EDITORIAL

The COVID-19 Pandemic and Research in Resource-Limited Settings

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In December 2019, distant murmurs were heard of a possible zoonotic virus somewhere in a wet-market in Wuhan, China. Subsequently, alarm bells began to ring when the first human-to-human transmission of a novel Coronavirus was reported in January 2020.[1] Pakistan reported its first case on February 26th[2] and found itself in the midst of the global pandemic of the SARS-CoV-2, Covid-19. In Pakistan, like every other country, health-care workers have found themselves in the eye of the storm; as this editorial is being written, approximately 249,000 cases have been diagnosed and more than 5000 have succumbed to the pandemic.[3] Like the rest of the world, we also lived through an early scramble to save lives and obtain the basic needs for patients e.g. a face mask or oxygen, yet the importance of local research could not be and, even now, cannot be underscored enough to go hand-in-hand with the clinical needs of patients. Chinese doctors and scientists spearheaded Covid-19 research published by some of the leading journals such as The New England Journal of Medicine & The Lancet.[4-8] The commendable decision to share Covid-19 research via the net with open access has provided doctors all over the world with ever-evolving tools and insights to diagnose better, treat better, protect better and ultimately save more lives. The commendable decision to share Covid-19 research via the net with open access has provided doctors all over the world with ever-evolving tools and insights to diagnose better, treat better, protect better and ultimately save more lives. In recent weeks, the early recovery but lack of mortality benefit of hospitalized patients with Remdesivir,[9] In recent weeks, the early recovery but lack of mortality benefit of hospitalized patients with Remdesivir,[9] the mortality benefit of low dose Dexamethasone in severely ill patients[10] and the potential of aerosol transmission[11] are just some of the data which have helped better manage patients and understand the biology of the virus. the mortality benefit of low dose Dexamethasone in severely ill patients[10] and the potential of aerosol transmission[11] are just some of the data which have helped better manage patients and understand the biology of the virus. By now, it is clear that Covid-19 has geographical variations even within countries. Preliminary data shows that the approximate death rate per million of population at 24 in Pakistan, is considerably lower than that in both Italy and UK: 578 and 660 respectively[12] - even though health-care facilities in these countries are some of the best in Europe. Why so? Why the decline in cases in Lahore and Punjab whereas the disease continues elsewhere in the country at elevated rates? What are the manifestations in children? What is the psychological impact of the disease?

These are just some of the questions which can only be answered by fact-finding, scientific and methodical investigation and analyses. In Pakistan, research for Covid-19 requires organization, motivation and ethical considerations more than state-of-the-art medical facilities. Medical students, an untapped resource, have contributed to the research effort in many countries afflicted with dwindling man-power of health-care professionals during the epidemic. Irrespective of resources, now more than ever, local health-care professionals need to initiate a scientific inquiry into Covid-19 to better understand the disease and its myriad implications. In the long run, this is the only way to mitigate the human, psychological and economic impact in Pakistan. Shying away from problems, waiting for miracles, first-world resources and borrowed solutions are never the answer; research is.

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OBITUARY

HAFIZ MAQSOOD ALI, FCPS

On behalf of faculty of SIMS, we pass our deepest condolences on the sudden demise of our highly intelligent and professionally competent anesthesiologist Dr. Hafiz Maqsood Ali . Recent pandemic COVID - 19 has snatched a genius, highly skilled, pious, humble and down to earth man who cannot be described in words. He has always been the heart and soul of anesthesia team wherever he served.

He was born on 15th July, 1964 in a modest family in Lahore. He completed his elementary education at Dar- ul -Uloom Islamia, Tajpura road Lahore and to the pride of his parents became of Hafiz of Holy Quran when he was just 11 years old. For conventional schooling he was admitted to Islamia High school Lahore Cantt. He secured a merit seat in Punjab Medical College Faisalabad for Medical Education.

Post graduate qualification in anesthesiology he chose services Institute of Medical Sciences, Lahore. He served as Consultant anesthesiologist at Prime hospitals of his native city including General Hospital, Mayo Hospital and Services Hospital Lahore.

Dr. Hafiz Maqsood Ali joined Anesthesia Department at Services Hospital Lahore as Medical office. He never cared for his duty hours and could work continuously round the clock if such a need arose. Senior and juniors colleagues always benefited from his teachings regarding Holy Quran and Hadith.

He was a great trainer andmentor and had a motto "train the trainers". He was one of the elite supervisor and examiners of anesthesiology faculty of College of Physician and Surgeon Pakistan (CPSP). Anesthesiologists trained by him are working all over the country as well as in many countries of world.

He ultimately sacrificed his life while taking care of COVID 19 patients. Let us pray for him that Allah Almighty bless him with highest place in Jannah. We will always remember him in our hearts, prayers and thoughts.

Original Article

Work Related Musculoskeletal Disorders (WMSDs) And Their Coping Strategies Among Nurses of Services Hospital Lahore

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Objective: To determine work related factors of musculoskeletal disorders, frequency of WMSDs and the use of coping strategies to prevent WMSD samong nurses working in indoor departments of Services hospital, Lahore.

Methods: Nurses from indoor departments of Services Hospital (n = 200) using non-probability convenient sampling were included in this cross-sectional study. Musculoskeletal symptoms over the past year and past week were assessed using the Nordic Standardized Musculoskeletal Questionnaire. For qualitative variables frequency, percentages were calculated and chi-square test was applied to see the significant difference between variables. Data was analysed using SPSS statistics V-23.

Results: One hundred ninety four (97%) of the nurses had WMSDs once or more in the last 12 months or last 7 days' time period. Frequency shows that WMSDs occurred mostly in low back (56.1%), shoulder (38.2%), and ankle 34.4%.Working in the same positions for long periods (87.3%), treating an excessive number of patients in one day (74.5%) and continuing to work while injured or hurt (64.2%) were the most perceived job risk factors for WMSDs. Getting help in handling heavy patients (80.7%) and modification of nursing procedures in order to avoid re-injury (65.1%) were the top two coping strategies.

Conclusions: One hundred ninety four (97%)of nurses had an episode of WMSD which mostly affected the low back. Two coping strategies used by majority of nurses were getting help in handling heavy patients and modification of nursing procedures. Educational programs targeted on prevention and coping strategies for musculoskeletal disorders are recommended for nurses.

Introduction

Nursing is a healthcare profession that is concerned with the maintenance and health promotion of patients. The International Labor Organization ILO and the WHO consider MSD as a work related disease, which is also referred as a "new epidemic" that should be researched and solved.[1] WMSD is an injury of the musculoskeletal system which is caused or aggravated by work related tasks such as lifting, pushing and pulling and its symptoms include pain, swelling, stiffness, tingling and numbness.[2] Nursing population that constitute almost 33% of hospital workforce are at high risk of developing WMSDs with reported occupational injuries of 60%.[3,4] WMSDs not only have a significant impact on quality of life but also have huge impact on work related absence.[1] Therefore WMSDs have an impact on individual level as well as on health system.[5-7] MSD prophylaxis is needed in many countries to allow workers to avoid symptoms of MSDs and in result improve work productivity.[8,9] In developed countries many programs for prevention of MSD have been implied in hospitals with the following evidence based practices in use, (1) patient handling equipment/devices, (2) no-lift policies, (3) training on proper use of patient handling equipment/devices, and (4) patient lift teams. Multiple intrinsic and extrinsic factors have been implicated in the etiology of WMSDs. Repetitious movement, awkward postures and high force level are the three primary risk factors which are associated with WMSDs[10] in nurses.

The 2016 Global Burden of Disease (GBD) data for non-communicable diseases identified the profound burden of disease associated with musculoskeletal health. DALYs for musculoskeletal conditions was increased to 61.6% between 1990 and 2016, with an increase of 19.6% between 2006 and 2016.[11,12] Musculoskeletal conditions comprised the second highest global volume of years lived with disability in 2016.[13] In the healthcare sector, occupational musculoskeletal disorders are common, with prevalence rates of work-related MSDs reported from 28%to 96% over a one-year time period [14] including those among nurses, for example, in Europe from 10% to 50% in France[15] and 89% in Portugal,[16] from 35.1% to 47% in USA[17] and in Africa

In Asia 78.6% in China,[19] 85% in Saudi Arabia,[20] 88% in Iran[21] and 89.1% in India.[22] There is a little published data on WMSDs on nurses in Pakistan. According to the 2013 estimates, the nurse-to-patient ratio in Pakistan was 1:50, whereas the ratio prescribed by the Pakistan Nursing Council is targeted at 1:10 in general areas and 1:2 in specialized areas.[23] This is much higher than the ratio in developed countries. Therefore, a higher rate of WMSDs in Pakistani nurses can be anticipated. Unfortunately, this issue received little attention. Possible reasons can be a lack of awareness regarding the topic, lack of resources, funds for researchers and a communication gap between researchers and the target audience. We conducted this study with objectives to determine work related factors that predict musculoskeletal disorders, to access the frequency of WMSDs and to determine the use of coping strategies to prevent WMSD among nurses working in indoor departments of Services hospital, Lahore.

Methods

It was a descriptive cross-sectional study conducted among nurses working in indoor departments of Services hospital Lahore for a time period of 3 months. Sample size was 200. The sample size was estimated using WHO statistical software S size having confidence interval of 95% and Relative precision of 10% taking anticipated population frequency 66%.[26] Non-probability convenient sampling technique was used. All nurses including student nurses with two years of work experience were included into the study. Absence at work at the interview time. Nurses with any diagnosed musculoskeletal disorder. Nurses who had given birth in the last 3 months. Nurses with history of recent trauma. Nurses having co-morbid illness.

In this study we defined WMSDs as musculoskeletal symptoms (pain, numbness, aching, stiffness) that resulted from a work-related event. Questionnaire compromising of 4 sections were used. First section included socio demographic section to collect some general information of participants such as age, gender, height, weight, marital status and history of any comorbid illness. We also collected information on their working characteristics: department, seniority, working intensity, duration of shift work, and so forth. The second section of the questionnaire investigated WMSDs. It also assessed whether sick leave had been taken because of WMSDs. The data collecting team explained all the symptoms to nurses and was available to answer any query. The nurses responded yes or no to whether they had experienced these symptoms in last 7 days and last 12 months period. This section was adapted from the previously validated and modified version of the standardized Nordic Questionnaire of Musculoskeletal Symptoms (SNQ) that was established by Kuorinkaet al.[23] The SNQ was used to evaluate nine body areas including four upper limb segments (neck, shoulders, elbows and wrists/hands), three lower limb segments (hips, knees and ankles/feet) and two trunk segments (upper back and lower back). The third section inquired about the work factors that predict towards the WMSDs and the fourth section inquired about the use of coping strategies. The questionnaire was distributed among nurses working in different major and minor departments of services hospital Lahore. 84% of nurses were taken from major wards including Surgery, Medicine, Gynaecology, Paeds medicine and Orthopaedics. While the remaining 16 percent subjects were included from minor wards including Dermatology, Endocrinology, Psychology, ENT, Eye, Urology. Data was double entered in SPSS version 23.00 for validation. All discrepancies were corrected by referring to original questionnaire. Weight and height were used to calculate the BMI which was further coded into underweight, normal and obese. We used algorithms for descriptive statistics (frequency and percentage) to describe the socio demographic characteristics of the participants. The frequency of MSDs was calculated as the percentage of nurses who developed symptoms of MSDs in at least one of the nine positions on the body (showed in the Nordic Questionnaire). The chi-square test was used for qualitative data. A probability level of 0.05 or less was used to indicate statistical significance.

Results

The questionnaire was distributed among 220 nurses working in indoor departments of services hospital Lahore. Out of which 200 nurses agreed to be part of this research. A group of 6 students from class 4th year SIMS collected the data from nurses and rechecked every questionnaire that it was filled and answered any query of nurses regarding questionnaire. 194(97%)of nurses working in Services hospital Lahore was suffering from MSDs as shown in **(Fig-2).** The socio demographic characteristics **(Table-1)** showed 111 (55.5%) of nurses were in the age range of 20-29 years, 54 (27%)

(52.5%) nurses were married while 95(47.5%) nurses were unmarried. The BMI was calculated which categorized the respondents11(5.5%) of nurses as underweight, 107(53.5%) as healthy and 82 (41%) of nurses as overweight.71(35.5%) of nurses were working in surgical departments while 37 (18.5%), 31(15.5%) and18(9%) belonged to Medic- ine, Gynaecology and Paeds Medicine department respectively.141(70 %) of nurses had the service experience of 2 to 10 years, 38(19%) had the experi- ence of 11 to 20 years and 21(10.5%) had above 20 years job experience. 37(18.5%) of nurses had their first episode of MSD before training while majority of nurses that is 59(30%) had their first episode of MSD during training as a student nurse, 72(36%) had first episode during first 5 years of service. 72(36%)of nurses was doing no leisure time physical activity, 86(43%) was doing slow walk 20(10%) brisk walk while 22(11%) used to do aerobics and gym. As depicted in **(Table-2)** 169(87%) nurses out of 194 were working in the same position for long periods(standing, bend over, sitting, kneeling)and 143(74%) were treating large no of patients in one day. Figure-1 showed the percentage of different body areas affected by MSD in last 7 days and last 12 months. While analysing the results showed that the lower back, shoulder and ankle are the most affected sites. Number of nurses practicing different coping strategies to reduce the risk of developing WMSDs are shown in **(Table-3).** The relationship between different factors that contribute toward MSDs are shown in Table no 4. There is a significant difference (p value=0.04) between lower back pain and no of preschool children. A significant difference (p value=0.00)is also seen between working in the same posture for long duration and presence of MSDs. Long working shifts and MSD shows a significant difference(p value=0.04). Lifting/carrying heavy equipment and not enough breaks during heavy work in this sample showed insignificant relationship with

Table-1: Socio Demographic characteristics.

Variable		N	Percentage
Age	20-29 Years	111	55.5%%
	30-39 years	54	27%
	40-49 Years	28	14%
	50-59 Years	07	3.5%
Marital status	Married	105	52.5%
	Unmarried	95	47.5%
No of Preschool children	0	144	12.9%
	1-2	54	72%
	>2	02	27%
BMI	Under weight (<18.5)	11	5.5%
	Healthy (18.5- 24.9)	107	53%
	Overweight (>25)	82	41%
Duration of service	2-10 years	141	70.5%
	11-20 Years	38	19%
	>20 years	21	10.5%
Department	Surgery	71	35.5%
	Medicine	37	18.5%%
	Gynae/Obs	31	15.5%
Medicine minor (peads medicine, Derma, Psyc.)		31	15.5%
Endocrine, Surg Minors (ortho, Neuro, Eye, ENT, Urology)		30	15%
Duty Type	Permanent	167	83.5%
	On rotation	33	16%
First episode of MSD	Before training	37	18.5%
	As a student nurse	59	29.5%
	First 5 years of services	72	36%
	After 5 years	32	16%
Physical leisure time activity	No leisure activity	72	36%
	Slow walk	86	43%
Duration of service	Brisk walk	20	10%
	Acrobic/gym	22	115%

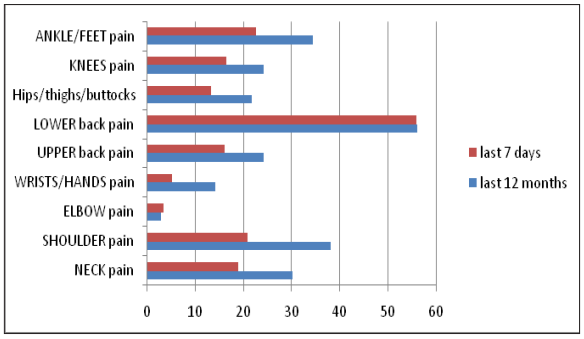

Fig-1: Pain in different body parts in last 7 days and 12 months

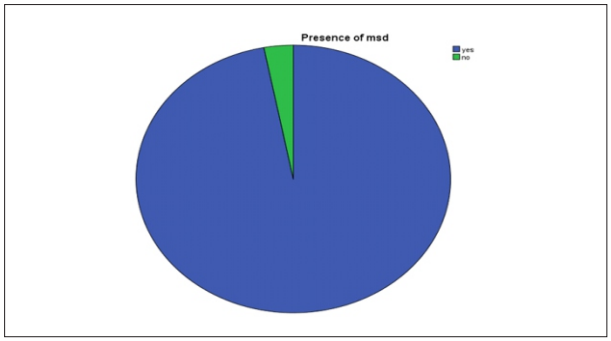

Fig-2: Frequency of WMSDs in nurses

Table-2: Frequency of WMSDs and its contributory work factors.

Contributory Factors	Frequency n (194)	Percentage (%)
Working in the same positions for long periods (Standing, bend over, sitting, kneeling)	169	87.3%
Treating an excessive number of patients in one day	143	74.5%
Carrying, lifting, or moving heavy materials or equipment (e.g., continuous passive motion machines)	144	22.6%
Not enough rest breaks or pauses during the workday	100	52.45%
Continuing to work while injured or hurt	124	64.2%
Working with confused or agitated patients	116	60.4%
Assisting patients during gait activities.	97	50.5%

Table-3: Frequency of WMSDs and its contributory work factors.

Strategies	Frequency n (200)	Percentage (%)
I get someone to help me handle a heavy patient.	161	80.7%
I select techniques/procedures that will not aggravate or provoke any discomfort.	130	65.1%
I got training to avoid musculoskeletal disorders.	98	49.1%
I thought of leaving nursing profession due to musculoskeletal disorders.	32	16%
I had to consult physiotherapist/doctor due to pain.	81	40.6%
Sick leaves due to WMSDs	118	59%

Table-4: Relationship of different work factors with MSDs.

Contributory Factors	Chi-square value	P-value
Age of Nurses	2.19	0.534
No of preschool children	9.39	0.042
Physical leisure time activity	4.55	0.207
Working in same posture for longer duration	16.10	0.006
Not enough breaks during work	6.30	0.17
Long working shifts	6.56	0.038
Moving /Carrying Heavy Equipment	0.002	0.50
Duration of service	0.81	0.66
Assisting patients during gait activities	0.03	1.00
Treating excessive no of patients in one day	0.56	0.37
Continuing to work while injured or hurt	0.005	0.62
Working with confused or agitated patients	0.019	6.62

Discussion

In Pakistan, where most of the hospitals lack the necessary equipment to assist nurses in their work, nurses are more prone to be affected by various problems especially musculoskeletal disorders. Moreover, public sectors hospitals have increased patient turnover as these provided free of cost treatment. In our study we found the overall frequency of WMSDs among nurses of SHL, Pakistan to be 97% which was higher than reported by previous studies conducted at different settings, 10% to 50% in France,[13] 89% in Portugal,[14] from 35.1% to 47% in USA,[16] 78.6% in China,[9] frequency of WMSD came out to be85% in a study conducted in Saudi Arabia[20],88% in Iran[21] , in Egypt to be 97%[24]and a comparatively lower frequency of musculoskeletal disorders of 31.6% among Pakistani nurses.[23] Prevalence of musculoskeletal disorders noted to vary across different occupational groups and nations. Variations in instrument use, organizational differences in work settings, and cultural differences in the perception and reporting of pain are adduced for the variation in rates of WMSDs in the different studies. In our study, a high percentage of nurses (36%) experienced first episode of MSD during first five years of job while 29.5% experienced it during their training as student nurses, these results are consistent with the study conducted among nurses in Zimbabwe.[25]The factors responsible for this might be not enough breaks for student nurses and strict

supervision by senior nurses. It is also observed that after 50 years of age and with more than 20 years of clinical practice the prevalence of musculoskeletal disorders decline.[26] The lower rate of WMSDs among very senior nurses in terms of both age and clinical practice may be attributed to less patient but more administrative duties that often come with rise in job cadre. Another explanation might be that experienced and older nurses have increased level of knowledge about injury prevention, avoid harmful physical load, and have developed better coping strategies for musculoskeletal problems than the less experienced and younger nurses.[26]

In the present study, having one preschool child and being much engaged in other tasks of a caring nature in the leisure time, such as caring for handicapped children or elderly relatives, predicted LBP, the results are consistent with the multiple previous studies.[27] The highest percentage of WMSDs in nurses over 12 months according to body sites is of low back (56%) followed by shoulder (38.2%) and ankle (34.4%). This distribution pattern is consistent with literature. LBP(low back pain) is one of the most important WMSDs among nursing professionals.[27] However, previous studies have documented various rates of work related low back pain (LBP) in nurses for a 12-month time period, a study conducted among nurses in Ibadan, southwest Nigeria[26] showed 44.1% LBP followed by neck and knees (28% and 22.4%). Similarly, a study conducted among nurses in Zimbabwe[25] found LBP was the most common WMSDs reported (67.9%). Likewise frequency of WMSDs in nurses of SHL over last 7 days followed a similar pattern with LBP (56%), ankle (22.6%) and shoulder (20.8%).

Working in the same posture for long duration, treating excessive number of patients and continuing to work when injured or hurt were the most happening job risk factors precipitating WMSDs among the nurses in our study with percentages of 87.3%, 74.5% and 64.2% respectively. These findings are not consistent with previous reports indicating manual patient handling, transferring or moving patients as important predictors of musculoskeletal disorders and low back pain among nurses. Different studies[26,28] implicated lifting patients as the most common mechanism for musculoskeletal disorders among nurses. In our study working in the same posture for longer duration and long working shifts showed a significant relationship with MSDs. In our setup nurses usually do not lift or transfer patients, particularly male patients. This aspect of direct patient care is often handed over to male nursing assistants. This is probably the reason we did not find a significant association between presence of MSD and lifting heavy patients.

Coping strategies play a crucial role in rehabilitation and prevention of injuries as well as musculoskeletal disorders. From this study, getting assistance or support from staff in handling heavy patients, modification of nursing procedure in order to avoid re-injury or stressing an injury and getting training to avoid MSDs were three mostly used coping strategies in reducing the risk of WMSDs (80.7%, 65.1% and 49.1% respectively). These coping strategies among Pakistani nurses seem like previous findings. Workers performing strenuous work are often advised to prevent problems and to cope with musculoskeletal symptoms by changing their working techniques, using lifting equipment, taking breaks and avoiding strenuous work tasks.[26,24] Less than half of those with WMSDs visited other health practitioners for treatment or engaged in self-treatment according to a study conducted in Nigeria[26]. Similarly in this study,40.6% of nurses consulted doctors or physiotherapist due to pain. This percentage is less than half of those suffering from WMSDs. It can be adduced that those who sought medical care represent the more severe cases and the more serious pathology. However, this study did not assess the severity of pain or discomfort from WMSDs of the respondents. As there is increased burden of patients in the public sector as well as private sector, more nurses including the male nurses should be appointed.To improve nurses' understanding regarding WMSDs and to reduce the incidence of WMSDs, workshops and seminars should be conducted regularly. Training should be held to familiarize nursing students with concept of ergonomics.

Conclusion

A high proportion of nurses of Services Hospital Lahore reported WMSDs at some body site (with percentage of 97%) in their occupational lives with the low back being affected most often.The knowledge about ergonomics was generally poor among the nurses. Working in the same positions for long periods and treating anexcessive number of patients in one day were the most perceived job risk factors for WMSDs. While getting help in handling

Less than half of those with WMSDs visited other health practitioners for treatment or engaged in self-treatment.

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Original Article

To Study the Spectrum of Acid Base Disorders in Critically Ill Patients

Rukhsana Gulzar, Rida Zahid, Rehma Dar and Hira Sajjad

Objective: To study the spectrum of ABGs in critically ill patients of Mayo hospital, Lahore in 15 days.

Methods: All samples received from ICU 23.10.18 to 6.11.18, referred to emergency laboratory for ABGs were included. The results and other relevant information were recorded on proforma. The collected data was analyzed by using Statistical package for social sciences (SPSS version 20).Quantitative variables like age was presented as mean ± SD. Qualitative variables like gender, single, double or triple disorder and type of disorder were presented as frequency and percentage.

Results: Out of total 200 samples, 126 (63%) and 74 (37 %) were of male and females respectively. Mean age ± SD was 40.4±10.7 years. The frequency of acid base disorders was 94%. Single disorder were121 (60.5%), 57 (28.5) were double, 10 (5%) were triple disorder and 12 (6%) were normal. 60 (50%), 6 (5%), 51 (42%), 4 (3 %) were metabolic acidosis, metabolic alkalosis, respiratory alkalosis, respiratory acidosis respectively. Hyperoxemia was present in 70 (35%) cases.

Conclusions: Metabolic acidosis is the most frequent disorder in our study and single disorder were common followed by double and triple disorder.

Keywords: ABGs, pattern, critically ill patients.

Introduction

Laboratory testing has an important role in the patient-centered approach for the delivery of health care services. 60-70% of the most important decisions on admission, discharge and medication are based on laboratory test results.[1]

Arterial blood gas analysis is frequently ordered laboratory test in emergency and intensive care unit (ICU).[2] It is used to monitor the acid base balance of patients.[3] Acid base disorders are common cause of high rates of morbidity and mortality in critically ill patients in our health care system.[4]The common indications for ABG analysis are shock, trauma, toxin/ poison ingestion, septicemia, burns, hypoxia, ventilated patients, cardiac failure, diabetic ketoacidosis, liver failure and respiratory failure.[5]

Artery is the preferred site for the sampling of blood gas analysis.[5] Radial artery is more preferred using heparin as an anticoagulant of choice.[2] Sample must be analyzed within 30 minutes. The sample should obtained in anaerobic conditions.[6]

Common parameters included in ABG analysis are partial pressure oxygen (PO_2), partial pressure carbon dioxide (PCO_2), pH and bicarbonates (HCO_3). Additional parameters are base excess, glucose, lactate, anion gap, serum levels of hemoglobin and electrolytes (Na^+, K^+ and chloride). Electrolytes are done for the calculation of anion gap.[5] Among these parameters, pH, PO_2, PCO_2 are measured parameters while HCO_3 is the calculated parameter.[7] Acid base balance is very important for the well-being of person.[8] The body functions normally at the optimal pH of 7.35-7.45.[9] The kidneys and lungs are the main regulators of acid-base balance in body.[5] In addition to them, buffers also play an important role. The main buffers of the body are bicarbonate, phosphate buffer and plasma proteins including Hemoglobin. Out of these, bicarbonate is a major contributing buffer.[7] ABG disorders are generally of respiratory or metabolic origin. Metabolic disorders are compensated by lungs and respiratory disorders are compensated by kidneys and other buffers of the body. Lungs regulate acid base balance by hyperventilation or hypoventilation whereas kidneys regulate blood pH by either reclamation or regeneration of bicarbonate and by secretion of H^+ ions. The compensation of ABG disorders of respiratory origin is done by kidneys and other buffers of the body. The compensation does not start immediately but efficient enough to achieve full compensation. On the other hand, the compensation of metabolic ABG disorders by the lungs is immediate but is not efficient enough to achieve full compensation.[7]There are five types of acid base disorders; respiratory acidosis, Respiratory Alkalosis, Metabolic Acidosis, Metabolic Alkalosis

In metabolic acidosis pH is less than 7.35 and a bicarbonate level is less than 22mmol/Land it is the result of bicarbonate deficiency or an excess of acids like severe diarrhea, laxative abuse, burns, severe dehydration, hypoxia, renal failure, starvation, lactic acidosis and salicylate poisoning.[10] In metabolic alkalosis pH is greater than 7.45 and HCO3 is more than 26mmol/L. Causes of metabolic alkalosis are vomiting, excessive us1e of antacids, Conns syndrome, aggressive gastric suction, hyper aldosteronism, pyloric stenosis and excessive use of diuretics.[10,11] Respiratory acidosis is caused by retention of Co_2 in the body, pH is less than 7.35 and PCO_2 greater than 45 mmHg.[11] Common causes of respiratory acidosis include narcotics, sedatives, anesthesia, neuromuscular diseases, respiratory distress syndrome and other disorders.[12] Respiratory alkalosis is caused by decrease in CO_2 level less than 35 mmHg and pH is greater than 7.45. Common conditions include fever, sepsis, pregnancy, central nervous system lesion, pulmonary edema, salicylates, trauma, infection and psychological response such as anxiety and stress.[13,14]

The timely diagnosis of acid base balance will help to prevent potentially deadly outcome.[5] It will help to guide clinician in adjusting the ventilator settings to meet the patient's needs.[15] In this background, this study was planned to study the pattern of ABGs in critically ill patients of emergency Laboratory of Mayo Hospital/ King Edward Medical University in 15 days.

Methods

It was a descriptive study conducted at emergency laboratory of Mayo Hospital/ King Edward Medical University, Lahore, after approval of the Institutional Review Board. The study included all ABGs done on critically ill patients in Emergency laboratory of Mayo hospital/King Edward Medical University. Clotted sample, hemolyzed sample, insufficient sample and sample in inappropriate vials were excluded. The duration of study was 2 months after the approval of synopsis. Sample technique was non probability convenient sampling.

Samples were collected over a period of15 consecutive days. Blood was collected in identical heparinized syringes and analyzed in M 348 (Siemens) blood gas analysis machine. The relevant information and results of ABG analysis were recorded on prescribed proforma. The result of each sample was analyzed and marked as normal or abnormal according to the type of disorder.

All collected data was entered and analyzed by using Statistical package for social sciences (SPSS version 20). Quantitative variables like age was presented as mean ± SD. Qualitative variables like gender, normal or abnormal reports, single, double or triple disorder and type of disorder were presented as frequency and percentage.

Results

Total samples in the study were 200. The mean age ± SD was 40.4±10.7 years. Out of 200 samples, 12 (6%) were normal and Acid Base Disorders were present in 188(94%) samples. Single disorders were 120 (60.5%) and 67 (33.5%) were mixed disorders. Out of 200 cases, 126 (63%) were male and 74 (37%) were female. The frequency of single, double, triple disorders and normal ABGs were 60.5%, 28.5%, 5%, 6% respectively. Out of 121 single disorders, n[illegible] d[illegible]

Table-1: Summary of results.

Study variable	Mean ±SD%
Age	40.4± 10.7years
Gender (M:F)	63%: 37%
Total Samples	200
Single	121 (60.5%)
Double	57 (28.5%)
Triple	10(5%)
Normal	12 (6%)
Metabolic Acidosis	60 (50%)
Metabolic Alkalosis	6 (5%)
Respiratory Acidosis	4 (3%)
Repiratory Alkalosis	51 (42%)
Mixed	76 33.5%)

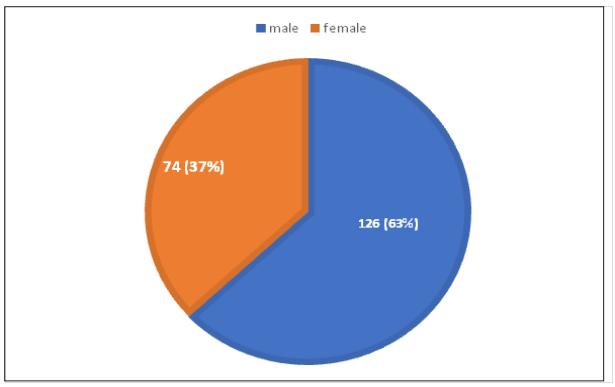

Fig-1: Frequency of male and female patients.

By respiratory alkalosis (42%), metabolic alkalosis (5%) and respiratory acidosis (3%) respectively.

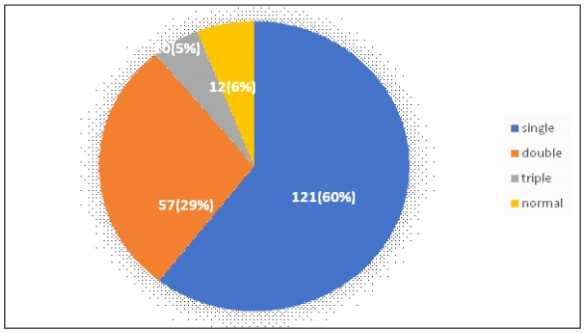

Fig-2: Frequency of Single, Double, Triple ABGs disorders.

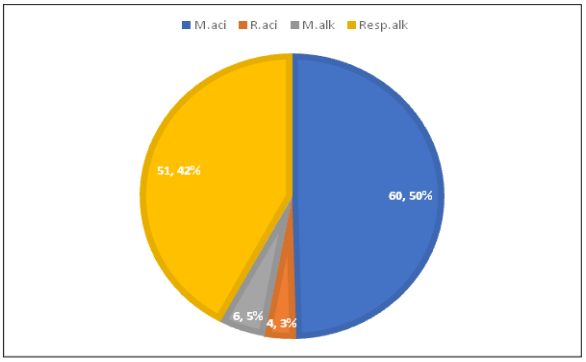

Fig-3: Frequency of different types of acid base disorders.

Discussion

Acid-base balance is very important for normal body function. The acid base disorders can complicate diseased state. It can disturb electrolyte balance and may affect optimal effectiveness of medications.[6] Arterial blood gas analysis is one of the most common investigation in intensive care units and emergency departments as ABDs are more frequent in emergency patients. It is utilized to establish diagnosis, guides treatment plan and helps to adjust ventilator settings of mechanically ventilated patients. The delay in the diagnosis of acid-base disorder can result in serious outcome. The timely management of ABD and its underlying cause significantly reduces morbidity and mortality. However, the pattern of acid base disorders among critically ill patients is not commonly reported.[8] So, this study was planned to study the pattern of ABDs in critically ill patients. ABG results should not be relied on alone in making clinical decisions. Rather it should be interpreted in the background of patient's medical history, present health condition and therapeutic intervention.[5] The accurate results of ABGs are pivotal for patients' management. This needs proper collection, transportation, handling and analysis of the blood sample as ABG measurements are particularly prone to preanalytical errors. The most common encountered errors are air bubbles in the sample, inadequate or excessive anticoagulant, inappropriate temperature for transportation or delayed transportation or analysis.[6,7] In our study, out of total 200 samples, 126 (63%) were males and 74 (37 %) were females. This is comparable to study by Kose et al in which 53.5% were male and 46.5% were female.[4] The mean age ± SD of patients in our study was 40.4 ± 10.7, in contrast with the study of Kose et al in which the mean age of patients was 60.7±17.1 years (4).Like our study, some other researchers also reported ABDs to be more common in males.[8,16.17] The frequency of ABD in our study was 94% that is comparable to studies carried out by Song et al, Ren et aland Zhao et al in which frequency was 97.3% and 94.2%-96.8% respectively. This reflects an increased burden of ABD in critical settings (8,18). In our study single disorders were the commonest (121, 60.5%) followed by double(57, 28.5%) normal (12,6%) and triple disorders (10,5%).This is in contrast with study by Songet alin which double disorders were the commonest (525, 70.5%). One possible explanation for it might be the age of patients (40.4 ±10.7 years) in our study which is less than that of study by Song et al in which mean age was 70.5±17.4 years.[8] In advanced age, patients are usually suffering from more than one comorbid condition like renal insufficiency, cardiac failure or chronic obstructive pulmonary disease that can also affect ABGs results. Moreover, medications like diuretics can also affect the results of ABGs in the elderly patients.[19] Another reason for this contrast might be that emergency laboratory in our study setting mainly deals with patients of general medicine and general surgery. The ABGs of patients of cardiovascular diseases, respiratory problems and burns are performed in their respective departments. Among the double disorders, the common combination in our study was metabolic acidosis and respiratory alkalosis followed by respiratory acidosis and metabolic acidosis. This is similar to study by Song et aland Kose et al.[4,8] The triple disorders were least frequent in our study. This is also comparable to study by Song et al.[8] In our study, the most common single disorder was metabolic acidosis 60(50%) followed by respiratory alkalosis 51(42%), metabolic alkalosis 6(5%) and respiratory acidosis, 4(3 %).This is in accordance with study by Song et al and Ahmad et al. [8,20] The underlying cause of metabolic acidosis could be hyperoxemia and poor systemic perfusion leading to lactic acidosis in end stage organ failure and shock patients.[8,20,21] The frequency of mixed acid base disorders was significant in our study 67(33.5%)

is comparable to study by Ahmad et al.[20] The patients in critical setting are actually suffering from multiple problems that can lead to mixed acid base disorders.[4] The prompt diagnosis and proper management of these abnormalities have a great effect on the outcome of critically ill patients. Hyperoxemia was observed in 70(35%) cases in our study. It is consistent with other studies showing 22% to 50% frequency in of mechanically ventilated patients in the ICU.[22,23] Hyperoxemia is defined as an increase in arterial oxygen partial pressure (PaO2) greater than 120 mmHg.[22,24] Hyperoxemia is associated with the duration of mechanical ventilation, the ICU stay and the hospital stay. It is also associated with a higher mortality rate in addition to hypoxemia.[22] Despite widespread use of oxygen supplementation in hospitalized patients, guidelines for the optimal use of oxygen are not available. Generally, in critical situations oxygen supplementation is started without checking for hypoxemia and often not adjusted to lower level despite partial oxygen pressures (PaO_2) within normal range.[2,25,26] The hyperoxemia results in mitochondrial dysfunction and depletion of cellular ATP levels resulting in formation of reactive oxygen species. It also results in peripheral vasoconstriction, cerebral vasoconstriction, neuronal cell death, and seizures, coronary vasoconstriction and a decrease in cardiac output while increasing peripheral vascular resistance.[27] Due to major neurologic and hemodynamic problems faced by critically ill patients, hyperoxemia must be addressed in this population in addition to ABD.

Conclusion

Acid base disorders are frequent in critically ill patients. They are more common in males as compared to females. Single disorders are more common than mixed disorders (double and triple disorders). Metabolic acidosis is the most frequent single disorder in our study.

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Original Article

Clinicopathological Concordance in Diagnosis of Dermatological Disorders; A Retrospective Analysis.

Hira Tariq, Rabia Mukhtar, Abeer Fahad, Wasfa Hayat, Saelah Batool and Tariq Rashid

Objective: To analyze the correlation between clinical and histopathological diagnoses in various dermatological disorders.

Methods: Histopathological reports of 669 patients were analyzed retrospectively, between March 2017 and March 2019, in the Department of Dermatology, Jinnah Hospital, Lahore. The consistency between clinical and histopathological diagnoses was analyzed in five groups, namely: (A) descriptive histopathological diagnoses favoring primary clinical diagnoses, (B) definite pathological diagnoses consistent with primary clinical diagnoses, (C) definite pathological diagnoses consistent with one of the provisional clinical diagnoses other than the primary diagnoses, (D) definite pathological diagnoses inconsistent with clinical diagnoses, and (E)inadequate sample requiring repeat biopsy. First three groups showed consistency while latter two groups showed inconsistence or inadequacy of sample.

Results: The histopathological diagnoses were consistent with clinical diagnoses in 464 biopsies (69.35%), and were inconsistent or inadequate in 205 biopsies (30.64%). Most of the biopsies were evaluated by the pathologists in the presence of clinical diagnoses.

Conclusions: In clinical dermatology, providing adequate clinical data is of utmost importance in order to get accurate dermatopathological diagnosis.

Keywords: clinicopathological consistency, dermatological disorders.

Introduction

Skin diseases are very commonly encountered in clinical setting. Their prevalence is often underestimated. Their distribution varies in different parts of the world and even within the same country.[1] These diseases are a source of significant physical and psychosocial disability. No age is immune to these disorders. Their clinical consequences vary from troublesome itching and can even lead to death.[2] Therefore, accurate diagnosis is of paramount importance for early treatment of these lesions. Skin biopsy is a simple and inexpensive procedure performed in the dermatology clinics.[3] Biopsy of skin is taken more easily than other organs. Biopsyhelps us immensely in finding out diagnosis, stages of lesions, pathogenesis and even etiological factors of these diseases. After biopsy, we can use many techniques such as histopathology, immunopathology, polymerase chain reaction and electron microscopy for accurate diagnosis of disease. A successful dermatopathological diagnosis needsevaluation of all clinical and histopathological findings.[4]

Sometimes we are perplexed by a rash and can't make a definite clinical diagnosis, histopathology solves this mystery for us.[5] In this study, our aim was to correlate clinical diagnoses with histopathological diagnoses as only a few studies have been done on this aspect in the world and none in our part of the world.

Methods

After getting approval from Ethical committee, we retrospectively analyzed clinical data and histo pathological reports of 669 patients at the Department of Dermatology, Jinnah Hospital, Lahore. These patients underwent biopsies from 1st April 2017 to 31st March 2019. Patients of either gender and all ages were included. Based on the primary clinical diagnoses, diseases were divided into following groups: (a) papulosquamous disorders, (b) bullous disorders, (c) eczemas, (d) neoplasia, (e) granulomatous disorders, (f) connective tissue diseases, (g) drug reactions, (h) vasculitides, (i) chronic ulcers and (j) miscellaneous disorders. The concordance between clinical and histopathological diagnoses was analyzed in five groups, (A) descriptive histopathological diagnoses favoring primary clinical diagnoses, (B) definite pathological diagnoses consistent with primary clinical diagnoses, (C) definite pathological diagnoses consistent with one of the provisional clinical diagnoses other than the primary diagnoses, (D) definite pathological diagnoses inconsistent with clinical diagnoses, and

Results

Out of total 669 biopsies, 152 cases had descriptive pathological diagnoses favoring the preliminary clinical diagnoses, 158 patients had reports consistent with primary diagnoses, 154 reports were consistent with one of the three differential diagnoses other than the primary diagnoses, 150 cases had definite pathological diagnoses inconsistent with any of the clinical diagnoses and 55 biopsies were inadequate to comment upon. This shows that reports of 464 patients (69.35%) were concordant with clinical diagnoses and 205 biopsies (30.64%) were inconsistent or inadequate.

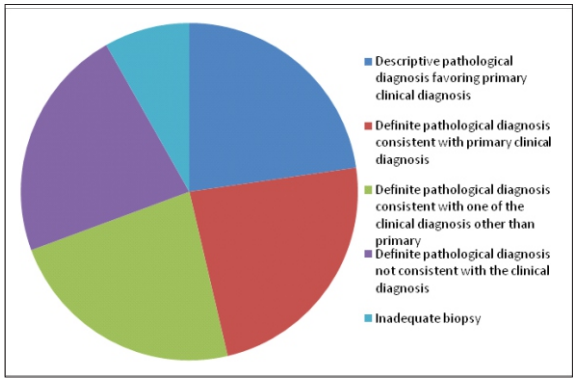

Fig-1: Clinicopathological concordance of cases.

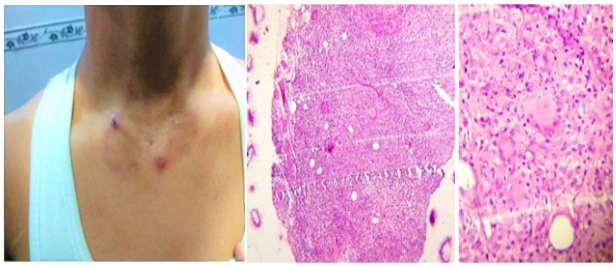

Fig-2: (Clinicopathological concordance in a patient of scrofuloderma: a)multiple draining sinuses on chest, b) and c) histopathology showing chronic granulomatous infiltrate with Langhan type of giant cells.)

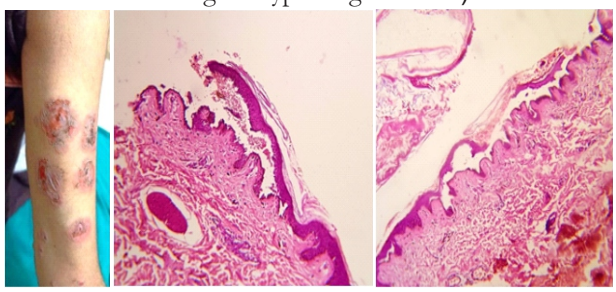

Fig-3:(Clinicopathological concordance in a patient of Pemphigus vulgaris: a) flaccid blisters and crusted erosions on limbs, b and c) histopathology showing suprabasal split in epidermis containing acantholytic cells and tombstoning of basal layer cells.)

Table-1: Clinicopathological concordance of cases.

Factors	No of Case	Percentage (%)
Descriptive pathological diagnosis favoring primary clinical diagnosis	152	22.7%
Definite pathological diagnosis consistent with primaryclinical diagnosis	158	23.6%
Definite pathological diagnosis consistent with one of the clinical diagnosis other than primary	154	23%
Definite pathological diagnosis not consistent with the clinical diagnosis	150	22.4%
Inadequate biopsy	55	8.2%

Discussion

After Dermatological disorders, whether acute or chronic have significant cosmetic and psychosocial impact on patient's life.[6] We as dermatologists have an edge over other clinicians that we can see the disease and reach a conclusion. However, many at times diseases mimic each other so much that supportive tools like histopathology and immunofluorescence are required to provide accurate diagnoses to patients. This clinico-pathological correlation helps us in understanding patterns of diseases in a better way.[7] Therefore, to assess the degree of this concordance we conducted this study over 2 years, as no such study has been conducted on this subject in our part of the world. According to this study, clinicopathological concordance was observed in 69.35% of cases. Narang et al[8] reported this correlation in 44% of the cases while Goyal et al[9] reported a consistence of 63%. Haugstved T et al[10] also conducted a study in non-neoplastic skin biopsies and found correlation in 57.5% cases. Factors responsible for low clinicopathological concordance in dermatological diseases have been evaluated in various studies. These include lack of adequate clinical history in the biopsy forms, inadequate biopsy samples and overlap

Between the histopathological findings of several dermatoses. Diagnostic yield of biopsies can be increased by appropriate choice of the lesion, biopsy technique and providing sufficient clinical infor- mation. Defective tissue fixation and processing, improper staining or lack of cooperation between the dermatologist and the dermatopathologist, may lead to poor outcome.[11-15] Another study reported that the rate of correct diagnosis without clinical information was 53%, however, the same rate was 78% after having the clinical information.[16] At times, repeated biopsies are needed for accurate diagnosis. Biopsy shouldbe compared with the previous one in repeated biopsies.[17] Retrospective nature of study and lack of facilities of immunofluorescence were the limitation of this study. Better cooperation and commun-ication between the dermatologists and the pathologists would have given us more definite diagnoses. Further studies can be planned to determine disease specific concordance.

Conclusion

Clinicopathological correlation is of immense importance in diagnosing various skin conditions. Providing adequate clinical information in the biopsy form along with interdepartmental cooperation between the clinical dermatologists and the reporting pathologists would lead to increased probability of a correct and definitive diagnosis.

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Original Article

Feto-Maternal Complications in Grand Multiparous Women Presenting in Gynaecology & Obstetrics Department, Sir Ganga Ram Hospital, Lahore, Pakistan: A Tertiary Care hospital

Sarwat Nazir, Rodaba Khan, Asma Sikandar and Saima Chaudry

Objective: To assess the frequency of maternal and fetal complications in grand multiparous women presenting in a tertiary care hospital.

Methods: A total of 300 grand multiparous women were included in this study. Any maternal and fetal complication like anemia, pre-eclampsia, placental abruption, post-partum hemorrhage, caesarean section rate, low birth weight and intra-uterine death were observed during delivery and within 24 hours.

Results: Mean age of patients was 34.1±4.8 years. More than one complication was encountered in most of the women and these suffered mainly from anemia (hemoglobin <10.5 g /dl) in 102 patients (34%), placental abruption in 35 patients (11.7%), pre-eclampsia in 71 patients (23.7%), post-partum hemorrhage in 60 patients (20%), and caesarean section was performed in 65 patients (21.7%). Regarding the fetal outcome, 39 (13%) babies were born with low birth weight and 37 (12.3%) babies were intrauterine death.

Conclusions: Grand multiparity is still a high risk pregnancy in our setup. Grand multiparity itself is not as hazardous, it is the lack of basic obstetric care during pregnancy and delivery, due to which grand multiparity is known as high risk pregnancy.

Keywords: grand multiparous, maternal complications, fetal complications.

Introduction

The term "grand multipara" was led in 1934 by Solomon, who called grand multiparas as "the dangerous multiparas".[1] Conservatively speaking, the older literature defines "grand multiparity" (GMP) as parity >7.[2,3] Additionally recent reports limited a definition of GMP to start from a parity of 5 because the threshold of risks of any obstetric complication, neonatal morbidity, and perinatal death increase markedly at parity ≥5.[4,5] Grand multipara are high risk obstetric patients who are liable to develop antenatal, intrapartum and adverse neonatal outcome[6] and these dangers of high order birth can be prevented by effective family planning methods.[7] In another study Grand Multipara (GMP) is not considered dangerous in developed countries with satisfactory health care system.[8] However reviewing literature from under developed countries, GMP is a risk factor for pregnancy related complications in both secondary and tertiary health care centres.[9] The majority of studies argued that GMP are more likely to be of old age which might be the reason for increased morbidity and mortality.[10]

In our clinical practice, such factor is difficult to remove because of women's age is the most important biological variable that influences the reproductive events which we study. The current study was conducted in a tertiary hospital where medical care is given free of cost to all mothers. The aims of the current study were to determine the prevalence of maternal and fetal outcomes related to grand multiparity like anemia, pre-eclampsia, placental abruption, post partum hemorrhage, caesarean section rate, low birth weight and intrauterine death.

Methods

This is a prospective, cross-sectional study done at Gynecology & Obstetrics department, Unit I at Sir Ganga Ram Hospital, Lahore, Pakistan. The mean annual average of deliveries are 24000 including primigravida 40%, multigravida 60% of all deliveries. The study population consisted of all multiparas defined as a woman who had 5 or more births after 24 weeks gestation. A total of 300 cases were collected from March 2019 to August 2019. Sociodemographic factors, obstetric complications, and neonatal morbidity for all cases were recorded. Maternal variables we assessed included anemia, placental abruption, preeclampsia, postpartum hemorrhage, cesarean section. Fetal variables we assessed were low birth weight and intrauterine death. Each of the maternal and fetal complications were assessed against each group. This study was approved by the Ethical Committee of the hospital. The Statistical

Results

Out of 300 grand multiparous patients, mean age of patients was 34.1±4.8 years. More than one complication was encountered in most of the women including anemia in 102 (34%) patients, placental abruption in 35 (11.7%) patients, pre-eclampsia in 71 (23.7%) patients, post partum hemorrhage in 60 (20%) patients, and caesarean section was performed in 65 (21.7%) patients. **(Table-1)** Regarding the fetal outcome, 39 (13%) babies were born with low birth weight and 37 (12.3%) babies faced intrauterine death. **(Table-2)**

Table-1: Pregnancy outcome in grand multipara (N=300)

Pragnancy Complications	Frequency(n=300)	Percentage
Anemia	102	34%
Palacental Abruption	35	11.7%
Pre-edampsia	71	23.7%
Post-partum Hemorrhage	60	20%
Caeserean Section	65	21.7%

Table-2: Perinatal outcome in grand multipara.

Birth Outcome	Frequency(n=300)	Percentage
Low Birth Weight	39	13%
Intra-uterine Death	37	12.3%

Discussion

This prospective cross-sectional study was conducted in order to explore whether parity has a harmful effect on maternal and fetal health. Our results showed that highparity pregnancies lead to multiple health issues of which anemia is to be the commonest with a average of 34%. In a healthy pregnancy, hormonal changes lead to an increase in plasma volume which causes reduction in hemoglobin level.[11] This hemodilution effect is considered normal if the hemoglobin concentration does not drop below a certain level e.g. 11.0 g/dl. Compared to the non-pregnant state, every pregnancy carries an increased risk of hemorrhage before, during, and after delivery. Therefore, higher parity exposes women more frequently to periods of hemorrhage risk that is supported by percentage of patients suffering with Postpartum Hemorrhage which turned out to be 20%. Although there is no consensus with regard to the exact mechanisms by which high parity increases the risk of hemorrhage, some reports have suggested intermediaries such as increased venous drainage to the lower part of the uterus, hyalinization of blood vessels, and decreased elasticity of the uterine wall.[12] None of these proposed mechanisms have been confirmed.

In the current study we found that there is a significant association between caesarean section and grandparity 21.7%. Certain other factors also lead to caesarean such as macrosomia , maternal diabetes and maternal hypertension which are not included in scope of our study however , a study done in Saudia Arabia have elaborated such risk factors and they stated the high rate of Caesarean section can be explained by fetal macrosomia, diabetes mellitus and pregnancy induced hypertension ($p<0.05$). All of these complications of pregnancy are well documented to increase the rate of caesarean delivery. This data showed that within grand multiparity 123(28.6%) of grand multiparas were less than 35 years of age, of whom 72 (60%) were delivered by Caesarean section with no significant differences compared to those greater than 35 years of age (60.0% VS 62.3% $p= 0.666$).[13] Our next variable that is pre-eclampsia have a very marked frequency of 23.7% which is far more than previous studies, in our neighboring country which comes out to be 9%.[14] Rayamajhi et al.[15] reported a strong association of grand multiparity with hypertensive disorders in pregnancy. This brings in a new door for clinicians to explore factors that may lead to increased risk of pre-eclampsia in our population as compared to European and other Asian population. Placental Abruption was of least frequency among all the variables we recorded as it was found in 11.7% of population. Also in literature not much of frequency of placental abruption in GMP has been reported so far. Considering peri-natal outcome in grand parity intrauterine death and low birth weight was found as 12.3% and 13% which is also supported by study by Sunder Pal Singh[16] in 2014 who reported perinatal outcomes to be of closest frequency as of our study.

Conclusion

In view of the results obtained in this study, we feel that grand multiparity continue to pose additional risk for pregnancy outcomes even in modern obstetrics care. In a community where large family is desirable, still there is a place for family planning. Further study is warranted to investigate the outcome of younger grand multiparty. Extreme parity poses a high burden on our healthcare system which should be dealt with extreme care especially in a setup like our country where unbooked deliveries poses a major burden on Obstetrics & Gynecological centres.

Department of Obst. & Gynae

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Original Article

Significance of Histopathological Examination in Appendicectomy Specimens

Samra Sameen, Iram Nadeem Rana, Amna Jahan, Athar Ali and, Tariq Zulfiqar

Objective: To analyze the clinical benefits of histopathological examination in appendicectomy cases with initial clinical diagnosis of acute appendicitis.

Methods: This is a retrospective study conducted in Histopathology section of Services Institute of Medical Sciences, Lahore spanning over a period of 15 months from Jan. 2018 to Mar.2019.

Results: Total 1147 cases of appendicectomy with presumed clinical diagnosis of acute appendicitis were received during the study period. Out of these 54% were males and 46% were females. Majority of the patients belonged to second and third decade of life. Histopathologic examination revealed acute appendicitis in 83.8% cases, lymphoid follicular hyperplasia causing obstruction in 8.4% cases, worm infestation in 0.3% cases, fibrosed appendix in 0.7 %, chronic granulomatous inflammation in 0.09% and neoplastic lesions in 0.5% of cases while no evidence of acute appendicitis identified on histological examination in 0.5% cases.

Conclusions: Routine histopathology examination should be performed in all cases so that any incidental finding is not missed which may affect the patient management

Keywords: Appendicectomy, appendicitis, histopathology.

Introduction

Acute appendicitis is most common surgical emergency and appendicectomy is one of the commonly performed surgeries all over the world.[1] The incidence of appendicitis is increasing in developing countries due to ever increasing trends towards western eating habits.[2] In spite of all recent advancements in diagnostic modalities, preoperative clinical diagnosis of acute appendicitis is accurate in only 60-80% of cases.[3] Therefore, histopathological examination of all appendicectomy specimens remains the gold standard method for confirmation of appendicitis.[4] Life time risk of appendicitis in children and young adults is reported to be about 7%. Appendicitis may be caused by a number of reasons which can be either obstructive or non obstructive. Luminal obstruction is one of the foremost causes of appendicitis and some of the classical causes of obstruction include fecolith, lymphoid hyperplasia and foreign bodies. However, there may be some uncommon causes as well including parasitic infestations, tuberculosis and tumors.[5]

Methods

It is a retrospective study conducted in Pathology Department, Services Institute of Medical Sciences(SIMS), Lahore spanning over a period of 15 months, starting from January 2018 to March 2019. All the surgically resected appendices, whether removed by open surgery or laparoscopy, submitted to department of Pathology, SIMS for histopathology were included in the study. A total of 1147 cases of appendicectomy were received during this period in Histopathology section, SIMS. Relevant clinical data was retrieved. Gross findings were noted. Specimens were fixed in 10% neutral buffered Formalin, routine tissue processing and paraffin embedding was done. Sections were prepared for microscopy after cutting at 5 micron thickness and staining with Haematoxylin and Eosin.3 Representative sections were taken from appendices after gross examination (one longitudinal section from tip and two transverse sections from base and body of appendix). In case of tumors, extra sections were taken according to recommended protocols including need of submission of entire appendices particularly in cases of mucinous neoplasms of appendix. Microscopic examination was performed in all specimens by a histopathologist and in case of a neoplastic diagnoses, second consultation from another histopathologist in the department was taken. Data was entered and analyzed by using Microsoft excel 2010 and results were prepared.

Results

Total 1147 appendicectomy specimens were received in the department of Pathology, SIMS spanning over a study period of 15 months from January 2018 to March 2019. Out of these 1147 cases, 621(54%) were males and 526(46%) were females, thus making a maleto female ratio of 1.2:1 **(Fig-1)**. Minimum patient age was 3 years and maximum age of presentation was 84 years. Mean age of the patients was 22 years with age group of 13-22 years of age

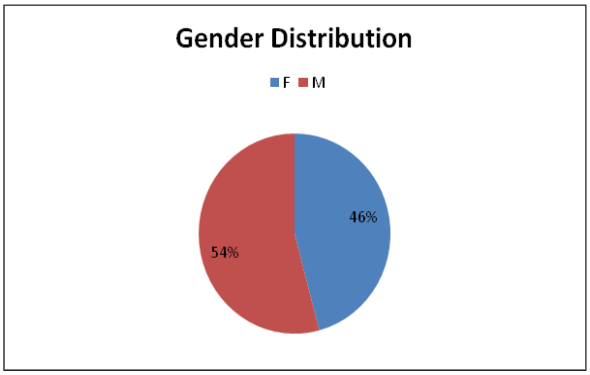

Fig-1: Gender distribution in appendicectomy specimens.

Out of these total 1147 cases, 961(83.8%) cases were proved histologically as acute appendicitis. Among these 738 (64.3 %) were confirmed histologically as acute appendicitis alone while 73 (6.4%) cases showed periappendicitis with acute appendicitis and 150 (13.1%) of the patients showed acute suppurative appendicitis. Lymphoid follicular hyperplasia was seen in 96 (8.4%) cases while worm infestation was seen in 4(0.3%) cases. 8(0.7 %) appendices were fibrosed and no evidence of acute appendicitis identified on histological examination in 6(0.5%) cases. One (0.09%) of the specimen had chronic granulomatous inflammation and neoplastic lesions were identified in 6(0.5%) of cases **(Fig-2).** 55(4.8%) cases were comprised of autolyzed appendix and 10(0.9%) of the patients had some other associated pathologies as well.**(Table -2)**

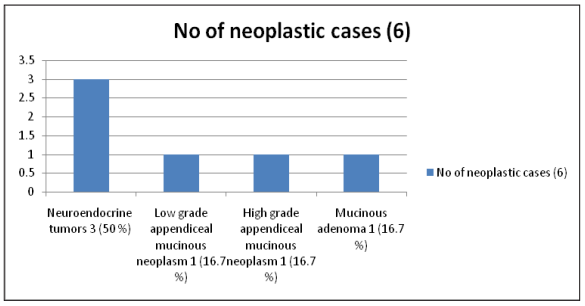

Fig-2: Histological diagnosis of neoplastic entities.

Table-1: Analysis of histopathological findings in appendicectomy specimens.

Histopathological Diagnosis	No of Cases	%
Acute appendicitis	738	64.3%
Acute appendicitis with periappendicitis	73	6.4%
Acute suppurative appendicitis	150	13.1%
Lymphoid follicular hyperplasia	96	8.4%
acute appendicitis with worm infestation	04	0.3%
Tumors	06	0.5%
Fibrosed appendix	08	0.7%
No evidence of acute inflammation seen	06	0.5%
Chronic granulomatous inflammation	01	0.09%
Associated pathologies	10	0.9%
Autolyzed appendix	55	4.8%
Total Cases	1147	100%

Table-2: List of associated pathologies.

Associated Pathologies	No of Cases	%
Haemorrhagic ovarian cyst	03	30%
Muture cystic teratoma	02	20%
Ovarian endometroitic cyst	02	20%
Folicular ovarian cyst	01	10%
Meckel's diverticulum	01	10%
Ovarian serous adenoma	01	10%

Discussion

The vermiform appendix is considered by most as a vestigial organ. Its clinical significance lies in its tendency to undergo inflammation which may lead to clinical presentation of acute appendicitis.[6]

There are many common and some uncommon causes of acute appendicitis. Common causes of appendicitis includes fecolith and lymphoid hyperplasia leading to luminal obstruction while uncommon causes include tumors, granulomatous inflammation and parasitic infestations.[7]

Appendicectomy is a common surgical procedure for the management of acute appendicitis. This current study reviews the histopathological findings of appendicectomy specimens received during 15 months period in Pathology department, SIMS.

During this study period 1147 specimens of appendix were received. Maximum number of patients belonged to age group 13-22 years of age. Number of appendicectomies performed was more in males (54%) compared to females (46%).

This is comparable to study by Al-Fatah which had 58% males and 42 % females in their study.[8] Among 1147 patients, 93 % of the patients showed inflammatory lesions whether in the form of acute appendicitis alone or associated with periappendicitis, suppurative appendicitis, lymphoid follicular hyperplasia or worm infestations. This rate is comparable to study by others like Patel M et al (91.3%)(8) and Divya R et al (92.3%).[9]

In our study 4(0.3%) patients had evidence of parasitic infestation with enterobius vermicularis **(Fig-3).**

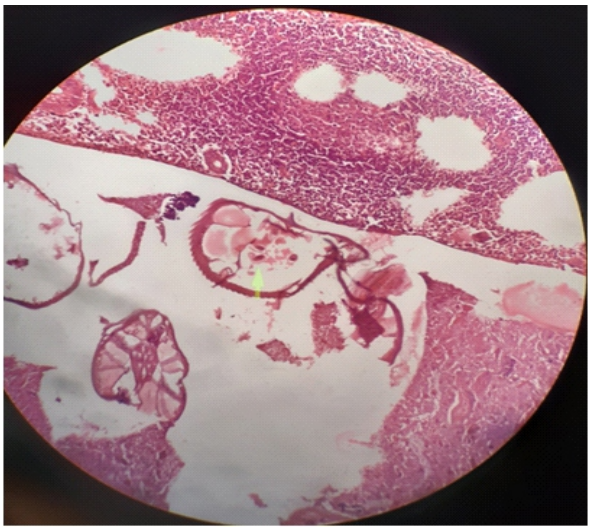

Fig-3: Appendix with enterobius vermicularis worm infestation.

There is a variability in reporting incidence of parasitic infections in appendicectomy specimens depending on geographic area and prevalence and it ranges from 0.2 to 41.8%.[10,11] Another significant finding was chronic granulomatous inflammation seen in one case **(Fig-4).**

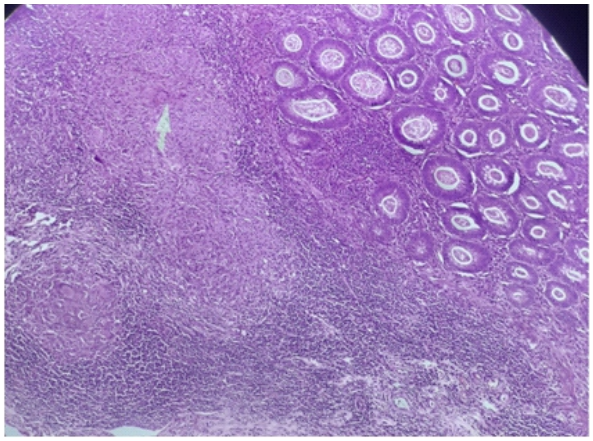

Fig-3: Chronic granulomatous inflammation involving appendix(Arrow pointing to a multinucleated giant cell).

Incidence of granulomatous inflammation in literature varies between 0.14-2.3%.[12,13] 6(0.5%) cases in our study had neoplastic disease which is comparable to study by Kunduz et al who reported 0.78% incidence of appendiceal neoplasms in their 3554 appendicectomy specimens examined.[14] Out of these 3 patients had neuroendocrine tumors **(Fig-5)**, while one case each was diagnosed of mucinous adenoma, low grade appendiceal mucinous neoplasm and high grade mucinous appendiceal neoplasm.

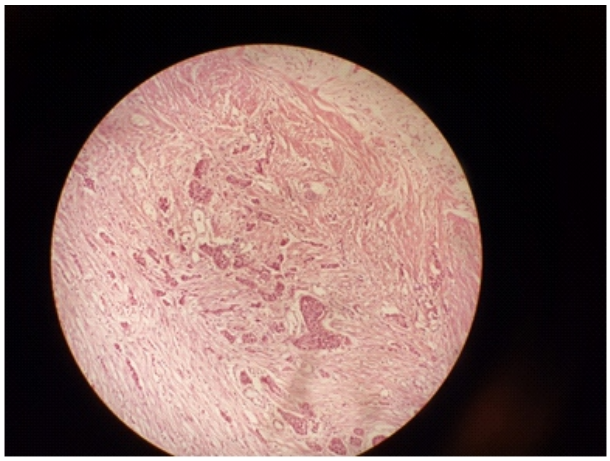

Fig-4: Neuroendocrine tumor of appendix found in tip of an appendix.

Whole of the appendix specimens were submitted in these tumors for microscopic examination. The case of low grade appendiceal mucinous neoplasm was associated with low grade pseudomyxoma peritonei and low grade ovarian mucinous neoplasm. Literature shows that a mucinous tumor of the appendix may coexist with morphologically similar tumor in ovary and may also show pseudomyxoma peritonei. Therefore it is imperative to perform follow up ultrasonography and CT scans to rule out any associated ovarian neoplasm and omental deposits.[5,15]

2.1% of the patients did not show any evidence of acute inflammation in our study. Out of these, 0.7 % were fibrosed appendices, 0.9 % had some other etiology for the clinical manifestations of the patients and 0.5% of the patients did not show any significant histological evidence of acute inflammation. These rates are much lower as compared to others like Sharma et al (5.7%)[16] and Sujhata et al (9.1%).[3] Another significant finding in our study was that of autolyzed specimens contributing 55(4.8%)of the patients. These specimens were sent without formalin which caused the specimen to be autolyzed, so we were unable to examine them histologically. This may have led to missing of some important pathology as mentioned above.

Conclusion

Appendicitis has peak incidence in second and third decade of life. It is important to send all the appendicectomy specimens for histopathologic examination with proper fixation in formalin in order to confirm the diagnosis of acute appendicitis as well as to rule out any possibility of incidental findings like parasitic infestation, neuroendocrine tumors or mucinous neoplasms of appendix.

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Original Article

Association of Liver Enzymes in the preeclampsia Patients Presenting In A Tertiary Care Hospital: Case Control Study

Jazba Yasin, Sadia Ilyas, Ateeqa Mubarak, Uzma Aziz, Nabeela Shami, Ameelia Sadaqat and Kumail Sajjad

Objective: To assess the association of preeclampsia with deranged liver enzymes of patients presenting in a tertiary care hospital.

Methods: It was case a control study including 100 females who fulfilled the inclusion criteria. They were enrolled in the study from OPD of Department of Obstetrics and Gynecology, Ghurki Trust Teaching Hospital, Lahore. Informed consent was obtained. Then two groups were formed i.e. cases with preeclampsia and controls without preeclampsia. Then blood sample was obtained in 3cc BD syringe. All samples were sent to the laboratory of the hospital for assessment of ALT and AST. Data was entered and analyzed by SPSS version 21.0. Odds ratio was calculated to find association between preeclampsia and deranged ALT and AST.

Results: The mean age of the patients was 33.30 (±4.45) years in cases and 32.96 (±4.72) in the control group. Mean gestational age was 33.88 (±4.07) weeks while 33.6 (±4.29) weeks in the control group. It was observed that body mass index was 28.90 (±2.32) in cases and 31.45 (±3.76). Parity was also almost similar in the both groups. It was observed that among cases 14 (28%) of the participants had deranged. ALT and AST value while 3 (6%) in the control group which was significant with Odds ratio >1.

Conclusions: Significantly deranged liver enzymes were observed in the eclampsia patients. There is a need to conduct further study to know its relationship with disease.

Keywords: preeclampsia, hypertension, liver function test, deranged liver function.

Introduction

Hypertension is the most common medical disorder in pregnancy. Hypertensive disorders of pregnancy are responsible for significant maternal and perinatal morbidity and the third leading cause of pregnancy related deaths (14.4%), superseded only by haemorrhage and sepsis. Preeclampsia is a multisystem disorder, unique to pregnancy that is usually associated with raised blood pressure and proteinuria after 20 weeks of gestation.[1] Maternal mortality ratio in 2015 was 178 per 100,000 live births in Pakistan.[2] In Pakistan, pre-eclampsia /eclampsia deaths represent one-third of maternal deaths reported at the tertiary care hospital settings.[3] Gestational hypertension and preeclampsia /eclampsia are hypertensive disorders induced by pregnancy; both disorders resolve postpartum. Gestational hypertension is the most common cause of hypertension in pregnant women.[4] The syndrome of hemolysis, elevated liver enzymes and low platelets (HELLP) is a severe manifestation of preeclampsia and complicates approximately 0.5-0.9% of all pregnancies and 10%-20% of cases with severe preeclampsia.[5]Ten to 50 percent of women initially diagnosed with gestational hypertension go on to develop preeclampsia in one to five weeks. HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) probably represents a subtype of preeclampsia with severe features in which hemolysis, elevated liver enzymes, and thrombo- cytopenia are the predominant features, rather than hypertension or central nervous system or renal dysfunction, although the latter do occur.

The majority of patients, but not all, have hypertension (82 to 88 percent) and/or proteinuria (86 to 100 percent).[6] Several studies have suggested that liver involvement in preeclampsia is serious and frequently accompanied by evidence of other organ system involvement, especially the kidney and brain along with hemolysis and thrombocytopenia.[7] The diagnostic work-up of abnormal liver function tests (LFTs) in pregnancy is challenging, as the condition peculiar to pregnancy have to be considered in addition to the causes affecting the non-pregnant population. The spectrum of disease is varied and the abnormal LFT can be mild with no long-term consequences, or it can be severe, leading to both maternal and fetal mortality.[6,7] AST is found in liver, cardiac muscles, brain, skeletal muscles, erythrocytes and kidney. ALT is found predominantly in liver. Therefore, increases in ALT are more specific than AST for hepatobiliary disease. In the hepatocytes, AST is cytoplasmic while ALT is intra-mitochodrial.

elevation in AST. Here is no agreement on the effect of pregnancy on serum AST and ALT. In a few studies, AST and/ or ALT levels slightly increase in the third trimester. However, in most studies, AST and ALT levels remain within the normal range for non-pregnant state.[8] As such, gastroenterologists and obstetricians are often faced with the dilemma of whether the abnormal LFT are related to pregnancy and whether immediate obstetric intervention in necessary.[9] In routine, LFTs are not evaluated in early stage, till the female is symptomatic. This may be due to lack of local evidence. So we conducted this study to find the association and prevent the life threatening consequences of liver dysfunction and preeclampsia.

Methods

This was a Case control study conducted in department of obstetrics and gynecology, Ghurki Trust Teaching Hospital Lahore from June 2019 to December 2019. 100 pregnant females were included; 50 females in each group. Non-probability, consecutive sampling technique was used. Inclusion criteria was decided preeclampsia females of age 18-40years, parity<5, presenting at gestational age>20 weeks (on LMP) presenting for antenatal check-up. While females with chronic hypertension, chronic, or gestational diabetes, anemia, eclampsia and abnormal LFT before pregnancy (on medical record), were excluded from study. Two groups were formed Group A cases (with preeclampsia) and Group B controls (without preeclampsia). Then blood samples were obtained by using 3cc BD syringe. All samples were sent to the laboratory of the hospital for assessments of ALT and AST. Females with abnormal results were managed as per hospital protocol. Data analysis: Data was entered and analyzed by SPSS version 21. Mean and SD ratio was calculated for quantitative variables like age, gestational age and BMI. Frequency and percentage was calculated for qualitative variables like abnormal ALT and AST. Parity will also be presented as frequency. Odds ratio was calculated to find association between preeclampsia and abnormal ALT and AST. OR>1 was taken as significant. Data was stratified for age, gestational age, parity and BMI. Post-stratification, adjusted OR was calculated with aOR>1 considered as significant.

Results

The mean age of the patients was 33.30±4.45 years in cases and 32.96±4.72 in the control group. Mean gestational age was found to be almost same in both group 33±4 weeks and body mass index was 28.90±2.32 in cases and 31.45±3.76 in control.

Table-1: Comparison of the Abnormal ALT and AST in the cases versus control

Group	Normal ALT & AST	
	Yes	No
Cases	14 (28.0%)	36 (72.0%)
Control	03 (6.0%)	47 (94.0%)

Odds Ratio=6.09

Table-2: Stratification of the abnormal ALT and AST in the cases versus control with respect to the age.

Group of age	Abnormal ALT & AST		P-Value	Odds Ration
	Yes	No		
18-30 Cases	5 (37.5%)	09 (64.3%)	0.20	3.0
Control	02 (12.5%)	41 (87.5%)		
>30 Cases	09 (25.0%)	27 (75.2%)	0.01	11.0
Control	01 (2.9%)	33 (97.1%)		

Table-3: Stratification of the Abnormal ALT and AST in the cases versus control with respect to the Parity.

Parity			Abnormal ALT & AST		Total	P-Value	Odds Ration
			Yes	No			
1.00	Group	Cases	02 (50.0%)	02 (50.0%)	04 (100.0%)	0.53	3.50
		Control	02 (22.2%)	07 (77.8%)	09 (87.5%)		
2.00	Group	Cases	04 (21.1%)	15 (78.9%)	19 (100.0%)	0.11	0.78
		Control	0 (.0%)	15 (100.0%)	15 (100.0%)		
3.00	Group	Cases	07 (35.0%)	13 (65.0%)	20 (100.0%)	0.20	5.38
		Control	01 (9.1%)	10 (90.9%)	11 (100.0%)		
4.00	Goup	Cases		09 (100.0%)	06 (100.0%)	-	-
		Control		10 (100.0%)	10 (100.0%)		
5.00	Goup	Cases	01 (100.0%)	0 (.0%)	01 (100.0%)	0.16	-
		Control	0 (.0%)	05 (100.0%)	05 (100.0%)		

It was observed that among cases 14(28%) and among control group3 (6%) had abnormal ALT and AST which was significant with Odds ratio of 6.09. Data was stratified for age, gestational age, body mass index and parity. Comparison of abnormal ALT and AST in both groups

Discussion

Pre-eclampsia occurs in 2%-8% of all pregnancies, with the incidence of severe pre-eclampsia being around 1%. In the U.K, an estimated incidence is 2.7 per 10,000 births(9, 10).The risk of pre-eclampsia is 4.1% in women in their first pregnancy and 1.7% in later pregnancies overall. However, this risk rises to 14.7% in the second pregnancy in women who had pre-eclampsia in their first pregnancy and 31.9% in women who had pre-eclampsia in their previous two pregnancies.[11]Pregnancy induces physiological, hormonal and physical changes. These changes may be responsible for the incidence of acute hepatic failure (AHF) in pregnancy both pre and post partum.[12,13] Acute fatty liver of pregnancy (AFLP), pre eclampsia and HELLP (haemolysis, elevated liver enzymes, and low blood platelet count) syndrome have been demonstrated as being the main causes of severe hepatic failure in pregnancy. They are thought to represent a spectrum of the same pathological process.[14,15] They are described as being specific to the trimester in which they appear, but this is not always the case.In a study, serum bilirubin and plasma levels of liver enzymes ALT, AST and ALK were measured. The mean BMI of the cases was 29.04±3.97 and that of controls was 26.54±3.11. The mean value of serum bilirubin in cases was 10.78±3.74 micromol/L and in controls it was 7.92±2.42 micromol/L (p< 0.001). The mean values of enzyme ALT in cases was 55.81±31.93 U/L while in the controls it was 15.22 ±3.30 U/L (p < 0.001). Mean serum AST in the cases was 41.34±10.76 U/L and in the controls it was 24±2.54 U/L (p<0.001). Mean ALK level of cases before delivery was 454.16±243.69 U/L, and in controls it was 181.34±66.76 U/L (p<0.001). Raised levels of serum bilirubin and liver enzymes ALT, AST and ALK were found in preeclampsia cases, Which was consistent with the findings of the current study. We also found a significant increase in Liver enzyme level in eclamptic females.[2,16] In another study, there was significant increase (p<0.001) in the levels of serum ALT and ALP in preeclampsia group compared to control and between high risk and PET group. Levels of AST also increased significantly (p<0.05) when preeclampsia group was compared with control and high risk group.[17] This study has limitations that it was a single centered study and the institute was a public institute. Majority of the patients were poor with bad hygienic conditions so similar studies are required in a controlled environment.

Conclusion

Conclusively, it is stated that there are high chances of raised liver enzymes levels in the patients presenting with preeclampsia. So it is needed to monitor the blood profile in such cases during and after pregnancy so that early on mortality or morbidity could be safeguarded.

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Original Article

Measurements of PM2.5, PM1, PM10, VOCs and HCHOs During a Building Fire in Central Lahore and its Possible Effects on Mental Health

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Objective: To measure the levels of various pollutants in a big fire in a building in Lahore.
Methods: A new specific measuring device was used to monitor the values during the fire and a week later at exactly the same spot and at the same time of the day.
Results: The values obtained of the PM2.5, PM1, PM10, volatile organic compounds and formaldehyde were markedly deranged. This was a warning sign for the fire men to wear proper protective gear on duty.
Conclusions: It is important to contain a building fire as soon as possible as it is a health hazard. It produces pollutants of various sorts such as the particulate matter of 2.5 to 10 micron sizes. It also produces volatile organic compounds and formaldehyde which can cause serious health problems from conjunctivitis and nasal irritation to cardiac arrhythmias anxiety, depression and cancer. It is equally important to make sure that the fire men are issued proper protective gear for fire fighting in addition to the mandatory professional training.
Keywords: fires, ecosystem, environmental, pollution, mental health anxiety depression.

Introduction

In August 2019, a large departmental store in the center of Lahore caught fire. The store had varied quantities and qualities of materials in it. This included textiles, foams, and in addition to that there were the structural materials themselves of the building including paint, wood, varnish, cardboard and MDF boards etc. Fire fighters almost took major part of the day to put out the fire. The major hallmark of a threatening fire, including heat, smoke and particulate matters were present. The fire fighters were very quick to arrive at the scene but were noted to be not adequately protected especially against smoke and particulate matters in the atmosphere. Fires can kill. Its smoke and toxic gases kill more people than flames do. The toxic gases thus released have the capacity to disorientate the person and cause drowsiness. Fires can kill by asphyxiation and their smoke is the main cause of death. Even delayed asphyxia can cause death.[1] Fire is lethal because of its carbon monoxide and cyanide fumes. These cyanide fumes are a result of combustion of many synthetic materials found commonly in ordinary homes such as plastics, rubbers and foams. Thus, synthetics polymers (teflon, nylon and polyester and polyethylene) are used in huge quantities in everyday house hold objects. In addition to these there are present other chemicals as well such as polyacrylonitrile, polyurethane and melamine but natural materials such as wool, horsehair, and silk. Paper is present in large quantities as well which aids the fire to burn more.[2] A by product of burning wool is hydrogen cyanide and on burning wood manganese and benzene are produced as by-products. These contain attached into their structure nitrogen and halogens as well. This is a lethal combination as when this burns in a fire, it produces hydrogen cyanide and inorganic acids. Humans inhale such deadly fumes which gives lethal levels of carboxyhemoglobin and cyanide in blood. The oxygen is used up as well and results in its depletion in the air as well later in the victim's blood. Thus, the fact that the combustion of certain household furnishings can produce cyanide has been proved by numerous studies. Thus cyanide poisoning results whose characteristics are hypoxia, metabolic acidosis and raised lactic acid levels. A fire will certainly give off heat but in a confined space of a room the temperatures can rises up to 1000 to 2100°F (5371160°C). Inside a room, there is a gradient of heat in the ascending order. At the feet it can be 100 degrees, rising quickly to 600 degrees at the level of the eyes and soaring up to 1500 degrees at the ceiling level. This is hot enough to burn the clothes and scald the skin, both sticking to each other like were never separate from each other. A person inhaling at this level will scald his respiratory tract up to the lungs with intense oedema. Although the name of a lethal gas like cyanide brings to mind instantaneous death, but in a fire the heat is a stronger role to play in human deaths.[3,4] Thus, Cyanide poisoning is not very frequent in fire fatalities, but when it is present it is

carboxyhemoglobinemia. An Australian study showed a correlation between elevated blood ethanol and whole blood cyanide levels ($r = 0.36$, $p < 0.001$) and between elevated carboxyhaemoglobin and hydrogen cyanide levels. Thus, there is a strong association between an elevated carboxy- haemoglobin level and cyanide levels. Once cyanide poisoning sets in, it can damage the cardiac function as well, resulting in it to stop contracting altogether, causing a cardiac arrest and imminent death unless treated in time.[5] Building fires can also affect the mental health of people in general and also among the fire fighters. Studies have shown high levels of stress among the sufferers.[6] Therefore various researchers have recommended psychological interventions to promote the mental health and enhance the knowledge. Moreover training can improve behaviours which can result in better outcome.[7]

Methods

A new multi-pollutant measuring device (Life Basis DM106A) was used to measure the pollutant levels. The device was calibrated before every new set of readings were taken. A week after the fire episode, ordinary day readings were also taken at the equivalent hour on the clock coinciding with the midway point of the total duration of the fire. Both readings were recorded after the device was given 5 minutes in the vicinity of the fire. During taking both the readings the same spot was used which was about 12 meters from the building ablaze.The readings were plotted in the table.

Results

It is evident from **(Table-1)**. That there is a stark difference between the concentrations of the particulate matters of all sizes (PM2.5, PM1, and PM10) during the blaze and a week after. In addition to these the concentration of the volatile organic compounds (VOC) is also increased and so is the level of formaldehyde (HCHO). It is show below why the concentration of these particulate matters and the other chemicals increases as the material they are a constituent of start to combust. The PM2.5 was so huge in concentration at the time of the fire that its concentration went beyond the scale of the device. The humidity went up as well despite the fire, because of the sheer amount of water the fire hoses were churning out.

Table-1: Measurements at the same spot during the blaze and a week after the fire. Recommendations for a safe level are included. The air quality index is colour coded and the indication on the fire day was at the maximum in the classification-' Very Unhealthy'(purple). This is equal to the score of 201-300. (https://webcam.srs.fs.fed.us/test/AQI.shtml)

	PM2.5 µg/m³	PM 1 µg/m³	PM 10 µg/m³	TVOC mg/m3	HCHO mg/m3	Humidity %	AQI colour indication
Ordinary days	59	36	71	0.45	0.17	64	Moderate
Fire	9.999	61.8	1444	2.4	0.3	73	Very Unhealthy
Recommendation	25 (WHO)	Not set yet	50 (WHO)	0.26(Japan)	0.12(Netherland)		

Discussion

Smoke, is defined by The American society of Testing and materials as "the airborne solid and liquid particulates and fire gases evolved when a material undergoes pyrolysis or combustion". If smoke is inhaled, this causes injury to the upper and the lower respiratory tract. There is supraglottic thermal injury, chemical irritation of the respiratory tract, systemic toxicity caused by cyanide and carbon monoxide. Once the respiratory tract is damaged by the heat, the cilia and the surface epithelium is disrupted and inflammation ensues. The lower tract especially is unable to clear the debris and stagnation leads to poor ventilator effort and infections leading to pneumonia and acute respiratory distress syndrome. The patient is unable to breathe and keep up the oxygenation which necessitates artificial ventilator support. Particulate matters can be either in the liquid or the solid forms. They can be naturally occurring or manmade as well. They originate from duct, ash or soot especially during combustion of solids, liquids. Car engines are also a big source of particulate matter. A high concentration of particulate matters, such as the PM2.5 and PM10 is already a problem in most developing cities of the world and is the same in Lahore. It is reported that fires 'significantly' elevate their concentrations. PM2.5 is 2.5 micrometer in diameter and are the 'fine' particles because they are so small (2.5 micrometers is one 400th of a millimeter) that they can enter the deepest parts of the lungs and cause serious problems. Fine

seen over Lahore. Human sources of these are more important than natural sources as these can cause systemic inflammatory and oxidative stress responses as seen in large polluted cities like in China.[8] It is seen that the synthetic materials will give rise to 12.5X more particles per mass as compared to natural materials like wood.[9] It is reported, not too surprisingly that the PM2.5 levels were significantly higher during a wildfire episode. A rise in Pm2.5 during a fire can lead to serious heart ailments. It has been reported that a certain increase in PM2.5 concentration in the atmosphere was associated with an increase in ischemic heart disease admissions (by 1.86%) in the hospitals. The researchers in the USA further tried to ascertain the reasons how the PM2.5 can lead to adverse cardiac events. They found out that the PM2.5 can lead to systemic pulmonary inflammation and increased release of various cytokines. They also reported that when these particulates get into the blood stream, being so fine in size, they can cause vascular events such as thrombus formation, increase in blood viscosity, disruption of the plaque and cardiovascular adverse events. Finally, these researchers also highlighted that these fine particulate matters can cause irregular or increased heart rates which can lead to cardiac arrest. Particulate matter causes a lot of health related problems such as asthma (3% increases for each10 µg/m3 rise in PM10) and others which necessitates increased (2%) hospital admissions. It is noted that the particulate matters which are in the 'ultrafine size range' can have 'surface transition metals' which can give rise to injurious oxidants with 'enhanced toxicity'.[10,11] The lungs thus take the main brunt of the particulate onslaught where these chemical can 'catalyze' an 'oxidative stress reaction' in the pulmonary tissue causing wide spread tissue damage. This was confirmed by alveolar lavage which confirmed that the inflamed lung tissue enhanced the 'metal-mediated oxidation' causing cardiopulmonary damage. The pulmonary damage by PM.5 and PM10, after fires can be significantly toxic to the alveolar macrophages. This has also been confirmed by another study which confirms the fact that the PM10 particulate matters are particularly more toxic (four times as much) to the macrophages in a fire than from exposure to ordinary urban pollution particulates. Out of 20,000 premature deaths in the USA, many were soot related due to sulphur dioxide and nitrogen oxide which combine to give acid rain. A Polish study confirmed soot in 80% of the fire victims in their airways. About 60% had inhaled enough carbon monoxide to be a reason for death.[12] Synthetic materials in the house tend to produce more smoke such as styrene used in disposable plates and glasses, insulation material in electronic appliances, toys and tires. Vinyl polymers like PVC pipes, plastic chairs and tables produce increased amounts of thick smoke. Toxins which are present on a long term basis including volatile organic compounds and formaldehyde with the particulate matter can result in thousands of deaths.[13] The smoke can contain heavy metals such as arsenic, cobalt, chromium, lead, and mercury. PM2.5 can damage the eyes as well resulting in ocular cell autophagy, and it is also reported that the Pm2.5 can damage the DNA in the corneal cells.[14,15] After tackling a fire the firefighters were reported to have a deposit of volatile organic compounds. There are numerous reports where the researchers have associations between cancers affecting the fire man after a career in fire fighting. There is evidence of DNA damage and epigenetic changes in specific gene promoters. Some mention the increased incidence of mesotheliomas, lung, leukaemia, prostate, brain, and haemopoietic malignancies.[16,17]

In the USA it is noted that certain cancer types have an increased association in fire fighters as compared to the general public. A few are enlisted below.[18]

Testicular Cancer	2.02 Times Greater Risk
Multiple Myeloma	1.53 Times Greater Risk
Non-Hodgkin's Lymphoma	1.51 Times Greater Risk
Skin Cancer	1.39 Times Greater Risk
Prostate Cancer*	1.28 Times Greater Risk
Malignant Melanoma	1.31 Times Greater Risk
Brain Cancer	1.31 Times Greater Risk
Colon Cancer	1.21 Times Greater Risk
Leukemia	1.14 Times Greater Risk

Higher rates of anxiety and depression were noted among people who suffered from wildfire at Alberta. These effects were more pronounced immediately after the episode. [19] This not only affects general population but also the personnel who are involved in fire fighting. This is the reason that mental health improvement plans have been devised to decrease mental stress and other negative consequences. This will result in overall improvement of mental health. [20]

Conclusion

It is important to contain a building fire as soon as possible as it is a health hazard. It produces pollutants of various sorts such as the particulate matter of 2.5 to 10 micron sizes. It also produces volatile organic compounds and formaldehyde which can cause serious health problems from conjunctivitis and nasal irritation to cardiac arrhythmias and cancer. It is equally important to make sure that the fire men are issued proper protective gear for fire fighting in addition to the mandatory professional training.

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in mice.[7] Carboplatin induces myelosuppression by increasing overall oxidative stress and decrease in the

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Original Article

Protective Effect of Malus Domestica (apple) Peel Extract on Carboplatin Induced Fall in Blood Platelet Count and Bone Marrow Megakaryocyte Percentage in Mice

Abdul Mudabbir Rehan, Rabia Naseer Khan, Sehrish Zaffar, Mahwash Malik, Sadia Chiragh and Amtul Hafeez

Objective: To evaluate the protective effect of Malus domestica (apple) peel extract on carboplatin induced fall in blood platelet count in mice and also fall in bone marrow megakaryocyte percentage in mice.

Methods: Forty adult male mice were divided into 5 groups. Group A was negative control and only distilled water was given to mice. Group B was disease control and mice in this group received carboplatin intraperitoneally in a dose of 125 mg/kg. Group C, D & E were experimental groups and carboplatin along with the apple peel extract in three different doses of 25, 50 & 75 mg/kg was given. After 7 days, blood & tissue sampling was done.

Results: The results revealed that apple peel extract significantly prevented the fall in platelet count and megakaryocyte percentage in all experimental groups treated with carboplatin.

Conclusions: Apple Peel Extract effectively prevented carboplatin induced fall in platelet count and megakaryocyte percentage and produced m,ore significant results in a dose of 50 mg/kg.

Keywords: thrombocytopenia, carboplatin, apple peel extract, bone marrow aspirate.

Introduction

Thrombocytopenia refers to decrease in platelet count <150,000/μL in blood (normal count is 150,000 to 450,000/ μL).[1] Thrombocytopenia is usually asymptomatic and it is picked up on a routine full blood count or peripheral blood smear examination. The individuals may experience external bleeding such as nosebleeds or bleeding gums. Women can experience heavier or longer periods or breakthrough bleeding. Bruising, particularly purpura can occur under the skin in forearms, whereas, Petechiae may occur on feet and legs.[2] Platelet counts of 75,000/ μL to 150,000/ μL are defined as grade-I thrombocytopenia, 50,000 to 75,000/μL as grade-II, 25,000 to 50,000/ μL as grade-III, and below 25,000/ μL as grade IV thrombocytopenia.[1] Platelets maintain vessel wall integrity, whereas thrombocytopenia is associated with a defect of primary hemostasis. The most common causes of thrombocytopenia are megalo- blastic anemia, idiopathic thrombocytopenia, infections, hematological malignancies, aplastic anemia, pregnancy, alcoholism and cancer chemotherapeutic drugs. Thrombocytopenia in cancer patients can result from chemotherapy, radiation treatment or from the underlying disease itself, but it is most frequently observed due to myel-osuppressive side effect of cancer chemotherapy and most of chemotherapeutic agents cause myelosuppression in a dose dependent manner.[3] Thrombocytopenia creates a number of problems in the care of a cancer patient. At platelet count<10,000/μL, spontaneous bleeding is increased and radiations/ chemotherapy are administered with caution for fear of worsening the thrombocytopenia and increasing risk of bleeding. At platelet counts <50,000/μL, surgical procedures are complicated by bleeding.[4] Therapeutic and prophylactic platelet transfusions create the additional risk of infusion complications. Clinicians' responses to thrombocytopenia in a cancer patient vary. Reduction of the dose intensity of chemotherapy or radiation is common and for some patients, treatment of the underlying cause of thrombocytopenia (e.g. stopping therapy with the offending drug) may work. Platelet transfusion is often the only readily available treatment. The discovery of thrombopoietin in 1994 generated great expectations and the 1st generation recombinant thrombopoietin agonists reduced chemotherapy-related thrombocytopenia in early clinical trials, but their subsequent development was halted due to antibody formation against endogenous thrombopoietin.[5] Whereas, two 2nd generation thrombopoietin receptor agonists have now been developed, but neither has yet been tailored for treating thrombocytopenia in cancer patients.[6] Carboplatin is an anticancer drug which belongs to alkylating class of cancer chemotherapeutic drugs. It is used effectively to treat many cancers. Experimentally, carboplatin has been used to induce myelosuppression

glutathione content inside bone marrow.[8] It also cross links the DNA and generates oxidative stress products such as malondialdehyde.[9] It is studied now that various substances like Glutathione,[10] Squalene[11] and L-Carnitine[8] have protective effects on carbo- platin induced myelotoxicity in animal models.

It can be concluded that toxicities of carboplatin are due to increase in the overall oxidative stress inside bone marrow and if this abrupt rise in oxidative stress could somehow be prevented then the serious untoward effects can be avoided. Apples are the most widely consumed fruit worldwide and contain five major polyphenols. Apple peel contains 3 to 6 times more flavonoids as compared to apple flesh that's why, apple peel extracts have more antioxidant potential than apple flesh extracts.[12] The aim of study is to observe the protective effects of apple peel extract on carboplatin induced thrombocy- topenia. Carboplatin suppresses the bone marrow production of various cells by interfering with redox reactions inside marrow cavity. Carboplatin shifts the redox equilibrium towards oxidative side, and apple peel extract by virtue of its antioxidant property will restore the redox equilibrium by reduction and will improve the bone marrow suppression.

Methods

It was an experimental study conducted at Postgraduate Medical Institute Lahore. Forty adult male mice were divided into 5 groups containing 8 mice in each group. Mice were kept in animal house of Postgraduate Medical Institute Lahore inside cages under hygienic conditions. They were given humane and veterinary care according to the criteria outlined in the "Guide for the care and use of laboratory animal" (Council, 2010). The temperature was maintained in a range of 19-22 °C with a natural day and night cycle. Before the onset of study, all mice were kept for a week for acclimatization and were provided with diet and water ad libitum. A single intraperitoneal injection of carboplatin (Injection Carpsol 150mg/15ml by Pfizer pharma) in a dose of 125 mg/kg was given to induce myelosuppression in mice.[7] Red delicious variety of local apples was selected because it contains the richest proportion of anti-oxidants among all the locally produced varieties.[13] Apples were washed with plain running water, air dried and peeled carefully so that peel may not contain flesh. The collected peel was spread and allowed to dry in shade for 2 weeks. The partially dried peels were then put in hot air oven at a temperature of 60 0 C for 3 hours. The completely dried peel was then coarsely ground with pestle and mortar. The powdered peel was soaked in 80% of ethanol (1:10, w/v) at room temperature for 3 days with daily shaking.[12] The filtration of solution was done by filtering it through What man filter paper No. 1 and was separated from the liquid extract. The excess of solvent was evaporated and concentrated extract was stored at 4 °C.[13] The five study groups were given drugs as described in the table below. The drug given to each mice in all groups via intraperitoneal route was administered once on day 0, whereas the drug given to each mice in all groups via oral route was administered once daily for 7 days starting from day 0.

Mice Groups	Drug by Intra peritoneal route (single dose on day 0 only)	Drug by Oral route (once daily\ dose from day 0 to 7)
A	Sterile water	Distilled Water
Normal Control	1.25mg/kg	4ml/kg
B	Carboplatin	Distilled Water
Disease Control	125mg/kg	4ml/kg
C	Carboplatin	Apple peel extract (25mg/kg)
Experimental 25mg/kg	125mg/kg	25mg/4ml/kg
D	Carboplatin	Apple peel extract (50mg/kg)
Experimental 50mg/kg	125mg/kg	50mg/4ml/kg
E	Carboplatin	Apple peel extract (75mg/kg)
Experimental 75mg/kg	125mg/kg	75mg/4ml/kg

Sampling:

Blood: On day 7 the mice were anesthetized with ketamine which was administered via single intraperitoneal injection in a dose of 100mg/kg 14 into the left lower quadrant of abdomen. The mice were dissected afterwards to expose the heart and 1.5ml blood was withdrawn directly from the right ventricle of heart with the help of 23 gauge needle and 3 ml disposable syringe. The blood was collected in EDTA vacutainer.

Bone Marrow:

Bone Marrow Aspirate Smear: The already dissected mice were euthanized by giving a single sharp cut at neck using surgical scalpel and further dissected to obtain the right femur bone. The contents of right femur were aspirated into 0.2ml of ice cold phosphate buffer saline by using 23 gauge needle and 10 ml syringe. The aspirate was then spread over slide and

Over the slide. Finally, the slide was stained with Geimsa stain, washed with plain running water andCover slip was applied.[15]

Parameters:

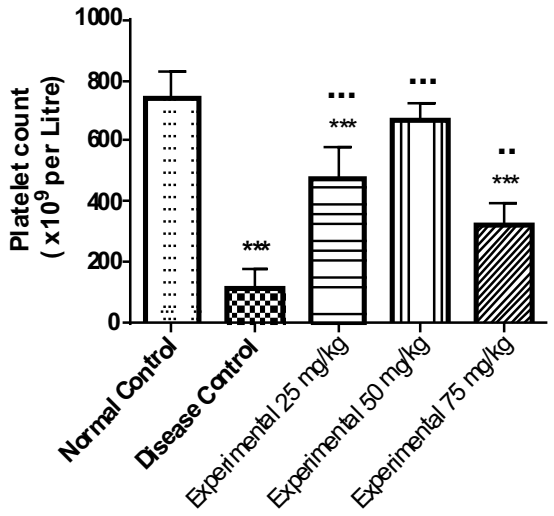
Platelet Count: The platelet count was analyzed by hematology analyzer in hematology lab of PGMI.

Bone Marrow Aspirate Smear: Differential cell count was done under oil immersion lens of light microscope. 200 cells were counted and relative percentage of platelets was entered in the proforma only.[15]

Results

1. Platelet Count:

The mean platelet count ± standard deviation of all the groups are illustrated in **Fig-1.** The comparison of means of all groups by ANOVA revealed a significant difference between the group means with a p value of <0.001.



The post hoc Tukey's test was applied to analyze platelet count difference between the groups. The disease control group had markedly lower platelet count as compared to normal control group, whereas all experimental groups had significant higher platelets count as compared to disease control group. All experimental groups had lower platelets count as compared to normal control, but the difference was insignificant with 50 mg/kg dose of APPE. When the experimental group were compared with each other, then the group with 75mg/kg dose had significant lower platelets count as compared to the groups with 25 & 50 mg/kg dose.

2. Megakaryocyte Percentage:

The mean megakaryocyte percentage±standard deviation of all groups are given in **Table-2.** The post hoc Tukey's test was applied to analyze the megakaryocyte percentage difference between the groups. The disease control group had markedly lower megakaryocyte percentage as compared to normal control group, whereas all experimental groups had significant higher megakaryocyte percentages as compared to disease control group.

Table-2: Comparison of effect of carboplatin & carboplatin with 3 differents doses of APPE on megakaryocyte percentage in bone marrow aspirate smear by post hoc Tukey's test (n=8).

Post hoc Tukey's multiple comparison test		Mean Difference	Significance
Group A Normal Control	Disease control	7.87	***
	Experimental (25 mg/kg)	2.87	***
	Experimental (50 mg/kg)	2.12	**
	Experimental (75 mg/kg)	3.87	***
Group B Disease Control	Experimental (25 mg/kg)	-5.00	***
	Experimental (50 mg/kg)	-5.75	***
	Experimental (75 mg/kg)	-4.00	***
Group C Experimental (25mg/kg)	Experimental (50 mg/kg)	-0.75	ns
	Experimental (75 mg/kg)	1.00	ns
Group D Experimental (75mg/kg)	Experimental (75 mg/kg)	1.75	*

*ns = not significant, * = p value < 0.05, ** = p value < 0.01, *** = p value <0.001*

All experimental groups had significant lower megakaryocyte percentage as compared to normal

Control. The group with 75 mg/kg dose had significant lower megakaryocyte percentage as compared to the group with 50 mg/kg dose.

Discussion

Cancer is the 2nd most common leading cause of death worldwide which causes severe morbidity and mortality in all age groups. Multiple preventive and treatment modalities like cancer screening, chemotherapy, radical surgeries & radiotherapy are available now a days, but among all these modalities chemotherapy is the prime option for initial medical management of various cancers. However, it is the acute or cumulative toxicity of chemotherapeutic agents which impairs treatment.[16] The adverse effects are many, but myelosuppression is the only treatment limiting toxicity in almost all of the cancer patients.[3] That is why adjuvants, neo-adjuvants and adjunct therapies are used along with the principal therapeutic strategy to abate cancers. The GM-CSF has been used in cancer patients to improve peripheral neutropenia,[17] and thrombopoietin to treat thrombocytopenia.[6] However, the indications of the above regimens are limited because of their adverse effects and high costs.[18] The ultimate solution to chemotherapy (CP) induced myelosuppression lies in the natural compounds which can prevent chemotherapy induced myelosuppression by virtue of their antioxidant capacity. We selected APPE of red delicious variety due to its maximum antioxidant potential[13] to observe the antioxidant effect on oxidative stress driven by carboplatin on bone marrow of mice. The statistical analysis revealed a significant decrease in peripheral blood platelet count which was accompanied by a significant decrease in megakaryocyte percentage in bone marrow aspirate smear of disease control group. The platelet count and the megakaryocyte percentage increased significantly in all experimental groups as compared to disease control group and the maximum increase was observed in group which received 50 mg/kg dose No similar study of effect of APPE is available for comparison, but studies utilizing other herbal preparations containing polyphenols/antioxidants have demonstrated similar results. A recent study conducted by (Tahir and her colleagues in 2014)[7] demonstrated the effect of Carica papaya leaf juice in preventing the fall in platelet count in mice induced by carboplatin. The Carica papaya leaf juice contains polyphenols which serve as antioxidants and reduce oxidative stress inside bone marrow of carboplatin treated mice. The increase in platelet count in all experimental groups is a remarkable finding because carboplatin has predominant effect on the decrease in platelet cell count[19] as compared to the red blood cells and white blood cells. In current study, 3 different doses of APPE were used to find out right therapeutic dose. The study results demonstrated that all 3 doses of APPE caused an overall numerical increase in peripheral blood cell counts and megakaryocyte percentage of all experimental groups, but statistics revealed that the APPE in a dose of 50 mg/kg is more significant as compared to the rest of 2 doses. The significantly better results of 50 mg/kg dose as compared to 25 mg/kg dose demonstrates dose dependent preventive effect, while inferior effect of 75 mg/kg dose may be explained by the fact that antioxidants in a high dose act as pro-oxidants.[20]

Conclusion

Apple Peel Extract is effective in preventing the fall in platelet count & megakaryocyte percentage induced by the carboplatin driven oxidative stress. Apple peel extract produced better significant results in a dose of 50 mg/kg.

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Original Article

A Comparison of Propofol and Sevoflurane for Smooth Laryngeal Mask Airway Insertion

Saadia Khaleeq, Muhammad Muazzam Butt, Umer Farooq, Ubaid-ur-Rehman, Sahir Shafeeq and Zulqarnain Butt

Objective: To compare the study the easiness of LMA insertion and its associated complications with sevoflurane and propofol.

Methods: 200 patients, aged 12-50 years, having ASA physical status I and II, undergoing elective surgical procedures in general anesthesia were allocated randomly in two equal groups. Group A received Propofol 2.5 mg/kg intravenously along with 100% oxygen through face mask while patients in Group B received 8% Sevoflurane in 50% N2O and O2 at flow rate of 8 litres/minute for 30 seconds. Losing eyelash reflex was taken as an end point of induction in two groups under study. Insertion of Laryngeal Mask Airway was attempted by an experienced anaesthesiologist who was blinded to technique of induction. Full mouth opening, LMA insertion at first attempt and complications including coughing, gagging, patient movements and laryngospasm, were recorded. Smooth LMA insertion was labeled if criteria fulfilled.

Results: Smooth LMA insertion was observed in 89 patients in Group A and in 83 patients of Group B. It appears that greater number of patients had smooth LMA insertion in Group A . There was no statistically significant difference between to groups (p-value=0.221). Complications associated with laryngeal mask insertion in both groups were not statistically significant as well.

Conclusions: Sevoflurane and propofol are equally good and safe for successful insertion of LMA and there is no significant difference in case of insertion and associated effects between the two study groups.

Keywords: laryngeal mask airway insertion, propofol, sevoflurane.

Introduction

The Laryngeal Mask Airway (LMA) has been used quite frequently above alternative to endotracheal tube. It is a supraglottic airway device which is made for provision of seal around the inlet of larynx for spontaneous ventilation and allows mechanical ventilation at modest level of positive pressure.[1,2,3,4] Coughing, gagging and laryngospasm are common undesirable responses associated with Laryngeal Mask Airway insertion.[5] An ideal induction agent is required for sufficient depth of anaesthesia, adequate relaxation of jaw and absent upper airway reflexes without compromising cardiorespiratory systems for successful insertion of Laryngeal Mask Airway.[3,4,6] Various anaesthetic agents such as thiopentone, propofol, ketamine, etomidate, lidocaine, halothane and sevoflurane (either alone or in combination with each other or with a muscle relaxant) has been used for insertion of Laryngeal Mask Airway.[4] Propofol, an intravenous induction agent is commonly used for laryngeal mask airway (LMA) insertion. It provides adequate suppression of oropharyngeal and cough reflexes.[7,8] But, certain adverse effects such as pain, hypotension, apnea, and excitatory patient movements are associated with its use.[7,9,10,11] Sevoflurane is a non-pungent inhalation agent which is not irritating for the airways and thus can be used for insertion of the LMA while preserving spontaneous ventilation.[9] It is known for lesser breath holding, cough and lower incidence of laryngospasm.[4] Sevoflurane is advantageous because of better hemodynamic stability and provides smooth transition towards the maintenance phase without an apnea phase as compared to propofol. But, sevoflurane is known for delay in relaxation of jaw and more time required to insert the LMA.[9] Many comparative studies have shown the induction of anaesthesia after inhalation of sevoflurane and intravenous propofol.[12] Previous studies have shown contradictory results on the comparison of sevoflurane and propofol for smoother insertion of Laryngeal Mask Airways. Thus the objective of this study is to compare the frequency of easier insertion of Laryngeal Mask Airway following induction of anaesthesia with intravenous propofol or sevoflurane inhalation and to observe any complications that might occur during insertion.

Methods

We conducted this randomized controlled trial in Services Hospital Lahore after approval from Institutional Ethical and Review Committee. Af written and informed consent, 200 patients having ASA physical status I and II planned for elective orthopedic, urological and general surgery were

randomly using random number table to one of the two groups (A&B) comprising 100 patient each. Patients having pharyngeal diseases (e.g. abscess) or obstruction, low pulmonary compliance (restrictive airway disease), diabetes mellitus, pregnancy, hiatus hernia gastro esophageal reflux disease, allergy to any anesthetic agents and all emergency surgical procedures were excluded from this study.

After arrival in the operation theatres, non-invasive blood pressure, heart rate, electrocardiography and oxygen saturation with pulse oximetry were monitored. According to the requirements of each patient and procedure, intravenous fluids were administered. Before induction of anaesthesia, patients were pre-oxygenated in both groups. Group A received intravenous Propofol 2.5 mg/kg along with 100% oxygen through the face mask in group B. The anaesthesia circuit was primed with 8% Sevoflurane in 50 % N2O and O2 at flow rate of 8 Litres/minute for 30 seconds every patient was advised for maximum exhalation followed by connecting the primed circuit to the face mask. All patients were adviced to take vital capacity breaths. Losing the eyelash reflex was taken as end point of anesthesia induction in both groups. Insertion of Laryngeal Mask Airway was attempted by an experienced anaesthesiologist who was blinded to technique of induction. The insertion of Laryngeal Mask Airway was considered smooth if there was full Mouth Opening (inter-inciser gap >three fingers or 6 cm), placement in 1st attempt and no patient movement, coughing or gagging. Anaesthesia was maintained by using 50% nitrous oxide (N2O) , 50% oxygen (O2) and Sevoflurane (1.5 MAC) in both groups. All the data was analyzed by utilizing SPSS version 24.0. The ages of the patients were presented by calculating mean and standard deviation. Gender and presence or absence of smooth insertion of Laryngeal Mask Airway was presented by calculating frequency and percentage. Frequency of smooth Laryngeal Mask Airway insertion and complications in two groups were compared by applying chi square test. P value ≤0.05 was taken as significant.

Results

Mean age of the patients was 31.58±11.05 years in two groups. In Groups A and B, average ages of patients were 30.57±11.46 and 32.60±10.57 years respectively. **(Table-1)** Gender distribution in both groups shows that in Group A 74 were male patients and 26 were females paients. Whereas Group B, 62 patients were male and 38 patients were female. x**(Table-2)** Statistically significant difference was not seen in complications associated with laryngeal mask insertion in both the groups. Only 3 patients had coughing in group A in comparison to 5 patients of group-B. Gagging was absent in both groups. Only 1 patient of group A had laryngospasm while none of the patients had laryngospasm in group B. Patient movement was seen in 5 patients of group A in comparison to 9 in group B. **(Table-3)** Smooth LMA insertion was observed in 89 patients of group A compared to 83 in group B.

Table-1: Age in both groups.

	Group A (n=100)	Group B (n=100)	Total (n=200)
Mean±SD	30.57±11.46	32.60±10.57	31.58±11.05

Table-2: Distribution of gender.

		Group A (n=100)	Group B (n=100)	Total (n=200)
Gender	Male	74 (74%)	62 (62%)	136 (68%)
	Female	36 (26%)	38 (38%)	64 (32%)
	Total	100	100	200

Table-3: Complications observed in patients.

		Group A n (%)	Group B n (%)	Total n (%)
Coughing	Yes	3 (3%)	5 (5%)	8 (4%)
	No	97 (97%)	95 (95%)	192 (96%)
	Total	100 (100%)	100 (100%)	200 (100%)
Gagging	Yes	0 (0%)	0 (0%)	0 (0%)
	No	100 (100%)	100 (100%)	200 (100%)
	Total	100 (100%)	100 (100%)	200 (100%)
Laryngospasm	Yes	1 (1%)	0 (0%)	1 (0.5%)
	No	99 (99%)	100 (100%)	199 (99.5%)
	Total	100 (100%)	100 (100%)	200 (100%)
Patients Movement	Yes	5 (5%)	9 (9%)	14 (7%)
	No	95 (95%)	91 (91%)	186 (93%)%
	Total	100 (100%)	100 (100%)	200 (100%)

Table-4: Smooth LMA insertion.

		Group A n (%)	Group B n (%)	Total n (%)	P-Value
Smooth LMA insertion	Yes	89 (89%)	83 (83%)	172 (86%)	
	No	11 (11%)	17 (17%)	28 (14%)%	0.221
	Total	100 (100%)	100 (100%)	200 (100%)	

It appears that greater number of patients had smooth LMA insertion in group A patients in comparison to group B patients but in terms of p-value, no statistically significant association was present. (p-value =0.221) **(Table -4)**

Discussion

Laryngeal Mask Airway (LMA) provides a clear airway in majority of patients and is easier to insert than a tracheal tube.[13] Appropriate depth of anaesthesia is required for easy, successful and proper insertion of LMA.[7] Inhalation of sevoflurane and intravenous propofol are commonly used for induction and maintenance of general anaesthesia with LMA.[14] Propofol is among the most commonly used induction agents for smoother insertion of LMA. Insertion of LMAs can be done with or without using neuromuscular blocking agents. However, adequately suppressing the upper airway reflexes is necessary for avoiding adverse responses ,e.g. cough, excessive gagging and laryngospasm.[13,15] Using propofol as induction agent for insertion of LMA is advantageous with quick onset and shorter duration of action and adequately suppresses the reflexes of upper airways. Sevoflurane has also been used as an alternative to propofol in recent times, being a preferred inhalational agent due to its smoother induction and recovery profiles, with lesser excitatory properties and hemodynamically stable as compared to propofol.[15] In this study we compared propofol and sevoflurane induction on the ease of insertion of LMA and the adverse effects that occurred during insertion. Smooth LMA insertion was seen in maximum number of patients of both groups (89% in group A vs 83% in group B), with no significant difference statistically (p=o.22) although successful LMA insertion was more in propofol group. This is in comparison to a study by Rehman et al who found propofol to be more effective than sevoflurane for successful LMA insertion .[3]The results of study by Prabhudev et al were in co-relation to our results. There was smooth insertion of LMA in each of 25 patients in propofol group and 23 patients belonging to sevoflurane group.[15] Chavan et al also showed excellent score of LMA insertion with propofol (83%) when compared to sevoflurane (80%) that was consistent with the results of our study.[4] Dwivedi et al also had similar findings in this respect. The overall insertion characteristic score was excellent in 92% of patients induced with propofol and 86% of patients induced with sevoflurane; this was statistically insignificant and hence comparable in both the groups.[16] A study comparing inhalation of vital capacity breaths with intravenous propofol versus sevoflurane in helping insertion of laryngeal mask airways in adults, Sarkar M et al also showed similar results favoring successful insertion with intravenous propofol (95%) vs sevoflurane (92.5%).[17] Dharmalingam also found ease of insertion with propofol in comaparison to sevoflurane without any significant difference.[6] Bakhshi S et al evaluated induction with sevofurane vs intravenous propofol for laryngeal mask airway insertion in children and found successful insertion of LMA in 98% patients in propofol group and 96% patients in sevoflurane group which was in accordance with the findings of our study.[14]Prakash et al compared vital capacity breath induction with sevoflurane to intravenous propofol for laryngeal mask airway insertion. He found that induction with intravenous propofol and induction with inhalation of sevoflurane vital capacity breaths were almost equally effective for successful insertion of LMAs. He placed LMA successfully in 90% of sevoflurane group and in 88% patients of propofol group. This could be due to difference in methodology.[7] Our results were not significantly different among the two groups regarding complications such as gagging, cough, laryngospasm and patient movements (p>0.05) Coughing in propofol group was seen in 3% vs 5% patients of sevoflurane group. 5% patients of propofol group showed movement vs 9% in sevoflurane. Gagging was not seen in any patient in both groups. Laryngospasm occurred in 1% of patients in propofol group only. (Table-3). These results of our study are comparable with that of Prakash et al who did not find any incidence of complications among two groups when they compared induction with inhalation of vital capacity breaths of sevoflurane with intravenous propofol for insertion of laryngeal mask airway.[7] Chavan et al also failed to show any statistically significant difference in two groups regarding complications [4]. Sarkar M et al showed no significantly different complications in the study groups. Patient movement was seen in 5%, coughing in 2.5% and gagging in 5%. [17]

Balakrishnan compared Propofol and sevoflurane for insertion of Laryngeal Mask Airway in Children for various Surgeries. In contrast to our study they found more coughing (20%) and gagging when 3mg/kg of propofol given intravenously. Movement of patients was significantly higher in the propofol group (43.3%

the propofol.[10] Ravi et al. compared Propofol and sevoflurane for insertion of Laryngeal Mask Airway in Children and found no incidence of cough, gagging and laryngospasm in two groups. Similar findings were observed by Bakhshi S et al when she compared the two groups in children.[13] Contrary to our study, gagging and laryngospasm was not noted by Prabudev et al. Coughing was seen in 8% of patients with sevoflurane which was not significant statistically.[15]

The limitations in our study was that the depth of anesthesia was not compared in the two induction techniques as we did not have BIS monitor. Also we did not measure the induction time. Further studies can be done to compare depth of anaesthesia and induction time.

Conclusion

We conclude that Propofol and sevoflurane are equally good for successful insertion of LMA and there in no significant difference in adverse effects during LMA insertion among the two study groups.

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Original Article

Placenta Accreta Spectrum and Modality of Choice For Placental Mapping as Confirmed with Intraoperative Findings

Bushra Haq, Wajid Ali, Tabeen Malik, Muhammad Asif and Shahid Malik

Objective: To find diagnostic accuracy of magnetic resonance imaging (MRI) and color doppler ultrasound for placenta accreta spectrum (PAS) by comparing them with intra operative findings.

Methods: This study was conducted at Lahore General Hospital, Lahore and Services Hospital, Lahore from 01-07- 2017 to 31-01- 2020. 36 pregnant patients with history of previous cesarean sections and ultrasound documentation of placenta previa at more than or equal than 32 weeks of gestation were included in the study. Both color doppler ultrasound and MRI evaluation for PAS were performed on all patients included in the study. Findings were confirmed intra operatively. Women with upper uterine segment placenta were excluded.

Results: Out of 36 patients enrolled for the study, color doppler USG confirmed diagnosis of PAS in 30 patients while MRI confirmed diagnosis of PAS in 31 patients. Intra operatively PAS was confirmed in 31 patients. Color doppler USG yielded 2 false negative cases and 1 false positive case with sensitivity, specificity, accuracy, positive predictive value and negative predictive value of 93.54%,(95% confidence interval [CI] , 77% to 98%), 80.0% (95% CI, 29% to 98%), 91.66%, 96.6%, 66.66% respectively while MRI yielded 1 false negative and 1 false positive case with all these values as 96.77% (95% CI, 81% to 99%), 80.0% (95% CI, 29% to 98%), 94.44%, 96.77%, 80.0% respectively.

Conclusions: Color doppler ultrasound and MRI are complementary investigations. MRI has superior sensitivity than color doppler USG but the specificity of both modalities are same for antenatal diagnosis of PAS.

Keywords: placenta accreta spectrum (PAS), magnetic resonance imaging (MRI), color doppler ultrasonography (USG), intra operative.

Introduction

Placenta accreta spectrum (PAS) is a relatively new obstetrical problem faced by obstetricians. Increasing number of cesarean sections over the past few decades have led to rising incidence of this life threatening condition. Accurate mapping of placenta is one of many other preoperative preparations. Gray scale ultrasound, color doppler ultrasound and magnetic resonance imaging (MRI) are among the different diagnostic modalities used for placental localization and defining the depth of placental invasion. Over the past few decades the increasing number of cesarean sections have lead to the dramatic rise in serious obstetrical complication called ` Placenta accrete spectrum` (PAS).[1] There is 25% to 50% reported incidence of PAS in patients with placenta previa with previous cesarean section.[2] The hallmark for placenta accrete spectrum is absence of decidua and invasion of trophoblast and villous tissue into the myometrium.[3] Placenta accrete spectrum is divided into placenta accreta, placenta increta and placenta percreta based on the depth of chorionoc villi invasion into the myometrium.[4] The morbid adherence of placenta to maternal myometrium may have serious sequels. This may include need for blood transfusion, anaesthesia complications, prolonged surgery, damage to surrounding viscera, need for extensive investigations prior to surgery, obstetrical hysterectomy and psychological and emotional disturbances associated with this life saving procedure.[5] Accurately defining and mapping the placenta prior to surgery is crucial to the successful outcome.[6] Coordinated peripartum management matters the most in the face of heavy blood loss encountered during surgery.[7] Ultrasound is the routinely followed, observer dependent diagnostic imaging modality to identify PAS. The sensitivity of ultrasound ranges from 82.4% to 100% and specificity 92% to 96.8% in different studies.[8,9] MRI on the other hand is another promising imaging modality for mapping the placenta. MRI can be of help in cases of posteriorly located placenta.[10] It can also warn about involvement of adjacent visceras. A recent study compared the ultrasound and MRI. The reported sensitivity and specificity of USG and MRI was 77% and 88% while specificity was 96% and 100% respectively.[11]

Methods

This study was conducted in Lahore General Hospital, Lahore and Services Hospital, Lahore from

With previous cesarean section having initial gray scale ultrasound documentation of placenta previa at gestation of≥ 32 weeks were included in the study. Women with ultrasound findings of upper uterine segment placenta were excluded. Informed and written consent of patients were taken. Both color doppler USG and MRI were performed and read for all the women in the study group by a radiologist who had more than 10 years of experience at Lahore General Hospital, Lahore. Patients were operated at Services hospital, Lahore. Ultrasound and MRI findings were recorded and tabulated. Findings were compared to intraoperative findings to identify the accuracy of imaging modality. These included location of placenta, loss of retroplacental hypo echoic clear zone, visualization of abnormal increased vascularity, presence of placental lacunae, decreased myeometrial thickness, loss of uterine serosa bladder interface and invasion of surrounded structures on color doppler USG. MRI findings for PAS included location of placenta, loss of junctional zone (heterogeneous signal intensity), presence of dark bands on T2W sequence, focal interruption in the myometrium, loss of uterine bladder interface and invasion of surrounding structures. Other findings suggestive of PAS on MRI included focal thinning of myometrium, localized outer bulge of uterus due to mass effect of placenta. All these findings were confirmed against gold standard intra operative findings. 31 out of 36 cases which were positive for PAS were statistically evaluated. Contingency tables were developed to identify the diagnostic accuracy of Color Doppler USG and MRI for PAS taking intra-operative findings as gold standard. p values for both USG and MRI were calculated. For comparison of categorical data Fisher Exact test was performed. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, positive likelihood ratio and negative likelihood ratio were also calculated for color doppler USG and MRI. p value less than 0.005 was considered statistically significant. Results were calculated with SPSS (Statistical Package for Social Sciences) version 20.

Sensitivity=Truepositive÷[True positive+False negative].

Specificity =True negative÷[True negative + False positive].

Positivepredictivevalue=Truepositive÷[True positive+ False positive].

Negativepredictivevalue=Truenegative÷[True negative + Falsenegative].

Overallaccuracy=[Truepositive+Truenegative]÷ All sample.

Positive likelihood ratio = sensitivity ÷ [1-specificity].

Negative likelihood ratio = [1-sensitivity] ÷ specificity.

Results

A total of 36 patients were included in the study. Age of patients ranged from 22-43 years. (mean age 29.16 years). **Table-1** shows the subdivision of placenta previa according to the placental position in relation to internal cervical Os.[12] Placenta previa was sub divided into low lying placenta, marginal previa, complete previa and central previa. Out of these 36 patients 31 had PAS confirmed intra-operatively. While pre-operativly 30 patients on color doppler USG and 31 patients on MRI had diagnosis of PAS as shown in **Table-2&3**. Color doppler USG overestimated 1 case and underestimated 2 cases while MRI overestimated and underestimated 1 case each. MRI has statistically higher diagnostic accuracy (p value 0.0004) than color doppler USG (p value 0.001). **Table-4** shows the diagnostic performance of color doppler USG and MRI. Color doppler USG has sensitivity of 93% (95% confidence interval [CI], 77%-98%) and specificity of 80% (95% CI, 29% to 98%). MRI has sensitivity of 96% (95% CI, 81% to 99%) and specificity of 80% (95% CI, 29% to 98%). We found no significant difference in specificity of both imaging modalities but sensitivity of MRI is more than color doppler USG. Visceral Injury was noted in 11.5% patients as given in **(Table-II)**.

Table-1: Subtypes of placenta previa

Placental Location	No of Patients	%Age
Low Lying Placenta	01	2.7%
Marginal Previa	06	16.6%
Complete Previa	13	36.1%
Central Previa	16	44.4%

Table-2: Color doppler USG and intra operative findings cross tabulation. N=36

Diagnosis on Ultrasound	Diagnosis on intra-operative findings: Morbidly Adherent Placenta	Non adherent Placenta	Total
Adherent Placenta	29	01	30
Non Adherent Placenta	02	04	06
Total	31	05	36

p value= 0.0012

Table-3: MRI and intra operative findings cross tabulation. n=36

Diagnosis on MRI	Diagnosis on intra-operative findings: Morbidly Adherent Placenta	Non adherent Placenta	Total
Morbidly Adherent Placenta	30	01	31
Non Adherent Placenta	01	04	05
Total	31	05	36

p value= 0.0015

Table-4: Statistical analysis of diagnostic performance of color doppler ultrasonography and MRI.

Statistical Analysis	Color Doppler USG	MRI
Placenta Previa (no invasion)	6/36 (16.6%)	5/36 (13.88%)
PAS(morbidly adherent placenta)	6/36 (83.33%)	31/3 (86.11%)
True positive	29	30
False positive	01	01
True Negative	04	04
False Negative	02	01
Sensitivity	93.54%	96.77%
Specificity	80%	80%
Accuracy	91.66	94.44%
Positive Predictive Value	96.6%	96.77%
Nagitive Predictive Value	66.66%	80%
Positive likelihood ratio [95% confidence interval]	4.67(0.80-27.06)	4.83(0.83-27.96)
Negative likelihood ratio [95% confidence interval]	0.08(0.01-0.33)	0.04(0.005-0.300)

Color doppler USG and MRI findings were matching in 29 out of 36 cases (80.55%) while they were discordant for diagnosis in 5 out of 36 patients (13.88%). **Table No-5** and 6 show color doppler USG and MRI imaging findings of PAS in positive cases. Multiple findings were present in single patient.

Discussion

Placenta accreta spectrum is a relatively new term . It encompasses placenta accreta, placenta increta as well as placenta percreta.[4] Risk factors for this disorder include manual removal of placenta, overzealous curettage of uterus prior to pregnancy, myomectomy, previous cesarean section and placenta previa. Cesarean section scar in the uterus causes abnormal anchoring of trophoblastic villi into the myometrium. Risk of PAS increases with increasing number of cesarean sections as well as with placenta previa.[13] Here placenta overlies the uterine scar which predisposes to deep anchoring of villi. Massive hemorrhage can lead to disseminated intravascular coagulation, adult respiratory distress syndrome, organ failure and even death.[14] Prenatal mapping of placenta can prove life saving. For prenatal diagnosis ultrasound remains the primary modality. In a meta analysis by D'Antonio F et al, the over all sensitivity of USG was 90.72 % and specificity was 96.94%.[15] According to this study color doppler USG had best predictive accuracy. In our study the sensitivity of ultrasound is 93.54% while specificity is 80.00 %. MRI is another promising investigation. It is of special help in posteriorly located placenta.[16] As fetal parts obscure the placenta, ultrasound may find it difficult to exactly define the depth of placental invasion into myometrium. Depth ofinvasion and extension of placenta into surrounding structures can be mapped with MRI. However inter observer agreement may vary for interpretation of different MRI features.[17] Features specifically looked For PAS

Table-5: Color doppler USG findings in proved cases of PAS (31 cases).

Item	abnormal clear space /loss of retroplacental zone	Decreased myeometrial thickness	Placental lacunae	Loss of bladder uterine interface	Invasion of surrounding structures	Hyper vascularity
No. of Cases	20/31	13/31	22/31	11/31	09/31	23/31
Sensitivity	64.51%	41.9%	70.96%	35.48%	29.03%	74.19%

Table-6: MRI findings in proved cases of PAS (31 cases).

Item	Heterogeneous signal intensity/ loss of junctional zone	Focal interruption in myometrium	Dark intraplacental bands	Loss of bladder uterine interface	Invasion of surrounding structures	Uterine bulging
No. of Cases	24/31	21/31	18/31	12/31	16/31	19/31
Sensitivity	77.4%	67.74%	58.06%	38.70%	51.6%	61.29%

However inter observer agreement may vary for interpretation of different MRI features.[17] Features specifically looked for PAS in MRI are heterogeneous signal intensity within the placenta, dark intraplacental bands on T2 weighted images, focal interruptions in myometrial walls, tenting of the urinary bladder and direct visualization of the invasion of pelvic structures by placenta.[18] Whereas abnormal uterine bulging is a unique feature picked up by MRI which is specific to placenta accreta.[19] In our study loss of junctional zone was present in 24/31 (77.41%) proven cases of PAS. It was the most significant MRI feature followed by focal interruption in the myometrium in 21/31 (67.74%)proven cases of PAS. In the study of Alamo L et al, the most significant MRI feature was dark intra placental bands.[17] Rahaim NS et al, reported the sensitivity of MRI as 75-100% and specificity 65-100%.[19] In our study sensitivity and specificity of MRI is found to be 96.77 % and 80.00 % respectively. While in the study of Hashem LB et al the sensitivity of MRI was 80.00% and specificity was 85.71% .[18] Ultrasonographic features of PAS include loss of the normal retro-placental clear zone, myeometrial thinning, hyper vascularity on color doppler USG, loss of bladder uterine serosa interface, intraplacental lacunae and extension of placenta into surrounding structures.[20] Intraplacental lacunae with turbulent flow create a`moth- eaten` or `Swiss cheese` appearance. These appear as dark bands on MRI.[21] It is the presence of these placental lacunae that has the highest sensitivity in diagnosis of placenta accreta spectrum on color doppler USG. Its sensitivity and specificity is reported to be 86.9-100% and 78.6-97.2% respectively by Yang JI et al,[22] Japaraj RP et al, reported interface hyper vascularity with abnormal vessels linking placenta and bladder as the most prominent color doppler USG feature for the diagnosis of placenta accreta.[23] Loss of retroplacental clear zone signifies the morbid adherence of placenta with uterus. However it is also seen in normal pregnancies.[24] In our study we found hyper vascularity with abnormal vessels as the most frequently encountered feature on color doppler USG in 23/31 (74.19%) proved cases of PAS. For the prenatal mapping of PAS, MRI and color doppler USG are supportive investigations.The strength of our study is that it compared the accuracy of color doppler USG and MRI against gold standard intra operative findings in the same group of patients. The limitation of our study is that we had a relatively small sample size as MRI is an expensive and time consuming modality. Second limitation is that only those patients were selected for the study who were high risk for PAS on the basis of clinical history and gray scale USG.

Conclusion

Color doppler ultrasound and MRI are complementary investigations. MRI has superior sensitivity than color doppler USG but the specificity of both modalities are same for antenatal diagnosis of PAS. Color doppler USG should be used as primary diagnostic tool however in doubtful cases of posteriorly located placenta MRI can be of valuable help.

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Original Article

Frequency of Unnecessary Tooth Extraction in Patients with Trigeminal Neuralgia

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Objective: To determine the frequency of unnecessary tooth extraction in patients with trigeminal neuralgia.

Methods: Observational Cross -sectional study. Study Duration: 1st Jan, 2019 -31st DEC, 2019. All patients of TGN were interviewed for tooth extraction as remedy of their pain before the final diagnosis. They were also asked about number of teeth extracted in range of minimum to maximum. Then all data was shifted to SPSS and analyzed in terms of frequency.

Results: 63/141 (44%) of patients with trigeminal neuralgia had undergone unnecessary teeth extraction before exact diagnosis of disease.

Conclusions: Our study has shown that a high percentage of patients that were treated for idiopathic TGN initially consulted their local dentist and received dental therapy first. This pattern has long been known, was first systematically assessed decades ago, and surprisingly has not changed since. Dentists should work in collaboration with neurologists to evaluate orofacial pain syndrome patients for possible idiopathic TGN. This would result in early diagnosis of trigeminal neuralgia and its proper management and prevention of unnecessary tooth extraction.

Keywords: tooth extraction, unnecessary, trigeminal neuralgia, orofacial pain.

Introduction

Trigeminal neuralgia (TGN) is a condition characterized by paroxysmal, excruciating pain and sudden, like a shock, which lasts a few seconds to two minutes. It is the most common among orofacial pain, returns in irregular periods, being triggered by stimuli not painful, as the simple act of speaking, or chewing .[1] Galassi, Blasi, Galassi et al. reported that the pain crisis may occur when the individual handling given areas of the face, called trigger zones. These areas are located ipsilateral to pain, usually around the nose and near the lips. The attacks often stimulate other responses such as salivation, facial flushing, lacrimation, or rhinorrhea. During a refractory period of pain, even in the presence of stimuli on the trigger zones, the painful process is not triggered.[2] In neuropathic pain it is common neuralgic pain in dentistry practice, so misdiagnosis is not uncommon due to lack of awareness, proper investigation and treatment.[8]

Clinically, the TGN can be confused with disorders related to teeth, facial bones and paranasal sinuses, leading to a variety of therapeutic incorrect. Disease severity is underscored by having one of the highest suicide rates in relation to any disease, and is considered one of the most painful diseases known.[3] Due to these symptoms, patients are likely to consult their local dentist when symptoms first develop and may receive further dental evaluation and treatment before they are referred to a neurologist.[2] Dentists should be accustomed with TGN to differentiate it from orofacial pain and prevent unnecessary tooth extraction. Facial pain has a considerable impact on quality of life. It has been recently shown that TGN is the most frequent type of facial pain[4] and that, among facial pain syndromes, the overall incidence of TGN has remained constant[5] ranging from 12.6/100,000/year[4]27/100,000/ year.[3]

Methods

Observational Cross -sectional study. Study duration: 1st Jan, 2019 -31st Dec, 2019. Objective of the study to determine the frequency of unnecessary tooth extraction in patients with trigeminal neuralgia. we interviewed and collected data of 141 patients presented at neurology out-patient clinic at Lahore General Hospital, with characteristic clinical features and diagnosis of Trigeminal Neuralgia. Diagnosis was purely based on history, clinical examination and specific nature of pain and presence of trigger zones, Patients with atypical facial pain and diseases mimics trigeminal neuralgia were excluded from study .

Results

We interviewed and collected data from 141 patients having diagnosis of trigeminal neuralgia. 84 were female's verses 57 males (F: M ratio 1.4:1) with age range 30-77 years. Out of these patients 63 (44.6%) of them got their teeth extracted before exact diagnosis of trigeminal neuralgia. Patients were divided into two groups on basis of their age. First group (30-40

Females and 15 were male. Total no. of teeth extracted were 2 to maximum of 8 teeth. **(Table-1)**

Table-1: Frequency of unnecessary tooth extraction in trigeminal neuralgia.

Study variable	Values
Total Number of Patients	141
Male	84
Female	57
F:M Ratio	1.4:1
Number of patients with teeth extraction before diagnosis of TGN	63 (44.6%)
Groups in reference to age	2 Groups
	Age < 40 Years
	Age > 40 Years
Age > 40 years	Female 14 Male 09
Age < 40 years	Female 25 Male 15
Number of Teeth extracted	Minimum 2
	Maximum 8

Discussion

Trigeminal neuralgia (TGN) is a syndrome whose patients suffer from episodes of excruciating facial pain in the territory of one or more divisions of the trigeminal nerve that can arise spontaneously or after a gentle tactile stimulation of a trigger point on the face or in the oral cavity or that can be triggered by natural activities, such as chewing, speaking, washing the face, or brushing the teeth. When the pain involves the maxillary or mandibular division of the trigeminal nerve, primary odontogenic syndrome should be considered as differential diagnosis. However, usually, it should be relatively easy, after a throughout anamnesis and clinical examination, to identify if the pain originates from the teeth or not. Therefore, if from a patient perspective, it is understandable to ask for a dental evaluation after the appearance of the first symptoms; it is surprising from a neurological point of view that many patients with a vibrant history of idiopathic TGN have their teeth extracted before a definitive diagnosis is made. A paper appeared in 1983 by Garvan and Siegfried[6] showed that 73 % of patients with trigeminal neuralgia had a dental assessment before diagnosis and that 65 % of them had a range from 1 to 32 teeth extracted.[6]

which corresponds to our study in which 63 patients (44.6%) despite having teeth extraction found no relief of their orofacial pain and presented to neurology department with no symptomatic relieve. On detailed examination and history taking we found that most of these patient presented to us with either preliminary diagnosis of TGN or definitive diagnosis had there multiple tooth extracted ranging from two to eight in number with no relieve in their pain otherwise.

Here I would like to highlight another important perspective of our study in which demographically out of 141 subjects of our study 63 got their tooth extracted whereas out of 63 majority that is 39 were female who responded poorly to tooth extraction as a management of their orofacial pain. Comparing to a study done in Pakistan back in 2013 with title of Spectrum of Trigeminal Neuralgia Out of 117 cases, 49 (41.9%) were males and remaining 68 (58.1%) were females. Among these 117 cases 108 underwent unnecessary dental extraction with no improvement in their symptoms.[7]

Despite an era of rapid advancements in science and medicine, there is no significant difference in unnecessary dental extraction in patients with trigeminal neuralgia. This is in part because of the treacherous nature of the disease that mimics the more common dental conditions. However, the solution to this problem is not just providing stronger educational provision for our dentist colleagues. "Facial pain" should be discussed with more frequency and in more depth in joint meetings between all specialties involved in the field. This paper also emphasizes the importance of what we recognize as "continuous medical education".

Conclusion

In our study has shown that a high percentage of patients that were treated for idiopathic TGN initially consulted their local dentist and received dental therapy first. This pattern has long been known, was first systematically assessed decades ago, and surprisingly has not changed since. Dentists should work in collaboration with neurologists to evaluate orofacial pain syndrome

patients for possible idiopathic TGN. This would result in early diagnosis of trigeminal neuralgia and its proper management and prevention of unnecessary tooth extraction.

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Original Article

The Frequency of c-erb-B-2 (her-2/neu) Over Expression in Different Grades of Transitional Cell Carcinoma of Urinary Bladder

Athar Ali, Qamar Jamal Muhammad Anwar and Samra Sameen

Objective: To determine the frequency of c-erb-B-2 over expression in different grade s of transitional cell carcinoma of urinary bladder.

Methods: This study was performed in our set up. Fifty cases were selected. During selection of cases, care was taken that the sections do not contain too mu ch fibrosis, necrosis, degenerative areas and haemorrhage. Care was also taken t hat the selected sections must contain heavy population of malignant cells representing the tumor.

Results: Regarding frequency of c-erb-B-2 over expression in all the 50 cases of transitional cell carcinoma, 15 (30%) cases were positive and 35 (70%) cases were negative for c-erbB-2 expression. The comparison between positive versus negative cases was highly significant with 95% confidence interval and p value of p< 0.01.

Conclusions: It is concluded that c-erb-B-2 over expression in 30% of transitional cell carcinoma suggests targeting of this tumor with Herceptin. c-erb-B-2 over expression occurs more in higher grade tumors.

Keywords: c-erb-B-2 over expression, transitional cell carcinoma, grades.

Introduction

c-erb-B-2(Her2/neu) expression has been studied in breast cancers where its expression is noted in 20% of the primary invasive breast carcinomas and is associated with poor prognosis.[1] c-erb-B-2 (Her2/neu) over expression in transitional cell carcinoma of urinary bladder ranges from 23% to 80% depending upon the grade of tumour.[2] Bladder cancer can occur in any age.

It is generally a disease of the middle age and elderly, however with the median ages at diagnosis for TCC being 69 for men and 71 for women respectively.[3] Moreover, the incidence of bladder cancer increases directly with age. In adults younger than 30 years, bladder cancer tends to express well-differentiated histology.[4] Younger patients appear to have a more favorable prognosis than in older ones.[5] Underwood et al (1995)[6] assessed c-erb-B-2 over expression by using immunohistochemistry.

They found 47% expression and 9% gene amplification of c-erb-B-2. Over expression was more i.e. 50% in recurrent tumors, as was gene amplification with P<0.05. They concluded and suggested that c-erb-B-2 can play a role as prognostic marker.

Chow et al (1997)[7] studied c-er b-B-2 over expression by using immunohistochemical techniques involving monoclonal antibody on formalin fixed, paraffin- embedded TCC of human bladder and analysis showed 18% expression of c-erb-B-2. They observed non-significant association between receptor over expression and tumor grade (P>0.01) but they suggested further studies.

Methods

This study was performed on formalin fixed paraffin embedded cases, diagnosed as transitional cell carcinoma of bladder, in our set up. Fifty cases were selected. During selection of cases, care was taken that the sections do not contain too much fibrosis, necrosis, degenerative areas and haemorrhage. Care was also taken that the cases must contain heavy population of malignant cells representing the tumor. The patients with incomplete clinical data were also excluded.

Results

The detail of results is given in **Tables 1 & 2 and Figures & 2.**

Table-1: Frequency of c-erb-B-2 over expression in transitional cell carcinoma of urinary bladder.

C-erb-B-2 over expression	N=%	95% CI	P-Value
Positive	15 (30%)	10.1-57.5	<0.01
Negative	35 (70%)	42.5-89.9	

Table-2: Grade wise c-erb-B-2 over expression in transitional cell carcinoma of urinary bladder.

Grades	C-erb-B-2 +ve Cases	C-erb-B-2 -ve Cases	Total
I	00 (0%)	03 (6%)	03 (6%)
II	08 (16%)	19 (38%)	27 (54%)
III	07 (14%)	13 (26%)	20 (40%)
Total	15 (30%)	35 (70%)	50 (100%)

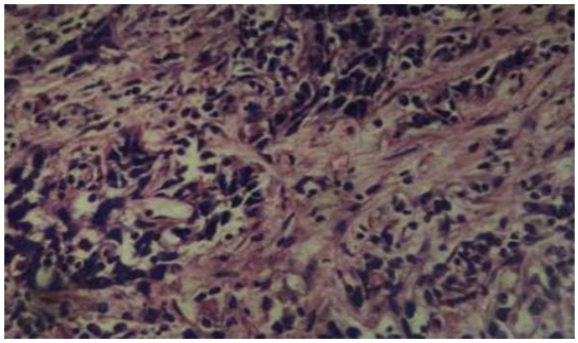

Fig-1: Transitional cell carcinoma grade III, H &E x 205.

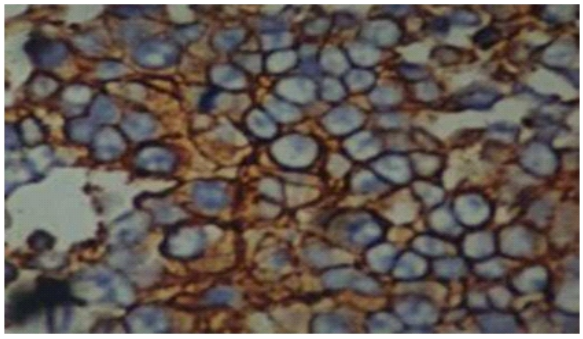

Fig-2: Transitional cell carcinoma grade lll intense membranous with cytoplasmic staining for c-erb- B-2 x416

Discussion

In this study, the overall frequency of c-erb-B-2 over expression in TCC of bladder is 30% (15 out of 50 tumors are positive). Positivity for the c-erbB-2 oncoprotein was easily identifiable as an intense brown staining localized predominantly at the cell membrane in agreement with, as reported by McCann et al (1990).[8] The review of the previous studies has shown the expression of c-erb-B-2 ranging from 2%-74.3%. The finding of 30% over expression in our study is nearly in concordance with the studies of Wei et al. (1993)[9], Moriyama et al (1991)[10] with the ranges of 31%-35% in all of these except that of Sato et al (1992)[11] which showed over expression of 26%. Other studies of Pitch et al (2002)[12] and Zhau et al (1990)[13] had reported expression from 36% - 72.3%. When frequency of c-erb-B-2 over expression was compared with the grade of the tumor, it was observed 0%, 29.7% and 35% in grade I, II & III tumors respectively. The absence of over expression in grade I tumors could be due to low number of cases in this group. Comparing grade II with grade III cases, frequency is higher in grade III tumors compared to grade II which was also statistically significant. Our results are similar to the outcome of studies by Moriyama et al (1991)[10] and Gardiner et al (1992)[14] who also reported greater over expression in grade III tumors as compared to grade I and grade II tumors. The over expression in grade III cases in our study has significant statistical value. This finding in our study and of the studies which are in concordance, support the idea that the more undifferentiated the tumor i s, the greater is the over expression.

Conclusion

It is concluded that c-erb-B-2 over expression is in 30% of transitional cell carcinoma. C-erb-B-2 over expression occurs more in higher grade tumors. Thus targeting of this tumor with new biological therapeutic agents like Herceptin is suggested in future modalities of treatment of this neoplasm.

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Original Article

Histological Changes in Epithelium of Hypertrophied Palatine Tonsils in Children

Saima Shahbaz, Munazza Sardar, Zahra Haidar and Attiya Mubarak

Objective: To study histological changes of tonsillar epithelium of enlarged tonsils and to co-relate the extent of these changes to the tonsillar hypertrophy.
Methods: Enlarged tonsils from thirty children with obstructive airway symptoms were obtained after tonsillectomy. Normal tonsils were obtained from children's at autopsy.
Results: In hypertrophied tonsils size, weight, epithelium and lymphoid compartment, all were affected. In tonsillar epithelium it was observed that there was increase in thickness and keratinization.
Conclusions: These epithelial changes are mainly physiological and probably immunological response to exposure to different antigens in an exaggerated manner and manifested by histological changes.
Keywords: hypertrophied tonsils, keratinized epithelium, lymphocytes.

Introduction

Enlarged tonsils have become the most frequent indication for tonsillectomy.[1] The commonest causes of enlarged tonsils in pediatric age group are reactive hyperplasia and chronic infection.[2] Tonsillar hypertrophy was observed in 11% school children in Turkey and adenotonsillar hypertrophy was observed 55.3% in school going children in Brazil.[3,4] In America the most commonly performed surgical procedure in children is tonsillectomy with or without adenoidectomy, the commonest indication being size i.e. tonsillar hypertrophy and its complication.[5] Generally tonsils start to hypertrophy during first three years of life which is the period of highest immunological activity during childhood[6]. The palatine tonsils increase in size throughout childhood and tend to regress or involute at puberty, when the reactive lymphoid tissue begins to atrophy.[7,8] Usually after 10 years of age tonsils start to atrophy, which is completed in adulthood[6]. This hypertrophy is not a disease but is due to increased immunological activity and is clinically known as tonsillar hypertrophy.[7] Sometimes this increase is very rapid and develops serious symptoms and complications.[9] Following 4 lymphoid compart- ments are present in all categories of tonsils: the follicular germinal centers, the mantle zones of lymphoid follicles, the extrafollicular area and the reticular cryptepithelium.[7] In physiological hypertrophy, tonsils increase in size and weight with absence of both visible congestion on anterior pillars and cheesy discharge on pressing. Tonsillar crypts contain dead and alive lymphocytes, desquamated epithelial cells and bacteria more than the normal tonsils.[10] Hypertrophied tonsils are characterized by enlarged follicles with significant enlargement of germinal centers.[10,11]

According to some researches interfollicular area is reduced because of the enlarged lymphoid follicles in tonsillar hypertrophy and it is relatively increased in diseased tonsils[12] while others stated that the interfollicular area remains unaffected.[13]

An equally reliable and useful feature that aids in differentiating tonsillar hyperplasia is the polarity of lymphoid follicles. Polarity is the mantle zone hyperplasia localized at one pole and is towards the antigenic stimulation.[14] In tonsillar hypertrophy the overlying epithelium is also thickened or even keratinized also known as hyperkeratosis.[15] Hyperkeratosis is the thickening of skin due to irritation from the sun, chemical or frequent friction or pressure. Epithelium of human palatine tonsil comprises of 2 different compartments i.e., epithelium of surface and crypt. The epithelium of tonsils is characterized as lymphoepithelium.[7,16] The epithelial area which is exposed to antigen is increased by 10 to 30 blind-ending crypts, and extends deeply into the tonsillar tissue.[17] The lymphoid tissue, which contains B lymphocytes (including some mature plasma cells) producing predominantly IgD and IgA, T lymphocytes and antigen presenting cells.[18] The lymphoid tissue of the tonsils is directly exposed to the outside environment through inspired air or by ingested food. Electron microscopic observations have demonstrated that the mature epithelium of tonsillar crypt is porous and allows the protrusion of lymphocytes through these pores that mediate the immune response.[19] It explains the functions of the palatine tonsils i.e. they sample the environmental antigens (which were inhaled or ingested) and participate in the initiation and maintenance of the local and systemic immune responses.[15]

Known. There is one possibility that during early postnatal life, respiratory viruses may modify the neuroimmunomodulatory networks within the tonsillar compartments, and in response to various exogenous stimuli promote different patterns of proliferation.[20] Healthy tonsils offer better immune protection and become more enlarged according to their demand for more immunity. In diseased tonsils there is decreased antigen transport, decreased antibody production above baseline levels, and increased chronic bacterial infection, and so these are less effective at serving their immune functions.[21]

Methods

It was a descriptive study of 6 months duration and conducted in the Department of Anatomy, King Edward Medical University, Lahore. Non hypertrophic tonsils from autopsies of ten children were collected from Department of Forensic Medicine, King Edward Medical University, Lahore. These were categorized as Group A (control group).

Thirty samples were collected from children who were diagnosed with obstructive tonsillar hypertrophy (after a detailed history taken on a proforma).

They underwent tonsillectomy at the Department of ENT Unit-II Mayo Hospital Lahore (15 children), Department of ENT Services Hospital Lahore (6 children) and Department of ENT Sir Ganga Ram Hospital Lahore (9 children). These were categorized as Group B. Prior to autopsy or surgery a written informed consent was obtained from the guardians or parents.

For the children undergoing tonsillectomies for hypertrophied tonsils, age range was 4-10 years (male and female children), with history of obstructive symptoms. For autopsies dead bodies of children both male and female of age 4-10 years received within 12 hours of death. The following gross and histological parameters were observed. The tonsils were examined for the colour and surface of epithelium.

The measurements were made by means of an occulometer at magnification of 10x objective. The sections were examined for the following parameters of epithelium. Type, thickness, lymphocytic infiltration and integrity of basement membrane.

Three random readings of three respective fields per slide of the above mentioned parameters of the tissues were taken under low power (10x objective) and mean was taken. Data were entered and analyzed using SPSS 13 version. All qualitative data was presented in form of multiple bar charts with respect to study groups. Quantitative data was presented in the form of mean ± S.D along with its minimum and maximum value. Chi-square test of association was used for the comparison of qualitative data in all study groups. Mann-Whitteny U Test was applied for the comparison of quantitative data in both study groups. A p-value less or equal to 0.05 was taken as significant.

Results

It was observed that there was no visible congestion, ulceration or pustule on the surface of hypertrophied tonsils. Surface epithelium in all specimens from group A and in 15 out of 30 specimens (50%) from group B was stratified squamous non-keratinized **(Fig-1)**, while in the remaining 15 specimens (50%) from group B it was stratified squamous keratinized **(Fig-2).**

Mean thickness of surface epithelium in group A was 70.32±6.49µm **(Fig-3),** while in group B it was 165.65±35.98µm **(Fig-3).**

The minimum thickness in group A was 63µm and and maximum thickness was 83.83µm. In case of group B the minimum thickness was 100.00µm and maximum thickness was 240.00µm.

The difference in mean thickness of epithelium b
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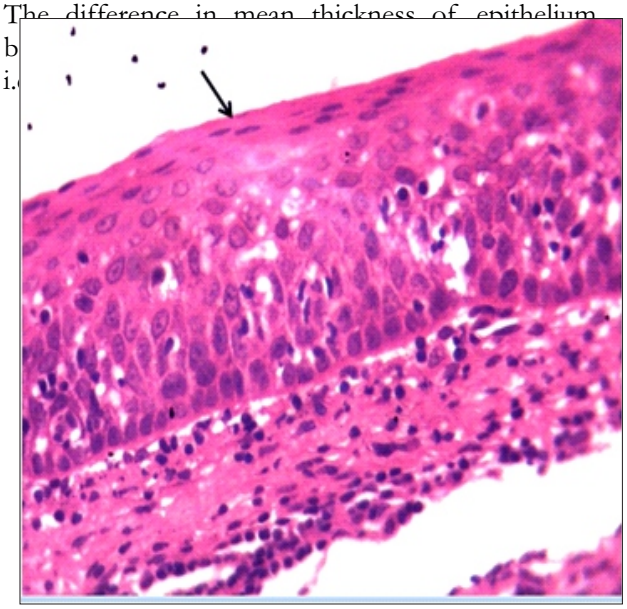

Fig-1: A photomicrograph of the surface epithelium of the tonsil from control group showing stratified squamous non keratinized epithelium (black arrow). H&E stain magnification 400X.

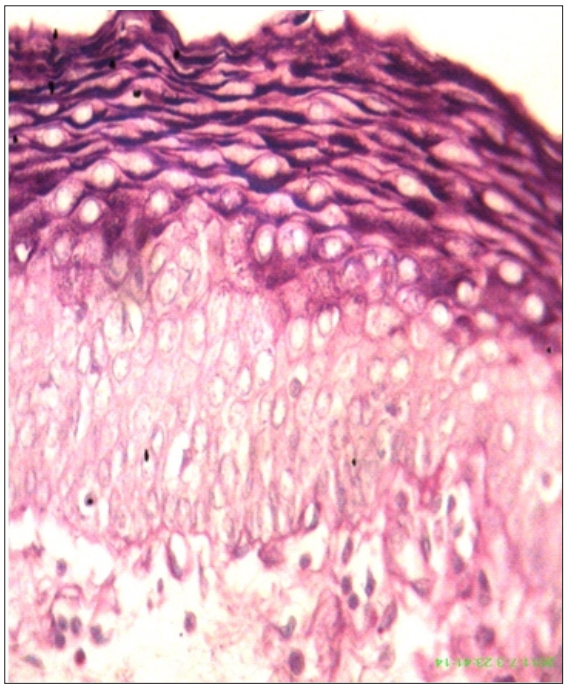

Fig-2: A photomicrograph of the surface epithelium of the tonsil from group B showing keratinization (green arrow). H&E stain magnification 400X.

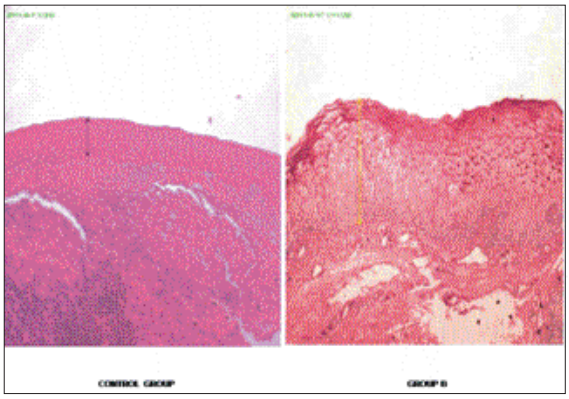

Fig-3: Aphotomicrograph of surface epithelia of both groups Showing comparison of thickness of epithelia in control (black arrow) and group B (yellow arrow). H&E stain magnification 100X.

Table-1: Type of epithelium in study groups.

Keratinization	Study Group		Total
	Group A	Group B	
Present	0 (0%)	15 (50%)	15 (37.5%)
Absent	10 (100%)	15 (50%)	25 (62.5%)
Total	10 (100%)	30 (100%)	40 (100%)

p-value = 0.006 (significant)

Table-2: Thickness of epithelia in study groups.

	Study Group	
	Group A	Group B
N	10	30
Mean	70.32	165.65
Std.	6.49	35.98
Deviatgion	2.05	6.57
Minimum	63.00	100.00
Maximum	83.83	240.00

Discussion

Tonsillar diseases i.e, tonsillitis or hypertrophy are common in children. In this study normal tonsils (Group A) were compared with hypertrophied tonsils (Group B) in children of 4-10 years of age. It was observed that there was no change in colour or any visible pathology on the hypertrophied tonsils. This visible pathology may be in the form of congestion, pus or ulceration. However on microscopic study we found epithelial changes regarding type and thickness. In present study surface epithelium of all the tonsils in group A was stratified squamous non keratinized which is the normal epithelium of palatine tonsils (fig. 12 & 13). In experimental or group B, epithelium of 50% tonsils was having stratified squamous non keratinized and 50% were having stratified squamous keratinized epithelium. This finding is in accordance with Yoko SATO et al (2011) who found the keratinization in the crypt epithelium of hypertrophied and infected palatine tonsils whereas surface epithelium was non keratinized[22]. In the current study keratinization of epithelium was observed both on surface as well as in the crypts. In 2015 another study was carried out on human palatine tonsils of patients of 19-26 years of age with history of chronic tonsillitis. Researchers found keratinization of crypt epithelium.[23] As for as thickness of epithelium was concerned, the mean thickness of surface epithelium in group A was 70.32±6.49 µm while in group B it was 165.65±35.98 µm. Ollfsson et al (1997) found 0.2-0.9 mm of epithelial thickness in hypertrophied palatine tonsils but the age range was 8-38 years.[24]In the current study the children are young (age range was 4-10 years) and their oropharynx are small. Increase in the size of the tonsils is causing obstruction. The increase in the tonsils size is due to increase in thickness of epithelium or tonsillar epithelium hypertrophy. This obstruction to inhaled or ingested matter may be the cause of surface epithelium keratinization due to continuous friction with inspired air and ingested

and may be due to exposure to ingested or inhaled antigens.

Conclusion

It was concluded from our study that keratinization and hypertrophy of epithelium are common features of hypertrophied tonsils in children. Some preventive and therapeutic measures should be taken, as prolonged obstructive tonsillar hypertrophy, especially in young children has many complications and may prove fatal.

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Original Article

Fetomaternal Outcome of Pregnant Patients with Valvular Heart Disease in a Tertiary Care Obstetrical Unit.

Summera Aslam, Faizan Kashif, Aleena Kashif and Tayyiba Wasim

Objective: To assess the incidence and types of valvular cardiac disease in pregnancy and to evaluate the Fetomaternal outcome in booked and unbooked patients.

Methods: It was a four-year cross-sectional data analytical study conducted at Gynae Deptt. SIMS/ Services Hospital, Lahore from January 2014 to December 2017. All the pregnant patients with valvular heart disease both booked and unbooked were included in this study. All the data from the registers and patients' files was reviewed and entered in a detailed proforma.

Results: During the period, 14473 deliveries were conducted. Out of these, 217 patients (1.5 %) had cardiac problem. 147 cardiac patients presented with valvular heart disease (10.15 per 1000). Out of total 147 pregnant patients with valvular heart disease, the mean age of the patients was 27.67±7.835 years and majority of the patients 70(47.6%) were between the age of 26-30 years.. Eighty-six (58.5%) patients were booked whereas 61(41.5%) patients were unbooked, 108 patients were multi gravida. Mitral stenosis was the commonest lesion (92%) with 42.1% had severe stenosis and 81% had ejection fraction >50%. As regards the treatment of valvular diseases in these pregnant cardiac patients, 31(21%) patients had PTMC, 32(22%) patients had valvular replacements whereas 62(42%) patients were on medical treatment. Regarding maternal outcome, no complications were noted in 79(53.74%) patients, 51(34.69%) patients suffered from pulmonary edema, 9 (6.12%) patients had atrial fibrillation, and stroke was noted in 2(1.36%) patients while 2(1.36%) patients suffered from pulmonary hypertension. There were 4(2.72%) maternal deaths. IUGR was noted in 40(27.21%) patients, there were 36(24.49%) preterm births, 23 (15.64%) miscarriages, 6(4.1%) still births, 3(2%) neonatal deaths and no fetal complications were noted in 38(25.85%) patients. Fetomaternal outcome was better in booked patients.

Conclusions: Pregnancy with cardiac disease especially valvular heart disease is still a major problem in our setup. Early booking and management with multidisciplinary approach in collaboration with a team of trained obstetricians, cardiologists, anesthetists and pediatricians may result in reduced morbidity and mortality of the disease.

Keywords: valvular heart disease, fetomaternal outcome.

Introduction

Pregnancy with cardiac disease is still a major problem worldwide especially in developing countries. The reported incidence of cardiac disease in pregnancy varies between 0.1 and 4%.[1-3] Improvements in health care facilities have significantly helped to identify more pregnant patients with cardiac disease at an early stage and thus reduce the risk of fetomaternal morbidity and mortality. At present the maternal heart disease is responsible for 10-25% of maternal deaths worldwide.[4] It is now the second most comm-oncause of death after psychiatric causes.[5] The rheumatic heart disease has decreased in recent years in developed countries but it continues to be a serious problem in developing countries like Pakistan with a prevalence of 5.7 per 1000patients.[6] Reason being poor socioeconomic conditions, overcrowding, purulent streptococcal infections and poor access to proper health Services.[7] Increased cardiac demands during the course of pregnancy potentially increase morbidity and mortality in women with underlying heart disease.[8] The physiological adaptation of pregnancy predisposes cardiac pregnant patients to decompensate. Detailed assessment of patient throughout pregnancy may lead to discovery of maternal cardiac disease at an early stage.[9] If diagnosed early and managed properly with multidisciplinary approach with collaboration ofteam of trained obstetricians, cardiologists, anesthetists and pediatricians may result in successful fetomaternal outcome in majority of cases.[10]

Methods

It was a 4 years cross sectional study from January 2014 to December 2017 conducted at gynecology department, SIMS, Services Hospital, Lahore. All pregnant patients with known valvular cardiac disease

Confirmed on echocardiography were included inthe study. Detailed history and clinical examination were undertaken in all the patients in collaboration with cardiologist. A Proforma was designed which included background information like age, parity, occupation, address, phone no if available, educational status of patients, known cardiac patients or diagnosed de. novo ,type of cardiac lesion , its timing of diagnosis and whether medical or surgical or both treatment takenand, echocardiographic findings , , number of antenatal visits in our hospital , obstetric history, family history especially of cardiac disease, maternal complications both cardiac and obstetrical during antepartum , intrapartum ,or postpartum period or fetal complication like prematurity , intrauterine growth restriction , or perinatal mortality , ,details of mode of delivery , maternal and fetal outcome ,neonatal follow up for one week and maternal mortality.

Allcardiac patients were assessed regarding modeof delivery and those without any contraindications were allowed spontaneous vaginal delivery while others had cesarean section forabsolute obstetrical indications. Instrumental delivery was under taken if maternal effort was poor in second stage of labour. Fluid overload was avoided during labour and so was ergometrine in third stage. Prophylactic antibiotic was given to selected patients such as metallic valvular heart replacement or preterm labour with premature rupture of membranes (PROM). Patients undergoing spontaneous vaginal delivery were given narcotic analgesia. Low molecular weight heparin was given to patients with prosthetic valve replacement and switch over to oral anti coagulants was made after 72 hours.Patients were kept in obstetrical ICU for 24 hours after delivery and discharged after three days for further follow up at PIC.

Results

During this study, a total of 14473 deliveries were conducted. Among these, there were 14256 (98.5%) non-cardiac patients whereas 217(1.5%) patients had cardiac disease. Among 217 cardiac patients, 147 (68%) patients had valvular heart disease. The mean age of the patients was 27.67±7.835 years and majority of the patients 70(47.6%) were between the age of 26-30 years.. Eighty-six (58.5%) patients were booked whereas 61 (41.5%) patients were unbooked, 108 patients were multi gravida. Mitral stenosis was the commonest lesion (92%) with 42.1% had severe stenosis and 81% had ejection fraction>50%. **(Table-1)**. Regarding fetal outcome, IUGR was noted in 40 (27.21%) patients, there were 36(24.49%) preterm births, 23 (15.64%) miscarriages, 6(4.1%) still births, 3(2%) neonatal deaths and no fetal complications were noted in 38 (25.85%) patients. There was only 1 (0.68%) anomalous baby Regarding maternal outcome, no maternal complications were noted in 79 (53.74%) patients, 51 (34.69%) patients suffered from pulmonary edema, 9 (6.12%) patients had atrial fibrillation, and stroke was noted in 2(1.36%) patients while 2(1.36%) patients suffered from pulmonary hypertension. There were 4(2.72%) n

Table-1: Patients characteristics.

Patient Characteristic	
Total no. Of deliveries	**14473**
Cardiac Patients	217 (1.5%)
Non-Cardiac Patients	14256 (98.5%)
Cardiac Patients	**217**
Valvular Heart Disease	147 (68%)
Non-Valvular Heart Disease	70 (32%)
Age (Years)	
<20	2 (1.4%)
20-25	48 (32.7%)
26-30	70(47.6)
31-35	21 (14.3%)
36-40	6 (4.1%)
Booking Status	
Booked Patients	86 (58.5)
Unbooked Patients	61(41.5%)
Gravida	
Prime Gravida	36 (26.5%)
Gravida2- Gravida4	76 (51.7%)
Gravida5 onwards	32 (21.8%)
Duration of Pregnancy	
More than 37 weeks	81 (55.1%)
Less than 37 weeks	43 (29.3%)

Valvular Heart Disease	
Mitral Valve only	92 (62.6%)
Multiple Valves	49 (33.3%)
Aortic Valve only	4 (2.7%)
TricuspidValve only	1 (0.7%)
Pulmonary Valve only	1 (0.7%)
Degree of Valvular Lesion	
Mild mitral stenosis	24 (16.33%)
Moderate Mitral stenosis	34 (23.13%)
Severe Mitral stenosis	62 (42.1%)
Mitral Regurgitation	17 (11.56%)
Aortic stenosis	2 (1.36%)
Aortic Regurgitation	4 (2.72%)
Pulmonary stenosis	2 (1.36%)
Mixed Valvular Regurgitation	2 1.36%)
Ejection Fraction	
>50%	119 (81%)
<50%	28 (19%)
Treatment of Valvular Heart Disease	
Medical Therapy	62 42%)
Valve Replacement	32 (22%)
PTMC (Percutaneous Mitral Transvenous Commissurotomy	31 (21%)

Table-2: Fetomaternal outcome.

Fetal Complication	
IUGR (Intra uterine growth restriction)	40 (27.21%)
No complication	38 (25.85%)
Pre-term Births	36 (24.49%)
Miscarriages	23 (15.64%)
Still Births	6 (4%)
Neonatal Deaths	3 (32%)
Anomalous Baby	1 (0.68%)
Maternal Complications	
No Complication	79 (53.74%)
Pulmonary Edema	51 (34.69%)
Atrial Fibrillation	9 (6.12%)
Stroke	2 1.36%)
Pulmonary Hypertension	2 (1.36%)
Maternal Deaths	4 (2.72%)

Table-3: Comparison of feto-maternal outcome in booked vs unbooked patients.

	Booked	Unbooked	Total	Chi^2	P-value
Maternal Outcome					
Maternal deaths	1 (0.6%)	3 (2.04%)	-	-	-
No Maternal Complications	73 (49.7%)	6 (4.1%)	6 (4.1%)	-	-
Maternal complications	13 (8.8%)	55 (37.4%)	79 (53.7%)	-	-
Total	86 (58.5%)	61 (41.5%)	147 (100.0%)	80.851	<0.05
Fetal outcome					
Still births	1 (0.7%)	5 (3.3%)	-	-	-
Neonatal deaths	1 (0.7%)	2 (1.4%)	-	-	-
No Fetal complications	12 (8.2%)	24 (16.3%)	36 (24.5%)	-	-
Fetal complications	49 (33.3%)	62 (42.2%)	111 (75.5%)	-	-
Total	86 (58.5%)	61 (41.5%)	147 (100.0%)	1.309	<0.05

Discussion

The frequency of cardiac disease with pregnancy in our study was 1.5%.This is comparable to various studies which report 0.2% to 4% incidence of all pregnancies complicated by cardiac disease.[11,12]

In our study out of a total of 217 cardiac patients, 147(68%) patients suffered from valvular heart disease.Valvular heart disease accounts for about 30% of the cardiac disease during pregnancy in developed countries whereas in developing countries 66-90% of the pregnant cardiac patients have valvular heart disease.[13,14] In our study, 92(62.64%) patients have mitral valve involvement which is the commonest valvular lesion. Priya et al reported 57% of isolated mitral valve lesions in their study of pregnant cardiac patients in India.[15] Rheumatic heart disease is still a burden in developing countries where weak health systems offer poor coverage of primary and secondary prevention. In our study, medical treatment was imparted to 62(42%) patients. This observation also correlates with the literature as most of the pregnant patients with cardiac disease are being treated medically in developing countries.[16,17] Surgical interventions in form of septoplasty and valve replacement are more common in developed countries. Poverty, lack of access to proper services, cost and dearth of specialized services are reasons for continuation of medical treatment. Regarding mode of delivery, 72 (49%) patients had vaginal deliveries whereas operative vaginal delivery was conducted in 7 (4.8%) patients. Priya et al and Sethuraman et al have reported vaginal delivery in 58% and 70% of patients

respectively.[15,17] Vaginal delivery is a preferred option for patients with cardiac disease as caesarean section poses more risk to mother in terms of hemodynamic instability. Regarding fetal outcome in our study, IUGR was noted in 40(27.21%) patients and there were 36(24.49%) pre term babies. Both are known complications in patients with valvular heart disease. Hemodynamic disturbances impede blood flow to the fetus and results in IUGR and preterm deliveries. The patients who were being treated for valvular heart disease had New York heart association (NYC) class III or IV had more complications. Mohamed Rezk has reported more NICU admissions and prematurity in patients with NYC class III and IV.[11] Regarding maternal outcome in our study, we had pulmonary edema in 51(34.69%) patients, atrial fibrillation in 9(6.12%) patients, stroke in 2(1.36%) patients, pulmonary hypertension in 2 (1.36%) patients and there were 4(2.72%) maternal deaths. Similar proportions of maternal morbidity have been reported from South Africa.[13] Developing countries have a great challenge of rheumatic heart disease with more than thirty million people living with RHD.[18] It adds a significant burden not only in terms of morbidity but also results in maternal mortality. We had 4 maternal deaths in our study which were mostly in unbooked patients. Booking status implies regular antenatal care and identification of deteriorating symptoms and starting treatment well in time. Booking status was an important determinant in maternal morbidity and mortality in our study as maternal complications like pulmonary edema, atrial fibrillation, stroke and pulmonary hypertension were noted in 55(37.4%) patients who were unbooked as compared to 13(8.8%) patients who were booked (P<0.05). Poor maternal outcomes have been reported from Bahloul M et al and Sawhney H et al in unbooked patients.[19,20] Regarding relation between fetal outcome and booking status, there were 5(3.3%) still births in unbooked patients compared with only 1(0.7%) still birth in booked patients. It was further seen that no fetal complications were noted in 12(8.2%) booked patients as compared to 24(16.3%) patients who were unbooked (P<0.05). Similarly, overall fetal complications including preterm labour, IUGR and miscarriages were noted in 49(33.33%) booked patients as compared to 62(42.2%) unbooked patients. This data shows that fetal outcome was better in booked patients. Regular antenatal care allows early detection of cardiac lesion and treatment is started which results in the hemodynamic stability and hence better fetal outcome. The data clearly showed that maternal and fetal outcome was better in booked patients with less complications in booked patients and this is comparable with the various studies conducted on the pregnant cardiac patients.[21,22]

Conclusions

Pregnancy with cardiac disease especially valvular heart disease is still a major problem inour setup. Early booking and management with multidisciplinary approach in collaboration with a team of trained obstetricians, cardiologists, anesthetists and pediatricians may result in reduced morbidity and mortality of the disease.

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Original Article

Evaluation of the Maternal And Perinatal Outcome in Unexplained Polyhydramnios: an Observational Study

Madiha Afzal, Samar Hussain and Uzma Aziz

Objective: To evaluate the maternal and perinatal outcome in patients with unexplained polyhydramnios

Methods: This observational cross sectional study was done in 80 pregnant females who participated in this study. The study was conducted in the Department of Obstetrics & Gynecology Unit 1, Arif Memorial Teaching Hospital for one year starting from January 2019 to January 2020. All the pregnant patients with confirmed unexplained polyhydramnios, diagnosed with ultrasound were included in this study. Females with congenital anomaly, gestational diabetes and twin pregnancy and rhesus isoimmunization were excluded.

Results: The mean age of the participants was 28.5±4.6 years. The mean gestational age at presentation was 33.12±7.41weeks. Out of 80 females, pregnancy induced hypertension was observed in 18 (22.5%) females, preterm delivery in 23 (28.75%) females, premature rupture of membrane in 23 (28.75%) females, while placental abruption in 11 (13.75%) females. 5 (6.25%) cases were found to be healthy with no associated complication with idiopathic polyhydramnios spontaneous vaginal delivery in 26 (32.5%) females, while cesareans section in 54 (67.5%) females, macrosomia was observed in 27 (33.75%) cases, poor Apgar score was 20 (25%) cases, NICU admission was required in 17 (21.25%) cases while perinatal death was noted in 3 (3.75%) cases while 13 (16.25%) newborns were alive and healthy .

Conclusions: We may conclude from our study that the unexplained polyhydramnios is associated with adverse outcome for both the mother and the fetus particularly with its increasing severity. The diagnosis of idiopathic polyhydramnios is of pertinent significance for identification of high-risk pregnancies and provision of proper antenatal care to ensure a better pregnancy outcome.

Keywords: polyhydramnios, unexplained, maternal and perinatal outcome, cesarean section, premature rupture of membrane, abruption.

Introduction

The origin of the amniotic fluid is fetal and maternal.[1] The fetus is surrounded by amniotic fluid which is essential for the growth and protection of the fetus. This amniotic fluid volume constantly changes throughout the gestation and increases from 35ml at 12 weeks to > 250ml at 17-18 weeks to 800ml at 37 weeks of gestation.[2] The amniotic fluid volume is controlled by dynamic interactions between fetal, placental and maternal systems. Abnormally increased amniotic fluid volume> 95thpercentile or AFI>24cm or deepest vertical pocket >8cm is termed as polyhydramnios which develops as a consequence of disturbed equilibrium between production, fetal resorption and secretion of amniotic fluid.[3] Polyhydramnios complicates about 3-5% of the pregnancies and is further divided into mild (25-30), moderate (30.1-35) and severe (>35).[4,5] Polyhydramnios may result from certain maternal medical disorders, fetal and placental conditions like maternal diabetes, rhesus isoimmunization, and multiple pregnancy, fetal congenital and chromosomal abnormalities.[6] This cause specific polyhydramnios has been found to be associated with adverse fetomaternal outcomes in clinical researches. However in half of the cases, no underlying causative factor can be identified and then it is referred as Unexplained/Idiopathic polyhydramnios. In such circumstances, a thorough maternal and fetal evaluation is undertaken to rule out the above mentioned conditions to label the case as unexplained polyhydramnios so it is the diagnosis of exclusion.[7] Unexplained polyhydramnios is significantly associated with high rates of maternal obstetric complications like preterm labor, premature rupture of membranes, macrosomia, increased caesarean section rate and also 2-4 fold increase in perinatal morbidity and mortality. All these fetomaternal complications increase with increasing severity of idiopathic polyhydramnios.[8]

As the presence of the isolated polyhydramnios at delivery yields an elevated perinatal mortality and morbidity and its effect on fetomaternal outcome has been a matter of clinical debate in modern obstetrics and the obstetricians consider the pregnancy with unexplained polyhydramnios as High Risk Pregnancy, that is why they recommend vigilant surveillance in advanced set up to evaluate and manage the associated maternal and fetal risks.[9]

Methods

This observational cross sectional study was carried out in theDepartment of Obstetrics & Gynecology Unit I, Arif Memorial Teaching Hospital for a period of one year starting from January 2019 till January 2020 on 80 pregnant females who participated in this study after taking written informed consent. Approval letter was taken from ethical committee of Rashid Latif Medical Complex. All the pregnant women aged 18-40yeas, presenting >28 weeks of gestational age with confirmed idiopathic polyhydramnios (AFI>24cm) diagnosed with ultrasound were included in this study. Females having polyhydramnios associated with congenital fetal anomaly, gestational diabetes, twin pregnancy, or those with rhesus isoimmunization were excluded from the study. The demographics of the participants were noted. The severity of unexplained polyhydramnios was ascertained by dividing the cases into 3 categories.[10]

1)Those with AFI between 24-29.9cm i.e. Mild polyhydramnios. 2)Those with AFI between 30-34.9cm i.e. mode- rate polyhydramnios. 3)Those with AFI >35cm i.e. Severe polyhydramnios.

Then all females were advised to present in labor room in case of active labor or premature rupture of membranes or any other problem. At time of delivery, maternal outcome was noted in terms of pregnancy induced hypertension, preterm delivery, pretermprelabor rupture of membranes, placental abruption and mode of delivery. Fetal outcome was noted in ters of macrosomia, low birth weight, low Apgar score, NICU admission and perinatal death after delivery. All this relevant information was entered in a predesigned proforma. Data was analyzed in SPSS version 22.

Results

The mean age of the participants was 28.5±4.6 years. The mean gestational age at presentation was 33.12±7.41 weeks. There were 16 (20%) primi gravida, 38 (47.5%) were multi gravida and 26 (32.5%) were grand multi gravida. The mean BMI of females was 24.92±9.23kgm/2. About 33 (41.25%) lived in rural area and 47 (58.75%) living in urban area. There were 41 (51.25%) females who belonged to low socioeconomic status, 29 (36.25%) belonged to middle class while 10 (12.5%) belonged to high socioeconomic status.**(Table-1)** Amongst 80 participants, 33 (41.25%) cases were having mild, 44 cases (55%) with moderate and 3(3.75%) were having severe unexplained polyhydramnios. **(Table-2)** Out of 80 females, pregnancy induced hypertension was observed in 18 (22.5%), preterm delivery in 23 (28.75%), premature rupture of membrane in 23 (28.75%), while placental abruption in 11 (13.75%) females.**(Table-3)** Out of 80 females, spontaneous vaginal delivery occurred in 26 (32.5%), while lower segment cesareans section was done in 54 (67.5%) **(Table-4).** During pregnancy, macrosomia was observed in 27 (33.75%) cases. The mean Apgar score at 1min was 6.9±1.3 & Apgar score at 5min 7.2±3.8 and poor Apgar score was seen in 20 (25%) cases. NICU admission was required in 17 (21.25%) cases while perinatal death was noted in 3 (3.75%) cases. **(Table-5)**

Table-1: Demographics of females participants.

Demographic Features	(N=80)
Mean Age (Years)	28.5±4.6
Gestational Mean age (weeks)	33.12±7.41
Parity	
Primi Gravida	16 (20%)
Multi Gravida	88 47.5%)
Grand multi gravida	26 (32.5%)
Mean BMI (kg/m$^{2)}$	24.92±9.23
Area of Living	
Rural	33 (41.25%)
Urban	74 58.75%)
Socioeconomic Status	
Low	41 (51.25%)
Midle	29 (36.25%)
High	10(125%)

Table-2: Division of cases according to severity of Unexplained Polyhydramnios.

Severity of unexplained polyhydramnios	Cases(N)T=80	Percentage
Mean Age (Years)	33	41.25%
Gestational Mean age (weeks)	44	55%
Severe (35)cm	03	3.75%

Table-3: Maternal outcomes in unexplained polyhydramnios according to its severity.

Maternal Outcome	Mild	Moderate	Severe	Total	Percentage
PIH	12	06	0	18	22.5%
Pre-term labor	08	13	02	23	28.75%
Premature rupture of membrance	07	16	0	23	28.75%
Placental abruption	03	07	01	11	13.75%
Healthy with no complication	03	02	05	05	6.25%

Table-4: Mode of Delivery in patients with unexplained polyhydramnios according to its severity.

Maternal Outcome	Mild	Moderate	Severe	Total	Percentage
Vaginal Delivery	16	10	-	26	32.5%
C/S	17	34	03	54	67.5%

Table-5: Perinatal outcome in patients with unexplained polyhydramnios according to its severity.

Perinatal Outcomes	Mild	Moderate	Severe	Total	Percentage
Macrosomia	09	18	0	27	33.75%
NICU Transfer	06	10	01	17	21.25%
Poor Apgar score	08	12	0	20	25%
Perinatal death	0	01	02	03	3.75%
Alive/Healthy	10	03	0	13	16.25%

Discussion

Amniotic fluid serves several roles during pregnancy. It creates a physical space for fetal movement, which is necessary for normal musculoskeletal development.[11] It permits fetal swallowing, essential for gastrointestinal tract development, and fetal breathing, necessary for lung development.[12] Amniotic fluid guards against umbilical cord compression and protects the fetus from trauma. It even has antibacterial properties.[13] Abnormally increased amniotic fluid volume is termed as polyhydramnios.[14] Fetal urination, fetal swallowing fetal lung fluid secretion intra-membranous flow across fetal vessels on the placental surface trans-membranous flow across amniotic membrane are major causes which effect the volume of amniotic fluid regulation late in pregnancy.[15,16] Polyhydramnios is present in approximately 1- 2% of pregnancies and it has been associated with a variety of adverse pregnancy outcomes that increase with increasing degree of polyhydramnios.[17] Approximately, 50-60% of cases are idiopathic with no known etiology.[18] Unexplained polyhydramnios is the most common type of polyhydramnios without definite etiological factors.[19] In our study, the mean age of females was 28.5±4.6 years and mostly females are above 25 years above. There were 16 (20%) primi gravida, 38 (47.5%) were multi gravida and 26 (32.5%) were grand multi gravida. The mean BMI of females was 24.92±9.23kgm/^{2}. Biggio et al., found a relationship between idiopathic polyhydramnios and rising maternal age and parity.[20] We divided the total cases according to the severity of unexplained polyhydramnios into three categories i.e. mild, moderate and severe and observed that there were 33 (41.25%) cases of mild, 44 (55%) cases of moderate and 3 (3.75%) cases of severe unexplained polyhydramnios. So the most common type of unexplained polyhydramnios in our study was of moderate severity. This was in contrast to the previous studies done by Dashe in 2002 and Lazebnik in 1999, where mild polyhydramnios was found to be the most common type (92.4%).[21,22] In our study, pregnancy induced hypertension was observed in 18 (22.5%)

cases in moderate unexplained polyhydramnios while no case reported in severe idiopathic polyhydramnios category. This high percentage of PIH seen in or study population is in contrast to the study done by Lallar M et al showing only 4.6% patients having pregnancy induced hypertension in study group. This high percentage of PIH in our patients can be justified by noncompliance towards taking antihypertensive drugs. The total cases of preterm delivery in our study were 23 (28.75%) with 8 (10%) cases seen in mild polyhydramnios, 13 (16.25%) cases with moderate and2(2.5%) cases with severe unexplained polyhydramnios, premature rupture of membrane in 23 (28.75%) females with 7 (8.75%) in mild,16 (20%) cases in moderate polyhydramnios, no case was reported in severe unexplained polyhydramnios category. When we compared the results of maternal outcome parameters like PIH, preterm delivery and PPROM with the study done by Raghuwanshi N et al[23], we observed that she reported 53%, 23%, and 13.3% cases of PIH, preterm labor and PPROM respectively in her research. The placental abruption in our study was seen in 11 (13.75%) females with 3 cases in mild, the highest number of cases i.e.7 (8.75%) in moderate polyhydramnios group and 1 case was seen in severe polyhydramnios category. This risk of placental abruption in patients with unexplained polyhydramnios is in comparison with the study done by Khazaei & Jenabi[24] who showed significant association between polyhydramnios and risk of placental abruption. In 5 (6.25%) patients, there was no added obstetric problem was identified.

Out of 80 females, spontaneous vaginal delivery occurred in 26 (32.5%) females with highest vaginal delivery rate in patients with mild polyhydramnios i.e. 16 cases (20%) followed by patients in moderate polyhydramnios category i.e. 10 (12.5%), while lower segment cesareans section was done in 54 (67.5%) females with high caesarean section rate in patients in moderate polyhydramnios group 42.5% followed by 17 (21.25%) patients in mild idiopathic polyhydramnios. The all 3 (3.75%) patients in severe polyhydramnios group ended up in having caesarean delivery. This overall high operation rate in our research was observed due to associated obstetric complications like macrosomia or placental abruption etc. This high caesarean section rate in our study is comparable to the study in 2016, done by Suleiman & Salim[25] who reported that overall incidence of caesarean section was significantly higher than vaginal birth amongst patients with polyhydramnios. Also Jodi S Dashe et al[21] reported rate of caesarean section of 55% in patients with idiopathic polyhydramnios. But the results of our study are in contrast to that done by Shazia Sheikh et al., who found that delivery occurred through cesarean section in 40% cases of idiopathic polyhydramnios with 60% patients delivering through vaginal route.[2]

In our study, macrosomia was observed in 27 (33.75%) cases with highest case reported in moderate polyhydramnios group i.e. 18 (22.5%) as compared to mild polyhydramnios group i.e. 9 (11.25%) cases. The poor Apgar score was seen in 20 neonates (25%). The highest number of cases with poor Apgar score was seen in newborns with mothers having moderate polyhydramnios i.e. 12(15%) cases.The overall NICU admission was required in 17 (21.25%) cases and again the babies of mothers in moderate polyhydramnios group required more NICU care i.e. 10 (12.5%) versus babies of mothers with mild polyhydramnios i.e. 6(7.5%) while perinatal death was noted in 3 (3.75%) cases with highest perinatal mortality observed in patients with AFI>35cm. So in general, for fetal outcome, we found an increasing trend of macrosomia, poor Apgar score, NICU admission and perinatal mortality with increasing severity of idiopathic polyhydramnios in our research. This is in contrast to the results shown by the study of Malas M O N et al where macrosomia was reported in only 20.3% cases, low. Apgar in 2.9% cases as the majority of the cases in her study were having mild polyhydramnios.[26] In another research by Panting-Kemp et al[27], the researcher did not find any association between increase risk of preterm delivery, low Apgar score, neonatal ICU admission or increased perinatal mortality rate in the pregnancies complicated by idiopathic polyhydramnios. However increased risk of macrosomia and caesarean delivery was observed at the same time Taskin S et al reported that low Apgar scores are associated with varying degrees of unexplained polyhydramnios,[28] whereas Khan S et al failed to demonstrate the significant difference between idiopathic polyhydramnios and low scores.[29] In the report of Pri -Paz et al., significantly low 5-min Apgar scores were noticed in the polyhydramnios group with AFI >35 cm when compared with controls. 16.25% of the neonates in our study remained alive and healthy with majority of the

Thus idiopathic polyhydramnios is associated with specific adverse maternal and fetal outcomes, such as PPROM, preterm labor, placental abruption, higher rate of caesarean delivery, fetal distress and NICU Admissions. Therefore, close surveillance of these pregnancies is required, especially near term.[30]

Conclusion

We have concluded from our study that thehigher proportion of cases of unexplained polyhydramnios in our research have been observed in moderate polyhydramnios category. Although unexplained polyhydramnios itself appears to be an independent risk factor for increased maternal and fetal morbidity but along with that we found that adverse fetomaternal outcome is strongly linked with increasing severity of unexplained polyhydramnios. So relatively higher complication rate like PPROM, abruption, preterm labor, macrosomia, NICU transfer, poor Apgar scores observed in patients with moderate polyhydramnios group than those with mild idiopathic polyhydramnios. Cases of severe polyhydramnios are rare but they are also associated with more maternal and perinatal morbidity and mortality as seen in our study like increased CS rate and PNM rate. So based on the current research findings, it is advised that any pregnancy with idiopathic polyhydramnios must be labelled as HIGH RISK andrequires a thorough strategic surveillance of the mother and fetus with timely intervention to optimize fetal and maternal outcome.

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Original Article

Comparison of Efficacy of Intense Pulsed Light Therapy Versus Fractional Carbon Dioxide Laser For Onychomycosis: A Randomized Trial

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Objective: To compare the efficacy of fractional carbon dioxide laser versus intense pulsed light therapy to treat onychomycosis in adults.

Methods: This randomized controlled trial was conducted on 26 patients of both genders, in the age range of 15-60 years, in the Department of Dermatology, Ameerudin Medical College, PGMI/ Lahore General Hospital for the duration of 6 months. Patients suffering from onychomycosis i.e. fungal infection of nails (confirmed on the basis of fungal scraping) were included. Patients in group A were given intense pulsed light therapy while in group B, fractional carbon dioxide laser therapy was given on weekly basis for 6 weeks. Follow-up fungal scraping was done one week after the last session to assess the effect of treatment.

Results: A total of 26 patients participated in the study which were equally divided into group A and group B. Group A received intense pulsed light treatment and in group B fractional carbon dioxide laser was given. In group A, out of 13 patients, 10 were cured while in group B, 7 were cured. In group A, cure rate was 76.9% while in group B, it was 53.8%. Although the number of patients cured were higher in IPL group as compared to CO2 group but it was statistically insignificant i.e. p-value=0.216.

Conclusions: Although cure rate was apparently higher in patients treated with intense pulsed light therapy but statistical difference among both treatment modalities was insignificant hence intense pulsed light therapy and fractional CO2 laser treatment both are equally effective in patients of all ages and both genders and can be safely used as an adjunct to the topical treatment of Onychomycosis.

Keywords: fractional carbon dioxide laser, intense pulsed light, onychomycosis.

Introduction

Onychomycosis is a common problem in adults. It has several treatment options but failures are very common as well as recurrence is also very frequent.[1] Onychomycosis is the chronic fungal infection of nails, which has poor impact on quality of life of a person as well as his physical and social well-being.[2] Several epidiological studies including 11 population-based studies and 21 hospital-based studies have been done. The average prevalence of onychomycosis was 4.3% [95% CI:1.96.8] for both; population-based studies, but was 8.9% (95% CI:4.313.6) for hospital-based studies. Both types of studies exhibited that onychomycosis is mostly diagnosed in toenails and is more common in men. The main causative organisms for onychomycosis are dermatophytes in 65% (95% CI:51.978.1) cases. Trichophyton rubrum is the commonest fungus cultured in about 45% (95% CI:33.856.0) cases. Moulds have been detected in 13.3% (95% CI:4.622.1) cases, while yeasts in 21.1% (95% CI:11.031.3) cases.[3] Onychomycosis cannot be controlled without treatment and can also infect other body parts.[4,5] Mycological investigations are necessary to confirm clinical diagnosis and identify the pathogen in order to select the most appropriate treatment.[6] Regardless of availability of several anti-fungal medicines, the rate of its cure is very low. Also, it has high recurrence rate after medical treatment.[4,7] Furthermore, because of the uniqueness of the biological system of fungus and prompt reproduction of fungal replicates, oral anti-fungal medicines may necessitate a prolonged course of treatment, which can cause an increase in the cost of treatment and likelihood of side effects.[8,9] So, there is an emergent necessity to pursue more effective methods of treatment which can avert the recurrence and reduce side effects.[10] Oral medicines showed usefulness in several trials and still is the most studied interventional way to treat onychomycosis. Treatment of onychomycosis via lasers is an attractive way for several dermatologists for many reasons.[11,12] Laser treatment is safe, harmless and a fast mode of treatment which can resolve several skin related disorders.[13] So in this study we compared the two most commonly used laser and light techniques for

This would help us to determine the more effective and successful of the two techniques that can be helpful in improving the outcome of therapy.

Methods

It was a Randomized Controlled Trial which was done at Department of Dermatology, Ameerudin Medical College, PGMI / Lahore General Hospital for a duration of 6 months i.e. 1st January-2018 till 30th June-2018. After approval from ethical review committee, written informed consents were taken and patients fulfilling the inclusion criteria were enrolled on the basis of non-probability consecutive sampling. They were randomized into group A and Group B. Patients of both genders and ages between 15-60 years, suffering from onychomycosis i.e. fungal infection of nail (clinical examination and positive microscopy after fungal scraping) were included in the study. Patients suffering from other onychopathies or nail deformities, total dystrophic onychomycosis, using systemic anti-mycotic agents, topical antifungal medication in last 3 months were excluded from the study. Intense pulsed light treatment: a treatment of 3 pulsed shots given on each affected nail with energy 20-22 joules, item: strong and skin type: normal. Fractional carbon dioxide laser treatment: a treatment of three pulsed shots given on each affected nail with point energy of 136-140 millijoules, power 20 watts, duration 6 milliseconds, distance 1.0 mm, interval 10 milliseconds, pattern normal, spot size variable. Patient in both groups were advised to: (a) apply 1% Clotrimazole Cream, twice a day, throughout the treatment and (b) wear gloves while doing wet work. Patients in group A were given intense pulsed light therapy while in group B, fractional carbon dioxide laser therapy was given on weekly basis for 6 weeks. Follow up fungal scraping was done one week after the last session. All the data was collected on predesigned proforma and was analyzed in SPSS v.22. P value of less than 0.05 was considered as significant.

Results

Our study included a total of 26 patients randomized into group A (IPL) and group B (CO2). Both groups included 13 patients each. In group A, 4 patients (30.8%) were in the age group 16-30 years, 7 patients (53.8%) were in the age range of 31-45years and 2 patients (15.4%) were more than 45 years of age. In group B, 5 patients (38.5%) were in the age range of 16-30 years while 4 patients (30.8%) were in the age range of 31-45 years and 4 patients (30.8%) were more than 45 years of age. **(Table-1).** In group A, all participants were female while in group B, there were 11 females and 2 males. **(Table-1)** In group A, 61.5% patients had 3-4 affected nails while 23.1% had 5-6 affected nails while in group B, 53.8% had 3-4 affected nails while 23.1% had 5-6 affected nails as shown in the **(Table-2).** In group A, the cure rate was 76.9% and in group B, 53.8% patients were cured as shown in the table 4. Although number of patients

Table-1: Age & gender distribution of patients in treatment groups.

	Rx IPL	Co2	Total	Pearson Chi Square	P-Value
16-30 Years	04 (30.8%)	05 (38.5%)	09 (34.6%)		
31-45 Years	07 (53.8%)	04 (30.8%)	11(42.3%)	1.596	0.450
> 45 Years	02 (15.4%)	04 (30.8%)	06 (23.1%)		
Total	13 (.0%)	13 (100.0%)	26 (100.0%)		
Male	0 (0%)	02 (15.4%)	02 (7.7%)		
Female	13 (100%)	11 (84.6%)	24 (92.3%)	2.167	0.141
Total	13 (100.0%)	26 (100.0%)	26 (100.0%)		

Table-2: Affected nails & treatment groups..

	Rx IPL	Co2	Total	Pearson Chi Square	P-Value
1-2	02 (15.4%)	03 (23.1%)	(05%)		
3-4	08 (61.5%)	07 (53.8%)	(15%)	0.267	0.875
5-6	03 (23.1%)	03 (23.1%)	(06%)		
Total	(09%)	(17%)	(26%)		

Table-3: Cured/ Not Cured in Treatment Groups

	Rx				
	IPL	Co2	Total	Pearson Chi Square	P-Value
Cured	10 (76.9%)	07 (53.8%)	17 (65.4%)		
Not Cured	03 (23.1%)	06 (46.2%)	09 (34.6%)	1.529	0.216
Total	13 (100.0%)	17 (100.0%)	26 (100.0%)		

Table-4: Result of Treatment in relation to Age & Gender of patients .

	Results				
	Cured	Not Cured	Total	Pearson Chi Square	P-Value
16-30 Years	06 (35.3%)	03 (33.3%)	09 (34.6%)		
31-45 Years	07 (41.2%)	04 (44.4%)	11(42.3%)	0.026	0.987
> 45 Years	04 (23.5%)	02 (22.2%)	06 (23.1%)		
Total	17 100(.0%)	09 (100.0%)	26 (100.0%)		
Male	02 (11.8%)	0 (0%)	02 (7.7%)	1.147	0.284
Female	13 (100%)	09 (100%)	24 (92.3%)		
Total	17 (100.0%)	09 (100.0%)	26 (100.0%)		

statistically significant i.e. p value =0.216. **(Table-3)** No significant association was seen between treatment results and age of patients. i.e. (p-value=0.987). Among cured patients 6(35.3%) were in the age group 16-30 years, 7(41.2%) were in the age group 31-45 years and 4(23.5%) patients were in the age group >45 years. **(Table-4).** No significant association was seen between treatment results and gender of patients (p-value=0.284). Among patients who were cured, 2(11.8%) were male and 15(88.2%) were female. While patients who were not cured all of them were females. i.e. 9(100%). **(Table-4)**

Discussion

The nail is the largest and relatively multifarious skin appendage. Nails are present on the dorsal side of the tips of fingers as well as on the tip of the toes. Nails play a very important role in protection of finger or toe tips. Development of nail starts in the womb (uterus) during 7th to 8th week of gestational age. But they are fully developed at the time of birth. For the accurate development of nails, there are several necessary signals. Structurally, nails are composed of four epithelial components:

i) Matrix, which forms the nail plate;
ii) Nail bed, which inflexibly attaches the nail plate to distal phalanx;
iii) Hyponychium, which forms the natural barrier at physiological point of the separation of nail from the nail bed; and
iv) Eponychium, which embodies the under-surface of proximal nail fold that is responsible to form the cuticle of nail.[14]

Onychomycosis is a rare condition of the pediatric age group. But is has been recently observed that the prevalence of onychomycosis is increasing in pediatric age group all over the world.[15] On the other side, onychomycosis is common skin disorder in adults and the prevalence is high among adults usually in men, as mostly cited in previous studies.[3] It is the fungal infection of nails and is usually difficult to discriminate it clinically from the other nail diseases/syndromes.[16]Onychomycosis is consid- ered as the decoder of nails and commonly occurs in adults. It accounts for about 15-40% of all nail disorders.[17] Several reports could not discriminate between dermatophytosis and other types of onychomycosis, or amongst infectious o non-infectious diseases of finger or toe nails. In UK, it was expected that around 3% of adult population of UK is at risk of developing onychomycosis.[18] The treatment of onycho- mycosis varies and depends on the clinical form of the onychomycosis, the number of nails involved and the brittleness of the involved nails.[19] Though many oral and topical anti-fungal drugs have been extensively used to cure the disease, but oral anti-fungal drugs can cause severe side effects and efficiency of topical anti-fungal drugs is insufficient. Recently, laser treatments have been evaluated to assess their efficacy to cure

machines have the capability to temporarily clear onychomycosis but they do not have on conclusive remedial data.[22] It is very difficult to treat the onychomycosis by applying only topical medicines /agents as these topical agents or medicine have low capacity to infiltrate through the nail and touch the exaggerated nail bed. Oral anti-fungal agents have also shown to be very effective, but as the course of treatment is long, they can cause several probable adverse effects to the systemic parts and also lead to the poor compliance and antagonistic events. So, laser treatments are proposed to be applied for management of the onychomycosis. This may be because of the minimal invasive nature of laser and also the probable require less sessions than other treatment modalities.[23] Numerous laser machines are available and applied to cure the onychomycosis. Most commonly applied lasers are Nd:YAG laser and diode laser. But the available evidence-based data regarding the efficiency of these lasers is still insufficient. Laser treatments can be applied in combination to different topical anti-fungal agents.[24] Treatment of onychomycosis by using laser therapy has been proved to be effective, but in non-randomized trials.[21] Therefore the evaluation of their abilities is still needs to be done to update the practitioners regarding the effectiveness of laser in long-term period. One review study, published in 2013, in which the application of laser technology for treatment of onychomycosis had been discussed, finalized that evidence regarding efficacy of lasers was deficient because of small scale trials and poor study designs, though, it was non-systematic.[25] In our trial, 7(53.8%) patients had complete cure with factional carbon dioxide while with intense pulsed light therapy, 10(76.9%) patients had complete cure. The calculated difference was insignificant, but intense pulsed light showed more cases with complete cure as compared to fractional carbon dioxide laser (p-value=0.216). No significant association was seen between treatment results and age of the patient i.e. p-value 0.987. Similarly both treatment results were not associated with gender of patients (p-value 0.284). Intense pulsed light is efficient in 80% cases, if applied as the treatment of toe-nails onychomycosis. So, lasers could be a good treatment option for the individuals presented with onychomycosis, which is the commonest nail disorder among all other nails disorders.[26] Fractional carbon dioxide lasers when applied in combination with 1% topical luliconazole for 6 months was found to be very much effective and harmless way to cure the onychomycosis among adults. The individuals given this combination treatment showed very high efficacy as compared to the individuals in whom fractional carbon dioxide laser was applied only. The experimental efficacy of carbon dioxide laser treatment was reported to be around 51% during 12 weeks and around 53% within 24 weeks.[27] Fractional carbon-dioxide laser treatment in combination with topical anti-fungal agents is proved to be highly effective found to be effective to cue the onychomycosis. But, randomized controlled trials are required to be done before its extensive application in dermatological clinics.[28] The side effects of laser treatment to cure the onychomycosis have also been reported in previous trials which ranged from mild pain to the tissue necrosis.[29,30] But, if the treatment executed with care and with responsibility, it can be the safest and most effective way to cure onychomycosis. The results of previous clinical trials have also shown strong correlation of overall patients' satisfaction with the laser treatment.[31]

Conclusion

Although cure rate was apparently higher in patients treated with intense pulsed light therapy but statistical difference among both treatment modalities was insignificant hence intense pulsed light therapy and fractional CO_2 laser treatment both are equally effective in patients of all ages and both genders. Now in future, for treatment of Onychomycosis we can recommend both intense pulsed light and fractional CO_2 laser as an adjunct to the topical treatment.

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Original Article

Positive Predictive Value of Colourdoppler in Predicting Malignant Thyroid Tumors Taking Histopathology as Gold Standard

Adnan Maqsood, Iram Iqbal, Wajid Ali, Hafiz Sheheryar Aamir, Nadia Mansoor and Nawaz Rasheed

Objective: To determine the positive predictive value of resistive index with a hope that results of present study provide a good noninvasive test for the preoperative diagnosis of patients with suspected thyroid lesions.

Methods: The study was conducted in the Department of Diagnostic Radiology, Mayo Hospital Lahore in collaboration with pathology department. 379 patients referred to Radiology Department for thyroid ultrasound were included in the study . The data was entered into SPSS version10 and simple percentages were calculated. This data was triangulated and compared with studies world-wide.

Results: In our study the age of the patients ranged from 18 years to 80 years with a mean of 49.45± 16.75 years. There were 84(22.2%) male and 295(77.8%) female patients. The size of the thyroid nodule ranged from 10mm to 42mm with a mean of 18.92±7.01mm.malignancy was confirmed in 313(82.6%) patients on histopathology. The study provided 313 true positive and 66 false positive cases yielding a positive predictive value of 82.6% for resistive index (RI >0.71) on color Doppler in malignant thyroid lesion taking histopathology as gold standard.

Conclusions: The positive predictive value of resistive index on Color Doppler was found to be 82.6% in the diagnosis of malignant thyroid nodule taking histopathology as gold standard. There was no statistically significant difference in the positive predictive value across patient's age, gender and size of the nodule.

Keywords: color doppler, resistive index (RI), histopathology.

Introduction

Thyroid malignancy is the most common endocrine tumor with an overall prevalence in Pakistan is 2.92%. Unfortunately; most of the patients undergo surgery with suspected benign disease which later proves to be malignant on histopathology after surgery and this significantly affects the outcome. Thus there is a need for excellent preoperative diagnosis so that patient´s surgery is well planned and is as extensive as required.[1] Fine needle aspiration cytology due to its high sensitivity and specificity is considered to be single best diagnostic procedure in differentiating benign and malignant nodules. However it is invasive and carries false negative results.[2] Anwar et al(2012)in Pakistan reported the frequency of malignancy to be 16.2% among patients who present with thyroid nodules.[3] Thyroid nodules are a common clinical dilemma; however the vast majority is benign and risk of malignancy occurs in 5-10%. Imaging plays an important role in providing an accurate preoperative diagnosis and in patients with proven thyroid malignancy for local tumor extent, presence of regional and distant metastasis and post- treatment surveillance. Thyroid carcinoma commonly present as thyroid nodule, cervical lymphadenopathy, recent onset of hoarseness, dysphagia and upper airway obstruction. Physical signs suggesting malignancy include hard consistency of thyroid nodule with an irregular edge fixation of nodule to adjacent structures, vocal cord palsy and ipsilateral enlarged cervical lymph nodes.[4] The American Thyroid Association published management guidelines in 2009 for patients with thyroid nodules and differentiated thyroid cancer. It is suggested that with the discovery of a thyroid nodule larger than 1-1.5cm, a serum thyrotrophic (TSH) level should be obtained as part of the initial evaluation.

FNA is inexpensive, widely available, easy to perform, accurate (90%) and cost effective method for evaluating thyroid nodules and commonly regarded as part of the initial investigation. Radionuclide imaging is recommended in patients with a thyroid nodule and subnormal TSH level. Hyper-functioning nodules rarely harbor malignancy.[2,5] 18FGD-PET has been utilized in differentiation of benign from malignant nodules. Although it appears to have a high sensitivity for malignant nodules, its specificity is low.

CT and MRI have only limited role in the investigation of a thyroid nodule. In locally invasive thyroid malignancy (such as anaplastic carcinoma), they help to evaluate the extra thyroid spread of tumor to the

Evidence of regional and distant metastases. Advances in ultrasound technology have made it possible to clearly evaluate the thyroid parenchyma and detect small nodules. The major role of ultrasound in thyroid malignancy includes detection, delineation and characterization of thyroid cancer, detection of cervical nodal metastasis, follow up of patients with benign disease, and follow up of patients after thyroidectomy, for early detection of local or regional nodal recurrence and for fine needle / core biopsy.[6] Sonographic evaluation of thyroid nodule includes Gray-scale, Doppler and Elastic imaging. Grey scale features such as size of the nodule hypoechogenecity, shape (taller than wider), irregular margin, absence of halo, micro calcification, local invasion and solid nature of nodule are useful inidentifying malignancy.[7] A combination of these features is better at predicting malignancy compared to any single feature. Features and combination of features which have a more reasonable predictive value for malignancy include presence of punctate micro calcifications and solid nature shows the highest accuracy (77%) ,specificity (96%), positive predictive value (75%) but a low sensitivity (30%).[4,7] Absent halo and the the presence of punctate micro calcifications has a specificity of 93% and sensitivity of 27%. The presence of micro calcification in a predominantly solid nodule increases cancer risk threefold compared to a predominantly solid nodule without any calcification while presence of coarse calcification increases cancer risk twofold compared to a predominantly solid nodule without any calcification.[8] A combination of an absent halo,

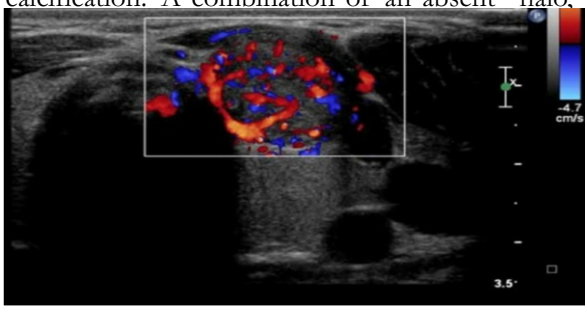

Fig-1: Malignant nodule, showing significantly increased intranodular flow.

and presence of punctate micro calcification has a specificity of 97% and sensitivity of 16%. Peripheral or egg shell calcification once thought to indicate benign nodule reported to have 18.5% prevalence in malignant thyroid nodule.[4,7,8] A pure cystic nodule, although rare (≤2%) is highly unlikely to be malignant. A spongiform appearance defined as aggregation of multiple microcystic components in more than 50% of nodule volume is 99.7% specific for benign thyroid nodule with a negative predictive value for malignancy of 98.5%.[4,9] Nodule size is not predictive of malignancy however nodule growth is an indication of repeat FNAC/biopsy. It is generally believed that follow up is better than FNAB of small nodules (<5mm). Patients with multiple thyroid nodules have the same risk of malignancy as those with solitary nodules. Benign hyperplastic nodules are slow growing and lack a true capsule.[9,10] The presence or absence of a halo is not a good indicator of the nature of the thyroid nodule as it is absent in about half of benign nodules[8] and 10-24% of all papillary carcinomas may have a complete/ incomplete halo around it.[10]

1. Well-defined, smooth suggestive of beni- gnity. **(Fig-2)**
2. Speculated, sharply demarcated: indicative of malignancy.
3. defined (where the edge of the lesion cannot be demarcated from adjacent thyroid parenchyma): seen in both benign and malignant lesions.

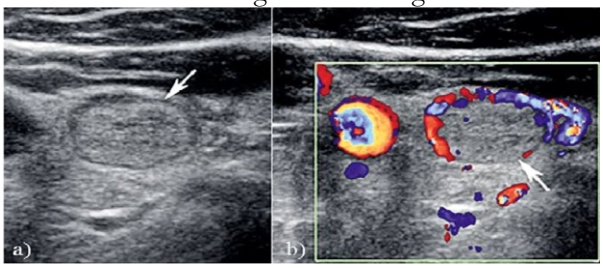

Fig-2: Benign well defined isoechoic nodule, showing a hypoechoic halo with perinodular vascularity.

A taller-than-wide shape is reported to be very specific (93% specificity) in differentiating malignant thyroid nodule from its benign counterpart.[11] Hypo echogenicity in a thyroid nodule is thought to represent its micro follicular structure on histology, whereas iso/hyper echoic nodules have a macro-follicular structure.[12] In routine clinical practice, most benign nodules have either absent vascularity (Type-I) or its perinodular vascularity is greater than intranodular vascularity (Type-II > Type-III). In malignant nodules, the intranodular vascularity is greater than peripheral vascularity (Type-III > Type II.[13] Though solid hyper vascular thyroid nodules have a high likelihood of malignancy (as high as 42%), the Doppler characteristics of a thyroid nodule cannot be used to exclude malignancy because 14% of solid non-hyper vascular nodules may be malignant. Type vascularity is a significant criterion to suggest malignant disease; intranodular blood flow is observed in 91.7% of malignancy and in 65.3% of

specificity of 43.7%.[7,14] Resistive index (RI) obtained from spectral Doppler analysis has been used to differentiate malignant and benign thyroid nodules.[4,6] Malignant nodules have a mean RI of 0.72±0.13 which is significantly higher than those associated with benign nodules (0.6±0.08) . The RI cutoff of 0.75 has a good accuracy (91%), specificity (97%), and negative predictive value (92%) in predicting malignancy, with relatively low sensitivity (40%) and positive predictive value (67%).Malignant nodules also have a higher pulsatility index (PI) (1.15±0.33) than benign nodules (0.91±0.19).[12,15] Although ultrasound is able to detect the presence of extracapsular spread (invasion of adjacent soft tissue and metastasis to regional lymph nodes), it may not be able to delineate its entire extent (partic- ularly for large thyroid masses). Invasion of prever- tebral muscle, esophagus, trachea are better demon- strated on cross-sectional imaging such as CT and MRI. Shadowing from the thyroid cartilage, trachea renders these areas sono- graphically invisible. Regional lymph node metastasis has been reported to occur in 19.4% of all thyroid malignancies.[6,12]

Methods

This cross-sectional study was carried out in the department of Diagnostic Radiology Mayo Hospital Lahore for a period of six months. Sample size of 379 cases was calculated using non-probability consecutive sampling with 95% confidence level,5% margin of error and taking expected percentage of positive predictive value of colour doppler in predicting malignant thyroid tumor to be 55.9%. Patients (18-80 years) with primary thyroid tumor who were labelled malignant on colour doppler RI>0.71 and who subsequently underwent surgical excision of the mass, followed by histopathology. Patients who gave written informed consent to participate in the study were included while those who were unfit for surgical operation or with inoperable thyroid tumors (having distant metastasis) or with secondary and recurrent thyroid malignancy were excluded . After approval from Hospital Ethical Review Committee and Informed consent, detailed history of these 379 patients were taken. They underwent ultrasound scan and resistive index(RI) values were obtained . A cut-off value of >0.71u/l was taken as diagnostic of malignant lesion. All the cases were followed for surgical excision, followed by histopathology. Result of histopathology were taken as gold standard and results of colour doppler were judged accordingly. All the patients were evaluated by a single consultant on a single machine and all the histopathology were acquired from same lab to eliminate bias. Confounding variables were controlled by exclusion. Histopathology diagnosis and case outcome (true positive/false positive) was recorded into the attached performa along with demographic details of the patients. All the collected data was entered into SPSS version 10: age has been presented by mean±SD. Gender and malignancy on colour doppler and histopathology have been pres- ented by frequency and percentage. Positive predictive value of colour doppler (RI>0.71) in the diagnosis of malignant thyroid lesion has been calculated by taking histopathology as gold standard and has been presented as frequency and percentagedata has been stratified for age, gender and size of nodule. Post-stratification chi-square test has been applied taking p<0.05 as significant.

Results

The age of the patients ranged from 18 years to 80 years with a mean of 49.45±16.75 years. There were 84 (22.2%) males and 295 (77.8%) females patients in the study group. The size of the thyroid nodule ranged from 10 mm to 42 mm with a mean of 18.92±7.01 mm. These findings have been summarized in **Table-1**.

Malignancy was confirmed in 313 (82.6%) patients on histopathology. This gave 313 True Positive and 66 False Positive cases yielding a positive predictive value of 82.6% for resistive index (RI>0.71) on color Doppler in the diagnosis of malignant thyroid lesion taking histopathology as gold standard as shown in **T**[illegible] si[illegible] across various age groups; 18-40 vs. 41-60 vs. 61-80

Table-1: Baseline characteristics of study population.

Characteristics			Participants n=379
Age (Years)		18-80	49.45±16.75
Gender	Male	84	22.2%
	Female	295	77.8%
BMI (Kg/m²)		20-35	27.83±3.87
Size (mm)		10-42	18.92±7.01

$$\text{Positive Predictive Value} = \frac{313}{313 + 66} \text{ X } 100 = 82.6\%$$

Table-2: Diagnosis on histopathology.

Characteristics	Frequency	Percentage
Malignant (True Positive)	313	82.6
Non-Malignant (False Positive)	66	17.4
Total	379	100.0

True Positive = 313 / False Positive = 66

Table-3: Comparison of positive predictive value across age groups n=379.

Age Groups	Diagnosis on histopathology		Total	p-value
	Malignant (n=313)	Non-malignant (n=66)		
18-40 Years (n=146)	122 (83.6%)	24 (16.4%)	146 (100.0%)	0.889*
41-60 Years (n=121)	100 (82.6%)	21 (17.4%)	121 (100.0%)	
61-80 Years (n=112)	91 (81.3%)	21 (81.8%)	112 (100.0%)	
Total	313 (82.6%)	66 (17.4%)	379 (100.0%)	

*Chi-square test, * observed difference was statistically insignificant*

Table-4: Comparison of positive predictive value across gender n=379.

Gender	Diagnosis on histopathology		Total	p-value
	Malignant (n=313)	Non-malignant (n=66)		
Male (n=84)	70 (83.6%)	14 (16.7%)	84 (100.0%)	
Female (n=295)	243 (82.4%)	52 (17.6%)	295 (100.0%)	0.838*
Total	313 (82.6%)	66 (17.4%)	379 (100.0%)	

*Chi-square test, * observed difference was statistically insignificant*

Table-5: Comparison of positive predictive value across size of nodule n=379.

Size of Nodule	Diagnosis on histopathology		Total	p-value
	Malignant (n=313)	Non-malignant (n=66)		
10-20mm (n=252)	207 (82.1%)	45 (17.9%)	252 (100.0%)	
21-31mm (n=104)	87 (83.7%)	17 (16.3%)	104 (100.0%)	0.943*
32-42 (n=23)	19 (82.6%)	4 (17.4%)	23 (100.0%)	
Total	313 (82.6%)	66 (17.4%)	379 (100.0%)	

*Chi-square test, * observed difference was statistically insignificant*

years (83.6% vs. 82.6% vs. 81.3%; p=0.889), genders; male vs. female (83.3% vs. 82.4%; p=0.838) and nodule size groups; 10-20 vs. 21-31 vs. 32-42 mm (82.1% vs. 83.7% vs. 82.6%; p=0.943) as shown in **Tables 3, 4 and 5** respectively.

Discussion

Thyroid cancer is the most common endocrine tumor with an overall incidence of 2.92% in Pakistan. Unfortunately, most of the patients undergo surgery with suspected benign lesion which later proves to be malignant on histopathology after surgery, and this significantly affects the outcome. Thus there is need for excellent pre-operative diagnosis so that patient's surgery is well planned and is as extensive as required.[1] Resistive Index (RI) on Color Doppler has been professed as a valuable tool in differentiating between benign (low RI) and malignant lesions (high RI) but the available literature contained conflicting evidence.[14,15] Also as the positive predictive value varies with prevalence of disease, there was need to perform such a study in local population to determine the positive Predictive value of resistive index on color doppler with a hope that the results of the present may provide a good, non-invasive test for the pre-operative diagnosis of patients with suspected thyroid lesion in future practice.[13,16] The objective of this study was to determine the positive predictive value of colour doppler in predicting malignant thyroid tumors taking histopathology as gold standard. It was a cross-sectional survey conducted at Department of Diagnostic Radiology, Mayo Hospital Lahore. This study involved 379 patients of both genders, aged between 18-80 years having thyroid mass suspected of malignancy on color doppler (RI>0.71) who subsequently underwent surgical excision and histopathology. Written informed consent was taken from every patient. The age of the patients ranged from 18 years to 80 years with a mean of 49.45±16.75 years. Algin et al. in 2010 reported a similar mean age of 49.3±13.2 years among suspected patients of thyroid cancer in Korean population [13]. However, Anwar et al. in 2012 in another local study reported much lower mean age of 37±12.48 years.[3] There were 84 (22.2%) male and 295 (77.8%) female patients in the study group giving a male to female ratio of 1:3.5. A similar female predominance has also been observed by Anwar et al. in 2012 (1:3.5) in Pakistani population, Soliman et al. (1:3.7) in Egyptian population and Algin et al. (1:2.1) in Korean population.[13,15] A much higher female predominance (1:7.2) has also been reported by Yunus et al. in 2010.[17] The size of the thyroid nodule ranged from 10 mm to 42 mm with a mean of 18.92±7.01 mm. Our observation is similar to that of Algin et al. who also observed similar size of lesion (10-42mm, 18±7mm) in Korean such patients.[13] Malignancy was confirmed in 313 (82.6%) patients on histopathology. This gave 313 True Positive and 66 False Positive cases yielding a positive predictive value of 82.6% for resistive index (RI>0.71) on color Doppler in the diagnosis of malignant thyroid lesion taking histopathology as gold standard. Our results are similar to those of Algazzar et al. in 2013 (81.8%) and Algin et al. in 2010 (100%).[13,16] Aslan et al. in 2013 reported much lower positive predictive value of 55.9%.[14] This conflict can be due to limited sample size of the study (n=199) as compared to the present study which was conducted over much larger sample size of 379, as well as population differences in the prevalence of disease. When stratified, there was no statistically significant difference in the positive predictive value across various age groups; 18-40 vs. 41-60 vs. 61-80 years (83.6% vs. 82.6% vs. 81.3%; p=0.889), genders; male vs. female (83.3% vs. 82.4%; p=0.838) and nodule size groups; 10-20 vs. 21-31 vs. 32-42 mm (82.1% vs. 83.7% vs. 82.6%; p=0.943). Thus positive predictive value of resistive index (RI>0.71) was unaffected by patient's age, gender and size of the nodule. The present study is first of its kind in local population and have found the positive predictive value of resistive index on color doppler to be 82.6% in the diagnosis of malignant thyroid lesion taking histopathology as gold standard. The results of the present study thus advocate the use of color doppler (RI>0.71) in the pre-operative diagnosis of thyroid lesion which is non-invasive and is readily available in common hospital setups. This pre-operative diagnosis will aid in better planning of treatment in such patients in future practice.

Conclusion

The positive predictive value of resistive index on

There was no statistically significant difference in the positive predictive value across patient's age, gender and size of the nodule.

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Original Article

Frequency of Visceral Injury in Septic Induced Abortions

Rabail Tariq, Afroza Abbas, Humaira Akram, Ayesha Ishaq, Hira Rauf and Sadaf Shaheen

Objective: To determine the frequency of visceral injury in septic induced abortions. .
Methods: It is cross sectional study that was carried out in MoulaBaksh DHQ Teaching Hospital Sargodha from December2017 to June 2018. Patients presenting with septic induced abortion in outdoor department and emergency were included in the study.An inclusion and Exclusion criterion was applied upon the patients. Patients were stratified with respect to their age, body mass index (BMI), marital status and socioeconomic status and relation. Frequency of visceral injury alone and in relation to selected variables was noted in patients. Study was carried after approval from the ethical committee. Data was taken after the informed consent and specifically designed Performa was used for this purpose.
Results: Total number of patients was 174. Out of these 174 patients that presented with septic induced abortion, visceral injury was in 20 patients. Among these 20 patients who have visceral injury 17 were in 18-30 years of age group, 12 patients were having body mass index (BMI)>25, 19patients were unmarried and 18 were having poor socioeconomic status. Statistical analysis program (IBM-SPSS.V.22) was used for analyzing the data.
Conclusions: This study shows the incidence of visceral injury in septic induced abortion and its relation with age, body mass index (BMI), marital status and socioeconomic status. We concluded from the study that septic induced abortion is mainly the problem of women of early reproductive age group and who are having an unwanted pregnancy. Most of the patients belong to low income families so are exploited at the hands of unskilled dais and Lady Health Visitors, leading to severe morbidities, being unaware of the circumstances. This can be overcome by effective ways of family planning counseling and making health facilities at easy approach to everyone.
Keywords: septic induced abortion, visceral injury

Introduction

The greatest destroyer of peace is abortion because if a mother can kill her own child, what is left for me to kill you and you to kill me? There is nothing between. *Mother Teresa:* Every year about 210 million of women became pregnant, and one fourth of them end up in an unplanned birth or the abortion.[1] Acorrding to World Health Organization, every 8th minute, in developing world a woman dies because of the consequences of an unsafe abortion.[2] In LMICs, the mortality rate due to un safe abortions is 55% as compared to 3% in developed countries.[3] Over the world millions of women pursue induced abortions that remain clandestine if they are completed and successful but are notified only when complication occurs and present at tertiary care level. So the data collected from hospitals just shows the tip of an ice berg. [4] Induced abortions in our country, due to being non-religious and illegal, are mainly performed by untrained birth attendants, lady health visitors and nurses in unhygienic and dirty environment, resulting in serious consequences like hemorrhage, infections and visceral injuries sometimes leading to death.[5] In Pakistan maternal deaths that are attributed to induced abortions are 9-15% as given in different studies.[6,7,8] Leading causes of maternal death as a result of an induced abortion are due to uterine perforations , infections , visceral injury, sepsis and shock.[9] A study conducted in Karachi has shown the incidence of 24% hemorrhage, 30% sepsis and 41% visceral injuries because of induced abortions.[10] In a study by Bhattacharya S and his associates' has shown 60% frequency of visceral injury in septic induced abortions.[11] Long term morbidities e.g. infertility, chronic pelvic inflammatory disease, rectovaginal and vesicovaginal fistulas are also the result of unsafe abortions.[12] It has been noted that in illegal abortions the percentage of infection is 51%. Multiple invasive methods have been in use for induced abortions and are subjected to increase risks. Tubes and liquids inserted into uterus are the most widely used and successful as compared to others.[13]

Data regarding the frequency of visceral injury due

To induced abortion in Pakistan is quite insufficient. The results of my study will encourage and help us to assess the burden of morbidity of septic abortion in our general population and to plan strategies to overcome the issue of unsafe abortion.

Methods

It was a descriptive cross sectional study and it was conducted at MoulaBaksh DHQ Teaching Hospital Sargodha after the approval of ethical committee. This study was conducted from 20th December 2017 to 20th June 2018. Sample size was calculated with WHO formula for sample size calculation. N=174. Sampling technique was non-probability consecutive sampling. In this study women age 18-40 years and presenting in emergency with septic induced abortion as per operational definition. Both married and unmarried. Unwilling to take part in study, History of miscarriage and History of Caesarean Section. Data was collected from all the patients that presented at Moulabaksh Hospital with septic induced abortion. Informed consent was taken before the study. Data regarding visceral injury was recorded as per operational definition on specifically designed Performa. Data was analyzed by statistical analysis program (IBM-SPSS.V.22).Chi square test was applied $p \leq 0.05$ was considered statistically significant.

Results

Age range for this study varies from 18 to 40years with mean age of 28.172±3.02 years, mean weight 65.287±8.94 Kg, mean height 1.586±0.06 meters & mean BMI was 25.995±3.60Kg/m2 as in **Table-I.**

Visceral Injury was noted in 11.5% patients as given in **(Table-II)**

Table-I: Mean±SD of patients according to age, weight, height and BMI.

Demographics	Mean±SD
Age (Years)	28.172±3.02
Weight (Kg)	65.287±8.94
Height (m)	1.586±0.06
BMI (Kg/m^2)	25.995±3.60

Table-2: Frequency and %age of patients having visceral injury.

Visceral injury	No of Patients	%Age
Yes	20	11.5%
No	154	88.5%
Total	174	100%

Table-3: Stratification of visceral injury regarding BMI.

BMI (Kg/m^2)	Visceral injury		P-value
	Yes	No	
1- <25	08 (11.1%)	64 (89.9%)	
2- >25	12 (11.8%)	90 (88.2%)	0.894
Total	20 (11.5%)	154 (88.5%)	

Table-4: Stratification of Visceral Injury with respect to Poor Economic Status.

Poor Economic Status	Visceral injury		P-value
	Yes	No	
1- Yes	18 (13.8%)	112 (86.2%)	
2- No	02 (4.5%)	42 (95.5%)	0.095
Total	20 (11.5%)	154 (88.5%)	

Discussion

Every year almost 670,000 to 680,000 females die because of unsafe and inappropriately treated abortions and its complications.[14,15] 13% of all the maternal deaths are attributed because of unsafe abortions. Among these 50% burden lies in Asia and most of the remaining in Africa.[16] Approximately 5000 unsafe abortions occur each day.[17] In different studies it is shown that among the patients having complications of abortion, majority are unmarried, secondary school students, nulliparous and the dependent family member.[18-22] In other parts of world ,induced abortion is considered a problem of single women mostly in their adolescence.[23,24] In contrast with this, in our study most of the females were multi Para considering abortion as a birth spacing tool due to lack of use of contraception methods. Worldwide females mostly prefer medications for self-induced abortions,like misoprostol and mifepristone[25-27], in contrast to our step. Most of the uterine perforations during the first trimester at the time of induced abortion by curettage remain untreated and hidden.[28] For disrupting the pregnancy multiple foreign bodies are inserted into uterus, resulting in damaging the uterus, bowel, bladder and other internal organs. For these purpose knitting needles, wooden sticks and roots, cannula and catheters are used.[13]

Avoiding undesirable pregnancies is a big public health issue, and by restricting the funds for managing contraception, these are more often encountered in women with low socioeconomic status.[29] By well-planned and systematic way, family planning can be made at foot step and easy accessible to each woman,

Status and who are educated are more concerned regarding the family size and attempt termination for an unplanned pregnancy.[30] In our study, we concluded that 11.1% visceral injuries were noted in septic induced abortions. Among them 76% were unmarried ended up in abortion due to unwanted pregnancy. 13.8% were of low socioeconomic status. Our studies are almost in line with the studies conducted in Pakistan. A study conducted by Jabeen A and associates have observed 13% visceral injuries in septic induced abortions,[31] that is in accordance to our study. In an Indian study 80% septicemia, 20% visceral injury and 4.5% DIC was recorded.[32]

It is the responsibility of state and health department to explain and emphasis on the short and long term complications of induced abortions and proper counseling regarding the effective ways of family planning and their availability.[33,34]

Conclusion

Induced abortion is one of the most crucial issue of our society. Most of the induced abortions are done by untrained dais and lady health visitors who being unaware of the consequences make the patient liable to serious hazards. From our study it is evident that females with poor socio-economic status and unmarried are most affected by unsafe abortions. Complications associated with these can only be reduced by effective methods of family planning and counseling.

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Original Article

Hepatopulmonary Syndrome in Patients of Chronic Liver Disease Due to Viral Etiology Presenting Tertiary Care Hospital Lahore

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Objective: To determine the frequency of hepatopulmonary syndrome in patients of viral cirrhosis presenting to a tertiary care hospital of Lahore.

Methods: This cross -sectional study was conducted in Medical Unit Iii Jinnah Hospital Lahore in 6 months.292 patients with chronic liver disease presenting to the medical unit III of Jinnah hospital Lahore and fulfilling the inclusion criteria were approached. An informed consent was taken from them before enrolling in the study and information regarding their demographic data was noted in the proforma. Arterial Blood samples were taken in sitting position using standard protocol to determine the alveolar arterial oxygen gradients. Blood samples were taken to determine serum albumin, serum bilirubin, PT / INR and ascites was confirmed by Ultrasound scan of abdomen to determine the Child Pugh class of Chronic liver disease patients. The results were noted in the proforma and Confidentiality of the data was ensured. Presence / absence of hepatopulmonary syndrome was labeled as per operational definition.

Results: From 292 patients, it was observed that the minimum age was found 25 years and maximum age was 60 years with mean and standard deviation of the age was 41.65±10.54 years. Male patients were 54.5% while female patients were 45.5%. Hepatopulmonary syndrome was present in 8.2% patients of viral cirrhosis while it was absent in 91.8% patients.

By using chi-square test it was observed that there was no significant association between age group and presence of Hepatopulmonary syndrome having p-value =0.520. Significant association was not found between gender and presence of Hepatopulmonary syndrome with p-value 0.210. There was no significant association between duration of chronic liver disease and presence of Hepatopulmonary syndrome having p-value=0.108. There was no significant association between type of viral and presence of Hepatopulmonary syndrome having p-value = 0.125. There was no significant association between Child Pugh and presence of Hepatopulmonary syndrome having p-value =0.966.

Conclusions: Presence of hepatopulmonary syndrome was found in 8.2% patients of viral cirrhosis. Effect modifiers like age, gender, duration of chronic liver disease, type of viral hepatitis and Child Pugh class showed significant association.

Keywords: hepatopulmonary syndrome, chronic liver disease, child pugh class, ascites.

Introduction

Hepatopulmonary syndrome is considered when triad of Liver disease, Impaired oxygenation and Intrapulmonary vascular abnormalities, referred to as intrapulmonary vascular dilatations (IPVDs) exists.[1-5] The unique pathological feature of hepatopulmonary syndrome (visualized by autopsy) is gross dilatation of the pulmonary precapillary and capillary vessels, as well as an absolute increase in the number of dilated vessels. A few pleural and pulmonary arteriovenous shunts and portopulmonary anastomoses may also be seen.[5] The presence of hepatopulmonary syndrome (HPS) worsens the prognosis of patients with cirrhosis and probably other liver diseases.[5,6] This was demonstrated by an observational study that included patients with HPS and controls that were matched according to the cause and severity of the liver disease.[7] Mortality occurred in 29 out of the 37 patients (78 percent) with HPS, compared to 20 out of the 47 patients (43 percent) without HPS. Patients with HPS had a median survival of 24 months and a five-year survival of 23 percent, while patients without HPS had a median survival of 87 months and a five-year survival of 63 percent. Survival was further worsened if the patients with HPS had coexisting medical conditions or were older adults.[5] The cause of death among patients with HPS tends to be multifactorial and related to complications of the liver disease (eg, hepatic failure, multisystem organ failure due to sepsis, hepatocellular cancer, gastrointestinal bleeding).[5,7]

Although oxygenation usually worsens over time (mean decline of 5.2 mmHg per year [range 0.4 to 8.3 mmHg per year]),[7] it is rare for progressive hypoxemic respiratory failure to be the primary cause of death. Spontaneous resolution of HPS and development of concomitant portopulmonary hypertension are unlikely.[5] There are no effective medical therapies for hepatopulmonary syndrome (HPS), although many approaches have been attempted to improve gas exchange and decrease hypoxemia. Liver transplantation offers the most promise for the successful treatment of patients with HPS.[3,5] Long-term supplemental oxygen is the most frequently recommended therapy for symptoms related to hypoxemia (e.g., dyspnea).[5] Various other medications have been tried, but anecdotal evidence and uncontrolled trials suggest that such medications cause little or no sustained improvement in oxygenation. Examples include methylene blue, allium sativum (i.e., garlic), N(G)-nitro-L-arginine methyl ester (L-NAME), curcumin, terlipressin, somatostatin analogues (e.g., octreotide), nitric oxide synthase inhibitors, cyclooxygenase inhibitors (e.g., indomethacin), almitrine bismesylate, antibiotics, chemotherapy (e.g., cyclophosphamide), glucocorticoids, beta blockers (e.g., propranolol), and inhaled nitric oxide.[3,5] Ransjugular intrahepatic portosystemic shunt (TIPS) placement is a medical intervention that has been associated with improvement of HPS in several case reports.[8] However, we do not advocate routine TIPS placement in patients with HPS because clinical outcomes have been variable.[3,9] In addition, there is a risk that the TIPS may worsen HPS by increasing the hyperkinetic state, leading to more pulmonary vasodilatation, shunting, and hypoxemia. Other medical interventions that have been tried unsuccessfully include plasma exchange and the occlusion of intrapulmonary vascular dilatations (IPVDs) via spring coil embolization. Agents that have been tested in animal models and appear promising include pentoxifylline (inhibits nitric oxide synthesis) and quercetin (a flavonoid antioxidant).[10,11] However, these medications still need to be studied in humans.

Methods

This cross-sectional studywas conducted for the duration of 6 months at medical unit III Jinnah hospital Lahore. Sample size of 292 cases was calculated with 95% confidence level, 25% margin of error and taking expected percentage of hepatopulmonary syndrome among patients of chronic liver disease as 5%.[5] Non probability consecutive sampling technique was used. All the patients having age range between 25 and 60 of both genders and having chronic liver disease due to viral etiology diagnosed with abdominal ultrasound were included in the study after informed consent. All the patients havingischemic heart disease and hypertension determined on history and medical record and having COPD determined by history and spirometry were excluded from the study.Arterial Blood samples were taken in sitting position using standard protocol to determine the alveolar arterial oxygen gradients.Blood samples were taken to determine serum albumin, serum bilirubin, PT / INR and ascites was confirmed by Ultrasound scan of abdomen to determine the Child Pugh class of Chronic liver disease patients. The results were noted in the proforma and Confidentiality of the data was ensured. Presence / absence of hepatopulmonary syndrome was labeled if there was an evidence of alveolar-arterial oxygen gradient (Aa02) 2 15 mm Hg in the arterial blood gas sample of a seated patient with evidence of viral cirrhosis.Data was entered and analyzed using SPSS version 17.0.Numerical variable i.e. age was summarized as mean and standard deviation. Qualitative variables like sex and hepatopulmonary syndrome were presented in the form of frequency and percentages. Data was stratified for age, gender, duration of chronic liver disease, type of viral hepatitis and Child Pugh class and Chi square test was applied to check statistical significance post-stratification. P-value < 0.05 was used as statistically significant.

Results

From 292 patients, it was observed that the minimum age was found 25 years and maximum age was 60 years with mean and standard deviation of the age was 41.65 $\pm$ 10.54 years. Male patients were 159 (54.5%) while female patients were 133 (45.5%). Hepatopulmonary syndrome was present in 24 (8.2%) patients of viral cirrhosis while it was absent in 268 (91.8%) patients. By using chi-square test it was observed that there was no significant association between age group and presence of Hepatopulmonary syndrome having p-value=0.520. Significant association was not found between gender and presence of Hepatopulmonary syndrome with p-value 0.210. There was no significant association between duration of chronic liver disease and presence of Hepatopulmonary syndrome having p-value = 0.108. There was no significant association between type of viral and presence of Hepatopulmonary syndrome having p-value = 0.125. There was no significant association between Child Pugh and presence of Hepatopulmonary syndrome having p-value 0.066 (Table-I).

Table-I: Presence of Hepatopulmonary syndrome.

Hepatopumonary Syndrome	Frequency	% Age
Yes	24	8.2%
Yes	268	91.8%
Total	292	100.0%

Discussion

The objective of the present research was to determine the frequency of hepatopulmonary syndrome in patients of viral cirrhosis presenting to a tertiary care hospital of Lahore. In this regard the present cross-sectional study was conducted in medical unit-III Jinnah hospital Lahore. 292 patients of viral cirrhosis were included by fulfilling the inclusion criteria by using non-probability consecutive sampling. From 292 patients, it was observed that the minimum age was found 25 years and maximum age was 60 years with mean and standard deviation of the age was 41.65±10.54 years. Male patients were 54.5% while female patients were 45.5%. Hepatopulmonary syndrome was present in 8.2% patients of viral cirrhosis while it was absent in 91.8% patients. Existing literature showed that the prevalence of arterial hypoxemia in cirrhotic patients was 14.6%. The presence of hypoxemia is increased in patients with advanced liver disease and the severity of hypoxemia was positively correlated with the severity of liver disease assessed by the Child Pugh score. HPS represents 64.1% of causes of hypoxemia. Pulse oximetry is a simple non-invasive method for detection of arterial hypoxemia as an initial screening test for HPS. Contrast enhanced echocardiography (CEE) is the gold standard method for the diagnosis of HPS by detection of intrapulmonary vasodilatation (IPV) characteristic of HPS, while CT chest assists in diagnosis by exclusion of intrinsic pulmonary disease.[12]

In present study by using chi-square test it was observed that there was no significant association between age group and presence of Hepatopulmonary syndrome having p-value = 0.520. Significant association was not found between gender and presence of Hepatopulmonary syndrome with p-value 0.210. There was no significant association between duration of chronic liver disease and presence of Hepatopulmonary syndrome having p-value = 0.108. There was no significant association between type of viral and presence of Hepatopulmonary syndrome having p-value = 0.125. There was no significant association between Child Pugh and presence of Hepatopulmonary syndrome having p-value = 0.966. The previous study showed that the prevalence of HPS was 25.28% (22 out of 87 cases). HPS is not uncommon in patients with hypoxemia and chronic hepatic disease. Diagnoses of such disorders are essential, especially in patients who are listed for liver transplantation.[13] In another study there was no significant differences found among related to sex, age, cirrhosis status or ascites. HPS frequency was 35% in Group 1 versus 64.7% among Group 2-Patients (P = .01). Taking into account the results, it was concluded that HPS frequency was related to cirrhotic etiology. Upon multivariate analysis a patient with cirrhosis from viral etiology showed significantly increased HPS frequency compared with those displaying cirrhosis of an alcoholic etiology.[14]

Conclusion

Presence of hepatopulmonary syndrome was found in 8.2% patients of viral cirrhosis presenting to a tertiary care hospital of Lahore. Effect modifiers like age, gender, duration of chronic liver disease, type of viral hepatitis and Child Pugh class showed significant association.

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Original Article

Bone Union After Percutaneous Fixation of Proximal 5th Metatarsal Fracture by Cannulated Steel Screw

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Objective: To determine bone union after percutaneous fixation of proximal 5th metatarsal fracture by cannulated steel screw in a tertiary care hospital.

Methods: Descriptive Case Series, Study was conducted in department of Orthopedics Unit- I, Jinnah hospital Lahore from September 2013 to February 2014. After taking an informed consent of 163 patients of either sex with radiological diagnosis of fracture of proximal 5th Metatarsal were treated with percutaneous cannulated screw fixation.

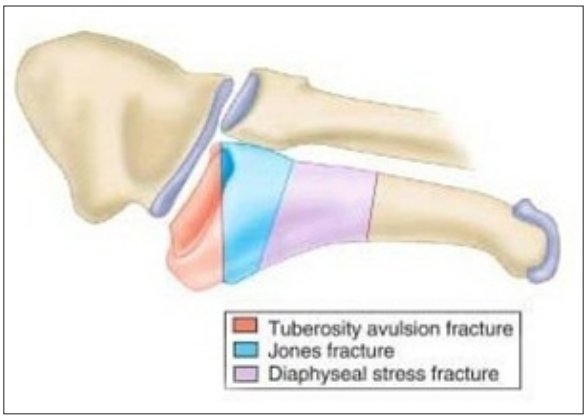
Results: Radiological union was assessed at 12th week.163 patients with mean age of 41.8 years ± 13 years were included. 63.2% were male. 147 patients (90.2%) achieved radiological union at 12 weeks 16 patients (9.8%) were unable to achieve. Gender, age distribution and time taken for partial and full weight bearing was similar in both groups with and without radiological union. It is concluded that radiological union is quite good (90%) in patients of proximal 5th metatarsal fracture being treated with percutaneous cannulated screw.

Conclusion: It is concluded that radiological union is quite good (90%) in patients of proximal 5th metatarsal fracture being treated with percutaneous cannulated screw. We hereby recommend its use in proximal 5th meta-tarsal fracture and it should be performed as early as possible. Limitation of current study is that we have not assessed the nutritional status and mode of injury in our population.

Keywords: proximal fracture of 5th metatarsal ,percutaneous cannulated screw fixation, jones fracture, effectiveness, radiological union.

Introduction

Proximal fifth metatarsal fractures occur commonly in athletes.[1] The fracture in the proximal part of the 5th metatarsal are divided according to the zone.[2] The area of the proximal phalynx is divided in 03 zone **(Fig-1)**.



The zone 1 fractures are the tuborisity , avulsion fractures and are usually result of inversion injury to the foot[3] zone II fractures extend from tuboristy to the metaphyseal/ diaphyseal junction. The fracture in this zone are called Jones fracture.[4] Due to the poor blood supply to this area these fractures are pron to non union.[5] These fractures result as a result of strong abduction force to the forefoot. Zone III extends to the proximal 1.5cm of the diaphysis. The fractures in this area are usually acute stress fracture.

The fractures in zone I usually heal well by conservative treatment in POP cast. The fractures of zone II & III have the tendency of non union after conservative treatment.[6] Although treatment options include both conservative treatment and surgery, the latter is often recommended due to the long treatment period in cast and high incidence of complications associated with conservative treatment like skin problems, muscle wasting, joint stiffness,[7] regional osteoporosis,[8] chances of displacement in cast and high rate of nonunion.[9] There is no consensus regarding the optimal surgical procedure.[10,11]

Different treatment options used are conservative method with cast application, percutaneous fixation with cannulated screw either made up of steel or titanium, open fixation with intra-medullary nail with or without bone grafting. In a study to determine union rate after fixation with either cannulated titanium screws or cannulated stainless steel screws of patients with fifth Metatarsal Fractures, the overall

came out 14/16 (88%) at 12 weeks.[12] We prefer conservative management in our setting due to cost effectiveness and feasibility. The available data for percutaneous fixation with cannulated screw is for younger athletes only and bone union is not studied in older population. Our population differs regarding bone mass density and nutritional status which are strong predictors of early healing.[13] As this procedure has not been studied in our population so the current study may help us to determine the efficacy of percutaneous fixation with cannulated screw as treatment modalities being used for treatment of base of fifth metatarsal fractures in our hospitals but no local data is available about the functional outcome of either option. Percutaneous fixation with cannulated screw is a cost effective technique but at same time there is indecisiveness regarding conservative management or fixation [14,15] . The purpose of present study is to establish the effectiveness of treatment of zone II, III fractures using intramedullary 4.5mm cannulated steel screw. The outcome union rate will help end this confusion and will help in decision making in treatment of fifth metatarsal fractures.

Methods

Study was conducted in Department of Orthopedics I, Jinnah Hospital, Lahore. Study was completed in Six months i.e. From Jan to July 2014. Study was descriptive case series and the calculated sample size was 163 cases, with 5% margin of error and 95% confidence level taking expected percentage of radiographic union (88%). An informed consent from 163 subjects coming to Orthopedics Department of Jinnah Hospital Lahore, fulfilling the inclusion criteria were taken from outdoor and emergency department within 72 hours of fracture. Under general or spinal anesthesia, with the help of Image Intensifier Intramedullary fixation with 4.5mm cannulated steel screw was carried out over a guide wire. POP splint was given for 04 weeks post operatively. Questionnaire containing background information i.e. age, sex, date of operation and contact was used as research instrument and data was recorded by researcher himself. Patients were followed for 12 week to determine the radiological union by x ray foot. Time of partial and full weight bearing (in weeks) and mode of presentation i.e. emergency and outdoor was treated as effect modifier and data was stratified subsequently. Data collected was entered and analyzed in the SPSS version 17. Results were projected using descriptive statistics e.g. mean with standard deviation in case of continuous variables like age and percentages and frequency in case of categorical variables like gender, and union of fracture. Time of partial and full weight bearing was used to stratify data in groups. Chi square test or Fischer exact test was used for categorical variables post stratification while independent sample 't' test was used for mean age and mean time for partial and full weight bearing. A p-value <.05 was labeled significant. The purpose of present study is to establish the effectiveness of treatment of zone II and III fractures using intramedullary 4.5mm cannulated steel screw.

Results

On hundred sixty three patients with fracture of 5th meta-tarsals were included in the study. 103 (63.2%) were male while rest were female. 135 patients (82.8%) presented through emergency while 28 (17.2%) presented through outdoor. 147 patients while treated with cannulated screw achieved radiological union at 12 weeks (90.2%) while 16 patients (9.8%) were unable to achieve **(Table-I).**

Table-1: Frequency distribution of sample population according toradiological union.

		Frequency	% Age
	Yes	147	90.2%
Valid	No	16	9.8%
	Total	163	100.0%

Mean age of the sampled population was the 41.8 years ± 13 ranging from 18 to 60 years. Mean time for partial weight bearing was 6.5 week±1.7 ranging from 4 to 10 weeks while mean time to achieve full weight bearing was 10.2 week±2.8 ranging from 6 to 14. When we cross tabulated the radiological union with gender there was a non-significant difference **(Table-I I)** .

Table-2: Cross tabulation between gender & radiological union.

		Radiological Union		
		Yes	No	Total
	Male	91	12	103
Sex	Female	56	04	60
	Total	147	16	163

Using Fisher's Exact Test, p value = 0.416 (Non-significant)

Similarly, opposite to this the mode of presentation was significant factor determining the radiological union of the sampled population as patients presenting through emergency had a batter radiological union (p<0.01) **(Table-III)**. When we applied independent sampled population 't' test on mean distribution of age in the sampled population with and without union we found a non-significant difference **(Table-IV).** Similarly, mean time for partial weight bearing was equal in patients with and

Table-3: Cross tabulation between gender & radiological union &mode of presentation.

		Radiological Union		
		Yes	No	Total
Mode of Presentation	Emergency	133	02	135
	Outdoor	14	14	28
	Total	147	16	163

Using Fisher's Exact Test, p value <0.001 (significant)

Table-4: Mean Age distribution in sampled population with and without union.

	Radiological Union	N	Mean	Std. Deviation	Std. Error Mean
Age (in years)	Yes	16	47.13	13.706	3.426
	No	147	41.20	12.843	1.059

Assuming Equal variances, using independent sample t test. P value = 0.08 (Non-significant)

Union . Mean time distribution for full weight bearing in both groups was almost equal when we applied independent T test P value came out were non-significant (p value= 0.91). We divided the patients into two age groups i.e. less than and more than 40 years and there was a non-significant difference. Similarly, complete weight bearing before and after 12 weeks was equal in both groups having union and not achieving union.

Discussion

In our sampled population almost 2/3rd were male while rest were female showing a more physical activity in male counterpart as compared to female counter part and decreased in stress fracture of proximal 5th metatarsal. This also determines the health seeking behavior in our community in which male are more prone to the fracture although this fracture is usually not due to sports activity only.

Similarly, to our surprise, the patients presenting in the emergency i.e. acutely with early treatment were more almost 82%. It shows that the health determinants and health seeking behavior is changing in our population more people complaints to the emergency of a tertiary care hospital.

Radiological union achieved in 90% individuals which is quite good and it is comparable with De-Vrieset al who showed 88% union. 16 person i.e. almost 10% sampled population was unable to achieve radiological union. Factors may be multiple.

In our sampled population mean age was about 41.8 years but ranging from 18 to 60 years. It means there is an early chance of stress fractures in 5th metatarsal bone. Partial weight bearing is quite good almost most of the patients achieved partial weight bearing within 10 weeks and full weight bearing in 14 weeks. To our surprise gender did not affect the radiological union i.e. the radiological union was similar between male and female although it is purposed that it vitamin-D deficiency and poor bone marks density is present in our female population due to local customs and decrease in calcium intake but to our surprise it was equal in both. The patients who presented in Emergency Department showed significantly good rate of radiological union compared with those who presented in OPD after a delay of 48 - 72hours. It means probably early fixation with percutaneous screw in such fractures result in both appropriate radiological union. Age has no effect on union similarly patients even with non-union started partial weight bearing and full weight bearing showing that this fracture is usually asymptomatic in our individuals. Age groups have no effect on it.

Conclusion

It is concluded that radiological union is quite good (90%) in patients of proximal 5th metatarsal fracture being treated with percutaneous cannulated screw. We hereby recommend its use in of proximal 5th metatarsal fracture and it should be performed as early as possible. Limitation of current study is that we have not assessed the nutritional status and mode of injury in our population.

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Original Article

Comparison Between Mekeown Subtotal Esophageotomy With Thoracotomy And Transhiatalesophagectomy Without Thoracotomy For The Surgical Treatment Of Carcinoma Of Lower 2/3rd Of Oesophagus.

Zen-ul-Abideen, Shaista Bhatty, Waris Farooqa and Nabeel Ahmad

Objective: To compare the two surgical procedures Mekeown subtotal esophageotomy with thoracotomy and transhiatalesophagectomy without thoracotomy for the surgical treatment of carcinoma of lower 2/3rd of oesophagus.

Methods: In 30 patients with carcinoma oesophagus two surgical procedures performed Meckeownsubtotaloesophagectomy (with thoracotomy) & Transhiataloesophagectomy (without thoracotomy for comparison regarding effective treatment.

Results: The median survival of these patients was 12 months (9-38 months) since majority of the results were comparable for the two procedures, but mortality associated with transhiatal approach was low.

Conclusion: Transhiatal is the better surgical procedure in terms of mortality when compared with Meckeown procedure.

Keywords: meckeowns subtotal oesophagectomy, transhiataloesophaectomy, carcinoma, oesophageal tumors, treatment.

Introduction

Oesophageal cancer is the ninth most common cancer in world.[1] In Pakistan a multicentre report of malignant tumor showed carcinoma oesophagus to be the eighth commonest tumor in males and fifth in females, with a male to female ratio 1.2:1.[2]

Carcinoma represent the vast majority of malignant oesophageal tumors. These are classified according to their cell type.

1- Squamous cell carcinoma 80-85%.

2- Adenocarcinoma 5-10%.

Oat cell carcinoma occurs occasionally. However, it is squamous cell carcinoma which is the commonest, but adenocarcinoma is the commonest type in most westernized countries and is increasing in incidence

Dysphagia is the most common presenting symptom and recent onset of dysphagia for solids in patients of middle age or older should alert the clinician to the need for urgent investigation.[3]

Presently the following two procedures are most commonly employed for the treatment of carcinoma oesophagus.

1. Meckeownsubtotaloesophagectomy (with thoracotomy)
2. Transhiataloesophagectomy (without thoracotomy.[4]

Transhiataloesophagectomy without thoracotomy can be considered a safe procedure,[5,6] it may be a useful procedure for lesions of the lower oesophagus, but may be hazardous for a middle third lesion that may be adherent to the bronchus or to the azygos vein. Transthoracic resection had significantly higher early pulmonary morbidity and mortality rates, 5-year survival was approximately 20% after both transthoracic and transhiatal resections.[7] Transhiatalesophagectomy is gaining increasing use as the preferred technique for esophagectomy, as the chest is not opened and oesophagogastric anastomosis is done in the neck.[8] However, tumor location and the possibility of direct mediastinal invasion may indicate the need for transthoracic dissection.

Methods

The study was carried out in Services Hospital, Lahore (SHL) Surgical Unit II, which is a tertiary care hospital in the central part of Lahore. It is 1000 bedded hospital with an annual turn over of surgical patients of around 21000. Number of patients studied were thirty, all who presented in out patient department (OPD) as well as referrals from other departments. Written consent taken from each patient, as these patients came on their own will for treatment. Two surgical procedures were done.

1.Transhiataloesophagectomy: In this procedure abdomen open by midline laparotomy, mobilization of stomach done. The left gastric artery, the short gastric vessels are all divided. Extended Kocker's-

posterior mediastinum. Gastro-oesophageal anastomosis done in the left neck.

2. Mckeownoesophagectomy: The stomach is first mobilized through a midline laparotomy incision and oesophagus is approached from aright thoracotomy fifth intercostals space. The Azygos vein is divided and iigated allowing easy access to thoracic oesophagus. A third incision is made in the left side of the neck for oesophagogastric anastomosis.

All patients had feeding tube jejunostomy, for anticipatinganastomotic leak and avoiding total parenteral nutrition(TPN).

Results

Analysis of results was done by percentage and student 't' test was used to compare between 2 groups. Level of significance was selected as P<0.05. Thirty patients were studied, (18)60% were referred patients and (12)40% were admitted through OPD.Patients were divided into four age groups:Five patients (16.6%) were 30-40 years old, Four(13.3%) were 40-50 years old, 7(23.3%)were in between 50-60 years & 14(46.6%) were in between 60-70 years. The income of 30 patients ranges between 12000 to 14000 in which (20)66.6% had income between 13000 to 14000, and (6)20% had income between 12000 to 13000 rupees. Among the risk factors associated with carcinoma esophagus was found out to be smoking (11)36.6% and beetle chewers (11)36.6%. Dysphagia was presenting symptoms in all cases (30)100% and mean duration of symptoms was four months range (1-15 months). While, (22)73,3% had weight loss amounting to more than 10% of body weight. Anemia was observed in (28)93.3% patients. In all patients base line investigations were performed. Haemoglobin percentage (Hb%), complete blood count (CBC), Erythrocyte sedimentation rate (ESR), complete urine examination (U/C). Renal function test (RFTs) Liver function test (LFTs), blood sugar level (BSL) were also done in all patients. Preoperative diagnosis was made by barium swallow, endoscopy and biopsy in 28 patients (93.3). Distant metastasis was sought by chest radiograph (CXR), abdominal ultrasound scan (USG), and 22(73.3%) cases by computed tomography (C.T). Bronchoscopy and indirect laryngoscopy ruled out involvement of tracheobronchial tree. None of the patients received radiotherapy or chemotherapy preoperatively. Out of 30 patients 93.3% were transfused fresh blood preoperatively and 10% were put on parenteral nutrition feeding The surgical procedures carried out were transhiataloesophagectomy without thoracotomy (50%), Mekeownoesophagectomy with thoracotomy (50%). The mean duration of operation was 3 hours. There were no complications regarding General anaesthesia as all the parameters were dealt with, in preoperative preparation of the patients. Anastomatic leaks were noticed in five patients (13.3% V/s 6.6%). These patients were treated conservatively. Six patients developed pleural effusion which was unilateral. One of them needed thoracocentesis other resolved on their own (13.3% V/s 26.6%). Temporary recurrent laryngeal nerve palsy occurred in 4 patients, one required tracheostomy for stridor. Primary haemorrhage occurred in 3 patients (6.6% V/s 13.3) in transhiataloesophagectomy. Patients who developed pneumothorax were six in number (6.6% V/s 33.3%) with Mckeownoesophagectomy. Two patients died of pulmonary embolism (6.6% V/s 6.6%). Death occurred within 30 days of post operative period. Median time until full establishment of feeding was 12 days. (80%) were found out to be cases of squamous cell carcinoma and (20%) of adenocarcinoma diagnosed on histopathological report. Thirty (100%) had evidence of transmural spread stage-III. Twenty six (86.6%) post-operative survivors died of recurrent carcinoma with involvement of vital structures. The median survival of these patients was 12 months (range 9 to 38 months).

Comparison of Complications:

Complications associated with both procedures were anastomotic leak (13.3% Vs 6.6%) P=1.5 NS, Pleural effusion (13.3% Vs 26.6%), P=0.92 NS, Haemorrhage (6.6% Vs 13.3), P=0.61 NS, Penumothorax (6.6% Vs 33.3%), P=1.94 NS, Pulmonary embolism (6.6% Vs 6.6%).(80%) were found out to be cases of squamous cell carcinoma and (20%) of adenocarcinoma diagnosed on histopathological report. 30(100%) had evidence of transmural spread (stage-Ill).26 (86.6%) post-operative survivors died of recurrent carcinoma with involvement of vital structures. The median survival of these patients was 12 months (9-38 months) since majority of the results were comparable for the two procedures, but mortality associated with transhiatal approach was low. Histopathology Adenocarcinoma in 6(20%) patients, Squamous ceii carcinoma in 24(80%) patients. On follow up Stricture occurred in

in the world.[1] As far as its incidence in Pakistan is concerned, it is 8th commonest tumor in males and fifth in females, with a male to female ratio 1.2:1.[2]
The main purpose of the study was to compare the two surgical procedure for the treatment of carcinoma of lower 2/3rd of the oesophagus. Iver Lewis and left thoracoabdominal approach has high incidence of chest complication related with surgery and post operative leakage.[9]
Different aspects were studied, age group, booking status, socioeconomic status, distribution of clinical symptoms, investigations, management options, complication, histopathology and follow up.
The number of patients studied were thirty. The age ranged between 30 to 75 years. Patient age and physical activity were also used to select an appropriate approach to oesophageal resection. The transhiatal approach was selected because it reduces the operating time and the chest is not opened thus minimizes the duration of Anaesthesia. In my study the association of carcinoma oesophagus with heavy tobacco and beetal leave, tobacco chewing complemented with advanced age was high. Although the findings were not consistent with the study carried out at National Cancer Centre Tokoyo, Japan by Kanamoto A (134).
As alcohol along with smoking was main associated factor while smoking with tobacco and beetal chewing were the predominant associations in set up of my patients. The present study showed that all patients with carcinoma oesophagus exhibit dysphagia. In a study conducted by Martin RE, University of Western Ontario,
London showed similar results[3] Base line investigations were done in all patients. As far as special investigations were concerned endoscopy and biopsy were found out to be the most useful and diagnostic test. In all patients endoscopy and biopsy was performed. So, it was found that sensitivity of endoscopy and biopsy for making the diagnosis of carcinoma oesophagus was 93.3%.
The majority of patients presented to us were under weight and their haemoglobin status was below normal, because of poor dietary intake. Resection is the main stay of treatment for neoplasm of the oesophagus. It is the best single modality for managing patients with early stage cancer. Surgical approach to resection includes a transthoracic operation in Mckeown and mobilization of the oesophagus via a transhiatal approach. Transhiatal- oesophagectomy without thoracotomy can be considered a safe procedure for resectable cancer of the mid oesophagus, the distal oesophagus or the oesophagogastricjunction.[10]
The selection of an operative approach is dependent in part on tumor location and histology. Squamous cell cancer are most often located in the middle and upper thoracic oesophagus, a location to which a transhiatal approach is often difficult except in the most experienced hands. So Mckeowno-esophagectomy was performed in this group of patients. 15 out of 30 patients underwent Meckeown procedure.
In contrast adenocarcinomas, which most often arise in the distal oesophagus or cardia, are easily amenable to transthoracic andtranshiatal approach but as complications of transhiatal approach are less so this group of patients were selected for this procedure and another 15 patients underwent Transhiatal-oesophagectomy. Anastomotic leak occurred in 4 patientstranshiatal approach and in one patient with Meckeown approach.
Conservative management for leak was done. Surgical technique used was hand sewing anastomosis. The other technique used for this is stappling Gun, as our patients belong to poor class. This expensive gadget was not affordable, so we were unable to use this technique.
The results were consistent with the study conducted by Chlapik D, at Slovenskarepublika.[11] Respiratory complications were most frequent, among them were pleural effusion, pneumothorax and pulmonary embolism were noticed. Subphrenic abscess developed in 2 patients, one was managed conservatively, and in other abscess was drained under the guidance of ultrasound followed by follow up ultrasound scanning and with antibiotic therapy. Frequency of haemorrhage was more in Meckeown approach as bleeding after blunt mediastinal dissection in transhiatal is less than expected because main feeding arteries divide some distance away from oesophageal wall and small perioesophageal vessels retract when torn.[12]
All these patients were followed by thoracotomy for the control of Haemorrhage and repair of tear's. The mortality observed with transhiatal approach was less as compared to Meckeown approach and the results were compareable with the study conducted by T. Mahmood at Allied Hospital, Faisalabad, Pakistan.[13] Transhiatal surgery also achieves longterm relief from dysphagia[13] and so happened in our patients, only 3(10%) had benign anastomotic stricture which responded well to repeated endoscopic dilatation.
Our study suggest that operative mortality is consistent with study conducted by Orringer M.B.[14]

Conclusion

Transhiatal is the better surgical procedure in terms of mortality when compared with Meckeown procedure.

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Original Article

Efficacy of Oral Propranolol in the Management of Infantile Hemangiomas

Feeroz Alam Khan, Naeem Liaqat, Asif Iqbal, Ghulam Mujtaba Zafar, Umar Hayat, Javaid Iqbal Khan, Asim Noor Cheema and Sajid Hameed Dar

Objective: To compare the effectiveness of propranolol versus prednisolone in the management of infantile hemangioma.

Methods: This was a randomized control trial in which a total of sixty patients with cutaneous infantile hemangioma were included and these patients were divided into two groups randomly by lottery method; Group A: Corticosteroid therapy and Group B: Propranolol therapy. Patients in group A were given 3 mg/kg of oral prednisolone while patients in group B were given 2 mg/kg of oral propranolol. Patients were followed up monthly for 5 months to see the change in color, consistency and size of the lesion along with monitoring of side effects.

Results: Demographic data including gender distribution, age and site of IH were comparable in both groups. Response to therapy on size of IH showed that there was significant difference in group B (average size from 10.39 cm2 to 1.2 cm2) as compared to group A (from 6.87 cm2 to 3.73cm2). Maximum response of the therapy in both groups was achieved in the first month of treatment. Favorable response (>75% reduction in size) was seen in 90% of patients who received propranolol compared to 36.6% with prednisolone. Response of therapy on color of lesion was better in group B than group A (100% vs. 80%).

Conclusion: It is evident from this study that propranolol is more effective than prednisolone in the management of IH and has fewer side effects as compared to steroids.

Keywords: propranolol; prednisolone; infantile hemangiomas.

Introduction

Infantile hemangiomas (IHs) are the most common benign vascular tumors in infancy.[1] The incidence is 4% to 10% in children less than 1 year of age, with a clear female predominance (female/male ratio: 2.5-4:1).[2] The etiology and pathogenesis of IHs is a subject of active research and debate. Currently it is thought that both vasculogenesis (synthesis of new vessels from cells/ progenitor cell denovo) and angiogenesis (synthesis of new vessels from preexisting vessels) play a role in the development of IHs.[3] Sixty per cent of infantile hemangiomas affect the head and neck area, whereas 25% occur on the trunk and 15% on the extremities. Usually 80% of all hemangiomas are single lesions, but 20% present as multiple tumors.[4] The life cycle of the vast majority of IHs can be summarized as appearance, rapid development, rest, and regression.[5] The majority of IHs requires no specific treatment other than observation. Only10% of IHsrequires treatment during the proliferative phase, because of life threatening & local complications, or cosmetic/functional risks. Treatment options includes; oral or intralesionalcorticosteroids, Propranolol oral or topical, interferon-α and Vincristine, pulsed-dye laser therapy and surgery.[6,7]

The first-line anti-angiogenic therapy for IHs has been systemic corticosteroids in the form of, oral prednisolone.[8] The overall response rate is 80% to 90% withpossible side effects of corticosteroid include Cushingoid faces, irritability, GI reflux, a slowing in the rate of height and weight gain, steroid-induced cardiomyopathy, and hypertension. Nearly all children (88%) return to their pretreatment curves for height and weight within 24 months.[8,9] ranolol is newly inducted for the treatment of IHs. It is a nonselective beta blocker and is being used with increasing frequency for the treatment of IHs.[11] The mechanism of action for propranolol is unknown.[12] There are still ongoing, prospective, randomized controlled trials which will help elucidate propranolol's safety, efficacy, and tolerability for the treatment of IHs. The purpose of the study was to compare the effectiveness of propranolol versus prednisolone in the management of IHs. The objective of this study was to compare the effect of oral propranolol and Prednisolone in the management of infantile hemangiomas.

Methods

This was a randomized control trial, carried out at the Department of Pediatric Surgery, Services Hospital, Lahore. Duration of this study was 4 years from April

infantile hemangiomas were admitted from out-patient department and included in this study. Previously treated or those who need urgent therapy due to impairment of vital organ were excluded. Cardiologist objection for use of propranolol for any reason were also excluded from this study. Selected patients were randomly divided into two groups; Group A (Corticosteroid group) and Group B (Propranolol group) by lottery method. Parents were informed in detail about the disease, treatment options and its complications. An informed written consent was taken from the parent for including their child's data in this research. A thorough clinical evaluation together with routine laboratory tests (peripheral blood count, serum electrolytes and random blood sugar) were done. Lesions were measured, photographed and whenever needed an ultrasound examination (measuring the maximum thickness of the lesion) was also done. The consistency and color of the lesion was noted. All the patients were evaluated by a pediatric cardiologist for cardiovascular status. At initiation of therapy, patients were admitted for a period of 48 hours and treatment (propranolol or prednisolone) was started at a dose of 1 mg/kg/day on the first day. It was given in three divided doses. All the patients were monitored for hypotension, bradycardia, hypoglycemia, hyperkalemia and bronchospasm. If tolerated, the dose of propranolol was increased to 2 mg/kg/day and that of prednisolone to 3 mg/kg/day on the second day and then the patients were discharged. This treatment was continued for a period of 5 months, as this period is sufficient to induce regression or stabilize the growth of infantile hemangiomas. Each patient was reviewed on monthly basis for a period of 5 months, at the end of which data was collected. During the visits the dose of the drug was also readjusted according to weight. The data was recorded and analyzed in SPSS version 20, Numeric data like age, lesion size, duration of treatment are represented as mean and S.D. Qualitative data are expressed in frequency and percentages. To find the significance difference between lesion size students tTest was used. Chi square test was used for qualitative data analysis. P value was ≤ 0.05, the power of study was equal to 90% and the level of significance equal to 5%. The sample size was 30 patients in each group.

Methods

A total of 60 patients were included in the study with 30 patients in each group. There were 14 male patients in group-A while 16 were female; in group-B, 13 patients were male while 17 were female. In group-A, the average age was 11.6±10.4 months & in group-B, average age was 13.6±17.4 months. Most common location in both groups was head and neck details are shown in **(Table-1).** Average size of the lesions in group-A at the time of presentation was 6.86cm^2 while in group-B it was 10.39cm^2. But at the end of treatment average size of the lesions in group-A was 3.35cm$_2$ while in group-B it decreased to 0.7cm^2. The response rate of treatment in both groups was compared but there was maximum decrease in size noted in both groups within 1st month of treatment. Similarly response rate was more in group-B than group-A details are given in **(Fig-1).**

Table-1: Demographic details of both groups

	Prednisolone (Group A)N=30	Propranolol (Group B) N=30
Mean Age (months)	11.6±10.43	13.6±17.47
Gender: Male	14 (46.67%)	13 (43.33%)
Female	16 (53.33%)	17 (56.67%)
Hemangioma Location		
Head and Neck	18 (60%)	16 (53.33%)
Limbs	6 (20%)	10 (33.33%)
Trunk	6 (20%)	4 (13.33%)
Adverse Effects		
Hypoglycemia	–	2 (6.67%)
Cushingoid faces	5 (16.6%)	–

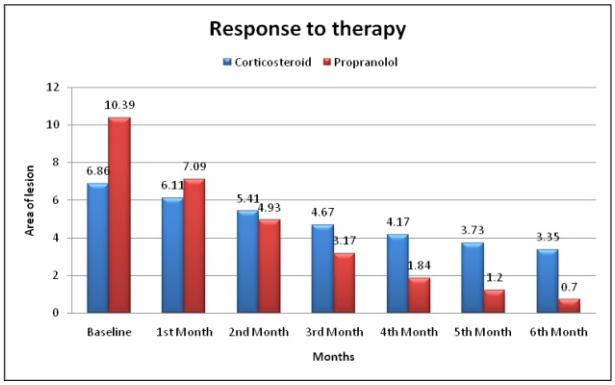

Fig-1: Response to therapy.

Discussion

IH is the most common vascular malformation noted in the infants. It involves head and neck region in 60% of cases, followed by trunk and limbs (20% each).[13] In our study similar findings were noted and IHs were present at head and neck region in 60% of patients in group-A and 53.33% patients in group-B. Similarly trunk involvement was seen in 20% patients in group A and 13.33% of patients in group-B. Response to therapy in IHs as an outcome has been measured by different researchers in a lot of different ways.[14] In our study we noted the size of the IH at time of presentation and then at each monthly follow up.

phase and treated them with systemic corticosteroids at a dose of 2 mg/kg/day as first-line treatment in 23 patients (56%) and as second-line therapy after failure of laser and/or cryotherapy in 18 (44%) patients. In their study mean duration of therapy was 129.0 and 137.6 days respectively. They noted that therapy was responsive in 86% cases in corticosteroids group and in all patients (100%) in the cryotherapy.[15] Buckmiller et al. evaluated 32 patients of IH and treated them with propranolol at a dose of 2 mg/kg/day. They reported that almost every patient responded to propranolol therapy. The outcome was excellent in 50% of the patients, where no additional therapeutic measure was required in 47% of the patients, there was improvement in the size of the IH, adjuvant therapy was required in addition to propranolol while 3% patient undergone further increase and this was designated as a non-responder.[16,17] In our study, size of IH decreased significantly in group-B treated with propranolol (90% of patients) as compared to group-A treated with corticosteroid (36.6% of patients). In a retrospective analysis of 110 patients with IHs showed more than 75% reduction in the volume of IH in 82% cases in propranolol group while in 29% cases of prednisolone group these results were comparable with our study results.[18]

We noted that maximum response was seen in 1st four weeks in terms of decrease in size. This response in 1st month was more in group-B than group-A, however Bagazgoitia et al. reported average reduction in size at weeks, in 60% of patients.[19] In our study, the side effect noted was cushingoidfacies in 5 patients (16.66%) in corticosteroid group while hypoglycemia was noted in 2 patients (6.67%) in the Propranolol group while no other adverse effects were observed. Prince et al reported almost similar adverse effects of both drugs i.e. hypoglycemia in one patient in propranolol group, while all the patients receiving prednisolone developed one or more adverse effects.[18]

There are many ongoing trials in different part of the world. So far, most studies and data have shown propranolol as superior, with better response and lower side effects. It is also cost effective.

Conclusion

From this study, it has been found that oral propranolol has clear and statistically significant advantages over prednisolone in the treatment of infantile hemangiomas. It has better outcome and fewer side effects as compared to corticosteroid. I would suggest propranolol to be used as first-line therapy in the management of Ihs.

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Original Article

Degree of Agreement Between Transvaginal Ultrasound Scan in Determining structural Uterine Abnormalities of Female Reproductive System Causing infertility Taking Hysteroscopy as Gold Standard

Wajid Ali, Bushra Haq, Rabia Akram, Tabeer Malik and Shahid Malik

Objective: To establish the degree of agreement between TVS and hysteroscopy in evaluating uterine structure abnormalities causing unexplained infertility.

Methods: It is a cross sectional study conducted at Lahore General Hospital Lahore and Services Hospital Lahore during a period of six months from 01-06-2018 to 31-12-2019. 385 patients fulfilling the inclusion criteria with informed consent were included in the study. Demographic data was collected from all patients. TVS was performed in the same cycle. Endometrial cavity was examined in two perpendicular planes. Endometrial echo pattern, thickness, irregularity and distortion were noted. All patients underwent hysteroscopy after TVS and hysteroscopic findings were noted and degree of agreement was calculated between TVS and hysteroscopy.

Results: Age ranged from 22 to 45 years of age with mean age 33.21±6.97 years. The mean duration of infertility was 3.15±2.13 years with minimum and maximum duration as 1 and 16 years. The mean BMI in this study was 28.21±4.06 with minimum and maximum BMI as 22 and 36.20. Agreement between trans-vaginal ultrasound scan and hysteroscopy in evaluating the uterine structural abnormalities causing infertility was assessed as statistically significant (kappa value 0.495 to 0.747, p<0.001).

Conclusion: This study proved a fair to substantial agreement between TVS and hysteroscopy to evaluate uterine structural abnormality in patient with unexplained infertility.

Keywords: infertility, trans-vaginal ultrasound (TVS), hysteroscopy, structural abnormalities. body mass index (BMI).

Introduction

Inability to conceive after 12 months of regular , unprotected sexual contact of couple is defined as infertility.[1] Many factors may cause difficulty in conception these include uterine structural abnormalities, endometrial pathologies, ovarian disorders and tubal factors. Uterine cavity abnormalities can be a contributing cause in 10 to 15% cases of female infertility; in approximately 50% of infertile women abnormal uterine findings are detected.[2] Endometrial morphology, thickness and shape of uterine cavity affect the blastocyst implantation.[3] Ovulatory problem is another common cause of female infertility. Among ovulatory disorders polycystic ovarian syndrome is most common. It affects 6% women of reproductive age group.[4] Tubal factors are responsible for 18% cases of female infertility.[5] Most important among these are endometriosis and tubal blockage. Blockage of fallopian tubes is due to infection or endometriosis.[6] Among uterine structural abnormalities most frequent cause is fibroid. Its prevalence is 8 -18% in women of reproductive age group.[7] Implantation failure and recurrent miscarriage can be caused by fibroid or septum.[8] Apart from fibroid endometrial polyps, congenital uterine abnormalities and intra uterine adhesions can also cause infertility among females.[9] Evaluation of uterine cavity is a routine investigation when investigating sub fertility in women. Different modalities are used for this purpose. These include transvaginal sonography (TVS), sonohysterography, hysteroscopy and rarely magnetic resonance imaging (MRI). Hysteroscopy is a commonly used gold standard procedure to evaluate the intrauterine abnormalities.[10] Hysteroscopy allows the direct visualization of cervical canal, endometrial cavity and tubal ostium.[11] It also enables the detection of vascular pattern of any abnormality, fibroids, endometrial polyps, Ashermans Syndrome, foreign bodies, uterine septa, structural uterine abnormalities, cervical stenosis and any lesion of uterotubal junction.[12] This endoscopic procedure has its risk of associated complications. These may include uterine perforation, infection, bleeding and air embolism.[13] TVS on the other hand is readily

Inexpensive first line investigation. It gives valuable information regarding uterine shape, uterine anomalies, ovarian morphology and follicle monitoring.[14] Hysterosalpangography (HSG) is another imaging modality which gives information regarding general configuration of uterine cavity. It is an indirect means for evaluation of uterine cavity and fallopian tubes. It is associated with hazard of radiation exposure, use of contrast media and patient discomfort.[15] Avoiding the radiation exposure but associated the patient`s discomfort hyster- osonography is another tool for uterine cavity evaluation. It allows single layer evaluation of endo- metrial lining by distending the endometrial cavity with saline or contrast medium.[16] In rare cases of diagnostic confusion MRI can be of valuable help especially in cases of Mullerian duct anomalies.[17]

Methods

It is cross sectional study conducted at Radiology Department of Lahore General Hospital Lahore and Services Hospital Lahore from 01-06-2018 to 31-12-2019. 385 married women of 22 to 45 years who were unable to conceive after one year or more than one year of regular unprotected intercourse were included in this study. Women with previous history of menstrual abnormalities, uterine surgery and women who did not give consent were excluded form the study. Informed consent was obtained from all patients who fulfilled inclusion and exclusion criteria. Demographic details were obtained. TVS with high frequency prob (6 to 11MHz) was performed during follicular phase (5 to 13 days) after cessation of menstrual bleeding. The endometrial cavity was examined in two perpendicular planes (sagittal and transverse planes). Endometrial echo pattern, thickness, irregularity and distortion were noted. Uterine abnormalities including polyps, fibroid, septum, adhesions, endometrial hyperplasia were also noted. Latter these patients underwent diagnostic hysteroscopy after informed consent in gynecology department with 5mm hysteroscope. Hysteroscopy was performed with full aseptic and antiseptic precautions in dorsolithotomy position. The cervix and vagina were swabbed. Bimanual pelvic examination was performed. Cervix was grasped with valsellum and gently dilated with hegar dilator where needed. Normal saline was used as distention medium. Hysteroscopic findings regarding cervix, cervical canal , endometrial lining, ostial openings, polyps , fibroid, septum or any distortion of endometrial cavity was noted. All information was recorded in pre designed performa.

Results

The mean age was 33.21±6.97 years with minimum and maximum age as 22 and 45 years. 136(35.32%) cases were <30 years old and 249 (64.68%) cases were 30-45 years old. The mean duration of infertility was 3.15±2.13 years with minimum and maximum duration as 1 and 16 years. A total of 302(78.44%) females had duration of <5 years and 83(21.56%) females had duration of infertility ≥ 5 years. The mean BMI in this study was 28.21± .06 with minimum and maximum BMI as 22 and 36.20.There were 138(35.84%) obese and 247(64.16%) non-obese females. The agreement between transvaginal scan and hysteroscopy in evaluating the uterine structural abnormalities causing infertility was assessed and found statistically significant with p value <0.001 and Kappa value 0.495 **(Table-1).** When data was stratified for age, duration and BMI, the agreement was statistically significant (p<0.001)as indicated in **Tables- 2,3 & 4.**

Discussion

Infertility is a widespread phenomenon that affects

Table-1: Agreement between trans-vaginal scan and hysteroscopy in evaluating the uterine structural abnormalities causing infertility.

HYSTEROSCOPY TVS	Endometrial-Polyps	Uterine fibroids	Adhesions	Endometrial hyperplasia	Didelphis uterus	Kappa/ P-Value
Endometrial- Polyps	73	02	07	01	04	
Uterine fibroids	08	52	12	11	23	0.495/ <0.001
Adhesions	05	06	31	11	18	
Endometrial hyperplasia	04	01	08	29	04	
Didelphis uterus	04	06	15	05	45	

Table-2: Stratification for age.

HYSTEROSCOPY TVS	Endometrial-Polyps	Uterine fibroids	Adhesions	Endometrial hyperplasia	Didelphis uterus	Kappa/ P-Value
Age < 30 Years (n=136)						
Endometrial- Polyps	73	02	07	01	04	0.495/ <0.001
Uterine fibroids	08	52	12	11	23	

Adhesions	05	06	31	11	18	
Endometrial hyperplasia	04	01	08	29	04	
Didelphis uterus	04	06	15	05	45	
Age ≥ 30 Years (n=249)						
Endometrial- Polyps	08	52	12	11	23	
Uterine fibroids	05	06	31	11	18	
Adhesions	04	01	08	29	04	0.495/ <0.001
Endometrial hyperplasia	04	06	15	05	45	
Didelphis uterus	73	06	15	05	45	

Table-3: Stratification for duration of infertility.

HYSTEROSCOPY TVS	Endometrial- Polyps	Uterine fibroids	Adhesions	Endometrial hyperplasia	Didelphis uterus	Kappa/ P-Value
Duration < 5 Years (n=302)						
Endometrial- Polyps	58	01	04	01	04	0.539/ <0.001
Uterine fibroids	07	43	07	07	19	
Adhesions	04	03	25	07	15	
Endometrial hyperplasia	03	01	07	26	01	
Didelphis uterus	02	04	11	03	39	
Duration ≥ 5 Years (n=83)						
Endometrial- Polyps	15	01	03	0	0	
Uterine fibroids	07	09	05	04	04	
Adhesions	07	03	06	04	03	0.334/ <0.001
Endometrial hyperplasia	01	0	01	03	03	
Didelphis uterus	02	02	04	02	06	

Table-4: Stratification for MBI.

HYSTEROSCOPY TVS	Endometrial- Polyps	Uterine fibroids	Adhesions	Endometrial hyperplasia	Didelphis uterus	Kappa/ P-Value
BMI<30(N=247)						
Endometrial- Polyps	40	02	07	01	03	0.357/ <0.001
Uterine fibroids	07	24	11	11	18	
Adhesions	06	06	19	07	13	
Endometrial hyperplasia	03	01	04	15	03	
Didelphis uterus	03	05	13	04	22	
BMI=30(N=138)						
Endometrial- Polyps	33	0	0	0	01	
Uterine fibroids	01	28	01	0	05	
Adhesions	0	0	12	04	05	0.743/ <0.001
Endometrial hyperplasia	01	0	04	14	01	
Didelphis uterus	01	01	02	01	23	

Congenital and acquired uterine structural abnormalities are major causes of female infertility. Congenital uterine anomalies account for 3% of all infertile female.[19] TVS is the 1st line, readily available,non invasive and cost effective imaging modality in term of diagnosis and characterization of uterine structural anomalies, ovarian disorders and other pathologies leading to female infertility. Hysteroscopy on other hand is invasive but can diagnose small intra uterine lesion

effect endometrial receptivity and implantation.[20] When finding degree pf agreement between TVS and hysteroscopy, Shiva M et al. conducted a study on 789 cases. TVS was conducted before hysteroscopy. TVS and hysteroscopy results revealed that there was significant agreement in diagnosis of uterine fibroids, intermediate agreement for endometrial hypertrophy, significant agreement for Asherman Syndrome and septate/arcuate uterus with Kappa coefficient as 0.3, 0.42, 0.16, 0.45 respectively for all these pathologies.[21] In agreement to this our study also revealed fair to substantial agreement between TVS and hysteroscopy in diagnosis of female infertility. In present study kappa value ranges from 0.356 to 0.747 and p value <0.001. In another comparative study by Shukla P et al. between TVS and hysteroscopy. TVS was succes- sful in explaining infertility with sensitivity of 51.21% and specificity of 100% while hysteroscopy had sensitivity 0f 90% and specificity of 100%. The final agreement between between TVS and hysteroscopy was moderate and significant.[22] In a study by Niknejadi M et al. hysteroscopy was taken as gold standard and the agreement between TVS and hysteroscopy was in 350 out of 394 pathological cases (88.1%).[23] In our study when stratified for age less than 30 years the Kappa value is o.747 and at age more than equal than 30 years the Kappa value is 0.356. It shows a substantial degree of agreement at age group less than 30 years and fair degree of agreement at age more than or equal than 30 years. When considering the duration of infertility as less than 5 years and more than or equal than 5 years the Kappa value is 0.539 and 0.334 respectively. It shows a moderate degree of agreement at less than 5 years of age and fair degree of agreement at duration more than or equal than 5 years. TVS is 1st line diagnostic modality among infertile couple for screening of structural uterine abnormalities and reducing the load of gynecologist in terms of hysteroscopic procedure. It also reduces the hazards of anesthesia and taking time off from work for the women suffering from infertility.

Conclusion

This study proves a fair to substantial agreement between TVS and hysteroscopy to evaluate uterine structural abnormality in patient with unexplained infertility.

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