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Details of papers published in the journals other than UGC notified journals 2018

S.N	Publication type	Publication title	Author name	Journal name	Year
1.	Original article	Effect of double straight leg exercise training on abdominal fat of adolescent population-An interventional study from Madurai, India	PSL Saravanan S Anu A Mohamed Rayeez G Rajalakshmi Preethi	Annals of International Medical and Dental Research.	2018
2.	Original article	Gender Differences on Pain Threshold, Body Temperature and Reaction Time among Elderly Population after Alternate Nostril Breathing Exercises-A Comparative Study	PSL Saravanan S Anu V Mathavakumar	Indian Journal of Clinical Anatomy and Physiology	2018
3.	Original article	Immediate effect of Slow Right & Left Nostril deep breathing Exercises on Reaction time, Pain sensitivity and Temperature in elderly population of Madurai	Mathava Kumar V, Anu S.	National Journal of Physiology, Pharmacy and Pharmacology.	2018
4.	Original article	Effect of breathing practices on visual and auditory reaction time of adolescent population in Madurai, India -A comparison of right and left nostril breathing	V. Suganthi, S.Anu, V. Mathava kumar, K. Rekha.	Indian Journal of Clinical Anatomy and Physiology	2018
5.	Original article	Analysis of Motor Nerve Conduction	Rekha K, Saravanan M, Anu S	Annals of International Medical and	2018

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		and Pain Threshold in Professional Drivers		Dental Research	
6.	Original article	Exam stress and choice reaction time in first year medical students.	Laxmi C, Saravanan M.	Journal of Evidence Based Medicine and Healthcare	2018
7.	Original article	Effect of body mass index on post-exercise hypotension in healthy adult males	Keba Jeeva, Paramita Bhattacharya	National Journal of Physiology, Pharmacy and Pharmacology.	2018
8.	Original article	Comparison of effect of aspartame (artificial sweetener) and aspartamesweetened diet drink on autonomic reactivity of volunteers	Kanietha Priya A S, Ganesh Prasath S	National Journal of Physiology, Pharmacy and Pharmacology.	2018
9.	Original article	A Comparative Study of Effects of Oropharyngeal Exercises and Continuous Positive Airway Pressure (CPAP) on Parameters of Sleep on Moderate Obstructive Sleep Apnea Syndrome (OSAS) Patients	Kanietha Priya A S, Ganesh Prasath S	National Journal of Basic Medical Sciences	2018
10.	Original article	Study on clinico microbiological profile and antibiotic susceptibility pattern of urinary tract pathogens with Special reference to susceptibility of Escherichia coli to fosfomycin	Sundaramurthy R, Tiruvanamalai R, Sivaraman S T, Arunagiri R, Charles J	Indian Journal of Microbiology Research	2018
11.	Original article	Study on prevalence of Methicillin resistant Staphylococcus	Rajendran Thiruvannamalai, Jhansi Charles, Raja	Journal of Evolution of Medical and Dental Sciences	2018

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		aureus: Comparison of four diagnostic methods for detecting MRSA-From a tertiary care hospital	Sundaramurthy, Ramesh Arunagiri, Vithiya Ganesan, Geni Veerathevar German Soundaram, Brindha Vetrinallathambi		
12.	Original article	Microbiological profile, comorbidity, incidence and rate analysis of catheter associated urinary tract infections in adult intensive care unit :Indian Journal of Microbiology Research	Ramesh A, Janagond A B, Raja S, Gobinathan S P, Charl J	Indian Journal of Microbiology research	2018
13.	Original article	A prospective observational study to compare the efficacy and safety of spinal Vs general anesthesia for laparoscopic cholecystectomy	Subbiah V., Palaniappan S.K	Surgical Review: International Journal of Surgery, Trauma and Orthopedics	2018
14.	Original article	study on Dimensions of Nasal Columella to Aid Aesthetic Rhinoplasty	Geetha K Siddapur, Kishan R Siddapur	Otolaryngology International	2018
15.	Original article	A comparative study of intravenous dexmedetomidine and midazolam on prolongation of spinal anesthesia	Malarvizhi T., Vidhya A., Lavanya R.	International journal of Research in Medical Research	2018
16.	Original article	A prospective observational study to compare the efficacy and safety of spinal Vs general anesthesia for laparoscopic cholecystectomy	Subbiah V., Palaniappan S.K	Surgical Review: International Journal of Surgery, Trauma and Orthopedics	2018

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17.	Original article	Gender Differences on the Effect of Non-HDL-C on Blood Pressure, Blood Flow Velocities and Arterial Wall Thickness; An Observational Analysis in Madurai Population	John Rajpathy, M. Mariappan, J. Vijay Anto	Annals of International medical and Dental Research	2018
18.	Original article	Sonographic Evaluation of Spectrum of Breast Diseases-A Study in a Tertiary Care Hospital of Southern Tamil Nadu	Krishna Kumar, S.Yogaraj, Poongodi	Annals of International medical and Dental Research	2018

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Effect of Double Straight Leg Raise Exercise Training on Abdominal Fat of Adolescent Population – An Interventional Study from Madurai, India

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ABSTRACT

Background:

Central/abdominal obesity is associated with metabolic and vascular complications than whole body obesity. High intensity exercises were generally proven to reduce total body fat as well as regional fat. Conflicting results were observed with the effects of specific abdominal exercises on abdominal fat. Hence the present study was done to find out the sole effect of double straight leg raise exercise on abdominal fat before and after 6 weeks of training and to compare with that of the control group.

Methods:

A total of 40 obese students of a private medical college were recruited for the study and divided into control (n=20) and leg raising group (n=20).The study was conducted for 5 days a week for 6 weeks during September to October 2017. Body Mass Index (BMI), Waist Hip Ratio (WHR) and Abdominal Subcutaneous fat using ultrasound was measured.

Results:

Paired and unpaired t test was used for statistical analysis. A significant decrease in BMI and Abdominal subcutaneous fat(p value < 0.001, < 0.017)was observed in the leg raising group with no significant change in WHR(p value<0.968). Control group showed no significant change in BMI& WHP (p value < 0.199, < 0.072) except for increase((p value < 0.035) in abdominal subcutaneous fat.

Conclusion:

Leg raising exercises help to reduce abdominal subcutaneous fat &Body weight but not the abdominal girth and if practiced along with other types of abdominal exercises may yield better results.

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Gender differences on pain threshold, body temperature and reaction time among elderly population after alternate nostril breathing exercises-A comparative study

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Abstract

Introduction: It is a known fact that elderly males have a faster reaction time than females, and females exhibit greater pain sensitivity than males. Results on body core temperature between genders are inconsistent. Alternate Nostril Breathing (ANB) exercises were known to modulate the autonomic nervous system. The present study was done to find whether such differences between elderly males and females on pain sensitivity, body temperature and reaction time still persisted after ANB exercises.

Objectives: 1. To measure the pain sensitivity, body temperature and reaction time in elderly males and females; 2: To compare the effects of 30 minutes of ANB exercises on all these parameters between elderly males and females.

Materials and Methods: 30 elderly males (n=14) and females (n=16) with a mean age of 70.3 years participated in the study. Pain sensitivity was measured with digital algometer, temperature with clinical thermometer and reaction time with choice time apparatus before and immediately after ANB exercises.

Results: A significant decrease (<0.001) in all the three parameters was observed after ANB exercises in both genders. No significant difference was observed between elderly males and females on pain sensitivity, body temperature and reaction time to red light, green light &click sound except for tone (<0.019).

Conclusion: Reaction time became faster; pain sensitivity and temperature decreased immediately after ANB exercise and this could be due to the balancing effect of the autonomic nervous system. No difference existed between genders after ANB except for tone.

Keywords: Breathing exercise, Gender, Elderly, Pain, Temperature, Reaction time.

Introduction

Aging is characterized by gradual deregulation of homeostatic mechanisms in all organ systems and this could be due to ample number of factors including oxidative stress, increasing inflammation and gene variation.[1] With aging, there is increase in blood pressure, development of arteriosclerosis, increase in blood sugar, altered motility in gastro intestinal tract and bladder, and decrease in lean body mass.[2] There is increased prevalence of hypertension in India among elderly ranging from 55% to 72% in rural and urban areas.[3] Around 30.4% of the elderly Indian population also suffers from diabetes mellitus.[4] Senility is also associated with deterioration of the circadian rhythm resulting in impaired sleep, and altered core body temperature. Impaired sleep is associated with disordered breathing leading to cardiovascular and metabolic complications. Insomnia is associated with increased sympathetic and decreased parasympathetic tone.[5]

Alternate Nostril Breathing (ANB) exercises have a balancing effect on autonomic nervous system. Regular practice of left nostril initiated ANB had shown a decrease in blood pressure and blood sugar indicating an increase in parasympathetic/decrease in sympathetic activity. Studies on the immediate and specific effects of ANB in non-yogic practitioners were inconsistent with varied results. This variation depends on multiple factors like breath rate, nostril with which breathing was initiated and the phase in which it was initiated.

Pain Threshold (PT) is the time at which pain is felt first when a stimulus was given. The stimulus for experimental pain may be of any type like electrical, pressure, thermal, chemical and ischemic pain. Studies had shown that largest changes in values are obtained mainly for pain induced by pressure and electrical stimulation. Women display greater pain sensitivity to all pain modalities than men.[6] This increased pain sensitivity in women could be due to hormonal factors, endogenous opioid function and genetic factors.[7] Though estrogen seems to exhibit both pro and antinociceptive effects, nociceptive effect dominates. Estrogen level seems to fluctuate during different phases of menstrual cycle, pregnancy and menopause.[8] Decreased pain sensitivity in males could be due to the fact that testosterone has more analgesic property and its level almost remains constant without much fluctuation in males. There is increased activation of mu-opioid system in men especially in amygdala and anterior thalamus in response to sustained pain, whereas women exhibited decreased activation of mu-opiod system especially in nucleus accumbens.[9]

Studies on pain perception in old age is inconsistent, with some studies reporting increase in pain threshold with age and few others reporting decrease in pain threshold with age.[10] But the sex

differences in perception of pain still continued in old age with women showing greater pain sensitivity than men. Controversial results were observed again with studies on the effect of slow breathing technique on pain threshold. An increase in pain threshold was observed after 6 weeks of slow alternate breathing practice in a study, whereas other studies reported no change in pain threshold immediately after slow breathing as well as after 6 weeks of training.[11-13]

Body temperature is normally kept within control by adjustments in the autonomic nervous system.[14] As Hypothalamic temperature regulatory mechanisms decompensate in old age, the body temperature of older individuals is less than the normal value of 36.5 degree celcius.[15] Few studies report no difference in body temperature between elderly males and females, whereas other studies had found an increased mean temperature in elderly females when compared with elderly males.[16,17] So far, no study was done to find out the effect of breathing practice exclusively on body temperature. This study aims to find out the effect of breathing practice on body temperature in elderly group as well as to find any gender difference in temperature after ANB.

Reaction time is the minimum time taken to respond to a stimulus and it helps in assessing the integrity of the nervous system. Reaction time is faster in males when compared with females of all the age groups.[18] Slow reaction time in elderly people accounts for falls and injuries. The present study also aims to find out whether such difference between elderly males and females persists after ANB exercise.

The purpose of the present study is to find out gender differences on immediate effects of ANB on pain threshold, body temperature and reaction time in elderly population.

Aim and Objectives

1. To measure the pain sensitivity, body temperature and reaction time in elderly males and females
2. To study the effect of 30 minutes of ANB exercises on pain sensitivity, body temperature and reaction time in elderly males
3. To study the effect of 30 minutes of ANB exercises on pain sensitivity, body temperature and reaction time in elderly females
4. To compare the effect of 30 minutes of ANB exercises on pain sensitivity, body temperature and reaction time between elderly males and females

Materials and Methods

The present study was conducted in a private medical college in Madurai over a period of 2 months from June 2017-August 2017. 30 healthy subjects of both the genders aged between 60-90 years were chosen for this study by simple random sampling. The mean age is 70.3 years. They were divided into 2 groups: Group A included 14 elderly males and group B included 16 elderly females. Elderly people who were attending General Medicine O.P were recruited for this study after obtaining their informed written consent and also after ruling out health issues. As we expected ANB to produce at least a 20 point difference in pain sensitivity value between males and females, the present sample size was chosen. This study was done after obtaining clearance from Institutional ethical committee.

Old individuals who had no prior exposure to pranayama and without clinical evidence of any physical illness like diabetes, hypertension, lung diseases and chronic pain syndromes were included in the study. Subjects with ophthalmologic and hearing disorders, with musculo skeletal deformities, suffering from any psychiatric disorder affecting their psychomotor abilities and on pain medication were excluded from the study.

Description of Intervention: Baseline data on VRT& ART, pain threshold and temperature was measured initially for both Group A & B. Then both the group participants were taught Alternate nostril breathing exercises to familiarize them with the technique by the author herself, who was a certified yoga instructor graduated under Tamil Nadu Physical Education and Sports University, 2010. ANB involves inhaling through right nostril for a count of 1-5 while the left nostril is occluded & then exhaling through the left nostril for a count of 1-5 while the right nostril is occluded with no pause in between. Then the same procedure has to be repeated with the left nostril and completing with the right nostril. This is one breathing cycle with duration of 10 seconds. Hence for 1 minute, there will be 6 breathing cycles. Slow breathing is breathing at a rate of around 5-6/min. Once the skill is acquired, in the same individual VRT & ART, Pain threshold and Temperature was measured immediately after 30 minutes of ANB exercises on the same day without further follow up.

Data Collection Method & Tools: Baseline data on all participants were collected using structured questionnaire. VRT& ART was measured with the help of discriminatory and choice reaction time apparatus (Anand Agencies, Pune) between 10am to 12pm every day. VRT was measured for green and red light stimuli and ART was measured for low and high frequency sound stimuli in the sitting posture at around 80cm distance. For recording the baseline VRT, initially the subject was instructed to keep pressing the finger on the response button and once he visualizes the stimulus, immediately he has to remove his finger. The response button terminated the clock counter & the value of VRT was displayed on the screen in milliseconds. This process has to be repeated for 3 times, and the lowest value was taken as the final reaction time. Baseline ART is also recorded in the same way for both for tone & click sound. After 30 minutes ANB, again VRT & ART was recorded.

Pain sensitivity was assessed with the help of a digital Algometer. After switching on the instrument, electrode attached with the algometer is placed on forearm of the subject and the baseline value is kept at 0. After that the knob was adjusted till the patient perceives pain sensation and then the final displayed reading at which pain is felt were noted. Temperature was measured with the help of oral mercury- in- glass thermometer before and after breathing exercise.

Statistics: The data was entered into MS excel and analysed using SPSS v16.0.VRT, ART, pain threshold and temperature values before and after 30 minutes of ANB were compared using paired t test. Between Gender differences were analysed using paired test. An arbitrary cut off of 0.05 was used to interpret significance of p value.

Results

Table 1: Mean age of subjects

		Age	
		Mean	**Standard Deviation**
Sex	Male	72.9	7.0
	Female	68.1	3.2
Total		70.3	5.8

Table 2: ANB induced changes in ART, VRT, pain and temperature before and after 30 minutes of training

		Mean	**N**	**Std. Deviation**	**P**
Pair 1 VRT-Green	Before	.23323	30	.040990	<0.001
	After	.22373	30	.044059	
Pair 2 VRT-Red	Before	.24673	30	.046819	<0.001
	After	.23690	30	.047739	
Pair 3 ART-Tone	Before	.23367	30	.040871	<0.001
	After	.22320	30	.046106	
Pair 4 ART-Click	Before	.25470	30	.038726	<0.001
	After	.24380	30	.044179	
Pair 5 Pain	Before	65.77333	30	15.015117	<0.001
	After	60.487	30	16.4396	
Pair 6 Temperature	Before	97.43333	30	.840498	<0.001
	After	97.427	30	.8769	

Table 2 shows a significant difference in all the parameters before and after ANB exercises in elderly population. A significant decrease in reaction time, pain sensitivity and body temperature was observed.

Table 3: Association of gender with 30 minutes of ANB induced differences in ART, VRT, pain and temperature

	Sex	**N**	**Mean**	**Std. Deviation**	**p**
Green	Male	14	.0096	.00970	0.941
	Female	16	.0094	.00977	
Red	Male	14	.0083	.01149	0.523
	Female	16	.0112	.01286	
Tone	Male	14	.0039	.01392	0.019
	Female	16	.0163	.01330	
Click	Male	14	.0095	.01961	0.675
	Female	16	.0121	.01424	
Pain	Male	14	5.9500	5.56054	0.715
	Female	16	4.7063	11.45964	
Temperature	Male	14	-.1571	.40137	0.078
	Female	16	.1500	.50332	

Table 3 shows a significant decrease only in tone of elderly females when compared with males. No significant difference was observed between elderly males and females on pain sensitivity, body temperature and reaction time to red light, green light &click sound.

Discussion

The present study shows a significant difference in pain sensitivity, temperature and reaction time before and after ANB exercises according to Table 2. Pain sensitivity had increased significantly (p value <0.001) and this could be attributed to increased sympathetic stimulation that occurs with right nostril associated ANB. Improved concentration and attention that occurs

with slow deep breathing exercises might also contribute to this.[19] The present study results differ from previous study results showing no change or decreased pain sensitivity after deep breathing exercises.[11-13]

Body temperature decreased significantly (p value <0.001) immediately after 30 minutes of ANB (Table 2). Generally there is decrease in body temperature with advancing age along with loss of diurnal variation in body temperature due to derangement of the temperature regulating mechanisms.[20] Decrease in body temperature is associated with increased longevity. This decreased temperature noted after ANB could be due to increased skin blood flow as a result of sympathetically mediated vasodilation. In healthy elderly people at rest, there will be a delay in the sympathetically mediated as well as total vasodilation in response to heat along with decreased sympathetic regulation.[21] Breathing exercises were shown to correct this defect by modifying the autonomic activity. As aging is associated with decrease in the number and myelination of Aγ fibres, this increased pain sensitivity would help them to be aware of injuries immediately so that proper measures could be taken.

According to Table 2, reaction time was found to decrease significantly for green light (p value <0.001), red light (p value <0.001), tone (p value <0.001) and click (p value <0.001) after ANB. The faster reaction time after ANB could be due to increased sympathetic activity and ascending reticular activity. The results of our study is in accordance with a study done on 16 adults where right nostril initiated ANB decreased reaction time and left nostril initiated ANB increased reaction time.[22]

There are two techniques of ANB. One is left nostril initiated ANB and another one is right nostril initiated ANB. Left nostril initiated ANB was shown to increase parasympathetic activity and right nostril initiated ANB was shown to increase sympathetic activity. In the present study, as breathing activity was initiated in the right nostril in inhalation and not in the left nostril, the increase in pain sensitivity, decrease in body temperature and reaction time might be due to increased sympathetic activity.

There was no significant difference in pain sensitivity, body temperature and reaction time for red light, green light and click between elderly males and females after ANB. This shows the modulating effect breathing exercises on autonomic nervous system. A significant decrease (p value< 0.019) was observed for tone in females when compared to males after ANB. This differs from a study done on young medical students where reaction time for tone and click remained the same for both males and females. The faster reaction time for tone could be due to the fact that auditory stimulus takes less time to reach the cortex than visual stimulus and this is in agreement with the results of a study in elderly Indian population which showed faster auditory reaction time in females when compared to males.[23,24]

Limitation

Study group was small and the response obtained was of short term. Long term study has to be done to obtain consistent results. As pain sensitivity varies with the type of experimental stimuli and the present study was done only with electrical stimulus, future studies should elicit pain sensation with other type of stimuli too.

Conclusion

Right nostril initiated ANB increased pain sensitivity, decreased body temperature and reaction time for light and sound in elderly males and females. This confirms the increased activity of sympathetic nervous system with this type of breathing. ANB can be practiced regularly to increase their alertness and concentration and to prolong their life span. There was no difference in pain sensitivity, body temperature and reaction time for red light, green light and click between elderly males and females. There is decrease in tone in females when compared to males.

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Conflict of Interest: None

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RESEARCH ARTICLE

Immediate effect of slow right and left nostril deep breathing exercises on reaction time, pain sensitivity, and temperature of elderly population in Madurai

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ABSTRACT

Background: Falls and fractures are very common in the elderly due to reduced swiftness of the response, decreased attention, and concentration. Normal reference point of temperature and pain threshold also varies in old age adding to their chronic illness. Important factor contributing to this is an imbalance in the autonomic nervous system (ANS). As nostril breathing exercises were known to modulate the ANS, the present study was done to find out the immediate effect of slow right nostril breathing (RNB) and left nostril breathing (LNB) exercises on reaction time, pain sensitivity, and temperature in the elderly population. **Aims and Objectives:** The objectives of the study were to measure the effect of 30 min of RNB and LNB exercises on auditory and visual reaction time, pain sensitivity, and temperature in elderly individuals. **Materials and Methods:** The study was done in the Department of Physiology of a Private Medical College in Madurai, on 30 healthy subjects aged 50–70 years. Reaction time was measured with discriminatory and choice time reaction apparatus, pain with digital algometer, and temperature with clinical thermometer. **Results:** A significant decrease in reaction time and pain threshold ($P < 0.001$ and <0.001) was observed with RNB exercises without change in temperature (0.909). A significant increase in reaction time, pain threshold, and decrease in body temperature ($P < 0.001$, <0.001, and <0.001) was observed with LNB exercises. **Conclusion:** RNB decreases reaction time and increases pain sensitivity without affecting body temperature. LNB increases reaction time but decreases pain sensitivity, and body temperature.

KEY WORDS: Breathing; Reaction Time; Pain; Temperature

INTRODUCTION

WHO global report states that there is an increasing incidence of falls in the elderly population all over the world and preventive measures have to be initiated. 70% of injuries are due to falls with multifactorial etiology.[1] An intact nervous system is essential for mobility and gait. With aging, there is a loss of neurons, especially in frontal and parietal lobes and alterations in the secretion of neurotransmitters.[2] Degenerative changes are seen in both myelinated and unmyelinated neurons and because of that speed of conduction in both sensory and motor nerves along with coordination decreases.[3,4] Due to this, the time taken to react to a stimulus increases (reaction time) and is unable to respond immediately to auditory and visual cues. There is synaptic delay in conduction of impulses from receptors to the brain and from brain to the effector organs. This

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increases the vulnerability of elderly population for falls and fractures.

Reaction time reflects sensory-motor coordination. A faster reaction time is essential for certain day to day activities such as crossing the road, catching a bus, and immediately responding to a call. A slower reaction time indicates damage in central and peripheral nervous system. Both auditory and visual reaction time (VRT) was found to increase with age.[5]

A balanced autonomic system activity is essential for the functioning of all vital organs in the body. There is also an age dependent decline in activity of both the parasympathetic and sympathetic components of the autonomic nervous system (ANS).[6] This imbalance in the ANS activity is associated with postural instability, hypertension, myocardial infarction, constipation, and insomnia, etc., in old age. Exercise does improve the vagal tone but only at specific intensity and duration.[7]

Deep breathing exercises alter autonomic function and that right nostril breathing (RNB) technique had shown to increase the sympathetic nervous system activity and left nostril breathing (LNB) technique to increase the parasympathetic nervous system activity. Literature shows that RNB practice increased basal oxygen consumption, increased basal metabolic rate, increased blood glucose levels, increased systolic, diastolic, and mean blood pressure LNB practice decreased basal oxygen consumption and metabolic rate, and decreased blood glucose levels, decreased systolic, diastolic, and mean blood pressure. RNB by activating the left hemisphere increases sympathetic activity and by activating right hemisphere increases parasympathetic activity. These evidence suggests the influence of RNB on sympathetic nervous system and LNB on parasympathetic nervous system.[8-10]

Sensitivity for hearing, vision and touch decrease with aging due to decrease in the number of specific sensory receptors and degeneration of afferent nerves.[11] In a study conducted on police trainees, 6 months training of breathing exercises along with yogasanas had shown improvement in the conduction in both sensory and motor nerves.[12] This could be confirmed with the help of the reaction time which is an index of central processing of the nervous system.

Persistent pain is a distressing factor more common in old age which could be due to loss of dorsal horn neurons and altered endogenous pain inhibition. According to the WHO report, 1 in 5 older individuals suffers from some kind of pain. Depression, anxiety, and sleep disturbance all add to increased pain sensitivity. Pain perception increases with aging and this is due to age-related increase in inflammation.[13] Pain also alters the autonomic function. As breathing exercises were reported to reduce stress, inflammation, and alter autonomic function, and few studies were done to identify the effect of slow deep breathing on pain perception but only in young subjects. The results showed increased pain tolerance, due to modulation in ANS.[14]

So far, no study was done on the role of breathing practices on pain sensitivity specifically in elderly population.

Mean body temperature decreases with age in healthy individuals.[15] Undiagnosed clinical illness might be reflected by the higher mean body temperature in the elderly. Previous studies had shown that decreased body temperature is associated with increased longevity.[16] The immediate effect of uninostril breathing exercises on body temperature was also not studied until now in older population. Hence, the purpose of the present study was to find out the immediate effect of 30 min of right and LNB practices on auditory and VRT, pain sensitivity, and temperature in older individuals.

Aim and Objectives

Among healthy elderly, aged 50–70 years in Madurai city, India, the objectives of the study are as follows:

1. To measure the immediate effect of RNB on VRT and auditory reaction time (ART), pain sensitivity, and temperature
2. To measure the immediate effect of LNB on VRT and ART, pain sensitivity, and temperature.

MATERIALS AND METHODS

A total of 30 healthy subjects in the age group of 50–70 years were chosen by simple random sampling. Healthy elderly people in the Private Medical College campus who were either working in the hospital or acquaintances of the patients were recruited for this study after obtaining their informed written consent. This study was done after obtaining clearance from Institutional Ethical Committee.

On the same subject, the effects of both right and LNB were assessed in a single day. This interventional study was carried out in the Department of Physiology, Velammal Medical College, Madurai, for a period of 2 months from June 2017 to August 2017.

Old individuals who had never practiced pranayama and without clinical evidence of any physical illness such as diabetes, hypertension, and lung diseases were included in the study. Subjects with ophthalmologic and hearing disorders, with musculoskeletal deformities, suffering from any psychiatric disorder affecting their psychomotor abilities and on medication were excluded from the study.

Description of Intervention

Baseline data on VRT and ART, pain threshold, and temperature were measured initially. RNB group participants were then taught RNB exercises, and LNB group were

taught. LNB exercises to familiarize them with the technique by a certified yoga instructor. RNB involves inhaling through right nostril for count of 5 while the left nostril is occluded and then exhaling through the same nostril for a count of 5 with no pause in between. LNB involves inhaling through the left nostril for a count of 5 while the right nostril is occluded and then exhaling through the same nostril for a count of 5 with no pause in between. Hence, for 1 min, there will be 6 breathing cycles. Once the skill is acquired, in the same individual VRT and ART, pain threshold, and temperature was measured after 30 min of RNB and LNB exercises in the same subject.

Data Collection Method and Tools

Baseline data on all participants were collected using a structured questionnaire. VRT and ART were measured with the help of discriminatory and choice reaction time apparatus (Anand Agencies, Pune) between 10 am and 12 pm every day. VRT was measured for green and red light stimuli and ART was measured for low- and high-frequency sound stimuli in the sitting posture at around 80 cm distance. For recording the baseline VRT, initially, the subject was instructed to keep pressing the finger on the response button, and once he visualizes the stimulus, immediately he has to remove his finger. The response button terminated the clock counter and the value of VRT was displayed on the screen in milliseconds. This process has to be repeated for 3 times, and the lowest value was taken as the final reaction time. Baseline ART is also recorded in the same way for both for tone and click sound. After 30 min of RNB and LNB, again VRT and ART were recorded.

Pain sensitivity was assessed with the help of a digital algometer. After switching on the instrument, electrode attached with the algometer is placed on forearm of the subject, and the baseline value is kept at 0. After that, the knob will be adjusted until the patient perceives pain sensation, and then the final displayed reading at which pain is felt is noted. Temperature was measured with the help of oral clinical thermometer before and after all these types of breathing exercises.

Statistics

The data were entered into MS Excel and analyzed using SPSS v16.0. VRT, ART, pain threshold, and temperature values before and after RNB and LNB were compared using paired *t*-test. An arbitrary cutoff of 0.05 was used to interpret significance of *P* value.

RESULTS

A significant difference is observed for all the parameters except temperature. There is no change in temperature. VRT, ART, and pain threshold had decreased from the basal value. Reaction time for green light is reduced more than that for red light after RNB. Reaction time for tone is reduced more than that for click after RNB [Table 1].

In Table 2, a significant difference is observed before and after 30 min of LNB for all the parameters. There is an increase in both VRT and ART and pain threshold. There is no much difference in the reaction time of red and green light. Increased reaction time is observed for click sound than for tone. Temperature had decreased from the baseline value.

DISCUSSION

In the present study, according to Table 1, a significant reduction in ART and VRT (<0.001 and <0.001) was seen after RNB exercises. There was also an increase in pain sensitivity. Although mean temperature increased, significant change was not observed. According to Table 2, a significant increase in ART and VRT (<0.001 and <0.001) was seen after LNB exercises. Pain sensitivity and body temperature had decreased significantly (<0.001).

This shows that practicing RNB increases conduction in both afferent and efferent nerve fibers. This could be attributed to increased stimulation of sympathetic nervous system and

Table 1: Comparison of parameters before and after 30 min of RNB among elderly (*n*=30)

Parameter	Baseline	RNB	*t*	*P*
	Mean±SD	Mean±SD		
Heart rate/min	83.5±5.3	85.9±4.7	−8.389	<0.001
VRT-green light (ms)	0.233±0.041	0.206±0.040	14.975	<0.001
VRT-red light (ms)	0.247±0.047	0.220±0.044	10.281	<0.001
ART-tone (ms)	0.234±0.041	0.205±0.041	14.779	<0.001
ART-click (ms)	0.255±0.039	0.229±0.044	10.889	<0.001
Pain threshold	65.8±15.0	49.5±16.3	12.213	<0.001
Temperature° F	97.4±0.8	97.5±1.6	−0.115	0.909

RNB: Right nostril breathing, SD: Standard deviation

Table 2: Comparison of parameters before and after 30 min of LNB among elderly (*n*=30)

Parameter	Baseline	LNB	*t*	*p*
	Mean±SD	Mean±SD		
Heart rate/min	83.5±5.3	80.3±5.0	10.116	<0.001
VRT-green light (ms)	0.233±0.041	0.265±0.042	-13.453	<0.001
VRT-red light (ms)	0.247±0.047	0.276±0.042	-11.005	<0.001
ART-tone (ms)	0.234±0.041	0.262±0.041	-14.211	<0.001
ART-click (ms)	0.255±0.039	0.280±0.042	-12.915	<0.001
Pain threshold	65.8±15.0	80.9±16.1	-13.394	<0.001
Temperature°F	97.4±0.8	97.0±0.9	4.072	<0.001

LNB: Left nostril breathing, SD: Standard deviation

increased catecholamine levels resulting in improved attention and concentration. This is supported by increased heart rate noted after RNB. This coincides with the results of the previous studies done on RNB techniques.[8-10] Sympathetic effects observed after 3 months of yogic breathing techniques could be elicited even after 30 min of RNB.

With LNB technique, reaction time increased due to decreased conduction in sensory and motor fibers. This could be due to decreased sympathetic activity after LNB practice. The present study reports that changes in VRT and ART after RNB and LNB practices were similar to that in the young individuals except for the basal increase in mean value in old age.[10] Reaction time for the green light (0.206 ms and 0.265 ms) is faster when compared to red (0.220 ms, and 0.276 ms) after RNB and LNB practice in old age. This is in contrast to the results obtained with VRT in young individuals where the reaction to red light is faster than green light.[17] This could be explained on the basis of the corpuscular theory of light which states shorter wavelength green light carries greater energy than the same quantum of red light.[18]

In the present study, subjects practiced breathing exercises at a rate of only 6 breaths/min, as only around that rate many studies had proved changes in autonomic function.[19] Fast breathing exercises practiced for the same period of time as slow breathing exercises were not shown to alter the autonomic activity. Increased pain sensitivity in aging might be due to oxidative stress, impairment in descending analgesic pathways and change in autonomic function.[13] Chronic stress results in dysfunction of hypothalamic pituitary adrenal axis resulting in decreased secretion of glucocorticoids leading to an increase in inflammatory mediators. This increases the sensitivity of nociceptive neurons decreasing pain threshold.[20] Chronic pain also alters autonomic outflow.[21] The decrease in pain threshold with RNB exercise could be due to increased sympathetic activation, whereas an increase in pain threshold seen after LNB exercise in old individuals could be attributed to increased vagal nerve stimulation and increased antioxidants. Descending analgesic pathways are activated through nucleus tractus solitarius by increased vagal stimulation.[22]

Body temperature is kept within normal limits by hypothalamic modulation of ANS. Decrease in temperature sensation after LNB exercise could be due to increased parasympathetic stimulation. Although no significant difference was seen in temperature sensation after RNB, there is a slight increase in temperature from the mean value of 97.4–97.5°F, and this confirms the effect of sympathetic mediated increase in body temperature.

Strength of Study

The study was conducted within a short period with excellent cooperation of small group of elderly subjects. Intervention did not require much expertise and easy to practice. Effect of uninostril breathing practices on pain threshold and body temperature is documented for the 1st time in an elderly population.

Limitation

Pain threshold varies with the type of stimulus. The present study was done with electrical stimuli alone. Future studies should focus on eliciting pain sensation with other type of stimuli. The effect observed is a short-term one. Longer duration study with regular practice of these breathing exercises has to be done to show consistent results.

CONCLUSION

The present study confirms the sympathomimetic effects of RNB by showing a decrease in VRT and ART, decrease in pain threshold/increase in pain sensitivity, but with no significant change in body temperature except a mean slight increase in temperature. RNB exercises can be practiced by elderly population in situations where improved attention and swiftness is required. The parasympathomimetic effects of LNB in old age were confirmed with an increase in VRT and ART, increase in pain threshold/decrease in pain sensitivity, and decrease in body temperature. LNB exercises can be practiced to decrease the pain perception in age-related illness, maintain the normal body temperature to improve the lifespan and to have a stress free life.

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Effect of breathing practices on visual and auditory reaction time of adolescent population in Madurai, India -A comparison of right and left nostril breathing

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Abstract

Introduction: Specific nostril breathing techniques are known to influence the autonomic function. Various studies have recorded that Right nostril breathing (RNB) exercises stimulate sympathetic activity and left nostril breathing (LNB) exercises stimulate parasympathetic activity. The present study was done to find out whether this is true by observing the immediate effect of specific nostril breathing on Visual Reaction Time (VRT) and Auditory Reaction Time (ART) of the same individual before and after training.

Aim and Objectives:

1. To assess the immediate effect of RNB & LNB on VRT and ART.
2. To compare the immediate effect of RNB &LNB on VRT & ART.
3. To assess the Gender difference in the RNB & LNB on VRT & ART.

Materials and Methods: 40 MBBS students in the age group of 18-20 years were randomly selected. Group A (n=20) consisted of male and Group B (n=20) consisted of female volunteers. Subjects were taught breathing exercises on the first day and after 30 minutes of RNB, VRT & ART and again after 30 minutes of LNB, VRT & ART were recorded.

Results: A significant reduction in ART& VRT and a significant increase in ART& VRT were seen after RNB & LNB exercises .No significant gender difference was observed on reaction time.

Conclusion: RNB stimulates sympathetic activity and LNB stimulates parasympathetic activity. ART is faster than VRT and no difference in reaction times between males and females were found after immediate breathing exercises.

Keywords: Autonomic function, Breathing exercises, Immediate, Reaction time.

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Introduction

The swiftness of the response to any stimuli depends on the speed of conduction of sensory nerves, motor nerves and the time taken for central processing. The time taken between application of a stimulus and the initiation of response is known as Reaction time. It serves as an index of sensory motor coordination. Audio visual (AV) reaction time plays an important role from the beginning to the end of the day. For example, the act of driving requires a faster AV reaction time, whereas a sound sleep requires a slow AV reaction time.

Specific nostril breathing techniques influence autonomic activity. At rest, in a normal individual uninostril dominance is seen, characterized by alternating patency of right and left nostrils in a 24 hour cycle.[1] Alterations in nasal cycle periodicity have been linked to various diseases. It has been reported that regular practice of breathing exercises are known to alter autonomic function and that Right Nostril Breathing (RNB) technique stimulates sympathetic activity by activating left cerebral hemisphere and Left Nostril Breathing (LNB) stimulates parasympathetic activity by activating right cerebral hemisphere.[2] A balancing effect on the left and right cerebral hemisphere was exhibited by Alternate nostril breathing.[3] These evidences confirm that nasal airflow influences the brain activity depending on nostril dominance.

Studies have recorded that RNB increases Systolic, Diastolic and Mean arterial pressure whereas LNB decreases Systolic and Mean pressure.[4] There is 37% increase in basal oxygen consumption after RNB and 24% increase after LNB. Forced RNB increased blood glucose levels; whereas LNB decreased it.[5] RNB produced a significant decrease in intraocular pressure by sympathetic stimulation.[6] All these evidences suggest that RNB may have been expected to decrease Visual Reaction Time (VRT) & Auditory Reaction Time (ART) by

stimulating sympathetic activity and LNB to increase VRT & ART by decreasing sympathetic and increasing parasympathetic activity.

It is a proven fact that males have a faster reaction time than females at rest. We want to elucidate in our study whether such differences in the reaction times between males and females existed after uninostril breathing exercises.

The direct and immediate effect of 30 minutes of specific nostril breathing practices, on the same individual on VRT & ART is so far not documented. Hence, the present study was designed to assess the immediate effect right and left nostril breathing exercises on VRT & ART.

Aim & Objectives

1. To measure the immediate effect of Right Nostril Breathing on VRT & ART.
2. To measure the immediate effect of Left Nostril Breathing on VRT & ART
3. To compare the immediate effect of Right and Left Nostril Breathing on VRT & ART of the same subject.
4. To assess the Gender difference in the Right and Left nostril breathing on VRT & ART

Materials and Methods

The study was conducted in the Department of physiology, Velammal Medical College, Madurai on 40 Adolescent individuals of First Year MBBS students of both the genders in the age group of 18-20 years who were selected randomly after obtaining institutional ethical clearance. Informed consent was obtained from the volunteers after briefing about the study. Male subjects were assigned to Group A (n=20) and female subjects (n=20) to Group B randomly by using a randomization sequence generated in Microsoft Excel.

Healthy volunteers who had never practiced pranayama and who were almost on the same diet (medical college hostel students) were included in the study. Subjects with clinical evidence of any physical illnesses like diabetes, hypertension, and upper and lower respiratory diseases, subjects with ophthalmologic and hearing disorders, subjects suffering from any psychiatric disorder affecting their psychomotor abilities and subjects on autonomic modifying medication were excluded from the study.

Description of intervention

The volunteers were instructed to refrain from tea, coffee or any caffeinated drinks on the day of the study. Study was carried out regularly in the evening between 4-5 pm to avoid the influence of circadian rhythm.

Baseline data on VRT& ART was measured initially after familiarizing them with the technique. The participants were then taught specific nostril breathing exercises by a certified yoga instructor. These exercises were practiced with subjects in the sitting posture as posture influences reaction time. RNB involves alternate cycle on inhalation & exhalation through the right nostril while the left nostril is occluded. There is no pause in between inhalation and exhalation and the subjects were asked to count 1-5 in their mind for each phase. The duration of one respiratory cycle is 10 seconds, so for 1 minute, there was 6 breathing cycles.

LNB involves alternate cycle on inhalation and exhalation through the left nostril while the right nostril was occluded. Once the skill was acquired, VRT & ART values were measured after 30 minutes of RNB exercises on the first day. Likewise on the second day, for the same individual values were taken after 30 minutes of LNB.

Data collection method & tools

Baseline & end line data on all participants were collected using structured questionnaire. The study was carried out with the help of discriminatory and choice reaction time apparatus (Anand Agencies, Pune) and done on the same time of the day for all subjects to avoid influence of circadian rhythm. It had two modes of providing stimulus- auditory & visual. VRT was measured for green and red light stimuli and ART was measured for low and high frequency sound stimuli. A distance of 80-100 cm should be there between the visual stimuli and the subject's eye. For recording the VRT, initially the subject was instructed to keep pressing the index finger on the response button and once he visualizes the stimulus, immediately he has to release his finger. The response button terminated the clock counter & the value of VRT will be displayed on the screen in milliseconds. This process has to be repeated for 3 times, and the lowest value was then taken as the final reaction time. Baseline ART has also been recorded in the same way for both for tone & click sound. Again after 30 minutes of RNB & LNB exercises, VRT& ART were recorded.

Statistical Analysis

The data was entered into MS excel and analysed using SPSS v16.0. VRT and ART values before and after nasal breathing were compared using paired t test. Sex wise differences in the effect of nasal breathing on

VRT and ART were analysed using unpaired t test. An arbitrary cut off of 0.05 was used to interpret significance of p value.

Discussion

In the present study, as shown in Table 1, VRT & ART were significantly decreased (<0.001) immediately after 30 minutes in the RNB group and increased (<0.001) in the LNB group reconfirming the fact that RNB stimulates sympathetic activity and LNB stimulates parasympathetic activity. This result coincides with the previous study done on 20 subjects who had undergone yogic breathing exercise training for a period of 3 months where RNB showed effects mimicking sympathetic activity and LNB showed effects mimicking parasympathetic activity.[7] The difference in reaction time is more for the RNB group than for the LNB group and this could be due to increased level of plasma catecholamines along with sympathetic stimulation.[8]

At rest nasal airflow is greater in one nostril than the other.[1] Persistent blockage of one nostril could affect this rhythmic alteration in the nasal cycle and can lead to health issues due to imbalance of autonomic activity.

Normally left hemisphere is specialized for language functions and right hemisphere is specialized for spatio-temporal functions. In a study conducted on adult volunteers, right nostril dominant individuals scored better on verbal tasks and the left nostril dominant individuals scored better on spatial tasks.[9] Uninostril breathing also showed increased EEG activity and Event related potential changes in the contralateral hemisphere.[10,11] Heart Rate Variability indices representing sympathetic activity were increased in the RNB group and indices representing parasympathetic activity were increased in left nostril breathing group following 6 weeks of breathing training.[12] All these evidences suggest that RNB technique stimulates sympathetic activity by activating left cerebral hemisphere and LNB technique increases parasympathetic by activating right cerebral hemisphere.

In the present study, subjects were asked to practice breathing exercises at a rate of only 6 breaths /minute, as regular practice of slow breathing exercises had shown significant changes in autonomic functions. Studies have proved that fast breathing exercises practiced for the same amount of time as slow breathing exercises had not altered the autonomic functions.[2,13] Reaction time also changed significantly with changes in duration of voluntary breathing.[14] In this study, even after 30 minutes of practice of specific nostril breathing exercises, significant changes were observed.

The mechanism by which these autonomic changes occur after breathing practices were so far clearly not documented and is still under debate. Suggested hypothesis could be that when cool air enters the nose during inspiration, trigeminal nerve gets stimulated.[15] This in turn activates brainstem reticular formation and increase arousal by stimulating wider areas of the cerebral cortex leading to changes in EEG and cognitive performance. Especially Cardiorespiratory centres in the brainstem which regulate the autonomic activity were influenced by breathing patterns.[16]

Reaction time to auditory stimulus was less when compared to visual stimulus before and after both the types of breathing which contradicts the results of a previous study where reaction time to visual stimulus was found to be lesser than auditory stimulus.[17] But many studies have concluded that not only in sedentary but also in sports trained subjects ART was faster than VRT .Though it is proved that light travels faster than sound, this could be explained on the basis that an auditory stimulus takes only 8-10 ms to reach the brain while on the other hand ,a visual stimulus takes 20-40ms.[18,19]

In the LNB group there was no significant change in reaction time to green light after breathing exercises though an increase in the mean value had been observed (from 0.190 to 0.200 ms). It is also shown in Table 2 that in both RNB & LNB group the reaction time for the red light (0.140ms, 0.183ms) is faster than that of the green light (0.154ms, 0.200ms) and this coincides with the results of a study done on young volunteers.[20] This could be explained on the basis of Trichromatic theory of colour vision which is based on three different pigments in the eye each absorbing a different range of wavelengths.[21] The spectral sensitivity of photopic human vision is dominated in order by the longer wavelength red (560 nm) cone, then by green (530nm) cone and then by the shorter wavelength blue cone which has one tenth absolute spectral sensitivity when compared with red and green. That means more number of red cones are stimulated than the other two.

There were mixed results regarding differences in reaction time between males and females.[17,22] The present study showed no statistically significant gender difference on reaction time(Table 3) after breathing exercises though the reaction time mean value for most of the parameters(except for green light in LNB and tone in RNB) is faster in males.

These results indicate that students can improve their performance in sports and academic activities by practicing RNB by increasing their alertness. But specific RNB exercises should not be practiced by hypertensive individuals with sympathetic over activity. Slow LNB techniques which could reduce blood pressure by increasing baroreflex sensitivity and decreasing sympathetic activity/chemoreflex activation should be advised.[23]

Limitation

As nasal cycle alternates periodically, nasal dominance patterns of the subjects should have been considered before the intervention. For example, if the subject was found to be in right nostril dominant period before the intervention, he should be suggested to practice RNB technique that hour to get a better result.

Results

Table 1: Comparison of VRT and ART before and after nasal breathing- Left and Right

Nostril breathing		Before		After		t test	p-value
		Mean	SD	Mean	SD		
Left	VRT(ms)	.175	.036	.191	.032	-3.841	<0.001
	ART(ms)	.155	.026	.171	.028	-6.538	<0.001
Right	VRT(ms)	.170	.026	.146	.024	9.284	<0.001
	ART(ms)	.156	.017	.137	.023	7.232	<0.001

There was an increase in the mean VRT &ART values (0.191, 0.171) after LNB from the baseline values and it was statistically significant (p<0.001).Mean VRT &ART values (0.146, 0.137) decreased from the baseline values (0.170,0.156) after RNB practice and was statistically significant (p<0.001).

Table 2: Comparison of VRT and ART before and after nasal breathing- Left and Right

Nasal breathing side	Reaction time (ms)	Before		After		t test	p value
		Mean	SD	Mean	SD		
Left	Green light	.190	.066	.200	.036	-1.136	0.263
	Red light	.160	.029	.183	.033	-6.389	<0.001
	Tone	.152	.021	.165	.023	-4.935	<0.001
	Click	.158	.033	.177	.037	-5.877	<0.001
Right	Green light	.177	.031	.154	.029	7.290	<0.001
	Red light	.163	.026	.140	.02	7.807	<0.001
	Tone	.153	.019	.134	.025	5.204	<0.001
	Click	.159	.019	.140	.027	6.148	<0.001

In the LNB group there was no statistically significant increase in the VRT for green light, though there was an increase in the mean value (0.200) from the baseline (0.190).

Table 3: Comparison of VRT and ART before and after nasal breathing- in Males & Females

Test (ms)	Side		Male		Female		t test	p value
			Mean	SD	Mean	SD		
VRT	Left	Green light	.021	.018	.000	.081	1.180	0.245
		Red Light	.020	.018	.026	.027	-0.915	0.366
	Right	Green light	.018	.019	.028	.021	1.456	0.154
		Red Light	.020	.023	.031	.017	1.687	0.1
ART	Left	Tone	.011	.017	.015	.016	-0.679	0.502

		Click	.015	.022	.022	.018	-1.123	0.269
	Right	Tone	.024	.022	.015	.026	-1.163	0.252
		Click	.015	.018	.023	.021	1.269	0.212

p value was not significant. No gender difference in reaction time.

Conclusion

Audio Visual reaction time has an important role in everyday tasks. This simple and cost-effective technique can be advised to students to overcome stress, for improvements in cognitive functions and to improve alertness and concentration. RNB has shown to stimulate sympathetic activity as evidenced by decrease in reaction time. LNB has shown to stimulate parasympathetic activity as evidenced by increase in reaction time. ART was faster than VRT. Reaction time for red light stimulus was faster when compared to green light. There was no gender difference in reaction time after breathing exercises.

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Analysis of Motor Nerve Conduction and Pain Threshold in Professional Drivers.

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ABSTRACT

Background: Professional drivers, who maintain the same sitting posture, a taut hand grip, erratic rotations of the trunk and holding the pedals in same place with foot makes them susceptible for sensory and motor nerve damage and its consequences. This study was aimed to assess the motor nerve conduction velocity and pain threshold for the professional drivers who are exposed to the constant vibration during driving. **Methods:** 40 professional drivers and 20 controls were included in the study for analysis of nerve conduction study and pain threshold in upper limb and lower limb. Drivers with significant medical illnesses, alcoholism, hypertension and diabetes were excluded from the study. **Results:** Among the study group, both in the upper limb and in the lower limb there is a significant reduction in the motor nerve conduction velocity when compared to the control group. Regarding pain threshold there is a significant statistical difference between control group and heavy motor drivers group. **Conclusion:** There is a significant decrease in the motor nerve conduction of upper limb in heavy motor vehicle drivers than low motor vehicle drivers and there is a significant decrease in the motor nerve conduction velocity in lower limb and decrease in pain threshold among the heavy motor vehicle drivers.We recommend that all the professional drivers, particularly heavy motor vehicle drivers, should have periodic medical screening to prevent neuropathic changes and its devastating complications.

Keywords: Professional drivers, Motor nerve conduction velocity, Pain threshold.

INTRODUCTION

Nowadays road traffic accidents have become an important public health issue, which has to be solved by a co-ordinated approach. Current scenario of the road traffic accident injuries and death is becoming alarming in both developed and developing countries including India. According to a census in 2010, more than 1.3 lakh people died on Indian roads. One of the many contributing factors for the increasing number of road traffic accidents is factors related to drivers.

Drivers, not like other professionals, work for a longer period of time on seat in shift basis. They do not have adequate breaks. As driving requires constant alertness, working for more than 12 hours at a stretch results in physical as well as mental fatigue and tiredness. The swiftness of the driving response requires an intact and faster conducting nervous system. There is a decline in the functioning of the nervous system with increasing age. Along with this, there is also an increased risk of nerve damage due to continuous exposure of the whole body to the engine heat and vibration during driving. The effect is more for heavy vehicle drivers. All these factors contribute to increased number of road traffic accidents. Than implementing more and more traffic rules, scientific measures have to be initiated earlier to prevent calamities.[1]

Constant vibration, work stress and poor nutrition will result in nerve damage. Nerve damage is associated with slower conduction velocity. Damage to the motor nerve results in muscle weakness and abnormal motor skills. Sensory nerve damage affects pain perception. To evaluate the functioning of motor and sensory nerves of the human body, Nerve conduction study is commonly done. It measures the speed of conduction of an electrical impulse through a nerve. It can determine nerve damage and destruction.[2]

Nerve damage also reduces pain sensitivity. In drivers, pain sensitivity has to be intact as otherwise they are at the risk of getting injured during the process of fixing mechanical glitches. Pain threshold is the point along a curve of increasing perception of a stimulus at which pain begins to be felt. It is the least stimulus intensity at which a subject perceives pain.[3]

Exposure to vibration, leads to peripheral nerve disorder such as vibration induced neuropathy.[4]

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Occurrence of features of peripheral neuropathy in the hands are common in people who are getting exposed to vibration.[5] The present study was done to assess the integrity of motor and sensory nervous system in professional drivers by analysing the nerve conduction velocity and pain threshold respectively.

MATERIALS AND METHODS

The study was approved by the Institutional Ethical board and study was done in accordance with the ethical standards suggested by the institutional body. Study was conducted in research laboratory of department of physiology, Velammal Medical College, Madurai. Study design is cross sectional study done on 40 male professional drivers and 20 controls over a period of three months. All the participants were male in the age group of 32-50 years. Subjects with driving experience of 10-20 years, with proper driving license were included in the study. Alcoholics, Smokers, individuals with Diabetes Mellitus, Hypertension and any other medical illnesses affecting nervous system were excluded from the study. Informed consent was obtained before initiating the study from all the participants. The participants were of three groups. Group I consist of 20 professional heavy vehicle drivers; Group II consist of 20 professional light vehicle drivers. Control group III consist of 20 volunteers of the same age group who are not involved in driving.

Baseline demographic data were collected before the beginning of the study using questionnaire. Motor nerve conduction velocity was recorded using Physiopac (Medicaid - Neurostim – NS2). Subjects were instructed to lie down on a couch and then skin over the placement of recording electrode was cleaned thoroughly with rubbing alcohol. The electrodes with conduction gel were fixed on the skin and secured with tape. Recordings were performed in the peripheral nerves: median nerve for the upper limb and common peroneal nerve in the lower limb. Recording electrode and reference electrode were placed distally in the course of the nerve and ground electrode was placed in between recording electrode and stimulating electrode. Nerve conduction velocity (in meter per second) was calculated by dividing the distance between the two points of stimulation by the difference of latency.[6]

Before starting the study, informed written consent was obtained from the participants. Vital signs were checked before the procedure. Room temperature was kept constant throughout the procedure. Subjects were asked to restrain themselves from drinking caffeinated drinks 1 hour before the procedure. Before the recording they were explained about the procedures clearly and made to lie down on the couch comfortably. Stimulation were made and the action potentials were recorded using surface electrodes, placed at the Right arm and Right leg (dominant side) in the median nerve and the common peroneal nerve respectively. Distance between the two points was measured and latent period was noted. Nerve conduction velocity (in meter per second) was calculated by dividing the distance between the two points of stimulation by the difference of latency. Calculations are performed by the following formula,

NCV= Distance (elbow-wrist) / latency (elbow) – latency (wrist).[10]

Pain sensitivity also was recorded after a brief period of rest. Pain sensitivity was recorded using Digital Algometer instrument (Medicaid, Pune). Probe was placed on the flexor aspect of the forearm and then the intensity of the stimulus was increased very slowly till the subject felt the pain. This value was taken as the pain threshold for that particular individual.[3]

The data were entered in to Microsoft Excel spread sheet. Mean and standard deviation was calculated in the spreadsheet. The data was then exported to SPSS version 21 and the three set of values were compared using ANOVA and student's unpaired t test for inter-group statistical significance.

RESULTS

The following table shows the mean ± SD of height and weight of three groups:

Table 1: Comparison of height and weight of three groups

	Control	Light motor vehicle drivers	Heavy motor vehicle drivers
Height (in cms)	160.1±5.51	167.78±4.91	162.7±5.49
Weight (in Kgs.)	55.45±4.42	72.35±5.12	68.3±9.39

The following table shows the comparison of motor nerve conduction velocity among the groups:

Table 2: Comparison of motor conduction velocity and pain threshold in three groups

		Control	Light motor vehicle drivers	Heavy motor vehicle drivers
Motor conduction velocity (in meter per second)	Upper limb	57.77±3.23	55.02±2.94	53.9±3.63
	Lower limb	60.13±2.62	59.99±3.86	42.14±5.72
Pain threshold	Fore arm	42±3.77	42±5.57	39±5.88

On applying ANOVA to the three groups of data, there was statistically significant difference ($p<0.05$) in both conduction velocity and pain threshold parameters. To identify the inter-group difference,

post-hoc test in SPSS and student's unpaired 't' test in EXCEL was applied.

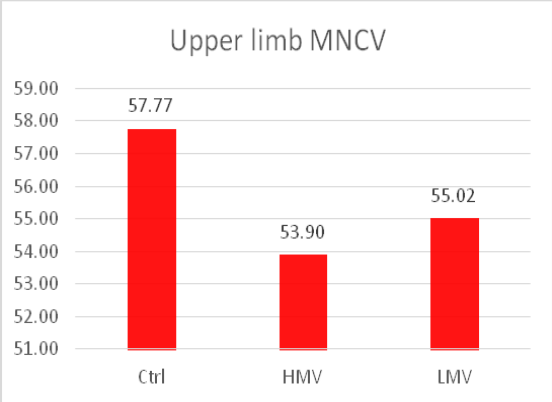

Figure 1: Comparison of motor conduction velocity – Upper limb

Table 3: Statistical comparison of motor conduction velocity – Upper limb

p value	LMV	HMV
Control	0.00384	0.00062
LMV	-	0.150

The motor nerve conduction velocity in upper limb is statistically decreased ($p<0.05$) in upper limb of light and heavy motor vehicle drivers when compared to control group. The decrease in motor nerve conduction velocity in heavy motor vehicle derivers when compared to light motor vehicle drivers is not statistically significant ($p=0.15$).

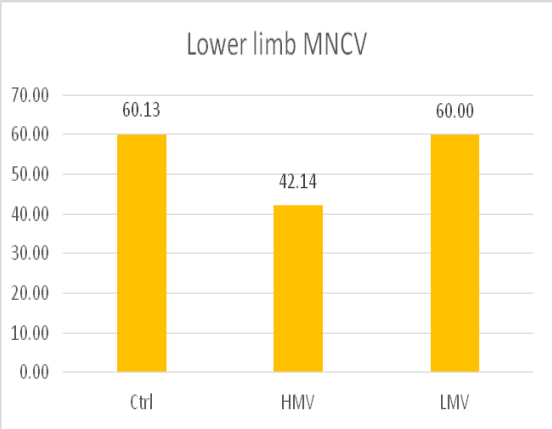

Figure 2: Comparison of motor conduction velocity – Lower limb

Table 4: Statistical comparison of motor conduction velocity – Lower limb

p value	LMV	HMV
Control	0.45	0.0003
LMV	-	0.0016

The motor nerve conduction velocity in lower limb is statistically decreased ($p<0.05$) in heavy motor vehicle drivers when compared to control group and light motor vehicle group drivers. Mean and p value of motor conduction velocity in controls and light motor vehicle drivers do not show significant difference.

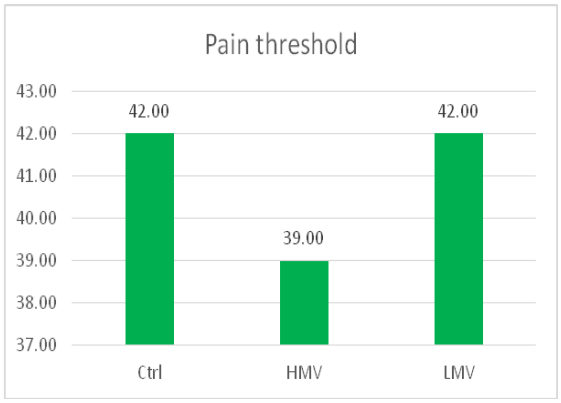

Figure 3: Comparison of pain threshold

Table 5: Statistical comparison of pain threshold

p value	LMV	HMV
Control	0.5	0.032
LMV	-	0.053

Pain threshold of control group and light motor vehicle drivers do not show significant difference in terms of mean or statistically. The pain threshold of heavy motor drivers showed significant decrease ($p<0.05$) in comparison with controls. Even though mean of pain threshold in heavy motor drivers were decreased it is not statistically significant with light motor drivers.

DISCUSSION

In this ever growing modern world, transportation has become one of the inevitable need. Professional drivers, who works for prolonged hours in a day are exposed to the continuous vibration produced by the motor vehicle, in that particularly hands and legs are getting affected commonly, and are at a risk of developing vibration induced neuropathic changes. There are very few studies done in the past to assess the vibration induced motor and sensory neuropathic changes in the professional drivers. Median nerve and common peroneal nerve are important for the motor and sensory functions of the limbs and commonly studied.[7] In the present study, we have assessed the long term exposure of vibration in the motor and sensory functions of these nerves.

Nerve conduction study is essential in the diagnosis of focal neuropathy.[8] Also studies had proven that motor nerve conduction velocity is an important forecaster in the onset of new foot ulcers in diabetic population.[9]

Our present study revealed that when compared to Control group and low motor vehicle group, Heavy motor vehicle group were having reduction in the motor nerve conduction velocity and increase in the pain threshold, so they are at more risk of developing long term hazards due to exposure to vibration for a longer period in a day. Indian Council for Medical

Research stated that the professional drivers are suffering from numerous health problems.[11] Symptoms like weakness, burning pain, tingling, pins and needles have to be reported and treated early.[12]

Regular rotatory shifts, periodic relaxations and life style modifications will be helpful in reducing the incidence of increased motor vehicle accidents and also will prevent later development of complications like chronic ulcers, It also reduces the incidence of sickness absenteeism.[13] These simple and cost effective electrophysiological test can predict the neurological complications on its earlier stages and proper treatment can be initiated earlier to avoid major neurovascular complications.[14] The median nerve is highly susceptible to damage by metabolic disturbances, entrapment neuropathies etc.[15] But, its abnormalities are often remain undiagnosed in a vast majority of patients, but with Nerve conduction study, more subclinical cases can be diagnosed at subclinical stages itself.[16]

CONCLUSION

- In upper limb, there is a significant decrease in motor nerve conduction for light and heavy motor drivers than in controls.
- In lower limb, the motor nerve conduction showed a significant decrease in heavy motor drivers.
- Pain threshold is significantly decreased only in heavy motor drivers.

Values implies a significant difference in motor nerve conduction velocity and decrease in the pain threshold values in the professional drivers who are occupationally exposed to the vibration than the controls, explaining the effects of vibration in motor nerve conduction.

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EXAM STRESS AND CHOICE REACTION TIME IN FIRST YEAR MEDICAL STUDENTS

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ABSTRACT

BACKGROUND

Medical education has always been regarded as highly stressful to students. The same stressors may be perceived differently by different medical students, depending on their cultural background, personal traits, experience and coping skills. Exam stress, inordinate hours, sleep deprivation, excessive workload, helplessness, increased psychological pressure, mental tension, adds to the stress of medical students. Reaction time is an index of sensory motor performance. Exam stress affects cognitive function.

The aim of the study is to find the effect of exam stress on auditory and visual reaction time in first year medical students.

MATERIALS AND METHODS

The study group consists of 63 healthy first year medical students of both genders in the age group of 18-20 years. The time between the auditory and visual stimulus given and response of the subject from the sensor will be taken as reaction time. The auditory and visual reaction times were recorded before and after the exam period. Statistical analysis of the data was done by using paired 't' test.

RESULTS

There was significantly prolonged visual and auditory reaction time values before exam on comparison with baseline stress free period. On comparing the same values between females and males also, the results were statistically significant. Exam stress affects the cognitive performance of the students. Prolongation of auditory and visual reaction time reflects the same in our study. Optimal stress relievers are needed in student life to cope with stress and ease out the stressful periods like exam stress.

CONCLUSION

1. Exam stress affects the cognitive performance of the students.
2. Prolongation of auditory and visual reaction time reflects the same in our study.
3. Optimal stress relievers are needed in student life to cope with stress and ease out the stressful periods like exam stress.

KEYWORDS

Stress, Reaction Time, Medical Students.

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BACKGROUND

Stress is defined as the body's nonspecific response or reaction to demands made on it, or to disturbing events in the environment.[1,2] It is a process by which we perceive and cope with environmental threats and challenges.[3] Personal and environmental events that cause stress are known as stressors.[4,5]

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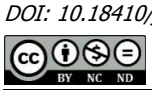

Medical education has always been regarded as highly stressful environment to students.[6,7] Stress in medical students can affect the physical and psychological well-being of the students.[8] Linn and Zeppa stated some stress in medical school training is needed for learning.[9] Stress which promotes and facilitates learning is called "favourable stress" and stress which inhibits and suppresses learning is called "unfavourable stress". They are also denoted as "Eustress" and "Distress". Eustress is attributed to positive outcome whereas distress is mostly correlated with negative outcome. Extreme magnitude of distress can cause burnout in many instances. The same stressors may be perceived differently by different medical students, depending on their cultural background, personal traits, experience and coping skills. Various studies conducted among medical students have reported prevalence of stress ranging from 27-73%.[10] Exam stress, inordinate hours, sleep deprivation, excessive workload, helplessness, increased psychological pressure, mental tension, adds to the stress of medical students. It is

observed that high stress causes deterioration in the academic performance of students.

Reaction time is the interval of time between application of a stimulus and detection of a response.[11] Reaction time is an index of sensory motor performance. Reaction time is a valid and easy method of analysing the cognitive function of the individual. Exam stress affects cognitive function.[12,13,14] The present study is designed to find the effect of exam stress on reaction time in first year medical students.

MATERIALS AND METHODS

The study was approved by Institutional Ethics Committee. The sample size was calculated on the basis of expecting a standard deviation of 10, Zα for α error of 5% as 1.96, Zβ for β error of 20% (power of 80%) as 0.84 and expecting a mean difference of 5 as 63. The study was conducted on 63 healthy first year MBBS student volunteers of both gender between the age group of 18 and 20 years. There were 49 female students and 14 male students in the participants. The participation to the study was made purely voluntary to the students. The subjects who were suffering from colour blindness, hearing impairment and sensory-motor disability were excluded from the study. As auditory and visual reaction time are prolonged in luteal phase[15,16] and menstrual phase,[17] the study group of females in the current study was included on mid follicular phase to keep the data unbiased. Informed consent was taken from all the subjects after they receive verbal explanation of the nature of the study.

The study was performed using the help of digital discriminatory and choice reaction time apparatus manufactured by Anand agencies, Pune. The study was performed in the same time of the day for all the participants to avoid influence of circadian rhythm. The volunteer was taken to the research lab which had optimal lighting and sound attenuated environment for better results of the study.

In this study a choice reaction time in the form of visual (red or green light) and auditory signals (high or low pitch sound) were used. The examiner sits with master (primary) controls and participant sat on other side with secondary controls. Once the unit is switched on, the examiner presents either with visual (red or green lights) or auditory signals (high & low pitch sounds) to the subject at random. Now, the subject immediately responded by releasing the corresponding switch on his/her side. The time duration between the application of stimulus by examiner and the response from the subject is the reaction time, which is recorded on reaction time apparatus in milliseconds. Ten such test recordings were done after two to three practice sessions. The lowest of these recordings were taken as final reaction time value for each subject. One set of recordings were taken in 'stress free' condition i.e. when the student was not under the stress of any upcoming exam and the second set of recordings were taken 30 minutes before the internal examination. Statistical analysis was done with the help of Microsoft Excel. After calculating the mean and standard deviation and confirming that the data was uniformly distributed, parametric test students' paired t test was used to compare the results. P value less than 0.05 was taken as statistically significant.

RESULTS:

The tables show the visual and auditory reaction time.

Reaction Time	During Stress free Period (m. sec.)		Before Exam (m. sec.)		P
	Mean	SD	Mean	SD	
Visual reaction time	110.1	11.3	124.5	5.3	0.0074
Auditory reaction time	81.9	10.7	103.1	10.0	0.01

Table 1. Visual and Auditory Reaction Time During Stress Free Period and Before Exam

Reaction Time	During Stress Free Period (m. sec.)		Before Exam (m. sec.)		P
	Mean	SD	Mean	SD	
Visual reaction time	111.6	11.3	124.7	5.2	0.0041
Auditory reaction time	81.8	10.5	101.9	10.5	0.0033

Table 2. Visual and Auditory Reaction Time During Stress Free Period and Before Exam for Females

Reaction Time	During Stress Free Period (m.sec.)		Before Exam (m.sec.)		P
	Mean	SD	Mean	SD	
Visual reaction time	104.9	10.2	123.9	5.7	0.017
Auditory reaction time	82.0	11.8	107.1	6.8	0.0049

Table 3. Visual and Auditory Reaction Time During Stress Free Period and Before Exam for Males

Considering the participants as single entity, there were significantly prolonged visual and auditory reaction time values between normal baseline stress free period and before exam. The difference in the readings during stress free and exam stress condition were statistically significant. On comparing the same values between females and males also, the results were statistically significant.

Both, visual and auditory reaction time were significantly prolonged for males and females enforcing that under stress full situation, the reaction time – the indicator of sensory-motor coordination is challenged by prolongation of these parameters.

DISCUSSION

The exam stress is a known acute stressor. Medical education also generates lots of stress in medical students. The volume of the subject, migration from school curriculum to college curriculum, introduction to new environment, peer adjustment, difference in study style, moving away from home etc. all lead to enormous stress in medical students. Added to these in addition to exam stress, the practical viva session is still more stressful, as the student has to face the examiner directly and answer. Particularly, the first-year students are more prone for this stress, as all together this is a new experience to them.

The aim of the present study was to observe the effect of exam stress on visual and auditory reaction time in medical students. It was observed that visual and auditory reaction time does get prolonged significantly when the students were exposed to exam stress as compared to stress free condition.

Reaction time is defined as an interval between the application of a stimulus to the appearance of appropriate voluntary response in a subject. Luce and Welford[18,19,20] described reaction time as simple reaction time and choice reaction time.

In simple reaction time, a single stimulus is presented with single voluntary response to it. In choice reaction time, more than one stimulus are presented and the subject is required to discriminate and respond accordingly. In our study we have used choice reaction time estimation. Either a red or green light is presented to the participant at random. The participant has to react by toggling the corresponding switch on his/her side. The minimal of ten trials was measured as the visual reaction time for that particular participant. Similarly, the auditory reaction time between a tone and click sound was measured.

This choice reaction time includes mental processing time and movement time.[13] Mental processing time involves time required by participant to perceive stimulus, identify, analyse and decide proper motor response. Movement time involves time required to perform the movement after selection of response. So, choice reaction time is a complicated process which involves recognition, discrimination, and analysis of stimulus and decision making for appropriate response selection. Reaction time is used as a cognitive test to measure the information processing speed.[21] Cognitive function reflects an individual's ability to think and reason in terms of temporal and spatial relationships and in symbols such as words and number. Simple reaction time test is usually considered a psychomotor test which refers to an individual's ability to co-ordinate timely and appropriate responses to stimuli but if the stimuli are complex and require decisions about how to respond then the test becomes more cognitive.[22]

In our study we decided to use choice reaction time as it reflects cognitive function of the individual. The results of our study show that, both visual and auditory reaction time is prolonged whenever the student in under exam stress. On comparing mean and standard deviation, during exam stress, the students showed prolonged reaction time. This prolongation is statistically significant on subject to student's paired t test.

Comparing among the males and females, females showed more prolonged visual reaction time during exam stress than males and males showed more prolonged auditory reaction time than females during exam stress.

The results show that exam stress affects the cognitive functions of students. Physiologically, this result can be explained on the basis of influence of hypothalamo-hypophysial-adrenal axis on higher functions. The stress, through hypothalamo-hypophysial-adrenal axis cause more cortisol and stress hormones like catecholamines to release which act on prefrontal cortex of the brain. Actions of glucocorticoid and catecholamines on pre-frontal cortex lead to a hyperdopaminergic response.[23,24] These neurochemical changes impair pre-frontal cortex signaling and neurotransmission during periods of stress and compromise pre-frontal cortex functions, thus affecting cognition and behaviour.[25]

Our results were consistent with the work done by Parikshit et al which also showed an increase in reaction times during exam stress in medical students.[13] Ganesh et al showed not only reactions times but also pulse rate, blood pressure and stress scores were increased in pre-examination settings among first year medical students irrespective of gender.[26]

So, the performance reduces because of acute exam stress. But this stress is unavoidable, and students have to undergo this stress for promotion to further years. So, we suggest, relaxation techniques like yoga, meditation, optimal sports and extra-curricular activities, break from regular work and early-well-planned preparation schedule will help in great for students to ease out their exam stress and perform well in the exams. Preparing the subjects regularly on day-to-day basis irrespective of exams, counselling and having campus mentor program will also help in overcoming the stressful situation.

CONCLUSION

1. Exam stress affects the cognitive performance of the students.
2. Prolongation of auditory and visual reaction time reflects the same in our study.
3. Optimal stress relievers are needed in student life to cope with stress and ease out the stressful periods like exam stress.

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RESEARCH ARTICLE

Effect of body mass index on post-exercise hypotension in healthy adult males

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ABSTRACT

Background: Post-exercise hypotension (PEH) is a physiological phenomenon of fall in blood pressure (BP) from basal value following exercise. Therefore, it can be used as a physiological method to treat hypertension. Obesity is known to be associated with hypertension. However, the association between body mass index (BMI) and PEH is unknown. **Aims and Objective:** The aim and objective are to compare the maximum PEH between healthy adult males with normal BMI and 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/m^2 (n = 30 in each group) were recruited. After recording basal heart rate and BP, the participants were made to walk on a treadmill at 50% of their VO_2 max for 20 min. Six post-exercise BP values at 5-min intervals were recorded. Data were analyzed using Mann–Whitney U-test. **Results:** The maximum systolic PEH was significantly greater ($P < 0.01$) in normal BMI group (median = 7 vs. 5) than the higher BMI group. However, the maximum post-exercise diastolic PEH was comparable between the groups. Spearman correlation test revealed a significant negative correlation between BMI and fall in systolic BP after exercise ($r = -0.52$, $P < 0.01$) for the pooled data. **Conclusion:** Therefore, it is concluded that BMI has a negative effect on the post-exercise systolic PEH. Hence, BMI must be taken into consideration while devising an exercise regimen for an individual as part of their lifestyle modification.

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

INTRODUCTION

"Physical fitness is not only one of the most important keys to a healthy body but also it is the basis of dynamic and creative intellectual activity." However, due to career and profession taking up ones time, and aided by technological advancement, the amount of physical activity has come down. Due to this, non-communicable diseases such as obesity, hypertension, and coronary heart diseases are on the rise and treating these diseases is fast becoming a public health problem. Physical exercise/activity is an easy and early physiological way to prevent and treat many such diseases. In patients with hypertension, 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 a prolonged decrease in resting BP in the minutes and hours following exercise."[2] PEH is seen not only in normotensive individuals but also in pre-hypertensive and hypertensive individuals.[3,4] Research is going on to see if a single bout of exercise itself can cause sufficient PEH.[5] PEH is seen in endurance exercises and is not evident in resistance exercises.[6] PEH occurs within minutes[7] to a maximum of

1 h after exercise.[8] PEH was found to last for even 12 h[9] after exercise, but the maximum fall occurred at around the 15th min[3] in the post-exercise period. Both central and peripheral mechanisms are implicated in PEH. Baroreceptor resetting to reduce the sympathetic outflow post exercise is the central mechanism,[10] while post-exercise vasodilation due to release of metabolites and histamine[11] is the peripheral mechanisms causing PEH. During the exercise recovery period, there is a combination of centrally mediated decrease in sympathetic nerve activity, as well as activation of local vasodilator mechanisms.[12] These are some of the mechanisms put forward to explain the phenomenon of PEH. The centrally mediated phenomenon of baroreceptor resetting has been put forward as a major mechanism to explain PEH. The arterial baroreflex is reset to function at a lower BP after exercise.[10] This will result in a reduction in sympathetic outflow post exercise. During exercise, the thinly myelinated and unmyelinated (Groups III and IV) muscle afferents are activated in response to muscle contraction. Input from these afferents releases the neurotransmitter substance *P* at neurokinin-1 receptors on GABAergic interneurons in the caudal NTS. These GABAergic interneurons release GABA at $GABA_A$ receptors on second-order barosensitive neurons within the NTS. The second-order barosensitive neurons convey information from baroreceptor afferents to the caudal ventrolateral medulla. GABA reduces their excitability, resulting in less inhibition of sympathetic neurons in the rostral medulla, greater firing of sympathetic vasoconstrictor neurons during exercise, and the observed resetting of the baroreflex to higher pressures during exercise.[12] As exercise continues, neurokinin-1 receptors internalize the GABA interneuron (a result of substance *P* release from muscle afferent stimulation during exercise) so that after exercise the neurokinin-1 receptors are less available for binding.[13] As a result, the GABAergic interneurons show diminished responses to tonic inputs and thus exert less inhibitory influence on the second-order barosensitive neurons.

This results in an overall decrease in sympathetic outflow from the rostral ventrolateral medulla after exercise. Another important mechanism underlying PEH is post-exercise vasodilation. Two vasodilatory phenomena are recognized during recovery from exercise: (1) Immediate post-exercise hyperemia and (2) sustained post-exercise vasodilatation.[11] The immediate post-exercise hyperemia can last from seconds to minutes. This should not be confused with PEH which lasts longer and is sustained. Recent studies show that sustained post-exercise vasodilatation is dependent on the activation of histamine H_1 and H_2 receptors.[14] In another study PEH following 60 min of moderate intensity unilateral dynamic knee-extension exercise was abolished by H1 and H2 receptor antagonist.[15] Several possible mechanisms may increase intramuscular histamine during recovery from exercise. Mast cells located within the connective tissue layer surrounding skeletal muscle fascicles and those also found near blood vessels may degranulate releasing histamine locally.[16] Antigen-dependent and antigen-independent mechanisms cause mast cell degranulation. However, in exercise, the antigen-independent methods predominate. Exercise-related factors that have been associated with mast cell degranulation include reactive oxygen species, a variety of cytokines, and increase in temperature.[17] These are some of the major mechanisms put forward to explain PEH.

Obesity is defined as a condition with excessive fat accumulation in the body to the extent that health and well-being are adversely affected (World Health Organization). Obesity is a silent killer. Obesity in India is rising in both the urban and in the rural population.[18] Sedentary lifestyle combined with unhealthy eating patterns is the major cause of obesity.[19] The first step in treating obesity is lifestyle modification which includes increased physical activity and dietary modifications.

A major concern about obesity is that it is almost always associated with other diseases such as hypertension[20] and diabetes[21] which make treatment even more difficult. A common solution for both hypertension and obesity lies in physical activity as it helps to reduce weight and BP.[2] Hamer and Boutcher[22] using 10 normal and 6 obese individuals studied the post-exercise hemodynamics between the two groups and concluded that changes in body mass index (BMI) were associated with variations in hemodynamic patterns in the post-exercise period. India is going through great epidemiological transition and must face the burden of dealing with the problem of both undernutrition and obesity. To the best of our knowledge, no such studies have been reported so far in the Indian population to evaluate the effect of BMI on PEH. Hence, this study was done to investigate the effects of BMI on PEH.

MATERIALS AND METHODS

Ethical Consideration

Ethical committee clearance (IEC: RC/13/103) from the institutional 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 in the study.

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/m^2.
Group II - Participants with higher BMI (25 and above) kg/m^2.

Sample Size

Based on an earlier study, 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%.

Exclusion Criteria

Participants who came under the following criteria were excluded from the study:

- Participants practicing yoga or trained athletes.
- Pre-hypertensives.
- Participants with previous history of 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 a well-ventilated room. Each participant was asked to report to the physiology laboratory in the morning around 9 a.m. after having light breakfast. They were instructed to refrain from rigorous physical activity for 48 h before the test and not to consume tea/coffee for 12 h before the study. A detailed medical history was obtained, and 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.

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 by dividing the participant's maximum heart rate by the basal heart rate and multiplying it with 15.3[24] (Uth-Sørensen-Overgaard-Pedersen estimation). The value obtained was divided by 2 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 max was then calculated by dividing the obtained O_2 consumption by 0.2.[25] This was the speed in m/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 maximum fall in systolic BP was calculated by subtracting the lowest recorded systolic BP in the post-exercise period from the basal systolic BP value. Similarly, the maximum fall in diastolic BP was calculated by subtracting the lowest recorded diastolic BP from the basal diastolic value.

Statistical Analysis

All the data were analyzed using SPSS version 21. $P < 0.05$ was considered to be statistically significant. The data were 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 significance of any difference between the groups in age, anthropometric parameters, basal heart rate, pre- and post-exercise BP values (both systolic and diastolic). Spearman correlation test was used to find out the association between the BMI and PEH values.

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 ($P < 0.05$) ones and had significantly lower body weight ($P < 0.01$) [Table 1]. 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 similar pattern, 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]. The maximum fall in systolic BP was found to be greater in normal weight subjects when compared with their overweight counterparts, and the difference was found to be statistically significant ($P < 0.01$) using Mann–Whitney U-test. Similarly, the maximum fall in diastolic BP was also higher in normal BMI group when compared with the higher BMI group in the post-exercise period, but it did not reach statistically significant values [Table 3]. Spearman correlation test showed that there was a significant negative correlation between BMI and fall

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 (m)	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*

P value is for Mann–Whitney U-test between the two groups. **P* value statistically significant. BMI: Body mass index

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*

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

Table 3: Comparison of PEH values among the groups with normal BMI (18.5–24.9) and above normal BMI (25 and above)

Variable	Normal BMI group median (25th–75th percentile)	Above normal BMI group median (25^{th}–75^{th} percentile)	*P* value
Maximum fall in systolic BP after exercise (mmHg)	7 (6–8)	5 (4–6)	<0.01*
Maximum fall in diastolic BP after exercise (mmHg)	4 (3–5)	4 (3–4)	>0.05

P value for Mann–Whitney U-test between the two groups. **P* value statistically significant. PEH: Post-exercise hypotension. BMI: Body mass index

in systolic BP in the post-exercise period ($r = -0.52$, $P < 0.01$) [Figure 1].

DISCUSSION

Among the two groups, the normal BMI group was significantly younger than the obese group ($P < 0.05$) and their weight was considerably lower than the higher BMI group which was statistically significant ($P < 0.01$). The height of the participants between the two groups was similar. There were differences in the basal BP and heart rate values between the two groups. Analysis revealed that the basal systolic BP of normal BMI group was significantly lower than (median, 25^{th} and 75^{th} percentile - 111 [108–116]) the above normal BMI group (116 [112–117]) ($P < 0.05$). A similar trend was seen in diastolic BP also. However, the difference was not statistically significant ($P > 0.05$). The higher BMI group also showed higher basal heart rate ($P < 0.01$) when compared with the normal BMI group.

The results of our study are consistent with those of Nageswari *et al.*[26] who found similar high basal BP values in obese individuals. These findings indicate that the basal sympathetic tone in the obese group is higher than the normal BMI group, whereas the peripheral resistance is similar between the two groups. In long-standing obesity, the sustained and prolonged hemodynamic burden induces structural changes in the left ventricle.[27] Therefore, the high basal BP could be due increase in cardiac output (CO) because of high BMI. Landsberg and Krieger in 1989[28] and Troisi *et al.*[29] in 1991 reported that diet intake has an important role in the activation of sympathetic system. Obese individuals also have elevated levels of insulin which is also a stimulator of the sympathetic system. Increased sympathetic activity in turn will gradually increase the BP from normal values. Higher sympathetic tone will also cause an increase in the heart rate. Therefore, high basal heart rate can be taken as a marker of sympathetic activity.[30] After exercise for 30 min, we compared the post-exercise fall in BP between the two groups using Mann–Whitney U-test. The normal BMI group had a greater fall in both systolic and diastolic BPs when compared to the above normal BMI group; however, the difference was statistically significant only in case of systolic fall ($P < 0.01$), whereas the difference in diastolic BP fall was not statistically significant ($P > 0.05$). The most important reason for the fall in systolic BP is due to centrally mediated baroreceptor resetting to reduce the sympathetic outflow after exercise.[10] The diastolic fall is due to the release of metabolites and local vasodilator substances like histamine.[14] The normal BMI participants have statistically significant greater fall in systolic BP than the participants with above normal BMI. This could be due to the

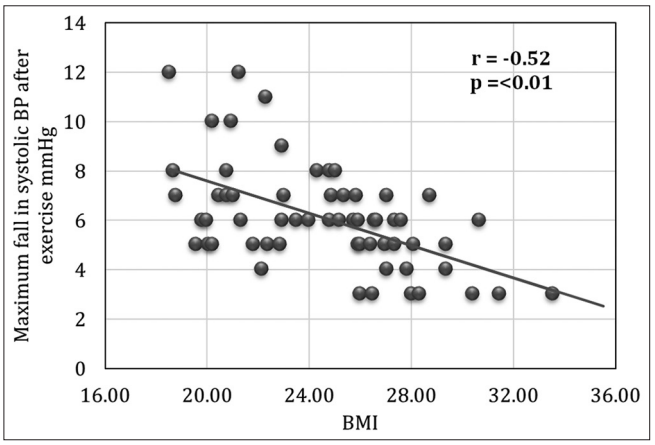

Figure 1: Scatter plot showing correlation between body mass index and maximum fall in systolic blood pressure in the post-exercise period

fact that obese individuals have higher sympathetic tone than non-obese individuals. Therefore, even after baroreceptor resetting, their sympathetic discharge would have been higher than the normal BMI individuals. Hence, normal BMI individuals have a statistically significant fall in systolic BP. In case of diastolic BP, the fall is due to the production of local metabolites which might be similar in both groups. Furthermore, Spearman correlation revealed a significant negative correlation between the maximum fall in systolic BP and BMI in the post-exercise period ($P < 0.01$, $r = -0.52$), but the correlation between maximum fall in diastolic BP and BMI was not statistically significant ($P > 0.05$).

Our study findings vary with the study findings done by Hamer and Boutcher.[22] They stated that BMI was associated with specific post-exercise hemodynamic responses between the normal BMI and obese group. Higher BMI was associated with greater reductions in CO and stroke volume but lower reductions in total peripheral resistance. Based on these findings, they concluded that BMI has no effect on PEH. However, they suggested that body composition has an impact on the mechanisms of PEH and should, therefore, be considered as an important confounding variable in future studies. This variation can be due to the fact that, in our study, a total of 60 subjects were recruited, whereas their study was done with only 16 participants in number. The inadequate sample size might be the reason their study did not show statistical significance.

Nevertheless, our study shows that BMI has a negative effect on post-exercise hypotension, particularly the systolic BP.

Limitations

1. Greater sample size might have given a better idea about the diastolic BP also.
2. Whether the effect is the same in women needs further investigation.
3. BP recording could have been done at 2-min intervals (or even continuous BP monitoring if possible) rather than 5 min for better knowledge about the BP fall after exercise.

CONCLUSION

From our study, it can be concluded that BMI significantly affects post-exercise hypotension, systolic PEH more than diastolic PEH, in the post-exercise period. This could be due to 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 with greater intensity or duration to attain the same beneficial effects of PEH as individuals with normal BMI. Therefore, while devising an exercise regimen for the treatment of hypertension, BMI of the individual must be taken into consideration for optimum benefit for the individual.

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RESEARCH ARTICLE

Comparison of effect of aspartame (artificial sweetener) and aspartame-sweetened diet drink on autonomic reactivity of volunteers

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ABSTRACT

Background: Obesity is the single most important risk factor in the onset of various diseases. Dieting is considered as an important part of today's daily life; the aim of our study is to explore the effects of aspartame on autonomic reactivity and compare it with the effects of aspartame-sweetened diet drink in human volunteers. **Aim and Objectives:** To study and compare the effect of aspartame and aspartame-sweetened diet drink on autonomic reactivity. **Materials and Methods:** This is a comparative study done in the department of physiology. After getting an Institutional Ethical Committee clearance and explained informed and written consent from all the participants. The study duration was for 2 months and the study population was 120 volunteers of age 20–30 years of both genders were randomly chosen and included in the study. They were divided randomly as 80 volunteers in the study group and 40 in the control group. The study Group A in whom aspartame (artificial sweetener) diluted in water was given. Group B in whom diet drink was given and Group C as controls who was fed with plain water and tested for various parameters of autonomic reactivity. **Results:** The findings in our study showed increased sympathetic activity after consumption of aspartame diluted in water and also showed further increased sympathetic activity in subjects who consumed aspartame-sweetened diet drink than the controls. **Conclusion:** Aspartame is causing various health hazardous to humans, it is no safer to consume aspartame as a sugar substitute.

KEY WORDS: Aspartame; Autonomic Reactivity; Diet Drink

INTRODUCTION

Obesity is the single most important risk factor in the onset of various diseases. Nowadays, everyone prefers taking some immediate steps to skip their calories either by doing strenuous exercise or dieting. Moreover, in dieting, consumption of diet drinks is considered as an important part of today's daily routine life.

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White granulated sugar 1 teaspoon (4 g) contains 16 calories and the complications produced by sugar intake are cardiovascular disease, nerve damage (neuropathy), kidney damage (diabetic nephropathy), or kidney failure and damage to the blood vessels of the retina (diabetic retinopathy).[1]

Aspartame packet each contains 1 g of aspartame 4 calories. 1 ounce of diet soda contains around 200 mg of aspartame. A 355 ml of diet soda will contain around 2.5 g of aspartame which is equal to 9 calories. On a weight basis, the metabolism of aspartame generates approximately 50% phenylalanine, 40% aspartic acid, and 10% methanol.[2]

"Artificial sweeteners" such as saccharin, aspartame, and sucralose are the alternatives for people who want to limit their sugar intake. Furthermore, maltitol and sorbitol are

often used, frequently in toothpaste, mouthwash, and in foods such as "no sugar added" ice creams.

Diabetics prefer sugar-substituted foods to lower the total carbohydrate in their meals and control their blood glucose level. Widely used sugar-free or diet foods include baked products, soft drinks, powdered drink mixes, candy, puddings, canned foods, jams and jellies, dairy products, beverages, instant breakfasts, breath mints, and sugar-free chewing gums.[3]

In carbonated drinks, acesulfame potassium is almost always used in conjunction with another sweetener, such as aspartame or sucralose.

All these sugar-free diets come into play with the idea of empty calories and zero fat. However, the most commonly used sugar substitute aspartame - the sweet silent killer, a major culprit of many diseases, and fatal conditions - is most commonly ignored.[4]

Methanol, a metabolite of aspartame, causes oxidative stress in the cardiovascular centers in the brain stem and/or sympathetic centers in the hypothalamus.[5,6]

Oral aspartame consumption at 40 mg/kg bodyweight/day has been found to cause oxidative stress in the brain,[7,8] liver and kidney,[9,10] and immune organs[11,12] in Wistar albino rats.

Studies also showed that long-term aspartame consumption in Wistar albino rats causes reduced cardiac parasympathetic modulation, increased low frequency (LF), decreased high frequency (HF), and decreased LF/HF ratio in heart rate (HR) variability. Total power, an index of overall heart rate variability (HRV), was also reduced in aspartame-treated animals.[13]

The inadequacy of past studies, combined with the general limited knowledge about the safety/potential toxigenic effects of substances widely present in the industrialized diet, motivated the design of this experiment. So far, no study has been done to find out the effect of aspartame on autonomic reactivity in humans. Therefore, the aim of our study is to explore the effects of aspartame on autonomic reactivity and compare it with the effects of aspartame-sweetened diet drink in human volunteers.

MATERIALS AND METHODS

This is a comparative study done in the department of physiology. After getting an Institutional Ethical Committee clearance and explained informed and written consent from all the participants. The study duration was for 2 months and the study population was 120 volunteers of age 20–30 years of both genders were randomly chosen and included in the study. They were divided randomly as 80 volunteers in the study group and 40 in the control group. The subjects with H/o of smoking, known DM/HT, obese, and neuromuscular disorders were excluded from the study.

The study Group A (n = 40) in whom aspartame (artificial sweetener) diluted in water was given. Group B (n = 40) in whom diet drink was given and Group C (n = 40) as controls who was fed with plain water and tested for various parameters.

All three group volunteers were instructed to take their meal 2 h prior before beginning the recordings and also were instructed to avoid caffeinated beverages on that particular day of the study, to avoid their influences.

The subjects were comfortably seated after explaining the procedure. Baseline data were recorded on day 1. Initially, resting HR and resting blood pressure were recorded for all the subjects using digitalized measuring apparatus, and their autonomic reactivity was assessed by recording when the volunteer was asked to do isometric handgrip (IHG) exercise for 5 min using handgrip dynamometer following which the HR and blood pressure were recorded. Then, the subject was asked to do deep breathing following which the HR and blood pressure were recorded and E/I ratio was calculated.

Then, the subjects were given two and a half packets of branded artificial sweetener containing 2.5 g of aspartame diluted in normal water. After ½ h, autonomic status of the subjects was measured once again using the same methods. On day 2, again baseline data were recorded for the same subjects and then aspartame-sweetened diet drink 355 ml (a can) was given. ½ h later, the autonomic status of the same subject was measured again. The same procedure was repeated individually for all the subjects in the same way for 2 consecutive days and the values were recorded. And now, the values of E/I ratio, blood pressure, and HR, before and after consumption of aspartame between the groups were assessed.

Data Collection Method and Tools

1. IHG dynamometer was used to assess sympathetic reactivity
2. Deep breathing (E/I) ratio was used to assess the parasympathetic reactivity.

The quantitative data were checked for normality and summarized using mean/median and standard deviation; the values obtained were compared using statistical Student's t-test. $P < 0.05$ was the cutoff to determine statistical significance.

RESULTS

Comparisons between the groups were using paired t-test and comparisons against the groups were done using unpaired t-test.

Table 1 summarizes the comparison of results of comparison of autonomic reactivity parameters - IHG and deep breathing (E/I) ratio in subjects before and after consumption of aspartame diluted in water.

After consumption of aspartame-sweetened water in Group A subjects, there was an increase significantly in the HR $P < 0.002$, systolic blood pressure (SBP) $P < 0.004$, and in diastolic pressure $P < 0.005$, along with reduction in parasympathetic parameter, deep breathing ratio (E/I).

Table 2 summarizes the comparison of sympathetic reactivity parameter - IHG in subjects before and after consumption of aspartame-sweetened diet drink after consumption of aspartame-sweetened diet drink in Group B subjects there was further an increase significantly in the HR $P < 0.003$, SBP $P < 0.005$, and in diastolic pressure $P < 0.005$, along with reduction in parasympathetic parameter, deep breathing ratio (E/I).

Table 3 summarizes the comparison of autonomic reactivity parameters - IHG and deep breathing (E/I) ratio in controls subjects before and after consumption of plain water. There was no significant increase in any of the autonomic reactivity parameters.

DISCUSSION

The findings in our study showed increased sympathetic activity (increase in systolic and diastolic blood pressure and increase in HR) while doing autonomic function test in the subjects after consumption of aspartame diluted in water and also showed further increased sympathetic activity significantly in subjects who consumed aspartame-sweetened diet drink than the controls.

which is In par with the study showing that long-term aspartame consumption in Wistar albino rats caused reduction in heart rate variability with sympathetic dominance and loss of vagal tone.[13]

Increased HR and blood pressure in our study are probably due to the aspartame changing the ratio of amino acids in the blood, blocking or lowering the levels of serotonin, tyrosine, dopamine, norepinephrine, and adrenaline. The present study deals with enforcing the toxic effects of aspartame, the artificial sweetener, and its metabolite products such as methanol and formaldehyde.

The association of hypertension with the consumption of cola beverages (Diet Coke [TM]) has been confirmed by Winkelmayer *et al*. in a large prospective study of female nurses - but not with caffeine consumption. They speculated that some other compound contained in soda-type soft drinks may be responsible for the increased risk of hypertension.[14,15] The causative role of aspartame products was indicted by (1) the striking improvement or normalization of blood pressure after stopping aspartame and (2) the prompt recurrence of hypertension following aspartame resumption. Which may be due to the conversion of phenylalanine (a molecule of aspartame)into pressor substances like dopamine, epinephrine and norepinephrine. Other aspartame reactors have evidenced peripheral vasomotor features including the Raynaud phenomenon and probable pulmonary hypertension.[16,17]

Phenylalanine being a component in aspartame when increased in the brain can elevate nor-epinephrine levels. which clinically manifest as hypertension. Nor-epinephrine increases blood pressure by increasing vascular tone through alpha-adrenergic receptors activation. So at least persons

Table 1: Comparison of autonomic reactivity parameters - IHG and deep breathing (E/I) ratio in subjects before and after consumption of aspartame diluted in water

Autonomic reactivity parameters	Before aspartame (mean)	After aspartame (mean)	*P* value
HR (min)	89.8	97.6	0.002*
SBP (mmHg)	123	134	0.004*
DBP (mmHg)	83	92	0.005*
E/I ratio	1.19	1.41	0.005*

**P*<0.05. IHG: Isometric handgrip, HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 2: Comparison of sympathetic reactivity parameter - IHG and deep breathing (E/I) ratio in subjects before and after consumption of aspartame-sweetened diet drink

Autonomic reactivity parameters	Before diet drink (mean)	After diet drink (mean)	*P* value
HR (min)	90.75	100.25	0.003*
SBP (mmHg)	125.25	139.35	0.005*
DBP (mmHg)	86.2	89.34	0.005*
E/I ratio	1.19	2.45	0.005*

**P*<0.05. IHG: Isometric handgrip, HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Table 3: Comparison of autonomic reactivity parameters - IHG and deep breathing (E/I) ratio in control subjects before and after consumption of plain water

Autonomic reactivity parameters	Before (mean)	After (mean)
HR (min)	75	72
SBP (mmHg)	110	112
DBP (mmHg)	83	84
E/I ratio	1.2	1.3

IHG: Isometric handgrip, HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

with hypertension have to avoid aspartame products. Another component of aspartame, methanol are noted for damaging mitochondria of the myocardium and the specialized form of myocardium called the cardiac conduction system. Damage to the mitochondria of the myocardium and conducting system produces lots of free radicals which leads to susceptibility to arrhythmias (irregular heart rhythm).

Moreover, the limitations of the study are failure in the estimation of levels of catecholamines in the individuals who were showing increased sympathetic reactivity due to aspartame consumption. The study is being planned to be further continued in animals in the future.

CONCLUSION

Since (artificial sweetener) aspartame is causing various health hazardous to humans, it is no safer to consume aspartame as a sugar substitute, either directly in the form of tabletop sweeteners or as diet products termed as "sugar free" prepared with aspartame. Diet drinks are no more a good alternative for weight reduction.

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Original Article

A Comparative Study of Effects of Oropharyngeal Exercises and Continuous Positive Airway Pressure (CPAP) on Parameters of Sleep on Moderate Obstructive Sleep Apnea Syndrome (OSAS) Patients

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ABSTRACT

Background: Obstructive sleep apnea syndrome is a highly prevalent serious chronic illness characterized by repeated, complete or partial obstruction of the upper airways during sleep, mainly at the level of the oropharynx. Upper airway dilator muscles are important for the maintenance of pharyngeal patency.

Objectives:

1. To assess the effects of Oropharyngeal exercises and CPAP on moderate OSAS patients
2. To compare effects of oropharyngeal exercises and CPAP therapy on moderate OSAS patients.

Materials & Methods: Recently diagnosed 20 Moderate OSAS patients of age group 25-60 years were included in the study. Group A consisted of 10 patients who practiced only oropharyngeal exercises (Tongue, Soft palate and Lateral pharyngeal wall) regularly 30 minutes a day for 3 months. Group B consisted of 10 patients who were on only CPAP therapy for 3 months.

Results: The results observed in Exercised and CPAP group were as follows: A significant decrease in day time sleepiness score ($p<0.005$, $p<0.001$), sleep quality index ($p<0.008$, $p< 0.001$), apnea-hypopnea index ($p<0.001$, $p< 0.001$), oxygen desaturation index ($p<0.002$, $p<0.001$), number of desaturations ($p< 0.013$, $p<0.002$), snoring events ($p<0.004$, $p<0.039$) was observed.

Conclusion: Though regular practice of Oropharngeal exercises/CPAP significantly reduced the severity in moderate OSAS patients, the effects observed with CPAP therapy had better results on comparison.

Keywords: Sleep apnea, Oropharyngeal exercises, Continuous Positive Airway Pressure

INTRODUCTION:

Obstructive sleep apnea syndrome (OSAS) is a most commonly present chronic illness, manifested by upper airways being repeatedly obstructed either completely or partially mainly during sleep. The obstruction occurs at the oropharyngeal level with repeated and continous stoppage of respiration causing oxyhemoglobin desaturation which leads to awakening and resumption of respiration. But the patients are not aware what is happening to them during sleep, and present with the history of only excessive tiredness, sleep disturbances and daytime sleepiness.[1] And when examined, they had enlarged tongue, elongated and floppy soft palate and uvula, associated with increase in adipose tissue in the oropharynx, causing obstruction in the airway.[2] Palatoglossus and palatopharyngeus are the upper airway dilator muscles which are most

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important for maintenance of pharyngeal patency.[3,4] The set of exercises practiced in this study were derived from a speech therapist. It consisted of isometric and isotonic exercises involving the tongue, soft palate and oropharynx, which were primarily developed to increase upper airway patency.[5,6]

Continuous positive airway pressure (CPAP) therapy is the most standard treatment for sleep apnea.[7] The patients are instructed to use CPAP device whenever they are asleep including naps at daytime too. The number of apneas and hypopnea is recorded by the CPAP device.

The apnea - hypopnea index (AHI) is defined as the number of apneas and hypopnea during pap usetime. CPAP treats OSAS by reducing snoring episodes, daytime sleepiness and improving subjective sleep quality.[8] Despite CPAP being the most efficacious treatment available to OSA patients, adherence is very minimal because the patients are able to use it only 3 to 5 hour per night sleep.[9]

The other therapies available for OSAS like weight reduction, repositioning the mandible intraorally and surgeries like uvulopalatopharyngoplasty have minimal benefits when compared to CPAP device.[10]

In our study we compared oropharyngeal exercises and continuous positive airway pressure results in moderate sleep apnea patients. Polysomnography was used to assess severity of sleep apnea by recording sleep symptoms including snoring episodes, daytime sleeping and sleep quality.

MATERIALS AND METHODS:

The present comparative study was done in sleep lab, pulmonary medicine department of velammal medical college and hospital, Madurai. For a study period of 3 months by random sampling 35 recently diagnosed moderate OSAS patients of both genders of 25-60 years age group were included, after getting an institutional ethical committee approval.

Ten patients were not willing for the study, rest of the twenty-five patients were put on baseline investigations and examination after obtaining an explained, written, informed consent. Five patients were excluded from the study because they were under the exclusion criteria taken up for the study, the exclusion criteria were subjects with BMI>40, craniofacial malformation, on regular sedatives & hypnotics, severe OSAS and any other medical illness. The remaining 20 patients were narrowed down to the study group, who were randomly divided into two Interventional groups Group A and Group B.

Group A consisted of 10 moderate OSAS patients who practiced only oropharngeal exercises (Tongue, Soft palate and pharyngeal wall) regularly each exercise for three minutes daily five times a day for three months duration.

Group B consisted of 10 patients who were on only CPAP therapy for 3 months.

BMI was calculated after measuring height in m^2 and weight in kgs. Baseline and End line values were collected before and after the interventional therapies.

Data Collection Method And Tools:

Collection of data using Questionnaire

1. Sleepiness at daytime was recorded with the Epworth sleepiness scale that evaluates sleep from No (0) to intense (3) in eight varying timings. Score when summed up if is more than 10 are then taken as excessive daytime sleepiness[11]

2. Sleep quality was recorded with the Pittsburgh sleep quality index (PSQI) which has 19 questions and 5 questions answered by accompanying person. Only self-answered questions were taken up in the scoring. The 19 self answered scores are added to form seven divisions of scores ,each of which has range of 0-3 points. In all cases, a score of "0" indicates there is no difficulty for the patients while a score of "3" indicates severe difficulty. The seven divided scores are then summed to one "global score" , with a range of 0-21 marks,"0" indicating no difficulty and "21" indicating severe difficulty in all sections.[12]

All the patients were evaluated with Polysomnography study which consisted of sensors like Oxygen saturation sensor to measure oxygen desaturation index, number of desaturations and levels of SPO^2. Nasal pressure cannula, oronasal thermistor &Thoracic belt sensor are used to measure apnea-hyperpnoea index (AHI) & respiratory distress index(RDI) which determines the severity of OSAS. Snoring sensor was used to measure snoring events.

Description of intervention:

Group A, OSAS patients were trained with oropharyngeal exercises under the instruction and supervision of a speech therapist. These exercises were practiced regularly to strengthen tongue, soft palate, oropharynx and jaw. The duration of each exercise was for three minutes daily and were asked to do it five times a day for three months duration. And to ensure adequate patient effort once a week they did it under supervision.

Tongue Exercises[5]

1. The tongue is placed in the floor of the mouth and gently brushed with a tooth brush on the sides and superior part of tongue, each movement should be done 5 minutes 3 times a day.
2. By keeping the tip of the tongue against the front of the palate and moving the tongue backwards 3 minutes totally throughout the day
3. Tongue is forcefully sucked upward against the palate by pressing the entire tongue against the palate for a total of 3 minutes throughout the day.
4. The tongue is forced back against the floor of the mouth while keeping the tip of the tongue in contact with the inferior incisor teeth for a total of 3 min throughout the day.

Soft palate exercises5

A vowel is asked to said by the patient either intermittently which is acting as isotonic exercises and when said continuously acting as isometric exercises. These exercises have to be done daily for 3 min at their house and were asked to do it in department once a week to assess if the procedure is properly followed by the patients.

Oropharynx & jaw exercises[5]

1. Buccinator muscles are contracted by sucking, with repetition acting as isotonic and same position as isometric exercise.
2. Buccinator muscle are taken against the finger and is put in the oral cavity and pressing the buccinators muscle outward.

3. Elevation of angle of the mouth is alternated which is acting as isometric and with repetition acting as isotonic exercises Patients are requested to complete 10 intermittent elevation three times.
4. Elevation of the angle of mouth by alternating lateral jaw movements acting as isometric exercises

Group B participants in this study were provided with PAP device which uses an electronic circuit to monitor the patients breathing and provides two different pressures, higher one during inspiration and lower one during expirations. The patients themselves are taught to wear the nasal mask of pap device whenever they are falling asleep including daytime naps.

RESULTS:

Comparisons of the values within two groups were by using paired t test and comparisons against the two groups were done by using unpaired t test. Table 1 shows the comparison of results of sleep related parameters in oropharyngeal exercised group before and after exercise for 3 months duration. After oropharyngeal exercises sleep quality has improved significantly with sleep quality score p< 0.008, there was a significant decrease in snoring episode p<0.004, apnoea – hypopnoea index p<0.001, snoring events p<0.004, respiratory index p<0.008 and oxygen desaturation index p<0.002, SPO^2 also improved, along with reduction in number of desaturations p<0.013 in exercised patients.

Table 1: Comparison of sleep related parameters before and after oropharyngeal exercises for 3months duration. (Group A)

Parameter	AFTER EXERCISE	BEFORE EXERCISE	P value
	Mean± SD	Mean±SD	
PSQI	13±2	10.7±1	*0.008
ESS	14.7±3	11.4±1	*0.001
ODI	18.6±8	10.9±6	*0.002
AHI	22.3±5	13.8±5	*0.001
SE	3320.2±1180	2104.±6	*0.004
RI	20.4±9	15.4±5	*0.008
SPO_2	76.1±10	84±4	*0.003
Number of desaturation	204.1±94	112±9	*0.013

*P value <0.05

PSQI – Pittsburgh sleep quality index, ESS – Epworth Sleepiness Score, ODI -Oxygen Desaturation Index, AHI-Apnea Hypopnea Index, SE – Snoring Episodes, RI – Respiratory Index, SPO^2 Blood Oxygen Saturation

Table 2: Comparison of sleep related parameters before and after CPAP Therapy for 3 months duration (Group B)

PARAMETERS	Before CPAP	After CPAP	Pvalue
	Mean±SD	Mean±SD	
ESS	16±3	11.8±1	*0.001
PSQI	15.2±2	9.8±1	*0.001
ODI	23.4±9	9.6±1	*0.001
AHI	22.2±6	9.9±1	*0.001
SE	3654.3±1822	3228.1±1474	*0.039
RI	23.6±7	11.2±3	*0.001
SPO_2	69.6±10	85.6±6	*0.001
No. Of desaturation	203.1±111	101.4±49.9	*0.002

*P value <0.05

Table 2 shows the comparison of results of sleep related parameters in CPAP group before and after therapy for 3 months duration

After CPAP therapy, sleep quality has improved significantly with sleep quality score p< 0.001, there was a significant decrease in snoring episode p<0.039, apnoea – hypopnoea index p< 0.001, respiratory index p<0.001 and oxygen desaturation index p<0.001, SPO^2 also improved, along with reduction in number of desaturations p<0.002 in exercised patients.

Table 3 shows the comparison of results of sleep related parameters between Oropharyngeal exercised group and CPAP group after therapy for 3 months duration

Though there were improvement both in exercised and CPAP therapy group statistically after three months of intervention, highly significant results were observed only in three of eight parameters in CPAP therapy, sleep quality showing P <0.005, respiratory distress index P <0.034 and SPO2 P<0.003

Table 3: Comparison of sleep related parameters of Oropharyngeal exercised and CPAP therapy groups (Group A & Group B)

Parameters	Oropharyngeal exercises	CPAP	p value
	Mean	Mean	
ESS	3	4	0.438
PSQI	2	5.4	*0.005
ODI	7	13.8	0.088
AHI	9	12.3	0.243
SE	1215.6	128	0.365
RI	5	10	*0.034
SPO_2	-10	-16	*0.003
No of desaturation	91.2	100	0.401

*P value <0.05

DISCUSSION:

Pharyngeal patency during breathing is mainly achieved by synchronized action of upper airway and thoracic respiratory muscles together. According to Fogel RB et al tongue posture appears to have greater effect on upper airway structures.[4] But in OSAS patients since tongue is enlarged, soft palate and uvula is elongated and floppy, the upper airway is getting obstructed leading to oxyhemoglobin desaturation followed by arousal and resumption of respiration. The results in the present study of both the oropharngeal exercised group and CPAP therapy group shows significant improvement in the quality of sleep, and oxygen saturation, reduction in - daytime sleepiness score, snoring episodes, apnoea –hypopnoea index (AHI) and number of desaturations.

Since the tongue, pharyngeal & oral cavity muscles get strengthened by the prescribed oropharyngeal exercises, which are proved by our study results, the upper airway patency is improved in OSAS patients and thereby oropharyngeal exercises acts as a corrective measure in OSAS.

Similarly, CPAP therapy is blowing continuous constant airflow through the nose and mouth and thereby it acts as a supportive measure to the OSAS patients by preventing collapse of the airway and improving upper airway patency.

CONCLUSION:

Both Oropharyngeal Exercises and CPAP therapy improves objective and subjective measurements of sleep related parameters on moderate OSAS patients. CPAP machine is not only costlier but also disrupts the sleep of the patient, the reason for the disruption of sleep is mask discomfort and pressure intolerance. And the patient's adherence could be substandard because it's also cumbersome wearing it each time they retire to sleep, especially elderly age group. But Oropharyngeal exercises are totally free of cost & easy for any age group to practice and, it gives much better results as CPAP therapy on moderate OSAS patients if done regularly and for a longer duration.

LIMITATIONS:

The limitations in the present study are, sample size is smaller, oropharngeal exercise was supervised only once in a week when the patients came to the OPD.

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Study on clinico microbiological profile and antibiotic susceptibility pattern of urinary tract pathogens with Special reference to susceptibility of *Escherichia coli* to fosfomycin

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Abstract

Aims: Urinary tract infections (UTI) is the most common infection seeking medical attention. Most of UTI cases were treated empirically with broad-spectrum antibiotics which invariably resulted in development of resistance even to carbapenem. Fosfomycin has broad spectrum of activity which may be useful against these resistant pathogens. Study aims to address microbiological profile, susceptibility pattern of UTI pathogens and fosfomycin susceptibility against all urinary isolates of *Escherichia coli (E.coli)*

Methodology and Results: All urine samples received in our central laboratory over a period of 2 months (May-June 2017) which showed significant growth were included in the study. After getting the written informed consent, data was collected using a questionnaire regarding demographic and clinical details. In vitro susceptibility of fosfomycin carried out for all *E.coli*. Among 1280 samples, only 156 (12.2%) yielded significant growth which emphasises the importance of urine culture for definite diagnosis of UTI. Females and >50 years of both gender showed higher prevalence. Majority of cases from medicine ward (41.7%) and ICU (23.1%) with diabetes (55.1%), catheter (34.6%) was common predisposing factor. *E.coli (63.2%)* was the predominant organism followed by Candida (11.6%) which has become an emerging threat. Higher resistance pattern seen with catheterised group. 40.4% were extended spectrum beta lactamase (ESBL), 12.8% inducible AmpC and 29.8% carbapenamases producers. All *E.coli* isolates including ESBL, carbapenamase producers showed susceptible to fosfomycin.

Conclusions: Study emphasis evidence based practice is the need of hour to combat with raising resistant pattern. Fosfomycin shown promising results to all ESBL and carbapenamase producing *E.coli*.

Keywords: UTI, Microbiological Profile, Clinical Profile, Fosfomycin.

Introduction

Urinary tract infections (UTI) - Microbial invasion of urinary tract is the second most common infection in the community, whereas it is the most common hospital acquired infection, accounting for 35% of all nosocomial infections.[1] About 10% of humans develop UTI in some part of their life.[2] The problem of UTI spans both male and female of all age groups including neonates.[3] Gender, age, malnutrition, low socioeconomic conditions with poor hygiene, structural and functional abnormalities of urinary tract are few of the main predisposing factors causing UTI.[4] *Escherichia coli*, *Klebsiella* spp., *Staphylococcus aureus, Staphylococcus saprophyticus, Proteus* spp., *Pseudomonas* spp., are the most common pathogenic microorganisms isolated in urine.[5]

Most of the UTI cases are treated empirically with broad-spectrum antibiotics over specific antibiotics. Treatment becomes even more challenging in the presence of risk factors such as higher age, comorbidity, and immunosuppression.[6] Extensive and inappropriate use of antimicrobial agents has invariably resulted in the development of antibiotic resistance which has become a major problem worldwide.[7,8] Emergence of drug resistance in uropathogens especially *Escherichia coli*, which is exhibiting high rates of resistance due to the production of extended-spectrum beta-lactamases (ESBLs) and carbapenamases are worrisome which has left us with limited treatment options.[9]

Fosfomycin is a phosphonic acid derivative has a broad spectrum of activity against Gram-positive and Gram-negative bacteria.[10] Only few studies addressed the invitro activity of fosfomyin against multidrug resistance pathogens.[10-12] Various studies done worldwide have shown changing patterns in the etiology of UTIs. The present trends of the uropathogens and their susceptibility to various antibiotics including Fosfomycin in all local geographic areas is essential to formulate guidelines for the empirical treatment of UTIs while awaiting the culture sensitivity.[5,8]

The present study aimed to address the common clinical presentation and risk factors for UTI, distribution of pathogenic strains isolated from UTIs and their resistance pattern against commonly used antibiotics and in vitro susceptibility of Fosfomycin against all urinary isolates of *Escherichia coli.*

Material and Methods

The study was carried out in a tertiary care hospital for a period of 2 months (May -June 2017) after obtained the approval from the Institutional Ethics Committee. Study was supported by Indian council of Medical

Research (ICMR) student project (Reference ID: 2017-07305).

Study included urine samples from all patients received in the central laboratory which showed significant growth in urine culture (>10^5 CFU/ml in a clean catch midstream urine; any colony count for supra pubic catheterization (SPC), Percutaneous Nephrostomy (PCN), Cystoscopic specimens) from suspected UTI patients. Probably significant or insignificant growth and mixture of more than 2 organisms even if it is >10^5 CFU/ml were ignored. After getting the written informed consent from the patients showing significant urinary bacterial growth, data was collected using a questionnaire regarding demographic and clinical details and recorded.

Procedure

Urine was cultured on Cysteine lactose electrolyte deficient media (CLED-Hi media cat no.MP792) for semi quantitative method – For isolation, calibrated 1 µL loop with a diameter of 1.3 mm (Hi media Cat.no:LA023) was used without intermittent heating and incubated at 35–37°C for 24 hours. Diagnosis of UTI was confirmed by means of a significant positive urine culture count of >10^5 colony forming units (CFU) per ml based on Kass concept. Pathogenic organism was further characterised upto species level using various biochemicals wherever applicable.

Antibiotic sensitivity test was done using Kirby Baeur disc diffusion method. Antibiotics were selected according to CLSI 2017 guidelines.[13] The anitbiotic discs selected were Amikacin (30ug), Gentamicin (10ug), Nitrofurantoin (300ug), Ceftriaxone (30ug), Ceftazidime (30ug), Cefepime(30ug), Piperacillin-Tazobactum (100/10ug), Cotrimoxazole (1.25/23.75ug),Ciprofloxacin (5mg), Imipenam (10ug), Vancomycin (30ug) and Teicoplanin (30ug), Penicillin (10U), Ampicllin(10ug), Linezolid(30ug), Colistin MIC E strip. Antibiotic discs and E strips were bought from Hi-Media diagnostic laboratory, Mumbai. In vitro susceptibility of Fosfomycin (200ug) against all urinary isolates of *E.coli* was also carried out by disc diffusion methodbased on CLSI 2017 guidelines.

Screening and confirmation of ESBL, Inducible AmpC and Carbapenamase: The screening for extended spectrum beta lactamase (ESBL) production was done using Ceftazidime (≤22 mm), and Ceftriaxone (≤25 mm). If the organisms showed a zone of inhibition lower than the minimum for the above said antibiotic disc, ESBL positivity was suspected.[14] If blunting was seen with either Ceftazidime, Ceftriaxone or Piperazillin –Tazobactum against Imipenam, inducible AmpC was suspected and it was confirmed by disc antagonism test. Lawn culture of the test strains made in Muller Hinton agar and disc of Cefoxitin was kept in between Ceftazidime and Ceftriaxone with a gap of 15 mm from centre to centre of the disc and incubated at35–37°C for 18-24 hours. If blunting was seen between discs, inducible AmpC positivity was confirmed. Carbapenem resistant was suspected if Imipenam disc showing a zone of ≤23 mm and it was confirmed by disc synergy test. Lawn culture of the test strains made in Muller Hinton agar and disc of Imipenam and Imipenam-EDTA discs were kept with a gap of 20 mm from centre to centre of the disc and incubated at 35–37°C for 18-24 hours. If zone size of Imipenam-EDTA shows >/-7 mm excess zone compared to Imipenam then it was confirmed as metallobetalactamase producers.

Statistical Analysis

The analysis was carried out using the software package SPSS. Age, gender, organisms causing UTI, their antibiotic sensitivity and resistance, symptomatology of these patients and risk factors for UTI were included as variables in the model.

Results

Clinical Findings: Out of 1280 samples received for urine culture with the clinical diagnosis of UTI, 156 (12.2%) samples showed significant growth. Among these, 820 samples were from male patients out of which 85 (10.4%) showed significant growth while in females, out of 460 samples, 71(15.4%) showed significant growth.

Among those 156 samples which showed significant growth, most common presenting age group was >50 years (105/156). **Table 1a &1b** shows gender with age group correlation among the study populations.

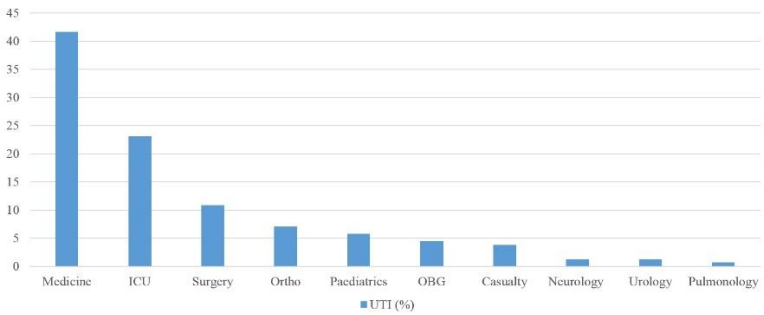

Fig. 1: Ward/Area wise distribution of UTI cases

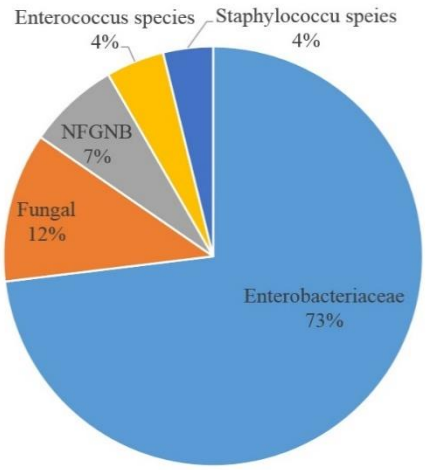

Fig 2: Isolates among the study population

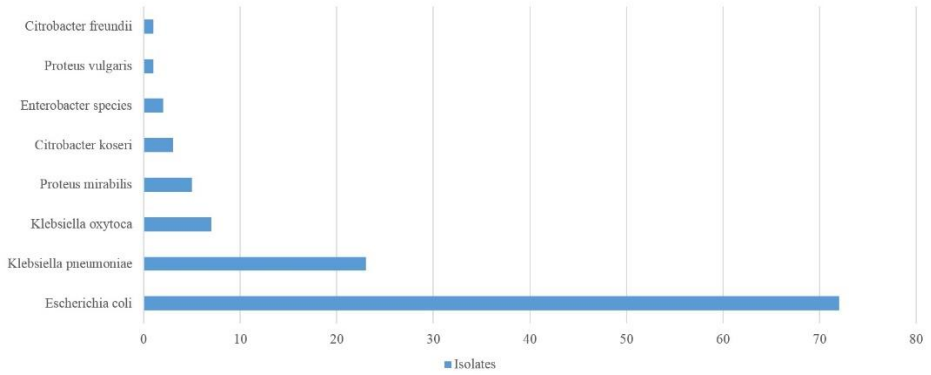

Fig. 3: Isolates among Enterobacteriaceae

UTI was most commonly seen in medicine ward 65(41.7%) followed by ICU 36(23.1%). **Fig. 1** explains the area wise distribution of UTI cases.

Common presenting symptom was fever, burning micturition, decreased urinary output and lower abdominal pain. **Table 2** represents the common presenting symptoms.

Most common presenting symptoms:
Female –Fever with lower abdominal pain-36.6% (26/71 cases)
Male-Fever with burning micturition -44.7% (38/85)
>50 yrs –Burning micturition with decreased urinary output-40% (42/105)
20-50 yrs- Fever with lower abdominal pain -78.8% (26/33)
<20 yrs –Vomiting and increase in frequency – 66.6% (12/18)
Diabetes mellitus-55.1% (86/156 cases) and catheter - 34.6% (54/156 cases) were the common predisposing factors. **(Table 3).**

Organism isolation:

Gram Negative: 125 isolates (80.1%)
Enterobacteriaceae- 114 isolates (73.1%)
Non fermenting Gram negative Bacilli-11 isolates (7%)
Gram Positive: 13 isolates (8.3%)
Enterococcus species-7(4.4%)
Staphylococcus aureus-4(2.6%)
Coagulase negative Staphylococcus-2(1.3%)
Fungal: 18 isolates(11.6%)
Candida species-17(11%)
Trichosporon-1(0.6%)
Figure 2 represents the Pathogenic isolates among the study population and
Figure 3 represents the isolates among Enterobacteriaceae.

Antibiotic susceptibility among the isolates: Among Gram negative isolates Cephalosporin showed 81.6% (93/114) resistant; Fluoroquinolones were the least active drug (98/125=80.7% resistance) against gram negative uropathogens followed by Cotrimoxazole(70/116=60.3% resistant) and Aminoglycosides [(Amikacin 66/125= 52.8%);Gentamicin 71/125=56.8%)]. Nitrofurantoin

showed sensitivity among 79% of our gram negative isolates. Fosfomycin was sensitive among all the isolates of *E.coli*. **Table 4** represents the Gram negative isolates resistant panel.

Among the Gram positive isolates more resistance was seen with Penicillin, Fluoroquinolones(11/13=84.6%) and Aminoglycosides(10/13=76.9%). Nitrofurantoin showed 77% sensitivity. All gram positive isolates were sensitive for Vancomycin, Teicoplanin and Linezolid. **Table 5** represents the Gram positive isolates resistant panel.

40.4 % (46/114) Enterobacteriaceae were ESBL producers; 12.8 % (16/125) were inducible AmpC producers and 29.8 % (34/114) were Carbapenem resistant isolates. **Table 6** represents ESBL, AmpC, CRE among gram negative isolates.

Table 1a: Gender with age group correlation among the study populations

Age (Years)	Male	Female	Total
<1	1	2	3
1-10	5	2	7
11-20	6	2	8
21-30	2	6	8
31-40	4	6	10
41-50	9	6	15
51-60	13	15	28
61-70	31	22	53
71-80	12	8	20
81-90	2	2	4
Total	85	71	156

Table 1b: Statistical analysis- Gender with age group correlation among the study populations

Age (Years)	Male n=85 (%)	Female n=71 (%)	Total n=156 (%)
0-20	12(14.1)	6(8.4)	18(11.5)
21-50	15(17.6)	18(25.4)	33(21.2)
>50	58(68.3)	47(66.2)	105(67.3)

Chi square statistic is 2.1863. p value is0.658915. Result is not significant at p<0.0

Table 2: Common Presenting Symptoms among the study population

Symptoms	Number
Fever	63
Burning Micturition	44
Lower Abdominal Pain	32
Decreased Urinary Output	32
Vomiting	30
Increased Frequency	24
Loin Pain	8
Blood in Urine	3
Pus in urine	2

Table 3: Predisposing factors for UTI among the study population

Predisposing factor	Number
Diabetes alone	40
Catheter alone	26
Diabetes + Catheter	22
Prostatic enlargement alone	24
Diabetes + Prostatic enlargement	20
Calculi alone	1
Calculi + Catheter	1
Calculi + Diabetes	1
Calculi + Diabetes + Catheter	2
Neurogenic bladder alone	2
Neurogenic bladder + Catheter	1
Neurogenic bladder + Catheter+ Calculi	2
Stricture alone	2
Stricture + Diabetes	1
Phimosis	1
Pregnancy	2
No specific factors	6

Table 4: Gram negative isolates resistance panel

Isolate(n=156)	CAZ	CTR	CPM	CIP	COT	AK	G	NIT	PIT	IPM	CL	FO
Enterobacteriaceae												
Escherichia coli(72)	59	60	60	59	38	37	41	5	20	12	0	0
Klebsiella pneumoniae(23)	19	19	19	19	16	15	15	14	14	12	0	
Klebsiella oxytoca(7)	7	7	6	6	6	5	6	3	6	2	0	
Proteus mirabilis(5)	3	5	5	1	2	1	1	-	0	0	-	
Citrobacter koseri(3)	3	3	3	3	3	3	3	3	3	3	0	

Enterobacter species(2)	2	2	2	2	2	2	2	2	2	2	0	
Proteus vulgaris(1)	1	1	1	1	1	1	1	-	0	0	-	
Citrobacter freundii(1)	1	1	1	1	1	0	0	0	1	1	0	
Non Fermenting Gram Negative Bacilli (NFGNB)												
Pseudomonas aeruginosa(9)	4	-	4	2	-	1	1	-	2	2	0	
Acinetobacter Species(2)	2	2	2	2	1	1	1	-	2	2	2	

CAZ-Ceftazidime; CTR-Ceftriaxone; CPM-Cefepime; CIP-Ciprofloxacin; COT-Cotrimoxazole; AK-Amikacin; G-Gentamicin; NIT-Nitrofurantoin; PIT-Piperacillin/Tazobactam; IPM-Imipenem; CL-Colistin; FO-Fosfomycin

Table 5: Gram Positive isolates RESISTANCE panel

Isolate	P	A	CIP	G	DO	COT	NIT	VA	TEI	LZ	CX
Enterococcus faecium(5)	4	4	4	5 (HLG)	2	-	2	0	0	0	-
Enterococcus faecalis (2)	1	1	2	2 (HLG)	1	-	0	0	0	0	-
Staphylococcus aureus(4)	4	-	4	2	2	2	1	0	0	0	3
Coagulase negative Staphylococcus(2)	2	-	1	1	1	1	1	0	0	0	2

P-Penicillin; A-Ampicillin; CIP-Ciprofloxacin; G-Gentamicin; DO-Doxycyclin; COT-Cotrimoxazole; NIT-Nitrofurantoin; VA-Vancomycin; TEI-Teicoplanin; LZ-Linezolid; CX-Cloxacillin

Table 6: ESBL, AmpC, CRE among gram negative isolates

	ESBL producers	Amp C beta lactamases	CRE
Escherichia coli(72)	39	8	12
Klebsiellapneumoniae(23)	5	2	12
Klebsiellaoxytoca(7)	1	1	5
Proteus mirabilis(5)	-	-	-
Citrobacter koseri(3)	-	-	3
Enterobacter species(2)	-	1	1
Proteus vulgaris(1)	1	-	-
Citrobacter freundii(1)	-	-	1
Total	46	12	34

ESBL-Extended Spectrum Beta Lactamases; CRE-Carbapenem Resistant Enterobacteriaceae. AmpC–Inducible AmpC

Discussion

For the appropriate empirical therapy of UTI, knowledge about present trends of the uropathogens and their susceptibility to various antibiotics in a local geographic area is essential as studies have shown that patterns of etiology and their susceptibility of UTI have shown changing trends over different periods of time from different places.[9,15-21] Though bacterial infection of the urinary tract is one of the most common cause for seeking medical attention in developing countries, only 156 of 1280 samples (12.2%) received in our lab with clinically suspected UTI yielded the significant growth. This emphasises the importance of urine culture for a definite diagnosis of UTI which will avoid unnecessary use of antibiotics.

Our findings revealed that female patients showed higher prevalence 15.4 % (71/460) compared to that of male patients 10.4% (85/820) which was in agreement with earlier studies.[19–21,23] Short urethra, close proximity of female urethral meatus to anus have been reported as factors which influence the higher prevalence in women. Age group analysis revealed that >50 years (105/156) was the most common presenting age group in both males 58(68.3%) and females 47(66.2%). Our finding is in concordance with Sood *et al.*,[19] who also reported that elderly patients had high prevalence (41.8%) and in discordance with other studies.[22,24-27] This is probably

because with advancing age, the incidence of UTI increases among males due to prostate enlargement and neurogenic bladder and in females due to urethral stricture and stone.

In our study, majority of cases were from medicine ward (41.7%), ICU (23.1%), and post-operative surgical ward (10.9%) which was similar to the results of Dash *et al*.,[3] who also reported high prevalence of UTI in medicine ward. This may be attributed due to the admission nature of the patients with diabetes and also use of catheter was more common in these premises.

Fever, burning micturition, decreased urinary output and lower abdominal pain were the most common presenting symptoms which is similar to the findings of Little *et al*., Eshwarappa *et al.,* and Sephai *et al*.[28,8,29]

Fever with lower abdominal pain was the common presenting complaints in more than 1/3rd of the female patients. In contrast, fever with burning micturition was the common symptom in half of the male patients. Still predictability of UTI by only these symptoms is to be questioned. None of the symptoms individually were potent enough to pick up most of the UTI. Combination of the symptoms has better predictability of UTI. Our findings indicate that clinical presentation plays a minor role in diagnosing UTI and reemphasizing the fact that urine culture is essential to diagnose UTI.

Our study analysis revealed that diabetes mellitus (55.1%) and catheter (34.6%) were the common predisposing factors which is similar to other studies.[21,22,24,25,27,30] Diabetic nephropathy, reduced immunity contributes to the increased risk for acquiring complicated UTI such as emphysematous pyelonephritis and emphysematous pyelitis among the diabetes patients. Catheter itself is the major predisposing factor for UTI as it favours the infection to spread by biofilm formation on both internal (intraluminal route) and external (periurethral route) catheter surface.

In our study gram negative isolates (80.1%) were the most common followed by fungal isolates (11.6%) which is in concordance with Gupta *et al*.[2] Among the Gram negative isolates the bulk was contributed by Enterobacteriaceae (73.1%) which is the normal inhabitant of large bowel and non-fermenting gram negative bacilli (NFGNB) contributes 7%. *Escherichia coli (63.2%)* was the predominant organism among the Enterobacteriaceae followed by *Klebsiella pneumoniae (20.2%),* this proportion of isolates are similar to the study results of Eshwarappa *et al*., Akram *et al.*, Dash *et al*.[8,9,3]

Among the gram positive isolates, *Enterococcus* species (4%) were the common isolates followed by *Staphylococcus aureus (3%) and* Coagulase negative *Staphylococcus(1.5%).* Prevalence of Gram positive isolates were not high in our study population which is concordance with the findings of Eshwarappa *et al.*,[8] but Coagulase negative *Staphylococcus*(CoNS), previously considered as normal flora, is now a major cause of nosocomial and opportunistic infections which is to be reported cautiously. Both CoNS isolates were associated with catheterised patients.

Among our total 156 isolates 17 were (11.6%) were *Candida* species and one was *Trichosporon*. *Candida* is the third most common isolate in our set up which is in concordance with the findings of Reshmi C Choudhury *et al*[30] who also reported the higher prevalence of Candiduria (12.3%) and in discordance with Yashavanth R.*et al*., and Rahul Kumar Goyal *et al*.,[31,32] who reported the lower prevalence of candiduria 2.27% and 2.36% respectively. All these patients were from ICUs. All the patients with these isolates had both diabetes and catheter as predisposing factors. Candiduria is an emerging threat which was previously assumed as non-pathogenic, now has acquired a greater clinical role in today's scenario of increasing risk factors like diabetes & catheter, emerging drug resistance and immunocompromised state. Caution has to be taken in reporting candida from urine and it should not be ignored because of risk of candidemia as 31.2% (5/16 cases) of our cases presented with candidemia.

Antibiotic susceptibility pattern in our study is similar to other studies.[23,27] Apart from beta lactum group, Fluoroquinolones were the least active drug (98/125=80.7% resistance) against gram negative uropathogens followed by cotrimoxazole (70/116=60.3% resistant) and aminoglycosides [(Amikacin 66/125= 52.8%); Gentamicin 71/125=56.8%)]. Increasing resistance rate necessitates a regular monitoring for drug resistance in local geographic areas to change the empirical therapy as per the susceptibility pattern. Nitrofurantoin showed some promising results as 79% of our gram negative isolates were sensitive. Colistin was 100% sensitive among the gram negative isolates. Among the gram positive isolates other than beat lactum group more resistance was seen with Fluoroquinolones (11/16=84.6%) and aminoglycosides (10/13=76.9%). Here also Nitrofurantoin showed some promising results as 77% of our gram positive isolates were sensitive. All gram positive isolates were sensitive for Vancomycin, Teicoplanin and Linezolid.

In our study, 40.4 % (46/114) Enterobacteriaceae *were ESBL* producers and among *Escherichia coli* (39/72) 54.2% were ESBL which is similar to the study results of Eshwarappa *et al*.,[8] where 52.2% of the isolates were ESBL-positive. Previous studies in India have reported an ESBL positivity rate between 26.9% and 48.3%.[16,23,26,28,30-32] ESBL producers do not respond to the usually prescribed empirical therapy of cephalosporins which will ultimately lead to increased risk of associated morbidity and mortality, and cost of therapy. Presently, alternative antimicrobial therapy to treat ESBL-positive UTI on outpatient basis is limited. Beta lactam with inhibitor combinations and Carbapenems are the most effective in this situation but need to be administered intravenously or -

intramuscularly. Nitrofurantoin and Fosfomycin which can be given orally were active invitro against 90% and 100% of the above mentioned ESBL isolates.

In our study 12.8 % (16/125) were inducible AmpC producers.These isolates do not respond to Beta lactum with inhibitor combinations. Carbapenems are the most effective in this situation. Fosfomycin among these resistant isolates also showed 100% sensitivity invitro against *E.coli* and 87.5% of Nitrofurantoin showed sensitivity against these inducible AmpC producers.

In our study 29.8 % (34/114) were carbapenem resistant isolates. Among these 52.2% *(12/23)* of *Klebsiella pneumoniae* and 71.4%(5/7) of *Klebsiella oxytoca* were carbapenem resistant and16.7% (12/72) of *E.coli* showed carbapenem resistance. The situation is worsening everyday as no new antibiotics against these multidrug-resistant organisms are in advanced stages of clinical development. Even Nitrofurantion showed only 11.8% (4/34) sensitive against these carbapenem resistant isolates. Fosfomycin showed promising invitro results against the CRE of *E.coli*.

In our study, all the *E. coli* tested isolates including ESBL producers, Carbapenamase producers were susceptible to fosfomycin invitro. Our study reveals some evidence that fosfomycin might be a promising solution for the treatment of such multi drug resistant infections.

The prevalence of infection by these organisms in our study is comparable to those of other studies from India as well as other countries.[23,27] The uropathogens identified in our study are similar to those of many other studies conducted in different countries, however different from some study results.[21,24] The similarities and differences in the type and distribution of uropathogens may result from different environmental conditions and host factors, and practices such as healthcare and education programmes, socioeconomic standards and hygiene practices in each country. Though diabetes was the most predominant predisposing factor, no difference was found among the uropathogenic profile or the antibiotic sensitivity pattern between diabetic and non-diabetic.But the second common predisposing factor (catheterised patients) had higher resistance pattern overall compared to other groups.

Conclusion

UTI was most common amongfemale patients and >50 years of both sex in our population too.

Medicine ward and ICUs had most number of cases due to the admission nature of the patients with diabetes and catheter which is also reported as an importance predisposing factor in our study. Though combination of the symptoms had somewhat better predictability of UTI, culture remains the gold standard. *Escherichia coli* was the predominant isolate followed by *Candida* species which emphasis that Candiduria is an emerging threat; similarly Coagulase negative *Staphylococcus*, previously considered as normal flora, is now a major cause of UTI in catheterised patients. No difference was found among the uropathogenic profile or the antibiotic sensitivity pattern between diabetics and non-diabetics. But catheterised patients had the higher resistance pattern overall compared to other groups. Increasing resistance of ESBL, Inducible AmpC and Carbapenamases is worrisome. In our study, all the *E. coli* tested isolates including ESBL producers, Carbapenamase producers were susceptible to fosfomycin invitro. Our study reveals some evidence that fosfomycin might be a promising solution for the treatment of such infections.

Limitations

Fosfomycin was tested only against *E.coli* isolates as disc diffusion guidelines was only available for *E.coli* as per CLSI. Due to non-affordability, MIC of fosfomycin for other isolates were not carried out. In vivo analysis of fosfomycin use for both complicated and uncomplicated UTI is at present the need of the hour as we are left with only few drugs against CRE isolates.

Implications

Only12.2% of the samples with clinically suspected UTI yielded the significant growth that emphasises that urine culture is essential to avoid unnecessary use of antibiotics. So evidence based practice is always essential.

All the *E. coli* tested isolates including ESBL producers, Carbapenamase producers were susceptible to fosfomycin invitro. Our study reveals some evidence that fosfomycin might be a promising solution for the treatment of such infections.

As nearly half of the isolates had ESBL, we have formulated the ideal choice for empirical therapy as beta lactum with inhibitor combinations like Cefaperazone - Sulbactum for complicated UTI in our set up.

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STUDY ON PREVALENCE OF METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS; COMPARISON OF FOUR DIAGNOSTIC METHODS FOR DETECTING MRSA– FROM A TERTIARY CARE HOSPITAL, MADURAI

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ABSTRACT

BACKGROUND

Prevalence of Methicillin-Resistant *Staphylococcus aureus* (MRSA) in India ranges from 30 to 70% which leads to high mortality, increased economic burden and high treatment failure when compared to MSSA. Rapid and accurate detection of MRSA is essential to take measures for infection control and also to prevent unnecessary use of antibiotics.

MATERIALS AND METHODS

Prospective observational study was carried out in our tertiary care hospital over a period of 6 months (May-October 2017). All *Staphylococcus* grown among 240 various clinical samples received were tested for MRSA by four phenotypic methods - cefoxitin and oxacillin disc diffusion test and MIC oxacillin E test and oxacillin resistant screen agar test (ORSA) with mecA-PCR as gold standard.

RESULTS

A total of 103 out of 200 (51.5%) bacterial isolates were *Staphylococcus aureus*. Pus from diabetic wound yielded high number of growth (42%) followed by blood (36%) which is alarming note. 55.4% were identified as MRSAs by PCR; most common presenting group was >50 years (36.8%) followed by infants (28%). Cefoxitin disc method has the highest sensitivity and specificity of 98.2% & 100% followed by E test (94.2% & 95.8%) and ORSA (87.5% & 94.2%). Oxacillin disc diffusion method had the least 79.5% & 92.9%. Most MRSA isolates were multi drug resistant.

CONCLUSION

Cefoxitin disc diffusion when combined with Oxacillin agar or E test will be helpful to detect all MRSA strains including hyper production of betalactamases. As these phenotypic assays are simple and relatively cheap, this can be used as an alternative to PCR in resource constraint settings.

KEYWORDS

MRSA; Prevalence; mecA Gene; Cefoxitin Disc; Phenotypic Tests.

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BACKGROUND

Methicillin-Resistant *Staphylococcus aureus* (MRSA) is an important cause of nosocomial and community associated infections throughout the world.(1) First MRSA was described among nosocomial isolates of Staphylococcus aureus in 1961, England which subsequently spread throughout the world.(2) In India the prevalence of MRSA ranges from 30 to 70% which leads to high mortality, increase economic burden.(3,4)

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MRSA treatment will be more problematic as these strains often show resistance to wide range of antibiotics compared to methicillin susceptible isolates.(3) Therefore, rapid and accurate detection of MRSA is very essential in order to choose appropriate therapy, to take necessary measures for infection control and also to prevent unnecessary use of glycol-peptides antibiotics.

MRSA strains harbour the mecA gene, which encodes a penicillin binding protein (PBP2a) with low affinity for all ß-lactam antibiotics including methicillin which has limited therapeutic option.(5) Hence methods used to identify MRSA from clinical samples should have high sensitivity and specificity and most importantly the result should be available within a short time. Different phenotypic methods such as oxacillin and cefoxitin disc diffusion test, oxacillin agar screening test, and determination of minimum inhibitory concentration (MIC) for oxacillin and cefoxitin are available in clinical laboratories.(6–9) Phenotypic expression is affected by various conditions such as temperature,

osmolarity of the medium and inoculum size that may affect the accuracy of the methods used to detect methicillin resistance.[9,10] Some strains of *S.aureus* hyper produce beta lactamase known as Borderline Oxacillin Resistant *S. aureus* (BORSA) will be oxacillin resistant, do not possess the usual genetic mechanism for MRSA resistance.[8]

Even though genotypic method which detects the mecA gene to identify MRSA among the *S.aureus* isolates is considered to be the gold standard test for detecting MRSA,[6,7,10] it could not be adopted as a routine method of screening MRSA in small laboratories since it requires costlier and sophisticated equipment. Hence the easily available, non- expensive phenotypic methods are the one needed to identify the MRSA isolates for many labs.

Our study is planned to know the prevalence of MRSA among different clinical samples received in laboratory with the aim to compare the PCR of the mecA gene with four phenotypic methods - cefoxitin disc diffusion test, oxacillin disc diffusion test and MIC of oxacillin by E test and screen agar test for detection of MRSA.

MATERIALS AND METHODS

Prospective observational study was carried out in Velammal Medical College Hospital and Research Institute, Madurai, Tamilnadu over a period of 6 months (May -October 2017).

A total of 240 samples received in the lab during the study period were tested for *Staphylococcus aureus* from various clinical samples like blood, pus, urine, sputum and throat swab. Isolates were identified as *S. aureus* by their colony morphology, gram staining, catalase and coagulase tests (both tube and slide coagulase tests).

All the *Staphylococcal* isolates were tested for antibiotic susceptibility by the Kirby-Bauer disc diffusion method. Following antibiotics were selected based on clinical and laboratory standards Institute (CLSI) guideline: Penicillin (10 u), Erythromycin (15 µg), Clindamycin (2 µg), Ciprofloxacin (5 µg), Cotrimoxazole (1.25/23.75 ug), Amikacin (30 µg), Oxacillin (1 µg), Cefoxitin (30 µg) and Linezolid (30 µg), Vancomycin E strip. Antibiotic discs and E strips were bought from Hi-Media diagnostic laboratory, Mumbai.[11]

Study Design

Phenotype Identification of MRSA:

Phenotypic methods for detection of MRSA strains were carried out according to CLSI guideline as follows:

Cefoxitin Disc Diffusion Test

Cefoxitin (30 µg) disc diffusion method was carried out on Mueller-Hinton agar (MHA) by using a 30 µg cefoxitin disc. The standardised inoculum was streaked on MHA and incubated at 37° C for 24 hrs. An inhibition zone diameter of ≤ 21 mm was reported as methicillin resistant and a diameter of ≥ 22 mm was considered as methicillin sensitive

Oxacillin Disc Diffusion Test

Oxacillin (1 µg) disc diffusion method was carried out on Mueller-Hinton agar supplemented with 4% NaCl. Plates were incubated at 35° C for 24 hrs. The isolates were considered as resistant when the diameter of inhibition zone of oxacillin was ≤10 mm, as intermediate when the diameter was 11-12 mm and as sensitive when the diameter was ≥13 mm.

Oxacillin E Strip Test

In Muller-Hinton agar plates supplemented with 4% NaCl, the test strain was lawn cultured, oxacillin E strip was placed on the medium and incubated for 24 h at 35° C. After incubation, inhibitory concentration studied as zone of inhibition intersected the strip in the form of ellipse and interpreted according to the CLSI criteria. MIC of ≤2µg/ml was considered as sensitive; ≥4µg/ml was considered as resistant.

Oxacillin Resistant Screen Agar Test (ORSA)

Muller-Hinton agar plates containing 4% NaCl, 6 µg/ml of oxacillin and chromogenic component aniline dye were prepared. Agar base were obtained from Himedia, Mumbai. Aloopful of 0.5 McFarland's suspension of the isolate was inoculated as a spot on the agar surface and it was incubated at 35° C for 24 h. The plates were observed for colour change from original grey to blue to identify as MRSA.

Genotype Identification of MRSA by PCR

Genotypic identification of mecA gene was carried out by conventional Polymerase Chain Reaction (PCR) using thermocycler in Helini Biomolecules, Chennai. DNA was extracted by the rapid cell lysis method using Helini extraction kit- 1.5 mL of an overnight culture of bacteria grown in Mueller-Hinton broth was harvested by centrifuging in a micro centrifuge tube at 10, 000 rpm for 5 mins. 400 µL of lysis buffer with 40 µL of proteinase K was added to the pellet and incubated at 70°C for 10 minutes. After adding 100 µL of isopropanol, the entire sample was pipetted into pure fast spin column and centrifuged for 1 min. Flow through was discarded and spin column washed with 500 µL wash buffer 1 & 2 and then 100 µL of pre-warmed buffer EB added and incubated for 2 mins. After the final centrifugation extracted bacterial DNA was collected for PCR assay.

PCR for mecA gene was performed using the following primers- Forward (5´ GCA ATC GCT AAA GAA CTA AG 3´) and Reverse (5´GGG ACC AAC ATA ACC TAA 3´) primers in the thermocycler (Eppendorf Master Cycler Gradient thermocycler, Germany) with a final reaction mixture volume of 50µl.Cycling conditions were 94^0 C-3 mins of initial denaturation followed by 30 cycles of Denaturation at 94^0 C–1 min, Annealing at 60^0 C- 1 min, Extension at 72^0 C– 1 min and a final extension of 72^0 C– 5mins. The amplicon for mecA gene was detected by the band at 220 bp on an agarose gel (2%) with ethidium bromide by electrophoresis.

Statistical Analysis

Data analysis was done using SPSS 16 version. Comparison of all phenotypic methods were carried out taking mecA PCR as a gold standard technique, sensitivity and specificity were expressed as percentage using Chi square test. Prevalence, Age, sex and risk factors analysis were expressed as percentage.

RESULTS

Among the 240 samples received during the study period, 200 samples showed growth. Total of 240 isolates were detected from those 200 samples. A total of 103 samples out of 200 (51.5%) yielded the growth of *Staphylococcus aureus* during the study period. Pus sample (40/103= 38.8%) followed by blood sample (37/103=35.9%) yielded the highest number of *S.aureus* growth (Figure 1).

Out of 103 *S.aureus* isolates 57(55.4%) were Methicillin Resistant *S.aureus* (MRSA) and 46 (44.6%) were Methicillin Sensitive *S.aureus* (MSSA) as detected by taking PCR as a gold standard technique. Sample wise analysis of MRSA showed that 29 out of 40 (72.5%) S.aureus strains isolated from pus followed by 19 out of 37(51.4%) from blood were MRSA (Table 1).

Age wise distribution analysis revealed that MRSA were most common among the older age group (21/57= 36.8%) followed by infants (28%) (Figure 2).

Among the 57 MRSA isolates 16(28.06%) were associated with risk factors. Analysis of risk factors revealed that 10 patients (17.54%) of MRSA wound infection had diabetes; 3 patients (5.26%) had chronic liver disease and 2 patients (3.5%) had a history of intermittent catheterisation; 1 patient (1.75%) had a history of prolonged self-medication with Quinolone antibiotic.

All the 103 *S.aureus* isolates were subjected to PCR to identify mecA gene. Among these 57 (55.4%) were identified as MRSA by PCR.

All the 103 *S.aureus* isolates were also subjected to methicillin susceptibility testing by disc diffusion method by using 30 µg Cefoxitin and 1 µg Oxacillin discs, E-Test (oxacillin), Oxacillin Resistant Screen Agar. Cefoxitin disc diffusion method identified 56 (54.4%) isolates of *S.aureus* as MRSA followed by Oxacillin E-Test identified 54 (52.4%) S.aureus strains as MRSA (Table 2).

Comparison of all phenotypic methods were carried out taking PCR as a gold standard technique. Among the 57 PCR positive MRSA strains, Cefoxitin disc identified one isolate as negative (false negative) (Table 3).

Cefoxitin disc method has the highest sensitivity (98.2%) and specificity (100%) and the PPV and NPV are 98.24% and 100% respectively (Table 4).

Most of our MRSA isolates were multi drug resistant (MDR) as 91% resistant to fluoroquinolones, 88% resistant to aminoglycosides, 83% cotrimoxazole (Table 5).

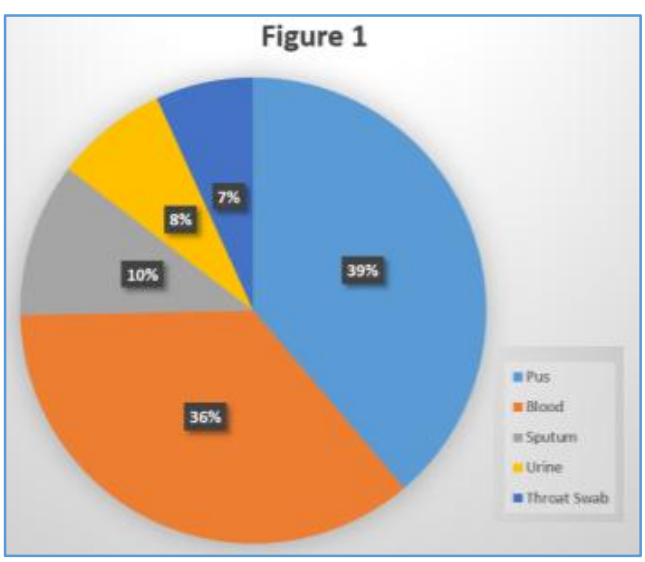

Figure 1. Staphylococcus aureus isolates among various clinical samples

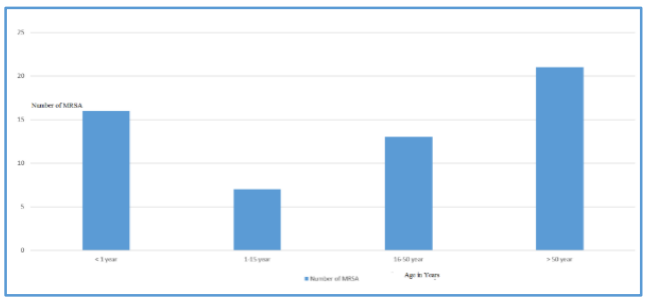

Figure 2. Staphylococcus aureus isolates among various age groups

Specimen	*S.aureus*	MRSA	Percentage
Pus	40	29	72.5%
Blood	37	19	51.4%
Sputum	11	4	36.4%
Throat swab	8	2	25%
Urine	7	3	42.91%
Total	**103**	**57**	**55.3%**

Table 1. Sample wise distribution of Methicillin Resistant Staphylococcus aureus (MRSA)

Test (n=103)	MRSA	MSSA
PCR (mecA gene)	57 (55.4%)	46 (44.6%)
Cefoxitin Disc	56 (54.36%)	47 (45.63%)
E-Test	54 (52.42%)	49 (47.57%)
ORSA	51 (49.51%)	52 (50.48%)
Oxacillin Disc	48 (46.6%)	55 (53.39%)

Table 2. Detection of Methicillin Resistant Staphylococcus aureus (MRSA) by various phenotypic and genotypic method

Methods	True Positives	False Negatives	False Positives
PCR	57	-	-
Cefoxitin disc	55	1	-
E-Test	49	3	2
ORSA	42	6	3
Oxacillin disc	35	9	4

Table 3. Comparison of PCR for mecA gene with phenotypic methods

TEST	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Cefoxitin disc	98.2%	100%	98.24%	100%
E-Test	94.2%	95.8%	96.42%	94.23%
ORSA	87.5%	94.2%	92.44%	90.22%
Oxacillin disc	79.5%	92.9%	88.30%	82.93%

Table 4. Sensitivity and Specificity of various phenotypic tests

	P	CD	E	CIP	AK	COT	VA	LZ
MRSA N=57	57 (100%)	32 (56.1%)	37 (64.9%)	52 (91.2%)	50 (87.7%)	47 (82.5%)	0 -	0 -

Table 5. Other antibiotic resistance pattern of MRSA isolates

P-Penicillin (10 u), CD- Clindamycin (2 µg), E-Erythromycin (15 µg), CIP-Ciprofloxacin (5 µg), AK- Amikacin (30 µg), COT- Cotrimoxazole (1.25/23.75 ug), VA-Vancomycin E strip, LZ-Linezolid (30 µg).

DISCUSSION

For the past 50 years, MRSA is probably the most challenging bacterial pathogen causing significant morbidity and mortality that affect patients in hospital as well as in the community.[12] Methicillin-resistant strains in all over the world have been posing a great difficulty in selecting anti-microbial agents for the management of the infections that leads to treatment failure. Hence, an accurate and rapid detection of methicillin resistance in *Staphylococci* is therefore important, not only for choosing the appropriate antibiotic therapy, but also to control of the endemicity of the MRSA.[2,3]

In our study, 51.5 % (103/200) of the isolates were *Staphylococcus aureus* which was isolated as the prime organism in all infections except urinary tract infection. Occurrence of *S.aureus* as the prime organism may be due to the presence of a number of enzymes and toxins produced by S.aureus which may inhibit the phagocytic and opsonic mechanisms.[1,12] Less frequent occurrence of *S.aureus* in UTI may be due to genotypic factors of *S.aureus* which may affect the uroepithelial susceptibility to the adherence molecules.[13]

Our study revealed *S.aureus* was the common isolate from pus samples from localised diabetic wound lesions(39%) which was in concordance with the findings of dechen C Tseringet al.,[14] who also reported 42% of isolation from pus samples. Localisation of pus is mainly due to the unique presence of coagulase in *S.aureus* which has the capacity of forming a wall of fibrin clot around the lesion. The challenging thing is nearly 36% of *S.aureus* was isolated from blood which was even higher than the other studies.[15,16] Bacteraemia due to *S.aureus* has increased dramatically in recent years which may end up in life-threatening complications like infective endocarditis and metastatic infections. This is driving as urgent need for improved strategies to prevent these infections.

In our study 55.4% were MRSAs which was much higher than other studies,[3,17,18] which indicates MRSA is steadily increasing which may be due to the adverse use of antibiotics or poor infection control practices in the environment. Among MRSA, 28.15% were isolated from pus samples of diabetic wound infection which is in concordance with finding of sgangaet al.,[19] reported 30% of MRSA. The increased incidence of MRSA in wound infection may be due to the production on Panton Valentine Leucocidin by MRSA which is shown too associated with tissue necrosis.

Age wise analysis revealed MRSA was commonly present in the extremes of age which is similar to the other study results.[20,21] Higher incidence in older age group may be due to immunosuppression caused by various factors like diabetes mellitus, chronic hepatitis, anaemia and non-adherence to antibiotic course and infants there may be poor development of immune system which may associated with acquired chemotactic or opsonic defects

Early and accurate determination of Methicillin resistance is of key importance in the prognosis of infections caused by *S.aureus*. Although many phenotypic methods of detection of this resistance have been developed they often show insufficient sensitivity and specificity to ensure appropriate treatment of the MRSA infected patients.[1,8,13] The sensitivity and specificity of these methods vary depending on the patients carrying them, environmental factors, and the techniques used.

Our study revealed disc diffusion using cefoxitin disc showed higher sensitivity (98.2%) and specificity (100%) which is almost similar to the study results of Pourmand et al.,[9] who also documented 99.1% sensitivity and 98.1% specificity by cefoxitin disc method. Even Swenson et al., Jain et al.,[22,23] showed 100% specificity and sensitivity with cefoxitin disc methods. Our findings also emphasis that cefoxitin disc method is close enough to PCR in identifying MRSA.

Oxacillin disc diffusion method had the least sensitivity (79.5%) and specificity (92.9%) followed by ORSA 87.5% sensitivity and 94.2% specificity. E test had better sensitivity and specificity (94.2% & 95.8%) when compare to ORSA and oxacillin disc but inferior to cefoxitin disc diffusion test. This may be due to the fact that detection of MRSA by Cefoxitin based methods will not be affected by temperature variations between 35^0 C and 37^0 C but Oxacillin method will be affected by temperature variations especially if it is increased above 35^0 C and also medium supplementations. Similar factors decrease the sensitivity and specificity of ORSA and E-Test.[24]

False positivity (resistant to oxacillin but sensitive to cefoxitin and negative for mecA gene) in ORSA methods and E-Test is due to the hyper production of betalactamase which may lead to phenotypic expression of oxacillin resistance do not possess the usual genetic mechanism for such resistance. Probably these strains under antibiotic pressure may evolve into fully resistant isolates subsequently.[25]

One more problematic fact is most of the MRSA isolates were multi drug resistant (MDR). Isolates have shown 91% resistant to fluoroquinolones, 88% resistant to aminoglycosides, 83% cotrimoxazole and more than 50 % to macrolides. This is an alarming note as only few therapeutic opinions available. So early diagnosis is will be helpful to avoid the unnecessary use of antibiotics.

CONCLUSION

Our study findings reveal that oxacillin disk diffusion method was found to be less sensitive for the detection of MRSA. Cefoxitin disc diffusion followed be Oxacillin E strip was in concordance with the results of PCR for mecA gene. As cefoxitin method is easy to perform, does not require special technique, media preparation, incubation temperature and more cost effective in comparison to other methods this can be used as an alternative to PCR for the detection of MRSA in resource constraint settings. Cefoxitin when combined with Oxacillin agar or E test will be helpful to determine the all MRSA strains including hyper production of betalactamase.

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Microbiological profile, comorbidity, incidence and rate analysis of catheter associated urinary tract infections in adult intensive care unit

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Abstract

Introduction: Catheter-associated urinary tract infections (CAUTI) being the commonest hospital-acquired infection (HAI) [40%], its burden, aetiology along with antibiotic susceptibility is essential to implement and monitor an effective infection control program.

Aims: To assess the incidence and rate of CAUTI in a tertiary care hospital and to identify the common organisms and their antibiotic sensitivity pattern.

Settings and Design: Prospective hospital based observational study was carried out in a tertiary care hospital in South Tamilnadu for a period of 2 months (June 2016 to July 2016) after obtaining the Institutional Ethics committee approval.

Materials and Methods: Total of 100 catheterized adult ICU patients were observed for signs of UTI on a daily basis. On clinical suspicion of UTI, urine sample was analysed microbiologically. CAUTI among various gender and age groups; pathogenic isolates, antibiotic sensitivity pattern and associated co-morbid conditions were expressed as percentages

Results: Incidence of CAUTI was 16/100 catheterization. Device utilization ratio was 0.72. CAUTI rate was 36.2/1000 catheter days. CAUTI was commonly seen among patients with >80 years, females with altered sensorium. Diabetes mellitus (35.7%) was the most common comorbid condition followed by TB (25%). Risk of CAUTI after 3-5 days of catheterization was 11.7% and proportionately increased with prolonged catheterization (100% if >20 days). *Escherichia coli* (37.5%) followed by *Candida Spp.* (25%) were common pathogens among 3-5days of catheterization. *Pseudomonas Spp.* was the commonest isolate after one week of catheterization. Imipenem, colistin resistance was highest among pseudomonas.

Conclusions: CAUTI rate was higher than the benchmark set by NHSN (0-4). Appropriate health education, strict infection control practices, appropriate antibiotic policy, proper guided bundle care of catheter are need of the hour to prevent the CAUTI.

Keywords: Adult ICU, CAUTI, Comorbidity analysis, Incidence, Microbiological Profile.

Key Messages: Incidence of CAUTI was 16 per 100 catheterization and the CAUTI rate was 36.2 per 1000 catheter days which was higher to the benchmark of NHSN (0-4). Risk of CAUTI proportionately increased with prolonged catheterization from 11.7% after 3-5 days to 100% after 20 days. *Escherichia coli* (37.5%) followed by *Candida* (25%) were common pathogens among 3-5days of catheterization. *Pseudomonas* was the common isolate after one week of catheterization.

Introduction

Hospital-acquired infections (HAI) are the leading cause of morbidity and mortality in healthcare settings globally, especially in intensive care units (ICUs).[1,2] HAIs also increase the economic burden on the patients in the form of prolonged hospital stay, lost work-days, laboratory and drug costs.[3]

Urinary tract infections (UTI) is the second commonest infection in the community, whereas it is the most common HAI, accounting for 40% of all HAIs.[4] Though, many predisposing factors like gender, age, malnutrition, low socioeconomic conditions with poor hygiene, structural and functional abnormalities of urinary tract are reported as risk factors for developing UTI; the indwelling catheter which is an essential part of modern medical care; inserted to monitor various clinical parameters, itself is the major risk factor for hospital-acquired UTI.[6] Approximately 25% of hospitalized patients and 70% critically ill ICU patients undergo urinary catheterization.[7]

CAUTI (CDC National Healthcare Safety Network (NHSN)) is defined as UTI where an indwelling urinary catheter was in place for more than two calendar days on the date of event, with day of device placement being Day one, and an indwelling urinary catheter was in place on the date of event or the day before. If an indwelling urinary catheter was in place for more than two calendar days and then removed, the date of the event for the CAUTI must be the day of discontinuation or the next day with culture positivity.[8] Each day when the indwelling urinary catheter remains, a patient has 3%-10% increased the risk of acquiring CAUTI and incidence of bacteriuria with catheter reaches nearly 100% in four weeks duration.[9]

Microbiological profile and antimicrobial sensitivity pattern of CAUTI vary considerably between regions and time to time.[10] Nearly 30-40% of the gram-negative septicemia acquired in the hospital originates in the urinary tract. Inappropriate and recurrent use of antibiotics to treat CAUTI can lead to antimicrobial resistance.[11] Multiple risk factors like quality of aseptic technique, duration of catheterization, hand hygiene and care of catheter can affect the occurrence of CAUTI. Also, HAI directly reflects on the quality care of the

healthcare setting; so knowledge about the rates of HAI and organism associated with their antibiotic susceptibility is essential to implement the infection control system in a proper manner.[12,13] The present study was aimed to assess the incidence and rate of CAUTI in a tertiary care hospital and to identify the common causative organisms and their antibiotic sensitivity pattern.

Materials and Methods

The prospective hospital-based observational study was carried out in a tertiary care multispeciality hospital in South, Tamilnadu for a period of 2 months (June 2016 to July 2016) after obtaining the Institutional Ethics committee approval.

A total of 100 adult patients including both genders with indwelling urinary Foley's catheter admitted in ICUs during the study period were included in the study. Catheterized ICU patients transferred to general ward were also followed up by two calendar days following the transfer (1st day being the day of transfer). Patients only on condom catheter or on nephrostomy tube/ suprapubic catheters were excluded from the study.

Urinary catheter insertion, maintenance, and removal were done based on standard guidelines. During the study period, catheterized study participants were observed for local and systemic signs of UTI, meticulously on daily basis. On clinical suspicion of UTI, a urine sample was collected by disinfecting a portion of the catheter tubing with alcohol & aspirating the urine aseptically by puncturing the tubing with a sterile syringe and sent to the microbiology laboratory for Culture and Sensitivity test immediately.

Sample Processing: The urine was cultured in Nutrient agar and MacConkey agar by a Semi uantitative method –calibrated 1 µL loop with a diameter of 1.3 mm (Himedia Cat.no:LA023) without intermittent flaming and incubated at 35–37°C for 24 h. The diagnosis of UTI was made by means of a significant positive urine culture count of $>10^5$ colony forming units (CFU) per ml. The pathogenic organism was further characterized to species level using appropriate biochemicals tests.

Antibiotic sensitivity test was done using Kirby Bauer disc diffusion method as per CLSI guidelines. Antibiotic discs were bought from Hi-Media laboratories, Mumbai.

Statistical Analysis

Incidence rate, Device utilization rate and CAUTI rate were calculated using the formula

1. Incidence Rate = (No. of CAUTI) x 100 /(No. of catheterized patients)
2. Device Utilization Rate = No. of indwelling catheter days/No. of patient days
3. CAUTI Rate = (No. of CAUTI) x 1000 /(No. of indwelling catheter days)

CAUTI among various gender and age; pathogenic isolates, antibiotic sensitivity pattern and associated comorbid conditions were expressed as percentage.

Results

Among the total 100 catheterized adult ICU patients, 66% were males and 34% were females. Catheterization was highest among 41-60 age group (51%). The incidence of CAUTI was 16% (16/100). A total number of patient days was 607; Number of indwelling catheter days was 441; Device utilization ratio was 0.72. CAUTI rate was 36.2 per 1000 catheter days.

The incidence of CAUTI was highest among the elderly (>80 years) individuals (50%) (Table 1). The difference in CAUTI incidence among females (17.6%, 6/34) and males (15.1%, 10/66) was statistically not significant. The incidence of CAUTI was higher in head injury patients with altered sensorium who were admitted in neuro ICU (42.8%) compared to the patients with other system involvements (Table 2). The commonest comorbid condition associated with CAUTI was diabetes mellitus (35.7%) followed by tuberculosis (25%) (Fig. 1). All the patients catheterized for more than 20 days had developed CAUTI (Table 3).

Common uropathogenic isolated was *Escherichia coli* (37.5%) followed by *Candida spp* (25%) (Fig. 2). All the *Escherichia coli* isolates were sensitive to Amikacin, Netilmicin, Colistin and Tigecycline. Most (66.7%) of the *Pseudomonas aeruginosa* isolates were sensitive to Colistin. Thus most of the Gram negative bacilli isolated from CAUTI were sensitive to Colistin, Amikacin and Tigecycline (Table 4).

Table 1: Incidence of CAUTI with age

Age group (Years)	No. of patients enrolled	No. of CAUTI cases	Percentage
15-20	2	0	0%
21-40	18	4	22.2%
41-60	51	8	15.6%
61-80	25	2	8%
>80	4	2	50%

Table 2: Incidence of CAUTI with respect to system involved in the primary disease/condition of patients

System involved in the primary disease	No. of patients enrolled	No. of CAUTI cases	Percentage
CNS	21	9	42.8%
RS	7	1	14.3%
CVS	6	0	0%
GIT	9	0	0%
Renal	19	4	21.1%
Metabolic	7	0	0%
Musculoskeletal	4	0	0%
Post Operative	25	2	8%
Poison	2	0	0%
CNS- Cardiovascular system, RS – Respiratory system, CVS – Cardiovascular system, GIT – Gastrointestinal system			

Table 3: Interval between catheterization and Appearance of features of UTI

Catheter days	No. of patients enrolled	No. of CAUTI cases	Percentage
1-2	35	0	0%
3-5	51	6	11.7%
6-10	5	3	60%
10-15	3	2	66.6%
15-20	3	2	66.6%
>20	3	3	100%

Table 4: Antibiotic Sensitivity Pattern (%)

Uropathogen (No.)	Escherichia coli (6)	Klebsiella pneumoniae (3)	Enterobacter spp (1)	Pseudomonas aeruginosa (2)
CTR	16.6	0	0	-
CPM	33.2	0	0	0
PIT	66.4	33.3	0	0
AK	100	33.3	100	50
GEN	66.4	33.3	0	50
CIP	16.6	0	0	0
NET	100	33.3	100	0
IMP	82.6	33.3	100	0
CO	66.4	0	0	-
CL	100	100	100	50
LE	16.6	0	0	-
TGC	100	100	-	-
NIT	82.6	66.6	0	-
OF	16.6	0	100	0
DOX	33.2	0	100	-
CAZ	16.6	0	0	0
CTR- Ceftriaxone; CPM- Cefepime; PIT- Piperacillin-Tazobactum; AK- Amikacin; GEN- Gentamicin; CIP- Ciprofloxacin; NET- Netilmicin; IMP- Imipenam; CO- Cotrimoxazole; CL- Colistin; LE- Levofloxacin; TGC- Tigecycline; NIT- Nitrofurantoin; OF- Ofloxacin; DOX- Doxycycline ; CAZ- Ceftazidime.				

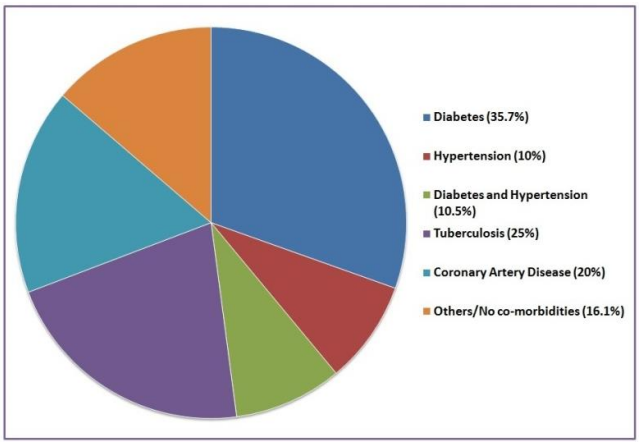

Fig. 1: Comorbid conditions associated with CAUTI

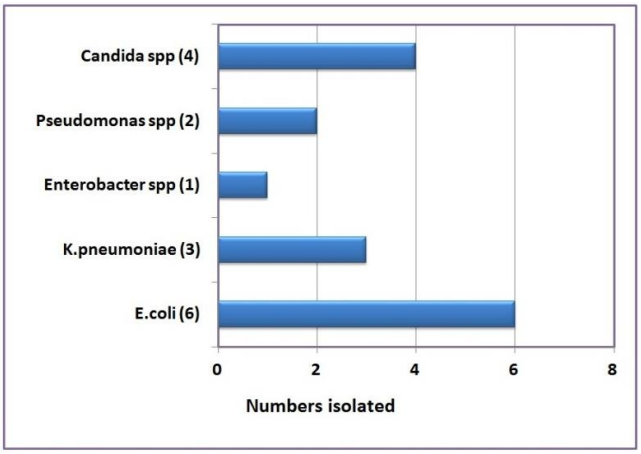

Fig. 2: Uropathogens isolated from CAUTI

Discussion

HAI directly reflect on the quality care of the healthcare settings. CAUTI which is the most common HAI was the first hospital-acquired complication chosen by the Centers for Medicare and Medicaid Services in 2008 as the basis for denial of additional payment to hospitals.[14] An acceptable CAUTI rate was up to four per 1000 catheter days as given by NHSN report of U.S.A.[15] If not aseptically inserted or maintained, the catheter itself may act as a portal of entry for the pathogen. Catheter-associated colonization is usually asymptomatic in healthy patients, which resolves spontaneously after removal of the catheter. In contrary, if the colonization persists that leads to infection in susceptible patients.[16] Cystitis, epididymitis, prostatitis, pyelonephritis and septicemia due to Gram-negative bacteremia are some of the complications encountered in high-risk group. Furthermore, in-patient deaths among the patients of CAUTI are two to three-times higher than that among the non-bacteriuric patients.[17]

In this study, device utilization ratio was 0.72 which was comparable to the study report of Choudhuri JA *et al*[14] in ICUs (0.77). In contrary to this, M. Todd Greene *et al*[18] reported the low device utilization ratio (0.5) in non ICU setup. This comparison clearly explains that catheter utilization is always high in ICU setup and thus the risk of CAUTI in ICU could be proportionately higher.

In this study, the incidence of CAUTI was found to be 16 per 100 catheterization which was lesser than the study report of Mahim Koshariya *et al* , Mangukiya JD *et al*, Gupta V, *et al*, Wazait HD *et al*, Chanda R *et al*, and Mulhall *et al*[12-20] who reported CAUTI incidence of 27,30.71,36.3,38.75,41,44 per 100 catheterization respectively. Even though its incidence appears lesser, it is not up to the standard of NHSN. This variability of incidence could be due to the varying place of surveillance as reported by Mangukiya JD et al[20] that CAUTI in Urology ward patients (33.33%) was higher than ICU patients (30.71%). This indicates that even though CAUTI incidence is higher in ICU setup; certain in-patient areas such as Urology/Nephrology wards may have a higher incidence, thus contributing to a significant percentage of CAUTI among non-ICU patients. Further research could be done in this angle to assess the burden of CAUTI in non-critically ill patients. These patients are more likely to have an acute or chronic renal functional compromise. In the latter case, device utilization may be at a higher rate than ICU

patients. This could probably explain the higher rate of CAUTI in these groups of patients.

CAUTI rate was 36.2 per 1000 catheter days which was higher than that reported by Sabir *et al*, Duszyńska et *al*, Derya keten *et al*.[5,25,26] who reported a CAUTI rate of 3.65, 7.16 and 9.6 per 1000 catheter days respectively and it is not meeting the NHSN standard too. This may be due to better infrastructure, availability of trained staff, strict infection control practices and an appropriate antibiotic policy, proper guided bundle care for both procedure and maintenance of catheter which we are planning to implement.

In the present study, CAUTI was most commonly seen among older age group (>80 years) which is in concordance with Chanda R *et al*,[23] who also reported old age itself as a predisposing factor for CAUTI(Table 1). Even though no statistical significance was found between the incidence of CAUTI and gender, CAUTI was slightly common (2.5% higher incidence) among the female patients, which is also comparable with other studies.[9,18] This increased risk in women is likely to be due to the shorter female urethra, urethra being in close proximity to the anus and hormonal influences.

Incidence of CAUTI was higher in head injury /altered sensorium patients (42.8%) who were admitted to neuro ICU compared to those patients with diagnosis/disease condition affecting other organ systems, which was in concordance with Umesh S Kamat et al.[27] Altered sensorium and also high severity of the underlying illness are important and common indications for urinary catheterization; both of them independently act as the risk factors for CAUTI **(Table 2)**.

In this study, diabetes mellitus (35.7%) was the most common comorbid condition associated with CAUTI which was also the major comorbid condition reported in other similar studies.[18,23,24] In the present study, when compared to above-mentioned studies, tuberculosis (25%) was also found to be the other important comorbid condition associated with CAUTI (Fig. 1).

In the present study, the risk of UTI after 3-5 days of catheterization was 11.7% and the risk proportionately increased with prolonged catheterization which reaches 100% if the catheter was in place for >20 days. This is similar to the study conducted by Dalen *et al*.[28] From this fact, the risk of CAUTI was almost 5 times higher after the 5th day of catheterization (Table 3).

Commonest uropathogen in this study was *Escherichia coli* (37.5%) which was similar to the results of several other studies.[9,16,18,23] *Escherichia coli* remains the common bacterial isolate for patients who develop symptoms of UTI in a short course catheterization (3-5days), in contrary Pseudomonas was the common isolate after one week of catheterization which is in concordance with the findings of Wazait HD, *et al*.[22] and *Candida spp* (25%) was the second most common isolate in our study. This emphasises the need to actively look for fungal causes of CAUTI in addition to bacterial causes.

Among the Enterobacteriaceae members, *E.coli, Klebsiella pneumoniae, Enterobacter spp* were uniformly sensitive (100%) to Colistin whereas *E.coli* & *Enterobacter spp* were 100% sensitive to Amikacin. *Klebsiella pneumoniae* differed in this aspect by only 25% being sensitive to Amikacin. Amomg the two *Pseudomonas aeuruginosa* isolates, one was resistant to colistin.

Imipenem-resistance was seen in 25% (3/12) Gram negative isolates. One Pseudomonas aeruginosa was resistant to colistin, an antibiotic that is considered as a last resort drug. This reveals that our isolates are multidrug-resistant and similar findings were observed by Kazi *et al*.[29]

This indicates measures like meticulous intervention in the form of hand hygiene, appropriate catheter maintenance practices, well defined antibiotic policy and properly guided infection control programs can reduce the extent of multidrug-resistant pathogen not only in CAUTI patients but also for the hospital in general.

Conclusion

HAI directly reflect on the quality care of the hospital and efficacy of interventions. CAUTI rate in our ICU was 36.2 per 1000 catheter days which is much high compared to the benchmark set by NHSN. So appropriate measures of educating the paramedical staff, strict infection control practices and an appropriate antibiotic policy, proper guided bundle care for both procedure and maintenance of catheter are the need of the hour to prevent the CAUTI which in turn can lessen the economic burden, work loss, and mental stress.

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Original Research Article

A prospective observational study to compare the efficacy and safety of spinal Vs general anesthesia for laparoscopic cholecystectomy

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Abstract

Background: Laparoscopic cholecystectomy is usually performed under General anesthesia, but in recent times many studies have proposed spinal anesthesia as a cost-effective alternative mode of anesthesia, specially for resource poor settings with comparable efficacy, safety. But there is a scarcity of literature on the subject. Hence the current study was conducted with an objective of comparing the efficacy and safety of spinal anesthesia, as compared to general anesthesia. **Materials and Methods:** The current study was prospective observational study, conducted in the department of general surgery and anesthesia, Velammal medical college, Madurai between April to December 2017. The study has included adult patients more than 18 years of age, with ASA grade I and II, posted for laparoscopic cholecystectomy. All the patients in the study period were administered with anesthesia as per their preference after explaining the pros and cons of each procedure. **Results:** A total of 73 subjects were included in the final analysis, with 28 subjects in spinal anesthesia group and 45 subjects in general anesthesia group. The median postoperative VAS score was statistically significantly lesser in spinal anesthesia group till 4-hour post-operative period, compared to general anesthesia group. After 4 hours the median VAS score was comparable between two groups. The ease of performing surgery score was similar in both the groups (2.63±0.62 in SA and 2.57±0.49 in GA, P value 0.647). The mean duration of surgery was also comparable between two groups (89.56±29.42 minutes in SA and 86.67±31.07minutes in GA, P value 0.694). Among the spinal anaesthesia group, 6(21.42%) had shoulder pain, 2(7.14%) had intraoperative nausea/vomiting, 9(32.14%) had hypertension. None of the GA group had intraoperative complications. The proportion of subjects with a post-operative headache was 25% and 17.78% in SA and GA group respectively (P value 0.61). The proportion of people with post-operative nausea and vomiting was 14.2% and 37.7% % in SA and GA groups respectively (P value 0.031). **Conclusions:** Spinalanaesthesia is a safe and effective alternative to general anaesthesia to perform laparoscopic cholecystectomy.

Keywords: Laparoscopic cholecystectomy, Spinal anaesthesia, Efficacy

Introduction

Symptomatic gallstone disease is one of the most common disease encountered in surgical practice [1]. Hence cholecystectomy is one of the most common surgical procedures performed by surgeons globally and in India[2]. Considering the rapid rise in the prevalence of various risk factors for gallstonediseases like obesity, alcoholism, the incidence of the disease and number of surgeries has been on the rise in recent years[3]. Laparoscopic cholecystectomy has gradually replaced and emerged as the gold standard for surgical management of symptomatic gallstone disease. As per reports as high as 98% of the cholecystectomies are being performed by this minimal access technique in some of the nations[4]. Various advantages like relatively lesser tissue dissection, lesser disruption of tissue planes, Lesser post-operative pain, Lower incidence of Intra and postoperative complications, early return to work and the Superior cosmetic outcome makes it an obvious choice over open cholecystectomy in the majority of the cases[5, 6].

Traditionally, the laparoscopic cholecystectomy has been performed under general anaesthesia [7]. But

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many studies in recent times have proposed spinal anaesthesia as a better alternative to general anaesthesia in terms of achieving better postoperative analgesia. Many studies have proposed it to be a more suitable alternative in resource poor settings like India, considering lower cost and possibility of shorter hospital stay[8-10] but there are some concerns regarding spinal anaesthesia including intraoperative shoulder pain, post spinal headache, post-operative nausea, and vomiting etc[11, 12]. Since the number of available studies on the subject is limited, clear evidence-based guidelines have not emerged in this regard. Hence there is a strong need for further studies on the subject, especially on the Indian population. In this background, the current study was conducted with the following objectives.

Objectives

1. To compare the efficacy of spinal anesthesia and general anesthesia in patients undergoing laparoscopic cholecystectomy

2. To compare the intra and postoperative complications between the two study groups

Materials and methods

Study design: Prospective observational study

Study setting: The study was conducted in the department of general surgery and department of anesthesia, Velammal medical college and Hospital, Madurai, which is a tertiary care teaching hospital.

Study period: The data collection for the study was done between April to December 2017.

Study population: The study population included patients, who were presenting to the department of general surgery OPD or emergency department subsequently posted for elective laparoscopic cholecystectomy.

Inclusion criteria

1. Adults aged more than 18 years
2. Both genders
3. ASA grade I and II
4. Clinically and radiologically confirmed cases

Exclusion criteria- Children below 18 years

All the patients were selected for the study by convenient sampling. The choice of anesthetic technique was based on the participants choice, after explaining the advantages and disadvantages of each anesthetic technique and the cost. Any patient who had a prior contraindication for any of the anesthetic technique were excluded from the study.

Ethical considerations: The study was approved by Institutional Human ethics committee. Informed written consent was obtained from all the study participants after explaining the risks and benefits of participation in the study. Confidentiality of the personal data has been maintained throughout the study.

Study procedure: After obtaining the informed written consent, all the patients had detailed preoperative evaluation and preparation for surgery as per the standard hospital protocol. All the necessary hemodynamic parameters like Blood Pressure, SpO2 and heart rate were monitored in the pre-operative room and necessary medication was administered.

The spinal anesthesiawas performed in sitting posture. Lumbar puncture was done with a 25 gauge spinal needle in the L2-L3 intervertebralspace following infiltration with a local anaesthetic. Following this intrathecal injection of 0.5% bupivacaine (3ml) and 25 micrograms of Fentanyl was done. After putting the patient in supine position and achieving sensory block at the T4 level, the approval was given to perform surgery. If the patient did not achieve T4 level sensory block after 5 minutes of supine position, Trendelenburg position was attempted and if at the end of 20 min if adequate sensory block level was not achieved, the patient was converted to GA.

All necessary haemodynamic parameters were measured intra operatively for every 5 minutes and if the mean arterial blood pressure (MAP) declined more than 20% below the pre-anesthetic level, it was labeled as intraoperative hypotension and managed with in termittent incremental iv boluses of Ephedrine 5mg. If any patient complained ofshoulder pain during the course of surgery, was managed with 25mcg fentanyl iv bolus repeated at every 5 minutes, till a maximum dose of 50mcg. GA was induced on the persistence of severe pain despite a maximum dose of fentanyl.

Following pre-oxygenation, the General anaesthesia group has received induction withPropofol (2mg/kg), Fentanyl (2mcg/kg,) and Atracurium (0.5mg/ kg). All subjects were intubated after 3min of ventilation and were maintained with air oxygen mixture enriched with Isoflurane (0.6-1.5%) and controlled mechanical ventilation. The surgery was performed by keeping the patients in a supine, reverse Trendelenburg position

with the arms fully abducted minimal possible tilt to facilitate exposure of the gallbladder. Pneumo-peritoneum was set at a pressure of 12mmHg, initial insufflation of Carbon Dioxide (CO_2) was done at a low flow rate (2L/min) and gradually increased to 5L/min. The surgery was performed using standard four-trocar technique using a zero-degree optical scope. Gallbladder dissection was done as per standard protocol starting from Calot's triangle. Following surgical removal of the gallbladder, the subhepatic drain was placed, as per standard institutional protocol.

Statistical methods: The data were analyzed using IBM SPSS statistical software version 21. Descriptive analysis was done using mean and standard deviation for quantitative variables, frequencyand proportion for categorical variables. Both the study groups were compared with respect to various baseline variables like age, gender, BMI and presence of relevant comorbidities. The primary outcome variable was postoperative pain assessed by 10-point Visual analog scale (VAS). Considering its non-normal distribution within each group, it was compared between two groups using Mann Whitney U test. The normally distributed quantitative variables were compared between two groups using unpaired t-test. Categorical variables were compared between two groups using Chi square test/ Fisher's exact test. P value < 0.05 was considered statistically significant.

Results

A total of 73 subjects were included in the final analysis, with 28 subjects in spinal anesthesia group and 45 subjects in general anesthesia group.

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

Parameter	Group 1 (Spinal) (N=28)	Group 2 (General) (N=45)	P value
Age	46.23±8.36	48.46±10.21	0.335
Gender			
Female	19(67.85%))	31(68.8%)	0.939
Male	9(32.15%)	14(31.11%)	
BMI	28.12±4.53	27.65±5.31	0.698
Presenting Symptom			
Pain abdomen	27(96.42%)	45(100%)	*
Vomiting	20(71.42%)	36(80%)	0.399
Fever	15(53.57%)	20(44.44%)	0.447
Jaundice	13(46.42%)	19(42.22%)	0.724
Presence of co-morbidities			
Diabetes mellitus	11(39.28%)	17(37.77%)	0.901
Hypertension	8(28.57%)	12(26.66%)	0.860
ASA grade			
ASA grade I	23(82.15%)	36(80%)	0.821
ASA Grade II	5(17.85%)	9(20%)	

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

Among the study population, the mean age of spinal anaesthesia group was 46.23±8.36 and 48.46±10.21 in general anaesthesia group. The difference between age and study groups was statistically not significant (P value 0.335). In both,thestudy groups the proportion of females was almost double as that of males, but no statistically significant differences were found between two groups. No statistically significant differences were found between the two study groups, in terms of Anthropometric parameters, presenting symptoms, the presence of comorbidities and ASA grade (Table 1)

Table-2: Comparison of baseline characteristics of the study population.

Parameter	Group 1 (Spinal)(N=28)	Group 2 (General)(N=45)	P value
Ease of operating conditions	2.63±0.62	2.57±0.49	0.647
Duration of surgery in minutes	89.56±29.42	86.67±31.07	0.694
Other Intraoperative events			
Shoulder pain	6(21.42%)	0(0.00%)	*
Intraoperative nausea/Vomiting	2(7.14%)	0(0.00%)	*
Hypotension	9(32.14%)	0(0.00%)	*
Conversion to GA	0(0.00%)	NA	*

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

Among the mean ease of operating conditions of spinal anaesthesia group was 2.63±0.62 and among the general anaesthesia group, 2.57±0.49. The difference between study groups and ease of operating conditions was statistically not significant (P value 0.647).

Among the mean duration of surgery of spinal anaesthesia group, was 89.56±29.42 and among the general anaesthesia group, 86.67±31.07. The difference between study groups and duration of surgery was statistically not significant (P value 0.694). Among the spinal anaesthesia group, 6(21.42%) had shoulder pain, 2(7.14%) had intraoperative nausea/vomiting, 9(32.14%) had hypertension. (Table 2)

Table-3: Comparison of Post-operative analgesia and use of adjuvant analgesic between two study groups

Postoperative analgesia (As assessed by VAS score)	Group 1 (Spinal) (N=30)	Group 2 (General) (N=30)	P value
Immediate post-operative period	0 (0, 1)	3(2, 6)	<0.001
30 minutes	0 (0, 1)	3 (2, 6)	<0.001
60 minutes	0 (0, 1)	4 (2, 7)	<0.001
90 minutes	0 (0, 1)	4.5 (2, 8)	<0.001
120 minutes	1 (1, 2)	4.5 (2, 8)	<0.001
4 hours	2 (1, 3)	4.5 (2, 8)	<0.001
8 hours	3.5 (2,5)	4 (2, 7)	0.326
10 hours	4 (2,6)	3.5(2, 6)	0.412
12hours	5 (2, 8)	4.5 (2,8)	0.512
24 hours	4.5 (2,8)	4.5 (2,8)	1

Among the spinal anaesthesia median VAS was 0(IQR0 to1) at immediate post-operative period, 0(IQR0 to 1) at 30 minutes, 0(IQR 0 to 1) 0f 60 minutes, 0(IQR0 to 1) of 90 minutes, 1(IQR1 to 2) 0f 120 minutes, 2(IQR 1 to30) of 4 hours, 3.5 (IQR 2 TO 5) OF 8 hours, 4 (IQR 2 to 6) 0f 10 hours, 5(IQR 2 to 8) of 12 hours, 4.5(IQR 2 to 8) of 24 hours. Among the general anaesthesia median was 3(IQR 2 to 6) of immediate post-operative period, 3(IQR 2 to 6) of 30 minutes, 4(IQR 2 to 7) 0f 60 minutes, 4.5(IQR 2 to 8) of 90 minutes, 4.5(IQR 2 to 8) of 120 minutes, 4.5(IQR 2 to 8) of 4 hours, 4 (IQR 2 to 7) of 8 hours, 3.5(IQR 2 to 6) of 10 hours, 4.5(IQR 2 to 8) of 12 hours, 4.5(2 to 8) 0f 24 hours pre-operative analgesia.

The difference across study groups and immediate post-operative period,30,60,90,120 minutes,4 hours were statistically significant (P value <0.001),The difference across study groups and 8,10,12,24 hours' post-operative analgesia was statistically not significant (P value >0.05) (Table 3).

Table-4: Incidence of various post-operative complications between two study groups.

Post operative Complications	Group 1 (Spinal)(N=28)	Group 2 (General)(N=45)	P value
Post-operative headache	7(25%)	9(17.78%)	0.61
Post-operative nausea and vomiting	4(14.2%)	17(37.78%)	0.031
Post-operative wound sepsis	0(0.00%)	0(0.00%)	ND

**ND+ not done as the data did not satisfy assumptions required to carry out chi square test/Fisher's exact test*

Among the spinal anaesthesia group, 7 (25%) people had a post-operative headache, which was 9 (17.78%) in general anesthesia group and the difference was statistically not significant (P value 0.61). The proportion of people with post-operative nausea and vomiting was 14.2% and 37.7% % in SA and GA groups respectively, with a statistically significant difference (0.031). None of the subjects in either of treatment groups had postoperative wound sepsis (Table 4).

Discussion

Laparoscopic Cholecystectomy has emerged as the safe and effective choice over open cholecystectomy in recent years. Even in developing countries,amajor portion of cholecystectomies is being performed laparoscopically [5].

In the current study, the operating time and ease of operating conditions and duration of hospital stay etc were comparable between both spinal and general anaesthesia groups. These findings were in line with the majority of the published literature on the subject. None of the subjects in spinal anaesthesia group required conversion to general anaesthesia. Tzovaras, G., et al.[13] In one of the first pilot study on the feasibility of spinal anaesthesia for Laparoscopic cholecystectomy have reported 100% successful execution.Yuksek, Y. N., et al.[12], have reported a conversion rate of 11.53% of cases to general anaesthesia due to severe right shoulder pain. Developed during spinal anesthesia. Gautam, B et al[8] have reported the failure very minimal operative difficulty. In a study by Sinha, R., et al[10] among laparoscopic cholecystectomy cases done under spinal anaesthesia, 0.52% patients required a conversion to GA. There were no differences between two study groups in operating time and other operative parameters.

In the current study, The spinal anaesthesia had resulted in better postoperative analgesia, especially in the first 4-hour post-operative period. The overall analgesic requirement was also lesser in this group, as compared to general anaesthesia. Tzovaras, G., et al.[13] have reported a postoperative median pain scores ranging from 1 to 1.5, with no major complications with spinal anesthesia.

Similar to current study findings, Tzovaras, G., et al. [14] in another study have reported that significantly lower pain until 4 hours. But in contrast to the current study, the superior painrelief with spinal anaesthesia had continued till 24 hours. In a study by Sinha, R., et al.[10] the overall post-operative injectable analgesic requirement was 34.36% and 91.45% in SA and GA groups respectively, indicating superior pain relief with SA. Bessa, S. S., et al.[15] have also reported similar findings to the current study, where for the first 2 to 4 hours, the mean pain scores were significantly lesser with spinal anaesthesia, as compared to general anaesthesia. The analgesic requirement in the first postoperative day was also significantly lower in SA group. Imbelloni, L. E., et al. [16] have reported significantly lower pain with spinal anaesthesia in the first 6 hours following surgery.

In the current study, among the spinal anaesthesia group, 6(21.42%) had shoulder pain, 2(7.14%) had intraoperative nausea/vomiting and 9(32.14%) had hypertension. None of the subjects in general anaesthesia group had the above-mentioned complications. In a study by Yuksek, Y. N., et al.[12], out of 26 patients attempted for laparoscopic chole-cystectomy under SA, 3 patients needed conversion to general anesthesia due to severe right shoulder pain. No major cardiopulmonary problems were reported by this study except transient hypotension Intra operatively. But almost 50% of the subjects had reported severe right shoulder pain, needing treatment by fentanyl, local washing of the right diaphragm with 2% lidocaine solution. As per a study by Gautam, B et al [8]the problems reported in the spinal anesthesia group were shoulder pain intraoperatively requiring treatment with by Fentanyl and anxietytreated by midazolam.Inastudy by Sinha, R., et al[10] among laparoscopic cholecystectomy cases done under spinal anaesthesia, the most common issues occurred during the intraoperative period were hypotension requiring

treatment in 20.05% of patients and, neck and/or shoulder pain in 12.29% of patients. Which was similar to current study findings. In a study by Kumar, A et al[9] commonest complaint reported was a pain in right shoulder and anxiety at the beginning of operation/ pneumoperitoneum. In the current study Among the spinal anaesthesia group, 7(25%) people had a post-operative headache, which was 9 (17.78%) in general anesthesia group and the difference was statistically not significant (P value 0.61). The proportion of people with post-operative nausea and vomiting was 14.2% and 37.7% in SA and GA groups respectively, with a statistically significant difference (0.031). None of the subjects in either of treatment groups had postoperative wound sepsis. Tzovaras, G., et al[14]in contrast to current study have reported comparable post-operative complication rate between spinal and general anesthesia. In a study by Sinha, R., et al[10] post-operative nausea and vomiting were present in 2.29% in SA group against 30.30% in GA. A postural headache was reported in 5.9% of patients following SA.

A randomized controlled trial by Bessa, S. S., et al[17] have reported higher proportion (8.8 % Vs 0%) of subjects in GA group requiring anovernight post-operative stay, as they had nausea and vomiting, inadequate pain control and unexplained hypotension.

Imbelloni, L. E., et al[16] have reported significantly lower pain with spinal anaesthesia in the first 6 hours following surgery. They have also specified the cost of spinal anaesthesia to be considerably lower as compared to GA and proposed it to be a more suitable option in resource-limitedsettings.

Conclusions

1. The spinal anaesthesia had resulted in better postoperative analgesia, especially in the first 4-hour post-operative period.The overall analgesic requirement was also lesser in this group, as compared to general anaesthesia.

2. The incidence of some of the intraoperative complications like shoulder pain and intraoperative hypotension, nausea, and vomiting were slightly higher in spinal anaesthesia group. A post-operative headache also was slightly higher in spinal anaesthesia group.

3. The incidence of postoperative nausea and vomiting was higher in general anaesthesia grou.

4. The operating time, operating conditions and post-operative stay were comparable between two groups.

Limitations: Since the study participant selection was not randomly done, the role of selection bias and the effect of potential unknown confounding factors and the magnitude and direction of their effect could not be estimated

Recommendations: There is a need for large-scale randomized controlled trials on the subject to generate more evidence on the subject to guide informed clinical decision making. Till such time the choice of anaesthesia should be made by carefully weighing the risks, benefits, cost of the procedure and patient preferences into consideration.

What this study adds to existing knowledge: The study further strengthens the evidence existing regarding the comparative efficacy and safety of spinal anaesthesia in patients undergoing laparotomy.

The study findings prove that the spinal anaesthesia can be used safely for laparoscopic cholecystectomy and achieve comparative efficacy, without any undue adverse effects. The study findings assume greater importance due to scarcity of studies on the subject in Indian population.

Author Contribution

Author 1: The first author has conceptualized the study, participated in developing appropriate study protocol, involved in all stages of the study from the design, data collection, data analysis, preparation and review of the drafts to submission of the manuscript for publication.

Author 2: The second author had provided a supportive role data collection, data entry. He had contributed to the preparation of the draft manuscript, editing of the drafts and also was involved in doing necessary modifications to the drafts as per reviewer'sinputs.

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Original Article

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Study on Dimensions of Nasal Columella to Aid Aesthetic Rhinoplasty

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Abstract

Aims: Thorough knowledge of an Indian nose is vital for performing aesthetic Rhinoplasty. Hence the present study was taken up with the aim to determine dimensions of nasal columella and columellar index of Tamil ethnic group; and also to statistically analyse gender wise difference in findings

Settings and Design: The present cross-sectional study, approved by the Institutional Ethics Committee, was done on Tamil speaking medical students of Velammal Medical College, Madurai, Tamil Nadu.

Methods & Material: Of total 142 medical student population, 106 Tamil speaking medical students participated. Consenting Tamil speaking students were included. Individuals with noticeable facial disfigurement and with history of previous facial surgery were excluded.

Statistical Analysis used: Unpaired t test

Results: The present study reports mean values for nasal columella width, length and index as 6.63mm, 13.8mm, and 48.6 for males; 5.61mm, 13.53mm and 41.9 for females; and 6.84mm, 13.65mm and 45 for the whole group.

Conclusion: The present study infers that nasal columella width greater than 5.9 mm belongs to male, and lesser than 5.9 mm belongs to a female; and nasal columella index is greater than 48 in males, and lesser than 45 in females. Nasal columella length findings were inconclusive.

Keywords: Otolaryngology; Columellar Length; Columellar Width; Columellar Index; Aesthetic Rhinoplasty.

Introduction

For aesthetic rhinoplasty, nasal columella is a major component. The columella has anterior lobular portion, the intermediate (or narrower) portion, and the basal (or wider) portion. The columella, ala, and lobule have now been included as an aesthetic complex for evaluation; and their interrelation may affect any nasal tip surgery, a fact that should be considered while planning surgery in that region. Thorough knowledge of an Indian nose is vital for performing aesthetic Rhinoplasty. Hence the present study was taken up with the aim to determine dimensions of nasal columella and columellar index of Tamil ethnic group; and also to statistically analyse gender wise difference in findings.

Columella is oriented vertically and is primarily responsible for nostril length and nasal tip projection and determines nasal tip size, shape, and nostril configuration. Hence, it is important to understand that individual, racial and ethnic variations within the structural compo-nents of the nasal tip are bound to exist. In general, the nose can be described as being platyrrhine (African), mesorrhine (Asian), or leptorrhine (Caucasian). The African and Asian noses do share many common features and can be described as less projected with a shorter colu-mella. A common finding with bilat-eral cleft lip nose is underprojection and a short columella, wherein,

V-Y advancement technique incision allows the surgeon to ex-pose and augment the nasal tip structures by lengthening the columella [1,2].

Material & Method

The present cross-sectional study was conducted during the months of January to April 2017. The study was approved by Institutional Ethics Committee and was ethically conducted in accordance with Declaration of Helsinki. Written informed consent was taken from the participants before data collection. 106 (49 males and 57 females) Tamil speaking medical students, 19-21years of age, participated in the study. Consenting Tamil speaking students were included. Individuals with noticeable facial disfigurement and with history of previous facial surgery were excluded. Sample size was calculated using Sample Size Calculator presented as a public service of Creative Research Systems: Survey software, 'The Survey System'. Sample size was 106 (Confidence Level at 95%, and Confidence Interval of 5) of total 142 students (population).

Participants were positioned as described by Farkas *et al. [3]*. Columellar measurements were taken manually using *Sliding Vernier calliper*. The Parameters assessed were, Columellar width (CW), Columellar length (CL), and Columellar index (CI). Columella Width was measured at the narrowest point at subnasale and Columellar Length was measured from sub nasale to nasal tip [4]. Columellar index (CI) was calculated using formula CI= CW / CL x 100. Statistical evaluation was done using *unpaired t test*. Statistical significance was determined at $p<0.05$.

Results

Columellar findings were tabulated in a Master-Chart. Statistical values namely, Mean, Standard Deviation (SD), Standard Error of Mean (SEM), and 95% Confidence interval ($CI._{95}$) of the difference in mean of male (m) and female (f) participants were estimated using unpaired t test. Intermediate values in calculation were t value, degrees of freedom (df), and standard error of difference (SED). Gender wise differences were significant at $p<0.05$ (*with unpaired t test*) in all measured parameters. Table1 indicates Statistical findings for columellar measurements in males, females and total participants and Table 2 indicates Statistical findings (*with unpaired t test*) on gender wise differences in analysed parameters.

Table 1: Statistical findings for columellar measurements

N=106		CW	CL	CI
Male Participants (n = 49)	Mean	6.63 mm	13.8 mm	48.6
	SD	0.73	1.79	6.23
	SEM	0.1	0.26	0.89
Female Participants (n = 57)	Mean	5.61 mm	13.53 mm	41.9
	SD	1.45	3.12	8.18
	SEM	0.19	0.41	1.08
All Participants (n = 106)	Mean	6.84 mm	13.65 mm	45
	SD	1.27	2.59	8.04
	SEM	0.12	0.25	0.78

CW-Columellar width, CL- Columellar length, CI- Columellar index, SD-Standard Deviation, SEM-Standard Error of Mean

Table 2: Statistical findings on gender wise differences in analysed parameters

	$CI._{95}$	t value	DF	SED	p value	Statistical Inference
CW	0.57 to 1.47	4.4607	104	0.228	Less than 0.0001	extremely significant
CL	0.73 to 1.27	0.5334	104	0.505	0.5949	Not Significant
CI	3.8 to 9.5	4.6729	104	1.431	Less than 0.0001	extremely significant

CW-Columellar width, CL- Columellar length, CI- Columellar index, M – Mean, SD - Standard Deviation, SEM - Standard Error of Mean, $CI._{95}$- 95% Confidence interval of the difference in mean of male (m) and female (f) participants, SED - Standard Error of Difference

Discussion

There haven't been studies of similar kind previously. Cho *et al.* reported columellar findings in infants which cannot be compared with the present study [5]. Farkas *et al.* and HeZ *et al.* reported smaller columella in Asians to that off Caucasians [6,7]. Poor development of medial and lateral crura could be the reason for short and narrow columella in Asian populations. Columella strut being one of the commonly performed procedures in Asian rhinoplasty justifies the aforementioned hypothesis [4].

Columellar morphology and orientation must be considered when deciding appropriate surgical pro-cedure for tip refinement and nostril shape augmentation. In rhino-plasty operation, aesthetics and function are objectives; and anatomy determines the op-erative technique. Changes in col-umella are performed to increase or decrease nasal tip projection. Col-umella can be viewed as the center pole of a tent, wherein, height alterations of the center pole results in an increase or decrease in nasal tip projection. Changes in projection, in turn affects nostril shape and ori-entation [8,9]. Nasal tip and the nostril shape are complex anatomical structures consisting of cartilaginous framework, skin and soft tissue. When preparing for rhinoplasty operations, it is important to con-sider ethnic and individual variations in the nasal tip, nostril shape, and internal structure. By categorizing nasal tip into its respec-tive subunits, the rhinoplasty surgeon can then formulate a systematic and pragmatic ap-proach to the nasal base, lateral wall, and colu-mella. Altering or augmenting one or all of these is bound to affect nasal tip, shape and orientation of the nostril [1,2].

In Rhinoplasty, post-operative complications result from nasal healing that causes changes in nasal morphology and function [9,10]. The surgeon should anticipate these healing forces and take into account support mechanisms of the nasal tip when planning an optimal approach for the surgery [11].

Conclusion

The present study infers that nasal columella width greater than 5.9 mm belongs to male, and lesser than 5.9 mm belongs to a female; and nasal columella index is greater than 48 in males, and lesser than 45 in females. Nasal columella length findings were inconclusive. The present study results will help surgeons avoid complications by anticipating healing forces and take into account support mechanisms of the nasal tip when planning an optimal approach for aesthetic nasal surgeries. The authors of the present study believe that knowledge of columellar morphology of a particular gender, geographical area and ethnic group is important for the surgeon to plan an approach for aesthetic nasal surgeries.

Key message

Knowledge of Nasal Columellar morphology of a particular gender, geographical area and ethnic group is important for the surgeon to plan an approach for aesthetic nasal surgeries.

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Article

A comparative study of intravenous dexmedetomidine and midazolam on prolongation of spinal anesthesia

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Abstract

Background: The present study was conducted to compare the efficacy and safety of intravenous dexmedetomidine and midazolam on prolongation of spinal anesthesia.Methods: The study population included people who were undergoing for spinal anesthesia for various surgeries. A total of 90 subject were randomized equally to Dexmedetomidine, Midazolam and saline groups using a computer generated random number sequence. Three study groups were compared with respect to all the baseline variables. The key outcome parameters and hemodynamic parameters were compared among the three study groups.Results: No statistically significant differences were observed in baseline paramters across study groups. The median values of patient satisfaction score and anesthesiologist satisfaction score were almost equal among three study groups, but the association was statistically not significant. The median VAS and the median HSL were slightly lower in dexmedetomidine group than other two groups (VAS-1,2,3 respectively and HSL -4,6,6 respectively) with statistically significant association (P<0.001). The proportion of Bradycardia and hypertension was slightly higher(12.2%) in

hours was 36.7% in saline group, 33.33% in midazolam group. The association between symptoms and study groups was statistically not significant (P value>0.05) except with number of patients requiring analgesic for the first 24 hours (P value<0.05).Co

Original Research Article

A prospective observational study to compare the efficacy and safety of spinal Vs general anesthesia for laparoscopic cholecystectomy

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Abstract

Background: Laparoscopic cholecystectomy is usually performed under General anesthesia, but in recent times many studies have proposed spinal anesthesia as a cost-effective alternative mode of anesthesia, specially for resource poor settings with comparable efficacy, safety. But there is a scarcity of literature on the subject. Hence the current study was conducted with an objective of comparing the efficacy and safety of spinal anesthesia, as compared to general anesthesia. **Materials and Methods:** The current study was prospective observational study, conducted in the department of general surgery and anesthesia, Velammal medical college, Madurai between April to December 2017. The study has included adult patients more than 18 years of age, with ASA grade I and II, posted for laparoscopic cholecystectomy. All the patients in the study period were administered with anesthesia as per their preference after explaining the pros and cons of each procedure. **Results:** A total of 73 subjects were included in the final analysis, with 28 subjects in spinal anesthesia group and 45 subjects in general anesthesia group. The median postoperative VAS score was statistically significantly lesser in spinal anesthesia group till 4-hour post-operative period, compared to general anesthesia group. After 4 hours the median VAS score was comparable between two groups. The ease of performing surgery score was similar in both the groups (2.63±0.62 in SA and 2.57±0.49 in GA, P value 0.647). The mean duration of surgery was also comparable between two groups (89.56±29.42 minutes in SA and 86.67±31.07minutes in GA, P value 0.694). Among the spinal anaesthesia group, 6(21.42%) had shoulder pain, 2(7.14%) had intraoperative nausea/vomiting, 9(32.14%) had hypertension. None of the GA group had intraoperative complications. The proportion of subjects with a post-operative headache was 25% and 17.78% in SA and GA group respectively (P value 0.61). The proportion of people with post-operative nausea and vomiting was 14.2% and 37.7% % in SA and GA groups respectively (P value 0.031). **Conclusions:** Spinalanaesthesia is a safe and effective alternative to general anaesthesia to perform laparoscopic cholecystectomy.

Keywords: Laparoscopic cholecystectomy, Spinal anaesthesia, Efficacy

Introduction

Symptomatic gallstone disease is one of the most common disease encountered in surgical practice [1]. Hence cholecystectomy is one of the most common surgical procedures performed by surgeons globally and in India[2]. Considering the rapid rise in the prevalence of various risk factors for gallstonediseases like obesity, alcoholism, the incidence of the disease and number of surgeries has been on the rise in recent years[3]. Laparoscopic cholecystectomy has gradually replaced and emerged as the gold standard for surgical management of symptomatic gallstone disease. As per reports as high as 98% of the cholecystectomies are being performed by this minimal access technique in some of the nations[4]. Various advantages like relatively lesser tissue dissection, lesser disruption of tissue planes, Lesser post-operative pain, Lower incidence of Intra and postoperative complications, early return to work and the Superior cosmetic outcome makes it an obvious choice over open cholecystectomy in the majority of the cases[5, 6].

Traditionally, the laparoscopic cholecystectomy has been performed under general anaesthesia [7]. But

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many studies in recent times have proposed spinal anaesthesia as a better alternative to general anaesthesia in terms of achieving better postoperative analgesia. Many studies have proposed it to be a more suitable alternative in resource poor settings like India, considering lower cost and possibility of shorter hospital stay[8-10] but there are some concerns regarding spinal anaesthesia including intraoperative shoulder pain, post spinal headache, post-operative nausea, and vomiting etc[11, 12]. Since the number of available studies on the subject is limited, clear evidence-based guidelines have not emerged in this regard. Hence there is a strong need for further studies on the subject, especially on the Indian population. In this background, the current study was conducted with the following objectives.

Objectives

1. To compare the efficacy of spinal anesthesia and general anesthesia in patients undergoing laparoscopic cholecystectomy

2. To compare the intra and postoperative complications between the two study groups

Materials and methods

Study design: Prospective observational study

Study setting: The study was conducted in the department of general surgery and department of anesthesia, Velammal medical college and Hospital, Madurai, which is a tertiary care teaching hospital.

Study period: The data collection for the study was done between April to December 2017.

Study population: The study population included patients, who were presenting to the department of general surgery OPD or emergency department subsequently posted for elective laparoscopic cholecystectomy.

Inclusion criteria

1. Adults aged more than 18 years
2. Both genders
3. ASA grade I and II
4. Clinically and radiologically confirmed cases

Exclusion criteria- Children below 18 years

All the patients were selected for the study by convenient sampling. The choice of anesthetic technique was based on the participants choice, after explaining the advantages and disadvantages of each anesthetic technique and the cost. Any patient who had a prior contraindication for any of the anesthetic technique were excluded from the study.

Ethical considerations: The study was approved by Institutional Human ethics committee. Informed written consent was obtained from all the study participants after explaining the risks and benefits of participation in the study. Confidentiality of the personal data has been maintained throughout the study.

Study procedure: After obtaining the informed written consent, all the patients had detailed preoperative evaluation and preparation for surgery as per the standard hospital protocol. All the necessary hemodynamic parameters like Blood Pressure, SpO2 and heart rate were monitored in the pre-operative room and necessary medication was administered.

The spinal anesthesiawas performed in sitting posture. Lumbar puncture was done with a 25 gauge spinal needle in the L2-L3 intervertebralspace following infiltration with a local anaesthetic. Following this intrathecal injection of 0.5% bupivacaine (3ml) and 25 micrograms of Fentanyl was done. After putting the patient in supine position and achieving sensory block at the T4 level, the approval was given to perform surgery. If the patient did not achieve T4 level sensory block after 5 minutes of supine position, Trendelenburg position was attempted and if at the end of 20 min if adequate sensory block level was not achieved, the patient was converted to GA.

All necessary haemodynamic parameters were measured intra operatively for every 5 minutes and if the mean arterial blood pressure (MAP) declined more than 20% below the pre-anesthetic level, it was labeled as intraoperative hypotension and managed with in termittent incremental iv boluses of Ephedrine 5mg. If any patient complained ofshoulder pain during the course of surgery, was managed with 25mcg fentanyl iv bolus repeated at every 5 minutes, till a maximum dose of 50mcg. GA was induced on the persistence of severe pain despite a maximum dose of fentanyl.

Following pre-oxygenation, the General anaesthesia group has received induction withPropofol (2mg/kg), Fentanyl (2mcg/kg,) and Atracurium (0.5mg/ kg). All subjects were intubated after 3min of ventilation and were maintained with air oxygen mixture enriched with Isoflurane (0.6-1.5%) and controlled mechanical ventilation. The surgery was performed by keeping the patients in a supine, reverse Trendelenburg position

with the arms fully abducted minimal possible tilt to facilitate exposure of the gallbladder. Pneumo-peritoneum was set at a pressure of 12mmHg, initial insufflation of Carbon Dioxide (CO_2) was done at a low flow rate (2L/min) and gradually increased to 5L/min. The surgery was performed using standard four-trocar technique using a zero-degree optical scope. Gallbladder dissection was done as per standard protocol starting from Calot's triangle. Following surgical removal of the gallbladder, the subhepatic drain was placed, as per standard institutional protocol.

Statistical methods: The data were analyzed using IBM SPSS statistical software version 21. Descriptive analysis was done using mean and standard deviation for quantitative variables, frequencyand proportion for categorical variables. Both the study groups were compared with respect to various baseline variables like age, gender, BMI and presence of relevant comorbidities. The primary outcome variable was postoperative pain assessed by 10-point Visual analog scale (VAS). Considering its non-normal distribution within each group, it was compared between two groups using Mann Whitney U test. The normally distributed quantitative variables were compared between two groups using unpaired t-test. Categorical variables were compared between two groups using Chi square test/ Fisher's exact test. P value < 0.05 was considered statistically significant.

Results

A total of 73 subjects were included in the final analysis, with 28 subjects in spinal anesthesia group and 45 subjects in general anesthesia group.

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

Parameter	Group 1 (Spinal) (N=28)	Group 2 (General) (N=45)	P value
Age	46.23±8.36	48.46±10.21	0.335
Gender			
Female	19(67.85%))	31(68.8%)	0.939
Male	9(32.15%)	14(31.11%)	
BMI	28.12±4.53	27.65±5.31	0.698
Presenting Symptom			
Pain abdomen	27(96.42%)	45(100%)	*
Vomiting	20(71.42%)	36(80%)	0.399
Fever	15(53.57%)	20(44.44%)	0.447
Jaundice	13(46.42%)	19(42.22%)	0.724
Presence of co-morbidities			
Diabetes mellitus	11(39.28%)	17(37.77%)	0.901
Hypertension	8(28.57%)	12(26.66%)	0.860
ASA grade			
ASA grade I	23(82.15%)	36(80%)	0.821
ASA Grade II	5(17.85%)	9(20%)	

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

Among the study population, the mean age of spinal anaesthesia group was 46.23±8.36 and 48.46±10.21 in general anaesthesia group. The difference between age and study groups was statistically not significant (P value 0.335). In both,thestudy groups the proportion of females was almost double as that of males, but no statistically significant differences were found between two groups. No statistically significant differences were found between the two study groups, in terms of Anthropometric parameters, presenting symptoms, the presence of comorbidities and ASA grade (Table 1)

Table-2: Comparison of baseline characteristics of the study population.

Parameter	Group 1 (Spinal)(N=28)	Group 2 (General)(N=45)	P value
Ease of operating conditions	2.63±0.62	2.57±0.49	0.647
Duration of surgery in minutes	89.56±29.42	86.67±31.07	0.694
Other Intraoperative events			
Shoulder pain	6(21.42%)	0(0.00%)	*
Intraoperative nausea/Vomiting	2(7.14%)	0(0.00%)	*
Hypotension	9(32.14%)	0(0.00%)	*
Conversion to GA	0(0.00%)	NA	*

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

Among the mean ease of operating conditions of spinal anaesthesia group was 2.63±0.62 and among the general anaesthesia group, 2.57±0.49. The difference between study groups and ease of operating conditions was statistically not significant (P value 0.647).

Among the mean duration of surgery of spinal anaesthesia group, was 89.56±29.42 and among the general anaesthesia group, 86.67±31.07. The difference between study groups and duration of surgery was statistically not significant (P value 0.694). Among the spinal anaesthesia group, 6(21.42%) had shoulder pain, 2(7.14%) had intraoperative nausea/vomiting, 9(32.14%) had hypertension. (Table 2)

Table-3: Comparison of Post-operative analgesia and use of adjuvant analgesic between two study groups

Postoperative analgesia (As assessed by VAS score)	Group 1 (Spinal) (N=30)	Group 2 (General) (N=30)	P value
Immediate post-operative period	0 (0, 1)	3(2, 6)	<0.001
30 minutes	0 (0, 1)	3 (2, 6)	<0.001
60 minutes	0 (0, 1)	4 (2, 7)	<0.001
90 minutes	0 (0, 1)	4.5 (2, 8)	<0.001
120 minutes	1 (1, 2)	4.5 (2, 8)	<0.001
4 hours	2 (1, 3)	4.5 (2, 8)	<0.001
8 hours	3.5 (2,5)	4 (2, 7)	0.326
10 hours	4 (2,6)	3.5(2, 6)	0.412
12hours	5 (2, 8)	4.5 (2,8)	0.512
24 hours	4.5 (2,8)	4.5 (2,8)	1

Among the spinal anaesthesia median VAS was 0(IQR0 to1) at immediate post-operative period, 0(IQR0 to 1) at 30 minutes, 0(IQR 0 to 1) 0f 60 minutes, 0(IQR0 to 1) of 90 minutes, 1(IQR1 to 2) 0f 120 minutes, 2(IQR 1 to30) of 4 hours, 3.5 (IQR 2 TO 5) OF 8 hours, 4 (IQR 2 to 6) 0f 10 hours, 5(IQR 2 to 8) of 12 hours, 4.5(IQR 2 to 8) of 24 hours. Among the general anaesthesia median was 3(IQR 2 to 6) of immediate post-operative period, 3(IQR 2 to 6) of 30 minutes, 4(IQR 2 to 7) 0f 60 minutes, 4.5(IQR 2 to 8) of 90 minutes, 4.5(IQR 2 to 8) of 120 minutes, 4.5(IQR 2 to 8) of 4 hours, 4 (IQR 2 to 7) of 8 hours, 3.5(IQR 2 to 6) of 10 hours, 4.5(IQR 2 to 8) of 12 hours, 4.5(2 to 8) 0f 24 hours pre-operative analgesia.

The difference across study groups and immediate post-operative period,30,60,90,120 minutes,4 hours were statistically significant (P value <0.001),The difference across study groups and 8,10,12,24 hours' post-operative analgesia was statistically not significant (P value >0.05) (Table 3).

Table-4: Incidence of various post-operative complications between two study groups.

Post operative Complications	Group 1 (Spinal)(N=28)	Group 2 (General)(N=45)	P value
Post-operative headache	7(25%)	9(17.78%)	0.61
Post-operative nausea and vomiting	4(14.2%)	17(37.78%)	0.031
Post-operative wound sepsis	0(0.00%)	0(0.00%)	ND

**ND+ not done as the data did not satisfy assumptions required to carry out chi square test/Fisher's exact test*

Among the spinal anaesthesia group, 7 (25%) people had a post-operative headache, which was 9 (17.78%) in general anesthesia group and the difference was statistically not significant (P value 0.61). The proportion of people with post-operative nausea and vomiting was 14.2% and 37.7% % in SA and GA groups respectively, with a statistically significant difference (0.031). None of the subjects in either of treatment groups had postoperative wound sepsis (Table 4).

Discussion

Laparoscopic Cholecystectomy has emerged as the safe and effective choice over open cholecystectomy in recent years. Even in developing countries,amajor portion of cholecystectomies is being performed laparoscopically [5].

In the current study, the operating time and ease of operating conditions and duration of hospital stay etc were comparable between both spinal and general anaesthesia groups. These findings were in line with the majority of the published literature on the subject. None of the subjects in spinal anaesthesia group required conversion to general anaesthesia. Tzovaras, G., et al.[13] In one of the first pilot study on the feasibility of spinal anaesthesia for Laparoscopic cholecystectomy have reported 100% successful execution.Yuksek, Y. N., et al.[12], have reported a conversion rate of 11.53% of cases to general anaesthesia due to severe right shoulder pain. Developed during spinal anesthesia. Gautam, B et al[8] have reported the failure very minimal operative difficulty. In a study by Sinha, R., et al[10] among laparoscopic cholecystectomy cases done under spinal anaesthesia, 0.52% patients required a conversion to GA. There were no differences between two study groups in operating time and other operative parameters.

In the current study, The spinal anaesthesia had resulted in better postoperative analgesia, especially in the first 4-hour post-operative period. The overall analgesic requirement was also lesser in this group, as compared to general anaesthesia. Tzovaras, G., et al.[13] have reported a postoperative median pain scores ranging from 1 to 1.5, with no major complications with spinal anesthesia.

Similar to current study findings, Tzovaras, G., et al. [14] in another study have reported that significantly lower pain until 4 hours. But in contrast to the current study, the superior painrelief with spinal anaesthesia had continued till 24 hours. In a study by Sinha, R., et al.[10] the overall post-operative injectable analgesic requirement was 34.36% and 91.45% in SA and GA groups respectively, indicating superior pain relief with SA. Bessa, S. S., et al.[15] have also reported similar findings to the current study, where for the first 2 to 4 hours, the mean pain scores were significantly lesser with spinal anaesthesia, as compared to general anaesthesia. The analgesic requirement in the first postoperative day was also significantly lower in SA group. Imbelloni, L. E., et al. [16] have reported significantly lower pain with spinal anaesthesia in the first 6 hours following surgery.

In the current study, among the spinal anaesthesia group, 6(21.42%) had shoulder pain, 2(7.14%) had intraoperative nausea/vomiting and 9(32.14%) had hypertension. None of the subjects in general anaesthesia group had the above-mentioned complications. In a study by Yuksek, Y. N., et al.[12], out of 26 patients attempted for laparoscopic chole-cystectomy under SA, 3 patients needed conversion to general anesthesia due to severe right shoulder pain. No major cardiopulmonary problems were reported by this study except transient hypotension Intra operatively. But almost 50% of the subjects had reported severe right shoulder pain, needing treatment by fentanyl, local washing of the right diaphragm with 2% lidocaine solution. As per a study by Gautam, B et al [8]the problems reported in the spinal anesthesia group were shoulder pain intraoperatively requiring treatment with by Fentanyl and anxietytreated by midazolam.Inastudy by Sinha, R., et al[10] among laparoscopic cholecystectomy cases done under spinal anaesthesia, the most common issues occurred during the intraoperative period were hypotension requiring

treatment in 20.05% of patients and, neck and/or shoulder pain in 12.29% of patients. Which was similar to current study findings. In a study by Kumar, A et al[9] commonest complaint reported was a pain in right shoulder and anxiety at the beginning of operation/ pneumoperitoneum. In the current study Among the spinal anaesthesia group, 7(25%) people had a post-operative headache, which was 9 (17.78%) in general anesthesia group and the difference was statistically not significant (P value 0.61). The proportion of people with post-operative nausea and vomiting was 14.2% and 37.7% in SA and GA groups respectively, with a statistically significant difference (0.031). None of the subjects in either of treatment groups had postoperative wound sepsis. Tzovaras, G., et al[14]in contrast to current study have reported comparable post-operative complication rate between spinal and general anesthesia. In a study by Sinha, R., et al[10] post-operative nausea and vomiting were present in 2.29% in SA group against 30.30% in GA. A postural headache was reported in 5.9% of patients following SA.

A randomized controlled trial by Bessa, S. S., et al[17] have reported higher proportion (8.8 % Vs 0%) of subjects in GA group requiring anovernight post-operative stay, as they had nausea and vomiting, inadequate pain control and unexplained hypotension.

Imbelloni, L. E., et al[16] have reported significantly lower pain with spinal anaesthesia in the first 6 hours following surgery. They have also specified the cost of spinal anaesthesia to be considerably lower as compared to GA and proposed it to be a more suitable option in resource-limitedsettings.

Conclusions

1. The spinal anaesthesia had resulted in better postoperative analgesia, especially in the first 4-hour post-operative period.The overall analgesic requirement was also lesser in this group, as compared to general anaesthesia.

2. The incidence of some of the intraoperative complications like shoulder pain and intraoperative hypotension, nausea, and vomiting were slightly higher in spinal anaesthesia group. A post-operative headache also was slightly higher in spinal anaesthesia group.

3. The incidence of postoperative nausea and vomiting was higher in general anaesthesia grou.

4. The operating time, operating conditions and post-operative stay were comparable between two groups.

Limitations: Since the study participant selection was not randomly done, the role of selection bias and the effect of potential unknown confounding factors and the magnitude and direction of their effect could not be estimated

Recommendations: There is a need for large-scale randomized controlled trials on the subject to generate more evidence on the subject to guide informed clinical decision making. Till such time the choice of anaesthesia should be made by carefully weighing the risks, benefits, cost of the procedure and patient preferences into consideration.

What this study adds to existing knowledge: The study further strengthens the evidence existing regarding the comparative efficacy and safety of spinal anaesthesia in patients undergoing laparotomy.

The study findings prove that the spinal anaesthesia can be used safely for laparoscopic cholecystectomy and achieve comparative efficacy, without any undue adverse effects. The study findings assume greater importance due to scarcity of studies on the subject in Indian population.

Author Contribution

Author 1: The first author has conceptualized the study, participated in developing appropriate study protocol, involved in all stages of the study from the design, data collection, data analysis, preparation and review of the drafts to submission of the manuscript for publication.

Author 2: The second author had provided a supportive role data collection, data entry. He had contributed to the preparation of the draft manuscript, editing of the drafts and also was involved in doing necessary modifications to the drafts as per reviewer'sinputs.

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Gender Differences on the Effect of Non-HDL-C on Blood Pressure, Blood Flow Velocities and Arterial Wall Thickness; An Observational Analysis in Madurai Population

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Gender Differences on the Effect of Non-HDL-C on Blood Pressure, Blood Flow Velocities and Arterial Wall Thickness; An Observational Analysis in Madurai Population.

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ABSTRACT

Background: Non-high density lipoprotein cholesterol has been shown to be a predictor of initial coronary heart disease events and arthrogenic. Women from Madurai have been shown to develop dyslipedemias from an early agerequiring surgical intervention when compared to women from other regions of India. This observational study was undertaken to find if the women had a higher risk for CHD when compared to men from the same region. **Methods:** 50 subjects (n=50) were inducted into this study with 26 (52%) of them were males and 24 (48%) of them were females.Patients with significant past history of major illness were excluded, including dyslipidemias, Diabetes mellitus, hypertension, myeloproliferative disorders, cardiac diseases and alcohol addiction. Blood lipid profile, Pulsed Doppler profile of right brachial artery blood flow velocities, Brachial arterial wall thickness, Blood pressure were measured. **Results:** In males there was significant correlation between Non HDL–C peak Systolic velocity (PSV), wall thickness (WT) and systolic Blood pressure (SBP) ($P< 0.01$) and End diastolic velocity (EDV) ($p<0.05$). Females in addition correlated significantly with diastolic blood pressure (DBP) ($p<0.05$) and without correlation with EDV. Total cholesterol (TC) in males were significantly correlated to PSV, EDV, WT and SBP ($p<0.01$). In females TC was significantly correlated to PSV, WT and SBP ($P<0.01$) and with DBP and Age ($P<0.05$). **Conclusion:** Our results show that females in Madurai develop higher risk for CHD from an early age than men because, Non-HDL-C was correlated significantly with SBP and DBP, SPV and WT, where as in men there was no correlation with DBP, and TC was additionally correlated significantly with DBP and Age in females and not in males. Early intervention with life style changes, Dietary modifications and exercise program may mitigate these risk factors for CHD.

Keywords: Arterial wall thickness, Blood flow velocity, Coronary Heart disease, Non-High density Lipoprotein.

INTRODUCTION

Non-high density lipoprotein cholesterol (Non-HDL-C) has been shown to be a predictor of initial coronary heart disease (CHD) events and also been associated with recurrent episodes of angina pectoris and nonfatal myocardial infarction (MI) in patients with multivessel coronary heart disease.[1,2] Non-HDL cholesterol is assessed by subtracting total cholesterol from HDL cholesterol which includes LDL cholesterol, very low-density lipoprotein (VLDL) cholesterol, intermediate-density lipoprotein (IDL) cholesterol, and lipoprotein (a) (LP(a)) all of which are circulating arthrogenic lipoproteins. Non–HDL cholesterol was shown to be an independent predictor of CHD regardless of the triglyceride level.[5] Several clinical studies have shown that arterial stiffness increases with age and hypercholesterolemia.[3,4] However non-HDL cholesterol affected arterial thicknessrather than arterial stiffness.[6-9] The increased arterial wall thickness(WT)is due to increase in the intima-media thickness (IMT).[7,10,11] Systolic blood pressure was found to be correlated with IMT.[12] In another study the IMT and End Diastolic velocity (EDV) in the carotid artery could jointly predict ischemic stroke. Significant and high correlations were found between Non-HDL cholesterol and systolic and diastolic blood pressure.[13] It is evident that CHD evolution is orchestrated by many interdependent factors and is more pronounced by the level of Non HDL-C. The National Cholesterol Education Program (NCEP) recommends that clinicians aim to

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reduce levels of non-high density lipoprotein (HDL) cholesterol as a secondary lipid-lowering target.[14] However there seem to be gender differences in lipid fractions and blood flow velocities, Women seem to have higher diastolic velocity components and lower systolic velocity components compared to men.[16] Madurai women have been show to develop dyslipidemias at an early age compared to men in the same region.[15] Accordingly this study was initiated to observe if there were gender differences in CHD risk factors particular Non HDL-C, blood pressure, Blood Flow Velocities and arterial wall thicknessto initiate an early intervention create and awareness in the more prone gender for CHD.

MATERIALS AND METHODS

All subjects who were inducted into this study were first time visitors to master health checkup clinic which is part of the OPD. 50 patients were included in this study of whom 26 were males and 24 were females. Medical history and personal data (blood pressure, weight, height and age) were recorded. Patients with significant past history of major illness were excluded,including dyslipidemias, Diabetes mellitus, hypertension, myeloproliferative disorders, cardiac diseases and alcohol addiction. Lipid profile, Ultra sonogram of the abdomen, were among the routine investigations of the master health checkup plan. Additionally for this study purpose blood flow velocitiesin the right Brachial artery weremeasured. Base line blood pressure was measured in the right upper arm in sitting position. For statistical purposes males and females were separately subdivided into four groups based on their age. Group 1 (age 22-32) Group 2 (age 33 to 42) Group 3 (age 43 to 52) Group 4 (age 53 to 62). The mean of individual variables from each group was graphically represented for comparison between male and female.

Pulsed Doppler sonographic measurements were carried out at the distal one-third of the right brachial artery, 1-2 cm proximal to the antecubital fossa while the subjects were in a lying position with the arm slightly abducted and the hand unclenched. The study was done in GE voluson P8 ultrasound machine (GE Medical Systems ,Milwaukee, U.S.A) using high frequency linear probe (7 -12 MHz) . B mode examination of vessel wall thickness , calcification and plaques were documented.The equipment was adjusted for filtering and gain to yield the most detailed information with no artifacts. The Doppler insonation angle was set under 60 degrees during velocity measurements. Flow parameters such as peak systolic maximum velocity (PSV) and enddiastolic minimum velocity (EDV) of each subject were measured .

For statistical analysis SPSS version 21 and Excel 2010 were used, Pearson's correlation was calculated for significance. P value < 0.05 was considered significant. Early intervention in women with life style changes

RESULTS

Table 1: Demographic details of respondents.

Demographic variables	Frequency (n)	Percent (%)
Gender		
Male	26	52.0
Female	24	48.0
Age group		
22-32	14	28.0
33-42	13	26.0
43-52	14	28.0
53-62	9	18.0

Table 2: Relationship between blood flow velocities, Wall thickness and cholesterol parameters of male respondents

	BA PSV	BA EDV	Wall thickness	Systolic BP	Diastolic BP	Age
TC	.728**	.510**	.598**	.812**	0.382	0.35
HDL	0.201	0.209	.468*	0.302	0.14	.437*
Non HDL	.722**	.501*	.567**	.816**	0.365	0.336

**P<0.01, *P<0.05

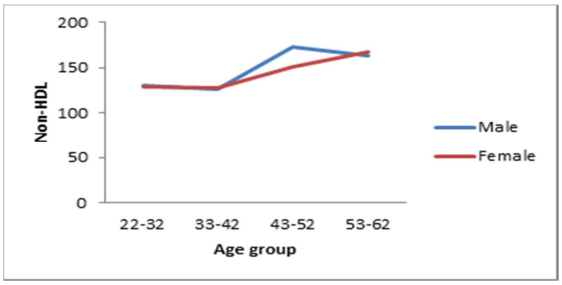

Figure 1: Gender wise non-HDL levels.

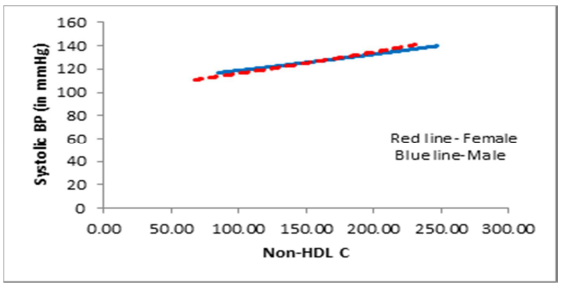

Figure 2: Gender wise relationship between Systolic Bp and Non-HDL C.

Statistical analyses are carried out in SPSS 20 version and MS-Excel. Percentage analysis is computed for demographic information of respondents and Pearson correlation analysis is used to ascertain the linear relationship between two variables.

50 subjects (n=50) were inducted into this study with 26 (52%) of them were males and 24 (48%) of them were females. Based on their age the maximum participants were found in 22-32 years age group and 43-53 years age group (28 % each) followed by

33-42 years age group (26 %) and 53-62 years age group (18 %) [Table 1].

Association between Non HDL–C and PSV, EDV, WT, SBP, DBP, Age

Non HDL–C in males correlated significantly with peak Systolic velocity (PSV) , wall thickness and systolic Blood pressure (SBP) (P< 0.01) and with Peak diastolic velocity (EDV) (p<0.05). Non HDL–C in females correlated significantly with peak Systolic velocity (PSV) , wall thickness (WT) and systolic Blood pressure (SBP) (P< 0.01) and with diastolic blood pressure (p<0.05).

Association between HDL–C and PSV, EDV, WT, SBP, DBP, Age

HDL-C in males correlated with wall thickness and age (P<0.05) and no correlations were found between HDL-C and wall thickness and age in females.

Table 3: Relationship between blood flow velocities, Wall thickness and cholesterol parameters of female respondents

	BA PSV	BA EDV	Wall thickness	Systolic BP	Diastolic BP	Age
TC	.565**	0.399	.576**	.631**	.480*	.406*
HDL	-0.094	0.119	0.112	-0.172	-0.069	0.058
Non HDL	.588**	0.372	.551**	.672**	.497*	0.393

**P<0.01, *P<0.05

Association between TC and PSV, EDV, WT, SBP, DBP, Age

Total cholesterol (TC) in males were significantly correlated to PSV, EDV, WT and SBP (p<0.01). In females TC was significantly correlated to PSV, WT and SBP (P<0.01) and with DBP and Age (P<0.05). [Table 2 & Table 3].

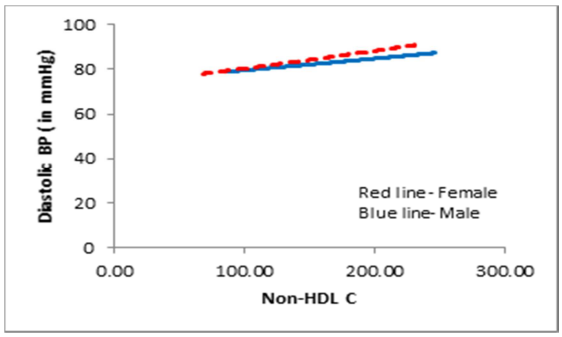

Figure 3: Gender wise relationship between Diastolic Bp and Non-HDL C

DISCUSSION

To our knowledge this is the first prospective study to investigate the relationship between NonHDL-C and PSV, EDV, WT, SBP and DBP. Wall thickeningat the early phase of atherosclerosis is related to atherogenic lipoproteins.In the males subjects increases in the Non HDL –C increased the wall thickness, resulting in increased SBP and both PSV and EDV. There was no relationship with DBP and Age. In contrast in the female subjects the Non HDL –C increased the arterial wall thickness, and increase of SBP, DBP and PSV. However it was not related to EDV or age [Table 2, 3]. Shear stress has been implicated in the pathogenesis of atherosclerotic lesions. Increase in blood pressure increases blood flow velocity which increases the momentum of RBC on the arterial wall increasing sheer stress resulting in intimal deposition of cholesterol into the wall leading to atherosclerosis.[19] Also hemodynamic alterations requiring an increase in blood pressure may provoke adaptive vascular remodeling and the attendant lower compliance of the vessel wall leading to lipoprotein efflux across the arterial wall and the development of atherosclerosis in the presence of dyslipidemia.[17,18] This indicates that the female subjects from Madurai seem to have a higher risk for CHD than men because SBP, DBP and PSV were in positive correlation with Non HDL-C compared to men where there was no correlation between non HDL-C and DBP [Figure 3].

When Mean Non HDL –C values were compared between male and female groups [Figure 1] the female show a steady increasing trend with Non HDL-C levels from an early age (33 to 42). Whereas men show a decreasing trend from Middle age (43 to 52).Total cholesterol increased with age along with SBP, DBP.PSV and WT in females the same was not evident in male where the total cholesterol did not increase with age and DBP. These findings indicate that the women from Madurai have a higher risk for CHD than men beginning at an early age, which agrees with our findings from our previous study where women require surgical cardiovascular intervention as compared to other women in India.[15]

Limitation

This study has a few limitations, Firstly this is an observational study and the sample size is very small. A study with larger population may yield better results for intervention. Secondly this study was performed only on population from Madurai district where generalizations are not justified. Finally the PSV and EDV were measured only once by experienced radiologist with good precision, we did not observe for the reproducibility of data.

CONCLUSION

Our present study observes that the female population develops risk for CHD at an early age compared to men from Madurai district. We recommend that women from this region be educated regarding their increased propensities for CHD risk and advised early lifestyle therapy with

dietary modification with a robust exercise regimen. A reduction in total calories, with brisk walking for weight reduction may be feasible in working women. omega-3 fatty acid-containing capsules should be provided for those women who cannot afford diets rich in omega-3 fatty acid. This may be included in the Governmental health care policy in CHD prevention programs.

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Sonographic Evaluation of Spectrum of Breast Diseases-A Study in a Tertiary Care Hospital of Southern Tamil Nadu.

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ABSTRACT

Background: Breast carcinoma has become one of the leading causes of death among women. Early clinical detection of breast carcinoma through screening has led to the detection of the tumor at a relatively earlier clinical stage, which definitely reduced the mortality. Breast ultrasonography (US) has gained widespread acceptance as a diagnostic tool for the evaluation of human breast disease and the ultrasound guided fine needle aspiration biopsy (FNAB) as the preferred method of tissue sampling. The present study aims to observe the diagnostic accuracy of US, in the assessment of breast masses compared to pathologic findings. **Methods:** This analytical, retrospective study was conducted on 246 patients that were referred for US scan in a tertiary care hospital of southern Tamilnadu, between January to December 2017. 110 breast masses from 246 patients were evaluated with US & US guided FNAB. BI-RADS US criteria combined with pathological findings were correlated in differentiation between benign and malignant masses. Sensitivity, Specificity & Accuracy were derived for US. **Results:**In our study the Sensitivity, Specificity, Positive predictive value (PPV) & Negative predictive value (NPV) of US, in detecting malignant breast nodule, was found to be 94%, 97.67%, 98.43% and 91.30% respectively. The overall accuracy of US in detection of benign & malignant breast nodule was found to be 95.45%. **Conclusions:** BI-RADS criteria combined with US guided FNAB, well correlated with pathological findings, increases the rate of detection of Breast cancer and reduces the number of unnecessary surgical & radiological procedures and the overall cost of medical care.

Keywords:Breast disease, Breast Carcinoma, BI-RADS, Mammography, Sonomammography, Ultrasonography.

1

INTRODUCTION

Breast lumps are common problem affecting females, which require proper workup, early diagnosis and treatment. Although most detected masses are benign, every woman presenting with breast mass should be evaluated to exclude or establish diagnosis of carcinoma.

Over 100,000 new breast cancer patients are diagnosed annually in India and according to WHO (2012) an estimated 70218 women died due to breast cancer.[1-3]

The established management of palpable breast lesions includes the triple assessment, which includes Physical examination, Imaging and Fine needle aspiration or core biopsy.[4]

US is currently considered the first-line examination in the detection and characterization of breast lesions including the evaluation of breast cancer.[5]

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For symptomatic women, US is the primary modality for the evaluation of palpable masses in younger women. In pathologic nipple discharge, for detection of intraductal mass or hypoechoic irregular subareolar mass, differentiating between intraductal papillomas and carcinoma in situ and invasive cancer, US is a useful diagnostic tool, superior to mammography and may be worth including in the routine evaluation.[6]

According to a multicenter trial of combined screening with mammography and US (ACRIN 6666),[7] that reported higher cancer detection in high risk women who underwent annual US screening in addition to mammography compared to those that underwent mammography alone, the combined screening detected an additional 4.2 cancers per 1000 women.[8]

High-resolution US, is a useful modality that helps to additionally evaluate breast lesions and also helps to characterize a mammographically non-detected palpable abnormality in dense breast.[9] Women with dense breasts run a four- to six-fold higher risk of developing breast cancer than other women.[10]

The high-prevalence of US-only detected carcinoma and tolerance of US scanning in women makes US screening implementation possible. Furthermore, the standardized scanning and BI-RADS interpretive criteria proved to be practicable for independent performance and interpretation and could be used for further implementation.

Hence, the aim of this study is to assess the value of US & US guided FNAB in evaluating breast masses, to compare it with Pathology results, and to evaluate its potential role in differentiating benign from malignant breast disease.

MATERIALS & METHODS

An electronic medical record search in Hospital Information System (HIS) at Velammal Institute of Medical Sciences and Research Institute hospital, Madurai, southern Tamilnadu, India, a large tertiary care referral hospital for patients referred for US to rule out Breast lesions, between January 2017 to December 2017, identified 246 patients.

All Patients irrespective of age and sex with clinically suspected breast lesions, palpable lump, breast complaints like nipple discharge, retraction, skin thickening were included in the study. Of the study group of 246 patients, 243 were female and 3 male. 2 male patients aged 24 & 30 years with BIRADS category 1 and another 76 years male patient who had proliferative breast disease (BIRADS 2) was eliminated from the study. Age of the patients ranged from 17 years to 82 years. The mean age of the patients was 47 years.

Among the 243 patients, 133 patients whose US were normal (BI-RADS category 1) or who did not undergo FNAC/ HPE were excluded from the study. The study was approved by the Ethics Committee and informed written consent was obtained from all patients.

One hundred & ten patients with one or more breast mass (BIRADS 2-6), who underwent US and US guided FNAB were enrolled in this retrospective study. Findings of Clinical examination, US examination and US guided FNAB were recorded for each participant.

All of the US examinations and US guided FNAB were performed by qualified radiologist using a linear array transducer 4-12 MHz (Voluson S6, S8 GE). Certain aspects of sonographic technique are unique to US examination of the breast, such as proper application of compression, transducer positioning, and image labeling. In order to stabilize, center, and thin out the breast tissue, the conventional position for breast US examination places the patient supine with the arm of the side being examined raised above the head. With larger breasts, a degree of elevation under the shoulder blade may be required in order to center the breast. This can best be accomplished with a foam wedge or roll of towels or sheets.

Scanning is performed with the degree of compression necessary to penetrate to the area of interest and eliminate superficial artifact. Scanning in the plane of ductal anatomy can be achieved by scanning in the radial and antiradial planes. Radial scanning is performed with the long axis of the transducer oriented along the long axis of the ductal and lobar anatomy (nipple to periphery of the breast in a branching pattern) and antiradial in the orthogonal plane (from the periphery of the breast inward toward the nipple).

Transverse and sagittal plane scanning are acceptable in the initial survey, and if a lesion is detected, radial and antiradial scanning are recommended, as the margins and extension of the mass may be better displayed and this approach increases the potential for finding other masses within the same ductal system . The position of the lesion should be labeled on the image according to the mammographic clock, noting distance from the nipple or areolar margin. It is important that this information be labeled on each image to ensure appropriate follow-up or localization for biopsy.

US findings were categorized according to the Breast Imaging Report and Data System (BI-RADS) lexicon using the following tumour classification,[11]: Shape (oval, round or irregular), orientation (parallel to the skin surface or not), margin (circumscribed or not, indistinct, angular, spiculated or microlobulated), echo pattern (anechoic, hypoechoic, hyperechoic or complex), posterior acoustic features (none, enhancement or shadowing), surrounding tissue change (absent or present), vascularity (none, focal or penetrating flow, or diffusely increased flow), presence of associated calcifications (none or microcalcifications in or out of a mass).

The BI-RADS lexicon requires the breast imaging report be summarized into 1 of 7 possible categories,[12]

BI-RADS 0 - Further assessment required;

BI-RADS 1 -Negative study;

BI-RADS 2- Benign finding (risk of malignancy similar to that of the surrounding parenchyma);

BI-RADS 3- Probably Benign finding (less than 2% risk of malignancies should be followed up at 6, 12, and 24 months, and then classified as benign category 2 after showing stability for 24 months or biopsied if concerning changes or growth are seen);

BI-RADS 4- lesion is Suspicious for Malignancy (biopsy is offered);

BI-RADS 5- lesions are Highly suggestive of Malignancy; and

BI-RADS 6- lesions are Biopsy-proven Malignant before surgery is obtained (it is suggested that appropriate actions should be taken for these categories).

"Positive" category were all those who had BI-RADS assessment category 4, 5 and 6. "Negative" category were all those with BIRADS assessment category 0, 1, 2 and 3.

All patients underwent pathological assessment either by FNAC or biopsy or both. Biopsies included either core biopsy or surgical excision biopsy. Surgical specimens had been fixed in 10% formaldehyde solution and cut into serial 5-mm thick slices. Histo-pathological slides in each tumor were reviewed by a pathologist independently. The cytology reports were classified as benign, suspicious for carcinoma, malignant, or inadequate. Histology was performed if cytology was suspicious or suggestive of malignancy.

BI-RADS criteria combined with US guided FNAB, were correlated with pathological findings to determine the Sensitivity, Specificity and Accuracy of the Sonographic examinations.

After the pathological assessment patients were reviewed in the out patients clinic with their pathology report to plan any further treatment.

RESULTS

In present study 243 breasts were examined amongst which 110 cases were included, rest of the cases were normal or failed to follow-up and refused for consent. Of the remaining consecutive 110 cases (BIRADS 2 to 6) were evaluated clinically, by sonomammography & FNAB. In this study the age range of patients presenting with breast lesions was 17–82 years with mean age 49.6 years. BIRADS Category score of patients in the study with reference to Age is depicted [Table1].

Table 1: BIRADS Category score of patients in the study with reference to Age.

Birads Score	Age group in years								Total
	10-19	20-29	30-39	40-49	50-59	60-69	70-79	>80	
0	0	0	0	0	0	0	0	0	0
1	1	18	33	31	24	21	5	0	133
2	1	3	8	9	4	4	2	0	31
3	1	1	2	5	3	0	0	0	12
4	1	1	0	4	2	0	1	0	09
5	0	1	3	20	12	10	9	2	57
6	0	0	0	1	0	0	0	0	01
Total	4	24	46	70	45	35	17	2	243

Age prevalence showed less than 2.7 % of patients in the age group of 10-19 years and 10.9 % of patients above the age group of 70 years were affected. Our study showed that 80% of breast lesions occurred in the age group of 40 years & above, the remaining were younger than 40 years. Most lesions were found in the upper outer quadrant and the right breast was affected more than the left in 55 lesions (50%) & bilateral lesions (19%) were detected in 21 women. Amorphous micro-calcifications were detected in 1 US test (0.9%).

Fifty seven lesions (51.81%) were assigned BI-RADS 5 category. The second most common category was BI-RADS 2 in 31 lesions (28.18%).

The patients with malignant disease underwent surgery. The surgical & histo-pathological findings were positive for carcinoma breast in 64 patients (58.18%) [Table2].

Table 2: Sonographic diagnosis of Carcinoma Breast compared with pathologic findings.

Sonography	Pathology		Total
	Negative	Positive	
Positive	4	63	67
Negative	42	01	43
Total	46	64	110

Among the total patients, 55 were diagnosed histopathologically as Infiltrating ductal carcinomas (IDC), 5 Poorly differentiated carcinoma, 2 Invasive mucinous carcinomas (IMC) & 2 Metaplastic carcinoma [Figure 1-3].

There were total of 46 benign (41.81%) cases, Fibroadenoma (17) being the commonest, followed by Fibrocystic disease (12), Mastitis (6), simple Cysts (4), Duct ectasia (2), Phylloides (2),Galactocele (2) and least being Papilloma (1) [Figure 4-6]. On pathological examination 1 benign case of fibroadenoma turned out to be malignant. A case of papilloma and 3 cases of fibroadenoma were misdiagnosed as malignant.

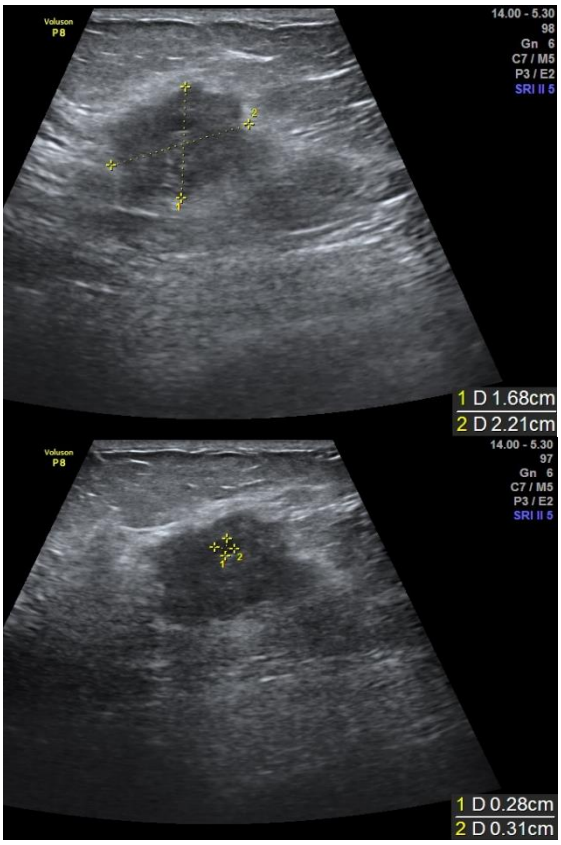

Figure 1(a,b): 40 years old female with infiltrating ductal carcinoma (IDC). US image reveals a hypoechoic mass that is Wider than taller, lobulated borders, internal tiny cystic component, peripheral marginal acoustic shadowing & no evidence of echogenic capsule.

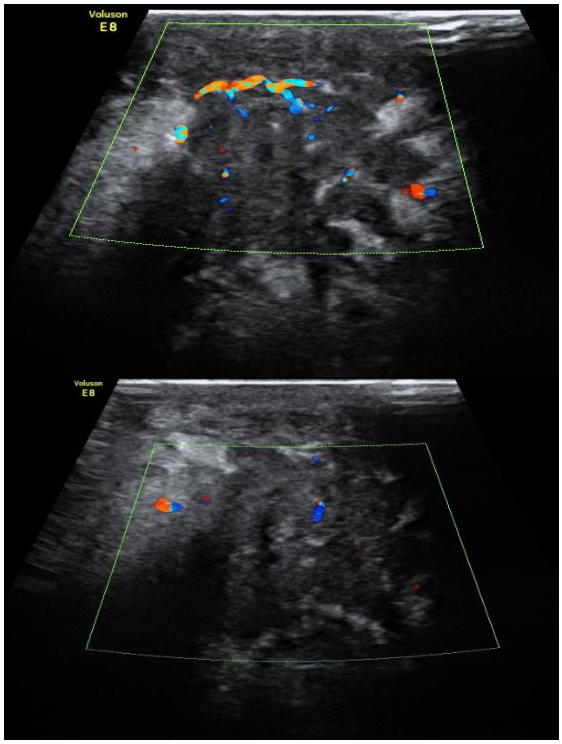

Figure 2(a,b): 71 years old female with Infiltrating ductal carcinoma. CDUS shows an irregular hypoechoic mass lesion with increased peripheral & central vascularity.

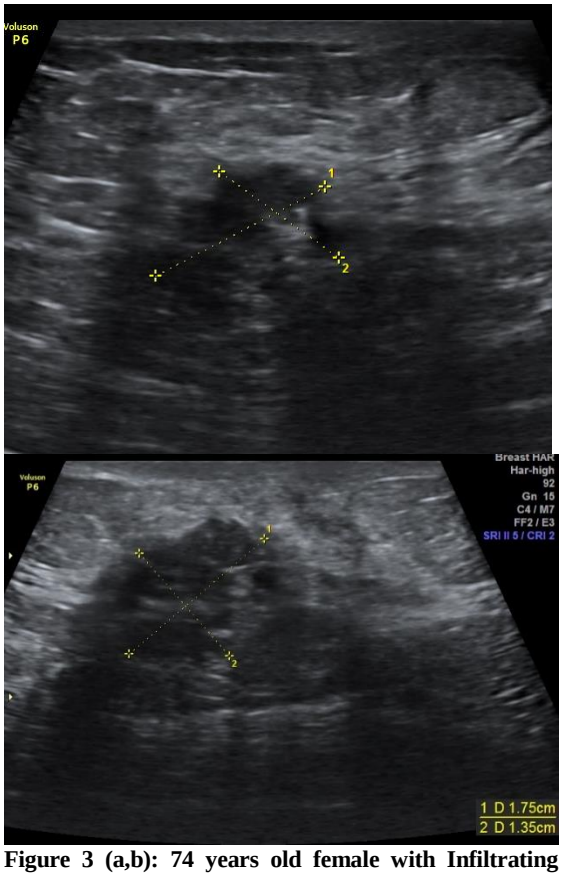

Figure 3 (a,b): 74 years old female with Infiltrating mucinous carcinoma(IMC). US shows lobulated heterogenous hypoechoic solid mass with tiny eccentric cystic components and peripheral acoustic shadowing.

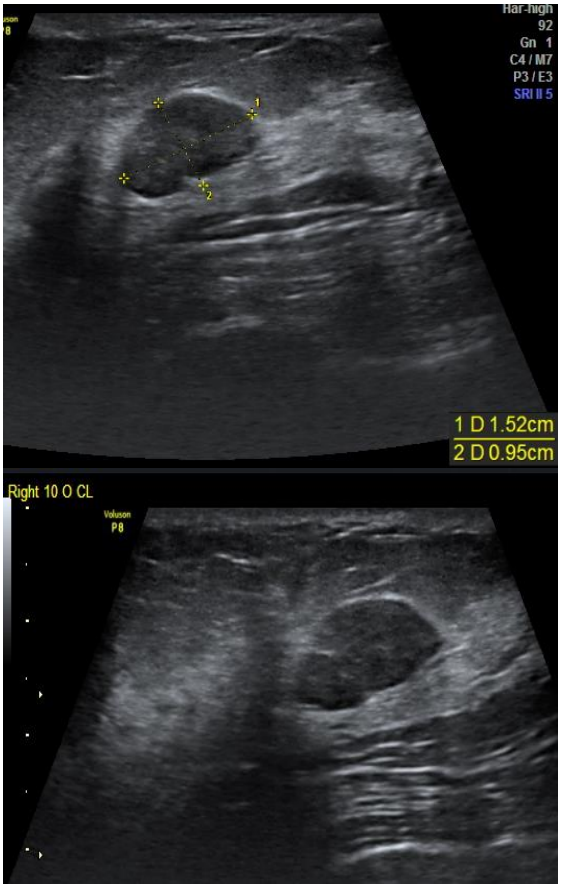

Figure 4 (a,b): 31 years old female with Fibroadenosis. Transverse sonographic image, showing an oval shape, hypoechoic mass with thin, echogenic capsule in right upper outer quadrant at 10'o clock position.

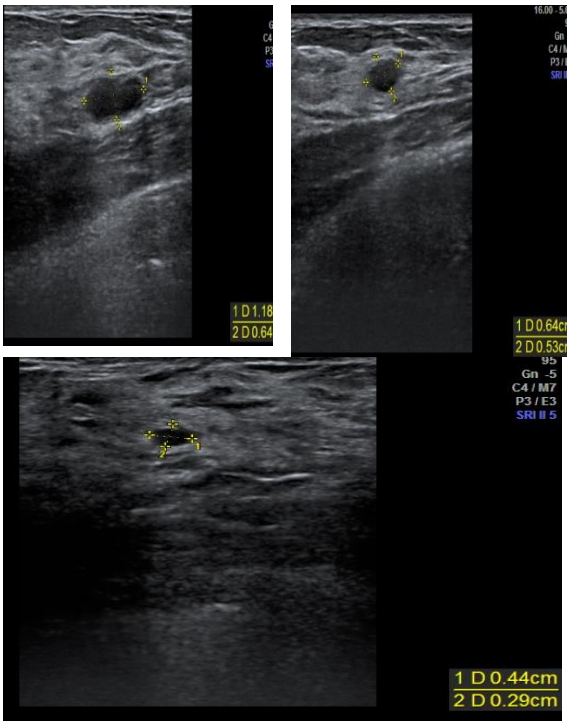

Figure 5 (a,b,c): 37 years old female with Fibrocystic disease.US images shows multiple tiny hypoechoic solid lesions & anechoic cysts.

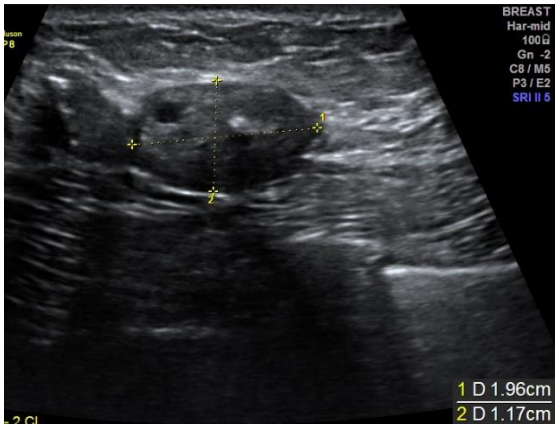

Figure 6: 44 years old female with Fibroadenoma. Transverse sonographic image, showing an oval shape, hypoechoic mass with thin echogenic capsule.

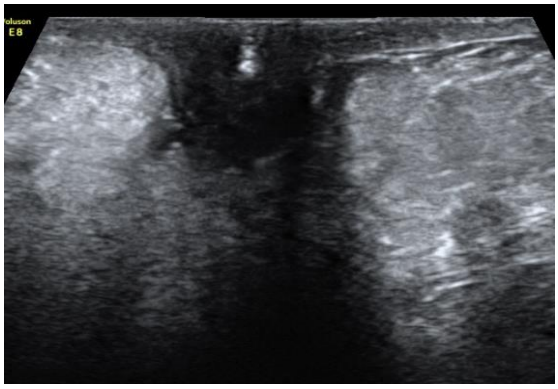

Figure 7: 57 years old female with acute suppurative inflammation. Transverse US image shows hypoecoic collection with thickened overlying skin & subcutaneous tissues.

Diagnostic role of US was evaluated by calculating Sensitivity, Specificity, Positive predictive value, Negative predictive value and overall diagnostic Accuracy using standard formulae and values obtained [Table 3 &4].

Table 3: Results of Sonographic studies in diagnosis of Breast Disease.

Breast disease	Proven on Histopathology	Sonography			
		True Positive	True Negative	False Positive	False Negative
Benign	46	42	63	4	1
Malignant	64	63	42	1	4

Table 4: Parameters depicting comparison of Benign & Malignant lesions by Sonography.

Sonography	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
Benign	97.67	94	91.30	98.43	95.45
Malignant	94	97.67	98.43	91.30	95.45

On the basis of the final diagnosis, the Sensitivity, Specificity & Positive predictive value of Sonography in detection of Malignant breast disease were 94 %, 97.67 % & 98.43 % respectively and Prevalence of 60.9% [Table4 & 5].

Table 5: Comparison of Sonomammographic results in different studies.

Study	Sensitivity (%)	Specificity (%)	Accuracy (%)
Texidor HS et al [13]	95.7	89.2	-
Taori K et al 2013 [15]	-	86.9	92.7
R E Mohamed et al 2014 [14]	92	90.24	91.03
Kumar et al 2016	85.45	89.31	82.7
Present study 2017	94	97.67	95.45

In conclusion, in our study Sonography was found to have a high Negative Predictive Value of 91.3 % for the exclusion of Carcinoma breast & Accuracy of 95.45% [Table4 & 5].

DISCUSSION

Breast cancer, the most frequently diagnosed and leading cause of death among women accounts for 23% of all cancer cases and 14% of cancer deaths globally,[17,18]whereas breast cancer in men accounts for only 0.7% with tremendous socio-economic, emotional,[19] and public health implications.

Benign breast disease is far more common than breast cancer. 50% of women will develop some form of benign breast disease during their lifetime. However, 1 in 9 of those presenting with a breast lump will be diagnosed as breast cancer.[20] Since it is not as yet preventable, its early detection gives the patient the best chance of a cure. Hence, breast screening programs have been implemented in many parts of the world.

The risk factors for breast cancer are numerous and can essentially be divided into hormonal, non-hormonal and genetic risk factors.[21] Patients with a benign lump but having a family history of breast cancer also have an associated increased relative risk for cancer. 50% of breast cancer patients do not have any specific risk factors.[21]

In our study, the enrolled women were with a wide age range between 17 and 82. The mean age was 49.6 years old. This study is similar to study by starves et al,[34] were mean age of the women was 47 years, with a range of 18-88 years and near similar to studies of Ayoade BA et al & Siddiqui MS et al,[22,23] were age range of 14-70 and mean age of 41years were reported.

In our study eighty eight women (80%), were aged 40 years and above & the remaining were younger than 40 years. Most of the patients with benign

lesions (32.55 %) and malignant breast lesions (37.31%) according to BI-RADS assessment were within the age range of 40-49 years. This finding is in agreement with the results of Okobia et al,[24] where they found patients with malignancy to be from the 4th decade of life.

The mean age of patients in the two benign and malignant groups in our study were 43.41 years and 54 years respectively , which is similar to study by Ozdemir A et alwho have reported significantly older age among the malignant breast lesions compared with the benign group.[31]

Patients with palpable breast lesion commonly present for radiology evaluation. Various imaging techniques like Mammography, Ultrasonography, MRI, Scintimammography, CT and PET are now available.

Mammography is primary method of detection and diagnosis of breast disease with sensitivity of 85%-95%.[25] The specific mammographic features of the breast mass help in diagnosis. Benign lesions show round to oval shape, well defined margins, few lobulations, low soft tissue density and fat containing lesions. Malignant lesions are high soft tissue density, irregular margins, multiple lobulations and spiculations with or without microcalcifications.[26]

Mammography is nearly 87% accurate in detecting cancer,[27,28] its specificity is 88% and its positive predictive value may be as high as 22%.[28] But the false negative findings in mammography in evaluation of palpable breast mass is high, estimated between 4% & 12%.[29,30] Hence many of the times, other modalities are needed to compliment the primary diagnosis given on mammography. A study has shown that using ultrasound in addition to mammography increases the sensitivity to 77.5% compared to that of mammography alone (50%) in women with dense breasts and increased risk of breast cancer.[31]

However, for screening, US is increasingly used to detect early breast cancer worldwide. The success of supplementary screening US might be attributed to the low cancer detection rate of conventional mammography in the dense breast population. Several studies have already shown that US can demonstrate small, non-palpable, invasive cancers that are not seen on mammography.[32-34] US is less sensitive, however, than mammography or MRI in the detection of ductal carcinoma in situ.[35-37]

Breast cancer in women younger than 40 years is rare and typically presents symptomatically. For symptomatic women, US is the primary modality for the evaluation of palpable masses in younger women.

Previous studies demonstrated that the following US features such as oval or round shape, parallel orientation, circumscribed margins, abrupt interface, enhancement or absence of posterior acoustic features, absence of surrounding tissue alterations represented a benign breast lesion [Figure 4-6], whereas, irregular shape, non-parallel orientation, echogenic halo, posterior acoustic shadowing and abnormalities of the surrounding tissue regardless of echo pattern were considered to be consistent with a malignant lesion [Figure 1-3].[38,39] It is also true that not all carcinomas fulfill these criteria and some do only partially.[39]

The BI-RADS in this study accurately predicted 43 benign breast lesions (39%) and 67 malignant lesions (60.9%), while histopathology identified 46 benign breast lesion (41.8%) and 64 malignant lesions (58.18%). The difference may be attributed to the limitation of relying purely on morphological appearances.

Infiltrating ductal carcinoma (IDC) and ductal carcinoma in situ (DCIS) represent 85% of malignant breast tumors.[40]Typically, infiltrating ductal carcinoma presents as a spiculate, irregular or focal asymmetrical mass, while ductal carcinoma in situ presents as pleomorphic or linear microcalcifications.[41]In our study IDC represented 85.93%, similar to the study by Khomsi F et al.[40]

Prognosis is unfavorable in cases of isolated IDC. Some histological types of breast tumors such as medullary carcinoma, mucinous carcinoma and tubular carcinoma are associated with a better prognosis.

US BI-RADS assessment from our study, has Sensitivity of 94%, Specificity of 97.67%, Positive predictive value (PPV) of 98.43%, Negative predictive value (NPV) of 91.10% and Accuracy of 95.45% in detection of breast carcinoma, which were similar to the results of R E Mohamed et al of 92%, 90.24%, 87.88%, 93.67% and 91.03% respectively and comparable to the results of Texidor HS et al with sensitivity 95.7%, specificity of 89.2% and accuracy of 92.7% by Taori K et al [Table5].

In a study by Jaipal R Beerappa et al,[42] the overall sensitivity, specificity & accuracy of US was 89.45%, 90.31% & 88.17%, which nearly correlates with our study of 95.83%, 95.83% & 95.45% respectively [Table5]. High prevalence (60.9%) of malignant breast disease in this region may be attributed to low socio-economic status of the population. Sensitivity of sonomammography in detecting benign lesions were high because small cysts and fibroadenomas are better seen even in dense breasts and US differentiates cyst from solid lesions. Specificity of US in detecting malignant lesions was less as microcalcifications were not well seen in US. These observations are similar to results of Texidor SH et al [Table5]. When histopathology results were compared with that of BI-RADS predictions in this study, no statistically significant difference was observed.

The use of color Doppler ultrasonography (CDUS) for characterizing breast lesions has increased in recent years. The presence and distribution of blood vessels associated with malignant lesions is visualized by CDUS [Figure 2]. Doppler criteria

such as resistive index (RI), pulsatility index (PI), and flow velocity are used to distinguish benign from malignant lesions.

Real-time ultrasound elastography (RTE) is a non-invasive dynamic imaging technique that assesses the strain of soft tissues and provides structural information other than the morphologic features shown by conventional B-mode US.[38] It can differentiate between benign and malignant lesions based on their elasticity. Benign lesions have elasticity similar to the surrounding tissue, while malignant lesions are harder than the adjacent tissue.[43] A 5-score system was described by Itoh et al,[43]to classify elastographic findings that can be easily correlated to the American College of Radiology (ACR) BI-RADS.

Contrast US seems to be a reliable method to differentiate breast lesions, because it provides typical enhancement patterns and perfusion curves, correlate well with MRI wash in & wash out curves. Rapid contrast uptake and rapid washout distinguishes benign from malignant lesions.[44]

New technical developments, such as three-dimensional (3D) US, computer-aided diagnosis (CAD) & automated breast US (ABUS) are now available on some machines.

Several new minimally invasive procedures, including radiofrequency ablation, interstitial laser ablation, focused US ablation, cryotherapy, and vacuum-assisted devices are currently under investigation and may provide treatment options that are comparable with that of traditional surgical therapies.[45]

US has a significant role in the postoperative assessment of patients with breast cancer. It is helpful in evaluating postoperative recurrent breast masses and postsurgical complications, such as seroma, infection and fat necrosis, as well as exclusion of recurrent disease.

MR Mammography can be useful in detecting distant, multifocal, or multicentric lesions when there is no clinical sign or suspicious mammographic finding. For diagnosis and evaluation of tumors of the nipple and retroareolar tumors, MR imaging has higher sensitivity than mammography. It also shows nipple involvement even when it is clinically unsuspected.[46] Contrast-enhanced breast MR imaging is known to help identify foci of cancer that are not detectable at physical examination, mammography or US.

CT & MRI has a major role in staging of locally advanced breast cancers. US is limited to detect the lesions with less than 1 mm in diameter ,whereas combined modalities such as US, CT and MRI increase the accuracy of detection from 86.4 to 93.8%.[47] Therefore, it has become very important that a variety of imaging modalities has been used for examining tumor extension and multifocality in breast cancer patients.

Scintimammography using 99mTc-sestamibi is a noninvasive and painless diagnostic imaging method that is used to detect breast cancer when mammography is inconclusive.

2-[fluorine-18]fluoro-2-deoxy-d-glucose (FDG) positron emission tomography (PET) / CT may have limited diagnostic value for detecting small primary breast tumors, well-differentiated breast cancer, or regional lymph node involvement, but it is superior to conventional imaging modalities for detecting distant metastases and recurrences and for monitoring the response to therapy. The most important advantage of FDG PET or PET/CT compared with other imaging modalities is the capability of detecting unsuspected distant metastases during a single whole-body examination.[48]

The American Joint Committee on Cancer (AJCC) staging system for breast cancer (7th edition) provides a tumor-node-metastasis (TNM) classification scheme for breast cancer that is important for determining prognosis and treatment.

Radiologic information that may alter stage, prognosis, or treatment includes tumor size; number of tumor lesions; total span of disease; regional nodal status (axillary levels I–III, internal mammary, supraclavicular); locoregional invasion (involvement of the pectoralis muscle, skin, nipple, or chest wall); and distant metastases to bone, lung, brain, and liver, among other anatomic structures. High-risk patients are screened for occult metastases with chest radiography, abdominal US, and bone scintigraphy, although the use of CT, MR imaging, and FDG PET is increasing .The staging information will help in choosing between breast conservation and mastectomy, preoperative and postoperative chemotherapy or hormonal therapy, sentinel lymph node biopsy (SLNB) and axillary lymph node dissection (ALND), and radiation therapy.[49]

Limitations

The study was done in a tertiary referral hospital, as a result some of the cases were already advanced at the time of evaluation. There was more number of malignant cases than benign for the same reason. Only patients attending the hospital were enrolled. It is not possible to know how many patients with a lump did not attend the hospital. It was not possible to do statistical analysis for all risk factor variables in this study. Despite these caveats the major aims and objectives of the study was achieved.

CONCLUSION

Ultrasound (US) has a significant role in diagnostic breast imaging. It is most commonly used as an adjunctive test in characterizing lesions detected by other imaging modalities or by clinical examination. US is recognized as the modality of choice in the evaluation of women who are symptomatic and

younger than 30 years of age, pregnant, or lactating and for guiding interventional breast procedures.

BIRADS US criteria combined with US guided FNAB, well correlated with pathological findings, increases the rate of detection of Breast cancer and reduces the number of unnecessary surgical & radiological procedures and the overall cost of medical care.

Elastography, 3D, CAD US, and automated whole-breast screening US are techniques that may have an impact on future clinical performance.

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