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Details of papers published in the journals other than UGC notified journals 2019

S. N	Publication type	Publication title	Author name	Journal name	Year
1.	Original article	Impact of Alternate Nostril Breathing Exercises on Vascular Parameters in Hypertensive patients- An Interventional Study	Saravanan P S L, Anu S, Vairapraveena R, Rajalakshmi Preethi G.	National Journal of Physiology, Pharmacy and Pharmacology.	2019
2.	Original article	Analysis of the effects of duration and quality of sleep on pain threshold and nerve conduction velocity on medical students	Kanietha Priya A S, Anu S, Pooja Devi	National Journal of Physiology, Pharmacy and Pharmacology.	2019
3.	Original article	Lung -specific yoga mudras on respiratory function in asthma patients	Saravanan P S L, Anu S, Kanietha Priya A S, Vijaybabu K, Rohit Paul.	National Journal of Physiology, Pharmacy and Pharmacology.	2019
4.	Original article	Doppler evaluation of Common carotid artery hemodynamic parameters in patients with essential hypertension after Alternate Nostril Breathing exercises	S. Anu G. Rajalakshmi Preethi R. Vaira Praveena K. Jeyashree	Journal of Evidence Based Medicine and Healthcare	2019
5.	Original article	Effect of Specific Yoga Mudras on Respiratory Efficiency in Asthma patients.	S Anu A S Kaniethapriya Rohit Paul Jeyashree	Indian Journal of Clinical Anatomy and Physiology	2019
6.	Original article	Effect of passive and active upper limb movements on muscles of the lower limbs in spinal cord injury patients	Anu S, Madhava Kumar V, Venkatesh, Vijay Anto J	National Journal of physiology	2019
7.	Original article	Non Infective Cough in Immediate Post Cardiac Surgery Patients.	Vijayakumar K Mohanakrishnan L Rieyaz HA John	International Journal of Contemporary Medicine,	2019

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			Rajpathy Selvakumar P Deneshkumar V	Surgery and Radiology	
8.	Original article	Assessment of memory and cognitive functions in controlled and uncontrolled Type 2 diabetes mellitus patients.	Shanthi M, Rekha K, Saravanan M, Shree Lakshmi KN	National Journal of Physiology, Pharmacy and Pharmacology	2019
9.	Original article	Effect of body mass index on time taken to attain maximum post-exercise hypotension in healthy adult males	Keba Jeeva, Rajesh Jeniton Fernando, Paramita Bhattacharyya	National Journal of Physiology, Pharmacy and Pharmacology.	2019
10.	Original article	Analysis of the effects of duration and quality of sleep on pain threshold and nerve conduction velocity on medical students	Kanietha Priya A S, Anu S, Pooja Devi	National Journal of Physiology, Pharmacy and Pharmacology	2019
11.	Original article	Genotype and viral load determination of hepatitis C virus from a tertiary care hospital, South India	Raja Sundaramurthy, Vithiya Ganesan, Ramesh Arunagiri, Rajendran Thiruvannamalai, Geni Veerathevar German Soundaram and Brindha Vetri Nallathambi	Journal of Evolution of Medical and Dental Sciences	2019
12.	Original article	Sexual Ambiguity based on the Length of Femur-A Statistical Analysis in South Indian Population	Yogesh C, Amirthvarshan A	Indian Journal of Forensic Medicine & Toxicology	2019
13.	Original article	A Retrospective Study of Annual Poisoning Profile in a Tertiary care hospital in south India for the year 2017-2018	Yogesh C, Priyanka, Amirthvarshan, Paranthaman	Journal of the Indian Society of Toxicology	2019
14.	Original article	Prevalence and Determinants of Depression among theElderly in Rural Field Practice Area of a Medical College	Karthikeyan K.; Sriandaal V.; Tamilarasan M	Indian Journal of Public Health Research & Development	2019

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		inPerambalur District, Tamil Nadu: A Cross-Sectional Study			
15.	Original article	Clinical profile and role of haematological parameters in the prognosis of dengue fever patients admitted in a tertiary hospital	Virgin Joena, Ananda Xavier Pragasam	International Journal of Contemporary Medical Research	2019
16.	Original article	Relationship between self rated health status &physical activity in obese south Indian patient's	Virgin Joena, Ananda Xavier Pragasam	International Journal of Advances in Medicine	2019
17.	Original article	Factors affecting carotid intimal medical thickness in patients with rheumatoid arthritis, an analytical cross sectional study	K. M. Prabhuswamy, M. Virgin Joena	International Journal of Advances in Medicine	2019
18.	Original article	Prevalence &profile of non alcoholic fatty liver disease among adults undergiong master health check up, a hospital based cross sectional study	A. Sangeetha, K.M. Prabhuswamy	International journal of contemporary medical research	2019
19.	Letter to Editor	Rainbow sign in dermatoscopy of nodular basal cell carcinoma	Nirmal B, Krishnaram AS, Sudhagar R	Indian Journal of Dermatopathology and Diagnostic Dermatology	2019
20.	Original article	A Study of Factors Associated with Relapse of Drinking during a 1 Year Follow-up: A Retrospective Cohort of 70 Males Treated as In-Patient for Alcohol Dependence Syndrome	Rena Stanley, Sugaparaneetharan Ayyanar, Ramanujam Venkatasamy, J. Vijay Anto	International Journal of Contemporary Medicine Surgery and Radiology	2019
21.	Original article	A prospective observational study to compare postoperative	Venkatesh Subbiah, Karpagavel Chandrabose	International Surgery Journals	2019

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		complications and quality of life between patients undergoing umbilical hernia repair by open and laparoscopic methods			
22.	Original article	Comparison of treatment outcome following rubber band ligation vs injection sclerotherapy for treatment of haemorrhoids	Karpagavel Chandrabose, Venkatesh Subbiah	International Journals of Surgery and Orthopedics	2019
23.	Original article	Profile and complication rate of thyroid surgeries performed interritiary care teaching hospital a prospective observational study	Vijaiaboobbathi Sathiah, Karpagavel Chandrabose	International Journals of Surgery and Orthopedics	2019
24.	Original article	A Clinical study on incidence of malignancy in solitary nodule of thyroid in rural area of tamilnadu	Jeyaganesh R, Vijaiaboobbathi Sathiah	MedPulse International Journal of Surgery.	2019
25.	Original article	A study to compare the effects of single dose intravenous dexmedetomidine and clonidine on bupivacaine spinal anaesthesia	P Ramadevi, T Nirmaladevi	MedPulse International Journal of Anesthesiology	2019
26.	Original article	Comparison of efficacy of Nebulized ketamine versus lignocaine for postoperative sorethroat	P Ramadevi, E Shanmugavalli	Indian Journal of Clinical Anaesthesia	2019
27.	Original article	Comparison of efficacy of intrathecal nalbuphine versus fentanyl as adjuvant to subarachnoid block in cesarean section	E Shanmugavalli, P Ramadevi, T Nirmaladevi	MedPulse International Journal of Anesthesiology	2019

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28.	Case Report	Congenital Primary Right Lung Agenesis in A Child – MDCT Imaging Features	M Krishna Kumar, H Kalyana, and S Yogaraj	Current Trends in Clinical & Medical Imaging	2019
29.	Original article	128 slices multidetector CT evaluation of Gastric carcinoma - Imaging and histopathological correlation	S. Yogaraj, M. Senthil Kumar	International Archives of Integrated Medicine.	2019
30.	Original article	Midline submental intubation	R Yoganandha	Journal of Indian Dental Association Tamil Nadu	2019

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National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Impact of alternate nostril breathing exercises on vascular parameters in hypertensive patients - An interventional study

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ABSTRACT

Background: Hypertension is characterized by overactivity of sympathetic nervous system. Sympathetic activation increases blood pressure both by stimulating heart and blood vessels. Breathing exercises are known to balance the autonomic function. Previous studies on hypertensives had shown that alternate nostril breathing (ANB) exercises reduce sympathetic activity by decreasing systolic and diastolic pressure. Since the effect of ANB on blood vessels was not documented so far, the present study was done to confirm the sympathetic lowering effect of ANB on vessel wall parameters immediately after 30 min of ANB exercises. **Aims and Objectives:** This study aims to measure and compare the immediate effect of 30 min of ANB exercises on the left brachial artery diameter, peak systolic velocity (PSV), and resistive index (RI) in hypertensive subjects. **Materials and Methods:** A total of 40 hypertensive patients in the age group of 45–65 years of both the genders were recruited for this study. The study group (interventional) and the control group included 20 hypertensive subjects each. Gray scale and Doppler ultrasound of the left brachial artery were done to assess the diameter of arteries, PSV, and RI before and immediately after 30 min of ANB. **Results:** In the study group, significant increase in vessel diameter (VD) ($P < 0.001$), and decrease in PSV ($P = 0.040$), RI ($P < 0.001$) were observed after ANB exercises. In the control group, no significant change in VD ($P = 0.485$), RI ($P = 0.789$), and PSV ($P = 0.777$) was seen after 30 min. **Conclusion:** ANB exercises reduced sympathetic activity in hypertensive patients.

KEY WORDS: Breathing Exercises; Brachial Artery; Essential Hypertension

INTRODUCTION

The increased demand of the present modern lifestyle has induced a lot of stress and stress-related disorders in all age groups. Hypertension is one such condition prevalent worldwide, increasing the risk of cardiovascular mortalities, and morbidities such as myocardial infarction, heart failure, and stroke. 95% of cases of the hypertension come under essential hypertension and though it is said that the cause is unknown, it is attributed to environmental and genetic factors. In essential/primary/idiopathic hypertension, secondary causes of hypertension such as endocrine or renal are not present. According to new American College of Cardiology/ American Heart Association 2017 Hypertension Guidelines, Prehypertension is characterized by systolic BP between 130 and 139 and diastolic BP between 80 and 89 and stage I Hypertension between 140 and 159 and 90–99 mmHg.[1]

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Known etiological factors for essential hypertension include obesity, insulin resistance, stress, sedentary lifestyle, high alcohol intake, smoking, high salt intake, and aging.[2,3] Most of these factors contribute to essential hypertension by overactivity of sympathetic nervous system (SNS). This increased adrenergic drive could be due to baroreceptor dysfunction, increased sensitivity of vascular chemoreceptors, and decreased parasympathetic activity.[4] The decrease in baroreceptor sensitivity is secondary to reduced vascular compliance or increased vasoconstriction.[5] Increased sympathetic activity increases vasoconstriction and decreased sympathetic activity results in vasodilation. Drugs prescribed to treat hypertension act by modulating autonomic activity. One of the non-pharmacological measures suggested to reduce sympathetic activity in hypertension is breathing practice. Breathing exercises are known to balance the autonomic function. Various studies had reported that alternate nostril breathing (ANB) exercises reduce heart rate and blood pressure by decreasing sympathetic and increasing parasympathetic activity. Deep breathing exercises decrease both systolic and diastolic blood pressure in hypertensive patients.[6-8]

Although the effect of 6-week yoga exercises and meditation on brachial artery reactivity is documented in a study on cardiovascular disease patients, the effect of breathing exercises alone on vascular parameter in hypertensive patients is so for not studied.[9] Doppler ultrasound is one of the standard non-invasive techniques used to measure vessel blood flow and arterial stiffness. The parameters that were measured commonly include peak systolic velocity (PSV), vessel diameter (VD) (DI), and resistive index (RI). PSV is used to measure arterial stiffness indirectly. Stiffer the tube, the pressure wave will be faster. RI indicates the resistance to blood flow as well as vessel wall extensibility. RI is calculated using the formula, RI = PSV-end diastolic velocity (EDV)/PSV, where EDV is EDV.[10] The aim of the present study was to confirm the sympathetic lowering effect of ANB exercises on vascular parameters before and immediately after 30 min of ANB exercises.

Objectives

The objectives of this study were as follows:

1. To measure and compare the vascular parameters of the left brachial artery in the control group before and after 30 min
2. To measure the immediate effect of ANB exercises on vascular parameters of the left brachial artery in the study group before and after 30 min
3. To compare the vascular parameters of the left brachial artery between the study and control group.

MATERIALS AND METHODS

The present study was conducted in the department of radiodiagnosis of a private medical college hospital in Madurai. 40 hypertensive subjects in the age group of 45–65 years of both the genders with mean systolic BP between 130 and 160 mmHg and diastolic BP between 86 and 106 mmHg attending general medicine operative between March and July 2017 were chosen by simple random sampling. 20 hypertensive subjects were assigned to the study (ANB) group who practiced ANB exercises and 20 to non-interventional (control) group who do not do any breathing exercise, randomly using a randomization sequence generated in Microsoft Excel. The study was conducted after getting clearance from the Institutional Ethical Committee.

Subjects with essential hypertension advised on lifestyle modification, who do not have prior exposure to pranayama/yoga and who gave their voluntary consent to participate were included in the study. Subjects with clinical evidence of any acute illness such as upper and lower respiratory tract infection, renal diseases, hormonal disorders, and subjects on medication and who had undergone major surgery were excluded.

Description of Intervention

On the day of the study, after obtaining informed consent from the subjects, baseline recording of blood pressure was done initially in the sitting position. Doppler parameters were then measured in the brachial artery for all the participants. The interventional group participants were then taught ANB exercises by a certified yoga instructor to familiarize them with the technique.

ANB involves inhalation through the left nostril for a count of 1–5 while the right nostril is occluded and exhalation through the right nostril for a count of 1–5 with the left nostril occluded with no pause in between. The same procedure is repeated in the right nostril again and completed in the left nostril. This completes one cycle. Hence, for 1 min, there will be 6 breathing cycles so that the respiratory rate could be maintained at 6/min. Once the skill is acquired, after 30 min of ANB exercise, Doppler values were then recorded for the interventional group. For the non-interventional group, Doppler values were assessed before and after 30 min of rest.

Data Collection Methods and Tools

Baseline data on all participants were collected using structured questionnaire. Blood pressure was measured using mercury sphygmomanometer (diamond). Gray scale and Doppler ultrasound (GE Voluson P8) of the left brachial were done for the assessment of the diameter of artery and Doppler parameters such as -PSV and RI. The left brachial artery was imaged in the cubital fossa using high-frequency linear probe, without giving any probe pressure. Brachial artery was chosen as it is easily accessible. VD was measured by placing the calipers in the outer wall and the vertical diameter was measured. On color Doppler, the spectral waveform

was obtained by placing the sample volume with the lumen of the vessel with standard Doppler angle of 60°. Doppler parameters such as PSV and RI were obtained from machine automated measurements based on auto or manual tracing of the spectral waveform. All the parameters were measured both before and after ANB exercise.

Statistics

The data were entered into MS Excel and analyzed using SPSS v16.0. The quantitative data were checked for normality and summarized using mean/median and standard deviation/interquartile range as appropriate. The change in readings within groups before and after intervention was analyzed using paired *t*-test (normal distribution of values). Between-group differences were analyzed using unpaired *t*-test. $P < 0.05$ was the cutoff to determine statistical significance.

RESULTS

According to Table 1, there was no significant difference in baseline values between the study and control group. Table 2 shows that there was no significant difference in Doppler parameters before and after 30 min in the control group. Table 3 shows that there was significant difference in all the Doppler parameters before and after 30 min of ANB exercises in the study group. Table 4 shows a significant difference in Doppler parameters between the control and study group.

Table 1: Comparison of baseline values between the study and control group

Brachial artery	Control	Study
	Mean±SD	Mean±SD
PSV (cm/s)	73.6±12.8	69.4±16.9
VD (mm)	4.0±0.6	3.9±0.6
RI	0.91±0.05	0.93±0.07

SD: Standard deviation, PSV: Peak systolic velocity, VD: Vessel diameter, RI: Resistive index

Table 2: Among the control group, comparison of before and after 30 min values

Paired samples statistics

Brachial artery	Mean	*n*	SD	Standard error mean	*P*
Pair 1					
PSV (cm/s) - before	73.600	20	12.7544	2.8520	0.777
PSV (cm/s) - after	73.645	20	12.5430	2.8047	
Pair 2					
VD (mm) - before	3.995	20	0.5680	0.1270	0.485
VD (mm) - after	3.984	20	0.5607	0.1254	
Pair 3					
RI - before	0.9130	20	0.04813	0.01076	0.789
RI - after	0.9125	20	0.04822	0.01078	

SD: Standard deviation, PSV: Peak systolic velocity, VD: Vessel diameter, RI: Resistive index

DISCUSSION

The present study results according to Table 3 show that 30 min of ANB exercises significantly reduced PSV ($P < 0.040$), increased VD ($P < 0.001$), and decreased RI ($P < 0.001$) in the study group. This confirms the effect of ANB exercises in reducing blood pressure in hypertensive patients. Increase in VD decreases the peripheral resistance which, in turn, decreases the blood pressure. As RI increases with increasing resistance in compliant vessels, decrease in RI indicates increase in vessel compliance.[11] In stenotic vessels, PSV increases through the area of narrowing depending on the diameter of narrowing.[12] Brachial artery is a muscular artery made up of many layers of the vascular smooth muscle cells and the tone of this vessel is mainly under the influence of SNS along with hormones such as NO and angiotensin II. The most commonly used parameter to assess the arterial stiffness is PSV. Brachial artery peak systolic velocities range between 50 and 100 cm/s (around

Table 3: Among the study group, comparison of values before and after 30 min of ANB

Brachial artery	Mean	*n*	SD	Standard error mean	*P*
Pair 1					
PSV (cm/s) - before	69.400	20	16.8879	3.7762	0.040
PSV (cm/s) - after	62.500	20	19.8667	4.4423	
Pair 2					
VD (mm) - before	3.905	20	0.5596	0.1251	<0.001
VD (mm) - after	4.261	20	0.6398	0.1431	
Pair 3					
RI - before	0.9340	20	0.06723	0.01503	<0.001
RI - after	0.8735	20	0.7876	0.01761	

SD: Standard deviation, PSV: Peak systolic velocity, VD: Vessel diameter, RI: Resistive index

Table 4: Comparison of difference in various parameters before and after intervention between the study and control group

Group statistics

Brachial artery	Study arm	*n*	Mean±SD	Standard error mean	*P*
PSV (cm/s)	Control	20	–0.0450±0.69998	0.15652	0.033
	Study	20	6.9000±13.97705	3.12536	
VD (mm)	Control	20	0.0115±0.07220	0.01615	<0.001
	Study	20	–0.3560±0.33401	0.07469	
RI	Control	20	0.0005±0.00826	0.00185	<0.001
	Study	20	0.0605±0.04763	0.01065	

SD: Standard deviation, PSV: Peak systolic velocity, VD: Vessel diameter, RI: Resistive index

60 cm/s). Stiffer the artery, higher will be the pulse wave velocity which increases the risk for disease.[13] In our study, after ANB exercises, PSV had decreased significantly. In the present study, subjects practiced breathing exercises only at a rate of only 6 breaths/min. This type of deep breathing, by stimulating the pulmonary stretch receptors, can result in sympathetic withdrawal of skeletal blood vessels resulting in widespread vasodilation. Decrease in blood pressure was also observed after breathing practices with a decrease in rate pressure product.[14,15] Blood vessels are under sympathetic tone. Breathing practice by reducing sympathetic overactivity would have dilated the brachial artery increasing VD. Baroreceptor insensitivity, leading to arterial stiffness, has been postulated to be the most important cause for essential hypertension. Deep breathing practices with equal inspiration and expiration were known to improve the baroreceptor sensitivity.[16]

The results of our study coincide with the results of the study which evaluated the effects of yogic intervention on brachial artery reactivity in coronary artery disease (CAD) patients.[9] Endothelium-dependent brachial vasodilatation was noticed after yoga and meditation only in CAD patients and not in those who do not have the disease. Another study had also reported an improved endothelium-dependent flow-mediated vasodilatation in brachial artery of only middle-aged and older individuals after yoga (along with breathing) practice and not in young individuals.[17] This study was done only on middle and older age group and not in younger individuals because in young age arterial wall stiffness may not be sufficient enough to change blood pressure as in old age.[18] With aging, there is increase in SNS activity. In essential hypertension, structural and functional changes occur in the blood vessels along with endothelial dysfunction and increased sympathetic activity, leading to arterial stiffness and raised PSV.[19] No significant change in parameters was observed in the control group after 30 min of rest [Tables 2 and 4]. Essential hypertensive patients alone were included in our study to rule out other medical causes. Recently diagnosed patients, not on drugs were included to avoid the impact of drugs on study results.

Strength of Study

This was the first study of its kind to assess the impact of breathing exercises alone on blood vessels in hypertensive subjects.

Limitation

The effect was of short term, and hence, long-term study must be planned to obtain stable results. Sample size could be increased and evaluation of other blood vessels could also be done in future studies.

CONCLUSION

ANB exercises reduced blood pressure in middle-aged and older hypertensives by increasing brachial VD, decreasing PSV, and RI when compared to the control group. This confirms the effect of ANB exercises in reducing the sympathetic overactivity by the parasympathomimetic effect. These simple, easy to learn breathing techniques could be practiced regularly to reduce the drug dosage as well to prevent the development of long-term complications of hypertension in future.

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RESEARCH ARTICLE

A cross-sectional study on effect of obesity on autonomic functions in a tertiary care center

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ABSTRACT

Background: Obesity is the most emerging problem in today's time. It is responsible for many metabolic as well as psychological ailments. Obesity and autonomic involvement have been studied, but evidence regarding the same is controversial. Obesity can no longer be considered as a silent epidemic in the new age scenario. Although people consider obesity a problem, it can still be regarded as one of the most overlooked public health issues. **Aims and Objectives:** This study aims to study the relationship between obesity and autonomic function tests. **Materials and Methods:** The present study was carried out in 86 male volunteers in the age group of 18–25 years. 40 of the subjects were included in the obese group, body mass index (BMI >30 kg/m^2) and the other 46 were included in the non-obese group (BMI <30 kg/m^2). Autonomic function tests in the form of heart rate variability and sympathetic skin response (SSR) tests were conducted in both the groups. **Results:** High frequency (HF) was significantly reduced in the obese group (240 ± 3.22, $P < 0.014$). Low frequency/HF was significantly altered in the obese group ($P < 0.05$). SDNN was significantly lesser in obese when compared to non-obese ($P < 0.05$). SSR latencies and amplitudes when compared between obese and non-obese did not reveal statistically significant results. However, both SSR amplitude and latency were lesser in the obese group when compared to non-obese. Tests indicate decreased parasympathetic activity in obese individuals. **Conclusion:** The link between obesity and autonomic functions if detected earlier in the long run will pave the way for a healthier life. This, in turn, may help in preventing cardiovascular morbidity which, in turn, reduces the burden on the society as a whole.

KEY WORDS: Body Mass Index; Autonomic Nervous System; Obesity; Autonomic Function Tests

INTRODUCTION

Obesity is emerging on the forefront as a health-care issue. It is an on-going epidemic heralding a new age crisis to both developed and developing countries. Both genetic and environmental factors interplay are observed in obesity.[1]

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Several factors such as sedentary lifestyle, lack of exercise or lack of motivation to continue exercising, intake of a calorie-dense diet, genetic and environmental factors contribute to the pathogenesis of obesity. Obesity results from a chronic imbalance between intake and energy expenditure. Hemodynamic and metabolic alterations occur in obesity. Obesity and autonomic involvement have been studied from times galore, but evidence regarding the same is controversial. Autonomic nervous system has two divisions sympathetic and parasympathetic. Autonomic system regulates body functions such as heart rate, respiration, urination, sexual function, and pupillary responses. Findings related to obesity and autonomic functions have been found to be inconsistent.[2,3] Hemodynamic instability in the form

of increased cardiac output, changes in vascular reactivity, hypertension, diastolic dysfunction, and cardiomyopathy have been documented. Cardiovascular diseases are often linked with obesity. Insulin resistance, hypertension, and reduced high-density lipoprotein have been suggested to cause cardiovascular diseases in obese individuals.[4] However, autonomic instability in obesity cannot be ruled out. Obesity can result in complications manifold, namely hypertension, insulin resistance, dyslipidemia, and coronary heart disease.[5]

Autonomic dysfunctions on a long-term basis pose a high risk for cardiovascular morbidity and mortality. In addition to cardiovascular risks, obesity has also been associated with diabetes, hypertension, cancer, and sleep apnea.[6] This may be the cause for an overall increase in mortality rate linked to obesity. Early detection of autonomic instability may prove as a key factor in promoting weight loss techniques in obese individuals by highlighting the nuances associated with the same, which may improve the quality of living if acted upon.

Various autonomic tests are available to study autonomic dysfunctions including heart rate variability (HRV), sympathetic skin response (SSR), and R-R interval variation. One of the most reliable methods to study cardiovascular autonomic status is HRV in addition to being noninvasive and sensitive. There are not many studies in the Indian scenario pertaining to correlation between obesity and autonomic functions. In addition, evidence concerning the relation of sympathetic skin resistance to obesity has been scarce. Keeping in mind the above facts, the present study has been undertaken to study the relation between obesity and autonomic functions. The study objective was to evaluate the link between autonomic functions and obesity.

MATERIALS AND METHODS

The present study was undertaken in a tertiary care center on 86 male volunteers, in the age group of 18–25 years. Ethical clearance was obtained from the institutional ethical committee. Informed consent was taken. After explaining the procedure to the subjects, anthropometric values were noted down. Obesity criterion based on the WHO cutoffs was added when the body mass index (BMI) was >30 kg/m^2. Group 1 consisted of 40 obese subjects and Group 2 had 46 non-obese subjects who were controls. Mean BMI of obese subjects (32.04 ± 2.66) was higher than that of controls (20.43 ± 2.34). Subjects on medication for cardiovascular and central nervous system disorders were excluded from the study. Subjects with a past/present history of cardiovascular disorders and history of smoking were excluded from the study. Subjects were asked to refrain from consuming tea/coffee/beverages on the day of the study. This was done to avoid any direct influence on cardiac autonomic activity. They were asked to report to the center after a light breakfast with light clothing.

The subjects weight was measured accurately using a digital weighing scale. Standing height was measured using a stadiometer. Both waist circumference and hip circumference were measured with the help of a flexible measuring tape. Measurement of HRV - ambulatory computerized electrocardiogram (ECG) system was used in this study. Frequency domain and time domain methods were used for analysis. ECG was recorded in the supine position for 5 min after 5 min of supine rest. ECG obtained was stored in the computer for analysis as an offline data.

Measurement of SSR - the instrument used in the study was NCV-evoked potential (EP)-electromyography (EMG) machine (RMS EMG EP MARK II, Recorders and Medicare Systems, Chandigarh). Surface disk electrodes were used in the current study. SSR was recorded using supramaximal electrical stimulus. The latency (defined as the time interval between the stimulus and the onset of the SSR waveform) and amplitude (defined as the peak-to-peak amplitude of the SSR wave) of SSR was noted for each of the recordings.

All the values obtained were charted and tabulated as mean ± standard deviation. Comparison between obese and non-obese group was performed using Student's unpaired *t*-test.

RESULTS

A total of 86 male volunteers were included in the study. 40 of them were obese (BMI >30, n = 40) and were grouped as test subjects. The other 46 were control (BMI <30, n = 46). Comparison studies between obese and non-obese group were done using Student's unpaired *t*-test. $P < 0.05$ was considered as statistically significant. Weight, BMI, waist circumference, and hip circumference were significantly higher in Group 1 obese subjects when compared to controls [Table 1]. High frequency (HF) is significantly higher in non-obese controls when compared to obese. Low frequency (LF)/HF when compared showed a significant sympathovagal imbalance in obese. SDNN is significantly lower in obese [Table 2]. Mean values of SSR amplitude and latency are lower in obese when compared to non-obese though no significance is attached [Table 3].

Table 1: Comparison of anthropometric values between Group 1 (obese subjects) and Group 2 (controls)

Parameters	Group 1 (n=40)	Group 2 (n=46)	P value
Age	23.07±7.25	21.48±8.011	0.428
Height in meters	1.57±0.97	1.63±0.10	0.036
Weight in kg	82.39±10.16	60.57±9.38	<0.001*
BMI (kg/m^2)	30.09±2.92	21.67±2.43	<0.001*
Waist circumference (cm)	99.33±13.96	61.98±11.33	<0.001*
Hip circumference (cm)	98.99±13.78	80.97±8.22	<0.001*

*P value<0.05: Significant difference

Table 2: Comparison of HRV indices between Group 1 (obese) and Group 2 (controls)

HRV indices	Group 1 obese subjects (*n*=40)	Group 2 controls (*n*=46)	*P* value
LF (ms^2)	480±3.56	248±3.55	0.063
HF (ms^2)	240±3.22	675±3.48	0.014*
LF nu	52±2.15	42±3.11	0.078
HF nu	44.28±3.92	54.29±3.87	0.078
LF/HF	1.33±3.66	0.78±3.78	0.043*
SDNN	30.65±3.6	42.53±2.08	0.037*

**P* value<0.05: Significant difference, HRV: Heart rate variability, LF: Low frequency, HF: High frequency

Table 3: Comparison of SSR parameters in obese and non-obese group

SSR parameters	Group 1 obese (*n*=40)	Group 2 controls (*n*=46)	*P* value
SSR amplitude	0.27±0.18	0.32±0.42	0.054
SSR latency	0.32±0.19	0.27±0.18	0.052

**P* value<0.05: Significant difference, SSR: Sympathetic skin response

DISCUSSION

Obesity alters autonomic effects on heart. The obese subjects had significantly higher ($P < 0.05$), body weight, BMI, waist circumference, and hip circumference in comparison to the controls. SDNN being a time domain variable, reflecting parasympathetic nerve activity was significantly lower in obese when compared to controls. Among the frequency domain variables, HF power (ms^2) and HF (ms^2) indicating parasympathetic activity were significantly lower in obese individuals. LF/HF ratio when compared between obese and non-obese showed significance indicating sympathovagal imbalance in obesity.

SSR values when compared showed that SSR amplitude was shorter in obese when compared to non-obese individuals. SSR latency was shorter in obese when compared to non-obese. Although no significance was attached to the values obtained through SSR, it can be safely said that parasympathetic activity was found to be reduced in the obese.

In a study by Poliakova *et al*., an independent association between HRV and age, waist circumference, and body fat was found. However, there was no association between BMI and HRV.[7]

All the above findings indicate autonomic imbalance in obese individuals. Parasympathetic activity was lower in obese when compared to controls. This shows poor autonomic control in obese. Our findings are suggestive of decrease in parasympathetic activity in obesity. The test results obtained are akin to that found by other researchers, indicating that parasympathetic activity is altered more than sympathetic in obese individuals.[8] Parasympathetic activity dysfunction is presented in obese when compared to non-obese. Some researchers have suggested insulin resistance as a culprit for the parasympathetic imbalance in obese individuals. Insulin resistance increases with increased body weight causing a state of hyperinsulinemia. This causes low vagal activity in obese individuals.[9] Decrease in vagal activity by itself is a threat to the cardiovascular status.

Nagai *et al*. reported alteration in both sympathetic and parasympathetic systems in obesity.[10] However, certain studies have recorded an increase in sympathetic activity and decrease in parasympathetic activity in an obese individual as age advances. Cardiac sympathetic activity alteration depends on the duration of obesity.[11] In addition, role of hypothalamus in altering the autonomic functions has been put forth. Hypothalamus houses both the satiety center and regulatory center of ANS. Lesions in the hypothalamus may lead onto obesity and autonomic dysfunction. Whether dysfunction is due to obesity or obesity facilitates dysfunction is a point to be pondered on.[12] On the other hand, studies have also detected decrease in sympathetic activity in obese animal models. Laitinen *et al.* have linked central body obesity and total body fat to alteration in autonomic activity.[13]

Although our study found a reduction in parasympathetic activity, other studies have shown autonomic function to be altered in obese based on the duration of obesity. Further cross-sectional studies involving a larger population dealing with obesity in a longer duration basis are warranted for in this regard. The alteration in parasympathetic activity could be owed to the fact that in obese there is a skew in the eating pattern. They usually have a higher carbohydrate intake when compared to fat and protein intake. This may result in a change in parasympathetic activity according to Valensi *et al*.[14] Inadvertent intake of food also increases sympathetic activation.[12]

The strength of the present study is the contribution in understanding the autonomic imbalance associated with obesity in young adults. Obesity is alarmingly increasing in the young adult population in India. In times to come autonomic imbalance along with metabolic disturbances could set in at a younger age. Limitations of the present study are that since the study population involved younger age group, it may be a possibility that noteworthy changes in sympathetic nervous system have not been detected.

CONCLUSION

Obesity and autonomic dysfunction can be correlated. Autonomic dysfunction on a long-term basis is responsible for cardiovascular morbidity and mortality. Autonomic function testing is one way of detecting the possibility of cardiovascular risks in future. If autonomic dysfunction is detected, early obese can be motivated to lose weight. Weight loss may help

in balancing the autonomic system which has been thrown off gear due to obesity. Poirier *et al.* in their study found an association between weight loss and parasympathetic activity which definitely paint a positive picture in the long run.[15] Obesity when detected early may help in preventing serious health issues which may occur as a consequence. In addition, it reduces the overburdening of the public health sector. Lifestyle modifications in the form of long-term exercise program, healthy diet is the need of the hour in the present era.

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RESEARCH ARTICLE

Lung-specific yoga mudras on respiratory function in asthma patients

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ABSTRACT

Background: Asthma is increasingly prevalent worldwide and still could not be effectively controlled with drug therapy alone. Non-pharmacological interventions such as yoga and pranayama were tried with promising results. Mudras are part of yoga tradition and it is said that specific hand postures stimulate cortical areas regulating autonomic nervous system (ANS). The present study aims to find out the role of lung-specific mudras alone in improving respiratory function by modulating the ANS. **Aims and Objectives:** The aims of this study were as follows: (1) To measure the effect of lung-specific yoga mudras on peak expiratory flow rate (PEFR), breath-holding time (BHT), Snider's test (ST), expiratory blast test (EBT), and respiratory endurance test (RET) in the study group after 6 weeks of mudra practice. (2) To measure and compare the PERR, BHT, ST, EBT, and RET values of control group with that of the study group after 6 weeks of mudra practice. **Materials and Methods:** This study was carried out on 50 stable asthma patients in the age group of 20–50 years who were randomly divided into control (n = 25) and study group (n = 25). The study group underwent mudra practice everyday for 30 min and 5 days a week for 6 weeks. Respiratory efficiency tests were measured before and after 6 weeks using peak flow meter and mercury sphygmomanometer. The tests include PEFR, BHT, ST, EBT, and RET.
Results: Statistically significant improvement (<0.001) was observed for all the parameters in the study group when compared with the control group. **Conclusion:** Lung-specific mudras improved the respiratory efficiency in asthmatic patients after 6 weeks of mudra practice.

KEY WORDS: Lung Mudras; Respiration; Asthmatics

INTRODUCTION

The overall prevalence of asthma in India is 2.05% in adults above 15 years.[1] Drug treatments may be useful in the early course of disease, but morbidity and mortality persist. One of 250 deaths is due to asthma worldwide. Hence, alternative non-pharmacological interventions such as yogic pranayama techniques and meditation are tried to prevent and treat asthma along with chemotherapy.[2] These techniques were shown to improve muscular efficiency and respiratory endurance and reduce wheezing episodes.

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Asthma is a chronic inflammatory disorder of the airways involving mast cells, eosinophils, T-lymphocytes, macrophages, neutrophils, and epithelial cells and is associated with bronchial hyperresponsiveness to various stimuli resulting in variable airflow obstruction.[3] It is characterized by recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning.

Autonomic nervous system (ANS) regulates the bronchial smooth muscle tone, bronchial secretions, and permeability.

Asthma is associated with ANS imbalance and characterized by increased bronchial sensitivity to cholinergic constrictors and decreased sensitivity to sympathetic dilators (increased α and decreased β receptor activity).[4] ANS contributes to asthma by acting not only on bronchial musculature but also on bronchial secretions, endothelial permeability, inflammatory mediator release, and pulmonary blood vessels tone. Genetic determinants as well as environmental factors play a role in asthma. Chronic inflammation obstructs the airways by accumulation of secretion, thickening of epithelial basement membrane, and contraction of bronchial smooth muscles. The inflammation results in high concentrations of interleukin 6, tumor necrosis factor alpha, and C-reactive protein in the blood plasma. To combat the excessive parasympathetic activity, there is increased release of Neuropeptide Y (NPY) from sympathetic nerves which, in turn, inhibit the release of acetylcholine. However, in asthmatic patients, NPY nerves are reduced.[5] These evidences suggest that asthma is characterized by abnormalities of both the components of ANS.

The most common precipitating factors for asthma include exercise, cold weather, exposure to air borne allergens, viral infections, and stress. Stress alters the responsiveness of the ANS and hypothalamo–pituitary–adrenal axis, thereby influencing immune system.[6] Stress by increasing the release of pro-inflammatory cytokines precipitates asthma exacerbations. Recent theory suggests that bronchial constriction is due to combination of vagal input plus inflammation.[7]

Respiratory efficiency tests employed in this study are simple bedside tests which help to assess mainly expiratory function of lungs. Peak expiratory flow rate (PEFR) is the maximum expiratory rate in liters/minute with which air is expelled with maximum force after a maximal inspiration. This test is generally used to assess larger airway obstruction and the normal value is 350–600L/m. The best measure for assessing airway obstruction is forced expiratory volume in 1 second (FEV1) which measures both larger and smaller airway obstruction. However, studies had reported that PEFR value correlates well with FEV1.[8] Furthermore, when an asthma attack resolves, larger airway obstruction reverses first than the smaller airway obstruction. Hence, peak flow meter, a tool for ongoing monitoring, is used to measure PEFR, as it is simple and reproducible. Breath-holding time (BHT) is the time taken by an individual to hold his breath as long as he can. The normal duration is around 45–60 s and duration depends on chemical and non-chemical stimuli. It is a measure for assessing the strength of the respiratory muscles and endurance of dyspnea. It could be positively correlated with FEV1 and forced vital capacity in evaluating obstructive diseases.[9]

Mudras were a part of yogic literature along with asanas and breathing exercises. Mudras involve body as a whole, or eyes, tongue, and hands specifically. Hasta mudras indicate delightful hand postures. They were a symbol of communication/expression in dance as well as in religion. The pressure exerted by the interplay of fingers stimulates the peripheral nerve ending which, in turn, sends signals to the central nervous system to bring about the specific response, depending on the type of mudra performed.[10] Few previous studies had depicted the importance of mudras in improving cardiovascular and neurological function.[11,12]

Literature says that lung-specific mudras could improve respiratory efficiency by causing bronchodilatation and reducing mucous congestion.[10] As there was no scientific evidence for this so far, the present study was done to find out the efficacy of yoga mudras in improving the respiratory function in asthma patients.

Aims and Objectives

The aims of this study were as follows:

1. To study the effect of lung-specific yoga mudras on respiratory efficiency in asthma patients.
2. To measure the effect of specific yoga mudras on PEFR, BHT, Snider's test (ST), expiratory blast test (EBT), and respiratory endurance test (RET) in the study group after 6 weeks of mudra practice
3. To measure and compare the PEFR, BHT, ST, EBT, and RET values of control group with that of the study group after 6 weeks of mudra practice.

MATERIALS AND METHODS

The present interventional study was done in the department of physiology of a private medical college and hospital, Madurai, between July 2018 and September 2018 at 4.00 pm everyday, 5 days a week for 6 weeks after obtaining institutional ethical clearance. Stable asthma patients of both the genders, between the age groups of 20 and 50 years, weight and height matched were enrolled for the study. Patients attending outpatient department in July 2018 and hospital workers in the medical college campus who were known asthmatics with disease duration of more than 1 year but not on routine drug treatment were included in the study after obtaining informed consent. Fifty asthma patients were chosen by simple random sampling from the list of all eligible subjects.

The patients were randomly assigned to control group ($n = 25$) and study group ($n = 25$) using a randomization sequence generated in Microsoft Excel. Asthmatics were selected based on adult asthma questionnaire, hospital records and only patients with intermittent and mild persistent asthma were included in the study[5] (WHO global initiative for asthma guidelines 2006).

Patients with acute asthmatic exacerbations and not willing to participate were excluded from the study. Subjects with other

types of lung diseases, mudra trained individuals, smokers, subjects with skeletomuscular disorders, subjects suffering from cardiac diseases, and on medication were also excluded from the study.

The subjects were instructed to refrain from caffeine, nicotine, and alcohol. Subjects on loose clothing were instructed to relax for 10 min initially in the sitting posture on ground except for linga mudra. Then, they were taught to perform all hand mudras by a qualified yoga instructor, along with smooth and deep breathing for 30 min a day.A common instruction was given to not to move their hands and put extra pressure on fingertips while doing hasta mudras.

The following were the mudras practiced in order, using both the hands:[10]

- Atmanjali mudra – Join the palms together in Namaste position (5 min)
- Bronchial mudra – Place the little finger at the base of the thumb, the ring finger on the upper thumb joint, and the middle finger on the pad of the thumb. Extend the index finger (5 min)
- Asthma mudra – Press the fingernails of both the middle fingers with other fingers extended (5 min)
- Bhramara mudra – Place the index finger on the base of the thumb. Place tip of your thumb on the side of your middle fingernail. Extend your ring and little finger (7 min)
- Linga mudra – Place both palms together and clasp your fingers. One thumb should remain upright; encircle it with the thumb and index finger of your other hand (8 min). Mudra was practiced in standing up position coordinating inhalation and exhalation.

Data Collection Method and Tools

The study was explained clearly to the participants and voluntary consent was obtained. Baseline data on all participants were collected using structured questionnaire. On day 1, between 10 am and 12 pm after recording vitals, all the respiratory efficiency tests were done for the control group and the study group. Then, the study group (n = 25) alone was taught yoga mudras by a certified yoga instructor for 30 min. All these yoga mudras were then practiced everyday in the evening under the supervision of the yoga instructor along with slow breathing (8 breaths/min). Values were collected again after 6 weeks of yoga mudra training. At the end of the 6th week, all were instructed to assemble in the department and the parameters were once again measured. The control group too assembled everyday in the department but took rest in the sitting posture, while they were instructed to concentrate on breathing (8 breaths/min).

Respiratory efficiency tests include BHT, EBT, ST, RET, and PEFR. PEFR was measured with the help of mini-Wrights peak flow meter (Ishneel Healthcare Private Limited) and EBT, RET with sphygmomanometer (Diamond agencies). All the parameters were measured in the following method:[13]

BHT

The subject was asked to sit quietly for a few minutes breathing normally. Ask the subject to pinch his nostrils with the thumb and index finger and to hold the breath after a normal inspiration and start the stopwatch. The time duration for which the subject was able to hold the breath was noted. Three such observations at an interval of 5 min were recorded. Similarly, record the BHTs after quiet expiration, deep inspiration, and deep expiration.

EBT

BP apparatus is required for this test. The rubber tube leading from the mercury reservoir to the cuff is disconnected. The subject was asked to take a deep inspiration and blow into the tube to raise the mercury column to the highest level possible. A normal subject can raise the mercury column to 55–100 mmHg or more during a single forceful expiration.

ST

A normal adult should be able to blow out a burning match stick or candle held at a distance of 30 cm in front of his face, with a single forceful expiration.

RET

The subject was instructed to take a deep breath, close his nostrils, and blow into the rubber tubing to raise the mercury column to 40 mmHg level in the manometer. He was instructed to maintain the mercury level at 40 mmHg as long as possible. Normal person can hold it at the same level for 40–70 s or more.

PEFR

The subject was instructed to take a deep breath and then to blow hard into the mouthpiece of the flow meter forcefully with his nostrils closed.

RESULTS

Statistics

The data were entered into MS Excel and analyzed using SPSS v16.0. The readings of PEFR, BHT, EBT, and RET were analyzed using one-way Wilcoxon signed-rank test and ST using McNemar test before and after 6 weeks of mudra practice. $P < 0.05$ will be the cut off to determine statistical significance.

Table 1 shows no statistically significant difference between the pre- and post-intervention values in the control group.

According to Table 2, a statistically significant difference exists between the pre- and post-values for all the parameters.

Table 3 shows a statistically significant difference between the control and the study group for all the respiratory parameters.

According to Tables 4 and 5, no statistically significant difference was observed in the control as well as in the study group

DISCUSSION

In the study group, according to Table 2, there was a significant improvement in all the respiratory parameters after 6 weeks of mudra practice (<0.001). No significant difference was observed in the control group for all the parameters [Table 1]. Table 3 shows no significant difference between the study and the control group. As increase in PEFR from the mean pre-value of 158 L/min to post-value of 240 L/min indicates that decrease in bronchoconstriction had happened after 6 weeks mudra practice, though the mean values were still <350 L/min [Table 2]. An increase in the duration of BHT shows the decreased response of respiratory centers to CO_2. An increase in BH allows air to move fast behind the secretions and also reduces respiratory rate (reduces dyspnea) by desensitizing CO_2 response.[14] The EBT values had increased from 32.52 mmHg to 56.80 mmHg which shows that the strength of the respiratory muscles had improved significantly to promote a strong expiratory effort [Table 2]. The patient's ability to hold the mercury column in sphygmomanometer at 40 mmHg also had increased dramatically from 8.05 s to 28.60 s in RET after 6 weeks, indicating the decrease in bronchial smooth muscle tone and improved respiratory muscle efficiency [Table 2].

Area for hand movements has a larger representation in the contralateral cerebral cortex. Pressing two palms together in Namaste position during Atmanjali mudra stimulates nerve endings in both the palms which have abundant sensory receptors. Pressure in both the palms will stimulate opposite cerebral hemispheres. Equivocal stimulation of both the cerebral hemispheres balances the activity of sympathetic and parasympathetic components of the ANS as the left hemisphere predominantly controls parasympathetic function and the right hemisphere sympathetic function. Hence, the different finger movements depending on the type of mudra performed bring the particular response. In the present study, the decrease in bronchoconstriction and inflammation could be due to lung-specific hand mudras which would have modulated the autonomic function. The connection between asthma and emotion was recorded in few functional magnetic resonance imaging studies. Along with increased inflammatory signals in the lung and airways with respect to asthma-specific stimuli, not only there is increase in inflammatory mediators but also there is activation of emotional area of the brain, i.e. anterior insular cortex.[5] As ½ h of mudra practice regularly calms down the individual, this relaxation could have reduced the stress, thereby reducing airway inflammation and improving asthma. Slow and deep breathing exercises were known to influence the autonomic activity.[15,16] As breathing is also regulated during mudra practice, this also could have contributed to modulation of ANS. This is supported by the fact that there is a decrease in heart rate, systolic blood pressure, diastolic blood pressure, and blood viscosity in a previous study after 15 min of mudra practice.[12] In the present study, mudra practice was carried over for a period of 6 weeks as well as for a minimum duration of 30 min, as in a previous study using electrophotonic imaging, a statistically significant change in the Electro photonoic imaging (EPI) parameter was observed only after practicing

Table 1: Comparison of pre- and post-intervention (after 6 weeks) values in the control group

Parameters	Duration	Mean	*n*	Standard deviation	Standard error mean	*P*
Pair 1 (PEFR)	Pre-value	202.40	25	71.664	14.333	0.100
	After 6 weeks	196.80	25	72.095	14.419	
Pair 2 (BHT-QI)	Pre-value	19.36	25	9.322	1.864	0.638
	After 6 weeks	19.84	25	8.260	1.652	
Pair 3 (BHT-QE)	Pre-value	14.76	25	6.851	1.370	0.618
	After 6 weeks	15.24	25	6.833	1.367	
Pair 4 (DI)	Pre-value	30.36	25	18.708	3.742	0.908
	After 6 weeks	30.60	25	14.329	2.866	
Pair 5 (BHT-DE)	Pre-value	17.04	25	5.070	1.014	0.696
	After 6 weeks	17.40	25	6.671	1.334	
Pair 6 (EBT)	Pre-value	37.76	25	16.179	3.236	0.717
	After 6 weeks	37.36	25	15.903	3.181	
Pair 7 (RET)	Pre-value	9.96	25	9.235	1.847	0.854
	After 6 weeks	9.76	25	7.524	1.505	

PEFR: Peak expiratory flow rate in L/min, BHT: Breath-holding time in seconds, EBT: Expiratory blast test in mmHg, RET: Respiratory endurance test in seconds

Table 2: Comparison of pre- and post-intervention (after 6 weeks) values in the study group

Parameters	Duration	Mean	*n*	Standard deviation	Standard error mean	*P*
Pair 1 (PEFR)	Pre-value	158.00	25	60.415	12.083	0.000
	After 6 weeks	240.40	25	72.599	14.520	
Pair 2 (BHT-QI)	Pre-value	14.34	25	8.315	1.663	0.000
	After 6 weeks	30.96	25	9.039	1.808	
Pair 3 (BHT-QE)	Pre-value	13.77	25	7.620	1.524	0.000
	After 6 weeks	27.52	25	8.598	1.720	
Pair 4 (DI)	Pre-value	15.39	25	8.663	1.733	0.000
	After 6 weeks	39.40	25	7.555	1.511	
Pair 5 (BHT-DE)	Pre-value	14.16	25	7.776	1.555	0.000
	After 6 weeks	32.24	25	8.378	1.676	
Pair 6 (EBT)	Pre-value	32.52	25	17.328	3.466	0.000
	After 6 weeks	56.80	25	13.304	2.661	
Pair 7 (RET)	Pre-value	8.05	25	8.354	1.671	0.000
	After 6 weeks	28.60	25	11.339	2.268	

PEFR: Peak expiratory flow rate in L/min, BHT: Breath-holding time in seconds, EBT: Expiratory blast test in mmHg, RET: Respiratory endurance test in seconds

Table 3: Comparison of values between the control and study group

Group statistics

Parameters	Control	*n*	Mean	Standard deviation	Standard error mean	*P*
PEFR 6 weeks	1	25	−5.6000	16.35033	3.27007	<0.001
	2	25	82.4000	61.93276	12.38655	
BHT-QI 6 weeks	1	25	0.4800	5.03422	1.00684	<0.001
	2	25	16.6200	7.52950	1.50590	
BHT-QE 6 weeks	1	25	0.4800	4.75324	0.95065	<0.001
	2	25	13.7468	8.59725	1.71945	
BHT-DI 6 weeks	1	25	0.2400	10.23181	2.04636	<0.001
	2	25	24.0100	8.46699	1.69340	
BHT-DE 6 weeks	1	25	0.3600	4.55412	0.91082	<0.001
	2	25	18.0800	8.23569	1.64714	
EBT 6 weeks	1	25	−0.4000	5.44671	1.08934	<0.001
	2	25	24.2800	10.48618	2.09724	
RET 6 weeks	1	25	−0.2000	5.36190	1.07238	<0.001
	2	25	20.5500	9.54921	1.90984	

PEFR: Peak expiratory flow rate in L/min, BHT: Breath-holding time in seconds, EBT: Expiratory blast test in mmHg, RET: Respiratory endurance test in seconds

mudras for more than 20 min.[17] In a 6-month duration study on 50 middle-aged women who practiced mudras, maximum changes were observed in autonomic variables and breathe rate. There was an increase in skin resistance and decrease in stress parameters.[18] Circadian rhythm exists for bronchial muscle tone. Hence, PEFR values vary significantly both in normal and asthmatic individuals due to biological rhythm.[19] To eliminate bias, all the tests were performed only between 10 am and 12 pm everyday. Asthma severity is directly related to autonomic dysfunction even when the patient is not in a period of exacerbation. Hence, the patients chosen for this study were not under acute exacerbation and not on routine drug therapy.[20]

Strength

This study is the first of its kind to measure the airway changes in asthma patients using mudras alone. The cooperation was very good from the patient's side, as many showed interest in learning theses simple techniques eagerly which were easy to perform.

Limitation

PEFR and other respiratory parameters could have been measured using computerized spirometer and a larger sample size could be used. The specific effect of each lung-specific mudra on respiratory function could have been noted.

Table 4: Snider's test value after 6 weeks in the control group

Test		Not able		Able	
		Count (no)	Row *n* (%)	Count	Row *n* (%)
Snider pre	Not able	15	93.8	1	6.2
	Able	1	14.3	6	85.7

Table 5: Snider's test values after 6 weeks in the study group

Test		Not able		Able	
		Count	Row *n* (%)	Count	Row *n* (%)
Snider pre	Not able	9	40.9	13	59.1
	Able	0	0.0	3	100.0

CONCLUSION

Lung-specific hasta mudras significantly increased all the parameters of respiratory efficiency after 6 weeks of mudra practice. No significant change was observed in the control group in all the parameters after 6 weeks. A significant difference existed between the control and study group. This simple, cost-effective, non-pharmacological technique if practiced regularly could improve lung function and reduce the need for drug dosage.

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DOPPLER EVALUATION OF COMMON CAROTID ARTERY HAEMODYNAMIC PARAMETERS IN PATIENTS WITH ESSENTIAL HYPERTENSION AFTER ALTERNATE NOSTRIL BREATHING EXERCISES

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DOPPLER EVALUATION OF COMMON CAROTID ARTERY HAEMODYNAMIC PARAMETERS IN PATIENTS WITH ESSENTIAL HYPERTENSION AFTER ALTERNATE NOSTRIL BREATHING EXERCISES

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ABSTRACT

BACKGROUND

Essential hypertension is a well-known predictor for cardiovascular disease, and it is mainly characterized by increased activity of sympathetic nervous system. As breathing exercises were known to reduce blood pressure by modulating autonomic nervous system activity, the present study was done to confirm the sympathetic lowering effect of alternate nostril breathing exercises in patients with essential hypertension by studying the haemodynamic parameters of left common carotid artery. We wanted to measure and compare the immediate effect of 30 minutes of ANB exercises on left common carotid artery diameter, Peak Systolic Velocity (PSV) and Resistive Index (RI) in hypertensive subjects.

METHODS

40 hypertensives in the age group of 45-65 years of both the genders were recruited for this study. Study group involved 20 and the control group involved 20 hypertensive subjects. Diameter of left Common Carotid Artery (CCA), PSV & RI before and immediately after 30 minutes of ANB was assessed with Gray scale and Doppler ultrasound.

RESULTS

A significant increase in vessel diameter (p <0.056) and decrease in PSV (p <0.010), RI (p=0.008) was observed after ANB exercises in the study group. In the control group, no significant change in vessel diameter (p =0. 485), RI (p<=0.789) & PSV (p=0.777) was seen after 30 minutes.

CONCLUSIONS

Sympathetic lowering effect of ANB exercises was evidenced by increase in vessel diameter, decrease in RI & PSV.

KEYWORDS

Breathing Exercises, Carotid Artery, Hypertension.

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BACKGROUND

In India, prevalence of hypertension is 25% in urban and 10% in rural population.[1] Hypertension is associated with increased risk of cardiovascular mortalities and morbidities. It increases the incidence of stroke, heart failure and end stage renal disease. The commonest type of hypertension is essential/idiopathic hypertension which accounts for 95% cases of hypertension. It is also known as primary hypertension since the secondary causes of hypertension like renal or endocrine disorders are absent. Both genetic and environmental factors play an important role. Obesity, insulin resistance, stress, sedentary lifestyle, high alcohol intake, smoking, high salt intake, low potassium intake and aging are known risk factors for essential hypertension.[2] Activation of sympathetic nervous system (SNS) seems to be the most important cause for essential hypertension.[3] This enhanced sympathetic activation in hypertension contributes to hyperlipidaemia, insulin resistance and left ventricular hypertrophy resulting in long term complications.[4] Increased sympathetic activity increases blood pressure by increasing cardiac output as well peripheral resistance, increasing renin secretion from JG cells and also by increasing sodium reabsorption from the kidney. Baroreceptors in carotid and aortic vessels were responsible for preventing rapid changes in blood pressure. Vagal tone of the heart is due to constant low firing rate of the baroreceptors, increasing the parasympathetic activity and decreasing sympathetic activity in normal young adults. Carotid artery thickness increases with aging which in turn decreases the vessel compliance thereby reducing baroreceptor sensitivity.[5] Decreased baroreceptor activity increase sympathetic discharge. Long term pressure on the carotid vessels in hypertension also

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decreases baroreceptor sensitivity reducing the sensitivity below the value of 7 ms/mmHg.[6] The increased adrenergic drive may not only due to altered baroreceptor function, but also due to increased sensitivity of vascular chemoreceptors, and decreased parasympathetic activity.[7] New ACC/AHA 2017 Hypertension Guidelines states that systolic blood pressure above 140 mmHg and diastolic blood pressure above 90 mmHg is considered as essential hypertension.[8] Anti-hypertensive drugs prescribed to treat hypertension act by mainly modulating autonomic activity. Non-drug interventions like Yoga, meditation, breathing exercises and stress reducing techniques were suggested as additional interventions and various studies had proved that these techniques reduce blood pressure by modulating autonomic function. Alternate Nostril Breathing (ANB) exercises were known to reduce heart rate and blood pressure by decreasing sympathetic and increasing parasympathetic activity in hypertensive patients.[9,10] In all these studies, changes in blood pressure was observed with direct measurement of systolic and diastolic blood pressure or with heart rate variability tests.[11] No study was done so far to observe the effect of breathing exercises on changes in vessel haemodynamic parameters. Doppler ultrasound is a non-invasive, cheaper and faster technique commonly used to measure vessel blood flow and arterial stiffness. It is used to study peak systolic velocity (PSV), Vessel Diameter (VD), & Resistive Index (RI). PSV is an indirect measure of arterial stiffness. Normal PSV in common carotid artery (CCA) is more than 45 cms/sec. If it goes above 125 cms/s, it indicates definite stenosis. Normal value of RI in CCA is 0.72 and 0.84.[12] RI indicates the resistance offered by the vessel to blood flow as well as vessel wall compliance. Resistive index is calculated using the formula RI= PSV-EDV/PSV where EDV is End Diastolic Velocity.[13] The normal value of vessel diameter of CCA is 6.5 mm &6.1 mm in males and females.[14] The aim of the present study was to observe the immediate effect of ANB exercises on diameter and haemodynamic parameters in left common carotid artery.

Aims and Objectives

1. To measure and compare the haemodynamic parameters &Vessel diameter of left common carotid artery in control group before and after 30 minutes.
2. To measure and compare the immediate effect of Alternate Nostril Breathing (ANB) exercises on haemodynamic parameters & Vessel diameter of left common carotid artery in study group before and after 30 minutes.
3. To compare the parameters of left common carotid artery between study and control group.

METHODS

The present study was conducted in the Radiology department of a private medical college in Madurai after obtaining Institutional ethical committee clearance. Among the patients who had attended the General Medicine OP between July to November 2017, recently diagnosed hypertensive patients, not started on drugs but advised life style modifications were recruited for this study after obtaining their informed written consent. Forty subjects with essential hypertension in the age group of 45-65 years of both the genders were chosen by simple random sampling. The subjects were assigned as the study (Interventional) group (n=20) who practiced breathing exercises and control (Non-interventional) group (n=20) who do not do any breathing exercises, randomly by using a randomization sequence generated in Microsoft Excel. Subjects with Essential hypertension whose systolic BP is between 130-160 mmHg and diastolic BP between 86-98 mmHg (Prehypertension & Stage I hypertension) and who do not have previous exposure to breathing exercises were included in the study. Subjects with clinical evidence of any acute illness like upper and lower respiratory tract infection, coronary artery disease, diabetes, chronic renal diseases, malignancy, subjects on medication and who had undergone major surgery were excluded from the study**.**

Description of Intervention

After obtaining a detailed history, baseline recording of blood pressure and common carotid artery parameters were measured initially for both the groups. Alternate nostril breathing exercises were then taught to the interventional group participants by a certified yoga instructor to familiarize them with the technique. ANB involves inhalation through left nostril for a count of 1-5 while the right nostril is occluded and exhalation through the right nostril for a count of 1-5 with the left nostril occluded. The same procedure is repeated in the right nostril again and completed in the left nostril. This completes one cycle. Hence for 1 minute, there will be 6 breathing cycles so that the respiratory rate could be maintained at 6/min. Once the skill is acquired, study group subjects were instructed to do ANB for 30 minutes in the sitting posture. Immediately after 30 minutes Doppler values were recorded. In the Non-interventional group, Doppler parameters were once again recorded after 30 minutes of rest.

Data Collection Method and Tools

Blood pressure was measured in the sitting posture using mercury sphygmomanometer (Diamond Agencies). Gray scale and Doppler ultrasound (GE Voluson P8) of left Common carotid artery was done for the assessment of diameter of left common carotid artery and Doppler parameters like- Peak Systolic Velocity (PSV) and Resistive Index (RI). Proximal Left common carotid artery was imaged in the neck, using high frequency linear probe, without giving any probe pressure.

Vessel Diameter (VD) was measured by placing the callipers in the outer wall and the vertical diameter was measured. On colour Doppler, the spectral waveform was obtained by placing the sample volume with the lumen of the vessel with standard Doppler angle of 60 degrees. Doppler parameters like PSV and RI were obtained from machine automated measurements based on auto or manual tracing of the spectral waveform. All the parameters were measured both before and after ANB exercise.

Statistics

The data was entered into MS excel and analysed using SPSS v16.0. The quantitative data was checked for normality and summarized using mean/median and standard deviation/ interquartile range as appropriate. The change in carotid artery readings within groups before and after intervention was analysed using Paired t test (normal distribution of values). Between group differences was analysed using Mann Whitney U test. p value <0.05 was the cut off to determine statistical significance.

RESULTS

	Control		Study	
	Mean	**Standard Deviation**	**Mean**	**Standard Deviation**
Carotid artery PSV (cms/s)	64.2	6.8	57.1	12.7
Carotid artery VD (mm)	6.3	.9	6.6	.8
Carotid artery RI	.76	.05	.77	.09

Table 1. Comparison of Baseline Values Between Interventional and Non-Interventional Group

Paired Samples Statistics						
Left Common Carotid Artery		**Mean**	**N**	**Std. Deviation**	**Std. Error Mean**	**P**
Pair 1	PSV (cms/s)- Before	64.150	20	6.8000	1.5205	0.494
	PSV (cms/s)- After	64.050	20	7.0223	1.5702	
Pair 2	VD (mm)- Before	6.330	20	.9460	.2115	1
	VD (mm)- After	6.330	20	.9257	.2070	
Pair 3	RI- Before	.7590	20	.05139	.01149	0.716
	RI- After	.7585	20	.05174	.01157	

Table 2. Among Control Group Comparison of Before and After Values

		Mean	**N**	**Std. Deviation**	**Std. Error Mean**	**P**
Pair 1	PSV (cms/s)- Before	57.079	20	12.6673	2.8325	0.010
	PSV (cms/s)- After	51.705	20	10.8202	2.4195	
Pair 2	VD (mm)- Before	6.620	20	.8180	.1829	0.056
	VD (mm)- After	6.789	20	.7781	.1740	
Pair 3	RI- Before	.7665	20	.09422	.02107	0.008
	RI- After	.6965	20	.06998	.01565	

Table 3. Among Interventional Group- Comparison of Values Before and After 30 Minutes

Group Statistics						
Left Common Carotid Artery	**Study Arm**	**N**	**Median**	**25th Percentile**	**75th Percentile**	**P**
PSV (cms/s)	Control	20	.0000	.0000	.5000	0.006
	Study	20	5.5000	.5000	8.5000	
VD(mm)	Control	20	.0000	.0000	.0000	0.096
	Study	20	-.1500	-.5500	.1000	
RI	Control	20	.0000	.0000	.0000	0.001
	Study	20	.0450	.0100	.1100	

Table 4. Comparison of Difference in Various Parameters Before and After Intervention Between Study and Control (to See if The Difference Observed in Study Arm was More than That Observed in Control Arm)

Table 2 shows that there was no significant difference in Doppler parameters before and after 30 minutes in the control group.

Table 3 shows a significant difference in all the Doppler parameters before and after 30 minutes of ANB exercises in the study group.

Table 4 shows a significant difference in Doppler parameters between control and study group.

DISCUSSION

The present study results show that 30 minutes of ANB exercises significantly reduced common carotid artery PSV (P <0.010), increased vessel diameter (p<0.056) and decreased RI (p<0.008) in the study group (Table 3). This confirms the effect of ANB exercises in reducing blood pressure in hypertensive patients. Narrower the tube, the pressure wave will be faster in hypertensives.[12] After ANB exercises, the mean PSV had decreased from 57 cms/s to 51 cms/s after ANB exercises in study group. Hence decrease in PSV is an indirect measure of decrease in arterial stiffness. The results of our study are in accordance with a study where a strong positive correlation was observed between systolic blood pressure and PSV between pressures of 135 and 160 mmHg and not below or above that in the left CCA.[15] Carotid artery is an elastic artery and resistance in these vessels is mainly influenced by peripheral sympathetic nervous system.[16] Excess activity of sympathetic nervous system in hypertension decreases Vessel diameter which leads to increase in peripheral resistance. This increased peripheral resistance along with decreased vessel compliance is responsible for increase in RI in hypertension. In the present study, VD had increased from the mean value of 6.620 to 6.789 mm in left CCA and RI had decreased from the mean value of 0.7665 to 0.6965. This confirms the sympathetic lowering effect of deep breathing exercises in hypertension. PSV, VD & RI almost remained the same before and after 30 minutes of rest in the control group hypertensive (Table 2). Hence an observable significant difference in parameters was noted between both the study and the control group. (Table 4) ANB exercises were shown to decrease blood pressure in hypertensives.[9,10] Slow breathing at a rate of 6/min stimulates the pulmonary stretch receptors which in turn results in vasodilation by causing sympathetic withdrawal of blood vessels. This could also be due to increased baroreceptor sensitivity which in turn can increase the vagal discharge and decrease sympathetic activity.[17] Improved endothelium dependant flow mediated vasodilation was also observed after breathing exercises in middle aged and older individuals and not in younger age group.[18] The results of our study coincide with the results of previous studies which showed decrease in sympathetic activity in hypertensive patients after ANB.[9,10,17,18]

In our study, carotid artery was chosen for evaluation as arterial stiffening was found to be more in elastic arteries than muscular arteries with increasing age.[19] Endothelium dependant NO production as well number of voltage gated calcium channels in vascular smooth muscle also decrease with age. Haemodynamic parameters of left common carotid artery were analysed and not the right, because left CCA arises directly from the aortic arch and has a considerable presence in thorax. The present study was done with only patients categorized as under Prehypertension & stage I hypertension since only in these groups, life style

modifications advised are sufficient to reduce blood pressure without taking drugs.[8] Pre-hypertension is characterized by systolic BP between 130-139 and diastolic BP between 80-89 and stage 1 Hypertension between 140-159 and 90-99 mmHg. We included only middle and old age hypertensive in our study as sympathetic nervous system activity increases with aging and change in arterial stiffness was adequate to obtain visible results.[20]

Strength of the study Doppler vessel parameters were recorded for the first time after ANB exercises. Limitation Future studies could be done on a larger sample size. The results measured were only temporary and to obtain consistent result, all the parameters could be measured after few months of breathing practice. Changes in muscular arteries could be recorded. The effects of ANB can also be studied in essential hypertensive on drug treatment.

CONCLUSIONS

Alternate nostril breathing exercises increase left common carotid artery peak systolic velocity, vessel diameter and decrease resistive index in patients with essential hypertension indicating a decrease in sympathetic activity. No significant change was observed in hypertensive patients who did not practice breathing exercises. ANB exercises could be practiced regularly along with other non-pharmacological interventions to decrease blood pressure as well as to reduce the drug dosage in patients who were already on drugs.

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Original Research Article

Effect of specific yoga mudras on respiratory efficiency in asthma patients

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ABSTRACT

Introduction: Hastha Mudras involves hand gestures. The pressure exerted by the fingertips stimulates the peripheral nerve endings. This in turn sends signals to the central nervous system to bring about the specific response by modulating the autonomic nervous system, depending on the type of mudra performed. The effect of mudras in improving cardiovascular and neurological parameters was recorded in previous studies. The present study was done to find out the efficiency of lung specific mudras in improving respiratory parameters in stable asthmatics.

Materials and Methods: 50 Asthma patients in the age group of 20- 50years were divided randomly into study group (n=25) who practiced mudras for 30 minutes and control group (n=25) who did not do the intervention. Respiratory efficiency tests were measured before and after 30 minutes using peak flow meter, and mercury sphygmomanometer. The tests include Peak Expiratory Flow Rate (PEFR), Breath Holding Time (BHT), Sniders T est (ST), Expiratory Blast Test (EBT) and Respiratory Endurance T est (RET).

Results: Statistically significant improvement was seen in all the parameters except for sniders test. Control group showed no significant change.

Conclusion: Lung specific mudras could improve the respiratory function in asthma patients when practiced along with focused breathing.

1. Introduction

Mudra means Gesture which may involve the whole body or simple hand position. It is a known fact that mudras help in communication. Mudras were also known to influence different body functions by enhancing connections with the cortex and influencing autonomic reflexes in these areas. [1,2] The hand and the fingers, as they have numerous sensory receptors have a larger area of representation in the sensory (homunculus) cortex of brain. Pressure signals from fingers and hands stimulate corresponding areas of both cerebral cortex promoting cross lateralization and sensory motor integration.

Asthma is a chronic inflammatory disease of the airways with variable airflow obstruction characterized by recurrent episodes of wheezing, breathlessness, chest tightness and cough particularly at night or in the early morning that is at least partially reversible either spontaneously or with treatment. [3] Genetic determinants as well as environmental factors play a role in asthma. With increased severity and duration, airway remodeling occurs with smooth muscle hypertrophy, hyperplasia and mucous plugging resulting in fixed narrowing of the airway. Common precipitating factors for asthma include exercise, cold weather, exposure to air borne allergens and viral infections.

Asthma is also a stress related disorder. [4] Stress by increasing the release of pro inflammatory cytokines precipitates asthma exacerbations. The inflammatory response is due to eosinophil infiltration, mast cell degranulation and lymphocyte activation resulting in airway hyper responsiveness. Both the components of Autonomic Nervous System (ANS) are essential for maintaining the airway caliber. Though there is no direct sympathetic innervation of the airway smooth muscle, stimulation α adrenergic receptors causes bronchoconstriction and

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stimulation of $\beta 2$ receptors in bronchial smooth muscle causes bronchodilation. In asthma, bronchoconstriction and increased glandular secretion is caused by increased activity of parasympathetic nervous system. To combat this, sympathetic activity increases to release Neuropeptide Y (NPY) which in turn could inhibit the release of acetyl choline. But it fails in its objective, since in asthmatic patients NPY nerves are reduced and direct sympathetic innervation of airway is negligible.[5] These evidences suggest that asthma is characterized by abnormalities of both the components of ANS. It is also hypothesized that as mudras create subtle connections with emotional areas of the brain, stress & related disorders could be reduced by balancing autonomic nervous system.

In asthma, airflow obstruction occurs mainly during expiration, unless the disease is very severe. Respiratory efficiency tests employed in this study are simple bed side tests which help to assess mainly expiratory function of lungs. PEFR is the maximum rate in liters per minute with which air is expelled with maximum force after a deep inspiration. This test is generally used to assess larger airway obstruction and the normal value is 350-600L/minute. PEFR value is considered almost equally important with respect to forced expiratory volume in one second (FEV1) for diagnosing asthma.[6] Peak flow meter values are almost identical with the PEFR values obtained by computerized spirometry in asthma patients.[7] Breath holding time serves as a screening test for obstructive lung diseases and it i s an index of onset and endurance of dyspnea. It also could be positively correlated with FEV1 and FVC in evaluating obstructive diseases.[8]

The overall of Prevalence of asthma in India is 2.05% in adults above 15 years.[9] In spite of tremendous advances in medical treatment, morbidity and mortality still persists. Hence alternative non-pharmacological interventions like yogic pranayama techniques and meditation are tried to prevent or treat asthma along with chemotherapy.[10]

It is said that specific lung specific mudras or hand gestures can improve respiratory efficiency by producing Broncho dilatation and reducing mucous congestion.[1] There were only few studies depicting the scientific importance of mudras on other systems.[11,12] Since no other study has reported regarding this, present study was done to find out whether these yoga mudras really improve respiratory efficiency and if so, whether it can be used as an additive measure to treat asthma.

2. Aim & Objectives

To study the effect of specific Yoga Mudras on Respiratory Efficiency in Asthma patients.

1. To measure the effect of specific yoga mudras on peak expiratory flow rate, breath holding time, sniders test, expiratory blast test and respiratory endurance test in study group before and after 30 minutes of mudra practice
2. To measure the peak expiratory flow rate, breath holding time, sniders test, expiratory blast test and respiratory endurance test values of control group before and after 30 minutes.
3. To compare the respiratory efficiency test values of the study group with that of the control.

3. Materials and Methods

The present interventional study was done in the department of Physiology of a private Medical College Hospital, Madurai after obtaining Institutional Ethical Clearance. Stable Asthma patients of both the genders, between the age groups of 20–50years, weight & height matched were enrolled for the study. Patients attending Respiratory Medicine O.P in July 2018 and hospital workers (especially housekeeping staff in the medical college campus) who were known asthmatics with disease duration of more than one year but not on routine drug treatment were included in the study. 50 asthma patients who were chosen randomly were assigned as control group (n=25) and study group (n=25) by using a randomization sequence generated in Microsoft Excel. Asthmatics were selected based on adult asthma questionnaire, hospital records & only patients with intermittent and mild persistent asthma were included.[5] (WHO Global Initiative for Asthma guidelines 2006)

Patients with acute asthmatic exacerbations and not willing to participate were excluded from the study. Subjects with other types of lung diseases, mudra trained individuals, smokers, subjects with skeleto-muscular disorders, subjects suffering from cardiac diseases and on medication were also excluded.

3.1. Description of intervention

The subjects were instructed to refrain from caffeine, nicotine and alcohol. Subjects on loose clothing were instructed to relax for 10 minutes initially in the sitting posture on ground. Then the study group patients were taught to perform all hand mudras by a qualified yoga instructor, along with smooth and deep breathing. A common instruction was given to not to move their hands and put extra pressure on finger tips while doing hasta mudras.

The following were the mudras practiced in order, using both the hands[1] :

3.1.1. Atmanjali mudra

Join the palms together in Namaste position (5 minutes)

3.1.2. Bronchial mudra

Place the little finger at the base of the thumb, the ring finger on the upper thumb joint, and the middle finger on the pad

of the thumb. Extend the index finger (5 minutes).

3.1.3. Asthma mudra

Press the fingernails of both the middle fingers with other fingers extended. (5 minutes).

3.1.4. Brahmara mudra

Place the index finger on the base of the thumb. Place tip of your thumb on the side of your middle finger nail. Extend your ring and little finger. (7 minutes)

3.1.5. Linga mudra

Place both palms together and clasp your fingers. One thumb should remain upright; encircle it with the thumb and index finger of your other hand. (8 minutes). Mudra was practiced in standing up position coordinating inhalation and exhalation.

3.1.6. Data collection method & tools

The study was explained clearly to the participants and voluntary consent was obtained. Baseline data on all participants was collected using structured questionnaire. On day 1, between 10am-12 pm after recording vitals, all the respiratory efficiency tests were done for the control group(n=25). Then they were instructed to take rest in sitting posture while concentrating on breathing (8/min) for 30 minutes and immediately after 30 minutes all the tests were once again recorded.

On day 2, all these parameters were measured initially for the study group. Then all were taught lung specific yoga mudras by a certified yoga instructor till they understood the technique properly. From day 2-day 6, every day test values of 4 patients were recorded after the practice of mudras for 30 minutes. Respiratory efficiency tests include Breath holding time, Expiratory blast test, sniders test, respiratory endurance test and peak expiratory flow rate.

PEFR was measured with the help of mini wright's peak flow meter (Ishneel Healthcare private limited). Expiratory blast test and respiratory endurance test was measured with the help of mercury sphygmomanometer (Diamond agencies). All the parameters were measured in the following method:[13]

3.2. Breath holding time (BHT QI)

The subject was asked to sit quietly for a few minutes breathing normally. Ask the subject to pinch his nostrils with the thumb and index finger and to hold the breath after a normal inspiration and start the stop watch. The time duration for which the subject could hold the breath was noted. Three such observations at an interval of five minutes were recorded. Similarly, record the breath holding times after quiet expiration (BHT QE), deep inspiration (BHT DI) and deep expiration (BHT DE).

3.3. Expiratory blast test (EBT)

BP apparatus is required for this test. The rubber tube leading from the mercury reservoir to the cuff is disconnected. The subject was asked to take a deep inspiration and blow into the tube to raise the mercury column to the highest level possible. A normal subject can raise the mercury column to 55-100 mmHg or more during a single forceful expiration.

Snider's test (ST)

A normal adult should be able to blow out a burning match stick or candle held at 30 cms in front of his face, with a single forceful expiration

3.4. Respiratory endurance test (RET):

The subject was instructed to take a deep breath, close his nostrils and blow into the rubber tubing to raise the mercury column to 40 mmHg level in the manometer. He was instructed to maintain the mercury level at 40mmHg as long as possible. Normal person can hold it at the same level for 40-70 seconds or more.

3.5. Peak expiratory flow rate (PEFR)

The subject was instructed to take a deep breath and then to blow hard into the mouth piece of the flow meter forcefully with his nostrils closed. The reading on the dial is the PEFR in liters /min.

Values were recorded immediately after 30 minutes of yoga mudra training.

4. Results

4.1. Statistics

The data was entered into MS excel and analysed using SPSS v16.0. The readings of Peak expiratory flow rate, breath holding time, sniders test, expiratory blast test and respiratory endurance test before and immediately after 30 minutes were analyzed using Wilcoxon signed rank test & Mc Nemar test. P value < 0.05 was the cut off to determine statistical significance.

5. Discussion

In the study group, according to Table 2, there was a significant improvement in all the respiratory parameters immediately after 30 minutes of mudra practice except for the Sniders test (Table 5). No significant difference was observed in the control group for all the parameters (Tables 1 and 4)

As asthma is associated with expiratory difficulty, PEFR, Expiratory blast test, sniders test & respiratory endurance tests were mainly used to assess expiratory function. As decrease in PEFR indicates larger airway obstruction, the immediate improvement in PEFR value

Table 1: Comparison of pre and post intervention (after 30 minutes) values of all the parameters in the control group

		Mean	N	Std. Deviation	Std. Error Mean	p
Pair 1(PEFR)	Pre value	202.40	25	71.664	14.333	.922
	After 30 min	202.64	25	74.750	14.950	
Pair 2(BHT-QI)	Pre value	19.36	25	9.322	1.864	.546
	After 30 min	18.72	25	8.127	1.625	
Pair 3(BHT-QE)	Pre value	14.76	25	6.851	1.370	.085
	After 30 min	15.92	25	7.123	1.425	
Pair 4(DI)	Pre value	30.36	25	18.708	3.742	.861
	After 30 min	30.04	25	15.957	3.191	
Pair 5(BHT-DE)	Pre value	17.04	25	5.070	1.014	.485
	After 30 min	17.72	25	5.849	1.170	
Pair 6(EBT)	Pre value	37.76	25	16.179	3.236	.823
	After 30 min	38.20	25	16.462	3.292	
Pair 7(RET)	Pre value	9.96	25	9.235	1.847	.621
	After 30 min	10.48	25	8.954	1.791	

According to Table 1, in the control group, there was no statistically significant difference in the values after 30 minutes of rest.

Table 2: Comparison of values between pre and post intervention (after 30 minutes) in the study group

		Mean	N	Std. Deviation	Std. Error Mean	p
Pair 1 (PEFR)	Pre value	158.00	25	60.415	12.083	.000
	After 30 min	196.80	25	71.979	14.396	
Pair 2 (QI)	Pre value	14.34	25	8.315	1.663	.013
	After 30 min	18.42	25	11.227	2.245	
Pair 3 (QE)	Pre value	13.77	25	7.620	1.524	.001
	After 30 min	18.45	25	9.177	1.835	
Pair 4 (DI)	Pre value	15.39	25	8.663	1.733	.000
	After 30 min	21.74	25	11.481	2.296	
Pair 5 (DE)	Pre value	14.16	25	7.776	1.555	.001
	After 30 min	19.40	25	9.152	1.830	
Pair 6 (EBT)	Pre value	32.52	25	17.328	3.466	.000
	After 30 min	43.44	25	14.101	2.820	
Pair 7 (RET)	Pre value	8.05	25	8.354	1.671	.001
	After 30 min	11.89	25	11.060	2.212	

Table 2 shows a significant improvement in all the respiratory parameters after 30 minutes of mudra practice in the study group

Table 3: Comparison of values between the control and study group

Group Statistics						
	Control	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**	
PEFR 30min	1	25	.2400	12.10124	2.42025	<0.001
	2	25	38.8000	40.65300	8.13060	
BHT- QI 30min	1	25	-.6400	5.21920	1.04384	0.014
	2	25	4.0788	7.64331	1.52866	
BHT-QE 30min	1	25	1.1600	3.22335	.64467	0.019
	2	25	4.6788	6.47341	1.29468	
BHT- DI 30 min	1	25	-.3200	9.01721	1.80344	0.006
	2	25	6.3540	7.31918	1.46384	
BHT- DE 30min	1	25	.6800	4.79340	.95868	0.008
	2	25	5.2400	6.64129	1.32826	
EBT 30 min	1	25	.4400	9.73858	1.94772	<0.001
	2	25	10.9200	9.26427	1.85285	
RET 30 min	1	25	.5200	5.19711	1.03942	0.028
	2	25	3.8380	5.13057	1.02611	

Table 3 shows the significant difference in the values between the control and the study group after 30 minutes.

Table 4: Sniders test after 30 minutes in control group

		not able		able	
		Count (no)	Row N %	Count	Row N %
Sni Pre	not able	17	100.0%	0	0.0%
	able	0	0.0%	8	100.0%

Table 5: Sniders test after 30 minutes in study group

		not able		able	
		Count	Row N %	Count	Row N %
Sni Pre	not able	22	100.0%	0	0.0%
	able	0	0.0%	3	100.0%

Tables 4 and 5 shows no significant change in the control as well as in the study group.

indicates the decrease in bronchoconstriction that had happened after mudra practice. An increase in the duration of breath holding time shows the decreased response of respiratory centers to CO2. An increase in BH allows air to move fast behind the secretions and also reduces res piratory rate (reduces dyspnea) by desensitizing CO2 response.[14] Improvement in expiratory blast test and respiratory endurance test also indicates the decrease in bronchial smooth muscle tone and improved respiratory muscle efficiency.

In a study conducted by Nagarajan et al in 2017, out of 100 volunteers in 25-40 years age group who underwent mudra training for 2 months, 71 subjects agreed that they could feel the improvement in health after mudra training.[11] In a previous study done on the immediate effect (after 15 minutes) of mudras on cardiovascular and neurological function in heart patients, a significant decrease in heart rate, systolic blood pressure, diastolic blood pressure and blood viscosity was observed. Coronary perfusion pressure, myocardial blood perfusion volume and brain tissue blood supply had increased.[12]

Large part of the motor cortex of the brain is dedicated to hand movements. Sensory nerves from the fingers occupy a larger area in the homunculus on the lateral side of the contra lateral hemisphere. In the present study, Mudra practice started with performing atmanjali mudra to bring calmness and breath control. Pressing two palms together in Namaste position stimulates nerve endings in the palms which has abundant sensory receptors. Pressure in right palm will stimulate the left cerebral hemisphere, whereas pressure in the left palm will stimulate the right hemisphere. Equivocal stimulation of both the cerebral hemispheres balances the activity of sympathetic and parasympathetic components of the autonomic nervous system. May be this could be the reason why we hold our both hands tightly when tensed.

MRI studies had postulated the connection between asthma and emotion, as it is a known fact that stress aggravates asthma by releasing inflammatory mediators. Along with increased inflammatory signals in the lung & airways with respect to allergens, there is also activation of emotional area of the brain i.e. anterior insular cortex.[15] Asthma represents an imbalance of the autonomic nervous system. It was a recorded in earlier studies that fronto insular cortex (ventral anterior insula), anterior and midcingulate cortices constitute the cortical autonomic control centers which respond to emotional stimuli.[16] Fronto insular cortex acts as afferent and anterior cingulated as efferent centers. Left hemisphere activation predominantly affects parasympathetic function and right hemisphere activation sympathetic function. It is understood from this that lung specific hand mudras could have modulated the autonomic function to reduce bronchoconstriction and inflammation.

Linga mudras were known to remove the phlegm in the body by increasing body temperature especially in asthmatics and not in normal subjects. To confirm this, for 3 new asthma patients, body temperature was recorded before and after 20 minutes of performing linga mudra alone. A 3º F rise in body temperature was recorded. This mudra could help in exercise induced asthma too, where hyperventilation leads to excess heat loss from the airway epithelium.[17]

Along with direct effect of mudras, focused attention & regulated breathing (slow & deep) during mudra practice could also have modulated the activity of the ANS.[18] It is an established fact that circadian rhythm exists for bronchial muscle tone. Previous studies had noted significant circadian variation especially for PEFR both in normal and asthmatic individuals.[19] Hence it was ensured that all the tests were performed only at specific time of the day between 10am-12pm.

6. Strength of the study

This study is the first of its kind to measure the airway changes in asthma patients using mudras.

The cooperation was very good from the patient's side, as many showed interest in learning theses simple techniques eagerly which were easy to perform.

7. Limitation

Pulmonary function test parameters especially FEV1 & PEFR could have been measured with computerized spirometer. Results would have been better with larger sample size and with long duration practice. Future studies should evaluate the role of mudras in assessing the function of all the other organ systems in the body.

8. Conclusion

Lung specific hasta mudras significantly increased PEFR, BHT, EBT, RET immediately after 30 minutes of practice except for sniders test. No significant change was observed in the control group. This simple, easy to practice anytime, anywhere, cost effective technique must be practiced regularly to produce beneficial effects. When practiced along with pranayama, not only will they serve as an adjunct to chemotherapy but by reducing stress and balancing ANS can help to improve all the body functions.

9. Source of funding

None.

10. Conflict of interest

None.

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Effect of Passive and Active Upper limb Movements on Muscles of the Lower limbs in Spinal Cord Injury Patients

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Effect of Passive and Active Upper limb Movements on Muscles of the Lower limbs in Spinal Cord Injury Patients

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Abstract

Background: The coordination of limb movements during locomotion is by the central pattern generators (CPG's) in spinal cord, regulated by supraspinal centers. Stimulation/Movement of upperlimb muscles elicited electrical activity in lower limb muscles in neurologically intact subjects. The present study aims to record electrical activity in lowerlimbs of acute spinal cord injury (SCI) patients during passive and active coordinated upper limb movements. **Materials & methods:** Seventeen acute spinal cord injury patients in the age group of 30-60 years were involved in the present study.7 acted as control and 10 were in the study group. Electromyographic (EMG) activity was recorded in Quadriceps femoris, Hamstring, Tibialis anterior, Soleus, Gastrocnemius muscles of the lower limbs after different patterns of coordinated movements of the upper limbs using scorpio 2p/4p EMG, Allengers medical system limited, Chandigarh. Results were analysed with Fisher's Exact Test. **Results:** EMG activity in paretic lower limbs was greater for active (2kg > 1kg load) than passive upper limb movements**. Conclusion:** Rhythmic arm movements could generate activity in paretic lower limb muscles by stimulating CPG's and this would be an additional effective rehabilitative therapy.

Keywords:EMG, limb movements,spinal cord Injury

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Introduction

The neural connections between the cervical and lumbo sacral networks in spinal cord is responsible for mediating the rhythmic coordinated movements of the arms with the legs during walking in normal individuals.[1] Central pattern generators (CPG's) are group of interneurons present in spinal cord and midbrain that activate the motor neurons resulting in alternate contractions of flexors and extensors of limbs resulting in stepping like movements during locomotion. There are two spinal cord CPG's: one in cervical region for upper limbs and another in lumbar region for lower limbs. CPG's in spinal cord are activated by impulses from midbrain locomotion generator.

Due to these connections muscle stimulation in either right or left upper limb causes activation of muscles in right or left lower limb.[2] Studies had shown that active muscle movements produced in one leg lead to muscle stimulation in the opposite leg due to inter neuronal circuits as evidenced by bursts of electrical activity in Electromyogram (EMG).[3] One muscle can be a part of multiple muscles synergies and one synergy can activate multiple muscles which is measured in EMG.

Pattern of co-activation of Muscles is recruited by a Single neural command Signal. Strengthening exercises to one limb also increases the voluntary strength of homologous contra lateral limb and the interaction between the legs is stronger than the interaction between arms.[4] Rhythmic arm movements were shown to increase the EMG activity in leg muscles, specifically with increased load by stimulating proprioceptive activity in normal subjects.[5]

SCI is the injury from the foramen magnum to the cauda equina. Motor vehicle accidents and sports injuries were the commonest causes. In spite of the modern advances in treatment modalities, it still results in permanent disability. Paraplegia occurs due to impairment of motor /sensory function in thoracic, lumbar and sacral spinal cord segments. [6]According to ASIA impairment scale (revised 2000), in incomplete spinal cord injury, there is still some retention of sensory and motor function below the point of injury. In complete spinal cord injury, there are no motor or sensory functions preserved in sacral segments S_4-S_5.

As a result of paralysis, rapid atrophy of paralyzed muscle occurs increasing the formation of protein degradation by-products, causing more demands on the kidneys. Along with that, loss of muscle force also contributes to bone demineralization resulting in hypercalciuria, renal calculi aggravating renal failure.[7]Other frequent complications include pressure ulcers, orthostatic hypotension, fractures, deep vein thrombosis (DVT), spasticity and contractures.

The rehabilitative treatments are primarily focused on direct stimulation of paralyzed muscles using electrical stimulators eg. continuous vibration of the quadriceps and hamstring muscle groups ,continuous electrical stimulation of the peroneal or sural nerve, and magnetic stimulation of the spinal cord .Recently, the focus is on training the Central Pattern Generators using Assisted treadmill techniques by sensory patterned feedback mechanism.[8] Sensory stimuli from legs stimulate the CPG's directly and also indirectly by stimulating sensory cortex.The purpose of the present study was to show another possibility that regular practice of active upper limb exercises in paraplegic patients can stimulate and strengthen paretic lower limb muscles apart from lower limb strength training. Hence the present study was done to evaluate the influence of arm movements on lower limb paretic muscles.

Objectives

Among Spinal cord injury patients, using Electromyogram,

1. To record the baseline electrical activity in both study and control group

2. To measure the effect of Passive upper limb movements on right and left lower limb muscles in study group

3. To measure the effect of Active upper limb movements on right and left lower limb muscles in study group

4. To measure the electrical activity after 2 hours of rest on right and left lower limb muscles in control group

Methodology

This interventional study was conducted in the department of Neurology in a private Medical college &Hospital in Madurai, after obtaining Institutional Ethical clearance. The present study involved 17 acute SCI subjects between the age group of 30-60 years selected over a period of July-October 2017 who attended Neurology, Physiotherapy and Orthopedics Departments. They were randomly divided into control group (n=7) who did not undergo any intervention and study group (n=10) who underwent intervention in the form of passive and active simultaneous upper limb movements. Informed written consent was obtained from all the participants.

Inclusion criteria

Patients with weakness of both the lower limbs (ASIA scaling B & C), patients with injury duration within 12 months, and patients who come to physiothethapy department for the first time were included in the study.

Exclusion criteria

Old aged patients, patients with injury duration more than a year, patients on antispasmodic medication, patients with metabolic disorders and with viral infections were excluded from the study.

EMG activity in lower limb muscles of SCI subjects of both control and study group (after passive & active upperlimb movements) was recorded using **SCORPIO 2P/4P EMG (ALLENGERS MEDICAL SYSTEM LIMITED, CHANDIGARH).** The features of this EMG are Simultaneous display of 2/4 channel EMG acquisition , EMG data can be stored, reviewed and replayed with audio and with more than 80 pre-stored muscle site.

The skin was cleaned with alcohol before the needle insertion. After identifying the individual muscle location using anatomical landmarks, EMG electrodes were placed on the muscles in order to get sharp and crisp multi unit action potentials (MUAP) and inter electrode resistance was checked.

Needle electrodes were placed on Quadriceps femoris, Hamstring muscles, Tibialis anterior, Soleus, Gastrocnemius of the lower limbs as in these muscles the innervations zones are distributed in a narrow band around the muscle belly. For soleus, the needle was inserted medial to the tibia, slightly distal to the midpoint between ankle and knee.

For gastrocnemius, the needle was inserted into the rostral, medial posterior calf. The electrodes were placed along the muscle fiber direction and the reference electrode was placed close to the active electrode.

Initially spontaneous activity for each muscle was assessed at rest with a sensitivity of 50 µV per division. Spontaneous activity was defined as any activity at rest lasting for longer than 3 seconds. Once this is over, the sensitivity was changed to 200 µV per division for recording MUAP of each muscle, after each prescribed form of passive upper limb movement.

The muscle movements involved include Adduction, Abduction, Flexion, Extension and Circumduction movements of both the arms simultaneously.

The electrode array was moved from location to location at intervals of about 5mm to record MUAP. Active upper limb movements were then recorded initially against a load of 1kg in each hand followed by 2 kg in each hand. Values displayed on the computer were then recorded after each movement. The time required for recording a single subject was around 2hours.

Results

Statistical analysis

The data was entered into MS excel and analysed using SPSS v16.0. The EMG readings before and after upper limb movements were analysed using FISHER'S **EXACT TEST** &movement specific correlation with Spearman Rank Correlation analysis.p value < 0.05 was the cut off to determine statistical significance

According to Table 5, there was a strong positive relationship among the passive movement with 1kg and 2kg in the flexion movement in quadriceps femoris of left limb of the respondents but not in the right limb. For abduction movement in quadriceps femoris and tibialis anterior of right limb of the respondents, passive movementand 2kg was correlated.

Passive movement has linear relationship with 1kg and 2kg for abduction movement in hamstrings, gastrocnemius and soleus of left limb. But, these relationships were notstatistically significant in the right limb of the respondents.

Analogously, passive movementhas linear relationship with 1kg and 2kg circumduction movement in hamstrings of rightlimb.Passive movement, 1kg and 2kg were correlated with one another in the adduction movement in gastrocnemius and extension movement in soleus of left limb of the respondents.

Table 1: Effect of upper limb movements on Quadriceps femoris muscle

QUADRICEPS FEMORIS MUSCLE	P Value **RIGHT LIMB**	P Value **LEFT LIMB**
Spontaneous	1.000	0.303
Flexion passive	1.000	1.000
Flexion 1kg	0.070	0.656
Flexion 2kg	0.020*	0.020*
Extension passive	1.000	1.000
Extension 1kg	0.020*	0.170
Extension 2kg	0.020*	0.045*
Abduction passive	0.070	1.000
Abduction 1kg	0.070	0.045*
Abduction 2kg	0.020*	0.045*
Adduction passive	0.370	1.000
Adduction 1kg	0.070	0.170
Adduction 2kg	0.020*	0.045*
Circumduction passive	0.370	1.000
Circumduction 1kg	0.020*	0.170
Circumduction 2kg	0.020*	0.042*

Table 1 shows significant difference with active movements flexion 2 kg, extension 1 & 2 kg, abduction 1& 2 kg, adduction 2 kg and circumduction 1 &2 kg

Table 2: Effect of upper limb movements on Hamstrings muscle

HAMSTRINGS MUSCLE	P Value **RIGHT LIMB**	P Value **LEFT LIMB**
Spontaneous	1.000	0.582
Flexion passive	0.170	0.650
Flexion 1kg	0.023*	0.070
Flexion 2kg	0.005*	0.027*
tExtension passive	0.350	0.020*
Extension 1kg	0.023*	0.020*
Extension 2kg	0.005*	0.020*
Abduction passive	0.070	0.020*
Abduction 1kg	0.005*	0.020*
Abduction 2kg	0.005*	0.020*
Adduction passive	0.070	1.000
Adduction 1kg	0.023*	0.179
Adduction 2kg	0.005*	0.020*
Circumduction passive	0.028*	0.370
Circumduction 1kg	0.025*	0.070
Circumduction 2kg	0.005*	0.020*

According to Table 2, Significant difference was observed with active movements flexion 2 kg, extension 1 & 2 kg, abduction 1& 2 kg,adduction1& 2 kg and circumduction 1 &2 kg & Also with passive movements like extension ,abduction and circumduction.

Table 3: Effect of upper limb movements on Gastrocnemius muscle

GASTROCNEMIUS	P Value **RIGHT LIMB**	P Value **LEFT LIMB**
Spontaneous	0.303	1.000
Flexion passive	0.057	0.628
Flexion 1kg	0.001*	0.023*
Flexion 2kg	0.001*	0.005*
Extension passive	0.005*	0.070
Extension 1kg	0.001*	0.005*
Extension 2kg	0.001*	0.005*
Abduction passive	0.001*	0.023*
Abduction 1kg	0.001*	0.005*
Abduction 2kg	0.001*	0.005*
Adduction passive	0.020*	0.023*
Adduction 1kg	0.001*	0.005*
Adduction 2kg	0.001*	0.005*
Circumduction passive	0.057	0.170
Circumduction 1kg	0.001*	0.005*
Circumduction 2kg	0.001*	0.005*

Table 3 shows significant difference with all active movements in both the limbs & also with passive movements like extension, abduction and adduction.

Table 4: Effect of upper limb movements on Soleus muscle

SOLEUS MUSCLE	P Value **RIGHT LIMB**	P Value **LEFT LIMB**
Spontaneous	0.141	0.582
Flexion passive	0.001*	0.057
Flexion 1kg	0.001*	0.037*
Flexion 2kg	0.001*	0.005*
Extension passive	0.020*	0.005*
Extension 1kg	0.001*	0.001*
Extension 2kg	0.001*	0.001*
Abduction passive	0.020*	0.005*
Abduction 1kg	0.001*	0.001*
Abduction 2kg	0.001*	0.001*
Adduction passive	0.005*	0.037*
Adduction 1kg	0.005*	0.001*
Adduction 2kg	0.001*	0.001*
Circumduction passive	0.020*	0.057
Circumduction 1kg	0.001*	0.001*
Circumduction 2kg	0.020*	0.001*

According to Table 4, significant difference was observed with almost all the active movements and most of the passive movements.

Table 5: Effect of upper limb movements on Tibialis anterior muscle

Tibialis Anterior	p value **Right limb**	p value **Left limb**
Spontaneous	0.301	1.000
Flexion passive	0.003*	0.087
Flexion 1kg	0.001*	0.003*
Flexion 2kg	0.001*	0.001*
Extension passive	0.033*	0.003*
Extension 1kg	0.003*	0.001*
Extension 2kg	0.001*	0.001*
Abduction passive	0.001*	0.001*
Abduction 1kg	0.001*	0.001*
Abduction 2kg	0.001*	0.001*
Adduction passive	0.003*	0.003*
Adduction 1kg	0.001*	0.001*
Adduction 2kg	0.001*	0.001*
Circumduction passive	0.005*	0.011*
Circumduction 1kg	0.001*	0.003*
Circumduction 2kg	0.001*	0.001*

According to Table 5, significant difference was observed for both active movements and passive movements of both the limbs except for flexion passive in left limb

Spearman Rank Correlation analysis

		Left Limb			**Right Limb**		
		Passive Vs 1Kg	**Passive Vs 2Kg**	**1kg Vs 2Kg**	**Passive Vs 1Kg**	**Passive Vs 2Kg**	**1kg Vs 2Kg**
QUADRICEPS FEMORIS	Flexion	0.816**	0.655**	0.802**	0.408	0.272	0.667*
	Extension	0.408	0.272	0.667**	0.218	0.218	1.000**
	Adduction	0.500	0.333	0.667**	0.102	0.408	0.667*
	Abduction	0.333	0.333	1.000**	0.375	0.667*	0.667*
	Circumduction	0.408	0.272	0.667**	0.408	0.102	0.667*
HAMSTRINGS	Flexion	0.478	0.500	1.000**	0.612	0.408	0.667
	Extension	0.509	0.509	1.000	0.500	0.333	0.667*
	Adduction	0.535	0.272	0.509	0.218	0.509	0.667*
	Abduction	0.667*	1.000**	0.667*	0.509	0.509	1.000**
	Circumduction	0.612	0.408	0.667*	1.000**	0.667*	0.667*
GASTROCNEMIUS	Flexion	0.408	0.272	0.667*	0.408	0.408	1.000**
	Extension	0.509	0.509	1.000**	0.667*	0.667*	1.000**
	Adduction	0.667*	0.667*	1.000**	0.509	0.509	1.000**
	Abduction	0.667*	0.667*	1.000**	1.000**	1.000**	1.000**
	Circumduction	0.408	0.408	1.000**	0.408	0.408	1.000**
SOLEUS	Flexion	0.802**	0.408	0.509	1.000**	1.000**	1.000**
	Extension	0.667*	0.667*	1.000**	0.509	0.509	1.000**
	Adduction	0.509	0.509	1.000**	1.000**	0.667*	0.667*
	Abduction	0.667*	0.667*	1.000**	0.509	0.509	1.000**
	Circumduction	0.408	0.408	1.000**	0.509	0.048	0.509

TIBIALIS ANTERIOR	Flexion	0.535	0.272	0.509	0.509	0.509	1.000**
	Extension	0.764*	0.509	0.667*	0.333	0.333	1.000**
	Adduction	0.509	0.509	1.000**	1.000**	1.000**	1.000**
	Abduction	1.000**	1.000**	1.000**	0.667*	0.667*	1.000**
	Circumduction	0.756*	0.500	0.661*	1.000**	1.000**	1.000**

**P<0.01; *P<0.05

Discussion

The present study shows that passive upper limb movements showed significant difference for extension, abduction in left and circumduction in right hamstrings muscle (Table 2),for extension, adduction, abduction in right and adduction & abduction in left gastronemius muscle (Table 3), for all the movements in right &extension, adduction ,abduction in left soleus muscle (Table 4),for all the movements in right & left (except for flexion) in tibialis anterior muscle(table 5) and no significant difference in quadriceps femoris muscle (Table1).

According to Tables 1-5, Active upper limb movements with 1 Kg weight elicited significant electrical activity for all the movements in right and left gastrocnemius, soleus and tibialis anterior muscle. For extension and circumduction movements in right and abduction in left quadriceps femoris muscle, for all the movements in right and extension, abduction in left hamstrings muscle. Significantly increased activity is observed for all the active upper limb movements on all the five tested lowerlimb muscles with 2 Kg weight (Tables 1-5).

The results of this study coincides with the results of a previous study on neurologically intact subjects,where an increased muscle activation was observed with active upper limb effort than with passive upper limb effort**.** [2]Greater amplitude MUAP's with more distinct bursts were recorded prominently with active than with passive upper limb movements. Also in this study, increased activity was observed for all the upper limb movements with 2 Kg load than with 1 kg load, where only in three out of five muscles, all the upper limb movements elicited activity. This is in accordance with the results of a study done on quadriceps muscles after SCI, where significantly greater improvements in force, type 1 fiber composition, fiber cross-sectional area, capillary-to-fiber ratio, oxygenation, and citrate synthase activity were observed in muscles trained with high load than muscles trained with minimal load. [9]

Active arm movements increased leg muscle recruitment during recumbent stepping in intact individuals and this could be attributed due to spill over and adaptations in the control system for the untrained lower limb muscles.[10,4]In another study, Hand-walking elicited significant locomotor-like activity in EMG recording in the legs of 58% of the participants, when the subjects were involved in mental arithmetic.[11] Vice versa ,rhythmical activity was recorded in arms and shoulder muscles during walking. In the current study, sensory information from stretch- and load-sensitive mechanoreceptors located in the muscles and skin of upper extremities could have stimulated the CPG'S which also controls the locomotor pattern in lower limbs.

Only patients with injury duration around one year were selected for this study as previous studies had shown that within six weeks after SCI, the size of lower-limb muscles was 45 percent smaller than normal subjects.[12] Though a case study on a single patient has reported a late neurologic motor recovery after 5 years of injury, most of the previous studies had found that rapid motor recovery occurs maximum within first 6 months post injury(greatest change within 3 months).Motor recovery in second year was found to be slower and at a smaller degree. [13] Neurologic level of injury, the initial motor strength, and neurologically complete or incomplete injury also determines recovery rate. In a pilot study done by the authors of the present study on 2 patients of 4 & 5 years duration of injury, no EMG activity was recorded for passive as well as active upper limb movements. The patients were under routine drug therapy for medical treatment of SCI during the

study period and not under physiotherapy as we included only the patients who came to physiotherapy department for the first visit.

Supraspinal control does have a role in modifying CPG activity. During locomotion, along with CPG 'S, there is also activation of medial sensory motor cortex and supplementary motor areas.[14] Spontaneous reorganization occurred in cortex, cerebellum and brainstem over a period of one year indicating functional locomotor recovery after injury. This neuronal plasticity could also be further induced by functional training initiated within one year of injury.[15] Hence Regular task specific training with upper limbs could also increase the motor area for lower limb activity in the cortex.

Resistance exercises using dumb bells to strengthen the muscles of the upper extremity in paretic patients not only could improve activity in lowerlimb muscles paretic muscles but also provides sufficient strength for day to day activities like independent transfer from bed.

Conclusion

In acute lower limb paralysis patients, coordinated upper limb movements elicited EMG activity in 5specific lower limb muscle. The effect was more and complete for active than passive upper limb movements. In that the electrical activity was greater with 2kg than with 1kg load. These findings suggest that rhythmic arm movements could be effective in the rehabilitation of lower limb paresis. This would be an additional strategy to increase the excitability of spinal neuronal locomotor circuitries and this could also help in gait rehabilitation in Parkinson disease, stroke, cerebral palsy and other neurological injuries which disrupt interlimb coordination.

Limitations

1. This could have been done on a larger number of subjects to provide better result
2. Patients were not separated based on the etiology of injury
3. Familiarity with the testing procedures might influence the result

Acknowledgement : Nil

Conflict of Interest : Nil

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ORIGINAL RESEARCH ARTICLE

Non Infective Cough in Immediate Post Cardiac Surgery Patients

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A B S T R A C T

Introduction: Cough is seen to occur commonly in post cardiac surgery patients. This causes great discomfort by aggravating pain. Sufficient data are not available regarding the incidence and cause of this cough. Study was designed to assess the severity and progress of cough in each postoperative day, the difference in cough pattern between various cardiac diseases and surgical techniques, the influence of smoking, the relationship to fluid imbalance and the relationship to reduction of lung volume and its influence on cough pattern.

Material and Methods: 100 consecutive adult patients who underwent cardiac surgery in this centre were evaluated for cough. Those who needed prolonged ventilation or developed respiratory infection were excluded. The incidence and intensity of cough was compared between the type of surgeries, cardiac pathology, smoking habits, fluid balance, and the lung volume of the patient.

Results: Over 80% of patients were found to have cough with, intensity peaking by 3rdto 5th post operative day (POD) and gradually reducing by 8th POD. Even in 8th POD,74 patients had cough with 11 having moderate to severe cough and 63 mild. The incidence of cough was found to be similar irrespective of technique of surgery, smoking habits and fluid balance. No significant variation with cardiopulmonary bypass (CPB) time (p-0.44), ejection fraction (p-0.88) and number of grafts in off pump patients (p-1.00) were seen.

Conclusion: 80% of post cardiac surgery patients were found to have cough, with varying intensity. Reduction in lung volume, as assessed by breath holding capacity, was seen in majority of patients. Incidence of cough was found to occur more when breath holding capacity reduces to less than 65% of preoperative level (P 0.00).

Keywords: Cardiac Surgery, Cough, CAT

INTRODUCTION

Postoperative pulmonary complications are an important cause of morbidity following surgeries contributing to delay in post-operative rehabilitation, increases in hospital length of stay, health-care costs and quality of patients' life.[1] Postoperative pain and restrictive lung dysfunction are believed to be important factors associated with cough impairment. A patient's inability to cough effectively after surgery is often attributed to excessive accumulation of pulmonary secretions and increases the risk of obstructive atelectasis and respiratory infections.[2] Non infective post-operative cough is often seen in post-operative cardiac surgery patients and there is not much data available regarding the cause or its prevalence. This study was aimed to understand the cause and incidence of non-infective postoperative cough in patients following cardiac surgery.

The possible causes thought of for post cardiac surgery cough are cardiopulmonary bypass (CPB) and extracorporeal circulation related inflammatory reactions, cardiac pathology causing pulmonary congestion, rise of left atrial pressure during manipulation,certain cardiac and anaesthesia drugs and post operative phrenic nerve injury causing diaphragmatic palsy.

Study was hence designed to assess the severity and progress of cough in each postoperative day, the difference in cough pattern between various cardiac diseases and surgical techniques, the influence of smoking, the relationship to fluid imbalance and the relationship to reduction of lung volume and its influence on cough pattern.

MATERIAL AND METHODS

100 consecutive adult patients (>17 years) who underwent open heart surgery were included in this study. Those who needed prolonged ventilator support (>24 hours) and those with post operative respiratory infection and multisystem

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failure were excluded from the study.

Surgery and post operative care: The open heart surgeries done on these patients are shown in Table I. All the surgeries were performed by a surgical team with uniform \techniques of median sternotomy, opening of pericardium and cardioplegia (when used) and extracorporeal circulation. Pleura if opened was drained with intercostal drainage tubes. All patients were anesthetised by the same team with uniform techniques. Post operatively all were ventilated with FIO2 varying from 40 -60% and were extubated when haemodynamically stable.

Pain relief was administered to all patients by standard protocol. Intravenous Fentanyl infusion was maintained till mobilisation along with benzodiazepines on ventilator and on oral Paracetamol. Oral Tramadol and parental Tramazac were used selectively.

All patients were on a standard physiotherapy regime of breathing exercisesincluding cough exercises and range of motion exercises of shoulder girdle. They are made to sit up at the earliest and if off ionotropic supports, made to stand and mobilized to an arm chair. All received nebulisation with Duoline and Budecortand few who were uncomfortable with nebulisation, steam inhalation.

Coronary artery bypass grafting - Off pump	43
Coronary artery bypass grafting - On pump	20
Combined procedures(6)	
CABG+ Atrial septal defect	1
CABG + Aortic valve replacement	2
CABG + Mitral valve replacement	2
CABG + Double valve replacement	1
Valve surgeries (22)	
Double valve replacement (Mitral & aortic)	3
Double valve replacement + Cox Maze procedure	1
Aortic valve replacement	3
Mitral valve replacement	12
Mitral valve repair	1
MVR + Cox Maze procedure	2
Others (9)	
Atrial septal defect	4
Cotriatriatum with Mitral valve repair	1
Supra cardiac type total anomalous pulmonary venous connection	2
Bentalls procedure	2

Table-1: Surgeries performed on 100 patients included in the study

Data recording: Hospital records were used to record the demographic data. Operation notes were used to record the surgical details and intensive care unit monitoring sheet was used to collect data of intake - output balance.

The lung volume of the patient was indirectly assessed preoperatively and post operatively by breath holding test. Same person was assigned to do the test for every patient. The procedure followed was to explain the patient in detail about the test preoperatively. Following a trial the test was performed thrice and the average taken as the final value. The post operative preserved respiratory volume was expressed as a percentage of the preoperative basal breath holding capacity. The cough intensity was assesse during the classification given in Table II. Few subjective and objective parameters along with its effect on patient was used for classifying. This data was assessed with input from patient, attenders and the nursing staff.

STATISTICAL ANALYSIS

Statistical analysis with Chi square test and Cochrane armitage test was applied on the data to ascertain the significance of increasing or decreasing trends of cough with different variants.

RESULTS

Of the 100 consecutive surgery patients studied, 71 were males and 29 females. The surgeries done on these patients are given in Table I.

The number of patients who had no cough on each post operative day is shown in Table III. Irrespective of cardiac pathology and type of surgery majority have cough of varying severity. A graph was plotted, for on pump, off pump CABGs and for valve surgeries, with X-axis showing the post operative day and Y-axis showing the number of patients having moderate to severe cough. Consistently the cough intensity was found to increase by 3rd to 5th post operative day and gradually settle thereafter (Fig 1).

Parameters	No cough	Mild cough	Moderate cough	Severe cough
Frequency	Nil.only as part of breathing exercise	< 5 Bouts * / day	5- 10 bouts/ day	>10 bouts /day
Intensity	Nil	Mild intensity	Moderate produces pain	Severe with pain persisting
Discomfort	Nil	Mild	Moderate discomfort	Severe discomfort with fear of cough
Ability to lie down flat	No difficulty	No difficulty	Occasional difficulty	Not possible to lie down flat
Sleep disturbance due to cough	No disturbance	No difficulty	Occasional cough during sleep	Definite interference with sleep
Difficulty to talk	No difficulty	No difficulty	Occasional	Definitely gets cough with continuous talk
*bout of cough means multiple cough occurring in short gaps to the extent of producing discomfort				

Table-2: Cough classification

Post operative day	Off pump CABG (N – 43)	On pump CABG (n- 26)	Valve surgeries (n-22)	Others (N- 9)
2	4 (9.3)	2 (7.7)	3 (13.7)	2 (22.2)
3	3 (6.9)	3 (11.5)	2 (9.1)	1 (11.1)
4	3 (6.9)	2 (7.7)	1 (4.5)	1 (11.1)
5	4 (9.3)	3 (11.5)	1 (4.5)	1 (11.1)
6	8 (18.6)	4 (15.4)	2 (9.1)	3 (33.3)
7	7 (16.3)	7 (26.3)	2 (9.1)	4 (44.4)
8	10 (23.3)	9 (34.6)	3 (13.7)	4 (44.4)

Table-3: Number of patients without cough (within bracket is the% of that category)

Balance	->-500ml		-500 -200ml		-200 – 0 ml		0 - +200ml		+200-500ml		>+500ml	
cough	Nil	Moderate severe	Nil	Moderate severe	Nil	Moderate severe	Nil	Moderate severe	nil	Moderate to severe	nil	Moderate severe
On pump (n-26)	17.7	23.5	19.1	31.9	30.3	15.2	11.8	32.4	17.4	19.6	20	26.7
Off pump (n-40)	23.5	20.6	13.6	34.6	7.35	38.2	5.8	34.6	4.8	22.6	7.14	42.8

Table-4: Comparison of severity of cough based on fluid balance, between off pump and on pump CABGs (% of patients having no cough and moderate to severe cough is shown in relation to their fluid balance)

% of preoperative breath holding capacity	No cough	Mild cough	Moderate cough	Severe cough
< 50%(N 12)	-	4	7	1
50 -65% (N 63)	2	29	27	5
65 -80% (N 17)	5	6	5	1
>80%(N8)	3	4	1	-

Table-5: Relationship between breath holding capacity and cough (number of patients with the each type of cough is given).

	No Cough	Mild Cough	Moderate Cough	SevereCough	Total
Below 65%	2 (7.50)	33 (32.25)	34 (30.00)	6 (5.25)	75
Above 65%	8 (2.50)	10 (10.75)	6 (10.00)	1 (1.75)	25
Total	10	43	40	7	100
The P-value is .000306. The result is significant at P< .05.					

Table-6:

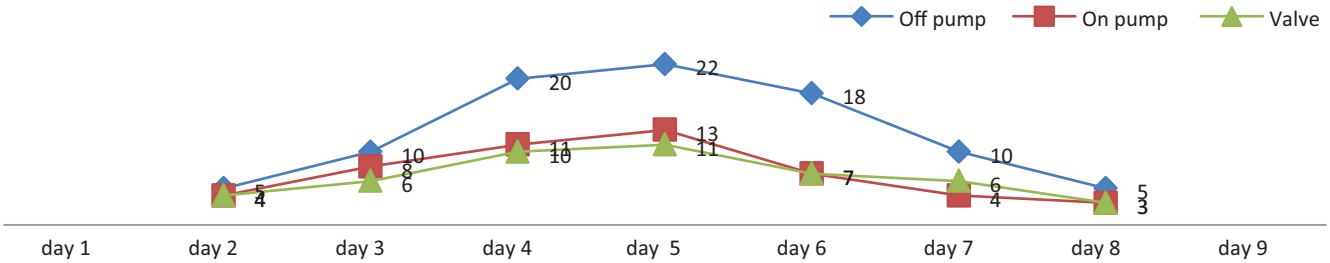

Figure-1: Graph depicting the number of patients having moderate to severe cough in each post operative day among three categories of surgical patients

As far as CABGs on pump were concerned we tried to see if the CPB duration has any influence on cough Of 26 patients who had on pump CABG 11 had a CPB time > 120 minutes (mts) and of this 6 had moderate to severe cough (54.5%). 12 patients had 90- 120mts CPB time and of this 5 had moderate to severe cough (41.7%). Of the 3 who had CPB time between 60 - 90 mts, 1 had moderate to severe cough(33%). When LV function was considered, of 11 patients who had ejection fraction below 50%, 5 (45.5%) had moderate to severe cough and of 15 patients with ejection fraction over 50%,7 (46.7%) had moderate to severe cough. The incidence of cough and severity, applying Cochrane armitage test, was thus seen not to be influenced by duration of CPB (p-0.44) and LV function (p-0.88).

In off pump CABGs the duration of manipulation of heart depends on the number of distal anastomosis. So the severity of cough was compared to number of grafts and they were plotted with post operative days in X axis and number of

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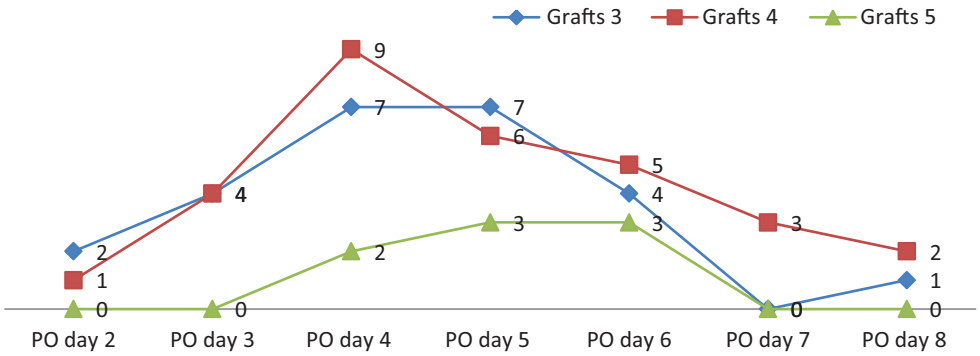

Figure-2: Graph depicting the number of patients having moderate to severe cough in each post operativeday, among off pump CABG patients in relation to number of grafts

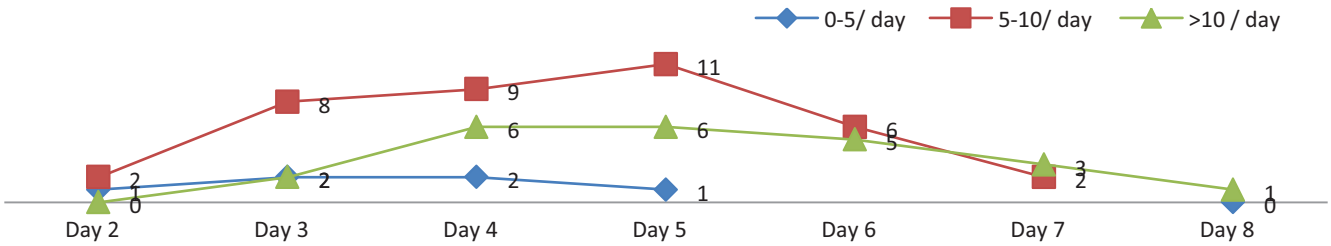

Figure-3: Graph depicting the number of patients having moderate to severe cough in each post operative day among smokers

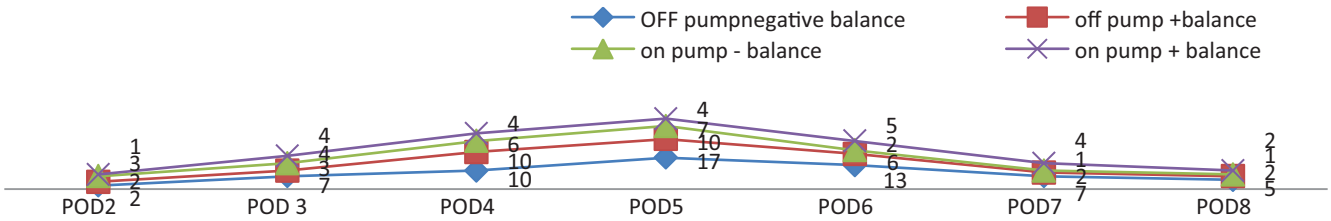

Figure-4: Graph depicting the number of patients having moderate to severe cough in each post operative day with relation to their fluid balance, and surgical technique.

patients with moderate to severe cough in Y axis (Fig 2).

Here too the cough severity peaks by 3-5 days and comes down by 7th day. Majority of patients had 4 grafts (20), 12 patients had 3 grafts, 7 had 5 grafts and 2 patients had 6 grafts and another 2 had 2 grafts. Moderate to severe cough occurred in 7 of 12 (58.3%) patients with 3 grafts and 9 of 20 patients (45%) with 4 grafts 3 of 7 (42.9%) patients with 5 grafts. Thus there was a uniform incidence of cough and its severity unaffected by the extent of manipulation.(p-1.00)

Cough pattern in smokers too was found to be identical. They were categorized as those taking less than 5 cigars a day(4 patients), 5-10cigars /day (22 patients) and more than 10 cigars a day (12 patients). The graph plotted showed the same pattern of cough intensity.(Fig 3)(p-0.95)

Moderate to severe cough occurred in patients irrespective of their fluid balance and showed the same pattern of peaking (Fig 4) around 3-5 days, the percentage being almost same in all categories. In off pump CABG patients, number of patients without cough was found to be more in those with more than 500ml negative balance.(Table IV)

All patients were found to have decrease in their lung volume after surgery. The breath holding capacity was considered as a measure of the lung volume. The postoperative preserved lung capacity was calculated as percentage of the preoperative capacity and it was tabulated against the intensity of cough. (Table V). The incidence of cough increases when the respiratory capacity decreases below 65% of the preoperative level. 25 patients had maintained > 65% of their respiratory capacity, while 75 had reduction of their respiratory capacity below 65% of the preoperative level. Of the 25 with > 65% capacity only 7 had moderate to severe cough (28%) while 8 had no cough(32%). Of the 75 patients who had reduction of their respiratory capacity, 40 (53%)had moderate to severe cough, and only 2 (2.7%) had no cough,remaining had minimal cough.(Table IV). By applying the statistical test of significance this increase in intensity of cough with reduction in respiratory capacity was found to be significant. (P- 0.000306)

DISCUSSION

Cough is one of the main defensive reflex which protects the airway from particulate and chemical pollutants, along with mucous secretions and ciliary movement. If there is hypersecretion of mucous or any ciliary dysfunction clearance by normal air movement may not be sufficient and cough becomes a necessity.[3] The mucus layer gets thinner as you go down the airway and the mucus secreting cells also decrease to such an extent that there are no mucus producing cells

in bronchioles. In alveoli the trapped materials are removed by macrophages or are removed by cough.[4] In the absence of ciliary movement cough becomes the major protective mechanism. This explains the cough which occurs in smokers. The mechanical events during cough are of three phases – inspiratory phase when air is drawn in to generate the sufficient volume, compression phase when the larynx closes and the muscles of chest wall, diaphragm and abdominal wall contracts to generate the intra thoracic pressure and then the final expiratory phase when glottis opens up and expels the high airflow with cough sound.[5]

During vigorous coughing, intrathoracic pressures may reach 300 mm of Hg and expiratory velocities may approach 800 km per hour.[6] This high pressures help expel the particulate matters and organisms with mucous. Though protective this high pressure causes discomfort, in postoperative situation after sternotomy, producing severe pain and distress. Cough induced rib fractures have been reported in literature especially in women with decreased bone densities.[7]

Assessing the severity of cough, is difficult, as it is a subjective matter inmost situations. Questionnaires were developed by various groups, to quantify cough as "cough severity index "published by Shembel AC et al.[8] Margret Vernon et al[9] had suggested that to address the severity of cough the three dimensions of cough namely frequency, intensity and disruptiveness must be considered. This aspect was taken care of in developing the assessment of cough in this study, and is given in Table II. 100 consecutive patients who underwent open heart surgery were followed throughout their hospital stayand was, assessed for cough severity, their breath holding capacity and their fluid balance.

We used simple bedside modified Sabrasez breath holding test to assess the respiratory volume as the patient compliance for spirometric equipment may not be good.[10] Patients were asked to hold breath after an usual deep inspiration. The duration of holding is noted. This gives an idea of their lung volume. Roughly > 25 sec is considered as normal and 15 -25 sec as limited reserve and less than 15 sec as very poor reserve. Studies correlating the breath holding capacity and the vital capacity had shown contradicting results. But here we compared the test result of the same patient before and after the surgery, hence the test can be reliably used for assessing the variation in effective lung volume.

All post cardiac surgery patients were observed for presence of cough and its severity was quantified. This data was analysed for any influence of type of surgery and the basic cardiac pathology in cough pattern. During cardioplegic arrest and cardiopulmonary bypass with extracorporeal circulation inflammatory responses may be stimulated leading to excessive secretions and reduced ciliary motion, which in turn may cause postoperative cough. However our data showed no significant difference between short and prolonged duration of CPB and in those who underwent surgery without CPB.

During coronary artery surgery done with off pump beating heart technique, inflammatory activation by extracorporeal circulation is avoided. Here pulmonary effect can be attributed to manipulation of heart leading to rise in left atrial pressure, which in turn increases the pulmonary venous pressure causing extravasations of fluid and added secretions. This can be a cause for cough in beating heart surgery. Manipulation will be more if the number of coronary grafts are more. This study compared the incidence of cough in patients with varying number of grafts and found the incidence and pattern to be identical.

Smokers are known to have excessive secretions and ciliary motility abnormalities. In these patients cough is a necessity to expel the excess mucous. We expected the smokers to have excessive cough postoperatively but found the incidence of cough similar to non-smokers.

Cardiac patients in general develops pulmonary edema with fluid overloading secondary to failure. The chance of pulmonary complications and cough are high when fluid balance becomes positive. However there was no significant correlation between cough severity and intake output balance.

Similar to other studies we found, there was a reduction in lung volume following cardiac surgery irrespective of cardiac pathology, the type of surgery and the technique. The breath holding test, revealed marked reduction to the extent of 65% of preoperative capacity in 75% post operative patients. Incidentally these were the patients who had more cough. Hence the cause of cough may be due to lung volume reduction.

A reduction in Forced Vital capacity (FVC) and Forced expiratory volume in 1 second (FEV1) was reported in most post cardiac surgery patients. While Nicholson et al reported a reduction of 40 -50% in FEV1 and FVC on first and second POD.[11] Matte et al reported a reduction of 53% on second post operative day.[12] Charlotte Urell et al observed 40% reduction in lung volume by second POD, in all patients irrespective of smoking habits. We found cough too peaks by third postoperative day. Lung volume reduction leads to peripheral atelectasis or airway constriction causing pooling of mucus. Cough may be a protective measure to expel the pooled mucus.[10]

This study too revealed reduction in respiratory volume in post operative patients and the incidence of cough was found to be more when the volume reduced to below 65% of preoperative level. Statistically using chi-square test it was found to be significant with p value .000306. This points to the fact that cough is related to the lung volume reduction probably due to peripheral atelectasis. Atelectasis may cause mucus secretion to accumulate, which gets expelled by cough.Intensity varying with the amount of accumulation of mucus and the efficiency of ciliary motility.

So to reduce cough in post cardiac surgery situation measures have to be taken to prevent post operative lung volume reduction. A combination of physiotherapy with breathing exercises, broncho dilatation by nebulisers and optimal pain management should be the main stay for managing this type of non infective cough.

CONCLUSION

The incidence of postoperative cough was found to be over 80% following open heart surgery., irrespective of the

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basic cardiac pathology, and the surgery performed. Cough was found to peak between 3rd and 5th postoperative day. The severity of cough was not significantly correlated with basic cardiac pathology, the type of surgery performed, the duration of cardiopulmonary bypass or the basic left ventricular function. The duration of manipulation of the heart in off pump CABGs and postoperative fluid balance and the smoking status of the patient too had no influence. All patients had a reduction in their lung volume and correlated significantly with severity of cough. A lung volume reduction to less than 65% of the preoperative level resulted in more severe cough. We conclude that post cardiac surgery cough primarily results from lung volume reduction following surgery. So control of this cough should be aimed at prevention of postoperative lung volume reduction.

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RESEARCH ARTICLE

Assessment of memory and cognitive functions in controlled and uncontrolled Type 2 diabetes mellitus patients

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ABSTRACT

Background: In Type 2 diabetes (T2D) mellitus, chronic hyperglycemia and hyperinsulinemia with resultant increased advanced glycosylated end products cause the acceleration of the brain aging in its structure and functions. This complication increases the risk of memory and cognitive dysfunctions. **Aims and Objectives:** This study was aimed to compare the memory and cognitive functions between controlled and uncontrolled T2D mellitus patients. **Materials and Methods:** The study is undertaken in the Department of Physiology, Velammal Medical College Hospital, Madurai. 100 known T2D mellitus patients aged between 30 and 50 years of both sexes are included after obtaining informed written consent. Patients with conditions and factors affecting memory and patients with defective hearing and speech are excluded from the study. Recent hemoglobin A1c (HbA1c), fasting blood sugar (FBS), and postprandial blood sugar (PPBS) values are collected from their hospital records. Cognition and memory assessment is done using Mini-Mental State Examination (MMSE) by 30-point questionnaire. **Results:** The average MMSE score of uncontrolled diabetes mellitus is less than the average MMSE score of controlled diabetes mellitus patients (HbA1c<7). Student's unpaired *t*-test among these two groups for MMSE was statistically significant ($P = 0.02$). The duration of diabetes mellitus, FBS, PPBS, and HbA1c showed negative correlation with MMSE score. **Conclusion:** The above result shows that there is more impairment in memory and cognitive functions in the uncontrolled than the controlled diabetes mellitus patients.

KEY WORDS: Type 2 diabetes mellitus; Memory and Cognition; Mini-Mental State Examination, Hemoglobin A1c

INTRODUCTION

Type 2 diabetes mellitus (T2D) is a worldwide prevalent disease and India places among the top three countries with diabetic population. The well-recognized complications of T2D mellitus are neuropathy, retinopathy, and nephropathy. Insulin resistance and hyperglycemia in T2D increases the oxidative stress, leading to these conditions.

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Angiopathy in T2D

Heredity, family predisposition, and obesity are the etiological factors for insulin resistance. Hyperglycemia as a result of insulin resistance leads to the production of reactive oxidant species (ROS). ROS activates protein kinase C and also increases the production of the advanced glycosylated end products. Activated protein kinase C causes the production of nuclear factor kappa B (NF_KB), angiogenesis, and increased cell growth. The receptors for the inflammatory products and thereby permeability to monocytes and the low-density lipoprotein (LDL) into the intimal layer are enhanced by the NF_KB. The monocytes transformed into macrophages engulf the LDL to form foam cells. Liberation of lipids and release of TNFα and IL1 from foam cells induces the production of inflammatory products and smooth muscle proliferation into the intimal layer of the blood vessels. The high level

of metabolic toxins and vascular inflammation causes endothelial dysfunctions ensuing micro- and macro-vascular complications.[1]

Angiopathy Effects on Brain

Effect of micro- and macro-angiopathy due to hyperinsulinemia and hyperglycemia on brain is quite significant to bring about deterioration in its structure and thereby its functions. Neuroimaging and neuropathological studies have confirmed the role of T2D in degenerative changes in the brain.[2]

Brain, significantly the Hippocampus, goes for the atrophic changes, more and faster in aging among T2D than in normal. The decreased blood flow coupled with the stimulation of thromboxane A2 receptor-induced vasoconstriction aggravates cerebral ischemia.[3]

Thickening of capillary basement membrane,[4] hyperglycemia-induced lactate accumulation, and glutamate brings about the neuronal damage accelerating the aging of the structure and functions of the brain.[5]

In a previous study carried out in diabetic patients, assessed cortical and subcortical infarcts and higher incidence of white matter lesions in their brain.[6]

Another study evaluated the cognitive functions and found that the diabetic patients thought processing and execution were low.[7]

Another important dysfunction is depression seen in T2D patients and its prevalence is twice more common than the controls. Depression that may be associated with the T2D also can be a causative factor for the cognitive dysfunction.[8]

Oxidative stress due to the insulin resistance and with the resultant hyperglycemia contributes to the future development of the Alzheimer's disease by tau hyperphosphorylation,[9] β-amyloid deposition, and mitochondrial dysfunction.[10] Considering the significant effect of T2D on brain structure and functions, cognitive dysfunction is assessed and compared between the controlled and uncontrolled diabetic patients in this study.

Aim

This study aims to assess and compare the cognitive functions in the controlled and uncontrolled T2D mellitus patients.

Objectives

The objectives of this study were as follows:

- To assess the fasting blood sugar (FBS), postprandial blood sugar (PPBS), and hemoglobin A1c (HbA1c) in T2D patients.
- To assess the cognitive and memory functions using MMSE questionnaire in controlled and uncontrolled T2D patients.
- To compare the blood parameters with cognition in both controlled and uncontrolled T2D patients.

MATERIALS AND METHODS

Institutional ethical committee clearance was obtained before the start of the study.

This comparative study was done in the Department of Physiology, Velammal Medical College Hospital and Research Institute (VMCHRI), Madurai, Tamil Nadu, India. 50 known T2D mellitus (T2D) patients of both the genders within 30–50 years of age attending the medicine Outpatient Department in VMCHRI are included in this study. The criteria of minimum high school education of the patients are considered for the assessment of cognition by MMSE scale. The informed written consent was obtained from all the participants before the study.

The duration of the study was 3 months. The recent blood parameters such as FBS, PPBS, and HbA1c are collected from their hospital records. HbA1c was done by high-performance liquid chromatography method and FBS and PPBS were done by glucose oxidase-peroxidase method in the hospital biochemistry laboratory.

Cognition and memory assessment was done by the Mini-Mental State Examination (MMSE).[11] MMSE is a 30-point questionnaire which is used extensively in clinical and research settings to measure cognitive impairment.

MMSE can also be used to estimate the severity and progression of cognitive impairment. Administration of this test takes between 5 min and 10 min. The domains of the cognition examined are registration, attention, calculation, recall, language, ability to follow simple commands, and orientation.[12]

This study excluded Type 1 diabetes mellitus patients, diabetes patients with hypertension and T2D <30 years and >50 years of age, those patients with the other ailments that might be causative factors for the decline in learning and memory, and finally, those T2D patients with speech difficulties, learning disorders, and mental disorders.

Statistical Analysis

Values were tabulated and analyzed in SPSS 20 version.

The following data have been done by:

- Frequency table
- Descriptive statistics: Mean, standard deviation, and Pearson correlation.

RESULTS

Tables 1-4 depict the distribution of the patients according to gender, diabetes status, drug intake, and treatment compliance, respectively. Controlled and uncontrolled patients highly differed on the basis of cognitive score, as the significance value is <1% level. Controlled patients have more cognitive score compared with uncontrolled patients [Table 5 and Figure 1]. Table 6 and Figure 2 show significant difference in the cognitive score among patients who took regular treatment and patients with irregular treatment. Since the difference is highly significant ($P < 0.01$), i.e., patients, who take regular treatment, did not have the cognitive impairment, while patients, who take irregular treatment, had the marginal level of cognitive impairment.

DISCUSSION

In the present study, the patients who were having HbA1c levels more than seven were considered to be in the uncontrolled state. From this study, the impact of age and sex of T2D mellitus patients over cognitive functions is not found to be present. High level of blood glucose was observed both in the fasting and postprandial state in the uncontrolled T2D patients. On comparison, MMSE score assessed in uncontrolled is lower than the controlled state T2D patients. The low MMSE score indicates the impairment of the memory and cognitive functions in these patients. 98% of T2D patients in this study are taking oral hypoglycemic drugs. These drugs induce endogenous secretion of insulin which may cause frequent episodes of hypoglycemia in these patients. T2D patients in this study with the regular treatment had good control over their HbA1c level and their MMSE score showed no decline in their cognitive functions, while patients who are irregular in their treatment suffer with marginal level of cognitive dysfunctions.

Table 1: Distribution of male and female patients

Gender	Frequency (%)
Male	24 (48)
Female	26 (52)

Table 2: Distribution of controlled and uncontrolled diabetics

Diabetes	Frequency (%)
Controlled	8 (16)
Uncontrolled	42 (84)

Table 3: Distribution of drug intake

Metformin and sulfonylurea intake	Frequency (%)
Yes	49 (98)
No	1 (2)

These findings of cognitive dysfunction with chronic hyperglycemia as indicated by the raised HbA1c level correlate well with the earlier reports.[13] The effect of prolonged hyperglycemia on cognitive function is attributed to the oxidative stress-induced changes in the structure and the metabolism in the neurons. These changes alter the electrophysiological properties of the neurons, culminating to advanced brain aging in the uncontrolled T2D patients. This finding can be referred with the previous study.[14] Hypoglycemic episodes are again another important risk factor for the neuronal degeneration, leading to subsequent cognitive decline in T2D patients may be correlated with supportive evidence of the earlier studies.[15,16] The effect of regular treatment compared with irregular treatment on cognitive functions correlates with the study of Meilly[17] and a study done by Gradman.[18] A previous study supports the fact that insulin resistance with hyperglycemia in T2D causes oxidative stress to the cerebral vasculature and promotes deposition of senile plaques of beta-amyloid which Christopher T Kodi denotes it as the hallmark of dementia in Alzheimer's disease.[5] All the above said factors have contributed to the cognitive decline in the uncontrolled T2D patients when compared with the patients who have good control over their HbA1c level with the regular treatment.

The finding that the patients with regular treatment and good control with HbA1c levels have better cognition when compared to the patients having uncontrolled HbA1c level with irregular treatment, is well established from their laboratory reports, and cognitive assessment is the strength of this study. Limitation of the study is the inclusion of patients who are over the age of 40 years may also have decline in cognitive functions due to aging.

Table 4: Distribution of treatment compliance

Treatment	Frequency (%)
Regular	32 (64)
Irregular	18 (36)

Table 5: Difference in the MMSE scores among controlled and uncontrolled T2D patients

T2D patients	MMSE score Mean±SD
Controlled	25.25± 4.17
Uncontrolled	21.26±3.28

*P value=0.004

Table 6: Difference in the cognitive score between T2D patients with regular treatment and irregular treatment

Treatment	MMSE score (Mean±SD)	*P*-value
Regular	23.13±2.45	0.007**
Irregular	19.72±4.55	

**P<0.01, T2D: Type 2 diabetes mellitus, MMSE: Mini-Mental State Examination

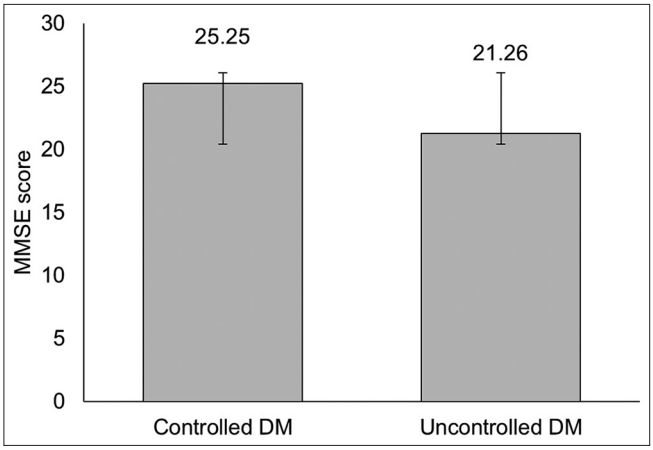

Figure 1: Mini-Mental State Examination scores for controlled and uncontrolled diabetes mellitus

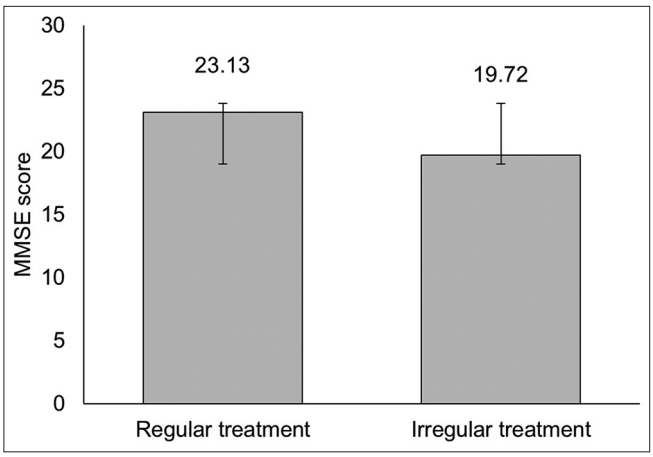

Figure 2: Mini-Mental State Examination scores for patients with regular and irregular treatment

CONCLUSION

T2D mellitus being a common prevailing disorder present globally, cognitive decline becomes a major health and social issue in these patients. Considering T2D is a risk factor to memory impairment and cognitive dysfunction, figuring out the ways to ward off effectively the complications of this disease becomes an important step to prevent this hazard. T2D patients on intensive blood glucose management with insulin and sulphonylureas must be closely monitored for hypoglycemic episodes which are a risk factor for further development of neurophysiological complications. A study states that hypoglycemia-induced neuronal damage may be prevented by the administration of the N-methyl-D-aspartate antagonists.[19] Another study indicates, minocycline prevents hypoglycemia-induced neuronal death.[20] Early management of blood glucose level, effective control of the HbA1c level, appropriate management of the diet with regular exercise, and treatment might help to alleviate the future cognitive decline and subsequent development of dementia in the T2D patients.

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RESEARCH ARTICLE

Effect of body mass index on time taken to attain maximum post-exercise hypotension in healthy adult males

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ABSTRACT

Background: Post-exercise hypotension (PEH) denotes a physiological fall in blood pressure (BP) from resting value after exercise. It is mainly due to decrease in sympathetic outflow after exercise. As obese individuals are known to have high basal sympathetic tone, we wanted to find a correlation between obesity and the time taken to attain maximum PEH. **Aim and Objective:** The aim of the study was to compare the time taken to attain maximum PEH between healthy adult males with normal body mass index (BMI) with those with above-normal BMI. **Materials and Methods:** Sixty healthy, young male participants with normal BMI (18.5–24.9) and BMI above >25 kg/mt^2 (n = 30 in each group) were recruited. The resting heart rate and BP were recorded. Then, the participants were made to walk on a treadmill at 50% of their VO_2 max for 20 min. BP was recorded at 5-min intervals for 30 min. **Results:** The time taken to attain maximum systolic PEH was significantly lesser ($P < 0.01$) in the normal BMI group (Median=20 vs. 25 min) than the higher BMI group. However, the time taken to attain maximum diastolic PEH was comparable between the groups. Spearman correlation test revealed a significant positive correlation between BMI and time taken to attain maximum fall in systolic BP after exercise ($r = 0.52$, $P < 0.01$). **Conclusion:** Therefore, it is concluded that as BMI increases the time taken to attain maximum systolic PEH also increases. Hence, when devising an exercise regimen, the BMI must be taken into consideration to attain maximum benefit.

KEY WORDS: Post-exercise Hypotension; Body Mass Index; Blood Pressure; Exercise; Time

INTRODUCTION

Physical fitness is not only most important to a healthy body but also the basis of dynamic and creative intellectual activity. However, due to scientific and technological advancements, the amount of physical activity has come down. As a result of this reduction, non-communicable diseases such as obesity, hypertension, and coronary heart diseases have increased in incidence, and treating them has become a huge public health issue. Physical exercise/activity is one of the easiest and earliest physiological ways of preventing and treating many such diseases. Particularly in patients with hypertension, lifestyle modification, which included regular physical activity is a well-known physiological method to bring down the blood pressure (BP).[1]

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Post-exercise hypotension (PEH) is "a phenomenon of prolonged decrease in resting BP in minutes and hours following exercise."[2] PEH is seen in pre-hypertensive, hypertensive individuals, and also in normotensive individuals.[3,4] There is sufficient evidence to prove that even a single bout of exercise (called acute exercise) itself

can cause sufficient PEH.[5] PEH is mainly seen in endurance (aerobic) exercises.[6] PEH can occur within minutes[7] to even an hour after exercise.[8] The maximum PEH occurs at around the 15th min[3] in the post-exercise period, but it was found to last for even 12 h[9] after exercise. The physiological basis behind PEH and the time taken to attain PEH has both central and peripheral mechanisms.[10] There is enough evidence to prove that during the exercise recovery period, there is a centrally mediated decrease in sympathetic nerve activity, and also activation of local vasodilator mechanisms.[10] The central mechanism is baroreceptor resetting to reduce the sympathetic outflow post-exercise[11] while the post-exercise release of metabolites and histamine[12] to cause vasodilatation is the peripheral mechanisms causing PEH. One of the major mechanisms for PEH is the centrally mediated baroreceptor resetting mechanism. After exercise, the baroreceptor reflex is reset to a lower BP level.[11] This causes a reduction in sympathetic outflow after exercise. During exercise, the myelinated and unmyelinated muscle afferents are activated in response to muscle contraction. At the caudal nucleus tractus solitarii (NTS), there is the release of substance P at neurokinin-1 receptors on gamma-aminobutyric acid (GABA) ergic interneurons due to the inputs from these afferent fibers. These GABAergic interneurons cause the release of GABA at $GABA_A$ receptors on second-order neurons within the NTS. The second-order neurons then convey the information from the baroreceptor afferents to the caudal ventrolateral medulla. The release of GABA reduces their excitability, which results in decreased inhibition of sympathetic neurons in the rostral medulla, which, in turn, leads to greater firing of sympathetic neurons during exercise and therefore the baroreflex is reset to a higher pressure during exercise.[10] As the person continues to exercise, due to the release of substance P from muscle afferent stimulation, neurokinin-1 receptors internalize the GABA interneuron, therefore after exercise, the neurokinin-1 receptors will be decreased in number for further binding.[13] As a result, there will be diminished GABAergic interneurons response to tonic inputs, and thus, the inhibitory effect on the second-order neurons will be decreased.

This, in turn, leads to an overall decrease in the sympathetic outflow from the rostral ventrolateral medulla after exercise. The second important mechanism underlying PEH is post-exercise vasodilatation. There are two vasodilatory phenomena which are recognized during the post-exercise recovery period: (1). Immediate post-exercise hyperemia and (2) sustained post-exercise vasodilatation.[12] The immediate post-exercise hyperemia lasts from seconds to minutes. This is not the same as PEH which will last longer and is sustained. There is sufficient evidence to prove that sustained post-exercise vasodilatation is dependent on the activation of histamine H_1 and H_2 receptors.[14] This was further supported by another study which showed that PEH following 60 min of moderate-intensity unilateral dynamic knee-extension exercise was abolished by H_1 and H_2 receptor antagonist.[15] Several possible mechanisms can cause an increase in intramuscular histamine during the post-exercise recovery period. The few exercise-related factors which are associated with mast cell degranulation include high temperature, reactive oxygen species, and a variety of cytokines.[16] Mast cells located in the connective tissue layer around the skeletal muscle fascicles will degranulate, releasing histamine locally.[17] In addition to these mechanisms, there is antigen-dependent and antigen-independent mechanism which causes mast cell degranulation, but with regard to exercise, the antigen-independent methods predominate. These are some of the major physiological principles put forward to explain PEH.

Obesity denotes a condition with excessive fat accumulation in the body to the extent that health and well-being are adversely affected (WHO). Obesity in India is prevalent in both the urban and in the rural population.[18] The major causes of obesity are a sedentary lifestyle and unhealthy eating patterns.[19] The first and most important step in treating obesity is lifestyle modification which includes regular physical activity and healthy dietary modifications.

The problem associated with obesity is that it is almost always associated with other diseases such as diabetes[20] and hypertension[21] which makes treatment even more difficult. Physical activity is a common remedy for both hypertension and obesity as it helps to reduce weight and BP.[2] The hemodynamic changes due to exercise and post-exercise are different between normal and obese individuals.[22] This study shows that body mass index (BMI) has a confounding effect on PEH. To the best of our knowledge, studies on the Indian population to evaluate the effect of BMI on time taken to attain maximum PEH are scarce. Hence, this study was done to investigate the effects of BMI on time taken to attain maximum PEH among healthy Indian adult males.

MATERIALS AND METHODS

Ethical Consideration

Ethical Committee Clearance (IEC: RC/13/103) from the Institute Ethical Committee was first obtained before the study commenced. An informed written consent was obtained after explaining the protocol to each participant before the commencement of the study.

Selection of subjects

Healthy adult male participants in the age group of 20–30 years with normal BMI and those with BMI above normal were included for the study.

Sample Size

Based on an earlier study,[22] a sample size of 30 was calculated for each group to detect a significant difference in

BP between normal and overweight groups, with 90% power and significance level of 5%.

Number of Groups

The participants were divided into two groups based on their BMI.

Group I – Participants with normal BMI (18.5–24.9) kg/mt^2 (n = 30)

Group II – Participants with higher BMI (25 and above) kg/mt^2 (n = 30)

Exclusion Criteria

The following criteria were excluded from the study:

- Participants practicing yoga or trained athletes.
- Prehypertensives.
- Participants with previous h/o musculoskeletal injuries.

Equipment Used

Omron M10-IT (HEM–7080 IT-E) digital BP monitor was used to record the BP of the participants before and after exercise. A motorized treadmill manufactured by AFTON (ACP087) was used to make the participant exercise at the desirable VO_2 max.

The exercise test was conducted in the exercise physiology lab. Each participant was asked to report at around 9 A.M. They were instructed to refrain from rigorous physical activity for 48 h before the test and not to consume tea/coffee as well as use tobacco for 12 h before the study. After obtaining the medical history, general physical examination was done to assess the health status of the participant. Anthropometric measurements were also recorded, and the BMI of each individual was calculated using the Quetelet's formula. Omron M10-IT (HEM-7080 IT-E) digital BP monitor was used to record the baseline BP in both the groups after 5 min rest.

The predicted maximum heart rate of the participant was calculated by subtracting their age from 220.[23] The participants VO_2 max (the maximum amount of oxygen utilization by the tissues) was calculated using the Uth-Sørensen-Overgaard-Pedersen formula.[24] The value obtained was divided by two to calculate the 50% VO_2 max. To eliminate the resting oxygen consumption 3.5 ml/kg/min was subtracted. The speed at which they must walk to make them exercise at 50% VO_2 maximum was then calculated by dividing the obtained O_2 consumption by 0.2.[25] This was the speed in meters/min. To get it in km/h, we multiplied it with 60 and divided it by 1000. This was the speed at which they walked on the treadmill to exercise at 50% VO_2 max. The speed would vary depending on the participant's age and basal heart rate; however, the work done by each would be the same.

Exercise Test

Each participant was instructed to walk on the treadmill (AFTON ACP087) for 20 min at the specific speed which was calculated for them. At the end of 20 min, the participants were asked to sit on a chair and their sitting BP immediately after exercise was recorded within 30 s. Subsequently, their BP was recorded for the next 30 min at 5-min intervals. Therefore, one immediate BP value measurement and six post-exercise BP values at intervals of 5 min were totally recorded. The time taken to attain maximum fall in systolic BP (Systolic PEH) below the resting value was noted. Similarly, the time taken to attain maximum fall in diastolic BP was also noted.

Statistical Analysis

The data were checked for normality and found to be not normally distributed, and hence, the variables are expressed as median and interquartile range.

Mann–Whitney U-test was used to compare the significant difference between the groups in age, anthropometric parameters, basal heart rate, basal BP, and time taken to attain maximum systolic and diastolic PEH. Spearman correlation test was used to find out the association between the BMI and time taken to attain maximum PEH values. All the data were analyzed using SPSS version 21. $P < 0.05$ was considered to be statistically significant.

RESULTS

The descriptive data of the study population demonstrated that there was no significant difference in height between the groups. However, the values of age, weight and BMI showed that normal BMI group participants were significantly younger than the higher BMI group ones ($P < 0.05$) and had significantly lower body weight ($P < 0.01$) [Table 1].

The basal BP and heart rate values of the participants in each group were expressed as median and interquartile range. The basal systolic BP of the normal BMI group was found to be lower than the above-normal BMI group, and the difference was statistically significant ($P < 0.05$). Although the basal diastolic values were also of a similar trend, the difference was not statistically significant. The basal heart rate was also found to be lower in normal BMI group, and it was statistically significant ($P < 0.01$) [Table 2].

While analyzing the time taken to attain the maximum fall in systolic and diastolic BP in the post-exercise period among the two groups, it was noted that normal BMI individuals have taken lesser time to attain maximum fall in systolic BP compared with the above-normal BMI group and the difference was found to be statistically significant using

Mann–Whitney U-test ($P < 0.01$). Although the time taken to attain maximum fall in diastolic BP in normal BMI group was also lower when compared with the above-normal BMI group, the difference was not statistically significant [Table 3].

The correlation between BMI and the time taken to attain maximum fall in systolic BP was analyzed using the Spearman correlation test. It was found that there was a significant positive correlation between BMI and the time taken to attain maximum fall in systolic BP in the post-exercise period ($r = 0.52$, $P < 0.01$) [Figure 1].

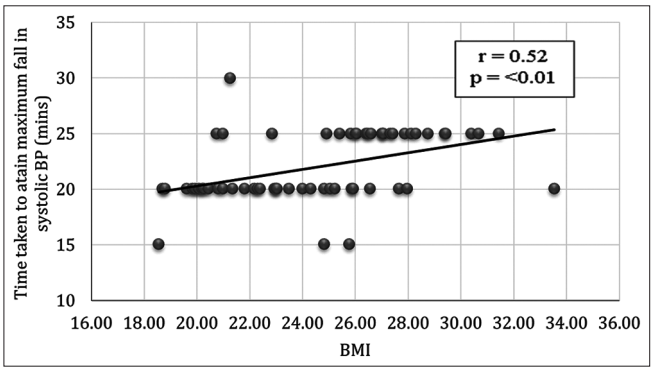

Figure 1: Scatter plot showing the correlation between body mass index and time taken to attain maximum fall in post-exercise systolic blood pressure using Spearman's test

DISCUSSION

The normal BMI group was significantly younger than the obese group ($P < 0.05$) and as to be expected their weight was considerably lower than the higher BMI group which was statistically significant ($P < 0.01$). The height variation between the two groups was minimal.

There was a significant difference in the basal systolic BP with the normal BMI group having a lower systolic BP than the above-normal group. The trend was similar in diastolic BP also, but it was not statistically significant. The basal heart rate of the above-normal BMI group was significantly higher than the normal BMI group. These findings are consistent with that of Nageswari *et al*.[26] who stated that obese individuals have a higher basal sympathetic tone when compared with non-obese individuals, whereas the peripheral resistance is similar between the two groups. The extra adipose tissue in obese individuals requires extra blood flow, which in turn leads to an increase in cardiac output. Thus, the high basal BP could be due to an increase in cardiac output in the obese individuals.

Landsberg *et al*. in 1989[27] and Troisi *et al*.[28] in 1991 reported that diet intake also has a role to play in the activation of the sympathetic system. They postulated that fat and carbohydrate in the diet of obese individuals stimulated the sympathetic

Table 1: Descriptive statistics of the study population

Variable	Normal BMI group Median (25^{th}–75^{th} percentile)	Above-normal BMI group Median (25^{th}–75^{th} percentile)	*P* value
Age (years)	23 (20–26)	26 (23–28)	<0.05*
Height (mts)	1.69 (1.65–1.72)	1.68 (1.64–1.72)	>0.05
Weight (Kg)	61 (55–69)	78 (72–81)	<0.01*
BMI (Kg/mt^2)	21 (20–23)	27 (26–28)	<0.05*

BMI: Body mass index. **P* value statistically significant for Mann–Whitney U test

Table 2: Comparison of cardiovascular parameters among the groups with normal BMI (18.5–24.9) and with above-normal BMI (25 and above)

Variable	Normal BMI group Median (25^{th}–75^{th} percentile)	Above-normal BMI group Median (25^{th}–75^{th} percentile)	*P* value
Basal systolic BP (mmHg)	111 (108–116)	116 (112–117)	<0.05*
Basal diastolic BP (mmHg)	74 (70–78)	77 (74–78)	>0.05
Basal heart rate (Beats/min)	70 (64–74)	76 (70–80)	<0.01*

BMI: Body mass index, BP: Blood pressure. **P* value statistically significant for Mann–Whitney U test

Table 3: Comparison of time taken to attain maximum post-exercise hypotension among groups with normal BMI (18.5–24.9) and above-normal BMI (25 and above)

Variable	Normal BMI group Median (25^{th}–75^{th} percentile)	Above normal BMI group Median (25^{th}–75^{th} percentile)	*P* value
Time taken to attain maximum fall in systolic BP (min)	20 (20–20)	25 (20–25)	<0.01*
Time taken to attain maximum fall in diastolic BP (min)	20 (15–20)	20 (20–25)	>0.05

BMI: Body mass index, BP: Blood pressure. **P* value statistically significant for Mann–Whitney U test

system. Insulin regulated glucose metabolism within the ventromedial hypothalamus plays an important role in the relationship between diet and sympathetic nervous system activity. These are the proposed mechanisms by which obesity is linked with increased activation of the sympathetic system and Grassi *et al*.[29] suggested that this increased sympathetic system activity is the cause of hypertension commonly associated with obesity. High sympathetic tone will also cause higher basal heart rate; hence, a high basal heart rate can be taken as a marker of sympathetic activity.[30] In an earlier study by us, we compared the maximum PEH between the two groups and found that the normal BMI group had a higher systolic PEH when compared with the diastolic PEH and that systolic PEH had a negative correlation with BMI.[31] This was postulated to be due to the higher sympathetic tone in obese individuals. In this study, we compared the time taken to attain maximum systolic as well as diastolic PEH between the two groups. The normal BMI group attained a maximum fall in systolic BP earlier than the above-normal BMI group ($P < 0.01$). The time taken to attain maximum fall in diastolic BP also followed the same trend, but, the difference was not statistically significant ($P > 0.05$).

The most important reason for PEH is the centrally mediated baroreceptor resetting which decreases sympathetic outflow following exercise and the diastolic was due to local vasodilator metabolites.[10,14] In the present study, normal BMI group attained maximum PEH (Systolic) faster than the above-normal BMI group. This could be due to the fact that normal BMI has a lower sympathetic tone than the obese group, so it will take longer time to reduce the sympathetic outflow after exercise in the obese group than the normal BMI group. Therefore, the systolic PEH is attained much quickly in the normal BMI group than the obese group. In case of the time taken for diastolic PEH, though the trend is similar it did not reach statistical significance which might be due to the fact that diastolic PEH is mainly due to the production of local metabolites which might be similar in both groups.

Scatter plot analysis also reveals than the majority of the men above BMI of 25 reached the maximum fall in systolic PEH around 25th min, and the majority of the normal BMI group reached around 20th min. This finding was similar with a previous study done by MacDonald *et al*. in 2000 who reported that the maximum reduction in BP in the post-exercise period has been shown to occur at around the 15th min after exercise.[3]

Nevertheless, our study shows that as the BMI increases the time taken to attain maximum fall in PEH also increases, particularly for the systolic BP.

Limitations

1. A greater sample size could have given a better idea about the time taken to attain maximum diastolic PEH also.
2. Whether there is any gender variation needs further investigation.
3. BP recording could have been done at shorter intervals (or even continuous BP monitoring if possible) rather than 5 min for more accurate time recordings.

CONCLUSION

From our study, it can be concluded that BMI significantly affects the time taken to attain maximum PEH, systolic PEH more than diastolic PEH. This could be due to a higher sympathetic tone in the higher BMI individuals. Clinically, by this study, it can be concluded that an above-normal BMI individual may have to exercise for a greater duration of time or at higher intensity to attain the same beneficial effects of PEH as individuals with normal BMI. Therefore, while devising an exercise regime for the treatment of hypertension or obesity, BMI of the individual must be taken into consideration for the optimum benefit for the individual.

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RESEARCH ARTICLE

A cross-sectional study on effect of obesity on autonomic functions in a tertiary care center

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ABSTRACT

Background: Obesity is the most emerging problem in today's time. It is responsible for many metabolic as well as psychological ailments. Obesity and autonomic involvement have been studied, but evidence regarding the same is controversial. Obesity can no longer be considered as a silent epidemic in the new age scenario. Although people consider obesity a problem, it can still be regarded as one of the most overlooked public health issues. **Aims and Objectives:** This study aims to study the relationship between obesity and autonomic function tests. **Materials and Methods:** The present study was carried out in 86 male volunteers in the age group of 18–25 years. 40 of the subjects were included in the obese group, body mass index (BMI >30 kg/m^2) and the other 46 were included in the non-obese group (BMI <30 kg/m^2). Autonomic function tests in the form of heart rate variability and sympathetic skin response (SSR) tests were conducted in both the groups. **Results:** High frequency (HF) was significantly reduced in the obese group (240 ± 3.22, $P < 0.014$). Low frequency/HF was significantly altered in the obese group ($P < 0.05$). SDNN was significantly lesser in obese when compared to non-obese ($P < 0.05$). SSR latencies and amplitudes when compared between obese and non-obese did not reveal statistically significant results. However, both SSR amplitude and latency were lesser in the obese group when compared to non-obese. Tests indicate decreased parasympathetic activity in obese individuals. **Conclusion:** The link between obesity and autonomic functions if detected earlier in the long run will pave the way for a healthier life. This, in turn, may help in preventing cardiovascular morbidity which, in turn, reduces the burden on the society as a whole.

KEY WORDS: Body Mass Index; Autonomic Nervous System; Obesity; Autonomic Function Tests

INTRODUCTION

Obesity is emerging on the forefront as a health-care issue. It is an on-going epidemic heralding a new age crisis to both developed and developing countries. Both genetic and environmental factors interplay are observed in obesity.[1]

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Several factors such as sedentary lifestyle, lack of exercise or lack of motivation to continue exercising, intake of a calorie-dense diet, genetic and environmental factors contribute to the pathogenesis of obesity. Obesity results from a chronic imbalance between intake and energy expenditure. Hemodynamic and metabolic alterations occur in obesity. Obesity and autonomic involvement have been studied from times galore, but evidence regarding the same is controversial. Autonomic nervous system has two divisions sympathetic and parasympathetic. Autonomic system regulates body functions such as heart rate, respiration, urination, sexual function, and pupillary responses. Findings related to obesity and autonomic functions have been found to be inconsistent.[2,3] Hemodynamic instability in the form

of increased cardiac output, changes in vascular reactivity, hypertension, diastolic dysfunction, and cardiomyopathy have been documented. Cardiovascular diseases are often linked with obesity. Insulin resistance, hypertension, and reduced high-density lipoprotein have been suggested to cause cardiovascular diseases in obese individuals.[4] However, autonomic instability in obesity cannot be ruled out. Obesity can result in complications manifold, namely hypertension, insulin resistance, dyslipidemia, and coronary heart disease.[5]

Autonomic dysfunctions on a long-term basis pose a high risk for cardiovascular morbidity and mortality. In addition to cardiovascular risks, obesity has also been associated with diabetes, hypertension, cancer, and sleep apnea.[6] This may be the cause for an overall increase in mortality rate linked to obesity. Early detection of autonomic instability may prove as a key factor in promoting weight loss techniques in obese individuals by highlighting the nuances associated with the same, which may improve the quality of living if acted upon.

Various autonomic tests are available to study autonomic dysfunctions including heart rate variability (HRV), sympathetic skin response (SSR), and R-R interval variation. One of the most reliable methods to study cardiovascular autonomic status is HRV in addition to being noninvasive and sensitive. There are not many studies in the Indian scenario pertaining to correlation between obesity and autonomic functions. In addition, evidence concerning the relation of sympathetic skin resistance to obesity has been scarce. Keeping in mind the above facts, the present study has been undertaken to study the relation between obesity and autonomic functions. The study objective was to evaluate the link between autonomic functions and obesity.

MATERIALS AND METHODS

The present study was undertaken in a tertiary care center on 86 male volunteers, in the age group of 18–25 years. Ethical clearance was obtained from the institutional ethical committee. Informed consent was taken. After explaining the procedure to the subjects, anthropometric values were noted down. Obesity criterion based on the WHO cutoffs was added when the body mass index (BMI) was >30 kg/m^2. Group 1 consisted of 40 obese subjects and Group 2 had 46 non-obese subjects who were controls. Mean BMI of obese subjects (32.04 ± 2.66) was higher than that of controls (20.43 ± 2.34). Subjects on medication for cardiovascular and central nervous system disorders were excluded from the study. Subjects with a past/present history of cardiovascular disorders and history of smoking were excluded from the study. Subjects were asked to refrain from consuming tea/coffee/beverages on the day of the study. This was done to avoid any direct influence on cardiac autonomic activity. They were asked to report to the center after a light breakfast with light clothing.

The subjects weight was measured accurately using a digital weighing scale. Standing height was measured using a stadiometer. Both waist circumference and hip circumference were measured with the help of a flexible measuring tape. Measurement of HRV - ambulatory computerized electrocardiogram (ECG) system was used in this study. Frequency domain and time domain methods were used for analysis. ECG was recorded in the supine position for 5 min after 5 min of supine rest. ECG obtained was stored in the computer for analysis as an offline data.

Measurement of SSR - the instrument used in the study was NCV-evoked potential (EP)-electromyography (EMG) machine (RMS EMG EP MARK II, Recorders and Medicare Systems, Chandigarh). Surface disk electrodes were used in the current study. SSR was recorded using supramaximal electrical stimulus. The latency (defined as the time interval between the stimulus and the onset of the SSR waveform) and amplitude (defined as the peak-to-peak amplitude of the SSR wave) of SSR was noted for each of the recordings.

All the values obtained were charted and tabulated as mean ± standard deviation. Comparison between obese and non-obese group was performed using Student's unpaired *t*-test.

RESULTS

A total of 86 male volunteers were included in the study. 40 of them were obese (BMI >30, n = 40) and were grouped as test subjects. The other 46 were control (BMI <30, n = 46). Comparison studies between obese and non-obese group were done using Student's unpaired *t*-test. $P < 0.05$ was considered as statistically significant. Weight, BMI, waist circumference, and hip circumference were significantly higher in Group 1 obese subjects when compared to controls [Table 1]. High frequency (HF) is significantly higher in non-obese controls when compared to obese. Low frequency (LF)/HF when compared showed a significant sympathovagal imbalance in obese. SDNN is significantly lower in obese [Table 2]. Mean values of SSR amplitude and latency are lower in obese when compared to non-obese though no significance is attached [Table 3].

Table 1: Comparison of anthropometric values between Group 1 (obese subjects) and Group 2 (controls)

Parameters	Group 1 (n=40)	Group 2 (n=46)	P value
Age	23.07±7.25	21.48±8.011	0.428
Height in meters	1.57±0.97	1.63±0.10	0.036
Weight in kg	82.39±10.16	60.57±9.38	<0.001*
BMI (kg/m^2)	30.09±2.92	21.67±2.43	<0.001*
Waist circumference (cm)	99.33±13.96	61.98±11.33	<0.001*
Hip circumference (cm)	98.99±13.78	80.97±8.22	<0.001*

*P value<0.05: Significant difference

Table 2: Comparison of HRV indices between Group 1 (obese) and Group 2 (controls)

HRV indices	Group 1 obese subjects (*n*=40)	Group 2 controls (*n*=46)	*P* value
LF (ms^2)	480±3.56	248±3.55	0.063
HF (ms^2)	240±3.22	675±3.48	0.014*
LF nu	52±2.15	42±3.11	0.078
HF nu	44.28±3.92	54.29±3.87	0.078
LF/HF	1.33±3.66	0.78±3.78	0.043*
SDNN	30.65±3.6	42.53±2.08	0.037*

**P* value<0.05: Significant difference, HRV: Heart rate variability, LF: Low frequency, HF: High frequency

Table 3: Comparison of SSR parameters in obese and non-obese group

SSR parameters	Group 1 obese (*n*=40)	Group 2 controls (*n*=46)	*P* value
SSR amplitude	0.27±0.18	0.32±0.42	0.054
SSR latency	0.32±0.19	0.27±0.18	0.052

**P* value<0.05: Significant difference, SSR: Sympathetic skin response

DISCUSSION

Obesity alters autonomic effects on heart. The obese subjects had significantly higher ($P < 0.05$), body weight, BMI, waist circumference, and hip circumference in comparison to the controls. SDNN being a time domain variable, reflecting parasympathetic nerve activity was significantly lower in obese when compared to controls. Among the frequency domain variables, HF power (ms^2) and HF (ms^2) indicating parasympathetic activity were significantly lower in obese individuals. LF/HF ratio when compared between obese and non-obese showed significance indicating sympathovagal imbalance in obesity.

SSR values when compared showed that SSR amplitude was shorter in obese when compared to non-obese individuals. SSR latency was shorter in obese when compared to non-obese. Although no significance was attached to the values obtained through SSR, it can be safely said that parasympathetic activity was found to be reduced in the obese.

In a study by Poliakova *et al*., an independent association between HRV and age, waist circumference, and body fat was found. However, there was no association between BMI and HRV.[7]

All the above findings indicate autonomic imbalance in obese individuals. Parasympathetic activity was lower in obese when compared to controls. This shows poor autonomic control in obese. Our findings are suggestive of decrease in parasympathetic activity in obesity. The test results obtained are akin to that found by other researchers, indicating that parasympathetic activity is altered more than sympathetic in obese individuals.[8] Parasympathetic activity dysfunction is presented in obese when compared to non-obese. Some researchers have suggested insulin resistance as a culprit for the parasympathetic imbalance in obese individuals. Insulin resistance increases with increased body weight causing a state of hyperinsulinemia. This causes low vagal activity in obese individuals.[9] Decrease in vagal activity by itself is a threat to the cardiovascular status.

Nagai *et al*. reported alteration in both sympathetic and parasympathetic systems in obesity.[10] However, certain studies have recorded an increase in sympathetic activity and decrease in parasympathetic activity in an obese individual as age advances. Cardiac sympathetic activity alteration depends on the duration of obesity.[11] In addition, role of hypothalamus in altering the autonomic functions has been put forth. Hypothalamus houses both the satiety center and regulatory center of ANS. Lesions in the hypothalamus may lead onto obesity and autonomic dysfunction. Whether dysfunction is due to obesity or obesity facilitates dysfunction is a point to be pondered on.[12] On the other hand, studies have also detected decrease in sympathetic activity in obese animal models. Laitinen *et al.* have linked central body obesity and total body fat to alteration in autonomic activity.[13]

Although our study found a reduction in parasympathetic activity, other studies have shown autonomic function to be altered in obese based on the duration of obesity. Further cross-sectional studies involving a larger population dealing with obesity in a longer duration basis are warranted for in this regard. The alteration in parasympathetic activity could be owed to the fact that in obese there is a skew in the eating pattern. They usually have a higher carbohydrate intake when compared to fat and protein intake. This may result in a change in parasympathetic activity according to Valensi *et al*.[14] Inadvertent intake of food also increases sympathetic activation.[12]

The strength of the present study is the contribution in understanding the autonomic imbalance associated with obesity in young adults. Obesity is alarmingly increasing in the young adult population in India. In times to come autonomic imbalance along with metabolic disturbances could set in at a younger age. Limitations of the present study are that since the study population involved younger age group, it may be a possibility that noteworthy changes in sympathetic nervous system have not been detected.

CONCLUSION

Obesity and autonomic dysfunction can be correlated. Autonomic dysfunction on a long-term basis is responsible for cardiovascular morbidity and mortality. Autonomic function testing is one way of detecting the possibility of cardiovascular risks in future. If autonomic dysfunction is detected, early obese can be motivated to lose weight. Weight loss may help

in balancing the autonomic system which has been thrown off gear due to obesity. Poirier *et al.* in their study found an association between weight loss and parasympathetic activity which definitely paint a positive picture in the long run.[15] Obesity when detected early may help in preventing serious health issues which may occur as a consequence. In addition, it reduces the overburdening of the public health sector. Lifestyle modifications in the form of long-term exercise program, healthy diet is the need of the hour in the present era.

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GENOTYPE AND VIRAL LOAD DETERMINATION OF HEPATITIS C VIRUS FROM A TERTIARY CARE HOSPITAL, SOUTH INDIA

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Abstract:

BACKGROUND

Hepatitis C Virus (HCV) is a leading cause of chronic liver disease which frequently progresses to cirrhosis and hepatocellular carcinoma. Genotype distribution of HCV in a geographical area and pre-treatment viral load are the prognostic markers of response to antiviral therapy which may help to decide the duration of treatment and to develop geographically tailored vaccine immunogens.

MATERIALS AND METHODS

A descriptive study with qualitative detection of anti-HCV in patients' serum was carried out by Chemiluminescent Immunoassay (CLIA) in VITROS. Samples positive in CLIA were further processed for viral load by Taqman Real Time PCR and genotype analysis was carried out by nested PCR using primers of core region to diagnose genotypes 1(1a/1b), 2, 3 and 4.

RESULTS

67 patients were newly diagnosed with HCV infection during our study period were included in

the study. Males were predominant 59.7%; most prevalent age group was 40-70 years (85%). Genotype 3 was predominant, 29 (43.3%), followed by genotype 1 in 28(41.8) and genotype 4 in 10 (14.9%) patients. High prevalence of genotype 3 was seen among female patients in contrary to genotype 4 in males. Among genotype 3, half of the patients had high viral load and in genotype 1b almost 60% had low viral load. But other genotypes 1a & 4 had high viral load in 3/4 of the patients.

CONCLUSION

Genotype 3 and 1 were almost equally distributed among our study population. Both genotype 1 and 4 showed increasing trend of prevalence. Our study emphasises that HCV genotyping in combination with quantitative evaluation of HCV RNA will be beneficial in selecting the duration of interferon treatment.

KEY WORDS

HCV; Genotypes; Viral Load.

Full Text:

BACKGROUND

Hepatitis C virus (HCV) is a globally prevalent pathogen, and is a major cause of chronic liver disease which frequently progresses to liver cirrhosis and hepatocellular carcinoma. [1] As per WHO globally >185 million people affected with HCV and nearly 30 million people affected in India. [2,3] Chronic hepatitis C infection is often silent, most of the times diagnosed only by routine serological testing. Many studies have been carried out to identify the natural history and progression of hepatitis C infection. Still, several aspects remain to be elucidated. [4] Several factors like age at infection, gender, mode of infection, genotype, and viral load have been reported as important predictors of outcome of the disease progression. Lack of a successful vaccine with high rate of chronicity makes HCV infection a serious public health challenge. [5,6]

HCV is a enveloped, single-stranded positive sense RNA virus belonging to genus Hepacivirus, family Flaviviridae. The genome of HCV is approximately 9.6 kb in length consist of structural core (C) and envelope (E1 & E2) and the nonstructural proteins (NS1, NS2, NS3, NS4A, NS4B, NS5A & NS5B) which prone for a high mutation rate of 10-2 mutations per nucleotide. [7] HCV has been classified into six recognized genotypes (G1-6) and five other genotypes (G7-11) regarded as variants of genotype six on the basis of phylogenetic and sequence analyses of the whole viral genome. Genotypes are further classified into 67 confirmed and 20 provisional subtypes. Also, HCV in chronically infected individuals exhibits as quasispecies. [8,9]

Age Group (Years)	Male (Percentage)	Female (Percentage)	Total
All	40 (59.7%)	27 (40.3%)	67
40-70	35 (87.5%)	22 (81.5%)	57 (85%)

Table 1. Age & Sex Distribution of Newly Diagnosed HCV

Therapy for HCV mainly depends on interferon--a (Standard or pegylated) and ribavirin. Response to therapy depends on genotypes, and the duration of treatment depend on rate of response. Almost 80% of the genotypes 2 and 3 can be cured with standard treatment for 24 weeks; while genotypes 1, 4, 5 and 6 have been reported to show poorer response with 48 weeks treatment. [10-12] Besides HCV genotypes, pre-treatment viral load has been shown to be another important prognostic indicator of response to antiviral therapy as increased pre-treatment viral load has been linked with low rates of response and a decline in HCV viral load during first 2-12 weeks has been shown high rates of response to antiviral therapy.!13-15! Furthermore, the first prophylactic T-cell vaccines which are currently in Phase II trail, to prevent persistent HCV infection contains a subtype-1b immunogen. But in countries where mixed

genotype infections are prevalent, cross immunity will depend on the generation of an immune response against the conserved antigenic target between genotypes which vary based on subtypes. An alternative strategy to this would be to develop a geographically tailored vaccine immunogens; for that comprehensive national-level understanding of relative subtype prevalence is mandatory. [16,17]

Globally, the geographic distribution of HCV genotypes is complex. Prevalence of genotypes differs considerably between geographical regions. Geographical distribution of genotypes and pretreatment viral load provide a clue about the outcome of liver disease and a prognostic marker for response to interferon therapy. [18,19] In India, only a few studies have been carried out in disparate regions within India. [3,19-21] Keeping this in mind, our study was planned to analyze the genotypes and pre-treatment viral load among newly diagnosed HCV individuals.

MATERIALS AND METHODS

A Descriptive study was carried out in our tertiary care hospital which includes the patients with a lab diagnosis of newly positive for HCV serology attended our hospital over a period of 12 months between Jan 2016-Dec 2016.

Qualitative Detection of HCV

Qualitative detection of anti-HCV from patient's serum was carried out by Chemiluminescent Immunoassay (CLIA) using VITROS ECi/ECiQ Immunodiagnostic Systems (Ortho Clinical Diagnostics- Vitros ECi/ECiQ fully automated immunoassay system, Buckinghamshire, HP12 4DP, United Kingdom). An immunometric technique is used, which involves the simultaneous reaction of HCV antibodies in the sample with recombinant HCV Ag antibody coated onto the wells and a horseradish peroxidase (HRP)-labelled mouse monoclonal anti-HCV antibody in the conjugate. After removing the unbound conjugate by washing, a reagent containing luminogenic substrates (Luminol derivative and peracid salt) and an electron transfer agent is added to the wells. The bound HRP conjugate catalyzes the oxidation of the luminol derivative, produces the light and electron transfer agent (Substituted acetanilide) increases the level of light produced and prolongs its emission which will be measured as cut off signal ratio by the system.The amount of HRP conjugate bound is indicative of the level of theanti-HCV present in the sample. [20]

Samples positive in qualitative detection of HCV by CLIA were further processed for viral load estimation and genotype analysis.

Quantitative Measurement of Hepatitis-C Viral Load

Viral load estimation was carried out by TaqMan Real-Time PCR system in SRL Lab, (Super Religare Laboratories) Mumbai. RNA was extracted from 100 pl patient's sera using Qiagen RNA extraction kit according to the kit protocol. Seven standards of different copy numbers (102 to 108 copies per ml) were included in HCV RNA quantification assay, and a known quantity of internal standard was included in each preparation. RT-PCR was performed in the 5' untranslated region (5'UTR) as per manufacturer's instructions (95[degrees]C for 20 secfollowed by 40 cycles at 95[degrees]C for 10 sec and 58[degrees]C for 15 sec and 72[degrees]C for 10 sec). The unit of the HCV RNA quantification was IU/ml. Lower limit of detection of this assay is 34 IU/ml.

Viral load was considered low if it was less than 6,00,000 IU/ml; intermediate 6,00,000 8,00,000; High if more than 8,00,000 IU/ml. [21,22]

HCV Genotype Analysis

HCV genotype analysis was carried in SRL Lab, Mumbai using the amplicons resulting from the

nested PCR using type-specific primers for the core region of the HCV genome to diagnose the genotypes 1(1a/1b),2,3 and 4. Briefly, 10 pl of HCV RNA was reverse transcribed to cDNA using 100 U of Maloney murine leukemia virus reverse transcriptase (MMLV RTEs) at 37[degrees]C for 50 minutes. Two pl of transcribed cDNA was used for amplification of 470-bp region from HCV 5'NCR by first round PCR amplification. The amplified first round PCR products were subjected to second rounds of nested PCR amplifications. Following amplification, the electrophoretic separation was carried out, and bands were detected by ethidium bromide staining, observed under a UV transilluminator.

Statistical Analysis

Genotypes	< 6 lakhs	6-8 lakhs	>8 lakhs
1a	2	2	**7**
1b	7	3	7
3	15	1	**13**
4	3	1	**6**
Total	**27 (40.3%)**	**7 (10.5%)**	**33 (49.2%)**

Table 2. Viral Load Distribution Among Various Genotypes

Data analysis was carried out by anSPSS version 16. Chi Square test was used to measure the association between categorical variables. Data presented as mean values or number of patients expressed as percentage. P-value of less than 0.05 was considered statistically significant.

RESULTS

Total number of newly diagnosed HCV positive patients during Jan 2016 -Dec 2016 was 67.

Among 67 HCV-positive patients, 59.4% were males, and the most common presenting age group was 40-70 yrs. (Table 1 and Figure 1). Almost 90% of males and 80% of females belong to 40-70 years of age. All of them had CLIA signal/cut off ratio of 20-42. Among the 67 HCV positive patients, Genotype 1 was positive in 28 (41.8%) patients, genotype 3 in 29 (43.3%) patients and genotype 4 in 10 (14.9%) patients. Within genotype 1, 1a in 11 (39.3%) and 1b in 17 (60.7%) patients (Figure 2).

Genotype Ia was mainly distributed among 41-50 years of age, Ib & 3 in all age groups and genotype 4 among 71-80 yrs. of age group (Figure 3). No significant statistical correlation among various age group with genotypes was observed. But statistically significant (p-value=0.0075 & 0.034 i.e. $p<0.05$) correlation was seen among the genotype 3 and 4 prevalence with gender. In our study, HCV genotype 4 was predominant among males (90%) and genotype 3 more prevalent among females (58.6%) (Figure 4).

No significant statistical correlation was present in the analysis of viral load distribution with various age group and gender (Figures 5 & 6). Nearly 15/29 (51.7%) patients infected by genotype 3 in our study population had low viral load and 14/29(48.3%) had intermediate and high viral load. 7/11 (63.6%) patients infected by genotype 1a & 6/10 (60%) patients infected with genotype 4 had high viral load (Table 2).

DISCUSSION

Currently, India harbors about 10-15 million chronic carriers of HCV, which is a major cause of liver-related morbidity and mortality. [8] Knowledge of genotypes is very essential for management of HCV infection and prediction of prognosis. Patients with HCV genotype 1 and 4 will have to receive IFN and ribavirin for a period of 48 weeks. Patients with these genotypes show a poor sustained viral response when tested 24 weeks after completion of therapy. On the contrary, persons infected with genotype 2 and 3 are reported to have a better response to therapy. Also, this remarkable heterogeneity of HCV must be studied to develop strategies for

designing a successful vaccine. [11, 15]

Our results indicated that high prevalence rate about 85% of HCV infection was found between the age group of 40-70 years. These findings were in agreement with the findings of Muhammad Waqar et al. [23] that high HCV prevalence rate was found in age group of 41-60 yrs. But our findings contradict from that of Ali et al. [13] Inamullah et al. [24] who reported highest rate of prevalence in the age group of <40 years.

Globally, geographic distribution of HCV genotypes is complex. 1-3 genotypes are widely distributed throughout the world. Subtype 1a is prevalent in North, South America, Europe, Australia and 1b is common in North America, Europe. Subtypes 2a and 2b are prevelant in North America, Europe, Japan, and subtype 2c in northern Italy. Genotype 3 is common in Europe, South America and Southeast Asia. Genotype 4 is prevalent in North Africa and Middle East and Genotype 5 is distributed in Southern Africa. In India, HCV genotypes distribution is variable in different region. In North India, genotypes 1, 2 and 3 have been identified with genotype 3 being the predominant one. Data from South India showed genotypes 1,2,3,4 and 6 were present with high occurrence of genotype 3 followed by 1. [2,25]

Our study reemphasizes that HCV genotype 3 is the predominant genotype (43.3%) along with genotype 1 (41.8%) in our study population. These findings were in agreement with Anita Chakravarti et al. Sompal Singh et al. and J Christdas et al. [3,26,27] Compared to previous reports from India, the prevalence of genotype 1 (About 25% previously) is increasing in trend (41.8%). Genotype 4 which was mainly distributed in Egypt and the Middle East is being increasingly reported in India. Compared to the previous report, the prevalence of genotype 4 has increased from 7.5% to 14.9%. [3,26,27] No significant statistical correlation among various age group with genotypes was observed.

But statistically significant (p-value=0.0075 & 0.034 i.e $p<0.05$) correlation was seen among the genotype 3 and 4 prevalence with gender. In our study, HCV genotype 4 was predominant among males (90%) and genotype 3 more prevalent among females (58.6%). These results are not in accordance with results of Amjad Ali et al. Akbar et al. Attaullah et al. who reported no significant correlation between gender and genotypes. [13,28,29] Also our results are in contrast to Idrees et al. who reported statistically significant association between genotype 4 and females. [30]

Previous studies highlighted that patients with higher viral load show lower response rates to standard antiviral therapy as compared to patients having a lower viral load [26,27]. No significant statistical correlation was present in the analysis of viral load distribution with various age group and gender. Our results were in agreement with Sompal Singh et al. [27] who also reported no correlation, but our results contradict with Nafees et al. [31] who reported that infected males have persistently higher HCV RNA levels than infected females.

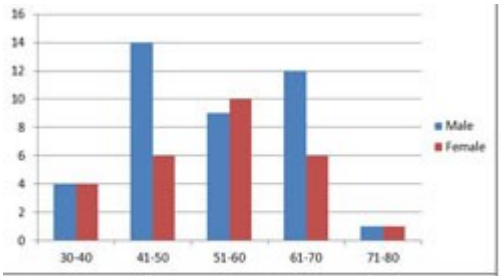

Figure 1. Distribution of Newly Diagnosed HCV Among Various Age Group with Gender Disparity

But our study findings carry some important implication for therapeutic purposes. Genotypes 3& 1 were the most commonly reported genotypes in India and also in our study population. HCV-infected patients with low viral load (HCVRNA< 6,00,000 IU/mL), more likely to attained a

sustained virological response (SVR) as compared to those with high viral load (HCV-RNA> 600000 IU/mL). [13,75]

We found that nearly 15/29 (51.7%) patients infected by genotype 3 in our study population had low viral load and 14/29(48.3%) had intermediate and high viral load. As per findings of Von et al [22] patients with genotype 3 and high viral load (> 6,00,000 IU/mL) should be treated for 24 weeks whereas patients with low viral load might be treated for 16 weeks if the patient's RNA level is undetectable at week 4 of treatment. Previous results suggested that genotype 3 is mostly associated with low viral load and it will have a good sustained viral response. In the present study, half of the patients with genotype 3 presented with a high viral load which needs longer duration of treatment. We also found that 10/17 (58.8%) patients infected by genotype 1b in our study populations had a low viral load. This is in contrast to Rong et al. Saba Riaz et al. who reported that genotype 1 was associated with higher HCV RNA levels than genotype 3. [32,33] So extensive information about HCV genotype and pre treatment viral load is essential when planning therapy strategies against HCV at the national level.

In our study population, 7/11 (63.6%) patients infected by genotype 1a & 6/10 (60%) patients infected with genotype 4 had high viral load, need the treatment for 48 weeks. These results also help to modify antiviral therapy individually for infected HCV patients with a particular genotype. HCV genotype 2 was not detected in our population.

Also, for optimal designing of serological sequencing and confirmatory assays for HCV diagnosis, antigenic differences between genotypes is essential. So to get the optimal sensitivity, future tests will need to incorporate antigens from various genotypes, especially genotype 3, 1 & 4 which were the most prevalent genotypes in our country as well as in this study region.

CONCLUSION

HCV infections were most commonly present among 40-70 years' age group. Genotype 3 and 1 were almost equally distributed genotypes among our study population. Both genotype 1 and 4 were showing increasing trend of prevalence. High prevalence of genotype 3 was seen among female patients in conflict to genotype 4 was prevalent almost in males. In contrary to previous thoughts, half of the patients with genotype 3 had high viral load, and 60% of genotype 1b had a low viral load. But other serotypes 1a & 4 showed high viral loads in 3/4th of the patients.

Our study emphasize that HCV genotyping in combination with pre treatment viral load will be essential in the management of chronic hepatitis C and in selecting the duration of interferon treatment. Before guidelines can be established, more studies are needed for the routine use of genotyping outside clinical trials and research laboratories.

Limitations

Only limited genotypes prevalent in our country (Genotypes 1, 2, 3 & 4) were looked for. Subtyping of other genotypes could not be done. Also, clinical correlation between the genotypes, pretreatment viral loads with response to treatment, if started were not analysed.

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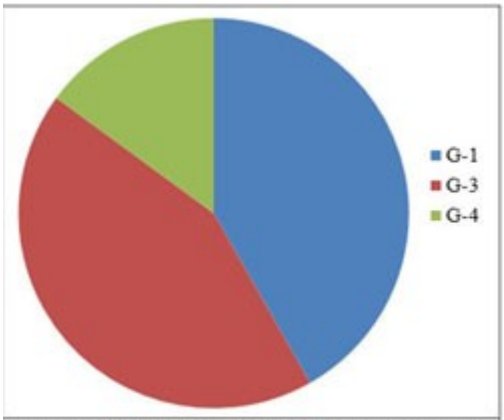

Figure 2. Genotypic Prevalence in Our Study Population

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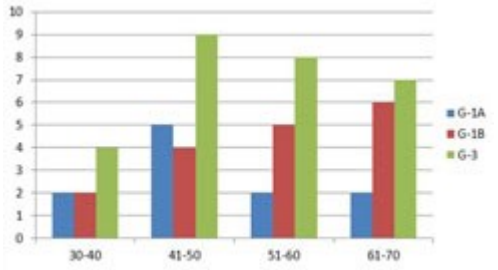

Figure 3. Genotypes Prevalence Among Various Age Group

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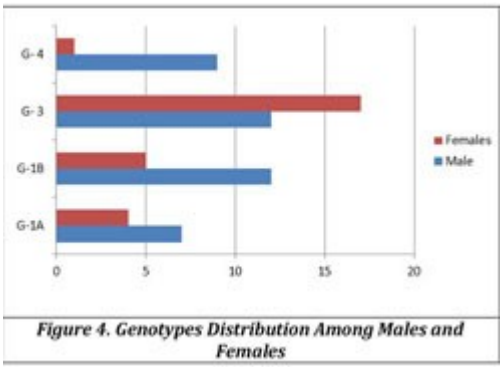

Figure 4. Genotypes Distribution Among Males and Females

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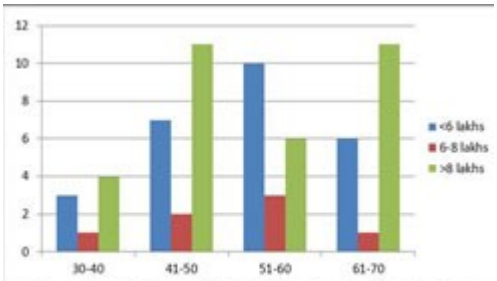

Figure 5. Viral Load Distribution Among Various Age Groups

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Caption: Figure 1. Distribution of Newly Diagnosed HCV Among Various Age Group with Gender Disparity

Caption: Figure 2. Genotypic Prevalence in Our Study Population

Caption: Figure 3. Genotypes Prevalence Among Various Age Group

Caption: Figure 4. Genotypes Distribution Among Males and Females

Caption: Figure 5. Viral Load Distribution Among Various Age Groups

Caption: Figure 6. Viral Load Distribution Among Males and Females

Table 1. Age & Sex Distribution of Newly Diagnosed HCV

Age Group (Years)	Male (Percentage)	Female (Percentage)	Total
All	40 (59.7%)	27 (40.3%)	67
40-70	35 (87.5%)	22 (81.5%)	57 (85%)

Table 2. Viral Load Distribution Among Various Genotypes

Genotypes	< 6 lakhs	6-8 lakhs	>8 lakhs
1a	2	2	7
1b	7	3	7
3	15	1	13
4	3	1	6
Total	27 (40.3%)	7 (10.5%)	33 (49.2%)

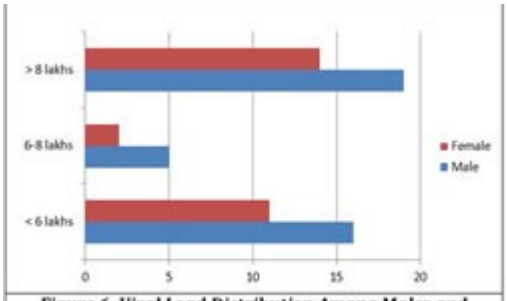

Figure 6. Viral Load Distribution Among Males and Females

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A retrospective study of annual poisoning profile in a tertiary care hospital in South India for the Year 2017–18

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Online published on 30 June, 2020.

Abstract

Introduction: Poisoning is a common medicolegal problem now days all over the world as it consumes not only the valuable health service resources but also causes considerable morbidity and mortality. *Aims and Objectives*: The present study was carried out with the objective to find out the pattern of acute poisoning in a tertiary care hospital in South India in one year. *Materials and methods*: A retrospective analytical content based analysis was made on 130 poisoning cases recorded in a tertiary care hospital in South India in one year from June 1st 2017 to May 31st 2018 and the results were tabulated. *Results*: Of the 130 cases, 52 were males and 78 were females with 31 cow dung poisoning cases (23.84%) as the most common followed by OPC poisoning with 22 cases (16.92%) and rat killer poisoning with 17 cases (13.07%). *Conclusion:*: Our study concludes that cow dung is the most common agent of poisoning followed by rat killer and OPC- all related to agricultural occupation with recommendation to establish a Poison Information Centre in all hospitals.

Top

Keywords

Poisoning, Cow dung, Agriculture, Mental vulnerability, Pesticide act, Rat killer poisoning.

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- **Author(s):** Karthikeyan K.; Sriandaal V.; Tamilarasan M.

- **Abstract:** 0Introduction: Depression is one of the most common psychiatric disorders worldwide, with the elderly population being the most vulnerable group. As a result of changing lifestyle & increase in nuclear families, elderly people lose their support & importance in their own family. They are often neglected, leading to loneliness & depression. It is commonly seen in the rural population. Objective: To estimate the prevalence of depression among elderly in the rural field practice area of DSMCH and to assess the socio-economic factors influencing the depression among the study population. Materials and Method: A community based cross-sectional study was conducted among 400 elderly people aged 60 years and above in the rural field practice area of Dhanalakshmi Srinivasan medical college and hospital, Perambalur district, Tamilnadu. The study subjects were contacted through household visits for data collection. The study was conducted for a period of 3 months (April 2017 to July 2017) using a pretested semi-structured proforma. The collected data was analyzed using SPSS software trial version. A p-value of <0.05 was considered statistically significant. Result: The prevalence of depression among the study subjects was 56%. A statistically significant association was found between the prevalence of depression and the elderly who were aged ≥70 years (p value = 0.0015), females (p value = 0.0048), illiterates (p value = 0.0071), class V socio economic status (p value <0.0001), living alone (p value = 0.0205), widows & separated family (p value = 0.0117%), economically dependent (p value <0.0001), neglected & just taken care by family members (p value <0.0001). Conclusion: The prevalence of depression was found to be higher in our rural population and many socioeconomic factors influence the depression among them. Health policy makers should take necessary steps to include a mental health programme for the elderly within the purview of the primary health care.

Clinical Profile and Role of Haematological Parameters in the Prognosis of Dengue Fever Patients Admitted in a Tertiary Hospital

Virgin Joena[1], Ananda Xavier Pragasam R[2]

ABSTRACT

Introduction: Even after the discovery of vaccines for dengue fever, it remains a major public health problem in developing tropical and subtropical countries, especially in India. The dengue fever has a varied clinical spectrum ranging from a mild headache to severe organ impairment or bleeding, depending on the virulence and susceptibility of the individual. The current study investigated the clinical profile of laboratory-confirmed dengue patients. A secondary objective was to find the role of haematological parameters in prognosis.

Material and Methods: This was a retrospective study conducted in a tertiary care hospital at Madurai following a dengue fever outbreak between August 2017 to November 2017 among laboratory-confirmed dengue patients older than 16 years. All the relevant clinical and laboratory investigation details of the patients were obtained from the medical records of the hospital.

Results: Fever was present in all the cases with an average duration of 4.86 ± 1.59 days followed by myalgia (57.39%), vomiting (46.96%), headache (30.43%) and abdominal pain (20%). Bleeding and hepatic complication was presented by 22.16% and 50.43%. The mean platelet recovery duration was 8.42 ± 1.74 days. A strong positive correlation between day of recovery (increasing trend of platelet) from the onset of fever and WBC recovery (r_s value: 0.0.713, P value: <0.001) was observed.

Conclusion: Dengue fever patients have varied clinical features varying from fever to severe hepatic complication. For assessing the prognosis of dengue fever, along with the continuous monitoring of clinical profile and platelet count, evaluation of WBC recovery is also recommended.

Keywords: Dengue Fever, Thrombocytopenia, Leukopenia.

INTRODUCTION

Dengue fever (DF), a vector-borne disease caused by dengue virus (DENV) infection has increased gradually over the past 10 years in India.[1] World Health Organisation has reported that around 390 million dengue infections occur per year (95% credible interval 284–528 million), of which 96 million (67–136 million) manifest clinically (with any severity of disease).[2] India is one of the seven identified countries in the South-East Asia region regularly reporting the incidence of dengue fever outbreaks and may soon transform into a major niche for dengue infection in the near future.[3]

Dengue fever has a wide clinical spectrum. This ranges from asymptomatic disease to undifferentiated fever (or viral syndromes), classical dengue fever (DF), dengue haemorrhagic fever (DHF), or dengue shock syndrome (DSS) and expanded dengue syndrome (EDS).[4] This is often characterised by high fever, headache, myalgia, body ache, vomiting, joint pain, transient rash and mild bleeding manifestations such as petechiae, ecchymosis at pressure sites and bleeding from venipunctures.[5] In the advanced severe dengue stage, patients may present with ascites or pleural effusion with or without respiratory distress, severe bleeding, and/or severe organ impairment.[2] The risk of severe bleeding in dengue is much higher with a secondary infection and is seen in about 2–4% of cases having secondary infection.[6,7] Atypical presentations are also encountered with acute liver failure, encephalopathy with seizures, renal dysfunction, lower gastrointestinal bleeding.[8]

During the course of dengue, the peripheral blood parameters changes. DF is characterised by leucopenia (White Blood Cells (WBC) < 5000 cells/mm^3), thrombocytopenia (< 150,000 cells/mm^3), rising haematocrit (5–10%) and there can be evidence of plasma leakage.[9] The platelets usually drop to below 100,000/mm3 in the febrile phase or around defervescence and may remain low for the first few days of recovery.[10] One study has observed that there is a progressive decline in white cell counts with sudden platelet drop which precedes plasma leakage and hence it could be the earliest prognosticator of severe dengue.[11] Leucopenia and the duration for recovery from it during dengue infection should be considered seriously since it increases one's susceptibility to various infection.

Most of the dengue cases are either underreported or misclassified,[2] or reported in an advanced stage. The most common reason being an underestimation of the clinical profile. Hence it is important to monitor the clinical profile of dengue fever properly. The present study aimed at presenting the clinical profile of laboratory-confirmed Dengue patients in a tertiary care hospital at Madurai. A secondary objective was to find the role of haematological parameters in prognosis.

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MATERIAL AND METHODS

This was a retrospective study done in tertiary care hospital at Madurai on patients suffering from dengue fever during an outbreak of the disease in August 2017 to November 2017.

Inclusion criteria

Patients admitted with the clinical suspicion of dengue fever and with NS1 antigen and IgM antibody positive for DF

Exclusion Criteria

Patients with fever positive due to other infections.
Patients who less than 16 years.

Study tools

Data was collected in a structured perform, and all the relevant clinical and laboratory investigation details of the patients were obtained from the medical records of the hospital.

Ethical considerations

Informed written consent in the mother tongue of the participants was obtained from the respondents before recruitment in the study. Confidentiality of the respondents was maintained. Respondents were given the option of quitting from the study if so desired by them. No element of compulsion was exerted.

STATISTICAL ANALYSIS

Data were collected in a structured perform, and all the relevant clinical and laboratory investigation details of the patients were obtained from the medical records of the hospital.

RESULTS

A total of 155 patients with a mean age of 30.53 ± 12.75 years with diagnosed DF constituted the study population. Equal male, the female proportion was observed. (Table 1)
The prevalence of secondary dengue infection was 53.3%. Fever was the presenting complaint of all patients (100%), followed by myalgia (57.39%), vomiting (46.96%) and headache (30.43%). Half of the study population has (50.43%) had a hepatic complication. Only 1 (0.8%) patient had a shock. Twenty-nine (25.22%) patients required a blood transfusion. (Table 2)
The fever lasted for an average of 4.86 ± 1.59 days, and DF patients took 8.42 ± 1.74 days (mean ± SD) for recovery from the onset of fever. The mean number of units of platelets transfused was 1.03 ± 1.97. The platelet level started declining at 4.95 ± 1.4(mean ± SD) from the onset of fever. (Table 3)
There was a strong positive correlation between days needed for recovery (increasing trend of platelet) from the onset of fever and WBC recovery (Rs value: 0.0.713, P value: <0.001) (Table 4 and figure 1)
The mean days for recovery from the onset of fever and mean WBC recovery days do not significantly differ (p value= 0.050; p value=0.367) with receiving a blood transfusion or not. However, a significantly a greater number of days (p value <0.05) was needed for MPV recovery among patients receiving blood transfusion compared to not receiving a blood transfusion. (Table 5)

Parameter	Summary
Age (Mean ± SD)	30.53 ± 12.75
Age group	
up to 20	28 (24.35%)
21 to 30	38 (33.04%)
31 to 40	29 (25.22%)
41 to 50	11 (9.57%)
51 to 60	6 (5.22%)
61 and above	3 (2.61%)
Gender	
Male	57 (49.57%)
Female	58 (50.43%)

Table-1: Baseline characteristics and clinical presentation (N=115)

Parameter	n (%)
Primary	49 (46.67%)
Secondary	56 (53.33%)
Symptoms	
Fever	115 (100%)
Myalgia	66 (57.39%)
Vomiting	54 (46.96%)
Headache	35 (30.43%)
Pain abdomen	23 (20.00%)
Oliguria	6 (5.2%)
Giddiness	1 (0.87%)
Diarrhoea	1 (0.87%)
Signs	
Bleeding	26 (22.61%)
Complications	
Hepatic	58 (50.43%)
Shock	1 (0.87%)
Received Blood transfusion	
Yes	29 (25.22%)
No	86 974.78%)

Table-2: Clinical presentation of the dengue in the study population

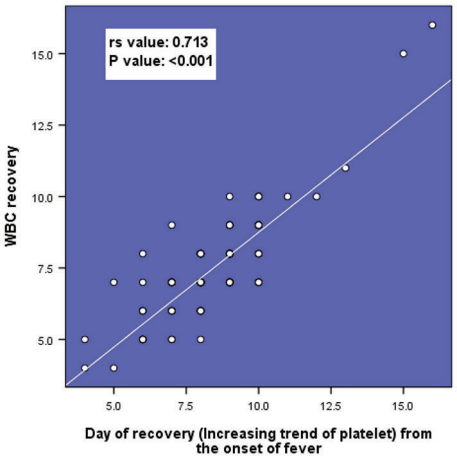

Figure-1: Scatterplot diagram of the correlation between day of recovery (increasing trend of platelet) from the onset of fever and WBC recovery

Parameter	Mean ± SD	Minimum	Maximum
No. of days of requiring IVF	0.44 ± 0.85	0	4
No. of unit's platelet transfused	1.03 ± 1.97	0	10
Day of fever requiring platelet transfusion	1.8 ± 2.95	0	10
Day of fever when platelet start falling	4.95 ± 1.4	0	8
No. of days the patient had a fever	4.86 ± 1.59	0	9
Day of recovery (Increasing trend of platelet) from the onset of fever	8.42 ± 1.74	4	16
Day of Fever when Liver Involvement	5.16 ± 1.31	3	9
WBC Recovery	7.48 ± 1.69	4	16
MPV Recovery	7.62 ± 1.42	3	12

Table-3: Summary of treatment and recovery in dengue fever patients (N=115)

Parameter	Spearman rank correlation	P value
WBC recovery	0.713	<0.001

Table-4: Correlation between the day of recovery (increasing trend of platelet) from the onset of fever and WBC recovery (N=115)

Parameter	Blood transfusion		P value
	Yes (N=29) (Mean ±SD)	No (N=86) (Mean ±SD)	
Day of recovery (Increasing trend of platelet) from the onset of fever	8.97 ± 1.5	8.23 ± 1.79	0.050
WBC recovery	7.72 ± 1.36	7.4 ± 1.78	0.367
MPV recovery	8.21 ± 1.57	7.41 ± 1.31	0.009

Table-5: Comparison of mean CBC parameters between the blood day of transfusion group (N=115)

DISCUSSION

Dengue fever is a major public health problem causing significant morbidity and mortality in the general population, especially in tropical and subtropical countries.[12] The clinical profile of patients with DF varies from mild fever to severe organ impairment and blood loss. We evaluated the clinical profile of patients with dengue fever admitted to a tertiary hospital in Madurai, India.

In the present acute infection was present in 46.67 % and secondary infection in 53.3%. Primary dengue infection was defined as an acute infection, as indicated by qualitative detection of NS1 antigen, and IgM or HI antibodies or RT-PCR positivity and absence of IgG antibodies against dengue virus.[13]

Secondary dengue causes more severe disease than the primary.[14] Secondary dengue infection is indicated by NS1 Ag positive with IgM + IgG positive. The prevalence of secondary dengue infection varied in different studies. Two studies by Sidique O et al[15] and Changal K et al[14] reported the prevalence of secondary dengue infection as 68.4 % and 66.7% respectively, which was higher compared to our study results. However, Kumar et al[16] reported the prevalence of secondary dengue infection as 50%. According to a meta-analysis by Ganesh Kumar P et al[13] of DF infection in India, the overall proportion of secondary dengue infection among laboratory-confirmed patients was 42.9% (95%CI: 33.7–52.6).

The clinical profile of dengue revealed that fever was the most common presenting symptom (100%) with an average duration of 4.86 ± 1.59 days. Many studies have reported fever as the foremost complaint of patients with dengue fever.[3,4,12,17-21] Other common presenting symptoms present were myalgia (57.39%), vomiting (46.96%) and headache (30.43%). This was in agreement with the study done by Agarwal VK et al[17], were the most common symptoms were fever (100%), followed by myalgia in 88%, chills in 74.5% nausea/ vomiting 65.5% and headache in 38% of patients. In the study by Laul A et al[4], headache was the chief complaint about 87% of patients, and 41% had typical retro-orbital pain. Mandal S. et al[22] reported headache in 62.16% of the patients. Matta L et al[21] reported the most common symptoms were fever (287;100%) followed by myalgia (223;78%), and headache (183:64%) similar to our study. The haemorrhagic manifestation was presentedby26(22.16%) patients. This was far high compared to the study done by Rajesh et al[19], were only 5% of the patients presented with bleeding. Twenty-four per cent of the patients presented bleeding in the study by Laul A et al.[4] Bleeding is a known manifestation of dengue fever, due to thrombocytopenia. The various reasons for thrombocytopenia include bone marrow suppression, immune-mediated clearance and spontaneous aggregation of platelets to virus-infected endothelium.[19]

The hepatic complication was found in half of the study population (50.43%). Agarwal VK et al[17] documented hepatic tenderness in 35.9% of patients. Twenty-five percentage had hepatomegaly in the study by Laul A et al.[4] DF has a profound effect on multiple organ systems, the commonest being the liver.[23] It is the major site for NS1 protein accumulation,and preincubation of hepatocytes with soluble NS1 enhances subsequent infection by a homologous strain of DENV.[24]

The average number of days required for the fever to subside was 4.86 ± 1.59 day (mean ±SD). However, 8.42 ± 1.74 days (mean ±SD) was required for the recovery to normal platelet level. This can be explained based on thrombopoiesis. The mean days for recovery from the onset of fever and mean

WBC recovery days do not significantly differ (p value= 0.050; p value=0.367) with receiving a blood transfusion or not. However, there was a strong positive correlation between day of recovery (increasing trend of platelet) from the onset of fever and WBC recovery (Rs value: 0.0.713, P value: <0.001). Leukopenia is usually observed in the course of dengue fever.[9,25] It is caused by virus-induced destruction or inhibition of myeloid progenitor cells.[26] Increased duration for the WBC to recover increase one's susceptibility to various infections. In the study by Joshi AA et al[27], 47 cases of leucopenia (36%) out of 132 total cases were associated with thrombocytopenia. They reported that leucopenia is an early marker of dengue and association of leucopenia with thrombocytopenia suggests that it could be one of the prognosticators of severe dengue.[27] Verdeal JC et al[11] reported that leukopenia could be a marker of severe dengue. This points to the importance of evaluating WBC count also in the prognosis of dengue fever and should be explored in further research.

A significant number of days (p value <0.05) was needed for MPV recovery among patients receiving blood transfusion compared to not receiving a blood transfusion. This can be explained by the fact that blood transfusion is usually done in patients with severe thrombocytopenia or hemodynamically unstable patients and therefore requires more time for recovery.

There were several limitations to the current study. First of all, due to the lack of data, we could not assess the baseline and post-treatment value of various haematological parameters. However, we considered the standard value to assess the days required for recovery. Secondly, our study did not assess the relationship between baseline platelet level with recovery duration or requirement of blood transfusion. This might have biased our study results. Even though our study raised the need for monitoring WBC count in DF patients, we couldn't assess the relationship of WBC recovery with the severity of DF, due to the retrospective nature of the study.

CONCLUSION

Dengue fever patients present with varied clinical features varying from fever to severe hepatic complication in the current study. Continuous monitoring of clinical profile along with haematological parameters is recommended

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Original Research Article

Relationship between self-rated health status and physical activity in obese South Indian patients

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ABSTRACT

Background: Regular physical activity can improve people's overall health and reduce various risks for morbidity and mortality due to a sedentary lifestyle. Although the evidence linking obesity with many chronic diseases is well established, the relationship with self-rated health is not clear. The study aimed to assess the relationship between physical activity and self-rated health and how it is related to obesity.
Methods: The cross-sectional study included 132 individuals above18 years, of both genders, with BMI above 25kg/m^2. Data was collected using a structured proforma which included apart from demographic parameters, anthropometry parameters, self-reported physical activity, health status and stress levels of the subjects. Chi-square test/Fisher's exact test was used to assess the association between BMI, physical activity and self-rated health.
Results: A total of 132 subjects were included with a mean age of 48.44±11.23 years, with an almost equal proportion of males and females. The mean of BMI was 29.54±3.99. Most of them reported having normal physical activity (61.36%) with only 3% of them having high physical activity. The self-rated health of the subjects revealed 45.45% of them is having fair health and 43.18% of them having poor health. The mean a number of hours spent by sitting/sedentary activity in a week were 32.32±21.09.
Conclusions: The study findings revealed that the irrespective of the degree of physical activity both overweight and obese subjects rated their health fair to poor.

Keywords: Obesity, Physical activity, Self-rated health

INTRODUCTION

Self-evaluation of general health status has been associated with actual health in that what people report about their health has been shown to predict mortality.[1] Self-rated health (SRH) is a paradigm based on an individual's perception and assessment of health. Recently it is often used the gauge in health research and has been found to be a reliable and precise indicator of physical and mental functioning.[2-5] Additionally, SRH has also been shown to be a predictor of health care utilization.[6]

Self-rated health (SRH) as a single survey question developed by the world health organization (WHO) has been validated as a tool to predict mortality in populations with and without cardiovascular diseases and functional ability.[1,6-9] Self-rating of health is a broad summary measure of different domains of health that includes psychosocial domain. Self-rated health has been identified as an important indicator of health that is associated with a wide range of outcomes, from well-being to health service utilization and even overall mortality in populations.[10-12]

It is well established that regularly engaging in physical activity has physical health benefits such as improved cardiovascular and metabolic health, weight status, bone density and psychological wellbeing of individuals.[13] According to WHO, insufficient physical activity is the fourth leading cause of non-communicable diseases, being responsible for 5.5% of all deaths.

The prevalence of overweight and obesity is increasing worldwide.[14] Epidemiologic studies have identified high body- mass index (BMI, the weight in kilograms divided by the square of the height in meters) as a risk factor for an expanding set of chronic diseases, including cardiovascular disease, diabetes mellitus, chronic kidney disease,16 many cancers, and an array of musculoskeletal disorders.[15-17]

Various studies have established that being overweight or obese is a risk factor for poor SRH.[18,19] Obesity is also related to low self-esteem and poor peer relationships.[20] Although the relationship between self-rated health (SRH) and physical health is well documented in developed countries, very few studies have analyzed this association in the developing world particularly in India.

International studies analyzing the relation between overweight/obesity and SRH show that overweight and especially obese people report poor SRH more often than those of normal weight.[21,22] However, little attention has been paid to whether the relation between overweight/obesity and SRH varies between different population groups. SRH is a broad summary measure of different domains of health that include the psychosocial domain. Hence the present study aimed to assess the association between self-rated health and physical activity among the south Indian population.

METHODS

The study was conducted in the department of general medicine, Velammal medical college hospital and research institute. The study was a cross-sectional observational study of the adult population attending the study setting for the screening master health check-up for 30 days period between May 2018 to June 2018. The study had included people aged above 18 years, of both genders, with BMI above 25kg/m^2. People with a known history of CAD, prior history of stroke, severe degrees of COPD, people with a physical disability affecting the physical activity or any other disease condition restricting their ability to do physical activity were excluded from the study.

All the study participants were recruited by convenient sampling. The data was collected using a structured proforma, which has assessed the participant's demographic parameters, anthropometry parameters, self-reported physical activity, health status and stress levels.

The data was analyzed by using IBM SPSS statistical software version 21. Descriptive analysis of quantitative variables was done by mean and standard deviation; categorical variables were done by frequency and proportion. The association between the self-reported health status physical activity was done by cross tabulation and comparison of proportions, using chi square test/Fisher's exact test. P value <0.05 was considered statistically significant.

RESULTS

The mean age was 48.44±11.23 in the study population. Among the study population, 6 (4.55%) participants were aged up to 30 years, 26 (19.70%) participants were aged between 31 to 40 years, 47 (35.61%) participants were aged between 41 to 50 years, 32 (24.24%) participants were aged between 51 to 60 years and 21 (15.91%) participants were aged >61 years. Among the study population, 65 (49.24%) participants were male remaining 67 (50.76%) participants were female. Among the study population, 4 (3.03%) participants had high physical activity, 18 (13.64%) participants had low physical activity, 2 (1.52%) participants had low/medium physical activity, 27 (20.45%) participants had medium physical activity and 81(61.36%) participants had normal physical activity (Table 1).

Table 1: Descriptive analysis of baseline parameter in the study population (N=132).

Baseline parameter	Summary
Age (Mean ±SD)	48.44±11.23
Age group	
Up to 30 years	6 (4.55%)
31 to 40 years	26 (19.70%)
41 to 50 years	47 (35.61%)
51 to 60 years	32 (24.24%)
61 years and above	21 (15.91%)
BMI (Mean ±SD)	29.54±3.99
Gender N (%)	
Male	65 (49.24%)
Female	67 (50.76%)
Physical activity N (%)	
High	4 (3.03%)
Low	18 (13.64%)
Low/medium	2 (1.52%)
Medium	27 (20.45%)
Normal	81 (61.36%)

Among the people who feel stress in our daily life, 19 (14.39%) participants had little stress, 38 (28.79%) participants had moderate stress, 18 (13.64%) participants had quite a lot stress and 5 (3.79%) participants had extreme stress. Among the study population, 5 (3.79%) participants had very poor health, 57 (43.18%) participants had poor health, 60 (45.45%) participants had fair, 8 (6.06%) participants had good health and 2

(1.52%) participants had very good health. The mean number of hours spent by sitting/sedentary activity in a week was 32.32±21.09 in the study population (Table 2).

Table 3 describes the relationship between physical activity with SRH and BMI. Among the 20 people who had low medium physical activity and low 19 (95%) participants had bad health status and 1 (5%) participant had good health status. Among the 81 people who had normal physical activity 77 (95.06%) participants had bad health status and 4 (4.93%) participants had good health status. Among the 31 people who had high and medium physical activity, all of them 31 (100%) participants had bad health status.

Among the 20 people who had low medium physical activity and low, 12 (60%) participants had over weight and 8 (40%) participant had obese. Among the 81 people who had normal physical activity 46 (56.79%) participants had over weight and 35 (43.20%) participants had obese. Among the 31 people who had high and medium physical activity, 19 (61.29%) participants had over weight and 12 (38.70%) participants had obese.

The difference in the proportion of BMI category across physical activity score was statistically not significant (P value 0.899) (Table 3).

Table 2: Descriptive analysis of self-reported health status in the study population (N=132).

Questionnaire	Summary
Do you feel stress in your daily life N (%)	
No	52 (39.39%)
Little	19 (14.39%)
Moderate	38 (28.79%)
Quite a lot	18 (13.64%)
Extreme	5 (3.79%)
How do you feel your present health is N (%)	
Very poor	5 (3.79%)
Poor	57 (43.18%)
Fair	60 (45.45%)
Good	8 (6.06%)
Very good	2 (1.52%)
Number of hours spent by sitting/sedentary activity in a week (Mean±SD)	32.32 ± 21.09

Table 3: Comparison of physical activity score between self-rated health status, body mass index (BMI) category (N=132).

Parameter	Physical activity score			Chi square	P value
	Low medium and low (N=20)	Normal (N=81)	High and medium (N=31)		
Self-rated health status					
Bad	19 (95%)	77 (95.06%)	31 (100%)	**	**
Good	1 (5%)	4 (4.93%)	0 (0%)		
BMI category					
Over weight	12 (60%)	46 (56.79%)	19 (61.29%)	0.214	0.899
Obese	8 (40%)	35 (43.20%)	12 (38.70%)		

**No statistical test was performed due to 0 subjects in the cells.

DISCUSSION

Self-rated health (SRH), generally captured by a single item inviting respondents to provide an overall assessment of their health using some form of a five-point scale, is currently one of the most commonly used health measures in surveys to assess the health status of adult populations in developed countries.[11,12]

SRH reflects a complex process of internalized reckoning that takes into account both disease exposure experiences and knowledge of disease causes and consequences. Self-rating of health is a broad summary measure of different domains of health that includes the psychosocial domain. The mean age of the study subjects was 48.44±11.23 years with 35.61% of them aged 41-50 years and 40% of them over 50 years. Research suggests that age is one of the most important socio-demographic factors affecting both what possible components of health a person considers and how they are taken into account in SRH.[23] Thus, according to social comparison theory, older people have lower expectations regarding health than do younger people, and these expectations can lead to more positive assessments among the elderly and more negative assessments in the young.[23,24]

Sex is another key variable that can modify the relationship between SRH and physical and mental health. Compared to men, women have been found to be less "stoic" and thus more likely to take less serious illnesses into account when assessing their health.[25] Case and Paxson C et al, showed that, even if women more often report worse health than men, women and men with the same chronic conditions have the same SRH.[26]

Among the study population male (49.24%) and female (50.76%) distribution was almost equal.

The mean BMI of the study subjects was 29.54±3.99 belonging to the overweight or obese categories. In comparison, a German study reported overweight in 10.2% of adolescents and obesity in 7.6% of them. Overweight and obese adolescents have, for example, reduced health-related quality of life, more mental health problems, and lower self-esteem than those of normal weight.

About 45.45% of the study population rated their health as fair while a considerable proportion of them (43.18%) felt they had poor health. Comparatively, Krause L et al, in their study on obese adolescents noted good SRH in half of the subjects (49.4%), fair SRH in 11% of them while only 0.4% of them reported poor SRH.[27] Although most studies suggest that there is a strong association between obesity and ill health, a few investigations have found a negative association between obesity and significant psychopathology.[28] Some investigators have suggested that the rationale behind some studies lacking a positive relationship between obesity and psychological health is due to biases and negative attitudes toward obese persons inherent in the study design.[29]

The mean a number of hours spent by sitting/sedentary activity in a week were 32.32±21.09 in the study population. Comparatively, Granger E et al, studying 12,770 European adolescents noted that 54.9% of them were sedentary for <4 hours/day while 39.3% of them were sedentary for >4 hours/day.[30]

Association between SRH with physical activity showed most almost all subjects in all the three categories of (100% in high and medium) physical activity reported bad health. Contrastingly Abu-Omar K et al, in their study on 16,230 individuals above 15 years concluded that there was a mild positive relationship between physical activity and self-rated health.[31] However, in most nations sufficient levels of physical activity were not positively related to self-rated health which might be explained by difficulties in assessing moderate forms of physical activity, and also differences of the context (at home, for leisure, at work, for transportation) where physical activity takes place.

BMI and its association with physical activity comparison showed a majority of them being overweight in all the three categories of physical activity, while a relatively lesser number of them (38.7%) being obese in high and medium physical activity and the difference was not statistically significant. Comparatively Young DR et al, reported that among overweight subjects, 24.6% of them belonged to moderate-to-vigorous physical activity (MVPA) and 20.1% of them in moderate physical activity (MPA), while those who were obese, 21.8% were in MVPA group and 17.3% in MPA group.[32]

Self-reported health status is known to be a strong and independent predictor of future health problems and mortality.[5] Accordingly, it is valuable to identify the modifiable risk factors that have an impact on health status. In this context, it is of concern that only 20.45% of the overall study subjects achieved the WHO physical activity recommendations of 60 minutes moderate or vigorous exercise per day. These findings highlight the necessity of increasing engagement in physical activity amongst adolescents and adults in South India.

In low-income and middle-income countries, the use of self-reported measures of health statuses, like the SRH item and other health status measures (diabetes, cancer, etc.), is viewed with scepticism as the respondents may fail to perceive illness or health deficits because of lack of awareness.[33] However, Cullati S et al in their construct validity study of SRH reliability in India concluded that the single SRH item is a reliable indicator of general health in the population of India.[34] Moreover, Falk H et al, supported the use of SRH as a simple measure in survey settings to identify vulnerable groups and evaluate targeted health interventions in resource-scares settings.[35]

A major limitation of this study is that as the study is cross-sectional, no causality can be established between physical activity and health status. There are a number of possible hypotheses to explain the relationship between physical activity and health status. There are two main physiological hypotheses. The first of these states the beneficial effects of increased endorphin release on pain reduction and therefore on health status following physical activity, and the second describes the role of physical activity in affecting the monoamine release in the brain, which affects neurotransmission patterns and results in improved health status.[36] The psychological hypothesis describes the beneficial effects of physical activity on self-concept, which in turn reduces anxiety and depression and increases resilience, thus improving health status.[37]

The WHO recommends that adults aged 18-64 should do at least 150 minutes of moderate-intensity aerobic physical activity throughout the week, Aerobic activity should be performed in bouts of at least 10 minutes duration and Muscle-strengthening activities should be done involving major muscle groups on 2 or more days a week. The updated recommendations by the American college of sports medicine (ACSM) and the American heart association (AHA) the promotion of physical activity in older adults should emphasise moderate-intensity aerobic activity, muscle-strengthening activity, activities that maintain or increase flexibility, reducing sedentary behavior, and risk management.[38]

CONCLUSION

The study findings revealed that the physical activity among the obese subjects was normal and their self-rated health was generally fair to poor. Present study findings

can have implications for public health interventions. Given the relationship between self-rated health with BMI, these measures could be a better option as the indicators to improve the self-perceptions of health among specific social and economic subgroups of the South Indian population, hence maximize the effectiveness of public health interventions towards obesity, diabetes and other metabolic diseases.

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Original Research Article

Factors affecting carotid intimal medial thickness in patients with rheumatoid arthritis, an analytical cross-sectional study

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ABSTRACT

Background: IMT assessment as a non-invasive imaging test is quite widely used especially among RA patients, the clinical applications of using such knowledge is scarce, hence study was conducted to compare the carotid artery intima-media thickness (CIMT) in patients with rheumatoid arthritis (RA) with healthy controls also to study the correlation between duration of rheumatoid arthritis, the activity of rheumatoid arthritis and other factors influencing (CIMT).
Methods: In analytical cross-sectional study, of 80 participants of RA and 40 healthy controls, "DAS28" was used to assess disease activity. Carotid intima-media thickness assessed using carotid ultrasonography.
Results: Mean age of the cases and controls was 43.9 and 44.38 years. Subjects with duration of disease <2 years, to 5 years and >5 years were 35%, 45% and 20%. The mean carotid intima-media thickness was 5.61mm in controls, and CIMT was 6.11mm in people below 2 years and 7.08 mm in people between 2 to 5 years and 8.00mm in people above 5 years which was statistically significant. The mean carotid intima-media thickness was 5.61mm controls and 6.86mm in people with low, 7.00mm in people with moderate and 6.95mm in people with high disease activity, which was statistically significant.
Conclusions: Study findings revealed risk of increase in carotid intima-media thickness higher among RA patients in the later stages and can increase the patients' susceptibility to cardiovascular events. The factors showing strong association with intimal medial thickness were the age and symptoms duration.

Keywords: CIMT, DAS28, IMT, RA

INTRODUCTION

Atherosclerosis is one of the leading causes of death across the globe not only in the developed but even in developing countries as well. Growing evidence has been consistently showing that it involves a chronic inflammatory process of the arterial wall set in a backdrop of dyslipidaemia.[1,2] The pathophysiology of atherosclerosis has its roots in early childhood, which usually is asymptomatic until later in life. The major risk factors of atherosclerosis and thereby coronary heart disease (CHD) are unhealthy lifestyles, clinical risk factors, psychological factors and public health transitions. ageing, urbanization and enhanced prosperity seem to be the underlying crucial drivers.[3] The impact of CHD has been huge in Asian countries with a mortality of 103 to 336 per 100, 000 adult populations.[3]

Asymptomatic thickening of the carotid artery is the strongest prognosticator of cardiovascular (CV) morbidity and mortality in general population. Carotid intima-media thickness (cIMT) displays structural

changes in the arterial wall even in initial subclinical phases of atherosclerosis. Mounting evidence suggests cIMT and CHD are directly related and that the former can predict events like myocardial infarction (MI) or stroke in apparently healthy individuals.[4] Blood pressure, altered lipid levels, increased body mass index among others present during childhood have been shown to increase IMT in adulthood by some prospective cohort studies.[5-7]

Such comorbidities cumulatively called metabolic syndrome have been frequently found in patients with rheumatoid arthritis (RA), a systemic autoimmune joint disorder that affects synovial joints with resultant chronic pain, bone erosions and progressive disability.[8,9] Cardiac events like angina, MI or cerebrovascular accidents are significantly higher among patients with RA than the general population and that the heightened CV morbidity and mortality among such groups could not be explained by traditional CV risk factors alone.[10,11]

Growing interest recently has pointed at a relationship between RA and CV risk markers like cIMT and carotid plaque formation, in particular by a couple of case-control studies that showed augmented atherosclerosis in RA patients.[10,11] A meta-analysis by Tyrrell PN et al, and van Sijl et al.[12,13] found those with RA showed a significantly higher IMT in contrast to the controls. However, some studies have debated such an interplay.[14,15] Though, IMT assessment as a non-invasive imaging test is quite widely used especially among RA patients, the clinical applications of using such knowledge is scarce. Hence the present study intends to explore the factors influencing cIMT in RA patients.[16,17] To compare the carotid artery intima-media thickness (CIMT) in patients with rheumatoid arthritis (RA) with healthy controls. To study the correlation between duration of rheumatoid arthritis, the activity of rheumatoid arthritis. Carotid intima media thickness (CIMT) To analyse the factors influencing carotid intima media thickness (CIMT) among rheumatoid arthritis patients.

METHODS

The study was an analytical cross-sectional study, conducted in the rheumatology outpatient clinic, Velammal Medical College and Research Institute, Madurai, Tamil Nadu, between January to July 2018.The study population was patients attending the study setting who was diagnosed with rheumatoid arthritis (diagnosed according to 2010 American College of rheumatology-European league against rheumatism (ACR-EULAR) criteria) and their age and gender-matched healthy controls.

Exclusion criteria

People who are having the following known risk factors for atherosclerosis were excluded from the study.

- Hypertension (BP >140/90mmHg) or the use of antihypertensive medications, hypercholesterolemia (Total cholesterol>240mg/dl, LDL>160mg/dl, triglycerides >200mg/dl) or use of lipid lowering medication, diabetes mellitus (diagnosed according to WHO criteria) or use of anti-diabetic medication, history of coronary artery disease, history of cerebrovascular accidents (CVA) or any other vascular event, known cases of hepatic or renal impairment.

Considering the mean difference in intimal-medial thickness to be detected as 0.69 with a standard deviation of 0.45 with 5% alpha error and 80% power of the study, the required sample size would be about 36 subjects in each group. To account for about 10%non-participantiopnrahe, it was decided to include 40 subjects in each of the study groups.

The cases who were attending the clinic, who satisfied, inclusion and exclusion criteria were selected consecutively into the study till the sample size is reached; hence no sampling was done. The controls were selected from among the people who were attending a local health-check program at local health-check program at Velammal Medical College Hospital Madurai, by convenient sampling.

The RA patients included in the study as subjects were divided into three groups based on the duration of disease. These were:

All the RA patients included in the study were evaluated for their disease activity using the disease activity score "DAS28". This score is calculated by using the formula: DAS 28 = $0.56\sqrt{TJC} + 0.28\sqrt{SJC} + 0.70$ (log ESR) + 0.014 GH where, TJC: tender joint count, SJC: swollen joint count, GH: general health status as assessed by the patient on a visual analogue scale (VAS).

All the subjects including the controls were evaluated for carotid intima-media thickness by using carotid ultrasonography. Carotid ultrasonography was carried out by skilled radiologist by using grayscale ultrasonography and then followed by color flow imaging.

Carotid intima-media thickness (CIMT) was measured in common carotid artery bilaterally by examining throughout common carotid artery up to 2cm proximal to the bifurcation. CIMT measurement was taken at the site of greatest thickness, and three readings were taken from each side at different points within the region of interest. All measurements were taken in diastole, measured in phase when the lumen diameter is at its smallest and IMT at its largest. The mean value of 6 readings (3 from each side) was taken as the final CIMT for evaluation. descriptive analysis of all the variables was done using mean and standard deviation for quantitative variables, frequency and percentage or categorical variables. Disease duration and activity were considered as primary

outcome variables. Intimal-medial thickness was considered as the primary outcome variable., the mean intima-medial thickness across the study groups was compared using one-way ANOVA. Mean differences along with their 95% CI were presented. Univariate and multivariate linear regression analysis was done to analyses the factors influencing the intimal-medial thickness in the study population.

Statistical analysis

IBM SPSS was sued for statistical analysis. The results obtained were subjected to one-way ANOVA test for statistical analysis.

Another 40 healthy (age and sex-matched) subjects were taken into group 4 as controls.

RESULTS

A total of 80 participants were included in the study, out of which 40 were cases of rheumatoid arthritis for variable duration, and the remaining 40 were controls.

The mean age of the cases and controls was 43.9 and 44.38 years respectively. Both the study groups were comparable concerning age and gender. The blood sugar values, renal parameters and lipid profile parameters also were comparable among both the study groups. The minor differences between the two groups in the above-mentioned parameters were statistically not significant. The proportion of smokers (12.5% in cases Vs none in controls) and alcoholics (5% in cases Vs none in controls) was slightly higher in cases when compared to controls (Table 1).

Table 1: Comparison of baseline variables among cases and controls in the study population (N=80).

Parameter	Cases (N=40)	Controls (N=40)	P -value
Age (Mean±SD)	43.90±10.52	44.38±9.41	0.832
Male: female	2.3:1	2.3:1	1.0
Blood sugar (Mean±SD)	95.38±20.90	89.20±22.17	0.204
Blood urea (Mean±SD)	26.43±7.40	27.78±9.07	0.468
Serum creatinine (Mean±SD)	0.86±0.13	0.89±0.13	0.275
Total cholesterol (Mean±SD)	166.3±21.84	168.5±16.99	0.625
TGL(Mean±SD)	150.53±16.01	153.48±11.98	0.354
LDL (Mean±SD)	89.63±14.90	92.65±13.21	0.340
VLDL (Mean± SD)	35.73±4.70	35.03±3.59	0.457
HDL	39.15±2.91	39.28±2.59	0.840
Alcohol N (%)	5 (12.5%)	0 (0.0%)	0.021
Smoking N (%)	2 (5.0%)	0 (0.0%)	0.152

All the 40 cases of rheumatoid arthritis have shown EMS (Early Morning Stiffness) positivity.

Table 2: Descriptive analysis of disease related parameters among cases (N=40).

Parameter		Frequency	(%)
EMS		40	100.0
Deformity		37	92.5
C reactive protein		17	42.5
RA factor		31	77.5
Duration of symptoms	<2 years	14	35
	2 to 5 years	18	45
	>5 years	8	20
Disease activity	High	15	37.5
	Low	3	7.5
	Moderate	22	55

Deformity raised CRP level and raised RA factor were seen in 37 (92.5%), 17 (42.5%) and 31 (77.5%) of the patients respectively. The proportion of subjects with a duration of disease <2 years, 2 to 5 years and >5 years were 35%, 45% and 20% (Table 2).

The mean carotid intima-media thickness was 5.61mm in controls, and CIMT was 6.11mm in people below 2 years and 7.08 mm in people between 2 to 5 years (mean difference 1.47, 95% CI 0.79 to 2.16, P value <0.001) and 8.00 mm in people above 5 years (mean difference 2.39, 95% CI 1.45 to 3.33, P value <0.001), which was statistically significant. The mean carotid intima-media thickness was 5.61 mm in controls and 6.86 mm in people with low, 7.00mm (mean difference 1.13, 95% CI 2.07 to 3.06, P value 0.15) in people with moderate and 6.95mm (mean difference 1.13, 95% CI 0.061 to 2.08, P value <0.001) in people with high disease activity, which was statistically significant (Table 3).

Univariate linear regression analysis was carried out to evaluate the factors influencing the intima medial thickness in the study population. The factors which have

shown statistical significance (presence of rheumatoid arthritis, age, duration of symptoms, total count, smoking and disease activity) with p value <0.05 were included in the multivariate regression analysis (Table 4). After controlling for other variables in multivariate analysis, the factors which retained the positive association with intimal medial thickness were presence of rheumatoid arthritis (regression coefficient 1.31, 95% CI 0.86 to 1.76, P Value <0.001), age of the patient (Regression coefficient 0.04, 95% CI 0.021 to 0.058, p value <0.01) and duration of symptoms (Regression coefficient 0.04, 95% CI 0.021 to 0.058, P Value <0.001) (Table 5).

Table 3: Comparison of carotid intimal medial thickness among cases and controls (N=80).

Duration of symptom	Mean	Mean difference	P value	95% CI	
				Lower	Upper
Duration of disease					
Controls	5.61±0.458				
<2 years	6.11±1.00	0.50	0.457	0.25	1.25
2 to 5 years	7.08±1.22	1.47	<0.001	0.79	2.16
>5 years	8.00±1.41	2.39	<0.001	1.45	3.33
Grading of the disease					
Controls	5.61±0.45				
Low	6.86±1.58	1.25	<0.001	0.42	2.10
Moderate	7.00±0.86	1.139	0.157	0.27	3.06
High	6.95±1.29	1.13	<0.001	0.061	2.08

Table 4: Univariate regression analysis showing the factors influencing the intimal-medial thickness among the study population (N=80).

Parameter	Linear regression coefficient	95% CI		P-value
		Lower	Upper	
Case vs control	1.31	0.86	1.76	<0.001
Age	0.048	0.023	0.073	<0.001
Gender (baseline=male)	0.107	0.695	0.482	0.719
TC	0.016	0.003	0.030	0.017
LDL	-0.006	0.014	0.025	0.563
HDL	-0.044	0.055	0.143	0.377
Smoking (baseline=present)	-1.103	0.016	2.190	0.047
Alcohol (baseline=present)	-1.265	0.44	0.297	0.144
Duration of symptoms (baseline=controls)	0.768	0.581	0.956	<0.001
Disease activity(baseline=controls)	0.451	0.266	0.637	<0.001

Table 5: Multivariate linear regression analysis of socio-demographic factors affecting intimal medial thickness among the study population (N=80).

Parameter	Linear regression coefficient	95% CI		P-value
		Lower	Upper	
Case vs control	1.31	0.86	1.76	<0.001
Age	0.040	0.021	0.058	<0.001
TC	0.009	0.018	0.001	0.073
Smoking	-0.272	0.471	1.015	0.468
Duration of symptoms	0.736	0.483	0.988	<0.001
Disease activity	0.008	0.224	0.209	0.944

DISCUSSION

The collateral consequence of rheumatoid arthritis is that it affects the CVS, which in turn could be the main cause of death among those affected decreasing their life expectancy by 3 to 10 years.[18,19] The combined effect of CV risk factors and sequelae of RA inflammation is overtly manifested by a significant rise in carotid

atherosclerosis in patients with RA, and each may modify one another's effects.[10]

The mean carotid intima-media thickness (cIMT) significantly increased with increase in the duration of the RA among the cases (6.11mm in cases below 2 years and 8.00mm in those above 5 years of having the disease while it was 5.61mm among controls). The cIMT also varied and was higher among patients with different degrees of severity of RA (6.86mm in those with low RA and 6.95mm in those with high RA). I'm et al, and Kisiel et al, reported similar findings stating that the mean cIMT and carotid plaque thickness was higher among RA patients than in controls.[20,21]

Considerable epidemiological and clinical evidence have been showing that accelerated atherosclerosis may be one of the key aspects of RA.[2,4,22] The clinical significance of such findings can be understood when authors consider that the risk of myocardial infarction increases by up to 43% for every 0.163mm increase in cIMT.[2,12,13]

Recently numerous studies seem to the point that atherosclerosis risk is higher among those with rheumatological disorders, especially RA and systemic lupus erythematosus (SLE) due to accelerated vascular processes.[23,24] It is plausible that the inflammatory cascade and alterations in the immune response inherent to the pathogeneses of autoimmune conditions like RA and SLE may play a critical role in accelerating atherosclerosis due to increased risk of arterial wall damage and endothelial dysfunction.[25,26]

Patients with RA also have elevated C-reactive protein (CRP), a classical marker of inflammation that is often associated with CV risk.[8,20,21] This is in line with present study finding wherein 42.5% of RA patients had elevated CRP. Apart from this elevated ESR levels, which reflect cumulative inflammatory burden be independently associated with carotid plaque thickness, even suggesting a synergistic interaction with traditional CV risk factors.[20,27]

One of the limitations of present study, which is inherent to non-longitudinal studies is that the inflammation markers measured at a single point of time may fail to be associated with cIMT.[28] There are two possible explanations for this. First, the patients included in present study and others of a similar kind have a wide range of disease activity with associated inflammatory markers. Second, it is the cumulative effect of prolonged inflammation that increases the susceptibility to accelerated atherosclerosis.[28] Two studies from Japan, one by Kumeda et al, and another by Nagata-Sakural et al, confirmed that longitudinal studies assess the markers of inflammation more accurately than cross-sectional studies.[29,30] Considering the lower sample size, the role of various potential confounders, which are already proven risk factors for increasing carotid intimal medial thickness could not be evaluated. Long-term prospective studies, with higher sample size, can help us in understanding the attributable factors of carotid intimal medial thickening and related cardiovascular sequelae, after adjusting for the effect of all the proven risk factors.

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Prevalence and Profile of Non-Alcoholic Fatty Liver Disease among Adults Undergoing Master Health Checkup, A Hospital based Cross Sectional Study

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ABSTRACT

Introduction: Non-alcoholic fatty liver disease (NAFLD) has emerged as a major public health problem in recent times. It is one of the neglected conditions in developing nations like India, due to scarcity of studies on the subject. Study objective was to assess the prevalence of NAFLD among patients undergoing master health check-up in a tertiary care teaching hospital and to analyze the profile of NAFLD cases.

Material and materials: The study was a hospital based analytical cross-sectional study. Conducted in a tertiary care teaching hospital in south India. People attending the master health checkup in the study setting from June 2015 to July 2018 were included. Chi square test was used to test statistical significance.

Results: A total of 818 patients were included, out of whom 130(15.89%) had NAFLD. The proportion of grade 1, 2 and 3 fatty liver was 79.23%, 13.84% and 6.92% respectively. The difference in waist circumference and HDL values were statistically significant between male & female (P value <0.001 and 0.007 respectively). No other components of Metabolic syndrome had shown statistically significant difference between males and females. The difference in grade of NAFLD across the age group is found to be significant with a P- value of 0.035. Grade of NAFLD was not associated with any other diet or lifestyle related parameters.

Conclusions: Significant proportion of healthy subjects are affected by NAFLD, some of them with severe grades, with key gender differences in some of the factors associated with NAFLD. Patients and clinicians needs to be sensitized regarding NAFLD.

Keywords: Non-Alcoholic Fatty Liver Disease, Adults Undergoing Master Health Checkup

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is histopathologically characterized by fatty infiltration of liver parenchyma, resembling alcoholic liver diseases, without a history of significant alcohol consumption or other established liver disease.[1] Some researchers have proposed around 5% infiltration of liver parenchyma may be considered as fatty infiltration.[2] The spectrum may range from simple fatty infiltration to associated inflammatory changes, presenting as NASH (Non Alcoholic Steato Hepatitis) to fibrosis of hepatic tissue, frank cirrhosis and even hepatocellular carcinoma (HCC) in minority of cases.[3] It can also lead to plethora of thrombotic, vascular complications.[4] It is associated with wide range of other metabolic conditions, more importantly metabolic syndrome, diabetes mellitus and obesity.[5-7]

Even though, it has been perceived as a major public health problem of developed and western world, it has emerged as a major public health problem in Asian countries, including India.[8] The reported prevalence of NAFLD was ranging between 20 to 30%, with about 2 to 3% of them progressing to NASH in western countries.[9] But the exact large-scale prevalence studies are scarce on Indian population. Among the general population, the reported prevalence varied from 9% in rural populations to 32% in urban populations.[10] As per SPRINT study, which was one of the large scale multicentric study from 101 cities across India, the overall prevalence of NAFLD was 56.5% among T2DM patients aged between 25 to 84 years. The prevalence was lowest at 44.1% in western India to as high as 72.4% in northern states.[11,12] Considering the scarcity of studies documenting the profile of NAFLD cases and the magnitude heterogenicity within the country, it is highly essential to conduct studies on local ethnic population groups. These studies will provide more relevant data about the profile of NAFLD in local population to the clinical practitioners and aid in effective screening and management of the same. The current study was conducted with the objective of documenting the prevalence of NAFLD among patients undergoing master health checkup in a tertiary teaching hospital in south India and to analyze the profile of NAFLD cases.

MATERIAL AND METHODS

The study was a hospital based analytical cross-sectional study which included, people attending the master health checkup in the study setting. The cases included were people satisfying the inclusion criteria from June 2015 to July 2018

Sample size: A total of 818 patients attending master health checkup were included in the study by universal sampling.

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Inclusion criteria:

- Adults aged above 20 years
- Both male and female
- Undergoing master health check up

Exclusion criteria:

- Alcoholic patients.
- Study procedure

All the patients were evaluated by clinical history, anthropometric assessment, including Height, Weight, Waist circumference. BMI and Waist hip ratio were calculated. Blood sample was collected from the patient and it was sent to the laboratory for fasting Lipid profile, fasting blood glucose, post prandial blood glucose.

Metabolic syndrome was defined as presence of 3 or more of the following 5 components of (1) fasting glucose >100 mg/dL; (2) central obesity (waist circumference>102 cm [men] and >88 cm [women]); (3) arterial pressure >130/85 mm Hg or pharmacologically treated; (4) triglyceride levels 150 mg/dL or use of fibrates; and (5) HDL-cholesterol <40 mg/dL (men) and < 50 mg/dL (women)

Waist circumference: For male, normal was<102 cm. For female <88 cm was considered as normal.

Waist/Hip ratio: For male, ≤0.9 was considered as normal and >0.9 was considered as abnormal. For female, ≤0.85 and > 0.85 were considered as normal and abnormal respectively. Then patient was sent for an ultrasound liver and radiologist had given diagnosis of mild/moderate/ severe fatty liver based on the following criteria:

Mild: Increased echotexture when compared to that of right kidney.

Moderate: Increased echotexture when compared to mild obliteration of diaphragmatic echoes.

Severe: Increased echotexture when compared to non-visualisation of diaphragmatic echoes.

The patients in statin or in antihypertensive therapy, are noted. Blood pressure from the right arm was measured in sitting posture. Relevant details on dietary habits, physical activity, sleep etc. were also noted to provide appropriate counselling.

Ethical issues: Informed consent has been obtained from all the participants before getting information from them. Confidentiality of the data was maintained thought the analysis and presentation of the study findings.

STATISTICAL ANALYSIS

Quantitative variables were summarized by mean and standard deviation. Categorical variables were summarized by frequency and proportion.

RESULTS

A total of 818 patients attending master health checkup were observed (Table 1). Among the study population, 130 (15.89%) participants had NAFLD. (Table 1)

Majority of 49 (37.69%) participants were aged between 41 to 50 years, followed by 51 to 60 years, 31 to 40 years, 61 to 70 years, 21 to 30 years and >70 years age group was 27.69%, 13.84%, 12.30%, 6.15% and 2.30% respectively. Among the study population, 75 (57.69%) participants were male remaining 55 (42. 30%) participants were female. majority of 46.15% participants were BMI 25 to 29.9. The proportion of BMI 30 to 39.9, <25% and >39.9 was 36.15%, 15.38% and 2.30% respectively. (Table 2)

The difference in waist circumference between the gender is found to be significant with a P- value of <0.001. The difference in fasting blood sugar between the gender is found to be insignificant with a P- value of 0.282. The difference in HDL between the gender is found to be significant with a P- value of 0.007. The difference in triglycerides between the gender is found to be insignificant with a P- value of 0.849. The difference in blood pressure between the gender is found to be insignificant with a P- value of 0.870. (Table 3)

Out of 130, 103 (79.23%) had grade 1 fatty liver, 18(13.84%)

NAFLD	Number	Proportion
Yes	130	15.89
No	688	84.11

Table-1: Incidence of NAFLD among the study population

Parameters	Frequency	Percentages
Age group		
21-30	8	6.15%
31-40	18	13.84%
41-50	49	37.69%
51-60	36	27.69%
61-70	16	12.30%
>70	3	2.30%
Gender		
Male	75	57.69%
Female	55	42.30%
BMI		
<25	20	15.38%
25-29.9	60	46.15%
30-39.9	47	36.15%
>39.9	3	2.30%

Table-2: Age, gender and BMI distribution of NAFLD patients (N=130)

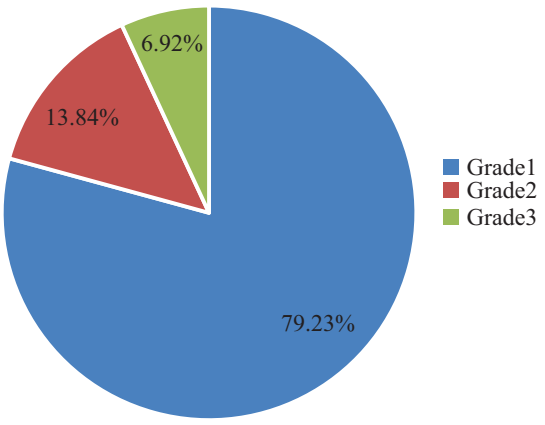

Figure-1: Grading of fatty liver among the study population.

Components of metabolic syndrome	Men (N=75)	Women (N=55)	P Value
Waist circumference (>102cm in men; >88cm in women)	26(34.66%)	40(72.72%)	<0.001
Triglyceride≥150 or treated	50(66.66%)	29(52.72%)	0.849
FBG≥ 100g/dL	58(77.33%)	43(78.78%)	0.282
HDL (>40 in men;> 50 in women)	45(60%)	48(87.6%)	0.007
Systolic BP >130m Hg or diastolic BP >85mm Hg or treated	42(56%)	30(54.54%)	0.870

Table-3: Summary of components of metabolic syndrome among NAFLD population

Parameters	Grade 1	Grade II	Grade III	P Value
Grading and age				
21-30(N=9)	9(100%)	0(0%)	0(0%)	*
31-40(N=18)	12(66.67%)	5(27.78%)	1(5.56%)	
41-50(N=49)	40(81.63%)	7(14.29%)	2(4.08%)	
51-60(N=36)	28(77.28%)	3(8.33%)	5(13.89%)	
61-70(N=15)	12(80%)	2(13.33%)	1(6.67%)	
>70(N=3)	2(66.7%)	1(33.3%)	0(0%)	
Vegetable consumed per day				
<=25 g(N=50)	42(84%)	5(10%)	3(6%)	0.70
26 to 50 (N=67)	50(74.63%)	12(17.91%)	5(7.46%)	
>50 (N=13)	11(84.61%)	1(7.7%)	1(7.7%)	
Non-veg consumption/ wk				
Once or twice(N=101)	82(81.2%)	12(11.9%)	7(6.93%)	*
3-4 times(N=13)	8(61.5%)	4(30.8%)	1(7.69%)	
Almost all days(N=10)	10(100%)	0(0%)	0(0%)	
nil(N=6)	3(50%)	2(33.3%)	1(16.7%)	
Oil consumption / month				
<1L(N=65)	53(81.5%)	8(12.3%)	4(6.15%)	0.76
>or = 1L(N=65)	50(76.9%)	10(15.4%)	5(7.69%)	
Exercise				
Doing exercise(N=49)	40(81.6%)	5(10.2%)	4(8.16%)	0.99
Not doing(N=81)	63(77.8%)	13(16.1%)	5(6.17%)	
*No statistical test was applied- due to 0 subjects in the cells				

Table-4: Association of lifestyle parameters with grade of NAFLD in the study population

had grade 2 fatty liver and 9 (6.92%) had grade 3 fatty liver. (Figure 1)

The difference in grade of NAFLD across the age group is found to be significant with a P- value of 0.035. The difference in grade of NAFLD across the vegetable consumed per day is found to be insignificant with a P-value of 0.70. The difference in grade of NAFLD across the non-veg consumption/week is found to be insignificant with a P-value of 0.15. The difference in grade of NAFLD between oil consumption/month is found to be insignificant with a P- value of 0.76. The difference in grade of NAFLD between exercise is found to be insignificant with a P- value of 0.99 (table-4).

DISCUSSION

The prevalence of NAFLD was 15.89% in our study. The reported prevalence of NAFLD is quite variable across the countries and even there were huge subnational variations reported from India. Majumdar, A., et al.[13] have reported 30.7% prevalence of NAFLD among rural Haryana population, which is considerably higher than the current study. Another study conducted on south Indian population has reported a overall prevalence of NAFLD of 32%.[14] The reported prevalence is ranged from 9% in rural populations to 32% in urban populations.[10]

In the current study, the proportion of male was slightly higher than the females. Many studies in the past had reported relatively higher risk of NAFLD in males compared to females. A study from south India had reported higher prevalence of 35.1% among men, compared to 29.1% in women.[14]

In the current study, BMI correlation with fatty liver is having clinical significance (p=0.05). NAFLD is more common in individuals with overweight and obesity than normal individuals. When compared with males (34%), a greater number of females (72%) had increased waist circumference which is clinically significant (p<0.001). The differences between the males and females with respect to various components of metabolic syndrome was analyzed in the current study. We have found waist circumference and HDL values to be significantly different between males and female NAFLD patients. A review by Lonardo, A., et al.[15] had pointed out the possibility of genetic composition, hormonal milieu and various other parameters to be responsible for key gender differences in the susceptibility to NAFLD and composition of the risk factor profile. Few candidate genes in hepatocytes were also proposed by few studies.[16]

In the current study, Out of 130, 103 (79.23%) had grade

1 fatty liver, 18(13.84%) had grade 2 fatty liver and 9 (6.92%) had grade 3 fatty liver. keeps on increasing till the age of 60 yrs. Grade 1 and Grade 3 incidence tend to fall beyond the age 50 & 60 respectively. This is having clinical significance ($p<0.035$). High vegetables intake, low non-veg intake, low oil consumption, regular physical activities had decreased incidence of fatty liver which is not having much significance. Severe grades of NAFLD were reported to be associated with coronary artery disease, even without metabolic syndrome by previous studies.[17] Hence studies have recommended screening of patients with higher grades of NAFLD for Coronary Artery Disease (CAD).[18]

CONCLUSION

Our report further highlights the association of NAFLD with features of the metabolic syndrome. Obesity, diabetes, hypertension, and hyperlipidemia have been repeatedly reported in NAFLD. So, it is of paramount importance in educating NAFLD patients about the association of metabolic syndrome and complications and the possible ways to prevent them like regular physical activity, maintain a normal BMI by gradually reducing their weight, adequate control oh blood pressure, sugar and lipids.

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Rainbow Sign in Dermatoscopy of Nodular Basal Cell Carcinoma

Sir,

Dermatoscope is considered a vital tool in the diagnosis of basal cell carcinoma (BCC), helping in the early diagnosis and differentiating from other clinical mimics. Dermatoscopy of nodular BCC shows arborizing vessels, ulceration, large blue-gray ovoid nests, and multiple blue-gray globules, whereas superficial BCC shows brown pigmented structures including concentric structures, leaf-like areas, spoke wheel areas, erosions, and superficial fine telangiectasia.[1]

A 75-year-old male patient presented with complaints of asymptomatic nodule over the face for 2 years. The lesion started as a small papule and enlarged insidiously to attain the present size. There was a history of occasional bleeding from the lesion. On examination, the nodule was firm in consistency and of size 3 cm × 3 cm present just beneath the ala of the nose [Figure 1]. Dermatoscopic examination was performed using a handheld dermatoscope Dermlite DL3 (3Gen Inc., USA) with ultrasound gel as interface fluid, and images were captured using a Sony DSC W-800 20.1 MP digital camera (Sony Corp., Tokyo, Japan). Dermatoscopy under nonpolarized light showed bluish-white structureless areas and ulceration [Figure 2]. Under polarized light, it showed white structureless areas, white crystalline structures, and multicolor structureless areas called "rainbow sign" [Figure 3]. When toggled between nonpolarized and polarized modes, rainbow sign appeared in polarized mode and disappeared in nonpolarized mode [Video 1]. Excision biopsy of the lesion showed basaloid tumor cells infiltrating dermis and subcutaneous tissue in the form of cords and nests, with peripheral palisading and dilated blood vessels in the stroma [Figure 4].

The rainbow pattern under dermatoscopy was first described in Kaposi's sarcoma due to diffraction of light passing through slits of blood vessels.[2] Rainbow pattern, however, was also found in lichen planus, stasis dermatitis, melanoma, atypical fibroxanthoma, and BCC.[3] Rainbow pattern is due to luminescence phenomenon of polarized light interacting with vascular structures present within the lesion.[4] Polarized dermatoscopic features of nodular BCC including rainbow pattern and crystalline structures as described in this case report are less reported in literature.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published

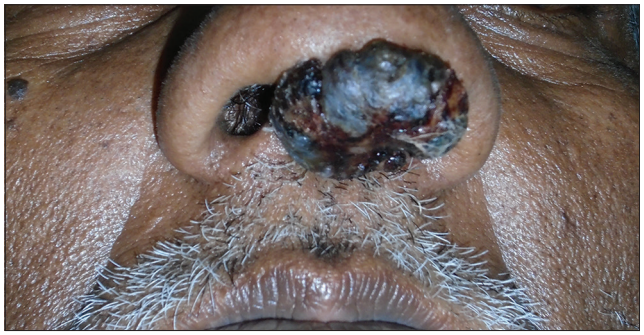

Figure 1: Nodule over the face just beneath the ala of the nose

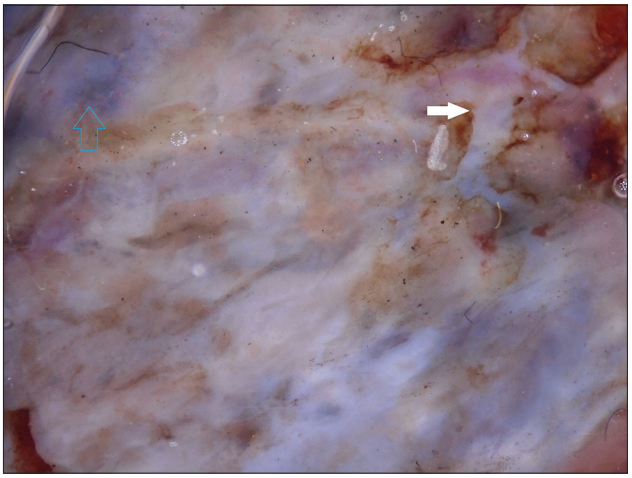

Figure 2: Nonpolarized dermatoscopy (×10) showing bluish-white structureless areas (blue arrow) and ulceration (white arrow)

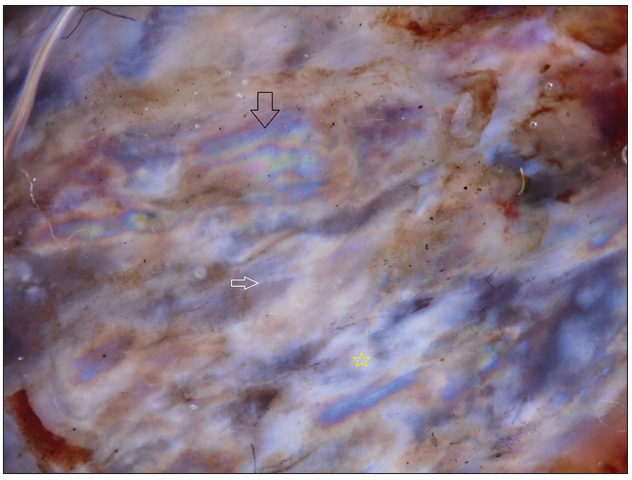

Figure 3: Polarized dermatoscopy (×10) showing rainbow sign (black arrow), white structureless areas (yellow star), and crystalline structures (white arrow)

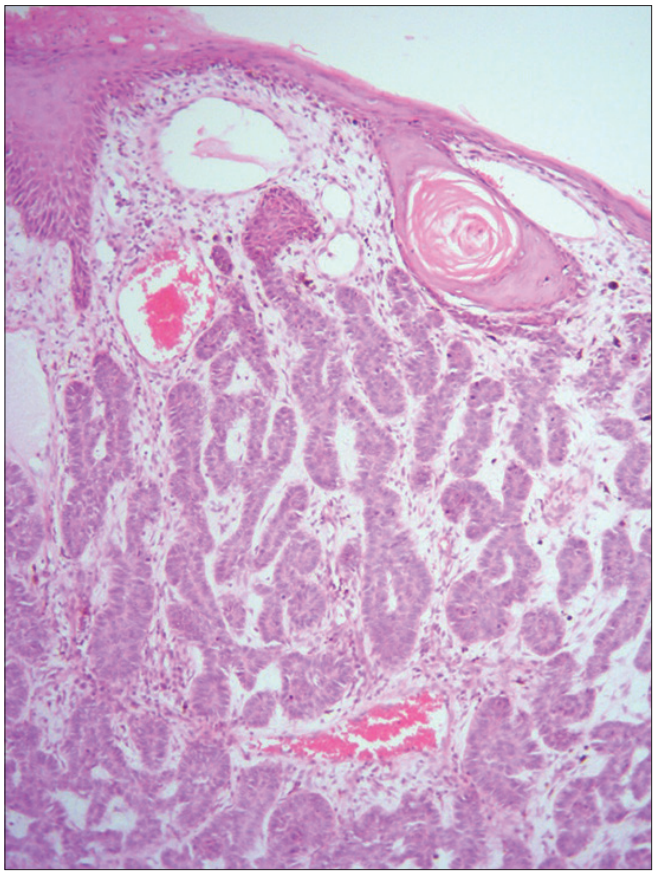

Figure 4: Histopathology showing islands of basaloid tumor cells with peripheral palisading and dilated blood vessels in the stroma (H and E, ×100)

and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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ORIGINAL RESEARCH ARTICLE

A Study of Factors Associated with Relapse of Drinking during a 1 Year Follow-up: A Retrospective Cohort of 70 Males Treated as In-Patient for Alcohol Dependence Syndrome

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A B S T R A C T

Intoduction: Relapse is a multi-factorial phenomenon and most likely to result from a combination of various factors. This study was conducted to determine factors associated with relapse of drinking in patients who underwent deaddiction treatment programme.

Material and Methods: This is a retrospective cohort study was done in patients who were admitted for in-patient de-addiction care programme between September 2017 and February 2018. The in-patient charts of the subjects were retrieved from the medical records department. The SADQ score at admission, CIWA - Ar score and The Brief Substance Craving Score at the time of discharge were taken from the record.

Results: A total of 70 patients were recruited and the mean age of participant was 41.27 ± 11.07 years. At the end of 1 year the mean total no. of lapses was 9.9 ± 12.67 in the study population and the mean total number of relapses was 0.84 ± 0.94. The mean duration of complete abstinence last 1 year (CDA) in days was 272.43 ± 109.12. The mean no. of readmissions for de-addiction last 1 year was 0.23 ± 0.57 in the study population. Univariate analysis shows age at first drink in years, total duration of drinking in months and use of disulfiram and graduation as educational status are associated with higher odds of relapse. However, multiple regression model showed no statistically significant association.

Conclusion: The complete abstinence was seen only in 31.43% of the population

Keywords: Alcohol Dependence Syndrome, Life Events, Relapse, Craving, Impulsivity, Relapse

INTRODUCTION

Despite increased awareness of the risks of alcoholism, it continues to present a serious public health problem and constitutes one of the most frequent, preventable cause of morbidity and mortality.[1] Continued excessive alcohol consumption can lead to the development of dependence that is associated with a withdrawal syndrome when alcohol consumption is ceased or substantially reduced.[2]

Relapse may be defined as the resumption of alcohol drinking following a prolonged period of abstinence. Clinically, vulnerability to relapse commonly is associated with an intense craving or desire to drink.[2] Management of substance use disorders is riddled with multiple relapses. Research studies show that 65–70% of abstinent alcohol-dependence subjects relapse within 1 year.[3,4] About 50% of detoxified alcohol users relapse within 3 months. There is evidence that approximately 90 percent of alcohol dependents are likely to experience at least one relapse over the 4-year period following treatment.[5,6]

Relapse is a multi-factorial phenomenon and most likely to result from a combination of various factors including the individual characteristics of the patient, the drug and environmental reinforcers.[7] Among treated individuals, more severe alcohol-related problems and depressive symptoms, lack of self-efficacy, poor coping skills and readiness for change have been associated with relapse in short-term.[7,8] Hence, in this study we propose to look for factors associated with relapse of drinking in patients who underwent deaddiction treatment as an in-patient in our hospital.

MATERIAL AND METHODS

This was a retrospective cohort study was done in patients who were admitted for in-patient de-addiction in "Nambikkai" addiction care programme between September 2017 and February 2018 were considered as the study population. The patient contact details were retrieved from the ward nominal register. Patients were contacted over phone and invited to participate in the study. The principal investigator reassessed

the patient on the day of reporting for participation in the study. Ethical approval was obtained from institutional review board before the start of study.

Inclusion criteria

- Subject over 18 years
- Fulfilling the ICD 10 criteria for Alcohol dependence syndrome at admission
- No comorbid BPAD/psychotic illness or cognitive or neurological disorder
- No evidence of intellectual disability
- No other drug/narcotic use disorder other than nicotine
- Patients who report with reliable informant
- Who give informed consent

Exclusion criteria

- Subjects less than 18 years of age
- Presence of Comorbid Psychotic/ BPAD/ cognitive disorder/ neurological disorder
- Intellectual Disability
- Comorbid drug abuse/dependence other than Nicotine
- No reliable informant
- Those who refuse informed consent

After informed consent the patient and reliable informant were interviewed by the primary investigator. Socio-demographic data was collected using a proforma. Details of lapse, relapse and abstinence periods were meticulously reviewed and recorded after confirmation with the reliable informant. A relapse was defined as "a complete return to earlier dependence pattern of drinking". A lapse was defined as "an intermittent drink not amounting to abuse or a full blown relapse". Abstinence was considered as "a state of zero lapse or relapse". Medical and alcohol history, readmission details during the period between March 2018 and February 2019 and other relevant information was noted.

The in-patient charts of the subjects were retrieved from the medical records department for additional information during admission in the deaddiction ward. The SADQ score at admission, CIWA - Ar score and The Brief Substance Craving Score at the time of discharge were taken from the in-patient record. Details of withdrawal phase, presence or absence of withdrawal seizures, delirium tremens and the cooperation, motivation and involvement of the patient with the treatment during the in-patient stay was noted from the daily progress notes of the doctor and nursing record. History regarding the medical complications of alcohol and results of relevant blood investigations results were also obtained from the case record. The drugs prescribed at discharge were noted. The standardised rating scales used for assessment were Severity of Alcohol Dependence Questionnaire (SADQ), Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar), Rosenberg Self Esteem Scale, General Self Efficacy Scale, Depression Anxiety and Stress Scale, and Brief Substance Craving Scale. The OP note of the patient was reviewed for checking regularity of review, drug compliance and additional information of medical complications and consultations sought were noted. Cross consultations sought and medical comorbidities like diabetes and hypertension were also recorded.

RESULTS

A total of 88 patients who were admitted for deaddiction treatment in "Nambikkai" addiction care ward. Out of the 88 patients 9 patients did not satisfy the inclusion criteria, 1 patient had died in an RTA (under effect of alcohol) and 8 patients were either not reachable or did not turn up for the study or did not review with a reliable informant to cross verify and were hence not taken for study. A total of 70 patients were finally recruited.

The mean age of participant was 41.27 ± 11.07 years in the study population, minimum level was 22 and maximum level was 70 in the study population. Among the study population 54 (77.14%) participants were referred by others and 16 (22.86%) participants were referred by self. The drinking parameters in the patients showed that the mean age of first drink in years was 22.99 ± 6.03 in the study population and the mean duration of dependent pattern of drinking in months was 64.67 ± 36.85 in the study population. There was high frequency of family history of alcohol among the study

Parameter	Mean ± SD
Age of first drink in years	22.99 ± 6.03
Total duration of drinking in months	207.86 ± 102.86
Duration of dependent pattern of drinking in months	64.67 ± 36.85
Age of onset of dependence pattern of drinking	35.17 ± 9.27
Family history of alcohol dependence	23 (32.86%)
Family history of mental illness	2 (2.86%)
Place of residence	
Urban	28 (40.0%)
Rural	42 (60.0%)
Literacy	
Primary	19 (27.1%)
secondary	24 (34.3%)
Graduate	24 (38.6%)
Marital status	
Single	16 (22.9%)
Married	40 (57.1%)
Separated/ Divorced/ Widow	14 (19.9%)
Financial debts	30 (42.9%)
Disulfiram	40 (57.1%)
Antidepressants prescribed	32 (45.7%)
H/O Jaundice after dependence drinking	14 (20.0%)
RTA under intoxication	17 (24.3%)

Table-1: Descriptive analysis of drinking related parameters in study population (N= 70)

Parameters	Frequency (%)
Withdrawal seizures	4 (5.71%)
Delirium tremens	8 (11.43%)
Cooperation during IP stay	56 (80.00%)
Motivation	53 (75.71%)
Disulfiram	40 (57.14%)
Antic raving medication	63 (90.00%)

Table-2: Descriptive analysis of clinical parameters in the study population (N=70)

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Parameter	Mean ± SD
Substance craving score at discharge	3.44 ± 3.61
Duration of complete abstinence after discharge in days	197.57 ± 173.77
Total no. Of lapses in the last 1 year	9.9 ± 12.67
Total number of relapses in the last 1 year	1 (0,1) (median (IQR)
Duration of complete abstinence last 1 year(CDA) in days	272.43 ± 109.12
No. of readmissions for de-addiction last 1 year	1 (0,1) (median (IQR)
No. of admissions for medical issues last 1 year	1 (0,1) (median (IQR)
Duration of IP stay for de-addiction in days last 1 year	14.16 ± 5.54
SADQ score at admission	23.5 ± 7.53
CIWA - ARSCORE after admission	29.97 ± 11.15
Rosenberg self esteem scale score	14.09 ± 3.87
General self efficacy scale score	21.66 ± 5.92
DASS depression score	10.53 ± 5.39
DASS anxiety score	11.94 ± 6.7
DASS Stress Score	14.46 ± 6.86

Table-3: Descriptive analysis of discharge related parameters in study population (N=70)

population (Table 1).

The difficulties in treatment included seizures, delirium tremens, poor motivation and use of disulfiram and anti craving medication (Table 2). At discharge the parameters such as craving and complete abstinence was mentioned in Table 3. At the end of 1 year the mean total no. of lapses was 9.9 ± 12.67 in the study population and the mean total number of relapses was 0.84 ± 0.94. The mean duration of complete abstinence last 1 year (CDA) in days was 272.43 ± 109.12. The mean no. of readmissions for de-addiction last 1 year was 0.23 ± 0.57 in the study population. The mean of standardised rating scales used for assessment were Severity of Alcohol Dependence Questionnaire (SADQ), Clinical

Parameter	Frequency (%)
Current alcohol use status (last 2 weeks)	
Abstinent	34 (48.57%)
Lapse	10 (14.29%)
Relapse	26 (37.14%)
Complete abstinence at one year	
Yes	22 (31.43%)
No	48 (68.57%)

Table-4: Descriptive analysis of alcohol use status (last 2 weeks) in the study population (N=70)

Parameter	Un adjusted odds ratio	95 % CI		P value
		Upper	lower	
Age of first drink in years	1.053	1.003	1.105	0.037
Total duration of drinking in months	1.151	1.046	1.267	0.004
Duration of dependent pattern of drinking in months	1.002	0.997	1.007	0.368
Age of onset of dependence pattern of drinking	1.058	0.999	1.120	0.052
Family history of alcohol dependence (Baseline=No)	0.684	0.226	2.073	0.502
Family history of mental illness (Baseline=No)	2.238	0.134	37.516	0.575
Place of residence (Baseline= Urban)				
Rural	1.667	0.576	4.825	0.346
Literacy (Baseline=Primary)				
secondary	5.100	0.948	27.423	0.058
Graduate	5.884	1.118	30.553	0.036
Marital status (Baseline= Single)				
Married	1.222	0.222	6.730	0.818
Separated/ Divorced/ Widow	2.200	0.527	9.176	0.279
Financial debts (baseline=No)	0.271	0.086	0.852	0.025
Disulfiram (baseline=No)	3.696	1.174	11.633	0.025
Antidepressants prescribed (baseline=No)	0.317	0.106	0.950	0.040
H/O Jaundice After Dependence Drinking (baseline=No)	0.125	0.015	1.023	0.052
RTA Under Intoxication (baseline=No)	0.095	0.012	0.773	0.028

Table-5: Univariate regression analysis of factors associated with Complete abstinence at one year (relapse) in study population (N=70)

Parameter	Un adjusted odds ratio	95 % CI		P value
		Upper	lower	
Age of first drink in years	1.029	0.958	1.106	0.431
Total duration of drinking in months	1.086	0.963	1.226	0.178
Financial debts (baseline=No)	0.289	0.075	1.110	0.071
Disulfiram (baseline=No)	3.417	0.743	15.718	0.114
Antidepressants prescribed (baseline=No)	0.354	0.094	1.329	0.124
RTA Under Intoxication (baseline=No)	0.153	0.016	1.437	0.101

Table-6: Multivariate regression analysis of factors associated with Complete abstinence at one year in study population (N=70)

Institute Withdrawal Assessment of Alcohol Scale, Revised (CIWA-Ar), Rosenberg Self Esteem Scale, General Self Efficacy Scale, Depression Anxiety and Stress Scale, and Brief Substance Craving Scale is mentioned in Table 4.

Univariate analysis had shown age at first drink in years, total duration of drinking in months and use of disulfiram and graduation as educational status are associated with higher odds of relapse. Having financial debts, prescription antidepressant intake and RTA under intoxication were associated with lower odds of relapse among the study population. (Table 5). None of the factors had shown any statistical significant association with relapse in the current study, on multivariate analysis. (Table 6)

DISCUSSION

The treatment of alcohol addiction has posed a bewildering challenge for modern society. Different individual characteristics are predictive of different types of treatment outcomes such as complete abstention, asymptomatic drinking, reduced but still problematic drinking, and unremitted impairment as drinking that leads to loss of control.[9] Therefore, relapse as a central issue in the treatment of alcohol dependence warrants further study.[10] Hence, in this study the factors associated with abstinence, lapse and relapse of drinking after an in-patient deaddiction programme was investigated.

The current study showed that only 22(31.43%) participant were abstinent meaning most patient either had a lapse or a relapse. The mean total no. of lapses in the last 1 year was 9.9 ± 12.67 and mean total number of relapses in the last 1 year was 0.84 ± 0.94. the Cüneyt Evren, et al.[11] Among 102 alcohol dependent inpatients, 61.8% (n=63) were considered as relapsed to alcohol abuse . Few other studies showed higher relapse.[7,10,12]

In the current study the, the univariate analysis had shown age at first drink in years, total duration of drinking in months and use of disulfiram and graduation as educational status are associated with higher odds of relapse. Having financial debts, prescription antidepressant intake and RTA under intoxication were associated with lower odds of relapse among the study population. None of the scoring systems showed any associations. Cüneyt Evren, et al.[11] showed that the relapsed was associated fewer regular visits to the outpatientclinic, attended the Outpatient Treatment Program on an irregular basis or not at all, made fewer social changes to protect themselves from a relapse or were not able to make any changes at all, and used the anti-craving medication irregularly or not at all.

Chauhan, V., et al.[10] found that patients who had relapsed were found to have significantly more positive family history of substance use, past history of alcohol-related comorbidity, experienced a higher number of undesirable life events, and higher negative mood states and social anxiety and dysfunction in social, vocational, personal, family, and cognitive spheres compared to patients who had remained abstinent.

This study showed various factors that influence alcohol relapse. However, there are several limitations to this study. This cohort of single-centred inpatient participants are small and are hardly representative of the general population. The study was observational study with convenience sampling technique. Thus, the paper's conclusions are suggestive but may not be applicable to other populations. The outcomes were based upon self-report and physician-report without confirmation from significant others. Self-reported measures may contain information or social desirability bias. Future study must include large scale cohort study with a larger sample size to determine factors associated with relapse.

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Original Research Article

A prospective observational study to compare postoperative complications and quality of life between patients undergoing umbilical hernia repair by open and laparoscopic methods

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ABSTRACT

Background: Surgery of umbilical hernias may be challenging due to the heterogeneity of presentation, multiple options for repair, and potential for complications, including infection and recurrence. Laparoscopic repair of a ventral hernia has gained the popularity in recent times for its advantage over the open surgery. Hence the study aimed to compare postoperative complications and quality of life between patients undergoing umbilical hernia repair by open and laparoscopic methods.
Methods: The study was a prospective cohort study, conducted in the department of general surgery of a tertiary care teaching hospital. Patients undergoing umbilical hernia repair by the laparoscopic method and by open surgery were included in the study. The interoperative time, postoperative hospital stays, post-operative complications and quality of life between patients undergoing umbilical hernia repair by open and laparoscopic methods were assessed after the surgery.
Results: A total of 64 people were included in the final analysis, with 32 subjects each in each group. 13 (40.6%) were males and 19 (59.4%) females in both the groups. The mean duration of open umbilical hernia surgery was 59.37±10.83, and it was only 46.87±12.74 for laparoscopic surgery. The difference was statistically significant ($p<0.05$). Post-operative period recovery time in days was significantly lesser for laparoscopic group. Pain score postoperative period was 6.52±0.87 for open surgery and 4.84±0.86 for laparoscopic surgery, and the difference was statically significant ($p<0.05$).The difference between individual Carolinas comfort scale scores and study group was statistically significant ($p<0.001$).
Conclusions: Laparoscopic umbilical hernia leads to lesser operative time, early postoperative recovery and comparatively superior quality of life, as compared to open umbilical hernia repair.

Keywords: Complications, Laparoscopy, Quality of life, Umbilical hernia

INTRODUCTION

An umbilical hernia(UH) is a rather common surgical problem.[1] They are the most common type of linea alba abdominis defects in adults with a prevalence of about 10%.[2] A true umbilical hernia is a defect in the anterior abdominal wall underlying the umbilicus, through which the intestine can protrude.[3] An umbilical hernia has gained little attention from surgeons in comparison with other types of abdominal wall hernias (inguinal, incisional).[4] Although UH are often thought of as simple hernias, they can be complex and, if not handled properly, can be irritating to patients and surgeons. An umbilical hernia has a tendency to be associated with

high morbidity and mortality in comparison with an inguinal hernia because of the higher risk of incarceration and strangulation that require emergency repair.[1]

Several things make umbilical hernias challenging, including the heterogeneity of presentation, multiple options for repair, and potential for complications, including infection and recurrence. The primary suture for an umbilical hernia resulted in recurrence rates of 19–54%.[5-7] The use of a variety of mesh materials for the repair of these hernias has resulted in a decreased recurrence rate when compared with that in primary suture closure.[8-10]

Laparoscopic incisional hernia repair has gained popularity for its superiority and has been reported to have better outcomes in terms of hernia recurrence and postoperative complications.[11] however, its role in the repair of an umbilical hernia remains controversial.[12-14]

Hence, the current study was conducted to compare the inter-operative time, postoperative hospital stays, post-operative complications and quality of life between patients undergoing umbilical hernia repair by open and laparoscopic methods.

METHODS

The study was a prospective cohort study, conducted in the department of general surgery of a tertiary care teaching hospital. The study cohort consisted of people undergoing umbilical hernia repair by the laparoscopic method, and the comparison group consisted of people undergoing umbilical hernia repair by open method, as per the institutional protocol

The sample size was calculated to be 32 subjects in each of the study groups. A total of 64 people were included in the final study, with 32 subjects each in open and laparoscopy groups. The data collection for the study was done between March 2018 to June 2018, for a period of 1 year.

The ethical approval was obtained from the institutional human ethics committee. Informed written consent was obtained from each of the study participants.

Study procedure

After obtaining the informed consent form and conducting thorough clinical assessment each participant was provided with the option of either choosing open or laparoscopic methods as per the institutional protocol. The advantages, disadvantages, cost and other relevant aspects of both the methods were explained to each participant, and they were allowed to take an informed decision about the procedure to undergo. Basing on the choice the participants were treated with the corresponding procedure and were recruited into the study in the corresponding group. Laparoscopy was performed. The interoperative time, postoperative hospital stays, post-operative complications and quality of life between patients undergoing umbilical hernia repair by open and laparoscopic methods were assessed after the surgery. Carolinas comfort scale was used to assess the quality of life post-surgical complication.[15] The CCS is a 23-item questionnaire that quantifies the severity of pain, mesh sensation, and movement limitation from a hernia or surgical site during the following 8 activities: lying down, bending over, sitting up, activities of daily living, coughing or deep breathing walking, climbing stairs, and exercise.[15] The answers were recorded on a 6-point Likert scale, which ranges from an absence of symptoms to disabling symptoms. It is a hernia- specific questionnaire aiming at patients treated with a mesh.

Statistical methods

The relevant demographic, clinical parameters, operative findings, post-operative complications and the quality of life were entered into Microsoft excel sheet and analysed using IBM SPSS statistical software. Numerical variables were compared between two groups using independent sample t-test or Mann-Whitney U test. Qualitative variables were compared between the two groups using the chi square test or Fisher's exact test. A $p<0.05$ was considered as the statistically significant.

RESULTS

A total of 64 people were included in the final analysis, with 32 subjects each in open and laparoscopic groups. The demographic details and the baseline characteristic of the patients were collected for both the groups, and there was no statistically significant difference between study group and different parameters like age, gender, size of the defect in cm and number of defects (Table 1).

The mean duration of open umbilical hernia surgery was 59.37±10.83, and it was only 46.87±12.74 for laparoscopic surgery. The difference was statistically significant ($p<0.05$). Post-operative period recovery time in days was significantly lesser for laparoscopic group. Pain score postoperative period was 6.52±0.87 for open surgery and 4.84±0.86 for laparoscopic surgery, and the difference was statically significant ($p<0.05$). Seroma formation and scar formation was significantly lesser for the laparoscopic surgery ($p<0.05$) (Table 2).

The scores of individual Carolinas Comfort Scale were more in open umbilical hernia repair compared to laparoscopic umbilical hernia repair. The difference between individual Carolinas Comfort Scale scores and study group was statistically significant ($p<0.001$). The mean the sensation of mesh total score in open umbilical hernia repair was 11.09±2.6, it was 1±1.44 for laparoscopic umbilical hernia repair. The mean of pain total score in open umbilical hernia repair was 16.61±3.63; it was 3.29±2.58 for laparoscopic umbilical

hernia repair. The mean of the movement limitations total score in open umbilical hernia repair was 10.46±3.18; it was 1.36±1.31 for laparoscopic umbilical hernia repair. The mean of movement total score in open umbilical hernia repair was 38.15±7.54; it was 5.65±4.19 for Laparoscopic umbilical hernia repair. The difference between study groups was statistically significant for all the parameters (p<0.001) (Table 3).

Table 1: Comparison of mean of demographical parameters across study groups (n=64).

Parameter	Open umbilical hernia repair (N=32)	Laparoscopic umbilical hernia repair (N=32)	P value
Age in years (Mean±SD)	48.7±14.69	50.42±11.36	0.603
Gender			
Male	13 (40.6%)	13 (40.6%)	1.000
Female	19 (59.4%)	19 (59.4%)	
Size of the defect in cm	4.62±1.39	Five±1.37	0.276
Number of defects			
1	31 (96.9%)	25 (78.1%)	***
2 or more merge	1 (3.1%)	1 (3.1%)	
3	0 (0%)	6 (18.8%)	
Primary, recurrent hernia (make it comparable between groups)			
Primary hernia	28 (87.5%)	21 (65.6%)	0.039
Recurrent hernia	4 (12.5%)	10 (34.4%)	
Spinal	26 (81.3%)	1 (3.13%)	

Table 2: Comparison of mean of pain score postoperative period, post-operative period and postoperative complications across study groups (n=64).

Parameter	Study group		P value
	Open umbilical hernia repair (n=32)	Laparoscopic umbilical hernia repair (n=32)	
Duration of surgery in mints	59.37±10.83	46.87±12.74	<0.001
Post-operative period recovery time in days	6.18±1.38	3.2±1.7	<0.001
Pain score postoperative period	6.52±0.87	4.84±0.86	<0.001
Urinary retention in the post-op period			
Yes	10 (31.3%)	4 (12.8%)	0.070
No	22 (68.8%)	28 (87.5%)	
Seroma formation in the post op period			
Yes	28 (87.5%)	2(6.25%)	<0.001
No	4 (12.5%)	30 (93.75%)	
Surgical site infection			
Yes	5 (15.6%)	1 (3.13%)	0.086
No	27 (84.4%)	31 (96.87%)	
Scar formation			
Yes	26 (81.3%)	1 (3.1%)	<0.001
No	6 (18.8%)	31 (96.87%)	
Recurrence			
Yes	2 (6.3%)	0 (0%)	***
No	30 (93.8%)	32 (100%)	

DISCUSSION

Umbilical hernias generally develop from small facial defects. The umbilicus is one of the potential weak areas of the abdomen and a relatively common site of herniations. An umbilical hernia is common in adults and is characterised by an acquired defect because of their size. Mesh repair became the gold standard in the elective management of most open umbilical hernias with significant improvement in terms of recurrence. However, the laparoscopic surgery is known to have a better outcome compared to the open surgery. With

advances in knowledge and improvement in clinical outcomes, attention is directed to functional outcomes, such as quality-of-life measures.

Table 3: Comparison of median in Carolinas comfort scale total scores in study group (n=64).

Parameter	Mean±SD		P value
	Open umbilical hernia repair (n=32)	Laparoscopic umbilical hernia repair (n=32)	
Laying down	2.36±0.7	0.13±0.5	<0.001
Bending over	4.03±1.91	0.26±0.68	<0.001
Sitting up	3.76±1.12	0.07±0.25	<0.001
Performing activities of daily living	4.36±1.73	0.19±0.6	<0.001
Coughing	4.61±1.41	0.52±0.85	<0.001
Walking or standing	5.36±1.41	0.71±1.1	<0.001
Walking up or down stairs	5.79±1.43	1.23±1.45	<0.001
Exercising total score	7.88±1.67	2.55±1.39	<0.001
Sensation of mesh (total score)	11.09±2.6	1±1.44	<0.001
Pain (Total score)	16.61±3.63	3.29±2.58	<0.001
Movement limitations (total score	10.46±3.18	1.36±1.31	<0.001
Overall total score	38.15±7.54	5.65±4.19	<0.001

In the current study, the mean of age of the subjects was comparable across both groups in which, OUHR group was 49.68 years while it was 51.56 years for LUHR group. Similar mean age among OUHR group (49 years), but slightly younger aged patients were present in LUHR group (48 years) was noted in the study by Gonzalez et al.[8] In their retrospective cohort study Cassie et al, also reported similar age group about 49.7 years in both the groups.[16] Gender wise, females were higher in both the groups (56% in OUHR group and 64% in LUHR group). Contrastingly higher proportions of males were present in the studies by Gonzalez et al, (72% in OUHR and 56% in LUHR) and Cassie et al (69% in the former group and 65% in the latter).[8,16]

In the current study, Seroma formation and scar formation was significantly lesser for the laparoscopic surgery ($p<0.05$). This was in accordance with the study by Malik where the post-operative complication was more in open group.[17] Gonzalez et al found that the number of postoperative complications were significantly ($p<0.05$) high in patients with open mesh repair (30%) than laparoscopic repair (6%).[8] The incision for OUHR is generally longer and located in a heavily contaminated area, thereby rendering it more susceptible to wound infection. None of the subjects in the LUHR group had seroma while most of them (84%) had it in OUHR group. Contrary to this, Gonzalez et al found a higher proportion of patients with seromas in LUHR group (56%) than OUHR group (40%).[8] Surgical site infections (SSI) are not benign complications. Multiple studies have demonstrated that SSI is related to higher rates of hernia recurrence, longer-hospital stays, higher incidence of hospital readmission, and increased likelihood for reoperation.[18] Regarding the post-op urinary retention few of them were reported in LUHR group (8%) than the OUHR group (28%). Contrastingly Gonzalez et al, observed 5% of patients in the OUHR group, and none in the LUHR group had urinary retention.[8] In our study, SSI was only seen in the OUHR group in 16% of them. Similarly, Gonzalez et al noted no wound complications LUHR group, but 15% of patients in the OUHR group had wound infections.[8] Laparoscopy has helped to reduce the risk of SSI for most abdominal surgeries, in particular, obese patients.[11,19] It may decrease rates of SSI by simply decreasing incision length. In line with this finding Gonzalez et al observed recurrences of a hernia only in the OUHR group (20%).[8]

Regarding the mean duration of surgery, LUHR procedure took significantly ($p<0.001$) less time 45.6 minutes than the OUHR procedure (67.8 minutes). Gonzalez et al though, noted that the operating time of LUHR was relatively short (62 minutes) compared to that of OUHR (82 minutes), but the difference was not statistically significant.[8] But the duration of surgery in the study by Korukonda, et al, was 1:49±0:19 for the laparoscopic group and it was 1:09±0:11 for the open surgical group.[20] However, there was no statistical significance between the group.

Post-operative recovery time was significantly ($p<0.001$) less in the LUHR group (3.04 days) than the OUHR group (7.4 days). The LUHR group experienced significantly less pain as indicated by their pain scores (4.84) than the OUHR group (6.520). The laparoscopic technique for umbilical hernia repairs results in decreased postoperative pain and LOS, shorter RTNA, and lower recurrence rates.[13]

In the current study, the scores of individual Carolinas comfort scale were more in open umbilical hernia repair compared to laparoscopic umbilical hernia repair. The difference between individual Carolinas Comfort Scale scores and study group was statistically significant ($p<0.001$).

Colavita et al, made a prospective long-term comparison of QOL among 720 patients who had undergone either open surgery or laparoscopy.[21] They found that at 1-month postoperatively, the frequency and severity of

symptoms was significantly higher in the LVHR (laparoscopic ventral hernia repair) group than in the OVHR (open ventral hernia repair) group. Discomfort was reported by 56% of LVHR versus 37% of OVHR patients, activity limitation in 47% versus 33%, and overall symptoms in 59% versus 43% ($p<0.001$ for each domain and overall). Beyond one month, there were no differences between LVHR and OVHR in regard to symptoms or pain. Evaluation of individual CCS scores for individual activities showed similar trends to previously mentioned situations, with increased symptoms being associated with LVHR. Exceptions were pain with walking at 1-month follow-up ($p=0.115$) and exercise movement limitation at 1 month ($p=0.335$). For all other activities 1 month postoperatively, LVHR patients experienced more discomfort and movement limitation than OVHR repair.

Our study findings overall reveal that all the parameters of CCS were significantly more noticed in patients with OUHR and hardly any patient in LUHR had any positive scores. This is contrary to that reported by Colavita et al.[21]

The median of laying down the score in Open umbilical hernia repair group was 2; it was nil for Laparoscopic umbilical hernia repair. The median of bending over the score in open umbilical hernia repair group was 3; it was nil for laparoscopic umbilical hernia repair. Conversely, Colavita et al found 40.4% of subjects in the LVHS group and 23.7% in OVHS group had a limitation in the bending over activity ($p<0.001$).[21]

The median of sitting up the score in open umbilical hernia repair group was 4; it was nil for laparoscopic umbilical hernia repair. Contrastingly Colavita et al noted 27% in LVHS and 15.1% in OVHS group having difficulty in sitting up ($p<0.001$).[21]

In their large-scale study of 710 patients Colavita et al noted more patients in LVHS group compared to OVHS group having difficulty in performing daily activities (37.3% vs. 20.5%), coughing (32.6% vs 21.3%), walking or standing difficulty (22.2% vs 15.5), walking upstairs (25% vs 15.7%) and difficulty in exercising (25% vs 20.2%) and all the differences were statistically significant ($p<0.001$).[21] Contrastingly in our study, the median of performing activities of daily living in OUHR group was 4, it was nil for LUHR group. The median of coughing in OUHR group was 4; it was nil for LUHR group. The median of walking or standing in OUHR group was 2; it was nil for LUHR group. The median of walking up or down stairs in OUHR group was 6; it was 1 for LUHR group. The median of exercising in OUHR group was 8; it was 3 for LUHR group. All the differences were statistically significant ($p<0.001$).

However, in their study of 56 patients, Hope et al observed the findings using CCS that are similar to the present study findings, which is as follows: lying down (LR-1.93; open-2.50), bending over (LR-3.15; open-5.87), sitting up (LR-2.51; open-5.13), daily activities (LR-2.48; open: open-5.75), coughing (LR-2.95; open: open-5.75), walking (LR-2.36; open: open-4.62), upstairs (LR-2.77; open: open-4.31), exercising (LR-3.19; open: open-6.14) and overall comfort (LR-17.62; open: open-40.23).[22] The median of the total score in open umbilical hernia repair group was 39; it was 5 for Laparoscopic umbilical hernia repair. There was a statistically significant difference between all scores in the study group ($p<0.001$).

In the current study, the median sensation of mesh (Total score) in open umbilical hernia repair group was 12; it was 1 for laparoscopic umbilical hernia repair. This is in line with that of Colavita et al, who noted that there was a trend within the OVHR group toward increasing mesh sensation over time as indicated by a significant rise ($p=0.008$) in the frequency of mesh sensation from 17.1% at one month to 26.0% at six months.[21]

The median of pain (Total score) in open umbilical hernia repair group was 18; it was 3 for Laparoscopic umbilical hernia repair. The median of movement limitations (Total score in open umbilical hernia repair group was 10, it was 10 for laparoscopic umbilical hernia repair. The difference in study group between the sensation of mesh, pain, movement limitations totals scores was statistically significant ($p<0.001$). The sensation of the presence of mesh was noted in 4% of the LUH group while 48% of them in the OUH group felt it. The overall pain score was 3 in LUH group, and it was 18 in the OUH group. The movement limitations were noted more often in OUH (10) group than the LUH group (1). Colavita et al, reported that the adjusted QOL outcomes for LVHR versus OVHR for the significant pain it was 1.9, for activity limitation (1.6), for mesh sensation (1.3) and overall symptoms it was 1.6 and all the differences except mesh sensation was statistically significant.[21]

A recent meta-analysis by Hajibandeh et al concluded that best available evidence (randomised and non-randomised studies) suggests that laparoscopic repair of umbilical or paraumbilical hernias may be associated with a lower risk of wound infection, wound dehiscence and recurrence rate, shorter length of stay but longer operative time.[23]

Laparoscopic umbilical hernia leads to lesser operative time, early postoperative recovery and comparatively superior quality of life, as compared to open umbilical hernia repair. The key limitation of the current study was non-randomized nature of the study participants into the study. The differences in the demographic, which influenced the selection of a particular procedure by the patients would have an influence on the outcome. This would have introduced some bias in attributing the outcomes to the procedure alone, the direction and magnitude of which is difficult to estimate. Also, the lack of blinding would have resulted in ascertainment bias, even though we have made all efforts to assess the outcomes in an objective manner, using standardised

study tools. Scientifically designed randomised controlled trials may provide a better quality of evidence on the subject. Also, there is a need to study the influence of various patient-related factors on quality of life. Till such time, patients should be provided with detailed information regarding various aspects both the methods and shall be allowed to make an informed choice regarding the procedure.

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Original Research Article

Comparison of treatment outcome following rubber band ligation vs injection scleratherapy for treatment of hemorrhoids: a prospective observational study

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Abstract

Background: Most common anorectal diseases seen in the community is hemorrhoids. The treatment aspect of each stage of hemorrhoids varies. Conservative treatment for first and second stages is preferred. Failure of conservative treatment and advanced diseases hasother options like sclerotherapy, ban ligation, cryosurgery and stapling. The objective of the present study is to compare treatment outcome of rubber band ligation and sclerotherapy in stage 2 hemorrhoid cases. **Methods:** Prospective observational study including uncomplicated stage 2 hemorrhoids cases was conducted in department of general surgery, Velammal Medical College. Madurai. The study population was divided into two groups by random allocation treatment procedure of rubber band ligation or sclerotherapy was allotted. The study was conducted during March 2018 to December 2018. **Results:** Total of 116 patients were included for analysis. The mean of group I was 53.2±4.63yrs and in group II was 52.7±5.37 yrs. The male and female distribution was almost similar in both groups. 41 of the group I patients and 37 of group II patients had stage 2 disease. 29% in group I and 36% in group II had stage 3 disease. In group I, 82.75% participants had complete recovery and 10.35% participants had partial recovery. In group II, 79.31% participants had complete recovery and 17.51% participants had partial recovery. The difference in the proportion of post-operative outcomes between study groups was statistically not significant. Comparison of pre and post-operative SS score between the two study groups was statistically significant. **Conclusions:** Stage 2 and 3 hemorrhoids warranting OPD based interventional procedures were presented with almost similar set of symptoms. The rubber band ligation and injection sclerotherapy both had similar post treatment outcome. Based on the patient's willingness and surgeons' decision any method can be chosen for the benefit of the patient.

Keywords: Hemorrhoids, Rubber band ligation, Sclerotherapy

Introduction

Hemorrhoids are most common, affecting up to one quarter of all adults according to some estimates. Large number of interventions exists for their management. These range from topical and medical therapies to outpatient treatments and surgical interventions that aim to fix or excise[1]. Hemorrhoids are polysymptomatic, making it difficult to judge on the management course.

Recently introduced novel hemorrhoid management techniques, such as stapled haemorrhoidopexy, Ligature excision and hemorrhoidal artery ligation, aim to reduce harm whilst maintaining or improving on outcome[2].

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"These new techniques are universally more expensive, and available good quality data suggest the additional cost does not necessarily equate to universally better outcomes compared with traditional older interventions, such as rubber band ligation and excision hemorrhoidectomy [3]. Whatever the intervention selected for treatment, it is clear that this should be tailored to the individual based on patient choice, convenience and degree of hemorrhoids.

Hemorrhoids represent pathological changes inthe anal cushions, a normal component of theanal canal involved in aiding evacuation of stooland fine-tuning of anal continence. These pathological changes include rupture of the supporting connective tissue within the cushions,

resulting inenlargement of the vascular plexus[4]. The pathogenesis of hemorrhoids explains the symptoms associated with the condition: bleeding, swelling and prolapse, seepage due to the disruption of thefine tuning of continence and consequent irritation of the perianal skin. More severe symptoms may include thrombosis leading to pain[5].Treatment options for hemorrhoids are varied; however, the evidence base for many of the seoptions has, until recently, been poor.

Despitethe poor scientific substantiation, some of the set treatment options have stood the clinical test of time. However, many new options have been introduced since the turn of the century[6]. There isrecent scientific support for some of these neweroptions that allow an evidence-based update to management [4].

The objective of the present study was to compare treatment outcome among patients undergoing rubber band ligation and sclerotherapy for hemorrhoids.

Methods

Study settings: The study was conducted in the department of general surgery Velammal Medical College. Madurai. Prospective recruitment of cases was done based on selection criterion. The study was conducted during March 2018 to December 2018. The study was approved by institutional ethical committee of Velammal Medical College, Madurai.

Study Participants: Patients diagnosed with grade 2 and 3 haemorrhoids were recruited after obtaining informed consent.

Sampling Methods: The sampling technique used was consecutive non probability sampling. The patients were divided into two groups based on computer generated list of random numbers. Group I was allocated Rubber band ligation and Group II was allocated Sclerotherapy.

Inclusion Criteria: Male and female patients of more than 20 years and above presenting with bleeding per rectum with or without associated symptoms like mucosal prolapse, discharge, pruritis and pain as well having being diagnosed on history and proctoscopy findings like visible bleeding and engorged anal cushions were included in the study.

Exclusion criteria: Patients having bleeding diathesis, or on anticoagulants, having anal fissure and/or peri-anal abscess, pregnant ladies or having any other advanced disease were excluded from the study.

Random Allocation: The procedure and its associated complications were explained to each patient in detail. SS score was noted at the time of presentation on the basis of history. Degree of haemorrhoids was ascertained on an proctoscopy in all patients. They were divided into two groups RBL and IST based on computer generated table of random numbers. Rubber band ligation was done in RBL group and IST was done in IST group patient as an OPD procedure.

Rubber band ligation: In RBL group, each patient was briefed about the procedure and placed in knee elbow position. Barron's Gun and Elise's tissue forceps were used to apply the Rubber Band at the base of each haemorrhoid.

Injection sclerotherapy: After anoproctoscopy and proper identification of position and degree of haemorrhoids, haemorrhoidal tissue was grasped with Elise's tissue forceps through Barron's Gun and rubber band was placed at insensitive area above the dentate line. In IST group, each Patient was briefed about the procedure and placed in knee elbow position. No bowl preparation was done.

Five percent phenol in almond Oil was taken in a disposable syringe with 20-gauge spinal needle and a well lubricated proctoscope was inserted gently into the rectum. Obturator was removed and proctoscope slowly withdrawn till the pedicle of the haemorrhoid to be injected became visible. Needle of the syringe was inserted into the submucosal plane of the pedicle above the dentate line. Suction with the needle was done to rule out any possibility of intravascular injection.

After confirmation of proper placement of needle in submucosal plane, 3-5 ml of the solution was injected into each pile in a single setting. No more than two haemorrhoids were injected at a time. After the withdrawal of the needle, oozing of the solution was stopped by applying local pressure with a gauze pack and forceps for 2-3 minutes which also helped in controlling the bleeding from injection site.

Patients were informed about the heaviness and occasionally desire to defecate after the injection. Post injection patients were advised not to try to defecate for next 24 hours. They were also advised not to strain and to contact the doctor in case of any problem in relation to treatment. Patients in both groups were observed for 30 minutes for immediate complications like pain and bleeding. Repeat anoproctoscopy was done to look for bleeding if necessitated in these patients.

Follow Up: Patients were then followed up on 15th post procedure day and improvement in SS score was noted. Patient's personal data, presenting complaints, findings on general physical and rectal examination, initial SS score, procedure done, any complications, final SS score and degree of improvement were noted on Performa. All the data collected was entered in IBM statistical package for social sciences (SPSS) version 21.0.

Results

A total of 116 patients, with 58 people in Rubber Band Ligation (group I) and 58 patients in IST (group II) were included in the final analysis.

Table-1: Comparison of baseline characteristics of study population.

Parameter	Group I(RBL) N=58	Group II (IST) N=58	P value
Age	53.2 ± 4.63	52.7 ± 5.37	0.592
Gender			
Male	33 (57%)	37 (63%)	0.447
Female	25 (43%)	21 (37%)	
BMI	26.8 ± 5.78	25.93±4.93	0.385
Mean duration of illness in days	37 ± 8.43	43±7.78	0.001
Presenting symptoms			
• Bleeding per rectum	58 (100%)	58 (100%)	*
• Mucosal prolapse	37 (63.79%)	33 (56.89%)	0.447
• Associated pruritus	10 (16%)	8 (13.79%)	0.608
• Associated Pain	15 (25.86%)	17 (29.31%)	0.677
• Discharge per rectum	12 (20%)	10 (17.24%)	0.635
Grade of haemorrhoids			
I	0 (0%)	0 (0%)	*
II	41 (70.69%)	37(63.79%)	
III	17 (29.31%)	21 (36.21%)	

*No statistical test was applied- due to 0 subjects in the cells

The mean age was 53.2 ± 4.63 years in people with group 1 (RBL) and it was 52.7 ± 5.37 years in people with group II (IST) group. The difference between two groups was statistically not significant (P value 0.592). In group I (RBL), 33(57%) participants were male and remaining 25 (43%) participants were female. In group II (IST), 37 (63%) participants were male and remaining 21 (37%) participants were female.

The difference in the proportion of gender between study groups was statistically not significant (P value 0.447). In group I (RBL), for all 58 (100%) participants had bleeding per rectum. In group II (IST), for all 58 (100%) participants had bleeding per rectum. The difference in the proportion of mucosal prolapse between study group was statistically not significant (P value 0.447).

The difference in the proportion of associated pruritus between study group was statistically not significant (P value 0.608). The difference in the proportion of associated Pain between study group was statistically not significant (P value 0.677). The difference in the proportion of discharge per rectum between study group was statistically not significant (P value 0.635). The mean BMI was 26.8 ± 5.78 in people with group 1 (RBL) and it was 25.93 ± 4.93 in people with group II (IST) group. The difference between two groups was statistically not significant (P value 0.385).

The mean duration of illness was 37 ± 8.43 days in people with group 1 (RBL) and it was43 ± 7.78 days in people with group II (IST) group. The difference between two groups was statistically significant (P value 0.001). In group I (RBL), 21 (70%) participants were grad II and 9 (30%) participants were grade III. In group II (RBL), 19(63.33%) participants were grad II and 11 (36.67%) participants were grade III.

Table-2: Comparison of post-operative outcomes between the study groups

Parameter	Group I(RBL)N=58	Group II (IST)N=58	P value
Complete recovery	48 (82.75%)	46 (79.31%)	0.425
Partial recovery	6 (10.35%)	10 (17.51%)	
No recovery	4 (6.89%)	2 (3.44%)	

In group I (RBL), 48 (82.75%) participants had complete recovery and 6 (10.35%) participants had partial recovery. In group II (IST), 46 (79.31%) participants had complete recovery and 10 (17.51%) participants had partial recovery. The difference in the proportion of post-operative outcomes between study group was statistically not significant (P value 0.425). (Table 2)

Table-3: Comparison of pre and post-operative SS score between the two study groups.

Parameter	Group I(RBL)N=58	Group II (IST)N=58	P value
Pre-operative SS score	4.49 ± 1.89	1.25 ±0.89	0.001
Post-operative SS score	4.52± 1.63	4.52± 0.78	1.000

The mean pre-operative SS score was 4.49 ± 1.89in people with group1 (RBL) and it was1.25±0.89in people with group II (IST) group. The difference between two groups was statistically significant (P value 0.001). The mean duration of illness was 4.52± 1.63in people with group 1 (RBL) and it was4.52± 0.78in people with group II (IST) group. The difference between two groups was statistically not significant (P value 1.000). (Table 3)

Discussion

Hemorrhoids develop from engorgement and prolapse ofthe submucosal anal cushion, which composed of an interlacingarteria-venous hemorrhoidal plexus, supported byconnective tissue and minute muscle fibres[7]. Hemorrhoids occur universally and are found since ancient times. The etiology remains indecisive and mostly patients present after the development of symptoms. The symptoms range from bleeding per rectum to prolapse of the mucosa.

All symptomatic cases need treatment indefinitely. Due to social stigma and hesitancy patient delay seeking medical care and mostly present with grade 2 or 3 hemorrhoids. So, every bleeding per rectum is considered are due to hemorrhoids until proved otherwise. Rubber band ligation is an optimal outpatient procedure for hemorrhoids and rectal mucosal prolapse.

A prospective randomized trial done by Murie et al [8]RBL was equally effective as that of haemorrhoidectomy in treating second grade hemorrhoids. RBL was effective 70% in treating third grade hemorrhoids. They proved that even the complications after the procedure was minimal and manageable. RBL being an OPD procedure reduced the need for hospital stay and resource wastage. A study done by Ambrose et a showed that infrared photocoagulation also was as good as RBL. However, the group randomized to the photocoagulation arm required furtherout-patient treatment more often than the RBL arm [2]. Poenetal [9] showed in a randomized controlled trial that RBL andinfrared coagulation were equally effective, but pain was significantly more common and more severe in the RBL group. In the present study the male preponderance was observed, similar to Khan et al study[10]. Half of men and women aged above fifty years have the chances of developing hemorrhoids in their life time[2]. In this present study, the mean age of participants was53.2 ± 4.63years, 52.7 ± 5.37 years respectively in groups. This was similar to the findings observed in various studies that hemorrhoids occurred more commonly among people above 50 yrs of age[11, 12]. Injecting sclerotherapy is indicated in first grade hemorrhoids with bleeding and second grade hemorrhoids.

Sclerotherapy is the gold standard in the first-degree hemorrhoid treatment similar to rubber band ligation, injection sclerotherapy may also be undertaking in the outpatients setting [4,13]. Among Treatments that prevents the progression of disease, sclerotherapy has less number of complications and good compliance [5]. Pain is the most common complain after the procedures. The patient often complains of intra anal discomfort. The reported incidence of pain following injection sclerotherapy ranges from 9% to 70% and in RBL 5 to 85% [14]. The other significant side effect reported is rectal bleeding. It is seen in 2-10% of casesafter sclerotherapy, 1 to 15% after rubber band ligation[15]. The Chew et al combined injection sclerotherapy with

RBL achieved 90 percent of success. The complication rate was of 3.1 percent with an overall recurrence rate of 16 percent. Only 7.7 percent of thesepatients required hemorrhoidectomy [16]. Proper technique and making office treatment for first to thirdgrade hemorrhoids tolerable and satisfying[17]. Kaman L et al reported a patient who underwent submucosal injection sclerotherapy for hemorrhoids andpresented with necrotizing fasciitis of the anorectum, perianal region and scrotum. Post-operatively, the patient developed septicemia and renal failure requiring an extended hospital stay[18].

In this present study after treatment with injection sclerotherapy, 79.31% had complete recovery. In a study Bhuiya et al using 5% phenol in olive oil as sclerosant satisfactory results were seen in 60.41% patients after the first dose, 15.78% patients after the second dose and 3.12% after the third dose injection sclerosant[19]. In Rubber band ligation group 83.3% had complete recovery. Proving that both RBL and injection sclerotherapy can be an effective treatment for grade 2 and 3 hemorrhoids. The overall success rate reported for these procedures in the past ranges from 80% to 90% [20-22]. In second grade and third grade hemorrhoids RBL had long term efficacy in terms of lower recurrence and less complications [6, 23-26].

Many comparative studies have been done in past between the two modalities, but none have given a clear advantage of one procedure over another. A meta analysis done by Johanson et al have shown that at the end of twelve months followup period, patients who underwent RBL had low pain and recurrence rate[1].

The advantages of these procedures being the time taken for completing the procedures are short. The patients recover fast after the procedure. Single outpatient sitting is enough for treating multiple hemorrhoids. These kind of outpatient procedures are less painful.

This study was hospital based and done on limited sample. Large community-based studies in future will help throw light on the prevalence of the disease and acceptance of treatment. Randomized controlled trials can be done to provide high quality evidence.

Conclusion

Based on thisstudies result it can be concluded that both rubber band ligation and injection sclerotherapy are equally effective in the treatment of hemorrhoids. The choice of the procedure should be done based on the patient's willingness and the surgeon's expertise. Early detection and correction can prevent development of complication at later stages.

Contribution by primary investigator: Karpagavel Chandrabose, **Guide:** Dr. Venkatesh Subbiah

What this study adds on to Existing Knowledge: This study is first of its kind in this region. This study has proven that for grade 2 and 3 hemorrhoidsoutpatients procedures like RBL and IST can be effectively used for management. These procedures have minimal side effects and good compliance. Thereby, reducing the need for hemorroidectomy

Declarations

Conflict of interest: None declared.
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Original Research Article

Profile and complication rate of thyroid surgeries performed in a tertiary care teaching hospital, a prospective observational study

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Abstract

Background: One of the most common endocrine disorder is the thyroid diseases. The prevalence and pattern of these conditions depends on sex, age, ethnic and geographic patterns. The incidence of thyroid nodules increases with the age hence benign and malignant thyroid disease is common in the elderly population. **Aim:** To compare the complication rate of various thyroid surgeries for benign and malignant diseases in a tertiary care teaching hospital. **Methods:** This study was a prospective observational study, Velammal medical college hospital at Tamil Nadu from December 2018-June 2019. The patients who underwent thyroid surgery for various thyroid disorders were enrolled in the study. **Results:** Out of117 cases, 107 were women and 10 were men. Multinodular goiter (MNG)was the most common (38.46%) condition, followed by solitary nodule (29.06%) and toxic MNG (18.8%). Among women, 40.19% were identified with multinodular goiter followed by solitary nodule (28.97%). Subtotal thyroidectomy was performed for 88.89% of MNGs, while 91.18% of the solitary nodule were managed by hemithyroidectomy Majority of the patients with toxic MNG underwent subtotal thyroidectomy with 99.91%. While 84.61% of the patients with thyroid cancer were treated by total thyroidectomy. The overall incidence of complications was 27.35%. The incidence rate of complications was high in patients with malignant disease, as compared to benign disease (69.23% in Malignant Vs 36.36% in toxic MNG and 24.44% in MNG). **Conclusion:** Through the present study, it was concluded that the complications associated with the different thyroid surgeries and various precautions that can be taken to reduce the complications.

Keywords: Thyroid, Thyroidectomy, Complications, Multinodular goiter, Surgery

Introduction

Worldwide, diseases associated with thyroid gland is one of the most common endocrine disorder. Various benign and malignant thyroid conditions are amenable to treatment by surgical intervention. These surgical procedures may range from hemithyroidectomy to sub-total, near-total and total thyroidotomies. The choice of surgical procedure may depend on the type and extent of the disease [1,2].

The surgical procedures on thyroid may be associated with a plethora of transient or permanent complications [3]. The most common immediate surgical complication of total thyroidectomy is post-operative hypocalcemia [4]. The permanent recurrent laryngeal nerve palsy and permanent hypoparathyroidism are the major complications followed by total thyroidectomy [5]. The pressure complaints, shorter complaining period, malignancy and more radical surgeries are the factors influencing thyroidectomy complications [3]. The risk of permanent complications is high in patients who performed surgery for the recurrence of benign thyroid disease [6]. Total thyroidectomy is considered as the treatment of choice for various thyroid diseases except in case of thyroid carcinoma and a few benign diseases due to its risk involved [1]. It is performed mainly in malignant thyroid disease as it can reduce the rate of recurrence and reoperations. The risk of recurrence is high with subtotal thyroidectomy performed for benign thyroid diseases [6].

The reported rate of complications after surgery for benign thyroid disease ranges from 0 to 1.8%. The risk of permanent complications reported is 3 to 4%. The complication rate of thyroid surgery for malignant thyroid is high as compared to benign thyroid disease.

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The reported incidence of permanent recurrent laryngeal nerve injury is 0 to 4% [7]. The patient condition, thyroid disease, surgeon's experience and type of surgery are the factors associated with the post-operative results from thyroid surgery [3]. The hyperthyroidism and goiter size are the independent factors for the development of complication in total thyroidectomy [8].

Complications associated with total thyroidectomy can be reduced by performing surgeon's experience, monitoring and identifying patients at risk [9].

A thorough understanding of the profile of thyroid surgeries and the likely complications is essential for surgeons dealing with them. This understanding can help them in minimizing the incidence of complications and effective risk communication to the patients. But the studies on the subject are scarce on the Indian population.

Hence, the present study was performed to compare the complication rates after thyroidectomy for benign disease and malignant disease and also to identify the ways to reduce the complication rates.

Aims and Objectives

1. The study aims to compare complication rates of subtotal thyroidectomy, near-total thyroidectomy, hemithyroidectomy and total thyroidectomy in a cohort of patients undergoing surgery for various thyroid disorders.
2. To compare complication rates after thyroidectomy for benign disease and malignant disease.

Materials and Methods

Study setting: The study was conducted on patients who underwent thyroid surgery, for various thyroid disorders at the Velammal medical college hospital, Madurai, Tamil Nadu, India.

Study design: The current study was a prospective observational study.

Study period: The study was conducted between December 2018 to June 2019.

Sample size: This study has 117 included undergoing thyroid surgery.

Inclusion criteria: The study had included, all the adult patients, of both genders, undergoing surgery for various conditions, including non-toxic multinodular goiter (MNG), toxic multinodular goiter, nontoxic solitary nodular goiter, colloid goiter and thyroid carcinoma.

Exclusion criteria: The study had excluded pediatric patients

Data collection procedure: Data was collected be retrospective case record review, using a structured proforma

Data analysis: Data was analyzed using IBM SPSS statistical software version 23. Descriptive analysis was done using mean and standard deviation for quantitative variables, frequency and proportion of categorical variables.

Ethical consideration & permission: Considering the retrospective nature of the study, the study was not subjected to approval of Institutional Human ethical committee and was also not possible to obtain informed written consent from the participants.

Confidentiality of the study participants was maintained throughout the reporting of study results.

Any scoring system: No scoring systems were used.

Surgical procedure: Operations were performed by different levels of faculty. When the procedures were performed by postgraduates, they were done under the close supervision of senior surgeons. For all the included patients a through history was elicited, followed by a complete physical examination.

The basic biochemical and hematological investigations were done for all patients. It was decided to request special investigation like thyroid hormone profile and serum calcium estimation only in selected cases, where a disturbance in the functional status was suspected.

Vocal cords were examined pre-operatively by indirect laryngoscope in all the patients, whereas postoperative vocal cord examination was performed only when hoarseness occurred. Patients were classified as having hypocalcemia (hyperparathyroidism) if both clinical and biochemical (a fall in corrected serum calcium supplementation supportive evidence were present.

FNAC was done for all patients based on the final diagnosis the treatment was given as advised by the experts. The details of each patient were documented as shown in a structured proforma.

Results

Table-1: Gender wise frequency of different types of thyroid surgeries performed.

	Male (N=10)	Female (N=107)	Total (N=117)
Colloid goiter	1 (10%)	2 (1.87%)	3 (2.56%)
Solitary nodule	3 (30%)	31 (28.97%)	34 (29.06%)
Multinodular goiter	2 (20%)	43 (40.19%)	45 (38.46%)
Toxic MNG	3 (30%)	19 (17.76%)	22 (18.8%)
Thyroid cancer	1 (10%)	12 (11.21)	13 (11.1%)

Out of 117 cases, 38.46% of patients underwent thyroid surgery for multinodular goiter followed by the solitary nodule, toxic MNG, thyroid cancer and colloid goiter with 29.06%, 18.8%, 11.1% and 2.56% respectively. Among females, 40.19% of the patients were identified with multinodular goiter followed by solitary nodule, toxic MNG, thyroid cancer and colloid goiter with 28.97%, 17.76%, 11.21% and 1.87% respectively whereas among males majority was identified with solitary nodule and toxic MNG with 30% each followed by multinodular goiter, colloid goiter and thyroid cancer with 20%, 10% and 10% (Table 1).

Table-2: Condition wise surgical procedure performed in the study population.

Disease	Total no of patients	Type of thyroid surgery			
		Hemithyroidectomy (no of PTS & %)	Subtotal thyroidectomy	Near total Thyroidectomy	Total Thyroidectomy
Colloidgoiter	3	-	-	-	3 (00%)
Solitarynodule	34	31 (91.18%)	3 (8.82%)		-
Multinodulargoiter	45	2 (4.44%)	40 (88.89)	1 (2.22)	2 (4.44)
Toxic MNG	22	-	20 (90.91)	-	2 (9.09)
Thyroid cancer	13	1 (7.69%)	-	1 (7.69%)	11 (84.61%)
Total (117)	**117**	**34 (29.06%)**	**63 (53.85%)**	**2 (1.71%)**	**17 (14.53%)**

Majority of the patients with multinodular goiter underwent subtotal thyroidectomy with 88.89% followed by hemithyroidectomy with 4.44%. 91.18% of patients performed hemi thyroidectomy surgery for a solitary nodule, followed by subtotal thyroidectomy with 8.82%. Out of 22 patients, 90.91% of patients performed subtotal thyroidectomy surgery for toxic MNG followed by total thyroidectomy with 9.09%. Majority of the patients with thyroid cancer performed total thyroidectomy with 84.61% followed by near-total thyroidectomy and hemithyroidectomy with 7.69% and 7.69% respectively. Total thyroidectomy was the only surgery performed in patients with colloid goiter (Table2).

Table-3: Incidence of complications in the study population.

Parameter	Total Number	Total number of people with complications	Percentage of complications
Overall complications	117	32	27.35%
Thyroid disorder wise			
Colloid and recurrent goiter	3	3	100%
Solitary nodule of thyroid	34	1	2.94%
Multinodular goiter	45	11	24.44%
Toxic multinodular goiter	22	8	36.36%
Thyroid carcinoma	13	9	69.23%
Type of surgery wise			
Hemithyroidectomy	34	1	2.94%
Subtotal thyroidectomy	63	15	23.80%
Near total thyroidectomy	2	1	50%
Total thyroidectomy	17	15	88.23%
Benign Vs Malignant			
Benign disorders	104	23	22.12%
Malignant diseases	13	9	69.23%

The overall incidence of complications was 27.35% in the study population. Among the disease conditions, all the 3 subjects with Colloid and recurrent goiter developed complications. Among the people thyroid carcinoma, 69.23% developed complications. The proportion of people with complications was 36.36% and 24.44% among the Toxic multinodular goiter and Multinodular goiter respectively. Among the surgical procedures, total thyroidectomy was associated with the highest incidence (88.23%) of complications, followed by Near total thyroidectomy (50%), Subtotal thyroidectomy (23.80%) and least by Hemithyroidectomy. The incidence rate of complications was high in patients with the malignant disease, with 69.23% as compared to 22.12% of the benign conditions reporting complications (Table 3).

Table-4: Histopathological diagnosis with the complication of each operative procedure.

Histological diagnosis	Total no of patients	Number of complications occurred in			
		Hemithyroidectomy	SBT	Near TT	Total Thyroidectomy
Colloid and recurrent goiter	3	-	-	-	3 (100%)
Solitary nodule of thyroid	34	1 (2.94%)	-	-	-
Multinodular goiter	45	-	8 (17.7%)	-	3 (6.66%)
Toxic multinodular goiter	22	-	7 (31.82%)	-	1 (4.54%)
Thyroid carcinoma	13	-	-	1 (7.69%)	8 (61.54%)

All the 3 subjects with Colloid and recurrent goiter, underwent total thyroidectomy, and all of them developed complications. The only complication among people with a solitary nodule of thyroid happened with hemithyroidectomy. Among the 45 multinodular goiter patients, 8 (17.7%) complications occurred with SBT and 3 (6.66%) complications occurred with Total thyroidectomy. Among 22 cases of toxic multinodular goiter 7 (31.82%) had complications with SBT and 1 (4.54%) complication occurred with Total thyroidectomy. Among 13 cases of thyroid carcinoma1 (7.69%), a complication occurred with near Total thyroidectomy, and 8 (61.54%) complications occurred with Total thyroidectomy (Table 4).

Discussion

Worldwide, thyroid disease is very common. In India, approximately around 42 million people are affected by the thyroid disease. It is considered as the common most endocrine disorder [10]. The prevalence of thyroid disease and thyroid malignancy is high, with an increase in age [11]. Globally, one of the common most surgery performed is thyroidectomy. The incidence of complications following thyroidectomy is associated with the difficulty involved in the procedure performed [12]. Thyroid surgery is performed based on the type and severity of the thyroid disease. In this study, the incidence of thyroid disease and the comparison of complications associated with various thyroid surgeries were carried out.

In the present study, the number of females was more as compared to males. The present study resembles to the study performed in Pakistan by Hussain N et al [13] in which out of 662 cases, 570 were females and 92 were males. In a retrospective study conducted by Salami B et al [14] in a population of 175 patients majority of the patients were females with 86.3% followed by males with 13.8%. Joseph E et al [15] performed a study in Kerala for a period of 6 years in a population of 801 in which 716 patients were females and 85 were males. In most of the published studies, the majority of the patients were females which indicates that the risk of developing the thyroid disease is high among the women as compared to men which can be due to various reasons. Among females, 40.19% of the patients was identified with multinodular goiter which is similar to the Kolur A et al [16] study published in 2014 in which majority of the patients with multinodular goiter was females with 92.24%.

Depending upon the gender, age, ethnic and geographical pattern the prevalence and pattern of thyroid diseases can vary. In the current study majority of the patients was diagnosed with multinodular goiter with 38.46%, followed by solitary nodule and colloid goiter with 29.06% and 2.56% which resembles the study result performed by Kolur A et al [16] in which 58.10%, 30.16% and 2.79% were identified with multinodular goiter, solitary nodule and colloid goiter. In the study performed by Haque GS et al [17] 48.5% of patients was diagnosed with multinodular goiter. The most common thyroid disease in Hussain, N et al [13] study was multinodular goiter with 61.63% of patients. In a retrospective study conducted by Joseph E et al [15], in Kerala 71.5% of patients was identified with

multinodular goitre. The present study resembles Darwish A, et al [18], study which was conducted in a population of 110 patients in which 45.5% of patients was identified with nodular goiter followed by malignancy with 24%. Out of 117 cases, 53.85% of cases underwent subtotal thyroidectomy followed by hemithyroidectomy, total thyroidectomy and near total thyroidectomy with 29.06%, 14.53% and 1.71% respectively.

In a study, Hussain A. et al [19] Performed in Pakistan the majority of the patients underwent subtotal thyroidectomy with 42.6% followed by hemithyroidectomy, total thyroidectomy and near total thyroidectomy with 36.5%, 15.2% and 3.9% respectively which is similar to the current study.

The type of thyroid surgery performed varies in different studies based on the type of thyroid disease and study population. In various studies, the subtotal thyroidectomy is the surgery performed mainly for the thyroid disease.

Chen KC et al [20] Conducted a study on 314 cases in which 13.5% of patients undergoing bilateral total thyroidectomy. The majority of the patients underwent total thyroidectomy with 61.1%followed by subtotal thyroidectomy and near total thyroidectomy with 36% and 2.4% respectively in a study performed by Vaiman M et al [21].

Majority of the patients identified with multinodular goiter in the present study underwent subtotal thyroidectomy and hemithyroidectomy. This was similar to the study conducted in Kerala by Kolur A et al [16] in a sample size of 179 participants in which patients presented with multinodular goiter was performed with subtotal thyroidectomy and hemithyroidectomy with 50.96% and 20.8% respectively. In the present study 84.16% of patients performed total thyroidectomy for thyroid malignancy.

Bhattacharyya N et al [4] presented a study in a population of 517 patients in which thyroid cancer was the most common indication for total thyroidectomy. The complications associated with thyroid surgery was high among total thyroidectomy and subtotal thyroidectomy.

The rate of complication varies between different thyroid surgeries. The complications which occur during and followed by the surgery can be reduced with the experience of the performing surgeon, monitoring and follow-up of the patients.

In the current study, the number of complications in total thyroidectomy and subtotal thyroidectomy performed for multinodular goiter was high with 6.66% and 17.7% respectively which is similar to the study done by Cifici F et al [22] in which 30.46% and 19.56% were the rate of complications followed by total thyroidectomy and subtotal thyroidectomy in multinodular goiter. The rate of complications varies based on the severity of disease and patient response.

In the present study, 11.11% of patients was identified with malignant disease. In a retrospective study conducted by Abdoulaye O et al [23] in a sample size of 53 patients for a period of 3 years 5.7% was reported with malignancy disease.

The rate of complications varies between patients with the malignant and benign disease based on the disease condition and management. The incidence rate of complications was high in patients with the malignant disease with 69.23% in the present study which is conflicting to the study result performed by Iddings D et al [9] in which majority of the patients had benign pathology with 68%. In a study conducted for the population size of 83, the complication rate for the malignant disease was 10% and 2% for benign diseases in Spear SA et al [7] study.

Limitations & recommendations: The study sample size was very limited; hence, there is a higher probability of chance findings. There is a need to conduct further large scale studies on the subject, for the more in-depth understanding of the complication rate and the factors influencing them. Also, clinicians need to be aware of the common complications and their incidence among patients undergoing thyroid surgery for effective risk communication and prevention of complications.

Conclusions

Majority of the participants undergoing thyroid surgery in the current study were women, emphasizing a significantly higher risk of thyroid disease among women. Multinodular goiter (MNG) was the most common condition, followed by solitary nodule and toxic MNG for which thyroid surgery was performed.

In women, MNG was the most common condition, and in men, solitary nodule and toxic MNG were relatively common. Subtotal thyroidectomy and hemithyroidectomy were the common procedures performed on mNG and solitary nodule patients, respectively. More than one-fourth of the subjects developed

complications. The incidence rate of complications was high in patients with malignant disease, as compared to benign disease (MNG and toxic MNG). All three cases of colloid goiter developed complications in the study.

What the study adds in the existing knowledge?

The prevalence of thyroid diseases is increasing therefore there is a need of updating knowledge regarding this condition. The present study enhances the present knowledge regarding various thyroid diseases.

The complications involved in thyroid surgery is high thereby patients is at high risk. By understanding more about the condition surgeons can make patient selection more appropriate for surgery and rate of complications can be reduced. Physicians and other health care professionals can make patient more aware about their disease condition and its associated complications. It can reduce the post operative complications.

Author's contribution

Dr. Karpagavel Chandra Bose had conceptualized the study, prepared the study protocol, and conducted the data collection, analysis and manuscript writing. He has verified all the drafts and approved the final draft.

Dr. Vijaiaboobbathi Sathiah had provided key inputs on methodology during protocol preparation, supported data compilation and analysis. He has also edited all the drafts and approved the final draft of the manuscript.

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A study to compare the effects of single dose intravenous dexmedetomidine and clonidine on bupivacaine spinal anaesthesia

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Abstract **Background:** Dexmedetomidine, also an α2-adrenergic agonist, used for pre-medication and as additive to general anesthesia. Dexmedetomidine when given intravenously decreases the inhalational anesthetic and opioid requirements during general anesthesia. This study has been undertaken as the hypothesis that dexmedetomidine and clonidine when given intravenously might prolong the duration of spinal analgesia. This technique may be helpful for increasing the duration of spinal anesthesia. **Aim and objective:** The aim of this study is to evaluate the effects of intravenous dexmedetomidine and clonidine on duration of spinal anesthesia and to assess the hemodynamic changes and the level of sedation. **Materials and methods:** It is a prospective Randomised study conducted at Government Rajaji hospital Madurai. A total of 90 patients were randomly allotted into three groups of 30 each. Group A received dexmedetomidine through intravenous route and Group B received clonidine through intravenous route and Group C received normal saline through intravenous route. **Results:** The average time taken for onset of sensory block is 57 seconds for dexmedetomidine group ,74 seconds for clonidine group and 93 seconds for control group. Thus dexmeditomidine has faster onset of sensory blockade. Mean duration time for two segmental regression in groupA is prolonged and was statistically significant than group B and group C. **Conclusions:** From our study it is concluded that dexmedetomidne can be safely used as preoperative sedation to hasten the onset of subarachnoid block and to prolong the sensory blockade without side effects.

Key Word: clonidin, Dexmedetomidine, spinal anesthesia

INTRODUCTION

Dexmedetomidine is used commonly in intensive care unit sedation and for any ambulatory procedural sedation. Like clonidine, it is an agonist of α_2 adrenergic receptor. Spinal anesthesia is commonly performed for infraumbilical surgeries. Additives are added to spinal anesthesia in order to prolong the duration of blockade and to reduce adverse effects due to local anesthetics. Thus procedures of longer duration can be done comfortably as block regression is slower. Agents starting from neostigmine, fentanyl to magnesium sulfate have been used as adjuncts to local anesthesia for prolonging the duration of spinal blockade. Small doses of dexmedetomidine (3 µg) used in combination with bupivacaine in spinal anesthesia resulted in shorter onset of motor block and prolongation in the duration of motor and sensory block with well preserved hemodynamics and minimal sedation. Clonidine an α2-agonists, has been used generally in the intrathecal route But when used intravenously within one hour after spinal block it extends the duration of spinal blockade for roughly one hour without undesirable effect.

AIM OF THE STUDY

To assess the efficacy and to compare the effects of single dose intravenous dexmedetomidine and clonidine effects on spinal anesthesia. Efficacy is assessed by, Onset of Sensory block, Onset of Motor block, Time for two segment level regression, Time for rescue analgesia, Intra operative sedation score, Hemodynamic stability.

MATERIALS AND METHOD

It is a prospective Randomised study conducted at Government Rajaji hospital Madurai. This study was proceeded after getting ethical committee's approval and informed written consent from the patients, who were included in this study.

Inclusion Criteria:

- Age between 35to 65 years
- Belonging to ASA I and II patients
- Either sexes
- Patients posted for lower abdominal surgeries.

METHODOLOGY

After securing good intravenous access all the patients were preloaded with 10 ml/kg of normal saline monitors: the monitors connected included spo2, ecg and nibp. Recording of baseline values: the baseline parameters were recorded (pulse rate, blood pressure, spo2, respiratory rate). Patient randomly receives either intravenous dexmedetomidine 0.5 µg/kg infusion over 10 minute or intravenous clonidine 0.8 µg/kg infusion over 10 minute or intravenous norml saline infusion over 10 minutes before spinal anesthesia. Performance of subarachanoid block: patient was placed in right lateral position and with strict asepsis and antisepsis of the region, subarachanoid block was performed at L3-L4 space using 23G quickes needle and injection Bupivacaine 0.5 % 15 mg given. Patient was then turned to supine position. Following parameters are noted:

1. Time taken for sensory blockade at T10.
2. Level of maximum sensory block.
3. Time of onset of complete motor block
4. Time for two segmental regression
5. Duration of surgery.
6. Time for rescue analgesia.

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7. Intraoperative sedation score.
8. Hemodynamic parameters, Blood pressure, Pulse rate, Spo2, Respiratory rate.
9. Complications if any.

The pin prick technique was used to locate sensory blockade level and Bromage score was used to asses the motor blockade. Score 0 for no block, Score 1 unable to raise extended knee Score 2 for not able to flex the knee, Score 3 for not able to flex ankle. Sedation was assessed with Ramsay sedation score Score 1 for patient frightened, nervous, restless Score 2 for patient is cooperative and tranquil, Score 3 for patient responds to oral commands only, Score 4 for exhibits brisk response to loud auditory or light glabellar tap, Score 5 for sluggish response to glabellar or auditory stimulus, 6 for patient exhibit no response. Vitals monitoring included pulse rate, Blood pressure, Spo2, respiratory rate for every^{2,5,10,15,30,45,60,75,90,105,120} minutes interval Fall in blood pressure more less than 25% from baseline was considered as hypotension and treated with 6 mg ephedrine and fall in pulse rate less than 50/min was considered as bradycardia and treated with Inj. Atropine.

STATISTICAL ANALYSIS

Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2010) developed by Centre for Disease Control, Atlanta. Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's chi square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

Figure 1: Onset time for sensory block

Group	Onset time for sensory block		
	Range	Mean	SD
Group A	40-90	57.7	11.9
Group B	50-140	74.3	23.3
Group C	60-140	93.5	23.0
'p' value between 3 groups	**<0.0001 Significant**		
Group A and B	**0.0009 Significant**		
Group A and C	**<0.0001 Significant**		
Group B and C	**0.0007 Significant**		

Mean duration of two segment regression in A group was 102.2 minutes and in Group B it was 93.8 minutes and in group C was 66.7. There was statistically significant prolongation of time for two segment regression in Group A than Group BandC. There was statistically significant prolongation of time for two segment regression in group B than group C.

Table 1: Time for onset of motor blockade (seconds)

Group	Range	Mean	SD
Group A	90-150	116.7	17.2
Group B	110-220	136.2	27.2
Group C	110-220	142.0	31.8

Table 2: time for first rescue analgesic (minutes)

Range	Mean	SD
120-125	195	46.4
120-220	168.3	30.3
90-200	141.3	26.5

Table 3: Time for 2 segment regression (minutes)

range	Mean	SD
90-140	102.2	18.4
60-120	93.8	16.1
50-90	66.7	15.8

Duration of motor blockade in group A is 205minutes when compared with group B and C which was about 194.5and 190.2 minutes respectively. There was statistically insignificant difference in duration of motor blockade in group A, B and C. Dexmedetomidine has extensive uses in the field of anaesthesia and intensive care medicine. It has analgesic, sedative properties without causing respiratory depression and hence can be used as an alternative to opioid. Following administration of clonidine and dexmedetomidine through intravenous route, both effectively inhibit the transmission of nociceptive impulse at spinal cord level from peripheral surgical stimulation and also has supraspinal effect at locus ceruleus, thereby acting as an additive to spinal anesthetic blockade. But dexmedetomidine is more potent alpha2 agonist with 8 time greater affinity for alpha 2 adrenoceptor than clonidine.

Demographic profile: The mean age, sex distribution, the BMI, ASA classification were comparable in all the three groups and there was no statistical difference between these groups.

Onset of sensory block: According to this study, the average time taken for onset of sensory block is 57 seconds for dexmedetomidine group ,74 seconds for clonidine group and 93 seconds for control group. Thus dexmeditomidine has faster onset of sensory blockade. This results is similar to that found in study conducted by Harsoor and colleagues.

Maximum height of sensory block: Mean higher level of sensory block in all three groups was T6. This shows that level of blockade is not affected by study drugs. This finding is similar to the results of study conducted by A Asada and colleagues.

Two segment regression time: According to this study, the mean two segment regression time is about 102 minutes in group A ,93 minutes in case of group B,66 minutes in Group C. Mean duration time for two segmental regression in group A is prolonged and was statistically significant than group B and group C with the p value of 0.0001. This is similar to that of study conducted by M Islam and colleagues.

Motor blockade: According to this study, onset time for motor blockade is 116 seconds in Group A ,136 seconds in group B and 142 seconds in group C shows early onset time of motor blockade in group A when compared to other groups. The mean duration of motor blockade is about 205 minutes in case of group A,194 minutes in case of Group B and 190 minutes in case of Group C shows duration of motor blockade is not affected by study drugs. Though motor blockade onset time in Group A has significant earlier onset with p value of 0.0008, duration of motor blockade were comparable between three groups and was statistically insignificant with p value of >0.05. This could be attributed to the fact that the conduction of sensory fibre may be more inhibited than motor fibre. The noradrenergic innervation of the spinal cord arise from the noradrenergic nuclei present in the brain stem. So, the disinhibition of the noradrenergic nuclei lead to descending inhibitory effect on spinal cord thereby prolonging the sensory block duration rather than motor block. This is similar to study conducted by those of Kaya and colleagues showed that the duration of motor blockade was not affected. **Hemodynamic**

parameters: Intraoperatively although the fall in systolic blood pressure was more in group A and group B compared to control group, the results were not statistically significant. Bradycardia occurred 6 % in group A ,3% in group B and nil in control group which was statistically insignificant. This is similar to study conducted by Jung and colleagues

Sedation score: The sedation score of most of the patients were between 2 and 3 grade i.e easily arosable with oral commands in group A and B when compared to control group where patients were anxious and restless. This is similar to study conducted by P Bansal and colleagues.

CONCLUSION

Dexmedetomidine or clonidine when administered as an infusion 10 minutes prior to the conduct of subarachnoid block using bupivacine, decreased the sensory and motor onset time, prolonged the two sensory regression time and increased the duration of sensory blockade without actually increasing the motor blockade duration. When compared to clonidine, dexmedetomidine had a statistically significant faster onset of sensory blockade, prolonged two segment regression time and duration of analgesia.

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Original Research Article

Comparison of efficacy of Nebulized ketamine versus lignocaine for postoperative sorethroat

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Keywords: Lignocaine, Ketamine, Sorethroat, Nebulization.

Abstract

Introduction: Post operative sore throat (POST) is a common post operative complaint following general anaesthesia with endotracheal intubation. Its incidence ranges from 30-75%. It may cause significant post operative morbidity and patient dissatisfaction.

Aim: The aim of the study is to evaluate the efficacy of ketamine and lignocaine nebulization.

Materials and Methods: This study is a Prospective randomised control study. After obtained Institutional Ethical Committee approval and written informed consent, 90 adult patients were randomized into three groups each consists of 30 participants. Group K received ketamine 50mg with 4ml of normal saline, Group B received lignocaine 2% 2ml with 2ml of normal saline nebulization 15 mins before induction and Group C did not receive any nebulization and is a control group.Postoperative sorethroat was monitored based on four point scale at immediate, 2, 4, 8, 12 and 24 hrs.

Results: The Severity of postoperative sorethroat was less in lignocaine and ketamine group compared to control group.On follow up for 24 hours, ketamine group provides better relief in sorethroat compared to lignocaine group.Hemodynamic parameters were comparable in all three groups.

Conclusion: Ketamine nebulization and lignocaine nebulization provides less discomfort to the patient and the severity of sore throat was less over 24 hrs in the post operative period. To conclude ketamine nebulization provides better relief of post operative sore throat when compared to lignocaine nebulization and no nebulization.

Introduction

Sore throat is a common postoperative complaint occurs in adults in the post operative period following general anaesthesia with endotracheal intubation.

Irritation and inflammation of the airway are considered to be the causes of post operative sore throat.

There are pharmacological and non pharmacological methods to decrease the incidence and severity of post operative sore throat.

The following factors influences the incidence of post operative sore throat, which includes Experience of anaesthetist, adequate relaxation of the patient, careful insertion technique, soft suction catheters, smaller tracheal tubes, minimal cuff-tracheal contact area, monitoring and adjustment of intracuff pressure and avoidance of local anaesthetic /steroid lubricants. Various methods to alleviate postoperative sorethroat has been reported in the literature. There are variable causes that can aggrevate sorethroat such as patient related factors, type of anesthesia and type of surgery. Steroids are commonly used intraoperatively to reduce airway edema and inflammation.Ketamine gargling has been used for sorethroat but due to risk of aspiration, palatability limits its usage. Lignocaine jelly applied over tracheal tube cuff may reduce sore throat but because of inaccuracy of instilled drug and short duration of action some additional management has to followed for postoperative sorethroat. Nebulization of lignocaine and ketamine prior to general anaesthesia confers good tube tolerability to patient as entire air passages is anaesthetized and attenuates sorethroat after extubation

Dexamethasone has been used to reduce the incidence of post operative sore throat. There is a reduction in incidence of sore throat following tracheal intubation after gargle with lignocaine or ketamine before induction of anaesthesia.

Materials and Methods

The study was approved by Institutional Ethical Committee and Patients were randomly allocated to Group K, Group B and Group C each group consists of 30 participants by computer generated random numbers. The anesthesiologist taking up the case is blinded to type of nebulization given to the patients.

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Inclusion Criteria
ASA physical status I, II, age group between 20 -60 years of either sex, duration of surgery less than 2hrs taken under general anaesthesia.

Exclusion Criteria
Head and neck surgeries, surgery in prone position, difficult airway and intubation attempts more than one.

Parameters monitored include postoperative sorethroat immediately after extubation, 2hrs, 4hrs, 8hrs, 12hrs and 24hrs. General anesthesia was given 10 minutes after nebulization. Standard monitors like blood pressure, ECG and SPO2 were monitored. Premedication inj glycopyrolate 0.2 mg, inj midazolam 1 mg iv given just before induction.GA induced with inj propofol 2mg/kg i.v, inj. fentanyl 2microgram /kg i.v and muscle relaxant inj. succinylcholine 2mg/kg i.v and intubation proceeded with 7-7.5 mm size endotracheal tube for women,8-8.5 mmsize for men. Position of endotracheal tube confirmed by auscultation and capnography. Endotracheal tube cuff is high volume, low pressure cuff and was inflated with air until no air leak heard with stethoscope. Cuff pressure monitor was connected and pressure in cuff is maintained between 20-22 cm H20 .Inj vecuronium 0.1mg/kg i.v loading dose given. Maintanence of anesthesia done with 50%nitrous oxide and isoflurane 1-1.5% and end tidal CO2 maintained between 30-35mmHg. Intravenous dexamethasone is given at the start of procedure. Tracheal tube cuff pressure monitored every 20 minutes and pressure is maintained between 20-22cm H2O. At the end of surgery, suctioning done and reversal inj. neostigmine 50mic/kg i.v and inj. glycopyrolate 10mic/kg was given. Patient is extubated after the patient is fully conscious and good muscle strength T4/T1ratio >0.9.Post operative pain is managed with IV paracetomol infusion 6th hourly. Postoperative sore throat, any cough, hoarseness of voice were assessed based on scores immediately after extubation, 2hrs, 6hrs, 12hrs, 24hrs postoperatively.

Post Score –severity
Grade 1: no sore throat
Grade 2: minimal says sore throat when asked
Grade 3: moderate complaint of sorethroat without question
Grade 4: severe change in voice

Primary outcome of the study was to find the incidence of postoperative sorethroat at 2hrs postoperatively in patients undergoing surgery of duration less than 2 hr. The secondary outcome of the study were to measure the incidence and severity of postoperative sorethroat at immediate recovery and 4hrs, 8hrs, 12hrs, 24hrs, and to compare the blood pressure after nebulization, at intubation and heart rate after nebulization, at intubation with baseline within these three groups.

Statistical Analysis and Interpretation
The study subjects namely lignocaine, Ketamine and control groups were described and compared between them in respect of their demographic profiles for homogeneity. The continous variables were compared by ANOVA and categorical variables by $\chi 2$ (Chi-square) test. The physiological variables such as SBP, DBP and HR of the three groups were compared by ANOVA and confirmed the groups by repeated measures of ANOVA. The sore throats between the three groups were compared within the groups by Friedman test and between groups by Krusca Wallis (KW) test. The P-values less than or equal to 0.05 ($P \leq 0.05$) were fixed as the level of statistical significance.

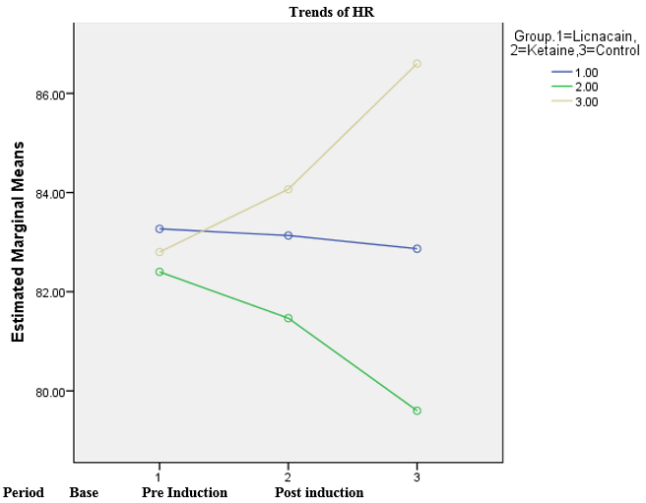

Fig. 1: Trends of HR of three groups at base through post induction

Results

Description of the Study Subjects
The demographical variables such as age and gender were compared between the three groups. The differences in age between the three groups were not statistically significant ($P>0.05$).

Table 1: Comparison mean BP at Base, pre induction and post induction between the three groups

Period	Lignocaine		Ketamine		Control		"F"	df	Sig
	Mean	SD	Mean	SD	Mean	SD			
Base	122.3	8.9	122.7	8.9	122.3	8.8	0.028	2,89	P=0.973
Pre Induction	121.6	8.2	119.0	14.0	123.0	9.1	1.090	2,89	P=0.341
Post induction	119.3	7.4	110.1	12.6	133.0	13.1	48.364	2,89	P<0.001

Table 2: Comparison of sore throat within the group from immediate throughout 24 hours

Groups (n=30)	Mean ranks at						Friedman χ^2	df	Sig
	Immediate	2 hrs	4 hrs	8 hrs	12 hrs	24 hrs			
Lignocaine	3.37	3.97	3.67	3.37	3.27	3.37	16.061	5	P=0.007
Ketamine	3.69	3.58	3.58	3.38	3.38	3.38	11.522	5	P=042
Control	4.38	4.53	3.15	3.07	2.98	2.88	49.220	5	P<0.001

Table 2 compares the sore throat within the groups from immediate through 24 hours. The level of sore throat in Lignocaine group was highly significant (P<0.01). The level of sore throat in Ketamine group was just significant (P<0.05). The level of sore throat in control group was very highly significant (P<0.001).

Table 3: Comparison of sore throat between groups at immediate

Sore throat Level	Lignocaine		Ketamine		Control		Results (K W)
	No	%	No	%	No	%	
Nil	28	93.3	27	90.0	3	10.0	
Mild	2	6.7	3	10.0	12	40.0	χ^2 =60.418
Moderate	0	0.0	0	0.0	10	33.3	df=2
Severe	0	0.0	0	0.0	5	16.7	P<0.001
Total	30	100.0	30	100.0	30	100.0	
Mean ranks	32.00		33.25		71.25		

Table 4: Comparison of sore throat between groups at 2hours

Sore throat Level	Lignocaine		Ketamine		Control		Results (K W)
	No	%	No	%	No	%	
Nil	22	73.3	28	93.3	0	0.0	
Mild	8	26.7	2	6.7	17	56.7	χ^2 =62.413
Moderate	0	0.0	0	0.0	9	30.0	df=2
Severe	0	0.0	0	0.0	4	13.3	P<0.001
Total	30	100.0	30	100.0	30	100.0	
Mean ranks	35.77		28.07		72.67		

The above table-5compares the sore throat at 2 hours. The mean ranks between the three groups were statistically significantly differed (P<0.001).

Table 5: Comparison of sore throat between groups at 8 hours

Sore throat Level	Lignocaine		Ketamine		Control		Results (K W)
	No	%	No	%	No	%	
Nil	28	93.3	30	100.0	6	20.0	
Mild	2	6.7	0	0.0	20	66.7	χ^2 =56.668
Moderate	0	0.0	0	0.0	3	10.3	df=2
Severe	0	0.0	0	0.0	1	3.3	P<0.001
Total	30	100.0	30	100.0	30	100.0	
Mean ranks	35.37		32.5		68.63		

The above table 5 compares the sore throat at 8 hours. The mean ranks between the three groups were statistically significantly differed (P<0.001).

Table 6: Comparison of sore throat between groups at 24 hours

Sore throat Level	Lignocaine		Ketamine		Control		Results (K W)
	No	%	No	%	No	%	
Nil	28	93.3	30	100.0	6	20.0	
Mild	2	6.7	0	0.0	21	70.0	χ^2 =56.702
Moderate	0	0.0	0	0.0	3	10.0	df=2
Total	30	100.0	30	100.0	30	100.0	P<0.001
Mean ranks	35.40		32.5		68.6		

The above table-6 compares the sore throat at 24 hours. The mean ranks between the three groups were statistically significantly differed (P<0.001).

Discussion

POST is more common problem encountered in post operative period. Irrespective of tube size and cuff pressure monitoring patient complaints of sore throat post operatively. Previous studies were done to alleviate POST by nebulization with steroid, gargling with various drugs, coating ETT cuff with lignocaine jelly etc. In our study, Ketamine nebulization 15 mins prior to general anaesthesia with endotracheal intubation offers good post operative sore throat relief and better comfortability for the patients.50mg Ketamine is least amount to enter into the circulation to have effect. Ketamine by acting directly in NMDA receptor relieve pain as it has peripheral anti nociceptive effect. Ketamine nebulization when compared to gargling provides less discomfort to the patient. Amingad B, Jayaram S.et al compared the ketamine nebulization with ketamine gargling in reducing post-operative Sore throat.[3] Kalil DM, Silvestro et al published a study on various pharmacologic methods that was used preoperatively helps in prevention of sore throat.[4] Ahuja V, et al proposed a study on ketamine nebulization reduces the incidence and severity of POST.[5] Zhu MM, Zhou QH, et al. studied in rats that have hyperresponsive airway with allergens and effects with ketamine nebulization.[6] D'Aragon F, Beaudet N, et al. studied the effects of intracuff lignocaine with lignocaine spray on post operative sore throat.[7] O'Callaghan C, Barry PW studied the mechanism of drug delivery with nebulization and its action on airway. Ketamine nebulization produces effects that lasts more than a hour after surgery when compared to Lignocaine nebulization.[8] Khatavkar SS, Bakhshi RG et al compared nasal midazolam with ketamine for children prior to surgery.[9] Aditya AK, Das Assessment of nebulized ketamine for reductions of incidence and severity of post-operative sore throat.[10] Reddy M Dose-dependent effectiveness of ketamine in POST.[11] Intraoperative hemodynamics was comparable with all the three groups in the study. POST can be effectively managed if prior proper steps are taken.

Conclusion

In our study both ketamine and lignocaine effectively reduced the POST, provided ketamine had extended duration of action when compared to lignocaine.

Source of Support: None.

Conflict of Interest: None.

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Comparison of efficacy of intrathecal nalbuphine versus fentanyl as adjuvant to subarachnoid block in cesarean section

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Abstract **Background and Aims:** Spinal Anaesthesia is the common technique for lower segment cesarean delivery. This research was conducted to observe the effects of intrathecal Nalbuphine or Fentanyl when added with hyperbaric bupivacaine in lower segment cesarean section under spinal anaesthesia. **Material and Methods:** This research was conducted after obtained proper ethical committee clearance from the institution and written informed consent from all the patients in a Prospective randomized, double blinded manner. Hundred patients of ASA physical status II planned for cesarean section were randomized into group 1 and group 2; each group consisted of 50 participants. Group 1 received Nalbuphine 0.8 mg (0.5 ml prepared by addition of normal saline); Group 2 received Fentanyl 25 mcg. Both groups were given inj.Bupivacaine 0.5% 10 mg as the basic drug so that all participants received a total volume of 2.5 ml. The time taken for the onset of sensory loss at the T6 dermatome level and Grade 3 modified Bromage motor blockade, two segment regression time of sensory blockade, total duration of motor blockade, Period of effective analgesia, Pain assessment using VAS scoring system and side effects were observed in groups. **Results:** Total period of effective analgesia was 264.6±10.0 minutes in group 1 and 191±5.7 minutes in group 2 and it was significant (p=0.001). **Conclusion:** Nalbuphine 0.8 mg and Fentanyl 25 mcg are can be used as an adjuvant for central neuraxial blockade especially in spinal anaesthesia. Nalbuphine has the advantage over Fentanyl in terms of better post-operative analgesic duration.

Key Words: Bupivacaine, Cesarean delivery, Fentanyl, Nalbuphine, Subarachnoid block.

INTRODUCTION

Opioids are used as adjuvant to local anaesthetics during subarachnoid block to improve the quality of intra operative and post-operative pain relief [1]. Fentanyl is a phenylpiperidine-derivative synthetic opioid agonist. Onset of action is rapid following intrathecal administration. Lipid solubility is more compared to morphine, which helps its passage across the blood brain barrier and the side effects were minimal.[2] Nalbuphine is an agonist and antagonist opioid and also acts on μ and kappa receptors.[3] Its agonistic effects are due to action on the kappa receptors. There is a study comparing addition of nalbuphine 0.4 mg (or) morphine along with hyperbaric Tetracaine and the side effects were comparatively less in the patients who received Nalbuphine.[4] Opioids acts as agonists on opioid receptors present in the pre synaptic and post synaptic sites mainly the brainstem and spinal cord. They also act on the peripheral tissues. There will be activation of antinociceptive system. Opioid receptors are G protein coupled receptor. μ type of receptors are important for spinal and supra spinal analgesia. In the spinal cord Substantia gelatinosa is the main site of action for opioids.[5] This study was done to look for the results of Intrathecal Nalbuphine or Fentanyl along with bupivacaine heavy 0.5% in cesarean delivery.

MATERIALS AND METHODS

After obtained Institutional Ethical committee clearance, patients under the inclusion criteria for this research that is physical status ASA II, aged between 20 to 35 years posted for cesarean section were randomized into group 1 which includes 50 participants and group 2 also had 50 participants by computer generated random numbers. All participants were explained about the procedure and written informed consent was obtained. Patients with contraindication for central neuraxial blockade were excluded from the study. All enrolled patients underwent routine preanaesthetic checkup and basic investigations. They were kept nil per oral as per WHO fasting guidelines and pre medicated with tablets (tablet. Metoclopramide 10 mg PO and tablet. Ranitidine 150 mg PO). Before commencement of anaesthesia in the pre-operative period all patients were educated in detail about the methods we are going to use for the assessment of sensory loss and motor blockade. The Visual Analog Scale pain scoring system was described in brief with the help of 10 cm paper strip which has 0 to 10 (0-no pain,10-worst pain.). On arrival to the operation theater all the patients were connected to standard monitoring like NIBP, ECG, and pulseoximeter and temperature probe. Base line values were noted. All patients preloaded with ringer's lactate solution (10 ml/ kg) after secured a peripheral intravenous line with 18G cannula.

Drug solution for the study was kept ready by the resident anaesthetist and the procedure was performed by another anaesthetist to ensure double blindness of the study. Data collection was done by a different person. All participants given spinal anaesthesia in the sitting posture using midline approach between L3-L4 space with the help of 25 gauge quincke babcock spinal needle .Group 1 patients received nalbuphine 0.8 mg which was 0.5 ml prepared by adding normal saline along with inj.bupivacaine 0.5% heavy 10 mg. Group 2 patients received Fentanyl 25 microgram along with inj.buphivacaine 0.5% heavy 10 mg, both the groups received a total volume of 2.5ml.After spinal anaesthesia, patients were positioned immediately in the supine posture with a wedge kept below the right hip in order to displace the uterus towards left side and avoid supine hypotension syndrome. 4L/min Oxygen was given by Hudson mask. Intra operative monitoring done continuously and recorded at five minutes interval up to 15 minutes then once in 15 minutes. If there is Hypotension (systolic blood pressure <100 mm hg or <20% from the baseline blood pressure) treated with Ringer's lactate solution and if needed vasopressor inj.ephedrine 6 mg intravenous at incremental doses was given. Bradycardia if occurs (Heart rate <60 beats /min) was treated with 0.6 mg of intravenous atropine sulphate. To assess the Sensory blockade pinprick method was used and Modified Bromage scale was used for assessment of motor blockade.[6] The time for the onset of loss of sensation to pinprick at the level of T6 dermatome level and the time taken for the grade 3 Bromage motor blockade to occur were noted. Entire motor blockade duration and time for regression of sensation 2 segment from the initial T6

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dermatome level also noted. Modified Ramsay sedation score [7] was used to assess the level of sedation in the preoperative and immediate post-operative period. In the Post-operative period VAS [8] scoring system was used to assess pain at 30 minutes interval till 300 minutes. First rescue analgesic dose requirement time is noted from the intrathecal drug injection and it is considered as duration of effective analgesia. Hypotension, bradycardia, pruritus and nausea are the expected complications and patients were observed for it. When participants complained of pain they were given inj.diclofenac 75 mg intramuscularly. Statistical package for the Social Sciences (SPSS) used for statistical analysis and alpha error of probability p value< 0.05 is considered as statistically significant and it is highly significant when p value is <0.01.

RESULTS

Table 1: Demographic profile of the study population

Demographic profile	Group 1 (total no=50)	Group 2 (total no=50)	Statistical p-value
Age (in years)	25.9±3.2	27.0±3.5	0.125
Height(cm)	156.6±2.6	156.4±2.6	0.729
Weight(kg)	66.2±7.2	63.7±5.7	0.057
Duration of surgery(minutes)	57.1±4.6	57.4±4.7	0.764

Group 1 received Intrathecal Nalbuphine and group 2 received Fentanyl as adjuvant to subarachnoid block. There is no statistical significance in terms of age, weight, height and duration of surgery among the groups. None of the variables were statistically significant. That is p value >0.05.

Table 2: Sensory and motor block

Characteristics of sensory and motor block	Group 1 (total no=50)	Group 2 (total no=50)	Statistical p-value
Time taken for Onset of sensory loss (minutes)	1.28±0.3	1.24±0.28	0.438
Time taken for Onset of motor blockade(minutes)	2.26±0.32	2.24±0.29	0.695
Onset time for two segment regression(minutes)	188.1±4.2	129.0±7.7	0.001
Duration of motor blockade(minutes)	234.7±6.3	164.7±8.6	0.001
Duration of effective Analgesia(minutes)	264.6±10.0	191.1±5.7	0.001
(first analgesic dose given time) Ramsay sedation score	2.18±0.4	2.0±0	0.002

There is no statistical significance in the onset of sensory and motor blockade between the groups. The time for the two-segment regression in group1 was 188.1±4.2 and that for group2 was 129±7.7 minutes and the difference was significant (p=0.001). The total duration of motor blockade and effective analgesia are more in nalbuphine drug received patients. Ramsay sedation score for group1 was 2.18±0.4 as compared to 2.0±0.0 for group2 (p=0.002) (Table 2).

Table3: VAS score measured at 120, 150 and 180 minutes

VAS score (Time in minutes)	Group 1 (Total no=50)	Group 2 (Total no=50)	Statistical p-value
120 minutes	0.68±0.47	2.0±0.0	0.001
150 minutes	1.02±0.14	2.06±0.24	0.001
180 minutes	1.86±0.35	3.0±0.0	0.001

VAS score at 120 minutes for group1 was 0.68±0.47 and it was 2.0±0.0 for group2 and the difference was seeming to be significant (p=0.001). VAS score at 150 minutes for group1 was 1.02±0.14 and it was 2.06±0.24 for group2 and it was significant (p=0.001). VAS score was 1.86±0.35 at 180 minutes in group1 and it was 3.0±0.0 in group2 and the p value is 0. 001.Since the VAS score was zero at 30, 60 and 90 min, it was not comparable. Graph: Comparison of VAS score at 120, 150 and 180th minute

Graph 1 **Graph 2**

Complications

Two patients in group 1 and one patient in group 2 developed bradycardia. Hypotension incidence was one in group2 whereas it was 2 in group1. Pruritus was noted one in each group. First analgesic dose requirement: The first analgesic dose requirement for group1 was very late at 300th minute for all 50 cases while it was occurred at 210th minute for 94% (47) of the patients in group 2.

DISCUSSION

We have decided to use Nalbuphine at a dose of 0.8 mg because jyothi *et al*[9] done a study and found that this is the dose at which Nalbuphine provides better analgesia without any adverse effects compared to 1.6 mg and 2.5 mg for lower abdominal and orthopedic surgeries. Bogra J *et al* [10] used Fentanyl along with bupivacaine for lower segment cesarean delivery under subarachnoid block and found that bupivacaine dosage can be reduced and so it's expected complications.

The time for the onset of sensory loss was not statistically significant in our groups, similar results were observed in Naaz *et al*[11], Umesh N Prabhakaraiah *et al*[12] and Gomaa *et al*[13]. In a study by Bhavana B Gurunath *et al* [14] the time taken for the two-segment regression in nalbuphine group was significantly prolonged as comparable to fentanyl group. The same results were noted in our research also. The time taken for regression of two segment from T6 level was found more in Nalbuphine group. As like in Tiwari *et al*[15] and Muhammad *et al*[16] the time for regression of two segment and duration of motor blockade were prolonged in nalbuphine group in our study also. The duration of Bromage grade 3 motor blockade and duration of effective analgesia were more in nalbuphine group in our research and the same observation is noted in tripat *et al* [2]and Ahmed *et al* [17].Sapate *et al* [18] done a study to see the quality of intrathecal Nalbuphine in patients underwent lower abdominal surgeries under subarachnoid block and it showed better results. Borah *et al* [19] conducted a comparative study to compare the Effects of spinal Nalbuphine along with Ropivacaine in lower limb procedures and found that Nalbuphine can be intrathecally used as a good alternative to other opioids as an adjuvant to produce a prolonged postoperative analgesic effect with reduced risk of side effects. Shraddha *et al* [20] done a research to see the effect of nalbuphine when used with Bupivacaine for spinal anaesthesia and proved that nalbuphine is an effective intrathecal adjuvant for postoperative analgesia. Kumaresan *et al* [21] conduted a study to find out what is the appropriate dose required for intrathecal nalbuphine in patients underwent lower limb orthopedic surgeries and concluded that intrathecal nalbuphine of 0.6 mg provides prolonged duration of post-operative analgesia without any increased outcome in the adverse effects. Ramsay sedation score was found to be significant in the post-operative period. However, at the end of procedure all the patients were arousable. The VAS score in our research was significant between the groups at 120, 150 and 180 minutes, it is more in fentanyl group which means nalbuphine group showed better post-operative analgesia. Requirement of first analgesic dose in the post-operative period was delayed in nalbuphine group compared to fentanyl group. The complications were not significant. Neelam singh *et al* [22] concluded that Nalbuphine used as adjuvant to intrathecal bupivacaine caused good quality of post procedure analgesia and there is less requirement for the analgesic dose in the post-operative period without any increased side effects or complications. Verma *et al* [23] studied the effects of intrathecal tramadol (50 mg) or nalbuphine (2 mg) when added to hyperbaric bupivacaine (12.5 mg) in patients underwent lower limb orthopedic procedure. There was a reduced requirement for post-operative analgesia. Shahedha Parveen *et al* [24] also showed similar results and reduced risk of side effects. The main aim of postoperative pain management is to reduce or eliminate the pain with minimal risk for side effects. Intrathecal opioids are preferably used to prolong and improve the quality of post-operative analgesia.

CONCLUSION

Intrathecally administered Nalbuphine as an adjuvant to hyperbaric Bupivacaine in central neuraxial blockade provides good quality of post-operative analgesia, without any significant increase in the side effects when compared to intrathecal Fentanyl.

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Case Report

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Congenital Primary Right Lung Agenesis in A Child – MDCT Imaging Features

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Summary

Go to

Pulmonary agenesis is a very uncommon congenital abnormality that represents the unsuccessful growth of the primitive lung bud. The cause may be a primary embryogenic defect or secondary to situations that restrict fetal lung growth. In the great majority of the cases, the diagnosis is usually made at or soon after birth, but some cases go unnoticed up to adulthood. It is generally associated with other congenital defects and must be suspected in the presence of a total radio-opaque hemithorax. In this article, we present a case of 8 years old female child with congenital pulmonary Agenesis who remained asymptomatic until childhood.

Keywords: Congenital Primary Pulmonary Agenesis, Pulmonary Hypoplasia, Pulmonary Aplasia, Pulmonary Artery Agenesis

Introduction

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Lung agenesis is a rare developmental anomaly which affects both lungs. Long term survival with unilateral lung agenesis is possible in the absence of associated severe anomalies. However, the condition is frequently associated with other congenital abnormalities, particularly esophageal atresia and the VACTERL syndrome (vertebral, anal, cardiac, tracheo-esophageal, renal and radial and limb anomalies) [1]. The prevelance of this condition has been noted to be 0.0034 - 0.0097%. There appears to be no sexual predilection for this condition. Most cases present in the neonatal period with cyanosis, tachypnea, dyspnea, stridor or feeding difficulties. The condition is often associated with fetal distress at birth. Yet, it may also be asymptomatic and manifest itself in adulthood. The cause may be a primary embryogenic defect or secondary to situations that restrict fetal lung growth [2]. Left-sided agenesis (70% of cases) is more frequent than right-sided. Right-sided defects have a poorer prognosis due to often coexisting cardiac anomalies or greater mediastinal shift and pressure on other structures [3]. We herewith report an 8 years old female child with right congenital Primary Pulmonary Agenesis and describe the MDCT imaging features.

CaseReport

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An 8 years old female child presented with complaints of dyspnea and left chest pain to the hospital for further investigations. General physical examination was non-contributory. Chest examination revealed absent air entry on right side, mediastinal shift to right side with hyper-resonance on left side. Cardiac examination revealed apex beat palpable in the right 4th intercostal space. Clinical examination of the abdomen revealed no abnormalities.

i. Routine biochemical and arterial blood gas analyses were unremarkable. Electrocardiographic assessment demonstrated a normal sinus rhythm pattern.

ii. The patient also had a cardiology consult to rule out any vascular, cardiac anomalies or effect of the agenesis on cardiac function.

iii. Echocardiography was suggestive of dextroposed heart with normal intracardiac connections.

Radiograph of chest revealed symmetric bony cage, opaque right hemithorax, mediastinal shift with herniation of the normal lung towards the right side (Figure 1). Ultrasonography done revealed absence of right lung tissue and shifting of heart towards the affected side. To exclude the diagnosis of a pulmonary thrombo-embolic event, the patient underwent further evaluation with contrast-enhanced MDCT scanning (General Electric (GE) Light Speed Multi Slice CT Scanner) of the thorax with dynamic bolus injection of contrast (100 ml Omnipaque 350 mg/mL, 4.5 mL/s). Multidetector Computed Tomography (MDCT) scan revealed that the volume of the right hemithorax

was reduced, Agenesis of right lung and bronchial tree with the mediastinal structures displaced towards the right .There was compensatory hypertrophy of left lung, while the superior lobe of the left lung was partially displaced towards the right hemithorax (Figures 2-4). MDCT Angiography revealed complete agenesis of right lung with non-visualization of right pulmonary artery and vein (Figure 5). On Bronchoscopy the patient had agenesis of the Right bronchial tree and no endobronchial lesions of left lung. Based on these findings a diagnosis of Congenital Primary Right Lung Agenesis was made.

Figure 1: Posterio-Anterior Radiograph of Chest revealed symmetric bony cage, opaque right hemithorax, mediastinal shift with herniation of the normal lung towards the right side.

(images/CTCMI.MS.ID.555619.G001.png)

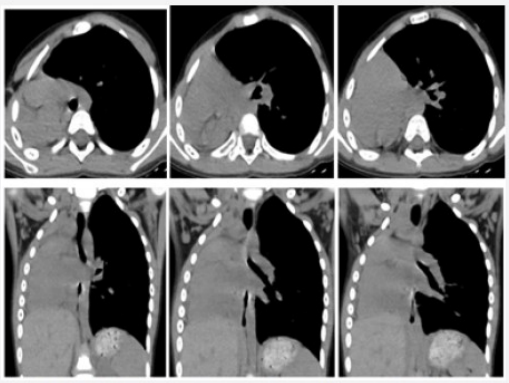

Figure 2: Non-contrast mediastinal window CT, Axial (A-C) and reconstructed coronal (D-F) sections shows reduced volume of the Right hemithorax, Agenesis of right lung and displaced mediastinal structures towards the right.

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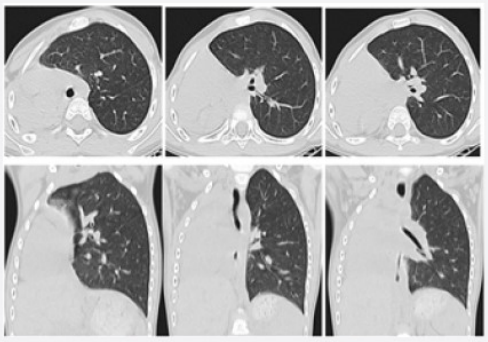

Figure 3: MDCT chest Lung window, Axial (A-C) and Reconstructed Coronal (D-F) sections shows Absent right lung and Bronchial tree, Compensatory hypertrophy of left lung and herniation of superior lobe of left lung towards the right hemithorax.

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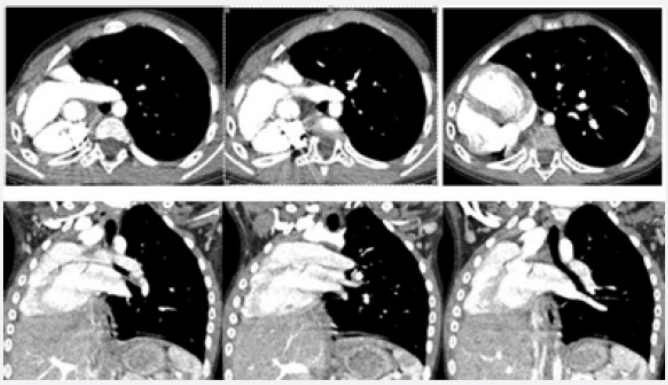

Figure 4: Contrast enhanced CT Arterial phase, Axial (A-C) and reconstructed coronal (D-F) sections shows Agenesis of right lung, Absent right pulmonary artery and displaced heart and mediatinum to right.

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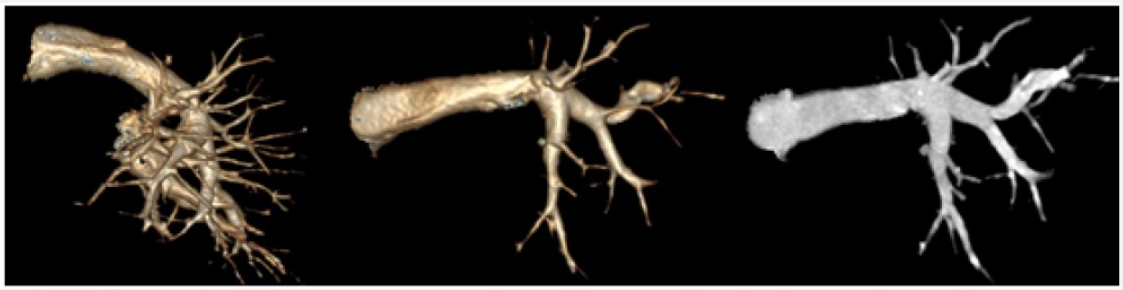

Figure 5: MDCT Angiography.3D Volume rendered images (A,B) and MIP images (C) revealed Non-visualisation of Right pulmonary artery and vein and normal left pulmonary artery and its branches.

(images/CTCMI.MS.ID.555619.G005.png)

Discussion

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Pulmonary Agenesis is a rare congenital anomaly characterized by complete absence of the bronchus, lung parenchyma, and pulmonary vasculature on that side. Unilateral lung agenesis has a birth prevalence of approximately 1 in 15,000 [4]. Normally the lung develops as a diverticulm from foregut in the 4th week of intrauterine life. Pulmonary agenesis results due to failure of the bronchial analogue to divide equally between the two lung buds, leading to normal development of one side, while failure of other side to develop either completely (agenesis/ aplasia) or partially (dysplasia or hypoplasia) [5].

Genetic, teratogenic and mechanical factors have been implicated in the etiology of pulmonary agenesis [6,7]. A history of recurrent chest infections during the first year of life is the usual history elicited; however, the patient may be completely asymptomatic and diagnosed accidentally from the radiograph or detected during autopsy [8]. Associated congenital malformations of the cardiovascular, skeletal, gastrointestinal, or genitourinary systems are present in half of the cases and may modify clinical presentation, course and outcome of patients with pulmonary agenesis [9]. Schneider classified pulmonary agenesis into three groups, which were later modified by Boyden in 1955 [8].

Type 1 (Agenesis) - There is a complete absence of lung and bronchus and there is no vascular supply to the affected side.

Type 2 (Aplasia) - There is a rudimentary bronchus with the complete absence of pulmonary parenchyma.

Group I: No bifurcation of trachea;

Group II: Only rudimentary main bronchus;

Group III: Incomplete development after division of main bronchus; and

Group IV: Incomplete development of subsegmental bronchi and small segment of the corresponding lobe.

Functionally, unilateral lung agenesis and lung aplasia are similar. Pathologically sole lung is larger than normal in pulmonary agenesis, and this enlargement is true hypertrophy and not emphysema [11]. Patients presenting late usually have readily detectable flattening and reduced movement of the chest wall on the affected side, with reduced air entry on auscultation. Breath sounds from the herniated, hypertrophied lungs may be heard on the side of agenesis except in the axilla and base Chest wall deformity can be quite pronounced, with an associated secondary scoliosis [11]. Diagnosis of Pulmonary Agenesis has been made on chest skiagram, bronchoscopy, bronchography and angiography. With the advent of CT scan, these invasive procedures which entail significant risk have become unnecessary [12].

As might be expected, Chest radiographs in patients with unilateral absence of a lung show loss of aeration and marked volume loss on the affected side. Volume loss is shown as elevation of the ipsilateral hemidiaphragm, shift of the mediastinum toward the abnormal side, and anterior herniation of the contralateral lung. There is usually characteristic wedge-shaped opacity in the inferior and lateral aspect of the affected hemithorax. This opacity is due to herniation of heart and mediastinum into the lower thorax and proliferation of fat to partially compensate for the absence of lung tissue. The obvious Differential diagnoses are acquired total lung collapse or prior pneumonectomy [13]. Other conditions to consider in the differential include hyperlucent and hypoplastic lung syndromes, obstructive lung lesions mainly

cancer, diaphragmatic hernia, adenomatoid cystic malformations and sequestrations and the Scimitar syndrome [14]. Pulmonary Angiography shows absence of ipsilateral pulmonary artery. Bronchoscopy demonstrates underdeveloped bronchus in agenesis. Other investigations e.g. echocardiogram, ultrasound abdomen etc. are required depending upon the presence of associated congenital abnormality [15]. The MDCT allows high-resolution isotropic imaging and is the ideal modality for diagnosing right lung agenesis and for diagnosing simultaneously any associated tracheobronchial anomaly. MDCT can very speedily acquire volumetric data sets, allowing for 2D, multiplanar, maximum intensity projection and volume rendering technique reconstructions, and has the capability to image both airway and vascular abnormalities. The characteristic MDCT findings include opaque hemithorax, Agenesis of lung with mediastinal shift towards the affected side and bony cage symmetry (Figures 2-4). Similar findings were seen in our case and a diagnosis of primary right lung Agenesis was made. However, no etiological diagnosis could be confirmed as genetic mutation analysis was not affordable in our case.

No treatment is required in asymptomatic cases. Treatment is necessary for chest infections. Patients having stumps (hypoplastic bud) may require surgical removal if postural drainage and antibiotics fail to resolve the infection. Corrective surgery of associated congenital anomalies, wherever feasible, may be undertaken [16]. Several methods have been proposed to reduce vascular compression and intrinsic stenosis such as mediastinal stabilization by an expansion prosthesis, aortopexy, aortic grafting and resection, detour of the left pulmonary artery and slide tracheoplasty [4]. Overall, prognosis depends on two factors. Firstly, the severity of associated congenital anomalies and secondly, involvement of the normal lung in any disease process. While bilateral Pulmonary agenesis is incompatible with life, 50% of those with even unilateral lung agenesis die within 5 years of life [17]. Right lung Agenesis carries a poorer prognosis because of the larger shift of the heart and mediastinum with a consequent distortion of the great vessels, especially aortic arch resulting in extrinsic compression over the trachea anteriorly [18,19]. In our case the child is surviving beyond 5 years of life.

Conclusion

Go to

Pulmonary Agenesis is an uncommon pathology. Clinical findings of recurrent respiratory infections and radiologic evidence of opaque hemithorax, bony symmetry and herination of normal lung to the affected side, along with associated congenital anomalies are suggestive of Pulmonary Agenesis. No treatment is required in asymptomatic cases. Management is mainly supportive, correcting associated malformations, prevention and treatment of repeated respiratory tract infections. MDCT imaging not only guides us to a proper diagnosis but also can identify the etiology, level of airway narrowing and associated congenital anomalies , thus helping in proper patient care.

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Original Research Article

128 slices multidetector CT evaluation of Gastric carcinoma - Imaging and histopathological correlation

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Abstract

Background: Multi-detector CT (MDCT) of the stomach is the first-line imaging for patients with suspected gastric pathologies. Hence, the study was conducted to explore the characteristics of variously differentiated gastric cancers on 128 slices multi-detector computed tomography (CT).

Material and methods: This prospective observational study was approved by our institutional review board, and informed consent was waived from January 2016 to January 2017. All the patients were selected by convenience sampling. All patients underwent an endoscopic biopsy that provided histologic confirmation carcinoma in the remnant stomach. CT examinations on a 128 slice CT scanner with a 0.7-second tube rotation (GE OPTIMA CT 660) were performed. The fasting time of at least six hours was recommended to patients for complete gastric emptying.

Results: A total of 26 people were included in the final analysis**.** The mean age was 56 ± 11.96 in the study population. 13(50%) participants were male and remaining 13(50%) were female. Most cancers were Adenocarcinomas and diffuse of higher grade and nodal involvement. Among the study population, 3(11.54%) participants were with T3 tumor stage, and 23(88.46%) were with T4 tumor stage. 13(50%) participants had nodal stage1, 10(38.46%) had nodal stage 2 and remaining 3(11.54%) had nodal stage 3. 15(57.69%) had M0 metastasis, and 11(42.31%) had M1 metastasis. 23(88.46%) Participants had overall stage 1V and remaining 3(11.54%) participants had stage IIIC as detected in CT. 18(69.23%) participants had surgery and the remaining 8(30.77%) underwent chemotherapy.

Conclusion: Stomach Multi-detector CT imaging is a functional imaging technology with potential clinical applications.

Key words

Gastric cancer, Computed Tomography, Operative staging, Histopathology, TNM.

Introduction

Gastric cancer is the second most common cause of cancer death globally, and fifth most common cancer among males and seventh most common cancer among females in India [1, 2]. For a complete cure of gastric cancer, complete surgical resection of the tumor at laparotomy has been the therapeutic method of choice [3]. Surgical resection is dependent on the GC stage at presentation, which incorporates the depth of tumor invasion, the extent of lymph node and distant metastases [3].

Multi-detector computed tomography (MDCT) with its ability to assess tumor depth, nodal disease and metastases is the preferred technique for staging GC and assessing treatment response for GC. MDCT has become a powerful imaging tool for non-invasive evaluation of the stomach and can assess locoregional and metastatic staging simultaneously [4]. This study was done with the aim of evaluation of Gastric carcinoma by Imaging and histopathological correlation.

Materials and methods

This prospective observational study was approved by our institutional review board, and informed consent was waived from January 2016 to January 2017. All the patients were selected by convenience sampling. All patients underwent an endoscopic biopsy that provided histologic confirmation carcinoma in the remnant stomach.

We performed CT examinations on a 128 slice CT scanner with a 0.7-second tube rotation (GE OPTIMA CT 660). To acquire a near-isotropic data set, we chose 4×1-mm collimation and reconstructed 0.625 mm-thick sections every 0.5 mm. An optimum CT technique requires high spatial resolution, proper gastric distension, and proper timing of contrast media injection to detect subtle changes in the gastric wall and to accurately stage tumors. A casting time of at least six hours was required for complete gastric emptying. For diagnostic viewing, we reconstructed 0.625 mm-thick axial sections either directly from the scanning data or the thin-section volumetric data set (the secondary raw data set) using the multi-planar reformation function of the scanner console. Also, we routinely performed coronal and sagittal reformation in the region of the stomach. Contrast material injection for the stomach was timed in a manner that ensured the arterial phase, portal phase imaging. In such cases, the scanning range included only the liver and stomach in the arterial phase and the upper abdomen down to the iliac crest for the portal venous phase.

We used 120kVp and 350-500 me like the exposure settings. The resulting volume CT dose index, as an indicator of average local dose, was~ 10.1 mGy for each multi-detector acquisition. This number may be varied with patient size: 125 kVp and 10 mGy appear sufficient for slim patients, but for very obese patients, 140 kVp and up to 30 mGy should be used for optimal image quality. Descriptive analysis was carried out by the mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Non-normally distributed quantitative variables were summarised by median and interquartile range (IQR).

Results

A total of 26 people were included in the final analysis**.** The mean age was 56 ± 11.96 in the study population. Among the study population, 13(50%) participants were male and remaining 13(50%) were female. The histopathological findings were as per **Table - 1**. Most cancers were Adenocarcinomas and diffuse of higher grade and nodal involvement. Among the study population, 3(11.54%) participants were with T3 tumor stage, and 23(88.46%) were with T4 tumor stage. 13(50%) participants had nodal stage 1, 10(38.46%) had nodal stage 2 and remaining

3(11.54%) had nodal stage 3. 15(57.69%) had M0 metastasis, and 11(42.31%) had M1 metastasis. 23(88.46%) Participants had overall stage 1V and remaining 3(11.54%) participants had stage IIIC as detected in CT (**Table - 2**). Among the study population, 18(69.23%) participants had surgery, and the remaining 8(30.77%) underwent chemotherapy.

Table - 1: Descriptive analysis of Histopathology in the study population (N=26).

HPE	Summary
HPE classification	
Adenocarcinoma	22(84.62%)
Signet Ring Cell Carcinoma	2(7.69%)
Metastatic adenocarcinoma	1(3.85%)
Carcinomatous	1(3.85%)
Type	
Mixed	1(3.85%)
Diffuse	23(88.46%)
Intestinal	2(7.69%)
Histologic Grade	
Grade ii	5(19.23%)
Grade iii	21(80.77%)
HPE Differentiation	
Moderate	11(42.31%)
Poor	15(57.69%)
Pathologic staging	
pT3 pN1	2(7.69%)
PT3PN2	1(3.85%)
PT4 endoscopy specimen	15(57.69%)
pT4 pN3	1(3.85%)
pT4 pN3b	1(3.85%)
pT4a pN1	1(3.85%)
pT4a pN3a	1(3.85%)
PT4APN2	1(3.85%)
pT4bN3aM1	1(3.85%)
PT4PN1	2(7.69%)
HPE Nodal Involvement	
Yes	10(38.46%)
No	16(61.54%)

Discussion

MDCT with isotropic volumetric imaging and various 3D images has increased the accuracy of T and N staging in patients with gastric cancer. Volume-rendering images including transparent or surface-rendering images enable radiologists to detect subtle mucosal abnormalities and provide an overview of the lesion in the stomach. Coronal and sagittal multi-planar reformatted images permit radiologists to select the optimal imaging plane to accurately evaluate tumor invasion depth of the gastric wall and perigastric infiltration and to differentiate lymph nodes from small perigastric vessels [5]. Another advantage as stated by Chen, et al. [6] was that MDCT is less skill-dependent, with less discomfort to the patient and thus more tolerable.

Table - 2: Descriptive analysis of CT in the study population (N=26).

CT	Summary
CT tumor stage	
T3	3(11.54%)
T4	23(88.46%)
CT nodal stage	
N1	13(50.00%)
N2	10(38.46%)
N3	3(11.54%)
CT metastasis	
M0	15(57. 69%)
M1	11(42.31%)
CT overall stage	
Stage IV	23(88.46%)
Stage IIIC	3(11.54%)

As in our study, it was seen that the histological findings correlated well with the CT findings which showed that Multi-detector CT was a good gastric imaging modality. Our study findings were in accordance to the study by Barros R.H., et al. [7] where it was found that 64-channel multi-detector computed tomography demonstrated clinically relevant accuracy in the preoperative staging of gastric adenocarcinoma as regards invasion depth (T) and metastatic involvement (M). Sharara S.M., et al. [8] found that MDCT T staging compared to pathological staging was highly significant and was better determined by Multi-detector Computed Tomography (MDCT). Lee, et al. [9] reported that three-dimensional imaging with the surface-

shaded display technique improved early gastric cancer detection rates from 64.5% to 93.5%.

Even though our study suggested that Multi-detector CT 3D imaging software is a great device in detecting gastric cancer, our study had certain limitations. First, statistical power was limited because the sample was relatively small. Furthermore, our study was done in a single centre. However, this study contributes to the literature that there could be a new treatment modality. Further multi-institutional studies with a large number of patients and prospective design are strongly warranted to confirm our study results and to generalise the study findings.

Conclusion

Multi-detector CT 3D imaging software and cheaper data storage capacities have allowed faster, simpler, and more accurate gastric imaging.

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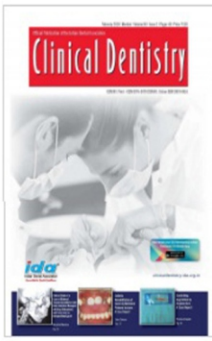

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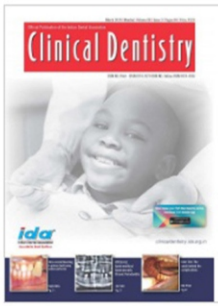

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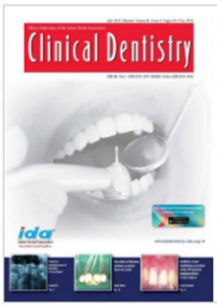

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Guidelines

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Title Page: Title page should include the title of the article and the name, degrees, positions, professional affiliations of each author. The corresponding authors, telephone, e-mail address, fax and complete mailing address must be given.

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CONTENTS

Dr. A.L. Meenakshi Sundaram

I'm very happy to meet you all again through the second issue of JIDAT. I can't believe we are halfway through 2018.Once again I congratulate Dr. Musthafa for the second issue of JIDAT. I request all the members to make use of this journal for their publications.

First of all I want to extend my thanks to all the members for their cooperation, dedication and support.

It is a great pleasure to witness growth in the membership and all the members surely put a lot of work helping us grow.

Speaking of events, in the previous months we had many events and conferences of highly valuable and educational and there was an incredible amount of sharing and learning.

These events help to rejuvenate and revamp the association.

I want to call your attention for the forthcoming events:

-6th Tamil Nadu State IDA Sports Meet on August 18 and 19, 2018 hosted by Marthandam Branch .

-33rd Annual Dental Conference on November 30,December 1 and 2, 2018.

-First ever Student Conference at Salem on November 9 and 10, 2018.

Before closing, I like to remind our special goals,

-reach membership growth of 10000

-reach 5 lakhs for Care and Concern.

Our members are strong, passionate and dedicated to our mission and look forward to continuing to make a difference together in 2018.

I'm humbled and honored to be able to serve you as the President of IDA, Tamil Nadu.

Thank you

Yours sincerely,

Dr. A.L. Meenakshi Sundaram
Hon-State President
IDA-Tamilnadu State Branch

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April - June 2018, 8(2)

Dr. K.P. Senthamaraikannan

Dear Members,

Warm regards from Indian Dental Association Tamilnadu State branch.

It's great that our Editor has coming out with 2nd issue of JIDAT on quick successful time. I as state secretary appreciate for his dedicated work towards JIDAT.

JIDAT is dedicated to dental health and providing results of studies based on research into various facts of dentistry. It's extremely happy to see that dental professionals are showing greater involvement in JIDAT. There is nothing greater than generation of enthusiastic response among the reader that publishers should come out with qualitative movements in the publication consistent with the global changes in the dental science.

JIDAT is the forefront of dental research that is of immense value for students, academician and private practitioner.

My best wishes.

Thanking you,

Yours sincerely,

k.p. Senthamarai

Dr. K.P. Senthamarai Kannan
Hon-State Secretary
IDA-Tamilnadu State Branch

Dr. H. Mohammed Musthafa

Warm wishes,

Happy to meet you all through this revamped and refurbished JIDAT.

My humble request to all the members is to equip yourself for the upcoming Clinical Establishment Act.

“Nothing is Stationary, except Changes”

There is no goback for the C E Act, as of now.

We, as law abiding citizens and responsible sculptors of this society, need to follow the rules enforced by the Government, with regard to C E Act.

Rules in C E Act needs to be amended further, for sure, and the Office of IDA Tamil nadu State is striving at its best, by all means for the same.

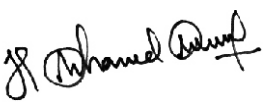
My suggestion to all the local office bearers is to acquaint yourself with the local government authorities for a better and placid sailing in the squall of C E Act.

Same way, My kind request to all the members is to make use of the Journal to evince your dexterity in the field of Dentistry which may familiarise you amongst the fellow Dental Fraternity as well as be helpful to fellow dentists' to pursue your footsteps for their successful Practice.

We at the Office of Editor of JIDAT take humongous efforts to bring out the issue on time with all your contributions.

United We Stand, Divided We Fall.

Jai IDA...!!!



Dr.H.Mohammed Musthafa,

Editor in Chief,

JIDAT.

INFORMING, SERVING, EDUCATING!.

Dr. G. P. Surendran
Dental Practitioner, Coimbatore.

Indian Dental Association (IDA) is an authoritative, independent and recognised voice of dental professional in India. We are asking you to join us, and here is why should you become a member?

"Working together works". From the minute you join, you can be confident that IDA is looking after your best interests. The association works towards acknowledging the members needs and requirements, appreciating our skills, awarding our talent and helping us achieve greater heights professionally.

IDA enhances the reputation of our profession and accelerates our practise by IDA Membership certification.

Empowers Dentists- IDA ensures that the voice of dentists and dentistry is heard in public and government forums, with the strength of 75000+ members in protecting our rights.

Networking- IDA teams up with trade, media and related organisations to gain maximum benefits, which is profitable for fellow members.

Education- Being in IDA is a way of staying current with the profession. Through CDEs, Fellowship programmes and educational training centre (ETC) and CE online, IDA conducts many lectures, hands-on courses and certification programmes which gives great scope for up gradation and access to research & training. State and national level conferences are held regularly for cohesive learning.

Service to the Community- If you believe in the saying," Service to Mankind is service to God", you have great opportunities as an IDA member to serve the society through various projects created by the team.

- Corporate and School dental health screening programs,
- TII: Tobacco Intervention Initiative
- OCF: Oral Cancer Foundation
- CDF: Child Dental Foundation
- EDC: Emergency Dental Centres
- HSF: Healing Smile Foundation, and
- IDRF: Indian Dental Research Foundation.

Legal Disputes- In case of medico-legal cases, IDA protects you, defends you and fights for you- if you are right. The power of information about law is the key to successful business.

Care and Concern Scheme- IDA has started the scheme for the families of deceased doctors wherein the family members will be provided with financial assistance. IDA is working out an exhaustive scheme for the benefit of family's at their loss.

Newsletter- To keep you abreast, IDA publishes newsletters with the information and technology trending in our field.

Channelize your inner leader- If you are a person who can take up responsibility, if you have administrative and leadership capabilities, you are most welcome to be a part of executive committee which will pave way further to the hierarchy of our association.

IDA Membership brings a whole wealth of benefits and any member of the IDA would unanimously agree that our organisation is all about improving oral health, quality of life and achieving `optimal oral health for all'. One would also say, we aim to represent the dental profession and support members in the provision of comprehensive and quality oral health care.

IDA can help you professionally, socially and of course as a trade union, wherever appropriate.

It is time to become a part of this prestigious association to create hope, possibilities and partnership for all individuals.

Cheers!

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Indian Dental Association Tamilnadu State Branch

ORIGINAL RESEARCH

EVALUATION OF DIAGNOSTIC ACCURACY OF KI – 67 (IMMUNOCYTOCHEMISTRY) AND AGNOR IN DETECTING EARLY CHANGES IN SMOKERS AND TOBACCO CHEWERS.

Dr.S.Prasanna*, Dr. Mohanavel**, Dr. S.Dinesh***

** Senior Lecturer, Dept.of Oral and Maxillofacial Pathology, Tagore Dental College & Hospital, Chennai.*
***Dental Surgeon, Kumaran Dental Clinic, Thiruvallur.*
*****Assistant Professor, Sumandeep College of Physiotherapy, Vadodara, Gujarat.*

ABSTRACT

The study was conducted to validate the accuracy of Ki – 67 (ICC marker) in identifying the proliferative and malignant changes occurring in the exfoliated buccal cells while comparing it with the standard AgNOR staining technique. The study group comprised of normal, smokers and tobacco chewers with a total of 30 subjects. The solutions for AgNOR staining was prepared as prescribed by Bukhari et al (2007) and Ki 67 was used for ICC procedure. The AgNOR number where more in smokers than in chewers. The AgNOR counts in chewers were also comparatively higher when compared to normal and close to smokers. The Immunocytochemistry (ICC) study, showed positive expression of Ki 67 in the nucleus of exfoliated cells which was significantly higher in chewers than smokers and normal.We conclude that even ICC (Ki 67) is even more sensitive than AgNOR and it could also be used as an adjunct to histopathological investigation. As literature states that proliferation is observable with AgNOR, this holds true for ICC technique with Ki 67also.

Keywords : AgNOR, Immunocytochemistry, Ki 67, Exfoliative cytology, Buccal smears.

Introduction

Cancer incidence in humans has gradually increased over the last century. Despite advances in diagnostic techniques and treatment protocol the disease is not under complete control. The World Health Organization (WHO) reported oral cancer as having one of the highest mortality ratios amongst all malignancies (Parkin et al., 2000). It ranks 12th among all cancers (Jemal et al., 2002). It is important to diagnose oral cancer in its early stages, since the management of small and localized tumors involves less morbidity and mortality than more advanced-stage disease, where treatment must be more aggressive.

Exfoliative cytology is the examination of exfoliated cells from the epithelial surface generally from oral mucosa. Cells in the deeper regions adhere to each other strongly in normal physiologic condition but in case of malignancy they tend to loose these adhesion and are exfoliated alone or along the cells of superficial layer.1Nucleus of a cell has an valuable role in the proliferation,regulation and protein synthesis.2 The nucleolar organizer regions (NORs) are the chromosomal loops of DNA involved in ribosomal synthesis. Some nucleolar proteins which are associated with these NORs stain with silver particles which are called AgNOR proteins. They correlate very well with cell proliferative activity and protein synthesis.3

Any type of screening test which works on biomarkers are amenable to automation, there by resulting cost savings and potential for applications in the developing world.4So the study aimed at performing AgNOR staining procedure from buccal smears collected from normal, smokers and tobacco chewer subjects and further validating it with Ki 67, a nuclear proliferative marker using Immunocytochemistry method.

Materials & Methods :

A total of 10 subjects were taken in each category of normal, smokers and tobacco

chewers with an age range of 25 – 50years, comprising a total of 30 subjects. The subjects were collected from those attending the Oral Pathology out patient department for routine dental check up and treatment. The smokers had the habit of smoking only using more than 5 cigarettes per day, the tobacco chewers had the habit of using smokeless form of tobacco for more than 5 years with a frequency of consuming it more than 4 times a day.

Patients who were included in the study subjects didn't had any oral lesions. The smears were taken from normal buccal mucosa of the subjects. Patients were asked to rinse with water and the area to be smeared was cleaned with gauze to remove excessive saliva and surface debris. The smears were collected by scraping wooden spatula along the buccal mucosa and smear was applied on the 2 glass slides and fixing one slide in alcohol for AgNOR staining according to Bukhari et al (2007) and other acetone fixing for Immunocytochemistry staining for half an hour.

Preparation of Working solutions :-3

Solution A – The solution was prepared by dissolving 500 mg gelatin powder in 25ml deionized water at 37 c and then 250 ml formic acid is added. Continuous shaking of the glass ware for about 10 min at 37 c was sufficient to dissolve the gelatin and a clear solution is obtained.

Solution B – It consist of silver nitrate and deionized water. 50% w/v concentrated solution of silver nitrate in deionized water

The final working solution was prepared by mixing one part of solution A with two parts of solution B and filtered using a filter paper into glass bottle and used immediately. Solution was prepared as an when required to avoid wastage and considering cost factor.

The slides are covered with the silver solution and kept in dark place for 20 – 30 minutes and dehydrated with alcohol (50%,70%,80%,96%,100%) for 5 min each and clarified with xylene for 5 min.5 The slides were dried in dark place and coverslip mounted with DPX.

For Immunocytochemistry procedure :-

The acetone fixed slides are subject to immuncytological procedures. The slides first hydrated with decreasing grades of alcohol (100%70%,50%) and water. Followed by 2 times PBS(Phosphate buffered saline) wash for 5 min each. Next step, is peroxide block for 5 min, protein block for 5 min, Ki 67 (primary block) for ½ hour followed by post primary for ½ hour , polymer link for 15 min and each step should be followed by PBS wash for 5 min x 2 times. DAB chromogen for 2 -3 min followed by running tap water wash and hematoxylin for 5 min, washing in water.

The slides are subjected to dehydration of alcohols (50%,70%,100%) for 5 minutes each and cleared with xylene for 5 minutes. Slides are dried and mount coverslip with DPX.

Results:

AgNOR dots were seen within the nuclei and viewed clearly as black dots. In Immunocytochemsitry slides, the nuclei showed brown dots which varies in intensity.

Subjects	AgNOR Staining (Mean)	Subjects	ICC Staining (Mean)
Normal	2.29	Normal	2.54
Smoker	4.58	Smoker	3.83
Chewer	4.17	Chewer	4.05

Table 1 : Mean value of AgNOR Staining & ICC Staining.

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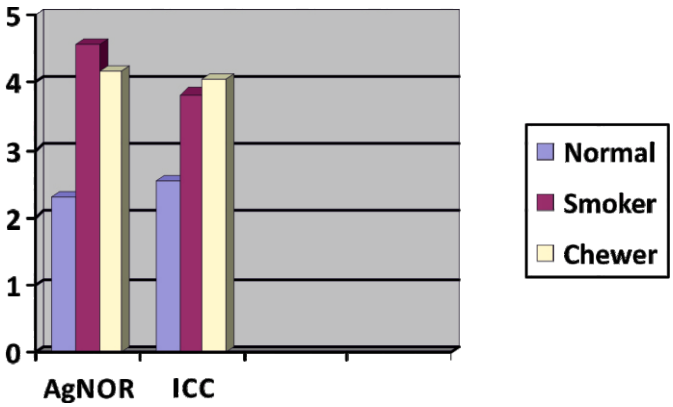
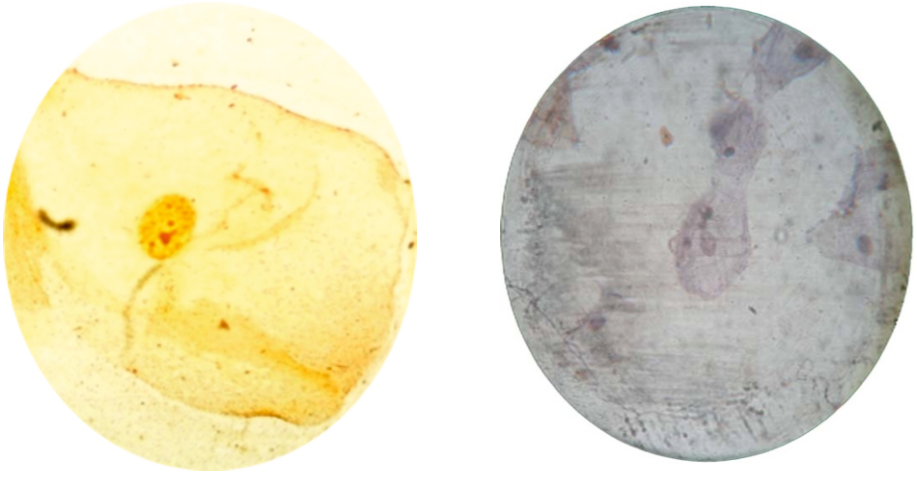


Graph 1 : Comparative mean between AgNOR and ICC staining



A B

Fig : 1- Cytological smear stained with (A) : AgNOR & (B) : ICC (Ki 67)

Discussion :

Cancer especially oral squamous cell carcinoma is quite common in India due to adverse use of tobacco in smoking and smokeless form.6 Oral squamous cell carcinoma has a poor prognosis inspite of advances in therapy. Diagnosis at early stage and treating them are the main tool in improving patient survival rate. Generally scalpel biopsy is used for diagnosis which is invasive and morbidity, so they are employed in severe suspected lesions and not in all conditions.7

To control the rapidly developing situation technqiues which are less expensive, non invasive, and well accepted by the patient needs to be developed and those which can be repeated frequently. It is an easy procedure that can be carried out at outdoor patient department to diagnose malignancy at early stage.6Exfoliative cytology is not a new science. In 1920, aspiration and exfoliative cytology were introduced. Johannes Muller (1801 - 1858), a pathologist in Berlin was first to show cancer cells in microscope on scrapings from the cut surface of surgically excised tumors.1The silver staining procedure which is used for identification of NORs has been frequently utilized in formalin fixed, paraffin embedded specimens but in this study we have used exfoiliative cytology. 9

Jahanshah Salehinejada et al has showed in their study that, in cytologic smears the analysis of AgNORs is more accurate as whole

nucleus can be assessed as in tissue sections and has used AgNOR technique successfully in oral smears1. This present study carried out AgNOR staining in cytologic smear also successfully carried out ICC staining in oral cytologic smears.

The Ki-67 antibody was first developed by Gerdes and coworkers who demonstrated the antigen to be present in G1, S, G2 and M phases of continuously cycling cells, but absent in G0 cells. To best of our knowledge there are no previous publication comparing AgNOR and ICC (Ki 67) marker but was suggested by Jahanshah Salehinejada et al (2007). 9In deep invasive fronts of tumours, the expression of Ki 67 is higher than those at the centre or surface of mucosal cancers. It shows that actively proliferating cells are more in number at deep tumour margin. The cytological assessment has certain difficulties like obscuring blood products, necrotic debris and contamination by bacterial and other components.9

In this study we have considered 3 or more black dots in the nucleus to have more cellular and proliferative activity and followed the same criteria for ICC counting. The AgNOR number where more in smokers than in chewers as not ususally expected because the silver granules may be counted as silver dots and were considerably high than normal. The AgNOR counts in chewers were also comparatively higher when compared to normal and close to smokers.

Regarding ICC study, it showed positive expression of Ki 67 in the nucleus of exfoliated cells. It showed a significantly higher value in chewers than smokers and normal. This shows that this procedure is more sensitive in detecting the nuclear alterations and miscounting of silver granules as silver dots could be eliminated.

Conclusion

Based on this study, we conclude that even ICC (Ki 67) is even more sensitive than AgNOR and it could also be used as an adjunct to Histopathological investigation. One of the main advantage in employing this technique is that counting will be accurate as we will be avoiding counting silver granules as silver dots in nucleus and it will detect even mild alterations in nucleus.

As literature states that proliferation is observable with AgNOR, this holds true for ICC technique with Ki 67also.

Further studies with larger population and certain other criteria for assessment could enable us to validate and improve the technique, so that it will help in formulating new diagnostic methodologies which are specific and can be performed at minimum laboratory set up.

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Indian Dental Association Tamilnadu State Branch

ORIGINAL RESEARCH

'COMPARISON OF TMA, STAINLESS STEEL AND TIMOLIUM FOR FRICTION, LOAD DEFLECTION AND SURFACE CHARACTERISTIC"

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Abstract:

OBJECTIVE

The present study aims at characterizing and comparing the mechanical property and surface characteristic of two arch wire alloys in orthodontics, stainless steel and TMA with newly introduced Timolium.

METHOD

An INSTRON 2366 testing machine was used for frictional characteristic and three points bend testing. Scanning electron microscope was used for surface evaluation and x-ray fluorescence for elemental analysis of Timolium wire specimen.

RESULT

Stainless steel was the strongest archwire alloy, and less friction at the archwire-bracket interface. TMA wires exhibited better load deflection characteristics with less stiffness than the other two wires. The surface of TMA appeared rough and exhibited very high values for friction at the archwire-bracket interface. Timolium appeared to be an alpha-beta titanium alloy composed of titanium, aluminum, and vanadium and intermediate in nature for all the parameters evaluated.

CONCLUSION

Timolium with its smooth surface, reduced friction and better strength can be considered as an introductive breakthrough in clinical orthodontic practice.

KEYWORDS

Friction, load deflection, scanning electron microscope, stainless steel, TMA, Timolium.

Introduction:

Gold alloy was one of the earliest orthodontic wire used .The gold wires have decreased usage in orthodontics because of their low yield strength and increasing costs. In 1940s austenitic stainless steel with adequate spring back, good formability, and moderate cost began to displace gold as primary alloy for orthodontic wires. Elgiloy, a chrome cobalt nickel alloy with excellent corrosion resistance was used. Nickel titanium alloy was introduced in orthodontics several years ago and find its application where deflection and low forces are required. These wires are not amenable to joining operations. With the introduction of b-titanium alloy distinctive features of good spring back, low force delivery, good formability, weld ability, high corrosion resistance, and excellent bio compatibility were available for orthodontist. The disadvantages are surface roughness and high friction. In 1995 a new TMA featuring dramatically reduced friction for a superior sliding mechanics was introduced by Burstone. Timolium ,a patented vanadium based high performance aerospace alloy, has been designed to produce a much smoother surface texture than other titanium molybdenum wires(TMA).Timolium as claimed by the manufactures has almost the same frictional resistance and half the stiffness of stainless steel making it ideal choice for finishing, aligning as well as leveling and torqueing through all phases of treatment.

MATERIALS AND METHOD

The following materials were used in the study

1. 0.016"x 0.022" stainless steel (ormco corporation Giendora CA) – 15 numbers.
2. 0.016"x0.022" TMA (ormco corporation Glendora CA) – 15 numbers.
3. 0.016"x0.022" Timolium (TP labs, Indiana polis IN) – 15 numbers.
4. 0.018" Edgewise canine brackets (American ortho.) – 45 numbers.
5. 0.010" ligature wires (ortho organizer).
6. Cold cure acrylic.
7. Stainless poles 5mm in diameter.
8. Instron machine with model number 2366.

METHOD

FRICTION ANALYSIS

In this study Tidy's (30) frictional test designs were used to stimulate canine retraction. The force acting on the surface of the tooth was simulated by single equivalent force acting at the center of resistance of the root. [27] . Four 0.018" slot edge wise bracket were fixed, at 8mm intervals with a 16mm space for a movable canine bracket at the center. A power arm of 10mm length from bracket slot was fixed at the base of each canine bracket. This distance was chosen according to Burstone finding relating to the location of center of resistance of canine. (3)

The wires stainless steel, titanium molibdinum and Timolium, were then evaluated for friction in the 0.018" slot edge wise brackets.

This jig assembly was mounted on to the lower jaw of instron machine. The canine bracket was then ligated to the test wires. The stainless steel ligatures 0.010" were initially fully tightened and then unwound by three turns; loose ligation was checked by rocking the brackets to confirm that there is play between both the spans of the bracket and the archwire.(21) the bracket was then moved over the archwire with the help of a 0.016"stainless steel wire which was suspended from a special jig which was attached to the upper jaw of the instron machine which was moved in the upward direction, at cross head speed of 5mm/min. In each test they were moved not less than 2.5mm across the central space and the load cell reading were recorded on the digital display.

The differences between load cell reading and load on the power arm thus represents the frictional resistance of the given material.

LOAD DEFLECTION ANALYSIS

The three point bending test was conducted as described by miura et al. (9)

A single bracket was attached on a steel pole, acting like a dental unit placed on a movable stage, so that the bracket span could be set at 14mm. the test wire was held in place with a ligature wire in the slot with a known quantity of force. This jig assembly was mounted on to the lower jaw of the instron machine.

A steel pole of 5mm in diameter was placed in an acrylic block, which was mounted on to the upper jaw of the instron machine. The steel pole which was attached to the upper jaw of instron machine was moved down so that mid portion of the wire segment was deflected to 2mm at the speed of 0.1mm/min under the pressure from the metal pole. The load cell reading in digital display was noted at 0.5mm, 1mm, 1.5mm and 2mm deflection.

The above tests were divided in to three groups comprising of 15 wires each.

Group 1 - 0.016"x0.022" stainless steel wires.

Group 2 - 0.016"x0.022" TMA wires.

Group 3 -0.016"x0.022" Timolium TM wires.

STATISTICAL ANALYSIS

Mean and standard deviation were estimated from the samples for each study group. The groups were subjected to one –way ANOVA to test the level of significance among the test groups. Multiple range tests by Tusky –HSD procedure was employed to identify the significant group if the p –value in the one- way ANOVA was significant.

In the present study, $p<0.05$ was considered as the level of significance.

SURFACE CHARASTERISTIC

In surface, characteristic study each wire was studied before and after sliding through the bracket with the help of a scanning electron microscope a 1cm specimen of each alloy wire was mounted and these wires were then scanned and viewed on the monitor at different magnification and representative micrographs (750 x) of the alloys were obtained.

RESULT

The result of the frictional resistance of the three wires which were analyzed in the study using instron testing machine are tabulated as follows (Table-1); and is graphically plotted in(chart -1)

Table-1

Frictional resistance between stainless steel, TMA, Timonium.

Group	Number of sample	Mean ± (grams)
I	15	203.2 ± 24.2
II	15	301.3 ± 27.5
III	15	222.5 ± 32.9

The above values were subjected to statistical analysis and tabulated as below (Table- 2)

Table-2

ONE-WAY ANOVA AND MRT

GROUP	ANOVA	Multiple range test
	P-Value	Significant group at 5%level
I	<0.001/(sig)	TMA VS STAINLESS STEEL
II		TMA VS TIMOLIUM
III		

- ANOVA test revealed a statistically significant difference among the three groups of the wires analyzed.
- Multiple range tests revealed a statistically significant difference between group-I and group-II and group-III.

The results of the three groups were analyzed for load deflection is tabulated as follows (Table 3); and are graphically represented in (chart 2).

Table-3

Load deflection between stainless steel, TMA and Timolium.

Group	Number of samples	Mean ± S. D (grams)
I	15	1576.3 ± 46.3
II	15	1189.3 ± 19.2
III	15	1319.6 ± 281

The above values were then subjected to statistical analysis and tabulated as below (Table 4)

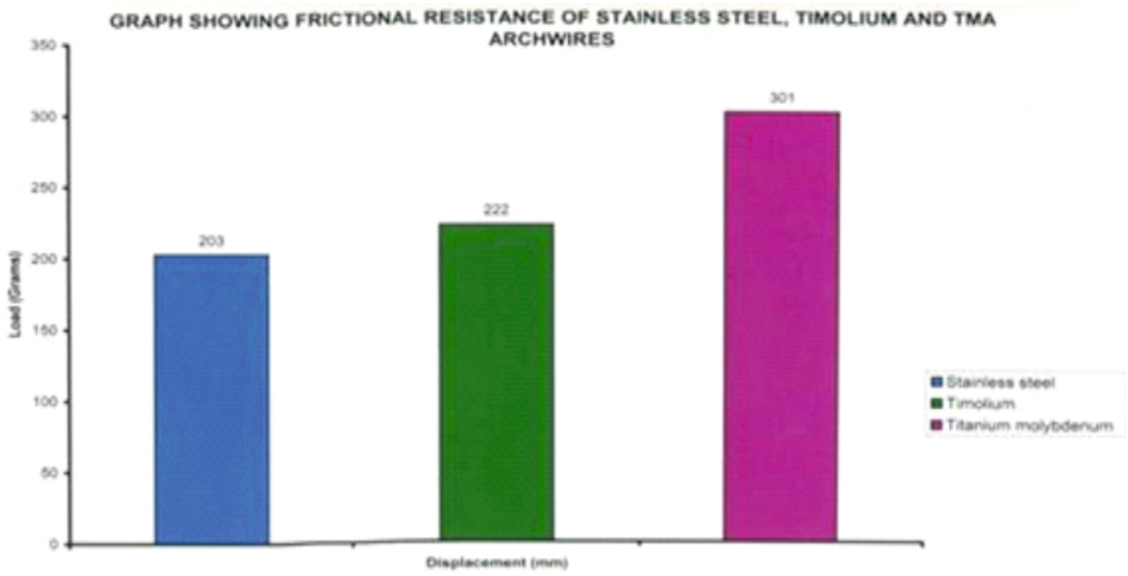
Table-4

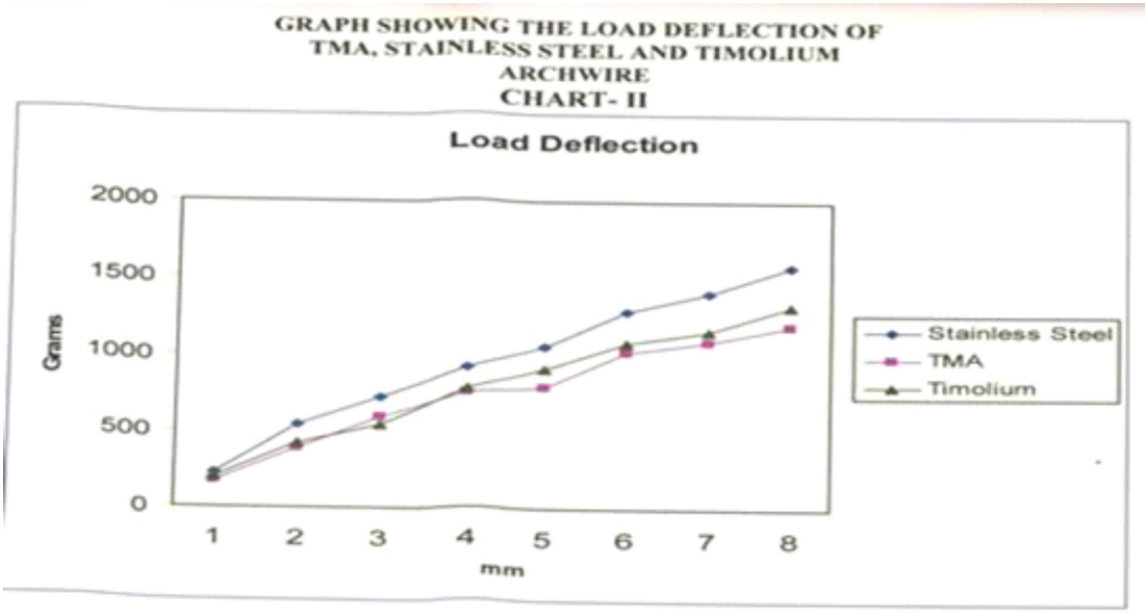
ONE-WAY ANOVA AND MRT

Group	ANOVA	Multiple range test
	P-Value	Significant group at 5%level
I	<0.0001/(Sig)	STAINLESS STEEL VS TMA
II		STAINLESS STEEL VS TIMOLIUM
III		TIMOLIUM VS TMA

- ANOVA test revealed a statistically significant difference among the three groups of wires analyzed.
- Multiple range tests revealed that there was a significant difference between Timolium and TMA wires.

All the three groups of wires which were



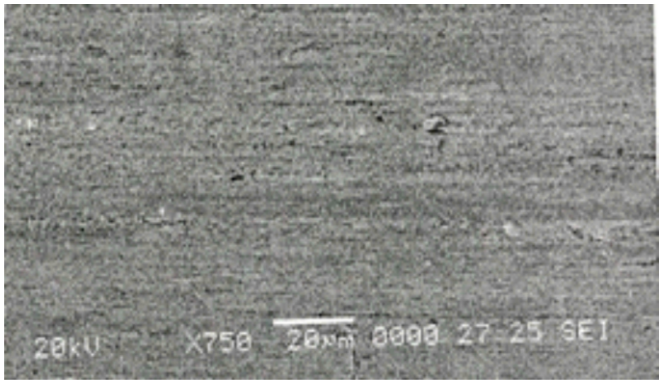


evaluated for the surface characteristic using scanning electron microscopy both before and after sliding of wire in the bracket, reveals that in

STAINLESSSTEEL (FIGURE -1)

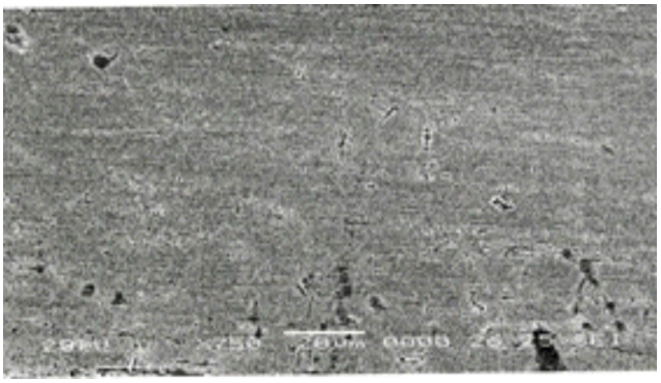
BEFORE SLIDING OF WIRE

(a)



AFTER SLIDING OF WIRE

(b)



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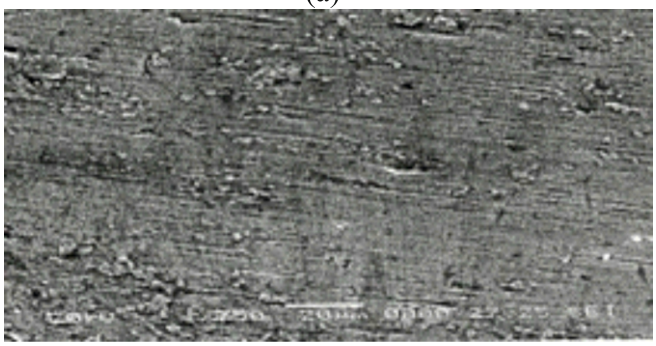
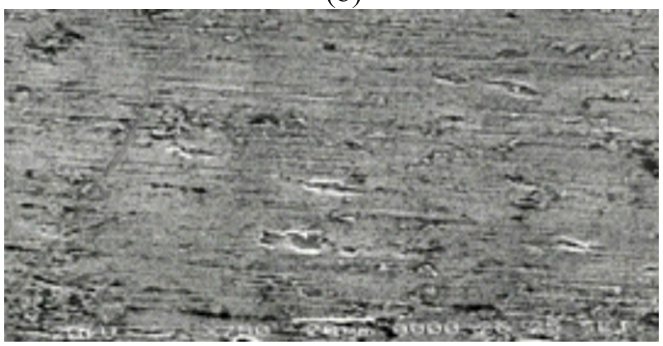
TIMOLIUM (FIGURE-2)

BEFORE SLIDING OF WIRE (a)

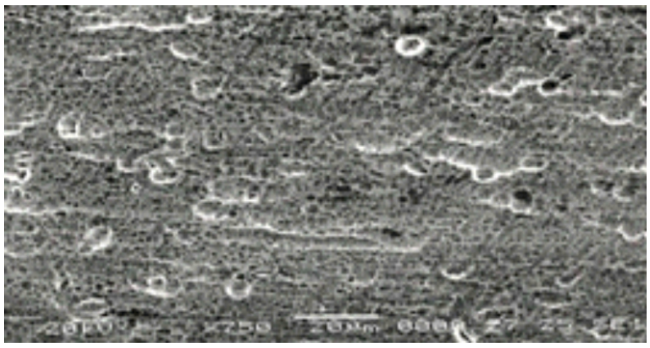


AFTER SLIDING OF WIRE (b)

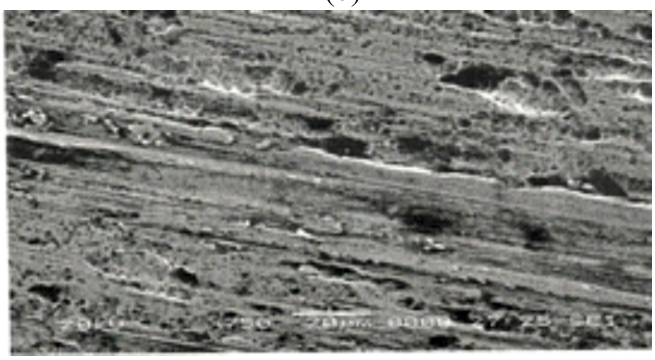


TMA (FIGURE-3)

BEFORE SLIDING OF WIRE (a)



AFTER SLIDING OF WIRE (b)

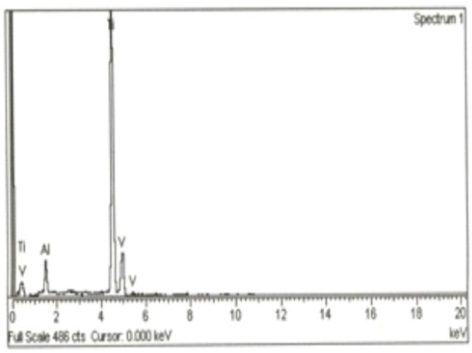


The composition of the timolium wires in (Table-5) and graphically represented in (Chart- 3.)

Table – 5

Element	Weight%	Atomic%
TiK	91.70	87.97
ALK	5.67	9.65
VK	2.63	2.37
Totals	100.00	

Chart -III



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DISCUSSION

Characterization of arch wire alloy forms an initial step towards understanding arch wire behavior in biomechanical requirement of the clinical situation from the plethora of the material available.

Frictional force has long been an important consideration in orthodontic mechanotherapy. It is a well-known fact that any force needed to retract teeth must overcome friction. (13)

Friction is a function of the relative roughness of two surfaces in contact [23].

Both static and kinetic sliding friction arises in any orthodontic situation of intended displacement, overtime, of an arch wire through a bracket (or) a bracket along an arch wire. (1)

Profit (2000) (26) reported that 50 per cent of the force necessary to initiate tooth movement required to overcome the regarding force generated between brackets, arch wires and ligatures. This implies that only 50 percent of the force applied reaches the tooth and its supporting tissues. The absolute value for the optimum force required to produce "biological tooth movement" is extremely difficult to quantity and it has been demonstrated that increasing the force increases the rate of orthodontic tooth movement up to a point (Andreasn and Quevedo,(1970)(1); Frank and Nikolai,(1980)(8); Garner et al; (1986)(10), Beyond this point tooth movement fails thus, the concept of optimal force. (8)

Kinetic friction was measured rather than static friction because of the variable nature of the frictional process. The result shows that the frictional resistance of Timolium lies between stainless steel and TMA with range being close to that of stainless steel.

The present study clearly indicates a greater friction when TMA wires are used, with a mean value of 301.3 (±) 27.5 grams. The least friction arch wire with stainless steel, with a mean value of 203.2 (±) 32.9 grams.

The result of the study conducted by Cash et al., (2004)(5) is similar to the present study.

The study conducted by Garner et al., (1986)(10), Dresche et al., (1989)(7), Kusy and Whitley, Kapila et al.,(1990)(14), Angolkar et al., (1990),(2) is similar to the present study stating that beta titanium arch wires developed frictional forces greater than stainless steel.

Surface evaluation of an arch wire alloy is important because of its influence on working characteristic as well as working potential. (18) Scanning electron microscopic evaluation of surface characteristics revealed a smooth surface with horizontal lines for Timolium arch wires as in accordance to, pradeep babu[30] . Stainless Steel exhibited vertically oriented cracks, and TMA, a very rough surface as reported extensively in the literature [4, 3, 6].

A modified version of the three-point test by Miura et al(9) was performed to evaluate the load deflection properties, the most important parameter determining the biological nature of tooth movement.(4) The result indicated beta titanium with a mean of 1189.3 (±) 19.2 grams. Stainless steel was more rigid among three arch wire alloy with very high loading value and less spring back properties with a mean of 1576.3 (±) 46.3 grams. Timolium was intermediate in nature 1319.6 (±) 281 grams.

According to cristiane [33] , Oltjen et al., (1970)[22] , vijayalakshmi RD [34] Timolium possesses comparatively low stiffness, better strength and behave as an intermediate between stainless steel and TMA.

Elemental analysis of Timolium with the help of EDS revealed the alloy, with

combination of alpha and beta phase of titanium alloy, exhibits an unusual combination of strength and surface smoothness.

CONCLUSION

In the study performed shows that in frictional studies, Timolium has almost has the same surface friction as stainless steel, unlike TMA (Titanium molybdenum) which have much higher frictional characteristics. This reduced frictional property of the Timolium helps in efficient canine retraction.

Timolium has the half the stiffness midway between TMA and stainless Steel making it ideal choice for finishing, aligning as well as leveling and torqueing throughout all phases of treatment.

Timolium bends easily in "T" boots and" loops" because it has a higher stiffness than TMA and fewer surface defects.

Timolium with its smooth surface, reduced friction and better strength can be considered as an introductive breakthrough in clinical orthodontic practice.

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Indian Dental Association Tamilnadu State Branch

CASE REPORT

DRUG INDUCED ORAL ERYTHEMA MULTIFORME: A CASE REPORT

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ABSTRACT

Erythema multiforme is an acute, self limited and sometimes recurring skin condition that is considered to be a type IV hypersensitivity reaction associated with herpes infection, medication and other various triggers. Here we report a case of Drug Induced Erythema multiforme in a 56 year old woman who developed oral lesions after taking antiepileptic medication.

Key words: oral erythema multiforme, drug reaction, oral mucosa, ulcerations.

INTRODUCTION

Erythema multiforme a self limited acute inflammatory disorder affecting skin,muous membrane or both was first identified by Bulkley and Bateman in 1817. In 1846, a first case was reported in America as “Herpes Iris.” Later, in 1866 Von Hebra, described this condition under the term “erythema exsudativum multiforme”. Erythema multiforme represents a spectrum of disease ranging from localized rash with minimal mucosal involvement to a more severe generalized rash with limited desquamation and involvement of mucous membranes with blister formation.1 The reaction comprises of polymorphous eruption of macules, papules, with a characteristic “target” lesions that are symmetrically distributed with a proclivity for the distal extremities. Other than EM minor and major, oral erythema multiforme (EM) is considered as a third category. The features include lip and oral ulcerations without any skin target lesions. No specific laboratory tests are indicated to make the diagnosis of Erythema multiforme, which should be arrived at clinically.Immunofluorescence and histopathological examination may be used to confirm the diagnosis of Erythema multiforme and to rule out the differential diagnosis.

This article reports cases of drug induced oral EM highlighting its importance of differentiating this disorder.

CASE PRESENTATION:

A 56 -year-old female patient reported to our department of Oral medicine and

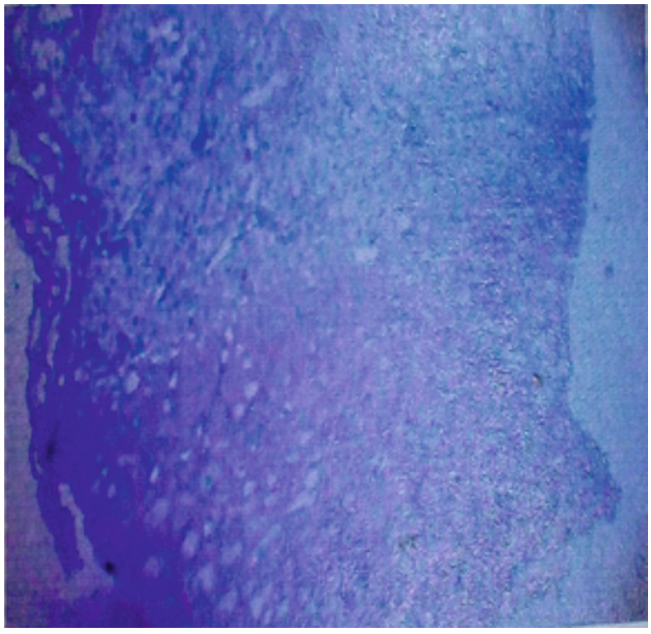
Radio diagnosis with a complaint of extensive oral ulcerations and hemorrhagic crusts on the lips due to which she was unable to take solid food and was on liquid diet since a week. Patient gave a history of seizures 15 days back for which she took Epitoin tablet 100 mg twice daily. Subsequently she developed multiple vesicles in the oral mucosa which eventually ruptured and transformed into extensive irregular ulceration.

On extra oral examination, both upper and lower lips showed extensive, fissured irregular ulcerations, with blood encrustation. Bilateral submandibular lymph nodes were tender and palpable.

Intraoral examination showed multiple irregular ulcerations with yellowish base surrounded by erythematous borders on lip and palate. There was no extension into the pharynx.

The sudden onset, drug history, extensive ulcerations of the oral cavity cracking and fissuring of lips with bloody crustations lead to the provisional diagnosis of oral erythema multiforme.A incisional biopsy followed by immunofluoresence study was done after revealing no abnormality in blood investigation

Histopathological examination of the specimen showed surface squamous epithelium showing acanthosis, necrosis of deeper keratinocytes and vacuolation of basal layer. Sub epithelial layer shows edema, increased vascularity and infilteration by lymphocytes and few polymorphs. Direct immunofluorescence study shows no deposition of Ig G,IgA,IgM and fibrin.



The clinical and histopathological findings were considered diagnostic for Oral Erythema multiforme.

The patient was advised to alter the drug after consulting her physician and was treated with systemic corticosteroids, (prednisolone 20 mg BD for 3 days followed by tapering the dose for 10 days), mild analgesics, and topical application of

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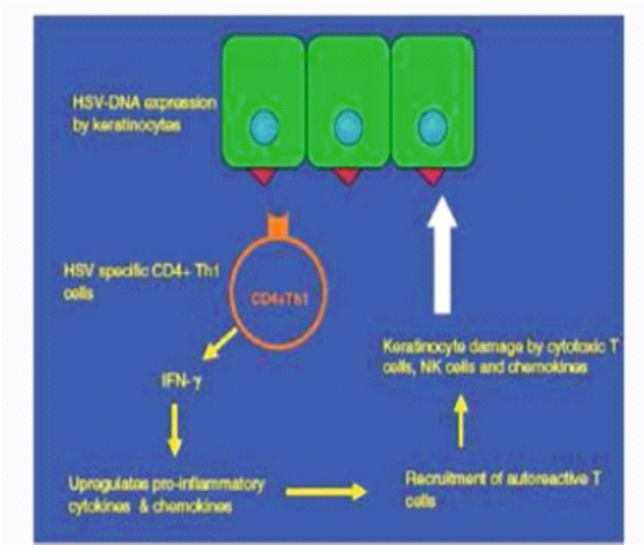
lignocaine gel to facilitate oral fluid intake. Patient responded to the treatment well and healing occurred within 10 days.

Review photos

DISCUSSION

Erythema multiforme a self limited acute inflammatory disorder affecting skin,muous membrane or both was first identified by Bulkley and Bateman in 1817. In 1846, a first case was reported in America as “Herpes Iris.” Later, in 1866 Von Hebra, described this condition under the term “erythema exsudativum multiforme” .2 According to him the patients with this condition should have raised edematous cutaneous papules. or acrally dispersed typical target lesions . In1968 Kenneth described an inflammatory oral disorder typial of EM but without any skin involvement.3

The disorder results from T-cell-mediated immune reaction to the triggering agent, leading to cytotoxic immunological attack on keratinocytes expressing non-self antigens, leading to subepithelial and intra-epithelial vesiculation forming widespread blisters , erosions and ulcerations. In drug-induced EM, the drug metabolites induce the disease. Tumor necrosis factor alpha (TNF-A) is responsible for keratinocyte apoptosis causing tissue damage.1



The sites commonly involved were cheeks, tongue and lips. Large irregular ulcers

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bordered with necrotic tags are usually seen .When lips are involved bloody encrustation were seen frequently.4 Patients initially may experience burning and itching sensation at the site followed by eruption of sharply demarcated numerous macules progressing to papules with crustation occurring in the center of the lesions.1 The characteristic "target" or "iris" lesion has a regular round shape with three concentric zones: a central dusky or darker red area, a paler pink or edematous zone, and a peripheral red ring.5

The differential diagnosis of oral EM includes autoimmune vesciculobullous lesions such as bullous pemphigoid or pemphigus vulgaris and other patterns of drug reactions and ulcerative lesion like herpes6.

Keratinized mucosa are most prompt for herpetic lesions and also the ulcers are smaller having regular borders .7But in our case irregular ulcers are seen in the lining nonkeratinized mucosa which is not a feature of herpes infection.

The onset is acute and does not show any desquamative gingivitis is not a feature in oral EM unlike pemphigus vulgaris.

The features of anaphylactic stomatitis include urticarial skin reactions which is not seen in oral EM

Erythema multiforme major is more aggressive form involving multiple mucosa with typical target skin lesions; while lesions of EM minor are single mucosal ulcerations and typical target lesions of skin. The oral ulcers are large with necrotic tissue tags.8 Bloody encrustation of lips is commonly seen. The third category of EM is known as oral EM having lesions confined only to oral mucosa and lips without cutaneous involvement.9

The drugs triggering EM lesions are co-trimoxazole, long acting sulfa drugs especially phenytoin, sulphonamides, carbamazepine and nonsteroidal anti-inflammatory drugs such as diclofenac, salicylates and ibuprofen.10

Management of oral EM involves identification of triggering agentand treatment of lesions palliatively with analgesics and antibiotics.11 Mild case respond to topical steroids, while for severe cases systemic corticosteroids are recommended.

CONCLUSION

Oral EM, is a rare variant of Erythema multiforme often triggered by HSV infections and rarely by adverse drug reactions. Even though initial attacks are confined only to oral mucosa, subsequent attacks can produce more aggressive forms involving skin. Hence, early clinical recognition of this disease remains essential to promptly initiate appropriate treatment.

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Indian Dental Association Tamilnadu State Branch

CASE REPORT

THE VERSATILITY OF SUBMENTAL INTUBATION SIMPLE ROUTE OF INTUBATION IN COMPLEX MAXILLOFACIAL TRAUMA

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Abstract

Achieving a secure airway is of utmost importance in patients under general anesthesia. The two most common methods of airway management (intubation) in such patients include oro-tracheal and naso-tracheal intubation. However, both may be contraindicated in complex maxillofacial trauma, like pan-facial fractures requiring surgical access to oral and nasal cavity in the same surgery. Traditionally, the only other alternative available in such situation is tracheostomy, which is associated with a high risk of iatrogenic complications. This report presents our experience of airway management using submental intubation in complex maxillofacial trauma.

Key words: Submental intubation, maxillofacial trauma, airway management.

Introduction

Achieving a secure airway is of utmost importance in patients under general anesthesia. The two most common methods of airway management (intubation) in such patients include oro-tracheal and naso-tracheal intubation. However, both may be contraindicated in maxillofacial trauma, like pan-facial fractures requiring surgical access to both the oral and nasal cavity at the same time.

Hence, management of airways in the presence of midface or pan-facial injuries with mandibular involvement requires special consideration. Tracheostomy remains an excellent procedure for establishing a definitive surgical airway. This procedure may involve a significant risk of iatrogenic complications, such as tracheal stenosis, internal emphysema, damage to the laryngeal nerves, tracheosophageal fistula and scarring.

Indications for alternative route of intubation

For fractures that do not involve the occlusion such as nasal, zygoma, naso-orbito-ethmoidal (NOE), frontal and orbital blow out fractures, oral intubation is indicated. For fractures that involve the occlusion such as mandibular and Le Forte fractures, oral intubation inhibits appropriate resolution of occlusion. In these situations, nasotracheal intubation is indicated.

However, under certain circumstances, such as persistent cerebrospinal fluid leakage, pan-facial fractures, stenosis of the nasal airway by deviated nasal septum, hyperopic turbinate, and nasal polyps, an alternate method of intubation is sought.

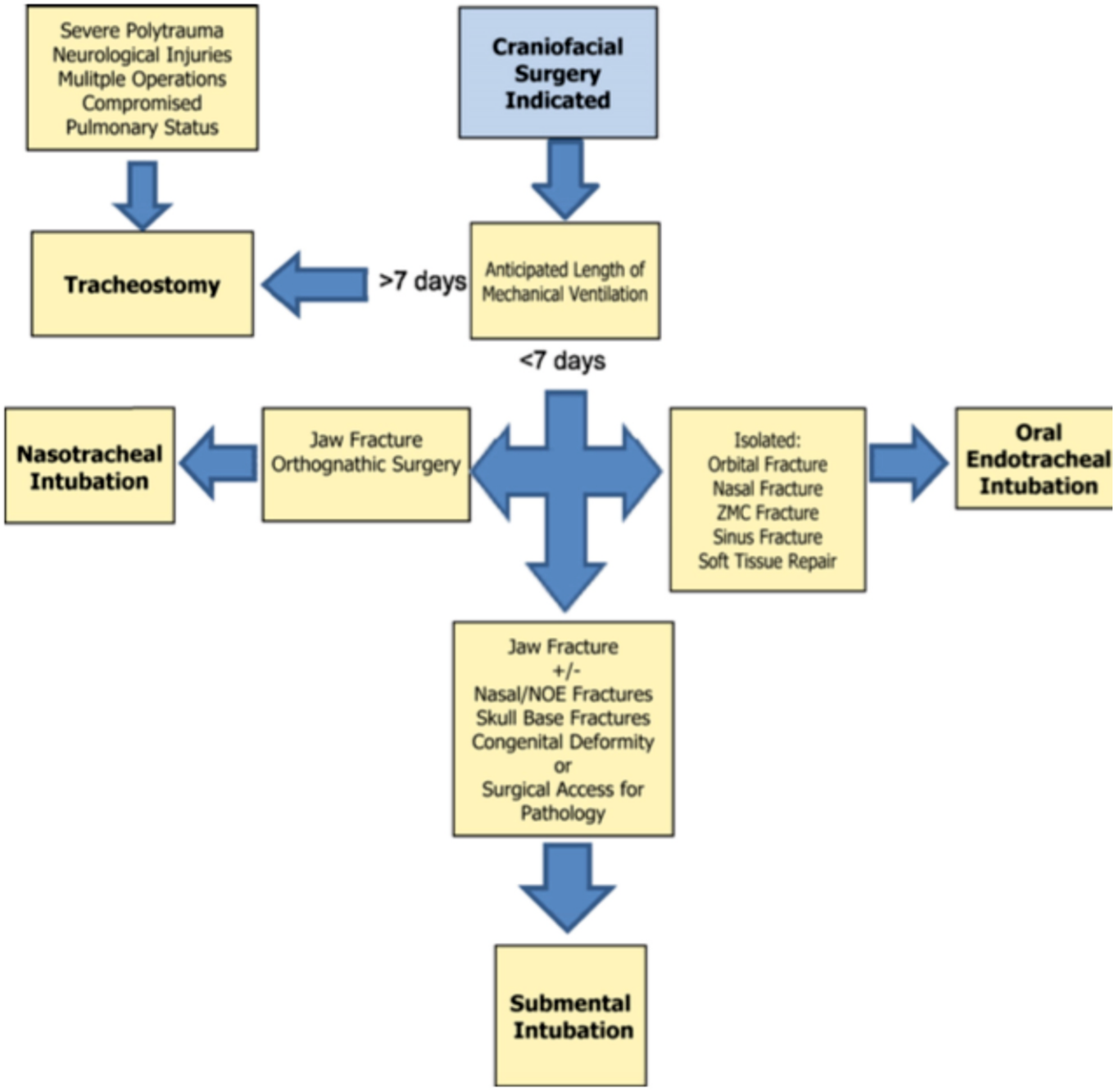
In some cases, tube exchange is possible, while tracheostomy is the preferred option in other situations. Retromolar intubation or dividing the surgery in to two separate procedures (nasal and oral intubation) are other options.

Submental intubation

An alternative to the classic methods is the submental route for tracheal intubation. Introduced by Hernandez Altemir in 1986,

this method has gained wide acceptance, and with some modifications, is an excellent alternative to tracheostomy. The technique consists of diverting the proximal end of an orotracheal tube through the floor of the mouth and submental region. This allows free intraoperative access to the dental occlusion and nasal pyramid without endangering patients with skull base trauma, and at the same time avoids transtracheal dissection.

Maxillofacial Airway Algorithm



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Case Presentation

A 24-year-old male patient presented to VMC ER following Road Traffic Accident. Following detailed clinical examination and CT evaluation, he was diagnosed with bilateral Leforte II fractures with derangement of occlusion; and was planned for open reduction and internal fixation under GA. The involvement of naso-orbital-ethmoidal complex, mobile midface and deranged occlusion, warranted the need for submental intubation.

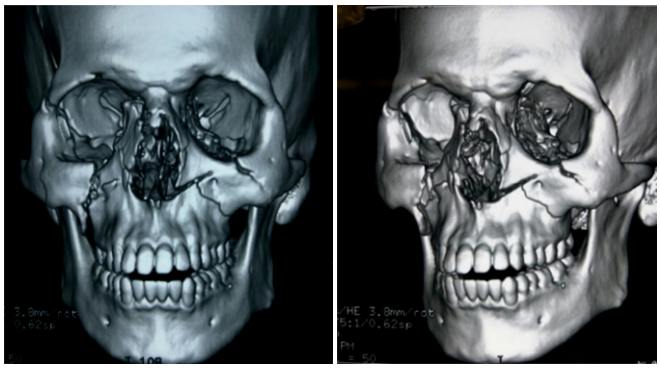

Figure 1 & 2: Fractures involving bilateral midface region at Le Forte II levels

Technique of submental intubation:

After establishing orotracheal intubation, a 2 cm skin incision is made on the median region of the submental area, directly adjacent to the lower border of the mandible. Following blunt dissection of the platysma and mylohyoid muscles, and maintaining close continuity to the lingual cortex of the mandible, a tunnel is created by placing an incision on the mucosal layer of floor of the mouth, in front of the sublingual caruncle.4 It is important to establish adequate width of the submental access to allow free passage of endotracheal tube. (Figures 3 & 4)

Figure 3: Skin Incision in submental area

Figure 4: Blunt dissection to the floor of mouth

After the surgical access was made, the pilot balloon with inflating tube was first passed through the tunnel with the forceps. ET tube was held firmly in position by an assistant while maneuvering the tube from oral to submental position. The tube was then disconnected from the ventilator and the universal connector briefly, and the tube brought out through the submental tunnel. Finally, the tube was positioned, the ventilation restored after checking bilateral air entry. Sutures were used to fix the tube in position.2,4,5 After the surgery, the submental intubation was converted to an orotracheal intubation by replacing the tube in the mouth and extubated in the conventional manner. The skin was sutured with 5-0 prolene and mucosal layer over the floor of the mouth with 3-0 vycril (Figures 5 & 6).

Figure 5: Submental Position

Figure 6: Reconverted to oral route

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Discussion

Submental intubation allows for mobilization of the dental occlusion, and those of orotracheal intubation, and allows access to frontonasal fractures. It also avoids the risk of iatrogenic meningitis or trauma of the anterior skull base after nasotracheal intubation, as well as complications of tracheostomy.5,6

Nonetheless, tracheostomy is indicated in patients who present with a neurologic deficit or thoracic trauma and need more than 7-14 days of post operative ventilatory support or in patients with multi-trauma who require long periods of assisted ventilation.1,2,5

Although the incision for gaining submental access can be placed laterally/ paramedially, midline access is most versatile because there are only a few anatomic structures present, and there is a minimum risk of nerve or vascular damage. Secondly, the scar is less visible behind the symphyseal region.3,6

Conclusion

Submental intubation should be chosen whenever possible in cases of purely maxillofacial trauma. It demands certain surgical skill, but it is simple, safe, and quick to execute. It also allows for operative control of the dental occlusion and the concomitant surgery of the nasal pyramid in major maxillofacial traumas and avoids iatrogenic placement of tube in skull base fractures.

Finally, it presents a low incidence of operative and postoperative complications and eliminates the risks and side effects of tracheostomy.

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Indian Dental Association Tamilnadu State Branch

REVIEW

LAB ON A CHIP "MINIATURIZED LABORATORY"

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Abstract

Since long oral cancer is considered as disfiguring and deadly disease of the oral cavity. Though there is increase in therapeutic modalities there is poor prognosis because of lack of early diagnosis and detection. For the timely care and prognosis,a mass screening procedure and rapid diagnostic test is required. Lab on a chip is a promising replacement of all the laboratory procedures into a miniaturized chip with all levels of identification of cancer biomarkers from gene profiling to proteins in cancer cells.

Introduction:

Even though there is great progress in the diagnosis and treatment of many diseases, malignancy has been the most common cause of death worldwide. Accuracy in early screening and diagnosis is the critical part of the day to day new invention in the field of medicine and diagnostics. The whole world is putting their hands together in the research of the informative cancer biomarker detection in the saliva and to simplify the cumbersome lab procedures into a pocket card that is lab on a chip also called as micro total analysis system μTAS.1

History:

It was in 2002 National Institute of Dental Craniofacial Research (NICDR) initiated the research effort on salivary diagnostics. NIDCR has funded the micro electro mechanical system for the salivary diagnostics. The important research group at the university of California Los Angles (UCLA) in developing the point of care micro-fluidic system for oral cancer and breast cancer ,metabolic diseases (e.g.) diabetes.2

Discussion:

Micro-fluidics technology also called as lab on a chip or μTAS micro total analysis system, is defined as the adaptation, miniaturization, integration and automation of analytical laboratory procedures into a single device or chip .Used in the analysis of disease diagnostics, control drug delivery, drug discovery, air and water quality control and monitoring.4 The sample introduced can be small biopsy or blood saliva etc. We will discuss about oral cancer diagnosis. 1

Typically micro-fluidic technology enables the activation of fluids and manipulation of the bioparticles (eg DNA, RNA, proteins and cell) at microscale. 1

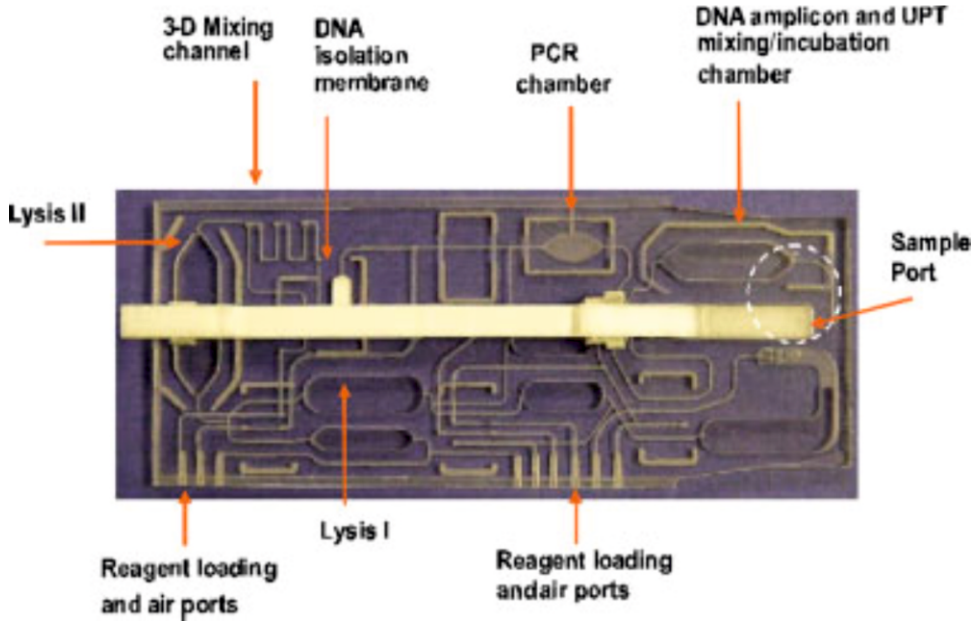
Microfluidic culture based studies gave way for integrated genomic, protemic and cytomic analysis to identify different novel biomarker potentially involved in tumerogenesis. 1

Types of microfluidic based analysis

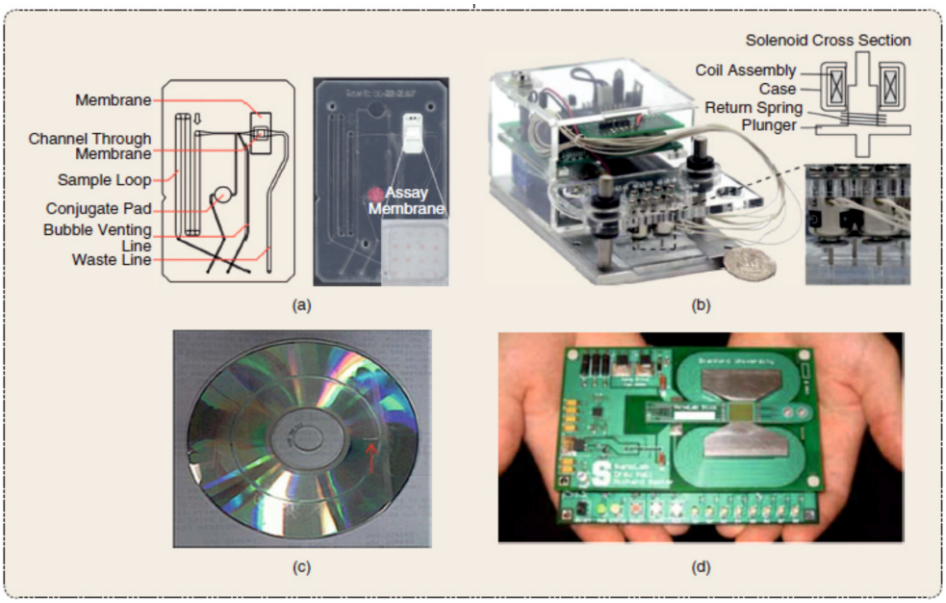
1. Microfluicidic –based gene analysis
2. Micro fluidic –based protein analysis
3. Microfluicidic –based cell analysis

There are two types of devices

1. Stationary configuration ,in which conventional PCR sample is held in a micro chamber and temperature of the chamber is cycled
2. Flow through configuration in which the sample flows through different thermal zones responsible for distinctive processes such as denaturation, annealing and extention.



Example of a microfluidic lab-on-a-chip. The saliva sample is introduced into the sample port. The saliva sample is lysed with enzymes, detergent, and chaotropic salts in a 2-step, 2-chamber lysis process. The nucleic acids are isolated from the lysate by solid-phase extraction using a porous silica membrane as a nucleic acid binding phase. Purified nucleic acids eluted from the silica membrane are amplified by PCR using specific primers. The PCR amplicons are labeled with up-converting phosphor particles and conjugated to antigens, then run on a blotted nitrocellulose strip, where they are captured by immobilized antibodies and detected by a laser scanner.



Examples of promising LOC technologies. (a) Microfluidic flow-through membrane immunoassay developed in the Yager laboratory achieves rapid and sensitive detection using dry reagents stored on the disposable card. (b) The Sia laboratory has demonstrated higher-level integration that is completely battery powered. (c) A CD-based approach for cell detection from the Liu laboratory reduces the requirements for pumps and valves. (d) The Wang laboratory has developed a wash-free multiplexed immunoassay based on magnetic nanotechnology. (All reproduced with permission from the Royal Society of Chemistry.)

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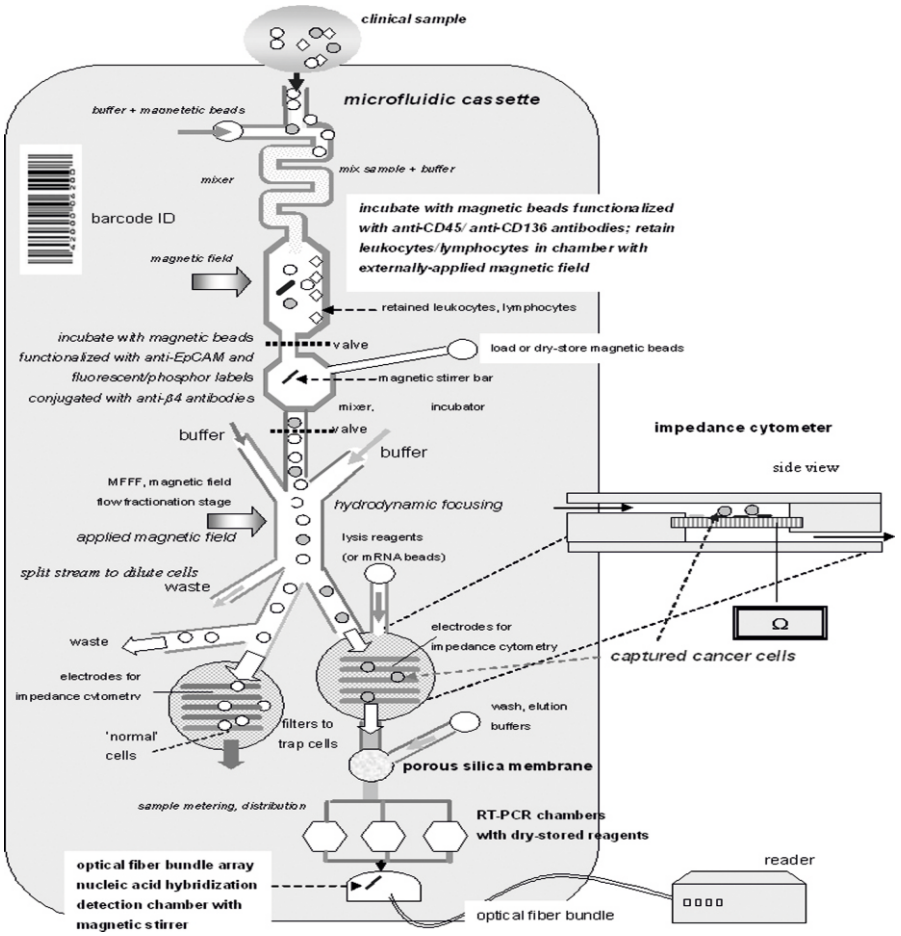
Microfluidic gene analysis or gene profiling : Genetic changes in cancer cells had lead to altered gene expression patterns which gives different biomarkers that can be used for detection of cancer cells .Gene expression profiling has shown many things in regards to progression of diseases ,intra and extra vascular invasion and tumor development also. Whereas somatic cells show various heterogeneity in its mutation so gene profiling them is a challenging one .

Capillary array electrophoresis (CAE) is the basic DNA sequencing method involved . The genetic changes in cancer cells have lead to altered gene expression patterns that can be identified before the expression of phenotype .The gene expression in OSCC tumor progression are P53,cyclin D, epidermal growth factor receptor (EGFR) gene. There is no single gene expression profiling for OSCC .They have found that 25 genes play a role in OSCC and 25 gene predicting Lab on a chip device is necessary to test a cancer patient saliva .

Along with DNA analysis free floating RNA or cell free RNA is also tried in cancer detection,the procedure in the Lab on a chip device is via ,capturing and isolation of cancer cells from normal cell with magnetic beads coated with antibodies to these cancer cells, then lysis,nucleic acid isolation via solid phase extraction or hybridization ,PCR , amplification labeling and detection.4

mRNA based detection of exfoliative cells in saliva analysis is done where mRNA can be isolated amplified using reverse transcription -PCR(RT-PCR) and gene expression can be profiled.4



Plan view schematic of a comprehensive cancer diagnostics lab-on-a-chip integrating microfluidic components for lymphocyte depletion, cancer cell isolation and lysis, mRNA isolation, multiplex amplification, and detection of a panel of mRNA.

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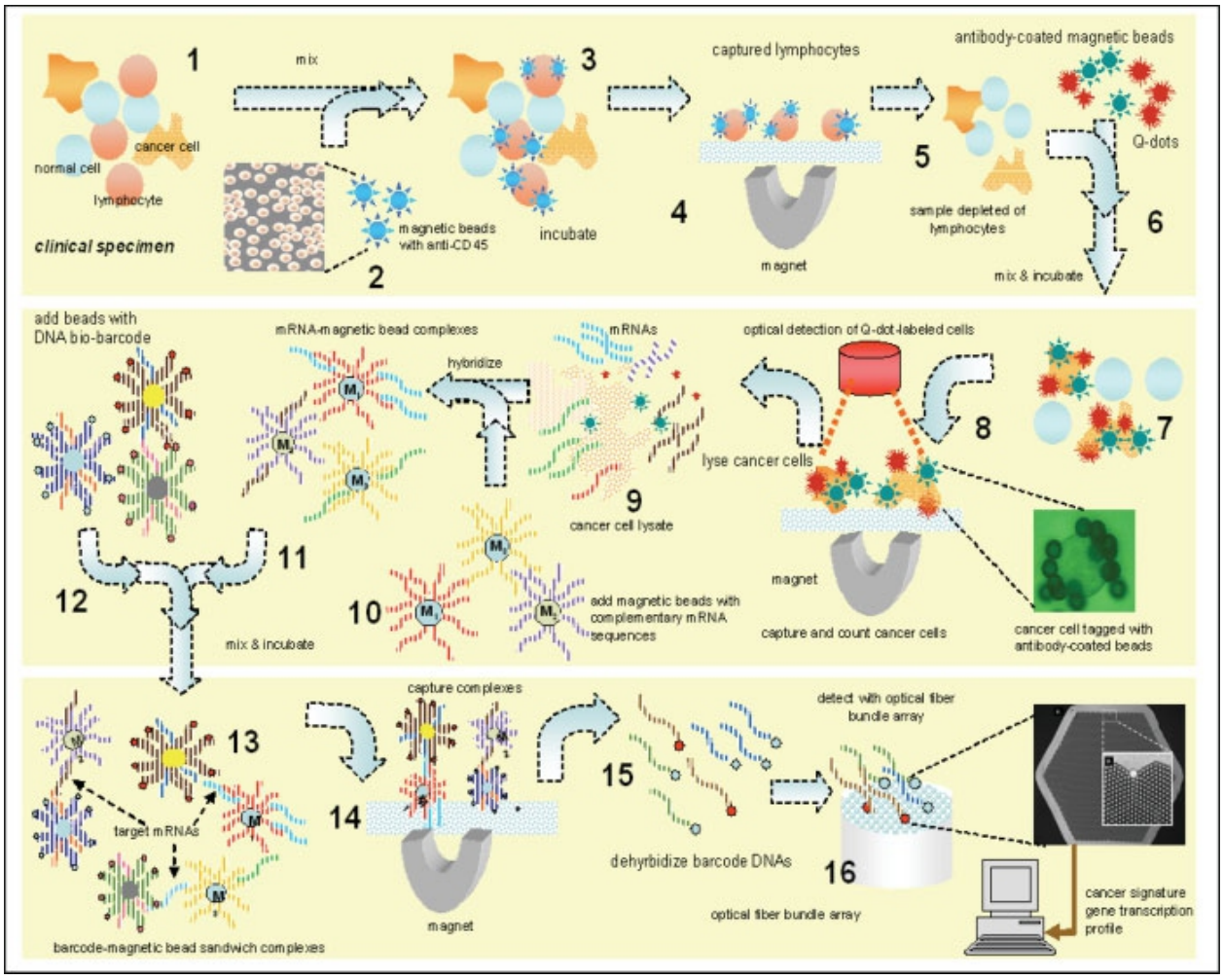

Cancer diagnostics format based on magnetic bead cell sorting and multiplex detection of a panel of mRNAs using biobarcodes. The cell-laden sample containing normal cells, cancer cells, and lymphocytes is introduced into the microfluidic cassette [1]. The cell suspension is mixed [2] and incubated [3] with magnetic beads functionalized with anti-CD45 antibody that specifically binds to lymphocytes. An external magnetic field isolates the lymphocytes-magnetic bead complexes from the solution [4]. The supernatant, depleted of lymphocytes [5] is mixed and incubated [6] with magnetic beads functionalized with antibodies to membrane glycoproteins specific to cancer cells (such as EpCAM and HSP47) and with quantum dots conjugated with the same antibodies as the magnetic beads or different antibodies specific to membrane proteins of cancer cells. The cancer cell-bead-quantum dot complexes are isolated from the solution with the aid of an external magnetic field [8]. The compartment is washed to remove any unbound quantum dots. An estimate of the number of cancer cells is obtained with a CCD camera. The immobilized cancer cells are lysed [9], and then mixed and incubated with magnetic beads functionalized with oligonucleotides complementary to a pre-selected set of mRNAs and to housekeeping genes [10]. The magnetic beads with captured mRNAs are isolated by application of an external magnetic field and thoroughly washed [11]. The captured mRNAs are hybridized with nanoparticles with oligonucleotides complementary to the specific cancer cell mRNA and the barcode DNAs [12] to form barcode-magnetic bead-selected mRNA sandwiches [13]. The magnetic beads are immobilized and the solution is washed [14]. The barcode DNAs are removed from the beads [15] and detected by fluorescence using fiber optic array [16]. The measured profile is compared with archived gene transcription profiles to determine the cancer type and stage. The detection method described here combines the bio-barcode format.

microfluidic -based protein analysis : There is a difference in gene expression in cancer cells along with instability, protein cancer biomarkers are direct expression of oncogenes. By determine the protein expression we can monitor treatment prognosis, microfluidics based immunohistochemistry is use for protein detection.1

Antibodies against cancer specific membrane protein conjugated with labels such as fluorescent antibodies and quantum dots or magnets can tag the cancer cells. They have found two membrane glycoprotein expressions in cancer and precancer dysplastic cells.

The Membrane Glycoproteins

1. Hsp 47- colligin

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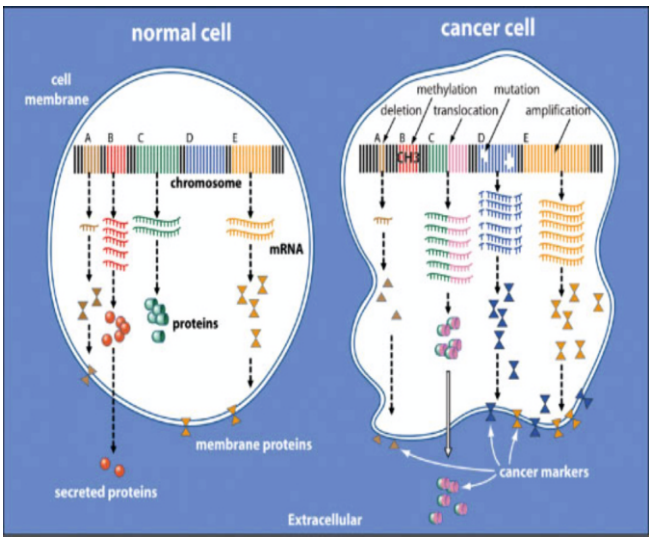
2. Ep CAM- epithelial trans membrane glycoprotein

   Hsp 47 -endoplasmic reticulum resident protein. Ep CAM expressed in several epithelial cancers. Found high in tongue cancer. Studied by Chaudal et al.

Cancer cytology analysis with micro fluidic system



Potential cancer biomarkers exemplified by genetic changes in the chromosomal DNA are illustrated in the cancer cell. Typical changes in the host DNA such as point mutations, deletions, translocations, amplifications, and methylations alter mRNA transcripts from these affected genes. These affected mRNA transcripts could be lost, mutated, or increased. As a result of the mRNA changes, cellular protein products from these affected genes are similarly altered. The altered proteins in the cancer cell are expressed intracellularly, on the cell surface, or secreted into the extracellular space at higher or lower levels compared to normal cells. Exploitation of specific changes that occur in the cancer cell's RNA or protein provides convenient targets to enrich the cancer cells from normal cells and other cell types.

Cellular analysis of cancer gives an assessment of single cell or cell to cell communication in the microenvironment.

Simple form of micro fluidic diagnostics devices are pregnancy test and saliva based HIV test commercially available ad ora sure test. 6

Latest advancement in oral cancer diagnosis called OFNACET Oral Cancer Nanosensor Test by university of California Los Angeles Collaborative Oral fluid diagnostic research laboratory led by David Wong developed point of care to detect oral cancer from saliva

Specific patterns of gene profiling in oral cancer four specific pattern of mRNA appears in saliva of patients with OSCC

- IL-8
- Ornithine decatbonylase
- Spermidine acetyltransferase
- IL-1B

Oral Fluid NanoSensor Test, a handheld, automated, easy-to-use integrated system that will enable simultaneous an rapid detection of multiple salivary protein and nucleic acid targets.

This is hand held automated easy to use integrated system which enables simultaneous and rapid detection of multiple salivary protein and nucleic acid targets.

Advantages :

1. Small sample volume
2. Automated operation

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3. Short time for processing
4. Reproducible and consistent
5. Reduces reagent consumption
6. Reduced exposure to hazardous materials /infections agents
7. Minimal risk of sample contamination and convenient disposal
8. Eliminate human errors
9. Easy to use

Conclusion:

The Recent diagnostic efforts in all fluids is developing tremendously and becoming a boon to the practitioners from laboratory diagnostic procedure which might take two days before is ready result in hard in 60 min. This Lab-on-a chip technology has made a significant impact on oral cancer screening and diagnostic and general healthcare.

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REVIEW

A REVIEW OF WEGENER'S GRANULOMATOSIS – A RARE GRANULOMATOUS DISEASE

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Abstract

Wegeners Granulomatosis is a rare multisystem autoimmune disease characterized by necrotizing granulomatous inflammation of the upper and lower respiratory tract, glomerulonephritis and vasculitis. The aetiology of WG remains unknown although a number of exogenous factors have been suggested to be of aetiological relevance. Most clinical characteristics of this disease are nonspecific, making the clinical diagnosis challenging. Histopathological examination of lesional tissue is not pathognomonic, but it remains an essential investigation to confirm the presence of disease and exclude other disorders. The present paper reviews the peculier aspects of this rare granulomatous disease with respect to diagnosis, laboratory features and treatment.

KEYWORDS:

Antineutrophil Cytoplasmic Antibodies , Autoimmune Disease, Gingival Hyperplasia, Granuloma,

INTRODUCTION:

Wegener's granulomatosis (WG) is a unique systemic inflammatory disease characterized by necrotizing granulomatous vasculitis of the upper and lower respiratory tract, pauci-immune segmental necrotizing glomerulonephritis, and small vessel vasculitis.1 WG was first reported by Friedreich Wegener in 1936, incorporating both clinical and histopathological criteria to describe what he believed represented a unique and distinctive syndrome.2 The cause of Wegener's granulomatosis remains obscure, although progress has been made on understanding the interrelation between granulocytes, endothelium, and antineutrophil cytoplasmic antibodies. Environmental factors, such as silicates and nasal carriage with Staphylococcus aureus, might trigger the onset of the disease.The most common oral lesion is hyperplastic gingivitis (Strawberry Gingivitis) which is red to purple with many petechiae that may remain localized in the oral cavity for unusually long periods of time before multiorgan involvement occurs.3,4

The diagnosis of Wegener's granulomatosis can be difficult, but is greatly helped by measurement of antineutrophil cytoplasmic antibodies with cytoplasmic staining (C-ANCA). For a proper diagnosis, histological evidence of granulomatous inflammation or small-vessel vasculitis, or both, in the appropriate clinical setting is needed, although a positive result for the C-ANCA test alone is not diagnostic. Management with appropriate therapy produces good response in most cases ,with occasional relapses.5 The present paper reviews the peculier aspects of this rare granulomatous disease with respect to diagnosis, laboratory features and treatment.

HISTORY OF FRIEDRICH WEGENER IN WEGENER'S GRANULOMATOSIS:

Friedrich Wegener was born on April 4, 1907, in Varel, a small town in northwestern Germany .Wegener began his medical studies in Munich in 1927, and completed his

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undergraduate training at the University of Kiel in 1932.6 By that time,Wegener had developed an interest in pathology, because of elective attachments with Karl August Borrmann (1870–1943), who is remembered for his classification of gastric carcinoma.

In June, 1934, Wegener did a post-mortem examination on a 38-year-old man who had died from uraemia after prolonged febrile illness. At autopsy, a saddle nose deformity was noted, and there was inflammation of nasal mucosa and cartilage with destruction of the nasal septum. Middle ear, larynx, pharynx, and trachea were similarly a□ected. Histological examination revealed granulomatous necrotising inflammation. The kidneys were large and swollen and showed histological evidence of necrotising glomerulonephritis.7

Wegener recognized the importance of his findings and it urged him to study the disorder in detail. Later he also encountered with many same disorder.Finally he said,"This disease was on the verge of being discovered. Somebody had to do it."8

In 1936, Wegener examined his cases in great detail, excluded an infectious cause, and presented his findings at the meeting of the German Pathological Society in Breslau.In 1967, Wegener published an extensive review on his study cases as Wegener's granulomatosis and also he witnessed the discovery of antineutrophil cytoplasmic antibodies as a marker of disease.9,10

AETIOLOGICAL FACTORS:

The specific aetiological factor for WG remains still unknown.Many clinical and experimental data suggested that microbial exogenous factors may highly prone to disease expression.

- Exposure to infectious agents such as Staphylococcus aureus,Mycobacterium avium- intra cellular or Parvovirus B19 and Fungi causes non specific activation of the immune system ,resulting in elevation of cytokine levels in the presence of ANCA and leading to cell destruction.11-14
- Environmental factors have also been implicated as a potential triggering factor for WG.It has been reported that ANCA associated Glomeruonephritis and Vasculitis can be associated with occupational exposure to crystalline silica or hydrocarbon, inhaled fumes and particulars – but the evidence is conflicting.15
- In WG inflammatory response is highly elucidated by pathergic reaction to certain foreign agent in which specific autoimmune response may occur.

CLINICAL PRESENTATION:

Wegener's granulomatosis can affect a wide spectrum of systems, and causes diseases involving Ocular, Cardiac, Aural, Cutaneous, Neural and vascular system.The quintessential features are seen in upper respiratory system , Lungs and kidney .

UPPER RESPIRATORY SYSTEM:

Upper respiratory tract disease occurs in 95% of patients with WG .16 The Sinusitis, solitary and most common initial presentation seen in 73% of patients,although may be unrecognized by clinicians for several months until other manifestations of WG arise.17 Patients may also complain of nasal obstruction, and crusting, foul-smelling rhinorrhea, purulent nasal discharge, epistaxis, hyposomia (due to mucosal swelling) and epiphora (caused by involvement of both the naso-lacrimal duct and the lacrimal sac) .18

PULMONARY AIRWAY:

Necrotizing granulomatous pulmonary inflammation may give rise to a variety of symptoms such as cough (which is usually unproductive), pyrexia, haemoptysis, dyspnea, thoracic pain and post- obstructive infection. Nodular(70%) and cavitary

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disease(35–50%)of patients with WG of lung involvement is usually sub-pleural.19,20

RENAL DISEASE:

The renal disease is usually initially asymptomatic, although with time it can leads to potential complications. In WG, ⩽20% to 80% of patients at the time of diagnosis is asymptomatic.During follow up 80% to 94% of patients invariably develop renal involvement, characteristic by the presence of focal, segmental, crescentic and necrotizing glomeruonephritis. The glomerulonephritis can lead to rupture of Bowman's capsule.17,21

ORAL MANIFESTATION:

Oral lesions are reported to be occur in 6-13% of patients.17 The gingivae, particularly the upper anterior region are the usual oral site of involvement of WG. A strawberry- like gingivitis is suggested to be a one of the characteristic sign of WG .It is thought to be an early manifestation, if present, is characteristic sign of WG.This manifest as enlarged, interdental papillae with red to purple in colour, have petechiae on its surface with granular appearance. Other intraoral sites that are rarely affected include the tongue, palate and lips. Palatal mucosal ulceration and inflammatory destruction is uncommon, but can arise as a down ward extension of WG from the nose and nasal septum. 22-24

DIAGNOSTIC CRITERIA:

In 1990, American College of Rheumatology proposed diagnostic criteria for diagnosis of WG, which requires atleast two features of following four criteria .25

Criteria	Description
Oral ulcer or Nasal discharge	Development of painful or painless oral ulcers or Purulent or bloody nasal discharge
Abnormal chest radiograph	Chest radiograph showing the presence of nodules, ?xed in?ltrates or cavities
Nephritic urinary sediment	Microhaematuria (= 5 red blood cells per high power ?eld) or red cell casts in urine
Biopsy	Histological change showing granulomatous In?ammation within the wall of an artery or in the perivascular or extravascular area.

DIAGNOSTIC METHODS:

BIOCHEMICAL INVESTIGATION:

If WG was suspected from clinical history,systemic and oral examination, then biochemical investigations should be done to detect the clinical course of this disease.It should include complete blood count, ESR, C-Reactive Protein, Serum Creatinine,Blood Urea Nitrogen levels, 24hr Proteinuria,Urinalysis and ANCA serology test.Besides this, special stains are also required for detection of microbial organisms to rule out systemic infections.

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ANCA SEROLOGY TEST:

The current recommendation for a mandatory ANCA testing for WG is essential when there is a strong clinical evidence of signs and symptoms.The association between WG and ANCA was first confirmed by Vanderwoude et al in 1985.26Initial screening of all sera by Indirect Immunofluorescent on ethanol fixed Neutrophils should be done to discriminate 2 main pattern of ANCA: Cytoplasmicpattern(C-ANCA) and a Perinuclear pattern(P-ANCA).27Myeloperoxidase and Proteinase 3 are the major target antigen for P-ANCA and C-ANCA which is present in the granules of neutrophils and lysosomes of Monocytes .C-ANCA is considered to be a sensitive and specific marker for multisystem WG and may be helpful in tracking disease activity and possible relapse.The detection of ANCA levels also plays an important role in the monitoring of patients response to treatment.28

RADIOGRAPHIC INVESTIGATION:

Chest radiographs and Computerized Tomography scan are mainly required to detect the specific characterized features of WG in Pulmonary system. The most common feature of pulmonary involvement is the radiological presence of single or multiple (usually less than 10) cavitary nodules of 5 to 100 mm diameter at cortical and sub-pleural sites.29

PATHOLOGY:

Biopsy is mandatory to confirm the disease, to rule out and differentiate it from other granulomatous diseases.Wegeners Granulomatosis has three specific pathological features and it serves as an element in diagnostic criteria:Necrosis, Granulomatous Inflammation,Multinucleated Giant cells and Vasculitis.30 The granulomatous in?ammation is characterized by collections of loose macrophages, multinucleated giant cells, acute or chronic in?ammatory cells, and the cellular composition of the granulomatous lesions of WG are composed of CD4+ T-cells, CD8+ T-cells, histiocytes, CD20+ B-lymphocytes, neutrophil granulocytes, CD68+ macrophages and CD68+ multinucleated giant cells that envelop the central area of necrosis.31,32

The central necrosis can be distinct and shows a serpiginous pattern of necrosis, Polymorphonuclear leucocytes and epithelioid histiocytes which may get arranged around the necrotic foci, occasionally. And the vasculitis of WG typically show ?brinoid necrosis affecting the walls of small to medium- sized arteries and veins, the affected vessel wall has acute/or chronic in?ammatory in?ltrate and occasionally accompanied by granulomatous in?ammation within the vessel wall. At the same time, most of the case reports with Gingival biopsy of WG shows pseudoepitheliomatous hyperplasia, Polymorph microabscess and giant cells .30,33..

TREATMENT

The choice of therapeutic agents for WG depends on severity of disease. If correct therapeutic decision is taken, most of the patient responds immediately to treatment within a week.Therapy is mainly aimed at inducing remission with oral prednisolone 1mg/kg and cyclophosphamide 2-3 mg /kg. Once remission is achieved prednisolone is usually tapered gradually to alternate days at 3 months and then discontinued, whereas cyclophosphamide is continued for atleast a

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year after remission induction.34 Resolution of oral lesions, clearing of pulmonary infiltrates with evidence of stable scarring and no further evidence of active renal sediment signifies complete remission. However, remission in some cases may soon be followed by relapse which usually coincides with tapering of immunosuppressive therapy.At present combination of Azathioprine and low dose prednisolone are mainly used as maintenance therapy.Because of high morbidity associated with standard therapy, intermittent intravenous treatment with cyclophosphamide has been introduced with the intention of reducing treatment related morbidity.35,36,37.

CONCLUSION

Wegener's granulomatosis is a multisystem disorder associated with significant morbidity and mortality. ANCA and other immunological analysis are relevant to its diagnosis but histopathological confirmation is vital.The oral health care provider's role is vital to the diagnosis of Wegener's Granulomatosis as "Strawberry Gingivitis" could be an early presenting symptom.Appropriate referral and relevant management of the oral lesions would be under the purview of the oral physician thereby ensuring early diagnosis and better outcome.

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CASE REPORT

MANAGEMENT OF PALATOGINGIVAL GROOVE ASSOCIATED WITH LOCALIZED PERIODONTITIS - A CASE REPORT

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Abstract

Palatogingival groove is a developmental anomaly which has been implicated as an initiating factor in localized gingivitis and periodontitis. These grooves which facilitate plaque growth can present as a challenge to the operator in diagnosis and treatment planning. This article describes the management of shallow palatogingival grooves present in the maxillary incisors. In the present case, a timely diagnosis was made and treated surgically with odontoplasty and sealing of the grooves with BiodentineTM and Mineral Trioxide Aggregate (MTA). On re-examination of the patient after 6 months, patient had good oral hygiene and no signs of disease progression.

Keywords: Palatogingival groove, odontoplasty, Biodentine, Mineral Trioxide Aggregate Glomerulonephritis

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The tooth is a specialized part of the human body, understanding the development of which is enigmatic and still challenging.1 Anatomical malformations of tooth often causes clinical problems and one such variant is the palatogingival groove(PGG).

The palatogingival groove is a developmental anomaly of the maxillary incisor teeth which has been reported to be associated with severe localized periodontal disease.2-5 Palatogingival groove also referred to as palato radicular groove (PRG), disto lingual groove, corono radicular groove or radiculo lingual groove is described in literature as a developmental malformation that exists on the palatal aspect of the incisor teeth and runs towards the mesial, distal or midpalatal root regions.3,7 It has a reported incidence ranging from 2.8 to 18%.6

In most cases, the course of the grooves is straight. According to their localization, they are differentiated as distal, mesial and central patterns, with the distal portion dominating, as it occurs in approximately 70 % of cases.8 The grooves also vary in depth. Deep grooves with direct communications with the pulp are seldom reported. With increasing depth of the goove, the thickness of the root cementum increases.9

The negative effect of palatogingival groove is related to their plaque accumulating effect. The groove may facilitate plaque growth by providing surface areas sheltered from cleaning efforts as well as from host defense mechanisms.

Prichard2 was the first to state that lingual grooves on maxillary incisor teeth are a predisposing factor to localized severe periodontal destruction.Lee et al3 reported on 13 patients who were seen with localized periodontal lesions associated with these anomalies. Simon et al4 described unsuccessful attempts to treat the periodontal defects associated with palatogingivalgrooves and felt that extraction of the involved tooth was the treatment of choice.

Various materials have been used for sealing the PRGs.In

the present case a tricalcium-based cement called BiodentineTM was used for sealing the palatogingival grooves in two teeth and Mineral trioxide aggregate (MTA) was used in the other tooth.

Biodentine, a tricalcium silicate-based material popularly known as “dentin replacement and repair material” was introduced commercially in 2009. It is recommended for use as both an endodontic repair material and a dentinsubstitute under resin composite restorations. It contains tricalcium silicate, dicalcium silicate, calcium carbonate and oxide, iron oxide, and zirconium oxide as its powder components; and calcium chloride and a water soluble polymer as its liquid components.

MTA is a powder that consists of fine trioxides (tricalcium oxide, silicate oxide, bismuth oxide) and other hydrophilic particles (tricalcium silicate and tricalcium aluminate) responsible for the chemical and physical properties of this aggregate which set in the presence of moisture. Hydration of the powder results in the formation of a colloidal gel. The gel solidifies to a hard solid in approximately 3 to 4 hours. This cement is different from other materials because of its biocompatibility, antibacterial properties, marginal adaptation and sealing properties and its hydrophilic nature.

It is important to note that it is the ability to adequately treat the periodontal defect that ultimately determines the prognosis of these teeth.14

ETIOLOGY

The etiology of PGGs is unknown. Similar to an invagination this seems to be a peculiarity of tooth development accompanied by a further anomaly. Black was the first to describe PGGs as a malformation during embryo development in 1908.10

Atkinson11summarised that the reason for its malformation is that there is no enough space during tooth development in the maxilla, resulting in folding in the area of the Hertwig's epithelial root sheath. In the opinion of Goon et al12 this could be also an attempt at a root partition. According to recent studies, PRGs may be caused due to genetic changes.9

CLASSIFICATION

MILD	Gentle depressions of the coronal enamel, which terminate at or immediately after crossing the cemento-enamel junction
MODERATE	Continue to extend some distance apically along the root surface in the form of a shallow or fissured defect
COMPLEX	Deeply invaginated defects that involve the entire length of the root or that separate an accessory root from the main root trunk

According to Yong - Chun Gu13

TYPE 1	The groove is short (not beyond the coronal third of the root)
TYPE 2	The groove is long (beyond the coronal third of the root) but shallow, corresponding to a normal or simple root canal
TYPE 3	The groove is long (beyond the coronal third of the root) and deep, corresponding to a complex root canal system

CASE REPORT

A 22-year- old female patient reported to the department of Periodontology, Best Dental Science College and Hospital, Madurai with the chief complaint of pain, intermittent discharge of pus from the upper front tooth region and bad smell for the past 2 days.

There was no history of trauma and the medical history was non-contributory. Dental history revealed that the patient was wearing removable orthodontic appliance for the correction of proclined upper incisors for the past 2 days. On intraoral examination, oral hygiene was satisfactory. On manual probing with William's periodontal probe, there was draining periodontal pocket in the distopalatal aspect (5mm) of 12,mesiopalatal aspect (7mm) of 11 and mesiopalatal aspect (6mm) of 21andthe teeth indicated concavity crossing CEJ extending to the root in the form of a groove (Goon et al- mild; Youn- Chun Gu – type1). These grooves on all the upper maxillary incisors were shallow and continue to extend for some distanceapically but not beyond coronal third of the root. These palatoradicular grooves which lead to plaque accumulation and act as a channel for the microbial deposits to carry subgingivally became evident to be the reason for the pathosis to occur. Mobility of tooth was within physiological limits. Thermal and electrical pulp testing showed normal response. Thus the endodontic treatment was not indicated. The pain initiated from the day she has started using the removable orthodontic appliance which was suspected to be the aggravating factor for the existing periodontal problem.

TREATMENT

Suggested treatment modalities were curettage of the affected tissues, elimination of the groove by grinding (saucerization), or by sealing with a variety of filling materials.14 The patient was instructed not to use the removable orthodontic appliance.Phase I therapy (scaling and root planning) was completed and medications (Amoxicillin 500mg TD and Metronidazole 400 mg BD) were given.

Phase II therapy was carried in two appointments. The first appointment involved the surgical management of 11 and 12 sealing the PRG with biodentin and the second appointment involved the surgical management of 21 with saucerization of the groove and sealing the PRG with respect to 22 with MTA.

SURGICAL PROCEDURE

Anesthesia was achieved after administering 2% lignocaine with 1:80,000 adrenaline. Sulcular incision was given and full thickness flap was elevated on the palatal aspect from

mesial to 13 to mesial to 21. Thorough debridement around the groove was performed by meticulous scaling and root planing. Granulation tissue was debrided using Gracey curettes number 1/2 (Hu-Friedy Manufacturing Co., Chicago, IL).

Next, the groove was shaped with high-speed diamond bur under continuous air-water spray and blended smoothly with the adjoining surface to receive the restorative material. Biodentine™ (Septodont, St. Maur-des-Fosses, France) was mixed according to the manufacturer's instructions and applied into the defect after proper control of bleeding. The material was allowed to initial set for about 9 min. During the setting phase, the tissues were kept hydrated using moist gauze piece. The flap was approximated and sutured using 3-0 silk suture. Analgesics and antibiotics were prescribed, and the patient was given regular oral hygiene instructions including chlorhexidine (0.2%) mouth rinse for 2 weeks.

After 7 days suture removal was done and irrigated with saline. The other palatogingival groove in relation to 22 was sealed with MTA (Mineral trioxide aggregate) in the same way by elevating full thickness periosteal flap. .Odontoplasty was done in 21 in which the groove was shallow.

DISCUSSION

Depending on the morphology of the palatogingival groove, localized periodontitis may develop accompanied by pathosis.This fissure like channel is a locus of plaque and calculus accumulation, which acts as a secondary local etiologic factor encouraging the development of periodontitis. An incorrect or delayed diagnosis decreases the prognosis and could result in the extraction of the tooth.

Several different approaches have been proposed for management of palatogingival groove. In most cases where the groove is shallow and not extended apical to CEJ, odontoplasty is sufficient to eliminate the groove by so called 'saucerization' or flattening the groove.This involves the grinding of the root surface, sometimes quite extensively which results in loss of tooth substance and exposure of cut dentin. One limitation of this technique is its impracticality in deep grooves that communicate with the root canal, and as concluded by Meister, “this treatment only can be successful if there is not a continuous opening along the length of the radicular lingual groove between the pulp canal and the periodontal tissues”.

However when the groove is more advanced with associated extensive periodontal destruction, the management becomes more complex. The reported treatment procedures in which the groove is extended too far apically include filling of the groove with amalgam17, or calcium sulphate18 or GIC19, or the intentional replantation after root planing and the insertion of emdogain20. In the last decades, with extensive knowledge of guided tissue regeneration, mechanical barriers have been used to halt epithelium downgrowth along the root surface, allowing periodontal ligament, cementum and bone to regenerate along periodontally diseased roots.

In some cases the periodontal pathosis may get driven more apically to involve periapical tissue leading to endodontic-periodontal lesion. In such cases, the treatment plan comprised of oral prophylaxis followed by endodontic management primarily and then periodontal pocket elimination and groove repair.14

In this case, the tooth was vital and had no bony defects associated with it. Localized flap surgery & restoration of defect with filling materials were done in 11 and 12 in which the grooves were quite deep and odontoplasty was done in the groove which is shallow in 22.

MTA was initially introduced as a root-end filling material for surgical endodontic

procedures. Since then, its clinical applications have broadened to include perforation repair, pulp capping, pulpotomy and apexification. During these procedures, the dental filling materials usually come into contact with the underlying tissues. The bond strength of most dental materials is significantly reduced by moisture contamination from the tissue, whereas MTA requires the presence of water for setting. Therefore, set MTA can acquire its optimal strength and produce excellent sealability in the presence of moisture21.

MTA offers a biologically active substrate for bone cells and permits cementoblast attachment, growth and the production of mineralized matrix gene and osteocalcin expression.22 Balto demonstrated that human periodontal ligament fibroblasts were well attached and grew on MTA.23 It has an antibacterial effect, biocompatible, optimal strength and excellent sealability in the presence of moisture, ability to form cementum layer. Because MTA has got all excellent properties in the field of regeneration for both hard and soft tissues, itwas used to seal the groove.

In a study by Zhou et al it was concluded that Biodentine caused gingival fibroblast reaction similar to that by MTA and can be safely used in procedures requiring close approximation with the periodontal tissues.24 It has proven bioactive properties, known to promote hard tissue regeneration and is biocompatible. Compared to glass ionomer cement, this material is more approving when adhesion and growth of fibroblasts is concerned. The ability to form hydroxyapatite crystals at the surface especially when formed at the dentin material interface is known to improve its sealing ability.

Sealing with Biodentine was better than MTA due to its better handling characteristics and short setting time whereas when using MTA in sealing of radicular groove it was difficult to control moisture during the setting of MTA causing degradation and poor marginal seal. In addition to documented uses of biodentine in diverse clinical applications like retrograde filling material, perforation repair, pulp capping and pulpotomy; our case shows successful application of Biodentine in management of complicated palatogingival groove compared to MTA.A 6 month follow up revealed reduction in pocket depth of 3mm and no signs of disease progression. In this case if the diagnosis was missed at an early stage, the tooth would have progressed for non-vitality and a combined approach by endodontist and periodontist would be needed..

CONCLUSION

This paper emphazises the early diagnosis of the silent killer PGG and its appropriate management to save the teeth from progressing to hopeless prognosis.

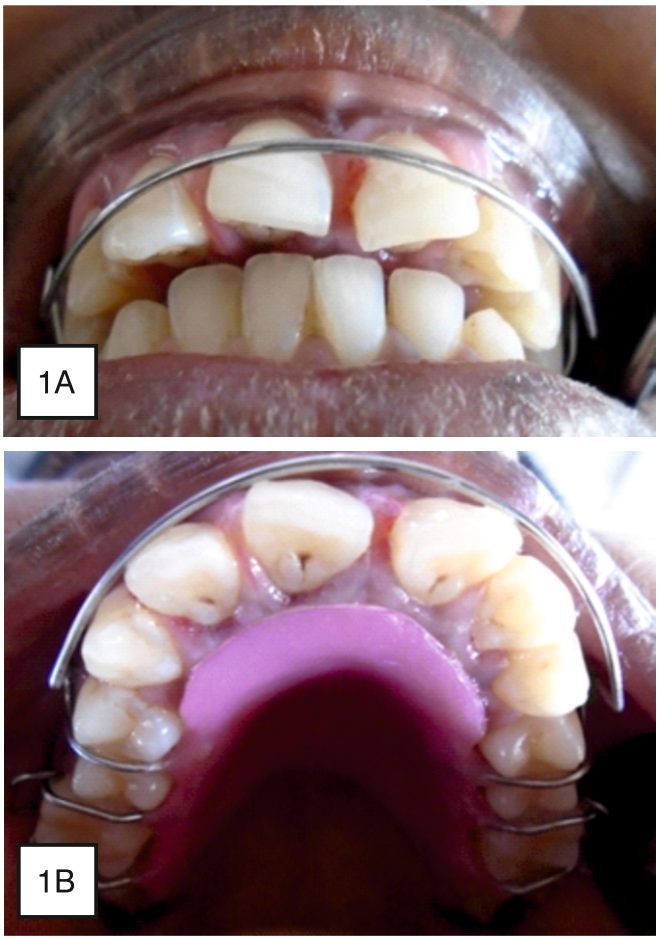

FIGURE 1A, 1B. Removable orthodontic appliance worn by the patient.

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FIGURE 2.Patient was having traumatic occlusion with deep bite

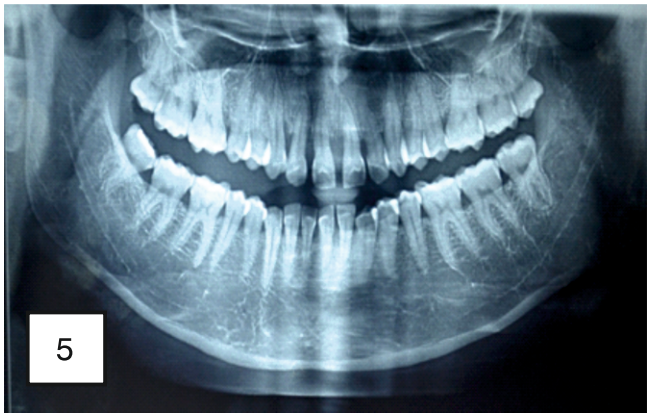

FIGURE 5.Orthopantomography of the patient showing horizontal bone loss in the maxillary anterior region.

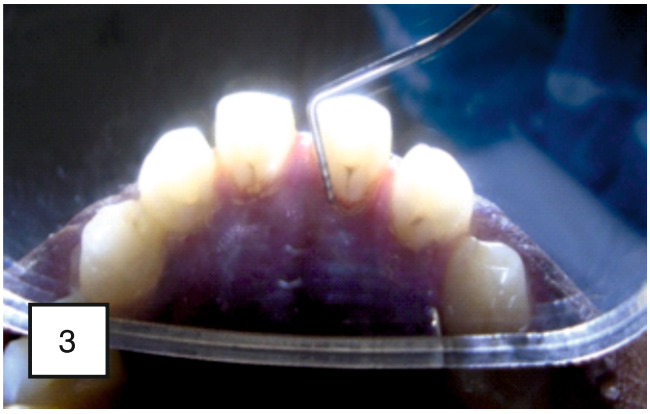

FIGURE 3.Palatogingival groove noticed in 11, 12 (pocket depth of 7mm in 11)

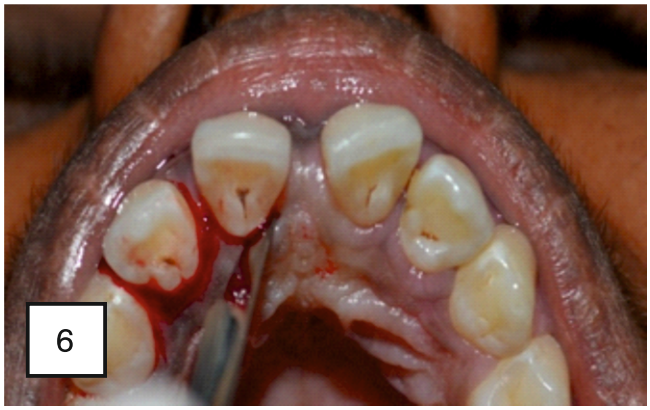

FIGURE 6.Intrasulcular incision was given at the palatal aspect

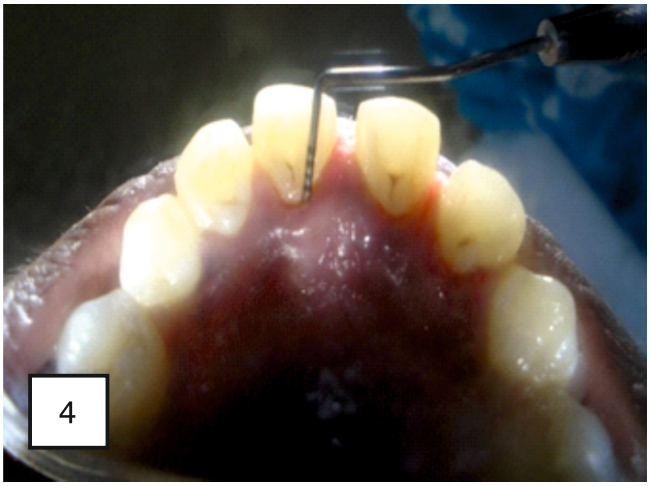

FIGURE 4.Palatogingival groove noticed in 21 (pocket depth of 7mm in 21)

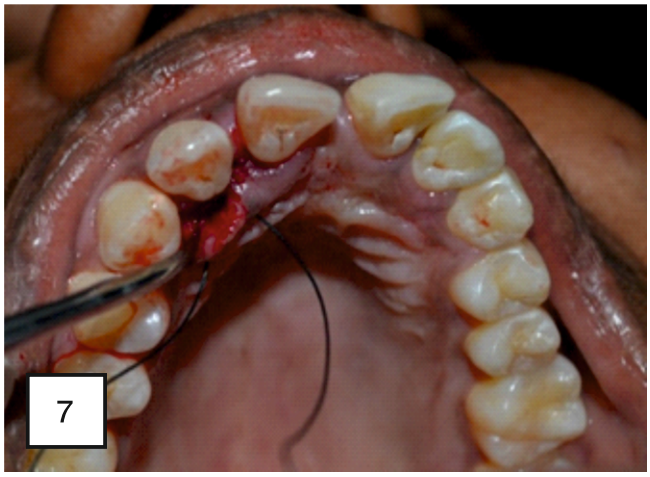

FIGURE 7.Palatal flap was elevated in relation in to 11, 12

FIGURE 8.Groove blended smoothly with adjoining surface with high-speed diamond bur to receive the restorative marterial

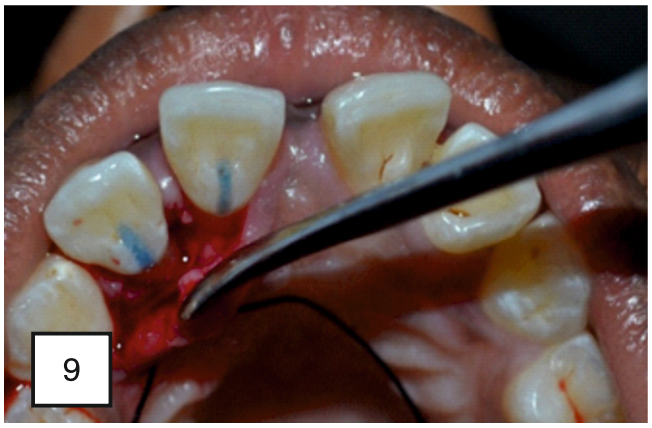

FIGURE 9.Palatogingival groove noticed in 11, 12

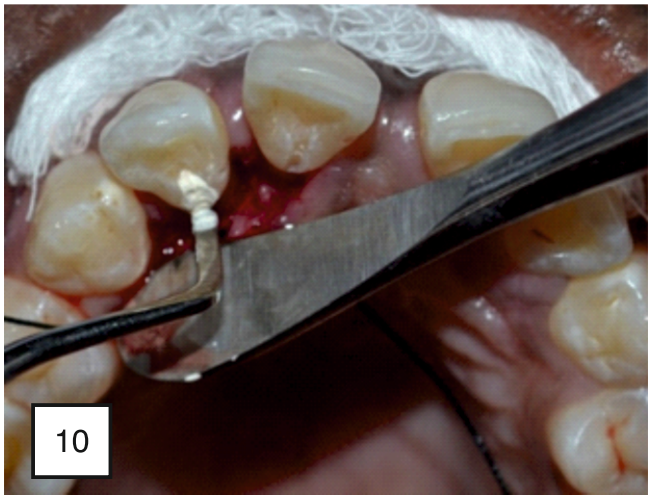

FIGURE 10.PRG sealing with Biodentine in 11

FIGURE 11.PRGs sealed with Biodentine in 11,12

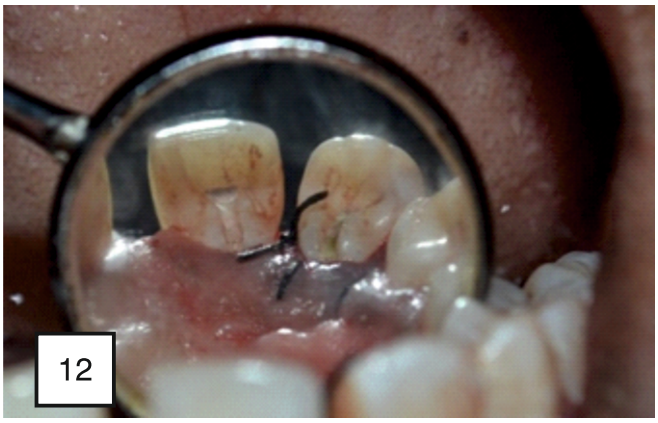

FIGURE 12.Flap closed with simple interrupted suture with 3-0 silk suture.

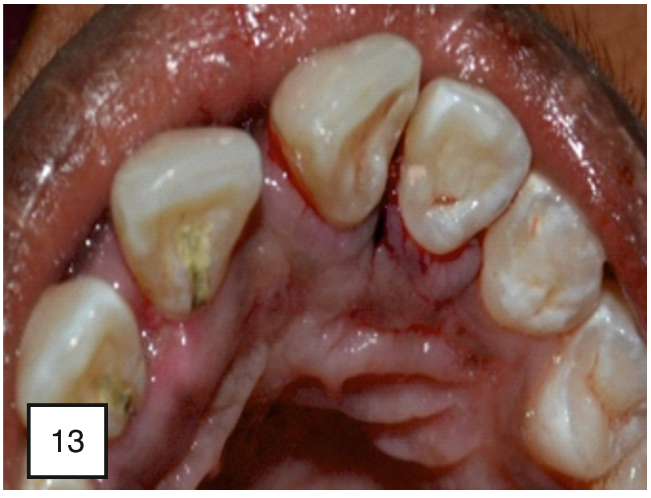

FIGURE 13.Palatogingival groove in 22 was sealed with MTA.Palatogingival groove in 21 was managed by saucerization.

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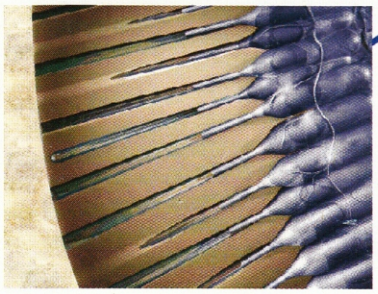

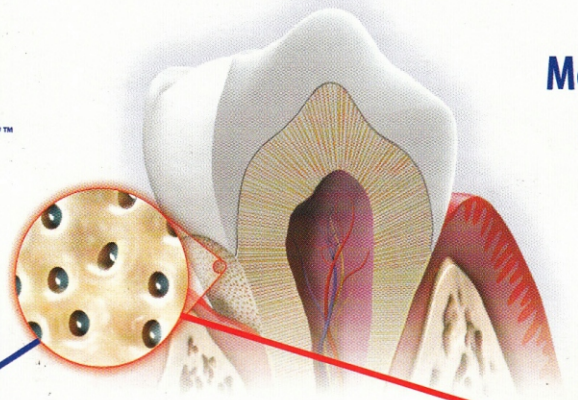

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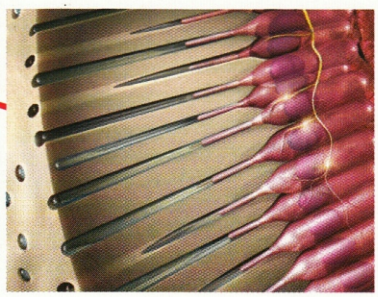

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