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Original Article

Determination of Age of Puberty Using Leptin Level in Male Popualtion

Ahmad Raza Khan, Memona Yasmin, Khalid Mahmood, Muhammad Abaidullah and Naveera Ahmed

Objective: Innovating puberty analysis via utilization of leptin as a biomarker to revolutionize existent archetype prototype paragon

Methods: It was a cross sectional study based on pubescence markers utilized as landmark criterion. Healthy volunteer males of disparate maturescens were selected. Their physical maturity was substantiated via gold standard tanner staging and correlative algorithm was established with serum leptin levels. Sample size calculative of 150 was collected.

Results: Leptin levels dependent on age groups were stratified. These leptin level ranged from a minimum pre-pubertal level of 0.174 ng/ml to maximum 7.704 ng/ml at puberty initiation, which exhibited a peak uprise of the leptin mean value of 3.57 ng/ml ± Std. Dev. 1.608 ng/ml, during the puberty startup averaging up to 12.5 years, with a progressive decline from mid-puberty to post-puberty age represented by the fall in leptin level from 2.539 ng/ml to 0.174 ng/ml respectively, with a mean value of 1.021 ng/ml ± 0.611 ng/ml

Conclusions: Leptin incentivized study was in pursuance of establishing a correlation between leptin in regards with juvenility along with evaluating range of leptin levels at which the maturity is initiated. The prospective study was deployed via utilizing pinnacle paradigm of tanner staging supplemented by leptin analysis. Data obtained was analyzed statistically for computation of puberty attainment age. Epitome of research conclusively analyzed a correlation between serum leptin and puberty initiation and an incontrovertible definitive leptin level range to assess the maturescence staging from initiation to complete adulthood.

Keywords: puberty, leptin, tanner, age of majority, forensic

Introduction

Maturescence into adulthood is a multisystem web of complex yet organized programmed pattern dependent on various physiological processes that once initiated at a particular time results in a cascade of events, generating sexual maturity.[1] The decisive time for sexual dimorphism is dependent on various prerequisites. The main initiation signal for the body to go into such transformation is thermogenesis. When the balance tilts in the favor of increased heat production in comparison to at which level heat is dissipated, is when the body knows it is time to develop sexual organs to its full functional level.[2] The second triggering feature of adipose tissue other than heat is hormone generated known as leptin.[3] Positive balance of the heat production signals the body to produce enough leptin to play triggering role in puberty initiation. Leptin is governed by multifactorial array of BMI, dexamethasone, insulin, NPY and T3. Cascading out the map of attainment of puberty has so far been traced up to trigger/permissive role of leptin. In pre-pubertal phase, leptin remains in the bound state to its receptors throughout the body. However, metabolic rates decline, signal the detachment of the leptin from its receptors in brain and subsequently from soluble receptors throughout the body. Hence, just at puberty initiation, surge of free form of leptin triggers the puberty process.

Finally coming to the legal aspect of the sexual maturity i.e. time of all sorts of experimentation under the multiple hormonal siege. A behavioral pattern trend studied by Peper and Dahl elaborates on the urges and surges of hormones having variable outcome mostly not positively driven.[4] This leads to juvenile criminological behavior resultantly producing sexual deviants and aggressive attitude personalities. This results in explicit extrovert behavior such as dacoity, rape, aggression and hostility towards society, leading to violence and disturbance of communal peace. A study conducted by Fakhurrnissa Talpur et al. narrates multiple influences on the youngsters leading them astray dependent upon the social factors, domination of peer impact and domestic crisis.[5] Hence the study outcome and its benefits would include suggested

proposal of reduction in legal age of majority to implicate the threat of punishment as an effective tool to curb the violence in society, rather than to apply the actual penalty after the unrest being created which itself is a source of disturbance. Statistical details exhibit the number of juvenile delinquents in Punjab jails in a research project by Khalid Mahmood and Mohammad Asghar Cheema. It analyses the causative factors resultantly producing unharnessed adolescent offenders.[6]

Methods

Sample size calculated according to the statistical formula was 160. This sample size was divided into 4 groups of different age ranges as shown in table 1. The male subjects were categorized in 4 groups as follows:

Table-1: Age stratification according to puberty range.

Groups	Age	Blood Sample
Group 1 (pre-pubertal)	9-11 years	3-5cc
Group 2 (initiation of puberty)	11.5-13 years	3-5cc
Group 3 (mid-puberty)	13.1-1 years	3-5cc
Group 4 (post-puberty)	15.1-18 years	3-5cc

The total number of 160 subjects included pre-pubescent, developing teenage, along with fully mature boys with an age range of 9-18 years.

Proper, valid and informed consent was taken from the parents/ guardians of subjects of age groups 1, 2 and 3 for the tanner staging and withdrawal of the venous blood. Informed consent of major subjects was obtained from themselves after elaborate information. All the major and consenting participants, willingly and actively cooperated in sample collection activity. None of the individuals had any chronic or debilitating disease.

Blood samples were collected from group 1, 2 and 3 from three schools of district Kasur and group 4 blood samples were collected from different individuals from Lahore. 5cc blood was withdrawn from vein in cubital fossa, of age ranging from 9-18 year old boys, in the disposable syringes, by the expert medical officer. The procedure was thoroughly elucidated regarding sample collection and likely risks accompanying it along with purpose of entire activity. Blood was preserved in the EDTA vacutainer tubes, stored with ice packs, maintaining the cold chain till transport to the laboratory.

Comprehensive global precautionary measures were taken, including alcohol swab use on skin, aseptic disposable syringes, with prompt dispensation of the used material in the disposal containers. Upon arrival in the laboratory in the department of Forensic Sciences, UHS, Lahore, the blood samples were centrifuged at 1000 rpm and stored at -20°C. Later ELISA was performed for serum leptin analysis.

A detailed biodata was collected on a proforma which stated the name, age and tanner staging of male subjects.

Results

Three schools were visited and 120 samples were collected from District Kasur and 14 samples were collected randomly from District Lahore. Random samples were taken from age 9-18 years and later the data was arranged as per tanner stages. 46 candidates were recorded in age group of 9-11 years, 51 in age group of 11.1-13 years and data of 14 was recorded in age group of 13.1-15 years and finally 23 candidates were in age group of 15.1-18 years. Later on according to tanner stages 70 sorted out as tanner 1, 18 as tanner 2, 12 each as tanner 3 & 4 and 22 as tanner 5. These groups were stratified as pre-pubescent, initiation of puberty, mid-puberty and post-puberty, which included 70, 30, 12 and 22 candidates respectively. In our cross sectional research project, boys of age ranging from 9 years up to 18 years in varying tanner stages were evaluated as per their physical and sexual developmental levels by criterion of pubic, axillary and face hair as secondary sexual markers. Penile length and testicular size were measured as genitalia characteristics. Pileouspuberal growth was one of the two pathways chosen for tanner staging, the other being the testicular volume measure. Some candidates exhibited spurt of scanty pubic hair initially without TV more than 3 ml, while others presented with a simultaneous virilization, i.e. nascent growth of pubic hair and increase in TV ranging from 4 ml to 8 ml initially ranging its way up from 12 ml to a maximum of 20 ml. Pre-pubescent age group according to tanner staging ranged from 9 years minimum up to maximum age of 14 years, with mean age of 10.764 ± Std. Dev. of 1.3125. Puberty initiation fell within the range of 9-16 years of age according to tanner assessment with mean age of 12.533 ± Std. Dev. 1.5916. Mid-puberty group was within range of 12-18 years, mean of which was 15.5 ± Std. Dev. 1.9188. The last group of post-puberty fell within the range of minimum 12.5-18 years maximum, with mean of 16.523 ± Std. Dev. 1.8158. Leptin levels dependent on age groups were stratified.

These leptin level ranged from a minimum pre-pubertal level of 0.174 ng/ml to maximum 7.704 ng/ml at puberty initiation, which exhibited a peak upraise of the leptin mean value of 3.57 ng/ml ± Std. Dev. 1.608 ng/ml, during the puberty startup, with a progressive decline from mid-puberty to post-puberty age represented by the fall in leptin level from 2.539 ng/ml to 0.174 ng/ml respectively, with a mean value of 1.021 ng/ml ± 0.611 ng/ml.

Comparative table in the statistical ANOVA displayed p = 0.000 for comparing the means of prepubescent vs puberty initiation depicting the presence of significant difference between leptin levels which were 1.035 ng/ml pre-pubertal as compared to 3.573 ng/ml at the puberty initiation. Pre-pubertal vs post-pubertal levels exhibited a p = 0.451, with the resultant evaluation that no meaningful difference, exists between the mean values of these two groups which were 1.035 ng/ml pre-pubescence vs 0.728 ng/ml in the post-puberty phase. Similarly the pre-pubertal levels vs mid-puberty also had a p = 0.000 showing a significant mean difference as 1.035 ng/ml pre-puberty vs 1.558 ng/ml in the mid-puberty age. Finally the mid-puberty vs post-puberty had a p = 0.036 which also showed a valid difference among means of the groups respectively as 1.558 ng/ml vs 0.728 ng/ml.

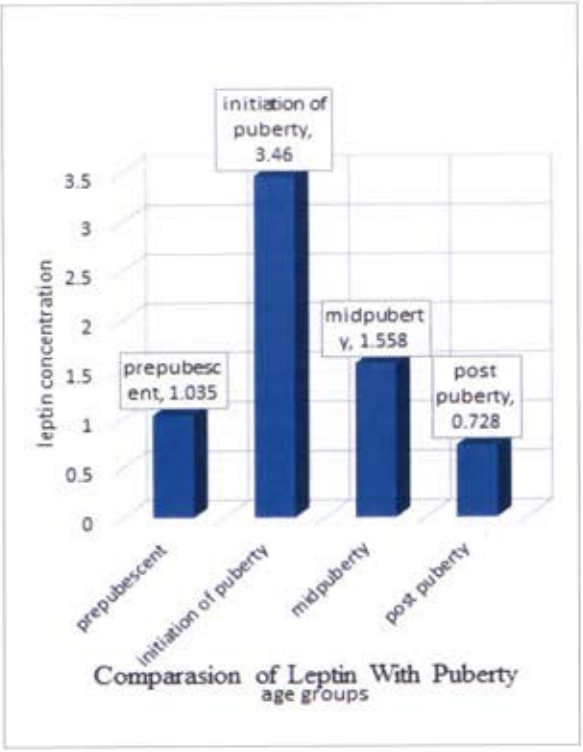

Fig-1: Laptin concentration.

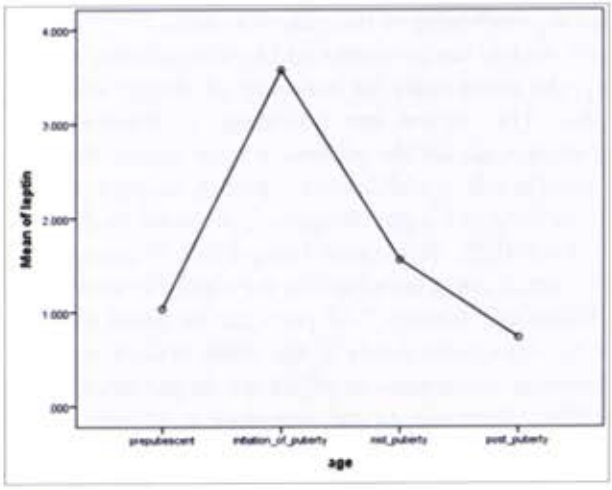

Fig-2: Means plot leptin association with puberty.

Discussion

Human body is a pool of amazing combination of multiple genetic codes and epigenetic factors influencing the outcome. The transitional phase of metamorphosing into an adult capable of procreation is a cascade with has yet not been completely deciphered. However so far the code has been traced up to leptin, an ob gene product, playing a mandatory role in puberty attainment.[7] Leptin although present throughout life playing different role in human biochemistry is only enhanced in enough effective exertive level to take the body into pubescence upon the various markers including thermal signal, insulin, triiodothyronine, glucocorticoids and neuropeptide Y.[8] The cumulative effect of all these signals, detaches the plasma-protein-mopped up leptin along with increased leptin production by the body fat resultantly initiating the puberty cascade.

Sexual desirability is a significant milestone of puberty emergence. This sexuality can be objectified by four landmarks, namely, sexual desire, vivification, attitude and activity. This tends to comprehend the advancement of sex sempiternity of human evolution into a procreative being, spanning from pubescence to adulthood. It is an interconnected web of desire, awareness, interpretation and respondent functionality[9]. Pattern of crime in adolescence is called juvenile delinquency. Puberty brings along various physical and hormone driven alterations, which if uncontrolled end up as delinquent behavior.

The covert alternating overt juvenile delinquent outcome among the young puberty attaining individuals is influenced by none other than peers, socio-economic factors as well as the electronic dilemma of internet, smart phones,

and easy availability of the cable television.

Every society has its norms and legal legislature to keep the community in harmony of decree and justice. The statute law prevailing in Pakistan, categorizes age for the punitive actions against the criminal rebels. A child under 7 years is exempt of any criminal and legal obligation, as stated in the sec. 82 of P.P.C. The reason being a lack of intent, in the act, if any, committed by the child. However an individual between 7-12 years can be penalized for his deplorable deeds if the child realizes the lamentable consequences of his act, as per sec. 83 of P.P.C. Next age in the annexure is of prime concern, declared as juvenility most prone to delinquencies of almost every kind, time of stepping up the maturation process, experimenting every thought. This is the age which if not exposed to proper paternalism, may become contingent with permanent atrocious, nefarious criminality. Finally 18+ years are treated as adults for all capital punitive actions due for the committed crimes[10]. This is the legal practice in most of the countries with the exception of Saudi Arabia, Iran, Sudan and Yemen, where the legal age for capital punishment is 15 years as Shariat law.[11] Despite of the legislature which states that a juvenile is to be sent to correctional facility, around 800 minors are on death row in adult jails of Pakistan. If the heinous crime obligates the court to go beyond clemency and award prime punitive sentence to a minor, may be its time to revise the legal age for criminal responsibility[12]. Deterrence is to be conceptualized in a reformed way, to discourage an act via introducing a fear of consequence. If effective threat is imposed in society, cognizance of risk would be a factor enough for dissuasion.[13] Presently, offenders even if apprehended, rarely go through the process of conviction. The reason behind is a legal technicality being so very conveniently manipulated by the solicitors, to benefit their clients, that any age below 18 years, is exempt of punitive action. The lawyers very successfully orchestrate the legal loophole maneuvers, to maximally exploit the situation[14]. The inception of reasonable uncertainty is seeded during the criminal proceedings which are eventually engineered strategically for the acquittal of the client. Recidivism is the repercussion of the ironic statutory rulings of the honorable court. These impudent juveniles when unleashed upon the society become a hideous audacity, as they have the understanding that the law gives them, benefit of doubt of being underage. Subsequently these unabashed delinquents become a malevolent element. This malignant element, ultimately is then uprooted, by extrajudicial killings, a most disapproved yet indispensable method which, still leaves behind the metastases[13]. Henceforth promulgation of the Sharia law is de rigueur, as it already states the age for capital crime is 15 years. Accountability needs to be liable, in the present scenario where "accidental hump" avows a secular decline in the age of pubescence from 18 years to 13 years. A pattern has emerged from mid-18th to 1900s, eliciting a 3 month decrease per decade in pubescence. 134 volunteer available ethnic individuals were taken for the research conducted by the author and his team. 70 candidates ranging from ages 9-14 years were sexually dormant, labelled as pre-pubescent. The next batch of 30 candidates exhibited puberty initiation signs, in the age range of 9-16 years.12 Mid-puberty individuals were of age range of 12-18 years. Finally the post puberty group of 22 candidates showed a variation of age from 13-18 years.

The disequilibrium of the fluctuating data exhibited a non-linear regression correlation. It showed that a pre-pubescent child had an age range from no minimum to a maximum of 14 years. Our present research quantifies the statistics that boys as young as 9 years are experiencing the initiation of puberty, as substantiated by tanner stage 2, backed up by leptin level.

Ages 10-12 years fell in the range of tanner 2 and 3, with age 13 years exhibiting full attained puberty with tanner 5 staging and corresponding serum leptin levels. However variability of the data does not preclude possibility of early initiation in the population of Pakistan. ANOVA results also discern the distinctive peak of leptin at puberty initiation. Hence this inflating generation gap amidst adolescence and adulthood enhances the time span for escalation of risk taking behavior. This shall consequently cause an upsurge of the erratic attitude and illicit predilection[15]. It is imperative to state here that most of the puberty attainment procedures, follow the trend of tanner staging backed up by radiological examination. It exposes an individual to entire body radiological irradiation, for age estimation, in cases of violence including sexual assault. This obsolete health hazardous technique can very conveniently be replaced by leptin analysis especially where puberty attainment is under scrutiny. A 3-5cc venous blood can efficiently support the physical tanner examination for the puberty staging.

Our study narrates the physical examination done as per tanner guidelines. This is further supported by the

serum leptin analysis showing marked corerlation with Puberty initiation. This would be of much help in settling legal disputes of sexual assaults by categorizing the individual as to prepubescent or otherwise, capable of accrediting sexual act. Hence the budding generation making a sexual debut at age of 12 years is definitely prone to vandalism, sexual experimentation besides sexual exploitation by other juveniles, and other risk taking behavior. Urbanization and industrialization has caused secular decline in the attainment of puberty[16]. This has consequently resulted in increase in "maturity gap". The system needs to be revitalized by revolutionary amends in social and legal architecture. Finally it is better to be safe rather sorry for a situation that could have been handled more competently. It is about time for a long due reformatory effort to improvise the legal framework. The harmonious prevalence is dependent only on the effective and just society.

Conclusion

In the conclusive summation, it is merely, not an understatement to narrate that although prevalent finale outcome of puberty is by and large, apparently survived by the youth, with not much perilous results. This approach shall be cliché, addressing only the triviality of the profound scenario. The many facet juvenile delinquent behavior includes vandalism, aggression, violence and sexual offences including deviances. Introduction of leptin analysis in Forensic Medicine, is an ancillary accessory for detection of puberty initiation. Puberty process is spread over years. The biochemical analysis of serum leptin, can help assess the pubescence initiation mid-puberty phase, clearly demarcating these stages from pre-pubertal and post-puberty phases[17].Therefore the medicolegal cases, being presented in the department of Forensic Medicine, in cognizance of sexual assault, can be processed by tanner staging supplemented by serum leptin analysis requiring only 3-5cc of blood.

Department of Forensic Medicine
SIMS/Services Hospital, Lahore
www.esculapio.pk

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Original Article

Changes in Number of Chondrons in Tangential Zone of Ageing Male Human Articular Cartilage

Shaista Ali, Ayesha Yousaf and Muhammad Amin

Objective: To study the changes in number of chondrons in tangential zone of male human articular cartilage in advancing age.

Methods: Forty samples of articular cartilage were collected from right knees of male dead bodies ageing between 21 60 years and placed into four groups. After tissue processing and cutting, staining with H&E was done. The number of chondrons containing chondrocytes was noted in each group.

Results: With advancing age the number of chondrocytes within chondrons in Tangential /superficial zone of articular cartilage were reduced.

Conclusions: In ageing, articular cartilage the number of chondrons in Tangential zone of articular cartilage is reduced leading to osteoarthritis. Presence of stem cells in this zone makes it an attractive target for preventive and therapeutic measures.

Keywords: articular cartilage, chondrons, tangential zone, osteoarthritis.

Introduction

Articular cartilage, hyaline in nature, is a specialized type of supporting connective tissue that covers the ends of the bones in synovial joints.[1] It is unique in its structure which gives it particular metabolic properties such as extraordinary resilience, enabling the articular cartilage to withstand enormous pressure.[2] In light microscopy, the articular cartilage presents four zones. Three of these zones namely tangential, transitional and radial are non-calcified while the deepest zone is the calcified cartilage zone.[3] In all zones, type II collagen is most abundant and constitutes about 95% of the total collagen content of cartilage.[4] The chondrocytes reside in chondrons and in each zone chondrons have specific shape, size, arrangement and number. These cells are responsible for the development, maintenance as well as repair of articular cartilage and by synthesizing and turning over the extracellular matrix. They are capable of creating specific microenvironment.[5]

Tangential/superficial zone makes up about 10-20 % of articular cartilage thickness. Collagen fibers in this zone are tightly packed and are aligned parallel to the surface. The densely packed collagen fibrils limit the access of large molecules, effectively isolating cartilage from immune system. Deep to collagen layer, this superficial layer of cartilage contains a relatively large number of flattened chondrocytes. This zone is in contact with synovial fluid and is responsible for most of the tensile properties of cartilage as well as the protection and maintenance of deeper layers[3]. In addition to the chondrocytes, this layer also contains the progenitor stem cells[6]. The secretions of the stem cells mediate tissue regeneration and can repair tissue injuries.[7]

Degeneration of articular cartilage leads to osteoarthritis, a most recognized major age related joint disease causing pain and disability. The disability is progressive and becomes more evident with advancing age.[8,9] It affects more than 15% of the adult population, becoming the second greatest cause of disability and poor life style throughout the world.[10] The cellular density in osteoarthritis is reduced which leads to changes in extracellular matrix secreted by these cells, clustering of chondrocytes, fibrillation and progressive cartilage degeneration. Aging also results in decreased number of cells in articular cartilage initiating the osteoarthritis.[11]

Methods

Forty samples of articular cartilage of knee joint were collected from unknown male dead bodies in Forensic department of King Edward Medical University Lahore, brought within six hours of death. All the bodies were between 21-60 years of age. The autopsy was performed within 12 hours and till that time the temperature of bodies was maintained at 4 degree centigrade. Samples with gross abnormality or deformity and signs of surgery or trauma of the knee joints were excluded. Depending upon the age of the cadaver, the collected samples of articular cartilage were divided in four groups A, B, C and D containing 10 samples each i. e. Group A: 21 30 years Group B: 31 40 years. Group C: 41 50 years. Group D: 51 60 years. For this study articular cartilage of femoral

condyle of right sided knee joint was selected. Transverse incision was given on the skin extending from medial to lateral epicondyle of femur. Skin was reflected upwards and downwards to expose the quadriceps tendon. This tendon was cut by giving inverted "U" shaped incision starting above the patella and extending downwards to the tibial condyle on either side of ligamentum patellae. The cut tendon was reflected downwards along with patella to expose the articular cartilage of femoral condyle. Knee joint was flexed and 1 cm x 1 cm full thickness piece of articular cartilage was removed with the chisel from the tibial surface of femoral condyle, 1 cm medial to the medial margin of intercondylar fossa. The specimens were immediately placed in 10% neutral buffered formalin for 48 hour, processed for paraffin embedding. Five micrometer (5µm) thick sections were made on rotary microtome and mounted on clear albumin coated slides. H & E staining was done and mean number of chondrons/HPF (mean of three non overlapping fields) in tangential zone was noted in all groups.

Results

In this study it was observed that in tangential zone the mean number of chondrons was 17.06± 1.67/HPF in group A , 15.3±1.62/HPF in group B, 12.74±1.15/HPF in group C and 7.66±1.52/HPF in group D. The mean number of chondrons was statistically significant in all study groups (p-value=0.000). The decrease in the number of chondrons with advancing age was very obvious **(Fig-1-2)**. Using multiple comparison test it was observed that the mean number of chondrons was maximum in group A. Number of chondrons gradually decreased from A to D. The difference in number in each group was statistically significant (p-value < 0.05).

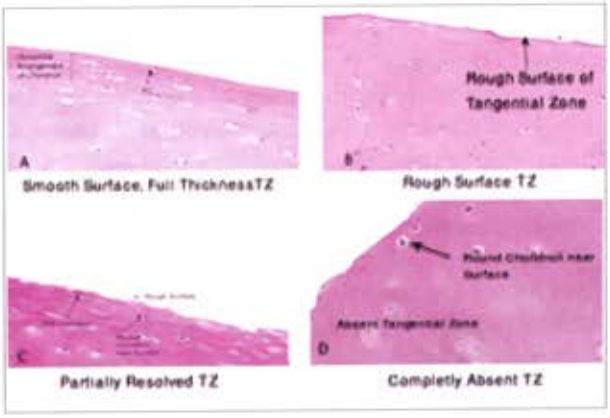

Fig-1: Histomicrograph showing decreasing number of chondrons in tangential zone of articular cartilage with advancing age.

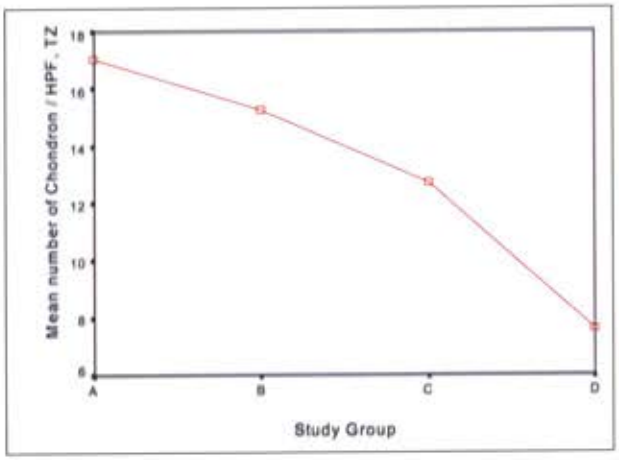

Fig-2: Graphical presentation of mean number of chondrons in tangential zone of articular cartilage in different study groups.

Table-1: Descriptive analysis of mean number of chondrons in tangential zone per hpf and multiple comparison test of number of chondrons in different study groups .

	Groups	n	Mean	Std. Devivation	Mininum	Maximum
Study Groups	A	10	17.067	1.6764	15.33	20.00
	B	10	15.300	1.6212	13.00	18.33
	C	10	12.741	1.1520	11.00	14.67
	D	10	7.6667	1.5275	5.00	9.33
	Total	40	13.667	3.6861	5.00	20.00

P-value over all

	A vs B	A vs C	A vs D	B vs C	B vs D	C vs D
Pair Wise	0.014	0.000	0.000	0.001	0.000	0.000

Discussion

This study described that the total number of chondrons in the tangential zone of the articular cartilage is decreased with the advancing age. The findings were similar to Lotz and Loeser (2012) who observed that the cellular density of articular cartilage is reduced profoundly in tangential/ superficial zone and the secretary properties of chondrocytes became abnormal with advancing age. Maintenance of normal extracellular matrix and functioning of articular cartilage is dependent on adequate number of chondrocytes. Superficial zone is unique in having large number of chondrocytes as well as progenitor stem cells which are capable of replacing chondrocytes after their destruction[11]. Chondrocytes are particularly prone to develop age changes affecting the mechanical properties of articular cartilage.[12] Main hindrance in the repair of articular cartilage is the limited intrinsic repair capacity of this avascular tissue.[13] The presence of large number of chondrocytes as well as stem cells in tangential zone and the fact that the cellularity of articular cartilage particularly in the tangential zone decreases with advancing age strongly indicates that this zone may play a critical role in the initiation of osteoarthritis.[14] Decreased cell count of surface layer during ageing results not only in thinning of articular cartilage due to less extracellular matrix but it also deprived the articular cartilage of the cells that might play a vital role in its regeneration by combating with the degenerative changes in the old age.[11,14] This might explain the failure of regeneration of articular cartilage after destruction. Tangential zone is one of the areas that should be focused upon for the attractive therapeutic measures to slow down or arrest the degenerative process.[15]

Conclusion

In ageing articular cartilage the number of chondrocytes in Tangential zone decreases which results in disturbance of normal orientation and composition of articular cartilage that leads to osteoarthritis. As this zone also contains the stem cells, reduction in the number of cells in tangential zone will further limit the repair of the cartilage.

Department of Anatomy
SIMS/Services Hospital, Lahore

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Original Article

Spectrum of Risk Factors of Myocardial Infarction and Their Associations with Age: A Cross Sectional Study from Gujranwala, Pakistan

Muhammad Shahid, Muhammad Irfan, Mubashar Zeeshan, Yasir Mahmud, Maryum Shafiq and Saqib Shafi Sheikh

Objective: To determine the prevalence of various risk factors of acute ST elevation myocardial infarction (STEMI) and their associations with age among patients admitted at tertiary care hospital, Gujranwala, Pakistan.

Methods: It was a cross sectional study of acute STEMI patients admitted from June 2017 to May 2018. After informed consent, data was collected by purposive sampling. Statistical analysis was done using SPSS version 25. Various risk factors of STEMI including smoking, hypertension, diabetes mellitus, obesity, personal H/O IHD, H/O of IHD in male family member of age <55years, and H/O of IHD in female family member of age <45years, were the qualitative variables while age of the patients was the only quantitative variable. Independent sample T test was used to compare the mean age of patients in two groups of each risk factor. The multiple regression analysis was also performed to predict the age at which STEMI may occur using different risk factors. The prediction by a risk factor was considered statistically significant if $p < 0.05$.

Results: Amongst 668 patients, 54.2% were smokers, 54% hypertensive, 29.5% diabetics, 22.9% obese, 28.9% had personal H/O IHD, 12.1% had H/O of IHD in male family member of age <55years, and 21.1% had H/O of IHD in female family member of age <45years. The mean age of the patients was 53.81 + 12.37 years. The mean age of the patients was statistically significantly less of smokers than non-smokers ($p<0.1$), diabetics than non-diabetics ($p=0.047$), and non-hypertensives than hypertensives ($p<0.1$). The mean age of the patients had no statistically significant association with H/O obesity ($p=0.264$), personal H/O IHD ($p=0.134$), H/O of IHD in male family member of age <55years ($p=0.700$), and H/O of IHD in female family member of age <45years ($p=0.265$). A multiple regression analysis suggested that age at which STEMI may occur can be statistically significantly predicted by 4 variables (Smoking, Hypertension, Diabetes mellitus, Obesity).

Conclusions: Smoking was the most prevalent risk factor for myocardial infarction in our studied population. Smokers and diabetic patients who suffered STEMI were younger than non-smokers and non-diabetic patients respectively. Among STEMI patients, hypertension was seen in relatively older group of patients. Smoking, Hypertension, Diabetes mellitus, Obesity are those four risk factors which significantly predict the age at which STEMI may occur.

Keywords: STEMI, risk factors, age, cross-sectional study, SPSS

Introduction

Acute myocardial infarction (MI) is the leading cause of death worldwide.[1] It occurs when blood flow to heart through one or more of the coronary arteries is blocked suddenly.[2] As a result, myocardial necrosis usually begins in the endocardium and spreads towards the epicardium.[3] In USA, the incidence of first MI in both genders is approximately stable during last 10 years, that is 1.1% and 1.7% per year in men and women, respectively.[4] The people of our subcontinent are more prone to MI, where annual incidenc is approx 6.44%.[5] The major known risk factors of MI include smoking, hypertension, diabetes mellitus, and dyslipidemia.[6] The recent studies have also associated these risk factors with premature coronary artery disease.[7,8] The known risk factors of first acute MI among youngs differ from that of eldely,[9] where smoking, dyslipidemidemia, family history of MI, and male gender are known common factors among youngs, while diabetes and systolic hypertension are common factors among elderly people.[10] The literature focusing such elaboration from Pakistan is lacking. Therefore, the author is keen to determine the prevalence of various risk factors of myocardial infarction among patients admitted at tertiary care hospital, Gujranwala, Pakistan. We will also find the associations of these risk factors with age of the

patients in our population.

Methods

This cross-sectional study was conducted in the Department of Cardiology, GMC Teaching hospital, Gujranwala from June 2017 to May 2018. Sample size calculation was performed using online Rao soft calculator. With a population size of 20000, response distribution of 50% and confidence interval of 95%, the minimum recommended sample size was 377. The written informed consent was taken from all patients and the data was collected by purposive sampling using a structured proforma. All the patients diagnosed with ST segment elevation myocardial infarction (STEMI) who were hospitalized were included in this study. The diagnosis of STEMI was made by ST segment elevation and raised cardiac enzymes in a patient with acute chest pain. Left bundle branch block or left ventricular hypertrophy cause secondary ST-T changes. Here cardiac troponins were especially used to help diagnosis. Statistical analysis was performed using the Statistical Package for Social Science (SPSS), version 25. Age of the patients was the only quantitative variable, while history of (H/O) smoking, hypertension, diabetes mellitus, obesity, personal H/O ischemic heart disease (IHD), H/O of IHD in male family member of age <55years, and H/O of IHD in female family member of age <45years were the qualitative variables. During descriptive interpretation of data, continuous variables were expressed as mean and standard deviation. Frequencies and percentages were computed for different categorical variables. Independent sample T test was used to compare the mean age of patients in two groups of each risk factor of MI i.e. with or without that risk factor. The multiple regression analysis was also performed to predict the age at which STEMI may occur using different risk factors. The prediction by a risk factor was considered statistically significant if $p< 0.05$.

Results

Amongst 668 patients who presented with STEMI, the percentage distribution of the risk factors was as follow: 54.2% (n=362) had H/O Smoking, 54% (n=361) had Hypertension, 29.5% (n=197) had Diabetes mellitus, 22.9% (n=153) had Obesity, 28.9% (n=193) had personal H/O IHD, 12.1% (n=81) had H/O of IHD in male family member <55years of age, and 21.1% (n=81) had H/O of IHD in female family member <45years of age. (F-**Fig-1).** The mean age of the patients was 53.81±12.37 years with a range of 24-90 years. The mean age of smokers who presented with STEMI was 2.74 years less than that of non-smokers, and the association between H/O smoking and the mean age of the patients was statistically significant ($p<0.01$). Similarly, the mean age of diabetics who presented with STEMI was 2.09 years less than non-diabetics, and the association between H/O diabetes mellitus and the mean age of the patients was statistically significant ($p=0.047$). The mean age of hypertensive patients who presented with STEMI was 5.85 years more than that of non-hypertensive patients, and the association between H/O hypertension and the mean age of the patients was statistically significant ($p<0.01$). The mean age of the patients had no statistically significant association with personal H/O IHD ($p=0.134$), H/O of IHD in male family member of age <55years ($p=0.700$), and H/O of IHD in female family member of age <45years ($p=0.265$) **(Table 1).**

A multiple regression was run to predict the age at which STEMI happened from presence / absence of different risk factors (H/O Smoking, H/O Hypertension, H/O Diabetes mellitus, H/O Obesity, Personal H/O IHD, H/O of IHD in male family member <55years, H/O of IHD in female family member <45years). These variables statistically predicted age at STEMI, $F(7,660) = 8.463$, $p<0.000$, $R2 = 0.082$. Among these 7 independent variables, 4 variables (Smoking, Hypertension, Diabetes mellitus, Obesity) added statistically significantly to the prediction, $p< 0.05$. Unstandardized coefficients indicate how much the dependent variable (i.e. age at STEMI) varies with an independent variable when all other independent variables are held constant. Hence, H/O Smoking, H/O Hypertension, H/O Diabetes mellitus, and H/O Obesity independently alter the age of the patient at which STEMI may occur **(Table 2).**

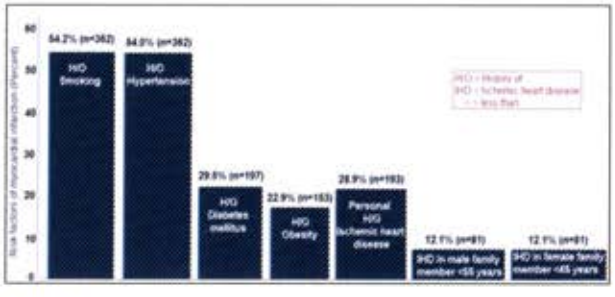

Fig-1: Percentage distribution of various risk factors among patients admitted with myocardia infraction.

Discussion

There are various modifiable and non-modifiable risk factors associates with myocardial infarction. It is also

Table-1: Comparison of factors with mean age of the patients admitted with myocardial infarction at GME, Gujranwala (n=668)*

Risk Factors of MI		Mean age (years)	Standard deviation	Mean differnce	P-value
H/O Smoking	Yes	52.56	11.87	-2.74	<0.01
	No	55.30	12.78		
H/O Hypertension	Yes	56.50	11.57	5.85	<0.01
	No	50.65	12.55		
H/O Diabetes Mellitus	Yes	52.34	11.51	-2.09	0.047
	No	54.43	12.67		
H/O Obesity	Yes	52.83	11.90	-1.27	0.264
	No	54.10	12.50		
Personal H/O IHD	Yes	54.94	12.11	1.59	0.134
	No	53.35	12.45		
H/O of IHD in male family member <55 years	Yes	54.31	9.90	0.57	0.700
	No	53.74	12.67		
H/O of IHD in female family member <45 years	Yes	55.25	8.08	1.64	0.265
	No	53.61	12.84		

Independent simple T-test was used

Table-2: Prediction of age at which myocardial infarction can occur by different risk factors: A multiple regression analysis (n=668)

Risk Factors	B coefficient	Standard error	t	p-value	95% C.I for B	
					Lower	Upper
H/O Smoking (Yes/No)	2.466	0.967	2.550	0.011	0.567	4.364
H/O Hypertension (Yes/No)	-5.878	0.959	-6.131	0.000	-7.760	-3.995
H/O Diabetes Mellitus (Yes/No)	2.963	1.043	2.842	0.005	0.916	5.010
H/O Obesity (Yas/ No)	2.392	1.131	2.114	0.035	0.170	4.614
Personal H/O HDX (Yas/ No)	-0.888	1.074	-0.828	0.408	-2.996	1.220
H/O of IHD in male family member <55 years (Yes/No)	1.048	2.560	0.409	0.682	-3.978	6.074
H/O of IHD in female family member <45 years (Yes/ No)	1.746	2.610	0.669	0.504	-6.871	3.379
Constant	52.339	4.710	11.113	0.000	43.091	61.586

known that addition of a risk factor results acute MI in younger age,[2,3] hence modifiable factors must be addressed to avoid earlier disease. In majority studies, the mean age of the acute MI was in 5th decades. In a study of 213 patients suffering acute MI by F kiani et al, the mean age was 58.3±12.6 years.[11] In a 331 patient's study from Multan, Pakistan, the mean age of acute MI patients was 54.99±11.25 years.[12] Similary, the mean age of the patients in our study was in same decade i.e. it was 53.81±12.37 years. In a study from Karachi, Arsalan Majeed Adam and colleagues found dyslipidaemia (91.2%) as the most frequent risk factor, followed by hypertension, diabetes, family history of disease, where smoking (29.2%) was the least common factor.[13] In our study from Gujranwala, Smoking (54.2%) was the most common risk factor of acute MI. Another mith that Obesity is prevalent at peak in Gujranwala people may not be true. In our data from this city about risk factors, prevalence of Obesity (22.9%) in acute MI patients comes at 4th number, after smoking, HTN, and DM. The findings of Abdul Ghaffar Memon form Hyderabad were in concordrant to our study, who noted Smoking (65.9%) being most frequent risk factor followed by hypertension (42.0%) and diabetes mellitus (34.1%).[14] Bahaaedin A. Elkhader found that Smokers have 3.71 times higher risk of myocardial infarction than non-smokers.[15] Emily M. Bucholz non-smokers, current smokers affected by acute MI were younger (mean age 77.20±7.40 vs 72.41±5.82 years) and the findings were significant (p<0.001).[16] Similarly, in our study, smokers were younger than non-smokers suffering acute MI (p<0.001). Diabetes mellitus is a well-established risk factor that increases the risk of coronary heart disease by two to four times.[17] This is because DM facilitates formation of atherosclerotic plaque and increases the rate of athersclerotic progression.[18] In a 216 patients study, for diabetic vs nondiabetic patients with AMI, there was no significant difference in age (64.0±13 vs 60.0±14 years, p = 0.13).[19] In contrast, in our study, diabetics suffering acute MI were 2.09 years younger than non-diabetics and relation of diabetes mellitus with younger age was significant (p=0.047). In old age, hypertension is even worse to heart and responsible for at least 70% of cardiac disease.[20] **In our study, hypertension** was seen in relatively older

group of patients suffering acute MI ($p<0.001$). Obese patients suffer coronary artery disease at a younger age.[21] On average, obese patients were 1.27 years younger than non-obese patients in our study. In a study from North Punjab, Pakistan, Riffat Iqbal et al noted that patients with a positive parental history of CHD experienced MI at a younger age ($P = 0.0001$).[22] In our study, presence or absence of personal history of IHD or history of IHD in male or female family member had no difference in the mean age of patients at time of acute MI. Similarly, in multiple reression analysis of our data, no such statistically significant correlation of age with these risk factors was seen.

Conclusion

Smoking was the most prevalent risk factor for myocardial infarction in our studied population. Smokers and diabetic patients who suffered STEMI were younger than non-smokers and non-diabetic patients respectively. Among STEMI patients, hypertension was seen in relatively older group of patients. Smoking, Hypertension, Diabetes mellitus, Obesity are those four risk factors which significantly predict the age at which STEMI may occur.

Department of Cardiology,
GMC Teaching hospital, Gujranwala
Www.esculapio.pk

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Original Article

Hepatoprotective and Antioxidative Effectso of Allium Sativum Var Chinese Exoticon Acetaminophen Induced Acute Hepatitisiin Male Albino Rats

Sauda Usmani, Aysha Zaheer and Hamid Javaid Qureshi

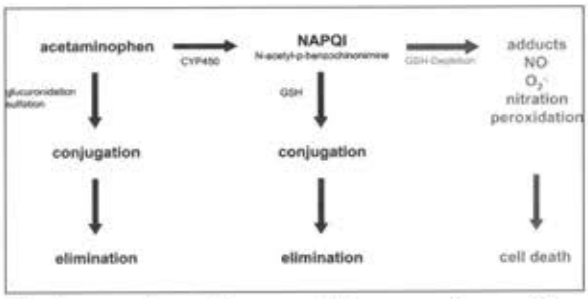
Objective: To determine the hepatoprotective and antioxidative effects of ethanolicextract of Allium sativumvar Chinese exotic on acetaminophen induced hepatotoxicity in male albino rats.
Methods: This study was carried out on 90 male albino rats. A single intraperitoneal dose of acetaminophen 750mg/kg was used to induce oxidative stress and hepatotoxicity. The rats were randomly divided into three groups of thirty each. Group A was given normal saline (negative control); group B was administered hepatotoxic dose of acetaminophen(positive control); group C (experimental) was pretreated with Allium sativum Var Chinese exotic extract for 7 days before receiving hepatotoxic dose of acetaminophen (Experimental). Serum ALT, AST, ALP, total proteins, albumin and glutathione peroxidase levels in each group were estimated from terminal blood sampling done 24 hours after acetaminophen administration under ether anesthesia.
Results: Allium sativumvarChinese exotic manifested hepatoprotective and antioxidative effects by producing highly significant (p=0.000) reduction in serum ALT and AST, but no significant (p=0.335) reduction in serum ALP levels. This garlic extract also produced highly significant (p=0.000) increase in serum albumin and significant increase in serum total proteins (p=0.027) and glutathione peroxidase (p=0.025) levels.
Conclusions: Allium sativumvar Chinese exotic has potent hepatoprotective and antioxidative potential.
Keywords: allium sativum, chinese exotic, glutathione peroxidase, antioxidative, hepatoprotective, acetaminophen.

Introduction

Acute hepatitis results in massive necrosis of liver cells leading to severe impairment of liver functions.[1] An estimated 1600 cases of acute hepatic failure occur each year in United States. Acetaminophen toxicity is the most common cause, accounting for at least 45% of the cases.[2]

Acetaminophen (AAP), which is also named paracetamol, is a commonly used antipyretic and analgesic. Overdose of acetaminophen can lead to acute liver injury and histopathological changes characterized by centrilobular necrosis.[3] Chronic alcohol use may greatly increase susceptibility to hepatotoxicity from acetaminophen because of depleted glutathione stores.[4]

Treatment of healthy adults with acetaminophen taken at the maximum daily recommended dose of 4g for 4 or more days frequently cause elevations in serum aminotransferases which often persist when acetaminophen concentrations are no longer measurable in plasma.[5] In some patients, chronic ingestion of therapeutic doses may produce hepatic necrosis and hepatitis, which persist long after the drug has been discontinued.[6] In most cases, there is no effective treatment other than stopping the dug and providing general supportive care. N-acetylcystine (NAC) has been used, as an antidote for acetaminophen toxicity.[7] The oxidative metabolite of acetaminophen is more toxic than the drug. Hepatotoxic doses of paracetamol deplete the normal levels of hepatic glutathione. The hepatic cytochrome P450 enzyme system metabolizes paracetamol, forming NAPQI (*N*-acetyl-*p*-benzo-quinone imine). NAPQI is then irreversibly conjugated with the sulfhydryl groups of glutathione. Conjugation depletes glutathione, a natural antioxidant. The highly reactive active metabolite NAPQI appears to mediate much of the acetaminophen-related damage to liver tissue by forming covalent bonds with cellular proteins and subsequent activation of inflammatory mediator TNF-α that in turn contribute to tissue necrosis.[8] **(Fig-1)** Allium sativum, or "garlic" is widely used in culinary preparations.[9] Two varieties of Allium sativum grown in Punjab are Chinese (exotic), LehsonGulabi (local).[10] Traditional uses of Allium sativum include; use in intestinal disorders, diarrhea, flatulence, worms, respiratory infections, skin diseases, wounds, symptoms of aging, headache, flu, sore throat, fever and otitis media.[9]



Garlic contains sulfur-containing constituents like γ-glutamyl-S-alkyl-l-cysteine and S-alkyl-l-cysteine, sulfoxides, allicin, steroidal glycosides, lectins, prostaglandins, fructan, pectin, essential oil, adenosine, vitamins B_1, B_2, B_6, C and E, biotin, nicotinic acid, fatty acids, glycolipids, phospholipids, anthocyanins, flavonoids, phenolics and essential amino acids.Allicin and other thiosulfinates instantly decompose to other compounds, such as diallyl sulfide (DAS), diallyl disulfide (DADS) and diallyltrisulfide (DAT), dithiins and ajoene. At the same time, γ-glutamylcysteines are converted to S-allylcysteine (SAC).[9,10] These sulphur compounds of garlic have proved to be promising antioxidants against drug induced hepatitis.[11-13] The liver is a vital organ. Search for new drugs for limiting hepatic injury has been of interest. The present study was aimed to explore new drug for curing acute hepatitis and delaying its progression to hepatocellular carcinoma by evaluating antioxidant and hepatoprotective properties of Allium sativum. Garlic is a natural component of diet in Pakistan and the Chinese exotic variety is commonly available in market. The objective of this study was to determine the hepatoprotective and antioxidative effects of ethanolic extract of Allium sativumvarChinese exotic on acetaminophen induced hepatotoxicity in albino rats.

Methods

Ninety Ninety male albino rats weighing 200-250 grams from were obtained from National Institute of Health (NIH), Islamabad. Animals were housed in groups of 30 per cage for at least one week before the start of experiments. Housing conditions were thermostatically maintained at 26±2 °C and a light/dark cycle (lights on: 0900-2100).[14]The animals were fed with commercially available standard pellet diet ad libitum and were provided with tap water in clean bottles. Allium sativumVarChinese exotic was obtained from local market of Lahore. Ethanolic extract of Allium sativumVarChinese exotic was made and standardized using facilities available at Applied Chemistry Research Centre, PCSIR labs, Lahore. The extract obtained, was filtered and the solvent (ethanol) evaporated in vacuum with a rotary evaporator. After evaporation a dark brown concentrate was obtained. This concentrate was kept at 4 °C prior to use. The crude extract was then dissolved in normal saline and then diluted to the desired concentration.[15]

A single intraperitoneal dose of acetaminophen 750 mg/kg[16] dissolved in normal saline was used to induce acute oxidative hepatic injury. Ninety male albino rats were divided into:Group A (Negative Control, n=30): was given normal saline 10ml/kg body weight intraperitoneally for 7 days. Group B (Positive Control, n=30): was given a single dose of acetaminophen 750 mg/kg[16] dissolved in normal saline intraperitoneally.

Group C (Experimental, n=30): was pretreated with Allium sativumVar Chinese exoticethanolic extract in a dose of 500mg/kg body weight intraperitoneally[17] daily for 7 days before a single intraperitoneal dose of acetaminophen 750 mg/kg[16] dissolved in normal saline. After 24 hours of acetaminophen administration, each rat was anesthetized using ether. Three-milliliter blood was drawn by cardiac puncture and was kept in the test tube for about 15-20 minutes, and allowed to clot. After 15-20 minutes, samples were centrifuged at 5000 rpm for 15 minutes. The serum, thus obtained, was preserved in labeled polypropylene storage tubes. Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total protein and albumin were determined on the same day of blood sampling. About 0.5mL of each of these samples were stored at -20 °C for determination of serum glutathione peroxidase at later stage. Data was analyzed using PASW18 (formerly SPSS). The arithmetic mean and standard deviation for quantitative variables were calculated. The statistical significance of difference amongst the three groups were determined by applying one way ANOVA followed by post hoc LSD (multiple comparison) test. The values were considered significant if the p value was less than 0.05; and, highly significant if the p value was less than 0.001.

Results

After pretreatment with ethanolic extract of Allium sativumvarChinese exotic followed by acetaminophen hepatotoxicity, there was highly significant (*p<.000) decrease in liver enzymes including serum ALT, AST and ALP in experimental

group as compared to both negative and positive control groups **(Table-1).**

The positive control group (group B) having acetaminophen toxicity showed highly significantly (p=0.000) raised values of serum ALT, AST and ALP as compared to the negative control group (group A) as depicted in **(Table-2).**

After pretreatment with ethanolic extract of *Allium sativum*VarChinese exotic followed by acetaminophen toxicity, the experimental group C showed highly significant (p=0.000) decrease in serum levels of ALT and AST but no significant (p=0.335) decrease in serum level of ALP as compared to the positive control group (group B) as depicted in **(Table-3).**

Table-1: Comparison of serum ALT, AST and ALP in groups A, B and C. (One way ANOVA)

Parameters	Group A (N=30)	Group B (N=30)	Group C (N=30)	P-value
Serum ALT (U/l)	53.53±4.46	177.50±6.53	82.83±6.36	0.000*
Serum AST (U/l)	65.80±3.46	102.43±7.19	83.03±5.87	0.000*
Serum ALP (U/l)	124.30±5.81	575.90±4.69	574±2.80	0.000*

*Values are presented as mean± SD *p<.000 highly significant*

Table-2: Comparison of serum ALT, AST and ALP in groups A and B. (Post hoc LSD)

Parameters	Group A (N=30)	Group B (N=30)	P-value
Serum ALT (U/l)	53.53±4.46	177.50±6.53	0.000*
Serum AST (U/l)	65.80±3.46	102.43±7.19	0.000*
Serum ALP (U/l)	124.30±5.81	575.90±4.69	0.000*

*Values are presented as mean± SD *p<.000-highly significant*

Table-3: Comparison of serum ALT, AST and ALP in groups B and C. (Post hoc LSD

Parameters	Group B (N=30)	Group C (N=30)	P-value
Serum ALT (U/l)	177.50±6.53	87.73±3.68	0.000*
Serum AST (U/l)	102.43±7.19	61.70±4.46	0.000*
Serum ALP (U/l)	575.90±4.69	572.47±3.54	0.335**

*Values are presented as mean± SD *p<.000-highly significant **p>.05-not significant*

After pretreatment with ethanolic extract of Allium sativum followed by acetaminophen hepatotoxicity, there was highly significantly (*p<.000) less decrease in serum total protein, albumin and glutathione peroxidase in experimental group as compared to both negative and positive control groups. **(Table-4)** The positive control group (group B) having acetaminophen toxicity showed highly significant (p=0.000) decrease in serum total protein, albumin and glutathione peroxidase as compared to the values in negative control group (group A) asshown in **(Table-5).** After pretreatment with ethanolic extract of Allium sativumVarChinese exotic followed by acetaminophen toxicity, the experimental group C showed highly significant (p=0.000) increase in serum levels of albumin, but only significant increase in total proteins (p=0.027) and glutathione peroxidase (p=0.025) as compared to those in the positive control group (group B) as shown in **(Table-6).**

Table-4: Comparison of serum total protein, albumin and glutathione peroxidase in groups A, B and C. (one way ANOVA).

Parameters	Group A (N=30)	Group B (N=30)	Group C (N=30)	P-value
Serum Total proteins (g/dl)	6.78±0.21	4.20±0.12	4.32±0.17	0.000*
Serum albumin (g/dl)	3.45±0.13	1.40±0.16	3.05±0.25	0.000*
Glutathione peroxidase (g/dl)	21.49±0.79	4.62±0.60	5.27±0.71	0.000*

*Values are presented as mean± SD *p<.000 highly significant*

Table-5: Comparison of serum total proteins, albumin and glutathione peroxidase in groups A and B. (Post hoc LSD)

Parameters	Group A (N=30)	Group B (N=30)	P-value
Serum Total proteins (g/dl)	6.78±0.21	4.20±0.12	0.000*
Serum albumin (g/dl)	3.45±0.13	1.40±0.16	0.000*
Glutathione peroxidase (g/dl)	21.49±0.79	4.62±0.60	0.000*

*Values are presented as mean± SD *p<.000-highly significant*

Table-6: Comparison of serum total protein, albumin and glutathione peroxidase in groups B, and C. (one way ANOVA).

Parameters	Group B (N=30)	Group C (N=30)	P-value
Serum Total proteins (g/dl)	4.20±0.12	4.32±0.17	0.027***
Serum albumin (g/dl)	1.40±0.16	3.05±0.25	0.000*
Glutathione peroxidase (g/dl)	4.62±0.60	5.27±0.71	0.025***

*Values are presented as mean± SD *p<.000-highly significant ***p<.05-significant*

Discussion

Our study evaluated the effects of ethanolic extract of Allium sativumVarChinese exotic on experimentally induced acetaminophen hepatotoxicity and noted effects on liver enzymes (ALT, AST and ALP), serum albumin, total proteins and serum glutathione peroxidase in male albino rats. This study showed that pretreatment of rats with ethanolic extract of this variety of garlic grown in Pakistan prevented the increase in liver enzymes and decrease in serum albumin, total proteins and glutathione peroxidase, due to acetaminophen toxicity. This adds to several reports on the pharmacological usefulness of garlic extracts as liver protective agents. Lee et al (June 2016) investigated the protective effect of fermented garlic extract by lactic acid bacteria (LAFGE) against acetaminophen

induced acute liver injury in rats. Their findings indicated lowered plasma ALT levels,inhibition of lipid peroxidation, glutathione and ATP depletion, and the elevation of antioxidant enzyme activities. These findings indicate that LAFGE ameliorated AAP-induced liver injury by preventing oxidative stress-mediated apoptosis, thereby establishing LAFGE as a potential supplement in the treatment of AAP-induced liver injury.[18] Allyl methyl disulfide (AMDS) has been identified as one of the bioactive components in fresh garlic paste and alleviates AAP-induced elevation of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) levels, significantly ($p < 0.05$) reduces the maleic dialdehyde (MDA) level in liver tissues and restores the activities of antioxidant enzymes superoxide dismutase (SOD), glutathione peroxidase and glutathione towards normal levels.[19]

Ozougwu et al (2014) investigated hepatoprotective effects of Allium sativummethanolic extracts on paracetamol induced hepatotoxic rats. Allium sativumreduced ALT and total serum bilirubin in a dose dependent fashion whereas it reduced AST, ALP and LDH level in a dose independent manner. Acetaminophen hepatotoxicity leads to leakage of cellular enzymes into the plasma such as ALT, AST, ALP and LDH showing increased permeability and necrosis of hepatocytes. These significantly increased levels of serum AST and ALT are due to hepatocellular damage because these enzymes are normally located in the cytoplasm and released into the circulation after cellular damage. The mechanism of action of garlic could be through preventing the intracellular enzyme release and by membrane stabilizing effects. This is because garlic is rich in antioxidants. The reduction in ALP and LDH levels by extracts may suggest repairing of rat liver by Allium sativumextracts. Thus it was suggested that the active ingredients in Allium sativum(allyl propyl disulfide) increased the levels of glutathione to bind with the toxic metabolites of paracetamol such as N- acetyl- p- benzoquinone imine (NAPQI) and increased its rate of excretion from the body. It might also have inhibited the levels of the cytochrome P- 450 enzyme system that decreased the formation of NAPQI from ingested paracetamol. These possible mechanisms of action of Allium sativumextracts may be through their antioxidative effects that are capable of free radical scavenging in living system.[20] Another study done in 2017 determined the antioxidative effects of Allium sativummethanolic extract against paracetamol induced liver toxicity. It was evident that garlic extract was able to significantly raise the intracellular contents of glutathione peroxidase.[21]

Rashed et al (2014) investigated the effect of garlic oil (GO) alone or in combination with low dose total body gamma ((γ)-irradiation (LDR) against paracetamol (AAP)- induced hepatotoxicity in rats. Findings showed that the combination of GO and LDR produced considerable comparable effects to either treatment alone in reducing serum elevations of ALT, AST, ALP, LDH, MDH, hepatic CYP2E1 activity and preventing the decreased hepatic glutathione content as a result of AAP toxicity. This ability of garlic to lower the raised levels of ALT, AST and to prevent decrease in levels of glutathione after AAP toxicity was in accordance with results of the present study. This remarkable synergistic protection against AAP-induced hepatotoxicity might be attributed partly to the suppressive effect of both GO constituents and LDR on lipid peroxidation by free radical scavenging properties or by restoration of glutathione content and cytochrome P4502E1 enzyme in the liver.[22]

Shin(2014) investigated the hepatoprotective effects of aged black garlic (ABG) in rodent modules of liver injury. ABG inhibited carbon tetrachloride induced elevations of ALT and AST. D-galactosamine induced hepatocellular damage was also suppressed by ABG treatment. However, ABG did not effect the elevations of ALP, which is also in accordance to with the results of present study.[23] Sharma et al (2010)studied amelioration of lead-induced hepatotoxicity by Allium sativum extracts in Swiss albino mice. Oral treatment with lead nitrate induced a significant increase in the levels of hepatic AST, ALT, and ALP. Hepatic protein levels in lead-exposed mice were significantly depleted. Aqueous garlic extract and ethanolic garlic extract restored the deranged parameters significantly.[24]This result was in accordance with our study regarding serum parameters of ALT, AST and total proteins.

Modulatory effects of dietary inclusion of garlic (Allium sativum) on gentamycin-induced hepatotoxicity and oxidative stress in rats were studied by Ademiluyi et al (2013). Hepatic damage, as revealed by significant elevation of liver damage marker enzymes (AST and ALT) and reduction in plasma albumin level, were restored following consumption of diet containing garlic. Elevations of serum levels of ALT indicated necrotic lesions in the liver cells while decreased serum albumin indicated that there was an impairment in both synthetic and

excretory activities of liver.[25] These results were in accordance with our results as ethanolic extract of garlic Chinese exotic variety prevented the decrease in plasma albumin while restoring liver damage marker enzymes to nearly normal values.

Conclusion

Thus garlic may be considered as a useful dietary supplementary compound to patients treated with regular high doses of paracetamol such as of tuberculosis, cancer, dengue fever and arthritis. The antioxidative and hepatoprotective potential of Allium sativum should be further investigated in in human studies. The medical implication of this finding could be that consumption of this variety of garlic might be a useful prophylactic and therapeutic strategy against oxidative stress of toxic hepatitis in Pakistan.

Department of Physiology
Akhtar Saeed Medical College, Lahore
www.esculapio.pk

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Original Article

Risk Factors and Outcome in Patients with Ruptured Uterus in Sahiwal Teaching Hospital, Sahiwal

Hina Ilyas and Safia Parveen

Objective: To determine the risk factors and feto-maternal outcomes among patients with ruptured uterus.

Methods: The study design opted for the present research was observational retrospective, where the mothers who delivered in the hospital were assessed for various demographic characteristics, indications and high risk factors. Maternal and fetal outcome were noted. The records were retrieved from June 2015 to Dec 2017 by using hospital records system. The exclusion criteria include all women with renal failure, past surgical history of heart disease. Women who deliver at hospital at or after 25 weeks of gestational age and experienced uterine rupture or went for hysterectomy at the time of delivery or afterward within the defined period of puerperium were included in the study.

Results: The data of 78 mothers were retrieved from the hospital record system. The mean age of the women was 39.85+4.99 with range 20-46. 54 (69.23%) of the mothers were in the age category of 20 to 30, 23 (29.48%) were 31-40 years of age and 1 (1.29%) was of above 40 years of age. The average gestational age was 35.42 weeks.70 (89.74%) of the deliveries were spontaneous and complete. The major causes of uterine rupture were, 57(73.07%) previous scar, 4(5.12%) Previous scar + Feto-pelvic disproportion, 3 (3.84%) with Previous scar + mal-presentation, 7(8.9%) Previous scar + oxytocic and 2 (2.56.28%) Mal-presentation.The average number of blood transfusion was 3.79.

Conclusions: We may conclude that feto-maternal outcomes like vaginal bleeding, palpable parts, and perinatal mortality were obvious among women with uterine rupture. Other probable risk factor may include previous scar history, multiparity, mal-presentation, feto-pelvic disproportion and hysterectomy.

Keywords: uterine rupture, emergency peripartum hysterectomy, maternal morbidity and mortality, multiparity.

Introduction

The split up of entire depth of uterine wall with extrusion of fetal parts and intra-amniotic substances into the peritoneal cavity named as uterine rupture.[1] This is not a common problem in pregnancy and is linked with potentially adverse outcomes for both mother and baby.[2] The uterine rupture incidence is controlled and less in developed than developingcountries. It is reported to be 1 in 8000-15000 deliveries.[3] From 1976-2012, literature reported the incidence of uterine rupture in 2,084 cases out of 2,951,297 pregnancies, yielding an overall uterine rupture rate of 1 in 1,146 pregnancies (0.07%). Spontaneous rupture of uterus in developed countries, the rate was 1 per 8,434 pregnancies (0.012%).[4]

The probable risk factors for uterine rupture may include, cesarean secession, hysterotomy, myomectomy, placenta percreta, mullerian anomalies of uterus, previous difficult uterine curettage convoluted by perforation.[5-9] The most common is the scarred uterus, multiparity and obstructed labor.[10] The fetal outcomes in uterine rupture may include the elongated affirmation of delivery.[11] In maternal outcomes may rarely include a maternal death due to uterine rupture, but constitute significant maternal morbidity that contained shock, renal failure, massive blood transfusion and hysterectomy.[12] Whereas in developing countries the uterine rupture is highly linked with maternal and fetal mortality and morbidity.[13] The main aim of the study was to determine the risk factors and feto-maternal outcomes among patients with ruptured uterus.

Methods

The study design opted for the present research was observational retrospective, where the mothers who deliver in the hospital were assessed for various demographic characteristics, indications, high risk factors and maternal and fetal outcome. The records were retrieved from June 2015 to Dec 2017 by using

hospital records system. The study duration was of six months. The venue of the study was DHQ Teaching hospital, Sahiwal. The exclusion criteria include all women with renal failure, past surgical history of heart disease whereas all the women who deliver at hospital with or after 25 weeks of gestational age and experienced uterine rupture or went for hysterectomy at the time of delivery or afterward within the defined period of puerperium were included in the study. The retrieved information contains demographics along with diagnostic history of all the mothers. All the required diagnostic values were collected from their results of blood samples which were produced by following their standard operating procedures in hospital laboratory. Ethical consideration was taken in to account by taking approval from hospital ethical committee and informed consent from patients. Statistical analysis: All the collected data was stored electronically & analyzed later by using SPSS version 20. Descriptive statistics were applied to calculate mean and standard deviation. Frequency distribution and percentages were calculated for qualitative variables like anemia and abdominal tendernessetc. Over all P-value≤0.05 was considered statistically significant.

Results

The data over 78mothers were retrieved from the hospital record system. The mean age of the women was 39.85+4.99 with range 20-46. 54 (69.23%) of the mothers were in the age category of 20 to 30, 23 (29.48%) were 31-40 years of age and 1 (1.29%) was of above 40 years of age. The average gestational age was 35.42 weeks.70 (89.74%) of the deliveries were spontaneous and complete. More of the mother's characteristics were given in **(Table-1.**

Table-1: The baseline characteristics of mothers..

Characteristic	Percentage
n	78%
Severe anemia	35 (44.87%)
Abdominal tenderness	76 (97.43%)
Vaginal bleeding	47 (60.25%)
Shock	14 (17.08%)
Uterus Conserved Repair	
With sterilization	23 (29.48%)
Without sterilization	42 (53.84%)
Hysterectomy	
Totla hysterectomy	4 (33.3%)
Subtotal hysterectomy	8 (66.76%)

The major causes of uterine rupture were, 61 (83.6%) previous scar, 4(5.5%) Fetopelvic disproportion, 5 (6.8%) with mal-presentation and 8 (10.9%) oxytocic **(Table-2).**

Table-2: Major causes of uterine rupture.

Major causes of uterine rupture	N(Percentage)
Previous scar	61 (83.6%)
Feto-pelvic disproportion	4 (5.5%)
Mal-presentation	5 (6.8%)
Oxytocic	8 (10.9%)

The average number of blood transfusion was 3.79±0.15 pints. The maternal morbidity include Bladder rupture was 4(66.67%), 1(16.67%) pack removed and 1(16.67%) mother expired during **(Fig-1).** More on the perinatal mortality is given in **(Fig-2).**

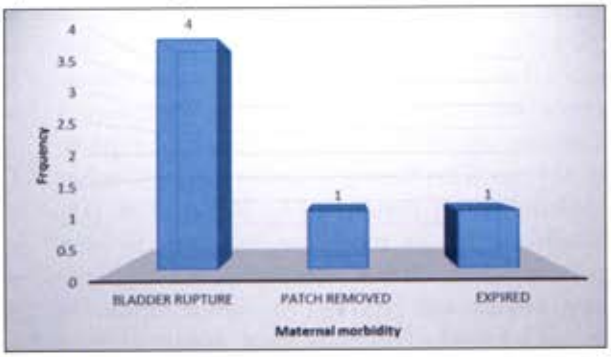

Fig-1: Maternal outcome.

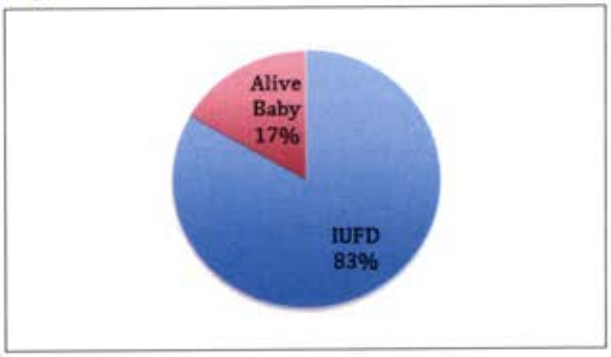

Fig-2: Fetal outcome.

Discussion

The study was planned to determine the risk factors and feto-maternal outcomes among patients with ruptured uterus. We not only report various risk factors but also the unfavorable outcomes in this study. Abdominal tenderness, vaginal bleeding, anemia, previous scar, mal presentation and fetopelvic disproportion were few prominent reason of maternal orbidity and mortality in women with uterus rupture. It is said to be a rare problem with appalling consequence for fetus as well as for mothers also. Uterine rupture is a Serious obstacle that is

linked with raised perinatal morbidity and mortality. The common cause may be obstructed labor with presentation of classing sign and symptoms. We observed in our findings the commonest cause for uterine rupture was previous scar and malpresentation along with feropelvic disproportions and indirectly leads to the fetometarnal morbidity and mortality. The incidence of the uterine rupture is high in our population. This finding is supported by other similar studies.[14-16]

Other developing countries like India, Nigeria and KSA were also reported with incidence up to 0.83%.[17,18] The developed countries like Ireland shows very less cases with uterine rupture during the gestational time.[18,19] The associated risk factors in developing and developed countries may include a previous history of uterine surgery. We also observed in our study with the previous scar history the morbidity increased. In our study we reported the average age of the women with uterine rupture was 31 years. This finding is almost similar to other population study conducted by Rouzi et al. [15] Though the age of mother is less likely to be a potential risk factor but multiparity with a scarred uterus proven with high risk of uterine rupture in our study. Similar findings were observed in a studies conducted in KSA.[17,20-21]

We observed in our findings that most of the cases were unbooked, Ekpo et al confirmed this finding but this is contrary to the findings of Jahan et al. [17,19] To the modern era of obstetrics, the vital risk factor classified as previous scar on uterus. This also confirmed by our study findings and similar findings of other studies.[22-23] We reported in our findings that the clinical presentation of the patients includes abdominal pain, abdominal tenderness, abnormalities and fetal deaths. Similarly the symptoms like vaginal bleeding and arrest of uterine contraction were also reported in our study. We reported in our study that major indication of Hysterectomy were due to the abnormal placentation and uterine atony and uterus injury or rupture. We also observed in our findings the cases with adherent placentation; the percentages were supported by other published studies.[24-25] Due to previous history of CS, adherent placentation become among one of the commonest indication. The study held by Kwee et al., testified that both previous CS and cesarean section in key pregnancy were associated with significant increased risk of Hysterectomy after uterine rupture.[26]

Conclusion

We may conclude that feto-maternal outcomes like vaginal bleeding, palpable fetal parts, and perinatal mortality were obvious among women with uterine rupture. Other probable risk factor may include previous scar history, multiparity, mal-presentation, feto-pelvic disproportion and hysterectomy.

Department of Obst. Gynae
Teaching Hospital, Sahiwal,
www.esculapio.pk

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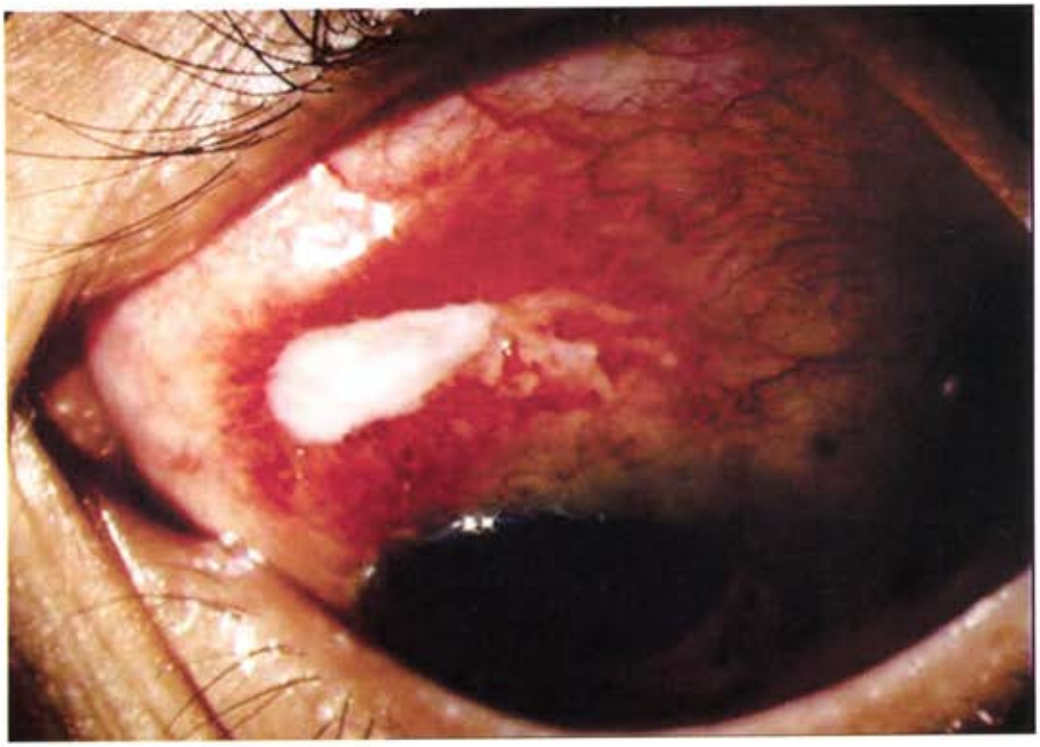
Picture Quiz

WHAT IS DIAGNOSIS

Questions

1 What abnormalities are seen in the photograph?
2 What is the most likely underlying diagnosis given his extraocular?



Original Article

Comparative Study Between two Techniques of Radiocephalic Fistula for Patients on Hemodialysis

Khalid Hussain, Rao Nouman Ali, Zahid Rafique, Maria Tariq, Attiq-ur-rehman and Muhammad Khalid butt

Objective: To compare the patency rate and complications of two different surgical techniques of radiocephalic arteriovenous fistula side to side anastomosis with distal vein ligation and without distal vein ligation in patients who are on hemodialysis (HD) due to end stage renal failure.

Methods: This prospective study was carried out on total 468 patients over the duration of two years. The fistulae were created between radial artery and cephalic vein, side to side anastomosis. In one group distal vein was ligated to compare with the other one without distal vein ligation. Patients were followed up to first dialysis by AVF to assess the overall outcomes and various complications. Data of Follow up was collected for 6 months from patient's dialysis staff.

Results: 468 patients were included in study. Patients were divided in two groups i.e. Group-X (without distal vein run off) and Group-Y (with distal vein run off). In group-X, patency rate was 171(73.1%), while 207(88.5%) patients in group-Y with a statistically significant p-value of 0.0001.

Conclusions: This study explained that there was a significant difference of patency rate and complications between the radiocephalic fistula with and without distal vein ligation. Hence we will prefer distal vein run off in our setup in future.

Keywords: radiocephalic, arteriovenous fistula, hemodialysis (HD), end stage renal disease (ESRD), chronic kidney disease (CKD).

Introduction

End stage renal failure or Chronic kidney disease is a serious illness because of damage to both kidneys. According to recent studies incidence of chronic kidney disease has increased from previous decades.[1] Arteriovenous fistula has been the vascular access of choice for hemodialysis due to less incidence of morbidity, mortality and lower cost.[2] Arteriovenous fistulas, arteriovenous fistula with graft material interposed in-between, and tunneled permacaths are three different ways of vascular access in hemodialysis. Among these, the arteriovenous fistula is best option for long-term hemodialysis because it has better primary patency rate, and requires the fewest manipulation for any access, and incidence of morbidity and mortality is less in this.[3-7] Benefits of arteriovenous fistulas over other types of vascular access are: Arteriovenous fistulas are related with less morbidity and mortality in patients on hemodialysis compared with central venous catheters and arteriovenous grafts.[8-10] Arteriovenous fistulas have the best primary patency rates, the less chances of thrombosis, and require the less secondary manipulations.[6,11-13] Arteriovenous fistulas generally provide longer hemodialysis access survival rates.[13-16] The total number of manipulations during the life of the access is considerably lower for arteriovenous fistulas compared with arteriovenous grafts.[6,11,15]

Methods

This prospective study was carried out on total 468 patients over the duration of two years. Fistulae were created using radial artery and cephalic vein side to side anastmosis between with and without distal vein ligation. Doppler ultrasounds were done before and after every operation to determine the velocity, volume of blood flow, depth from the skin, diameter of vessels and to access the time of maturation of AVF.

Patients were followed up to first dialysis by AVF to assess the overall outcomes and various complications. The inclusion criteria was; patients of both gender ages between 25-70 years with end stage renal disease on maintenance hemodialysis and patients with end stage renal disease that will require renal transplant surgery, now on HD. The exclusion criteria was previously operated AVF, previously operated complicated AVF and previously operated Failed AVF. Follow up information was obtained for 6 months from patients dialysis technician.

Results

During 24 months from December 2016, to Dec, 2018 total 468 patients were part of study. Patients were divided in two groups i.e. Group-X (without

distal vein run off) and Group-Y (with distal vein run off).

In group-X, there were 135(57.7%) were males and 99(42.3%) were females. In group-Y, 120(51.3%) were males and 114(48.7%) were females.

The mean age of patients in group-X was 47.3±13.6 years and in group-Y was 46.1±13.2 years. In group-X, there were 57(24.4%) in 25-35 years age group, while 69(29.5%) and 108(46.2%) were in 36-50 years and >50 years age groups respectively. In group-Y, there were 63(26.9%) in 25-35 years age group, while 84(35.9%) and 87(37.2%) were in 36-50 years and >50 years age groups respectively. In group-X, there were 54(23.1%) who were hypertensive, while 45(19.2%) patients in group-Y. In group-X, there were 75(32.1%) who had diabetes mellitus, while 57(24.4%) patients in group-Y. In group-X, there were 27(11.5%) who had post-operative infection, while 9(3.8%) patients in group-Y. In group-X, there were 12(5.1%) who had numbness at thumb, while 3(1.3%) patients in group-Y. In group-X, there were 6(2.6%) who had aneurysm, while 0(0.0%) patients in group-Y. In group-X, there were 12(5.1%) who had edema, while 3(1.3%) patients in group-Y. In group-X, patency rate was 171(73.1%), while 208(88.5%) patients in group-Y with a p-value of 0.0001, which is statistically significant.

Table-1: Comparison of gender distribution between groups.

Gender	Groups: Group-X (Without distal vein run off)	Group-Y (With distal vein run off)	Total
Male	135	120	255
	57.7%	51.3%	54.5%
Female	99	114	213
	42.3%	48.7%	45.5%
Total	234	48.7%	468
	100.0%	100.0%	100.0%

Table-2: Comparison of age groups distribution between groups.

Age Groups	Groups: Group-X (Without distal vein run off)	Group-Y (Withdistal vein run off)	Total
25-35 years	57	63	120
	24.4%	26.9%	25.6%
36-50 years	69	84	153
	29.5%	35.9%	32.7%
> 59 years	108	47	195
	46.2%	37.2%	41.7%
Total	234	234	468
	100.0%	100.0%	100.0%

Table-3: Comparison of diabetes mellitus and hypertension between groups.

Gender	Groups: Group-X (Without distal vein run off)	Group-Y (With distal vein run off)	P-value
Diabetes Mellitus	75	57	0.064
	32.1%	24.4%	
Hypertension	54	45	0.308
	23.1%	48.7%	

Table-4: Comparison of complications between groups.

Compliations	Groups: Group-X (Without distal vein run off)	Group-Y (With distal vein run off)	P-value
Infection	27	9	0.002
	11.5%	3.8%	
Numbness at thumb	12	3	0.018
	5.1%	1.3%	
Aneurysm	6	0	0.014
	2.6%	0.0%	
Edema	12	3	0.018
	5.1%	1.3%	

Table-5: Comparison of patency rate between groups.

Patency	Groups: Group-X (Without distal vein run off)	Group-Y (With distal vein run off)	Total	P-value
Yes	171	207	207	
	73.1%	88.5	80.8%	
No	63	27	90	0.0001
	26.3%	11.5%	19.2%	
Total	234	234%	468	
	100.0%	100.0%	100.0%	

Discussion

Increasing need for vascular access in patients of renal failure lead to importance of fistula surgery. In our study we compared two AVF (with distal vein run off) and (without distal vein run off) in terms of patency rate and complications documented. Generally fistula surgery at wrist encounter complications like carpel tunnel syndrome, venous hypertension, numbness at thumb, aneurysm formation, gangrene of limb and wound infection.[17] In a study, patency rate and complications rate is better in patients who are dealt with distal vein run off.[18] Their results are comparable to our study as patency rate in their study was 93% at the end of 6 months while in our setup it was 88.5% in patients without distal vein run off.[18] In another study, patency is superior in distal vein run off than without distal vein run off.[19] Vascular access related mortality and morbidity is internationally accepted. A large number of randomized control trial results focus the need of fistula creation for hemodialysis patients because of good results, better outcome and less complications.[20] Hammes et al stated that problems occur in nearly one-third of fistulas and include:

Aneurysms, infection, numbness at thumb and thrombosis.[21] Beathard GA et al in his study said that the distal vein run off is associated with less complications than without distal vein run off are seen with other types of vascular access, they do occur and they should be handled effectively.[22]

He stratified major complications that are seen in arteriovenous fistulas in different types e.g early failure, late failure, formation of anerysm and wound infection. Both kind of failures have multiple reasons. Fistula fails within three months of use should be classified as an early failure.[22] The complication that were encountered during this study were oedema of the hand, numbness at hand, infection and aneurysm. Mahakalkar CC et al in his study found that the rate of complications was more at Radiocephalic site. In the series ,complications were seen in 26 (18.57 %) patients out of 140.[23] In present study the overall complications were seen in 24(15.3%) patients out of 156. In Mahakalkar CC et al study mild swelling and redness around the operated site were seen in 16 (65.38%) all at wrist region.[23]

Conclusion

This study demonstrated that there was a significant difference of patency rate and complications between the radio cephate with and without distal vein ligation . Hence we will prefer distal vein ligation in our setup in future.

Department of Urology,
DHQ Hospital, Gujranwala

www.esculapio.pk

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Original Article

Imagnetic Resonance Imaging as Diagnostic Tool for Acute Invasive Fungal Sinusitis

Muhammad Imran, Tuba Tariq, Sadia Haleema, Ameena Nasir, Saadia Sajjad and Qanita Mahmud

Objective: To measure the diagnostic accuracy of magnetic resonance imaging for diagnosis of acute invasive fungal sinusitis taking histopathology as gold standard.

Methods: After obtaining permission from ethical committee of hospital, 150 patients meeting the study criteria were recruited in the study which was conducted in Department of Diagnostic Radiology, Sir Ganga Ram Hospital, Lahore. Informed consent was obtained. Demographic information (name, age, gender, contact) was also obtained. Then patients underwent MRI by using 1.5T magnets by a single senior radiologist. The imaging was performed with specified sinus views and sequences including T1-weighted images in axial plane, T2-weighted images with fat saturation in axial and coronal planes, and also contrast enhanced T1-weighted images with fat saturation in axial and coronal planes. Then patients underwent biopsy by a single surgical team under general anesthesia. Histopathology was then performed on the biopsy samples obtained during sinus surgery. Reports of MRI and histopathology were compared. Out of 150 patients who were clinically suspected of having fungal sinusitis 87 were negative for fungal disease on histopathology.

Results: Sensitivity and Specificity of MRI for diagnosis of fungal sinusitis was 92.06% and 93.1% respectively. However positive predictive and negative predictive value for MRI for diagnosing fungal sinusitis was 90.63% and 94.19% respectively. Overall diagnostic accuracy of MRI was 92.67% respectively.

Conclusions: Results of this study showed high sensitivity and specificity of MRI in making the diagnosis of fungal sinusitis. Considering the results of this study MRI can be used effectively for diagnosing of fungal sinusitis.

Keywords: fungal sinusitis, magnetic resonance imaging, histopathology

Introduction

Fungal sinusitis is increasing worldwide in the past two decades. It is divided into two types including invasive and noninvasive. Noninvasive types contain allergic fungal sinusitis (AFS) and fungus ball. AFS is a hypersensitivity reaction to fungal allergens in the mucosa of the sinonasal tract in atopic individuals. The fungus ball is a different type of noninvasive fungal rhinosinusitis which is delineated as an accumulation of debris and fungal elements inside a paranasal sinus.[1] Sandeep Suresh et al found the prevalence of fungal rhinosinusitis to be 30% with mucor being the most commonly isolated species.[2] According to another study conducted in India the prevalence of fungal rhinosinisuitis came out to be 44%.[3] In Pakistan, fungal sinusitis is present in 13% patients only.[4] It is observed that fungal infections involving the paranasal sinuses are not very common and usually occur in individuals with a compromised immune system. However according to one study, the incidence of fungal sinusitis has been increased in the immunocompetent individuals as well.[5] The commonest species involved are *Aspergillus* and *Mucor species*. Non-invasive as well as invasive forms of infections can be caused by Aspergillus. Mostly fungal infections of the sinuses tend to be noninvasive with the exception of infections occurring in immunocompromised population. But many studies have now shown invasive fungal infections in immunocompetent population as well. While non-invasive infections present with generalized symptoms of sinusitis on the other hand invasive variety tends to cause destruction of surrounding structures including the orbital walls and intracranial extension. Invasive infections produce greasy and dark coloured substance within the paranasal sinuses. Routinely the cultures obtained from the affected sinuses uncommonly show the growth of fungus. The fungal infection however is suspected when the images obtained from the computed tomography (CT) scan are reviewed and when the material removed from the affected sinus is examined.[5] Fungal sinusitis requires early diagnosis and treatment for optimum outcome. Fungal sinusitis is a distinct clinical entity with a highly specific

radiographic appearance based on computed tomography and magnetic resonance imaging (MRI).[6] The diagnosis of fungal sinusitis is based upon radiological, histopathological and laboratory investigations. Fungal sinusitis is defined radiologically on magnetic resonance imaging as the detection of mucosal thickening ranging from mild to complete filling of the sinus with the presence of fungal mass which is of intermediate to low signal on T1 weighted images and T2 weighted images associated with fluid or hemorrhagic material in other paranasal sinuses as well, and enhancement of sinus mucosa with non enhancing center. No mucosal enhancement is seen in case of necrosis. Clinically suspected fungal sinusitis is defined by the presence of any one or more of these: i.e. recurring sinonasal polyposis (polypoidal masses seen to be stuffing the nasal cavity on clinical examination), non resolving chronic sinusitis, immobility of the eyes, and altered status of consciousness.

Magnetic resonance imaging (MRI) findings of fungal sinusitis:

Contrast enhanced MRI is of value in evaluation of patients with allergic fungal sinusitis and in those who are suspected to have invasive fungal sinusitis. It is also valuable in assessing spread of disease to the central nervous system in case of invasive fungal sinusitis. Low signal intensity on MRI would be more in favour of fungal disease rather than a solid mass in case of allergic fungal sinusitis.[9]

Histopathology findings of fungal sinusitis:

Allergic fungal sinusitis shows allergic mucin containing non damaged as well as deteriorated eosinophils, cellular remains, Charcot-Leyden crystals, and little amount of hyphal forms. The fungi do not cause invasion of mucus membrane in allergic fungal disease and sinus mycetoma does not contain allergic mucin. The mucosa of sinus shows infiltration by eosinophils, plasma cells, and lymphocytes and the sinus shows substance that is dense and contains hyphae which are separate from the mucosa being present adjacent to it. In acute invasive fungal sinusitis, histopathology shows invasion of the mucosa by fungal hyphae as well as invasion of submucosa and blood vessels; tissue infarction and hemorrhage; vascular inflammation and thrombosis. Carotid arteries and cavernous sinuses may also be involved. In chronic invasive fungal sinusitis there is necrosis of the mucosa, submucosa, and blood vessels, with mild inflammation. In granulomatous invasive fungal sinusitis there is granuloma formation with multinucleated giant cells associated with erosion of sinus walls and pressure necrosis.[9]

Laboratory findings of fungal sinusitis:

In patients with allergic fungal sinusitis, raised levels of total fungus-specific IgE are frequently observed however it is uncommon in cases of sinus mycetoma.[10]

Rhinologists have not yet reached to any consensus upon the criteria for diagnosis of allergic fungal sinusitis.[11] Loury and Schaefer in 1993, put forward a diagnostic criteria, which included elevated serum eosinophils, raised total immunoglobulin E level, immunoglobulin G serum antibodies to fungal antigen or immediate skin reactivity, edematous nasal mucosa or sinonasal polyposis, characteristic MRI or CT findings and presence of allergic mucin with fungal hyphae not causing invasion histopathologically. Cody et al in 1994, made the diagnostic criteria more simple by including only characteristic allergic mucin and either cultures positive for fungus or non-invasive fungal hyphae in the obtained mucin. In the same year, Bent and Kuhn put forward a now widely accepted criteria for diagnosis. Five common characteristics were seen upon the analysis of fifteen cases. These include sinonasal polyposis, mucin containing eosinophils with no sinus tissue invasion by the fungus, Gell and Coombs type I (IgE-mediated) hypersensitivity to fungi, characteristic CT and MRI findings, and positive fungal stain of surgically removed sinus material. A similar five parameter criteria was described by DeShazo in 1997 consisting of radiological evidence of sinusitis, positive fungal stain or culture from the sinus material obtained during surgery, presence of allergic mucin (found either grossly or on histopathologic examination), no invasion by the fungus, lack of contributory factors (eg, immunodeficiencies and diabetes mellitus). Groppo et al. conducted a study on 23 patients and reported that sensitivity and specificity of MRI for diagnosis of fungal sinusitis were 86% and 75% respectively, taking histopathology as gold standard.[12]

Rationale of our study was to assess the diagnostic accuracy of magnetic resonance imaging for diagnosis of fungal sinusitis taking histopathology as gold standard. Now-a-days MRI is considered to be gold standard for diagnosis / differentiation of different tumors having > 95% accuracy. Literature has shown that for confirmation of fungal sinusitis, MRI is a reliable tool but still biopsy is in practice. This may be due to lack of local evidences which would help to implement the use of MRI. The study which has been mentioned above was conducted with

very low sample size (23 patients). We conducted this study with large sample size (150 patients) to get more reliable results, so that we can implement the use of MRI for diagnosis of fungal sinusitis in future.

Methods

A sample size of 150 cases was selected by non-probability, consecutive sampling technique. Patients of age 15-50 years of either gender, presenting with clinically suspected fungal sinusitis (as per operational definition), with size of mass >10mm planned to undergo biopsy for histopathology. Patients with septal defect (on x-ray) or with history of previous surgery for fungal sinusitis (medical record) were excluded. Patients with hypertension (BP ≥ 140/90 mmHg), asthma or COPD (medical record and clinical examination) were also not included.

True positive: When MRI and histopathology, both are positive for fungal sinusitis

True negative: When MRI and histopathology, both are negative for fungal sinusitis

False positive: When MRI is positive but histopathology is negative for fungal sinusitis

False negative: When MRI is negative but histopathology is positive for fungal sinusitis

After obtaining permission from ethical committee of hospital, 150 patients meeting the criteria of selection were included in the study referred to Department of Diagnostic Radiology, Sir Ganga Ram Hospital, Lahore. Informed consent was obtained. Demographic information (name, age, gender, contact) was also obtained. Then patients underwent MRI by using 1.5T magnets by a single senior radiologist. The imaging was performed with specified views and sequences for the sinuses including T1-weighted images in axial plane, T2-weighted images with fat saturation sequences in coronal and axial planes, and also contrast enhanced T1-weighted images with fat saturation sequences in coronal and axial planes. Then patients underwent biopsy by a single surgical team under general anesthesia. Histopathology was then performed on the biopsy samples obtained during sinus surgery. Reports of MRI and histopathology were compared. Out of 150 patients who were clinically suspected of having fungal sinusitis 87 were negative for fungal disease on histopathology. The obtained information was collected in proforma. Statistical analysis of the data was done with SPSS Version 20.0. Fungal sinusitis (on MRI and histopathology) was presented in terms of frequency and percentage. A 2x2 table was formulated for the calculation of specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of MRI taking histopathology as gold standard. p-value ≤0.05 was considered as statistically significant.

Results

Sensitivity and specificity of MRI for diagnosis of fungal sinusitis was 92.06% and 93.1% respectively. The positive predictive value and negative predictive value of MRI was 90.63% and 94.19% respectively. Overall diagnostic accuracy of MRI for diagnosis of fungal sinusitis was 92.67%. **(Table-1)**

Table-1: The baseline characteristics of mothers..

		Histopathology		
		Positve	Negative	Total
MRI	Positive	TP 58 (92.1%)	FP 6 (6.9%)	64 (42.6%)
	Negative	FN 5 (7.9%)	TN 81 (93.1%)	86 (57.33%)
	Total	63 (42%)	87 (58%)	150

Sensitivity=TP/(TP+FN)=58/(58+5)=58/63=92.06% (82.73 - 96.56).

Specificity=TN/(TN+FP)=81/(81+6)=81/87=93.1% (85.76-96.8).

Positive predictive value=TP/(TP+FP)=58/(58+6)=58/64 =90.63%(81.02-95.63).

Negative predictive value=TN/(TN+FN)=81/(81+5)=81/86=94.19% (87.1 - 97.49).

Diagnostic accuracy=(TP+TN) /(TP+TN+FP+FN) = 139/150 = 92.67% (87.35 - 95.86)

Discussion

Both the radiology and otolaryngology literature has described the radiologic features of invasive fungal sinusitis. Previously researchers focused on destruction of bone, which is depicted with CT. Destruction of bone, however, is a relatively late occurrence in the course fungal sinus disease. The high mortality of 50-80% which occurred previously may be explained to some extent by delay in the diagnosis. But now clinicians have focused more on detecting early minute features of invasive fungal infection and especially the abnormal findings in soft tissues outside the boundaries of the sinuses. There may be underestimation of the extent of invasive fungal disease when diagnosed using CT scanning alone. On this basis some researchers suggest MRI scanning early in the course of disease in patients with suspected acute fulminant invasive fungal *sinusitis*.[13] A definite advantage of MRI over CT is that MRI has clearer soft-tissue contrast resolution, which defines the ability to detect even minute differences in tissues

which otherwise appear similar. Unfortunately, the ideal imaging tool for diagnosing acute fulminant invasive fungal *sinusitis* in immune-compromised patients has yet to be established.[13,14,15] Invasive fungal sinusitis is a rather common disease and it has a high rate of mortality if diagnosis is delayed however it is often misdiagnosed. An early diagnosis is required for successful treatment, which can be achieved with radiologic imaging including CT and MRI each having its own advantages.[16] Whereas CT is better to assess for bone changes, MR imaging is superior in evaluating intracranial and intraorbital extension of the disease.[16] In our study 64 patients showed typical features of fungal sinusitis on MRI i.e. low signal intensity mucosal thickening and fungal mass on T1 and T2 weighted images and signs of intraorbital and intracranial extension. On histopathology 63 patients were positive for fungal sinusitis showing features of mucosal infiltration by eosinophils, plasma cells, lymphocytes and fungal hyphae. Findings of this study regarding sensitivity and specificity for MRI for diagnosis of fungal sinusitis were in line with the study of Groppo et al.[12] However the obtained sensitivity and specificity of MRI in this study was a bit higher as that of reported by Groppo et al.[12] Another study conducted by Kadri et al showed high sensitivity and specificity of MRI in diagnosing fungal sinusitis with intracranial extension however their sample size was of fifty patients with 30 females and 20 males, having mean age of 40 years.[17] It is recommended that incidentally made findings on MRI should be reported normal as these findings do not suggest that children whose MRI is performed for causes unrelated to sinus disease require sinus treatment.[18] MRI has an additional advantage that it does not involve use of ionizing-radiation, which is critical for patients who are undergoing frequent studies over their lifetime given the multiple co-morbidities and especially of importance for children. The use of computerized tomography is in planning surgery and image-guided navigation during surgery.[19] MRI sharply differentiates mass from adjacent inflammatory tissue and sinus secretions. It is to note that MRI has better soft tissue resolution, but it is inferior when it comes to evaluation of bones. On MRI the appearance of edematous membrane and mucus is distinct hyperintensity on T2-weighted images. The nasal polyps on the other hand return intermediate signals. A disadvantage of MRI is its inability to highlight bony anatomy for which CT scan can be used. Vascular and CNS complications (e.g. vascular invasion with infarction, pseudoaneurysm formation, intracranial invasion with enhancement of the meninges and cerebral grey and white matter involvement) are better assessed on MRI with contrast.[20] There is devascularization of mucosa in acute invasive fungal sinusitis which leads to no enhancement of mucosa after IV contrast and this is one of the earliest MRI findings of AIFRS. Moreover, invasion of the fungal disease into the orbit and post-maxillary fat pad can be clearly depicted. Additionally MRI is helpful in depicting disease extension in the orbit (extraocular muscles, extraconal post-septal fat, and intraconal fat) as well as intracranial extension (cavernous sinus, involvement of pachymeninges, leptomeninges and brain).[21]

Conclusion

It is concluded that magnetic resonance imaging can be used with significant diagnostic accuracy for the diagnosis of fungal sinusitis, taking histopathology as gold standard. Moreover magnetic resonance imaging is investigation of choice because of its lack of radiation hazards.

Department of Physiology
Continental Medical College, Lahore

www.esculapio.pk

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Original Article

Outcomes of Inguinal Hernia Repair Under Local Anesthesia

Luqman Ali Bajwa, Muhammad Asjad, Muhammad Imran Manzoor, Hassan Shaukat, Javaid-ur-Rehman and Muhammad Kamil Zulifquar

Objective: To evaluate the outcomes of inguinal hernia repair under local anesthesia in terms of post-operative wound pain and post-operative hospital stay.

Methods: This study included all 140 consecutive adult patients who were fulfilling the inclusion criteria and treated with surgery for an inguinal hernia under local anesthesia by using the Lichtenstein open mesh hernioplasty technique between 24 December 2014 to 24 June 2015. The primary endpoint was the early post-operative pain and the objectivity of pain was assessed by visual analogue scale (VAS) 6 hours post-operatively and the secondary endpoint was the hospitals stay measured in hours.

Results: There were no post-operative deaths and no major systemic complications. In our study, out of 140 Patients, all were male (100%) with their mean age of 41.44, SD ±12.75 years. 80 patients (57.2%) were having right sided unilateral inguinal hernias while 60 patients (42.8%) having left sided unilateral inguinal hernias while 30 patients (21.42%) were diagnosed as having direct inguinal hernias while 110 patients (78.58%) were having indirect inguinal hernias, Mean VAS score at 6 hours post-operatively was noted as 2.36, SD ±1.04 with maximum VAS pain score 5 and minimum score was 1,after 6 hrs of surgery, while the mean hospital stay in all the patients post-operatively was found to be as 6.36 hours, SD ±0.59 hours.

Conclusions: Lichtenstein open tension free mesh hernioplasty under local anesthesia is safe, feasible and effective technique. With this approach, there is reduced early post-operative pain and the hospital stay.

Keywords: lichen steins, open, tension free, mesh plasty (mesh hernioplasty).

Introduction

An Inguinal hernia is protrusion of abdominal cavity contents through the inguinal canal. Inguinal hernia is a common surgical problem and is one of the most common surgical procedures performed worldwide. It can be repaired by several methods but LICHENSTEIN open tension free mesh hernioplasty is the most frequently used technique and is considered to be Gold standard by American College of Surgeons.[1] Hernia repair by general surgery accounts for the 10-15% of all surgical procedures because of its high incidence worldwide.[2] High-quality surgical procedures, with least postoperative pain early discharge from hospital with reliable long term results and early return to occupation are the parameters that should be considered for inguinal hernia repair.

Anesthetic techniques recommended for inguinal hernia repair are general, regional (epidural or spinal) paravertebral block and local anesthesia. Open repair like Lichenstein repair under local anesthesia is safe, cost effective and results in good success rates.[3-5] Local anesthesia is gaining importance with its associated low peri-operative and post-operative risks like reducing post-operative nausea and pain and early return to normal social activities.[6-8] Local anesthesia is generally preferred because of its quick and safe induction with excellent outcomes and reduction in intervals between operations in operating theater[9]. Many patients specifically request local anesthesia due to short hospital stay. Benefits of local anesthesia are that test to repair can be performed by communicating with the patient. Patient remains ambulant throughout the procedure which may increase morale of the patient and subsequently his/her short hospital stay.

Local anesthesia is gaining ground and due to its safer induction, excellent outcomes, reduced risk of cardiopulmonary complications. It may become the anesthesia of the choice with growing awareness and advantages that it offers.[9] So there is a need to emphasis on the role and possible benefits and drawbacks of local anesthesia for inguinal hernia.

During literature review there was a great variability of results. According to one study conducted in 2012, it was observed that 28.70% patient developed wound pain and post-operative hospital stay was 27.27±9.91 hours (about 1 day) after hernia repair under local anesthesia. But in another study conducted in 2014,

inguinal hernia repair under local anesthesia was performed on 25 patients, they observed 92% patients experiencing wound pain and mean hospital stay was 1.76±1.2 days (>24 hours).

The rationale of study was to evaluate the outcomes of Inguinal hernia repair under local anesthesia in terms of post-operative pain and hospital stay in our local population as better outcome may help us to adopt local anesthesia for inguinal hernia repair over general anesthesia as General Anaesthesia is associated with risk in patients with comorbidities, and spinal anesthesia is mostly refused by patients due to post-operative backache and headache complications.

Despite various studies published in foreign literature, in Pakistan for multiple reasons, there was still a lack of significant data to support local anesthesia. The aim was to assess outcomes of inguinal hernia repair under local anesthesia in our population to avoid harmful effects of general anesthesia and spinal anesthesia in our population and providing cost effective means of surgery to non-affording patients. It will also be beneficial for patients not fit for general and spinal anesthesia, and for generating base line data to encourage further studies in the field of inguinal hernia repair.

Methods

This Quasi experimental trial was conducted at Department of Surgery, Services hospital, Lahore for 6 Months i.e. from 25th December 2014 to 24th June 2015. Sample size of 140 cases is calculated with 95% confidence level, 7.5% margin of error and tasking expected percentage of wound pain i.e. 28.70% in patients underwent inguinal hernia repair under local anesthesia. Non-probability, consecutive sampling was used in recruit the patients. Males of age between 18 to 60 years with Unilateral, Direct or Indirect, reducible inguinal hernia (assessed on clinical examinations and ultrasound) were included who underwent elective surgery.

General contraindications to surgery e.g. coagulopathy (PT>20sec, aPTT>30sec), and ascites, diabetic (BSR>186mg/dl), hypertensive (Bp≥140/90mmHg) mental disturbance, obstructed, Incarcerated or Irreducible inguinal hernia, conversion to any other form of anesthesia due to failure of local anesthesia were excluded from the study. Informed consent was taken. A demographic data like name, age, gender and contact were recorded. Then patients underwent inguinal hernia repair under local anesthesia. (Inj Xylocain & Inj. Bupicane) Intramuscular injections of Diclofenac Sodium BID was used as a routine analgesia. A single surgical team operated all the patients to control bias. Patients were shifted to ward and were followed-up there. Outcomes were defined as post-operative pain and post-operative hospital stay. Post-Operative pain using visual analogue scale was assessed.

If patient complaint of pain on surgical site, then post-operative wound pain was labeled (assessed by Visual analogue scale (VAS) ranging from 0-10 score with 0 suggestive of no pain and 10 suggestive of severe pain after 6 hours of surgery.) Patient was discharged after he returned to daily routine activities. Duration of hospital stay was noted (considered in hours from time after operation till discharge from hospital, on oral medications).

Data was collected on Performa. The collected data was entered and analyzed accordingly using SPSS 17.0. The mean and standard deviation was calculated for age, pain score and hospital stay. Frequency and percentage were calculated for post-operative wound pain.

Results

A sample of 140 consecutive patients with mean age of 42.99±15.32. Out of 140 patients, 80 patients (57.2%) had right sided unilateral inguinal hernias while 60 patients (42.8%) had left sided unilateral inguinal hernias.

There were 30 patients (21.42%) with direct inguinal hernias while 110 patients (78.58%) had indirect inguinal hernias.**(Table-1)**

The mean pain score of patients was 2.36±1.05 and 25 (17.9%) patients had pain ≥4. The mean hospital stay was 6.36±0.59 hours. **(Table-2)**

Table-1: Baseline characteristics of patients.

Baseline characteristics of patients	41.44±12.75
Laterality	
Left	60 (42.8%)
Right	80 (57.2%)
Obesity	21 (17.2%)
Type of inguinal hernias	
Direct inguinal hernia	30 (21.4%)
Indirect inguinal hernia	110 (78.6%)

Table-2: Outcome of treatment.

Outecome	Mean±SD
VAS Score	2.36±1.05
Pain (VAS=4)	25 (17.9%)
Hospital stay (hours)	6.36±0.59

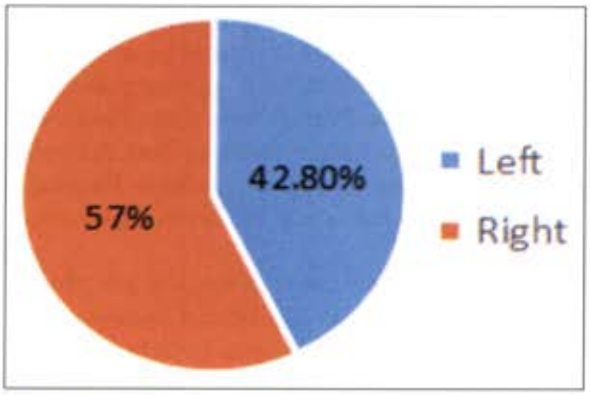

Fig-1: Laterality.

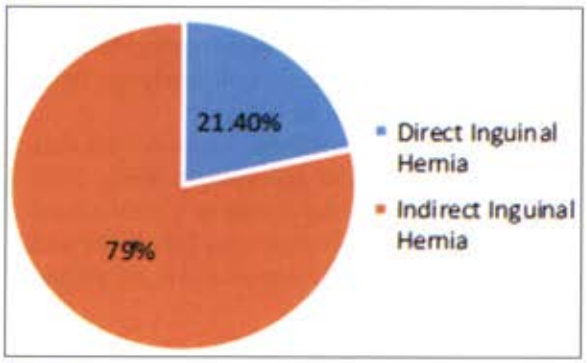

Fig-2: Type of inguinal hernia.

Discussion

Since Bassini's (1844-1924) period various methods of inguinal hernia repair have been discussed for better results. The ideal method of hernia repair is one that cause minimal discomfort to the patient during and after the surgery. It should be technically simple, and would have a low rate of complications and recurrence.[10] The Shouldice method remained acceptable for several years with a recurrence rate of 01 to 06 %. Inguinal hernia repair performed by suturing and displacement of anatomical structures may lead to excessive tension on the suture line and surrounding tissues, resulting in recurrence. The use of prosthetic mesh allows tension free repair of inguinal hernia with better results.[11]

The prevalence of inguinal hernia is high in old and middle age.[12] Most of the elderly patients having inguinal hernia also have some concomitant disease (cardiac, pulmonary and diabetes) that increases the surgical risk.[13] Cardiovascular, pulmonary and urinary complications can occur after inguinal hernioplasty, especially when the procedure is performed under general or spinal anaesthesia. On the other hand, patients operated under local anaesthesia do not generally have serious peri or post-operative complications. Several retrospective and randomised control trials have shown that L/A provide the best clinical and economical benefits to patients[14-16]. Inspite of all these benefits, the use of local anaesthesia in inguinal hernia surgery has not been established among surgeons on a wide scale. In this study, we aimed at assessing the safety and benefits of local anaesthesia in mesh hernioplasty for inguinal hernia in terms of post operative wound pain and hospital stay. In our study, 20 (14.28%) patients had minor problems during the procedure and no patient developed anaphylaxis. A study done by Davis L et al in 2003, showed the anaphylaxis rate of about 1% to local anaesthesia.[17]

Pain is the main factor in post-operative morbidity. In this study 3 patients complained of severe pain (VAS 5) six hours post-operatively, and 22 patients had moderate pain (VAS 4) after six hours. Most of the patients remained pain-free within the six-hour post-surgery period with 27 patients having of VAS 3, 59 patients experiencing VAS 2 and 29 patients having VAS score of 1. VanVeen and colleagues[18] between August 2004 and June 2006 noticed in their study that inguinal hernia repair under L/A had significantly less pain. Local anaesthesia is highly effective in alleviating post-operative pain when using both peripheral nerve blocking technique, and local wound infiltration at fascial level.[19] In Young's study,14 patients operated (inguinal herniorraphy) under L/A had lesser need for post-operative analgesia because most patients felt that the subsequent pain was more tolerable as it comes gradually, compared with those who had their surgery performed under general or spinal anaesthesia.

The incidence of post-operative nausea, vomiting and hypotension was negligible in our study and this is in line with other studies.[20] We also noted post-operative urinary retention in some patients because most of the patients were in the age of having enlarged prostate. Jenson et al[21] showed that urinary retention is definitely a problem after inguinal hernia repair when the procedure is done under spinal anaesthesia, but not when it is done under L/A. This is a very important observation and sheds light on a common old-age problem. Early post-operative mobilisation results in lesser morbidity and, hence, early discharge from hospital. Patients operated under L/A start physical activity earlier after surgery. Callese[22] also proves in his study that L/A facilitates the faster mobilisation and early discharge from hospital than the other anaesthetic techniques. Also in our study all patients tolerated local anesthesia well and there was no need of conversion to any other form of spinal or general anesthesia.

Conclusion

The open tension free mesh hernia repair offers many advantages. It is inexpensive and allows the surgeon to cover all potential defects with one piece of mesh. Lichenstein open tension free mesh hernioplasty under local anesthesia is feasible and effective technique. With this approach, there is reduced early post-operative pain and the hospital stay. For surgeons performing the Lichtenstein repair under general or spinal anesthesia, procedure under local anesthesia is a feasible and effective alternative.

Department of Surgery
Sims/Service Hospital, Lahore

www.esculapio.pk

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Original Article

Frequency Of Type 2 Diabetes Mellitus And Comparison Of The Mean ALT And AST Levels Between The Type 2 Diabetic And Non-Diabetic Patients

M.Saeed-uz-Zaman, Imran Taqi, M.Yousuf Jamal, Rozina Mustafa and Momna Ijaz

Objective: To determine the frequency of Type 2 diabetes mellitus and comparison of the mean ALT and AST levels between Type 2 diabetic patients and non-diabetic patients.

Methods: The study was conducted in Department of Medicine, Services Hospital Lahore. Randomly 300 patients were enrolled from outpatient department of medicine. Sample size of 300 cases was calculated with 95% confidence level and 3% margin of error taking expected frequency of diabetics to be 7.6% 2. Patients were selected with Non probability, consecutive sampling technique. Patients were invesigated by performing Fasting blood glucose level, oral glucose tolerance test and Glycated HemoglobinA1c (HbA1c) level and diagnosed as diabetics as per American diabetic association criteria4. Newly diagnosed diabetics were segregated as type 1 and type 2 on the basis of clinical criteria4 i.e. age of onset, body mass index (BMI), insulin requirement as initial therapy, previous history of diabetic ketoacidosis and associated autoimmune disorders.

Results: Frequency distribution of patients with Type 2 diabetes mellitus showed that among 300 patients, 19%(n=57) had Type 2 diabetes mellitus . Mean ALT levels were deranged more in Type 2 diabetics (38.2±13.4) as compared to non diabetic patients (29.7±12.6). Mean AST levels were were also deranged more in Type 2 diabetics (39.7±12.7) as compared to non diabetics (32.6±14.1).

Conclusions: Mean AST and ALT values in patients with type 2 diabetes mellitus were deranged more than that of non diabetic patients.

Keywords: type 2 diabetes mellitus, alanine aminotransferase, aspartate aminotransferase.

Introduction

Globally the number of diabetic patients has emerged as a challenge because of a significant increase in patients over past few decades.[1] Incidence of Type 2 diabetes mellitus for the South Asia region was observed to be 7.47% in 2005, and raised to 7.60% in 2010.[2] The frequency of Type 2 diabetes mellitus is rising in Pakistan because of our social and sedentary life style.[3] As Non insulin dependent diabetes is associated with liver insult including fat infiltration/steatosis and steatohepatitis,[9] So, deranged alanine transaminase (ALT) and Aspartate transaminase (AST) are commonly seen in these patients. Aspartate transaminase (AST) and alanine transaminase (ALT) are the enzymes that are used to predict liver damage in several conditions like viral hepatitis,[5] autoimmune hepatitis, pregnancy, Drugs, Alcoholic and in nonalcoholic Fatty liver disease.[6-7] Elmahi et al. in 2014 in a randomized controlled trial showed that ALT and AST were significantly raised in diabetic patients than in non-diabetics ALT (23±17 in diabetics vs. 15±4.0 in non-diabetics) and AST (34±15 in diabetics vs. 25±5.0 in non-diabetics).[8] Few studies have been observed in context with deranged liver transaminases in type 2 diabetics up till now in Pakistan.Therefore need exist to conduct this study in our population to assess the deranged liver enzymes with reference to diabetes. This will help us to see the progression of the disease in terms of early detection of liver disorders,associated with Type 2 diabetes mellitus; and timely management regarding poor glycemic control including life style modification of Type 2 diabetes mellitus.

Methods

The study was conducted in Department of Medicine, Services Hospital Lahore. This study was a cross sectional survey in which 300 patients were enrolled from outpatient department of medicine. Sample size of 300 cases was calculated with 95% confidence level and 3% margin of error taking expected frequency of diabetics to be 7.6% [2].Patients were selected with Non probability, consecutive sampling technique. Patients of both sex groups with ages in the range of 20-70 years and who sign written informed consent to participate in the study were

enrolled. Patients who were already known patients of Diabetes mellitus, history of fever associated with deranged serum transaminases in past four weeks, drug history regarding steroids/Hakeem medications/alcohol intake, pregnant patients, having hepatitis B and C (on viral serology) as per history and clinical record were excluded from study.

Written informed consent, detailed history and examination were done for each patient. Patients were invesigated by performing Fasting blood glucose level, oral glucose tolerance test and Glycated HemoglobinA1c (HbA1c) level and diagnosed as diabetics as per American diabetic association criteria[4]. Newly diagnosed diabetics were segregated as type 1 and type 2 on the basis of clinical criteria[4] i.e. age of onset, body mass index (BMI) ,insulin requirement as initial therapy ,previous history of diabetic ketoacidosis and associated autoimmune disorders. Both Type 2 diabetics and non diabetics were evaluated for their transaminase levels to make a comparison between the two groups. Data collected was entered and analysed into SPSS version 23.0. Numerical variables i.e. age, alanine transaminase level, aspartate transaminase level, fasting blood glucose and BMI were presented by Mean±S.D. Categorical variables i.e. gender and Type 2 diabetic were presented as frequency and percentage. Mean ALT and AST levels were compared between the Type 2 diabetics and non-diabetics. Independent sample t-test was applied for comparison of mean alanine transaminase level and aspartate transaminase level between the two groups taking *p*-value of ≤0.05 as statistically significant. Data were stratified for age and gender to address effect modifiers. Post stratification independent sample t-test was applied taking p-value of ≤0.05 as statistically significant.

Results

A total of 300 patients fulfilling the inclusion /exclusion criteria were enrolled in the study. Age distribution of patients was done and three groups were made. group I (age 20 -34 years), group II(age 35-49 years) and group III(age>50years).Age distribution of patients showed that 87 patients were in age group I ,90 were in age group II and 123 were in age group III.

Gender distribution of patients was done which showed that 62.7% were males while 37.3% were females. Frequency distribution of patients with Type 2 diabetes mellitus showed that among 300 patients, 57(19.0%) had Type 2 diabetes mellitus. Mean ALT levels were compared between Type 2 diabetics and non diabetic patients which showed that Mean ALT levels in Type 2 diabetic patients was 38.2±13.4 and in non diabetics was 29.7±12.6 with a p-value of p=0.000, which is statistically significant. Mean AST levels were compared between Type 2 diabetics and non diabetics which showed that Mean AST levels in diabetic patients were 39.7±12.7 and in non diabetics 32.6±14.1 with a p-value of p=0.001, which is statistically significant as well. Stratification with respect to gender for comparison of ALT levels in both groups was done which showed that it is significant for both males and females with P values 0.001 and 0.002 respectively which is significant.

Stratification with respect to gender for comparison of AST levels in both groups was done which showed that it is significant in female gender with a p value =0.007 but insignificant in male gender with p value=0.020.

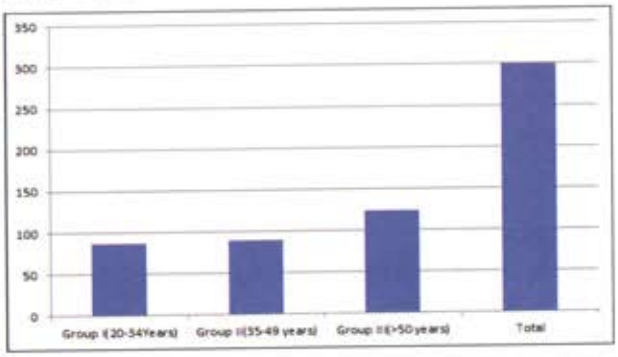

Fig-1: Distribution of age groups.

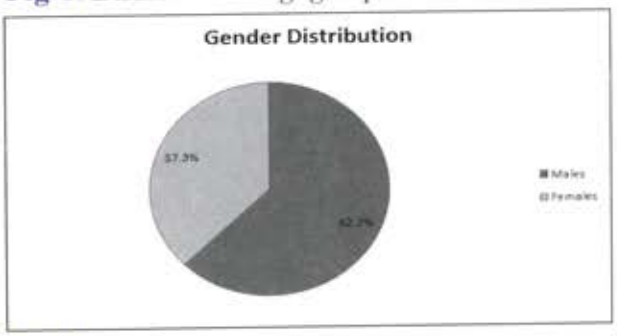

Fig-1: Distribution of age groups.

Table-1: Frequency distribution of Type 2 diabetes mellitus.

Type-2 diabetes mellitus	Frequency	Percentage
Yes	57	19.0
No	243	81.0
Total	300	100.0

Table-2: Comparison of ALT levels in both groups.

	Type-2 diabetes mellitus	N	Mean	Std. Deviation	P-value
ALT Levels	Yes	57	38.2	13.4	0.000
	No	243	29.7	12.6	

Table-3: Comparison of Mean AST levels in both groups.

	Type-2 diabetes mellitus	N	Mean	Std. Deviation	P-value
AST Levels	Yes	57	39.7	12.7	0.001
	No	243	32.6	14.1	

Table-4: Stratification with respect to gender for comparison of ALT levels in both groups

	Gender	Type-2 diabetes mellitus	N	Mean	Std. Deviation	P-value
ALT Levels	Male	Yes	38	36.4	13.0	0.001
		No	150	29.2	12.1	
	Female	Yes	19	41.8	14.0	0.002
		No	93	30.5	13.7	

Table-5: Stratification with respect to gender for comparison of AST levels in both groups

	Gender	Type-2 diabetes mellitus	N	Mean	Std. Deviation	P-value
AST Levels	Male	Yes	38	37.9	12.1	0.020
		No	150	32.0	14.1	
	Female	Yes	19	43.3	13.6	0.007
		No	93	33.5	14.3	

Discussion

Deranged Liver function tests have been reported in association with type 2 diabetic patients, higher ALT levels being most prime finding.[11]

In our study, the means of serum transaminases i.e. ALT/AST were within the normal values in non diabetic patients but significantly raised mean values in Type 2 diabetic patients. In a study on Mexican American patients, more deranged liver function tests were observed in diabetic patients as compared to non diabetic patients.[15] Serum transaminase measurements of type 2 diabetes patients were more elevated when compared with non diabetic patients which was observed in study done in Sudan by Hind M. Elmahi et al.; 2014,[8] which was also supportive in the background of our study.

Some studies on type 2 diabetics in India have reported abnormal Liver function tests with a prevalence of 50-70% [16,17,18,19].This is higher prevalence as compared to studies in Europe and United States where raised LFT in diabetics have been observed at a frequency of 7.822.9%.[20].The higher occurrence of these values in indian studies may be due to inclusion of patients with coexisting illnesses like non alcoholic steatohepatitis ,alcoholic liver disease and other causes of chronic liver disease. In our study we observed genderwise variability of deranged liver functions tests. In female type 2 diabetics, mean ALT/AST values were more raised when compared with male type 2 diabetics .But in other studies data is deficient for variability of LFT in diabetics on basis of gender. Our study emphasizes the monitoring of diabetic patients for Liver function tests and further required workup .Hepatic dysfunction is usually not assessed in diabetic patients as compared to systemic evaluation for cardiac, renal and neurological examination including eye assessment for diabetic changes. This is very common practice in primary care physicians, who manage a large number of diabetic patients.[21] .Early detection of deranged ALT/AST levels in type 2 diabetics will result in better patient care and lead to good prognosis and clinical outcome in these patients.[22,23]

Conclusion

Mean AST and ALT values in patients with type 2 diabetes mellitus were deranged more than that of non diabetic patients. So, liver function tests monitoring is highly suggested for Type 2 diabetic patients.

Department of Medicine
SIMS/Services Hospital, Lahore

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Original Article

Demographic Characteristics of Patients Presenting With Ischemic Stroke at Services Hospital Lahore.

Satia Waheed, Gauhar Mahmood Azeem, Awais Majeed, Ali Hassan, Nimrah Farooq and Ayesha Alam

Objective: To determine the demographic characteristics of patients presenting with stroke.
Methods: Retrospective cross sectional survey was conducted using a 20 point stroke questionnaire.
Results: 132 patients were included in study. The mean age of patients presenting was 62.1±12.3 years. 66.67% patients were diabetic. Patients reached the hospital on average within 2 hours 18 minutes from symptom onset. Most patients had onset of symptoms at night time. Motor symptoms were present in a vast majority of cases.
Conclusions: Patients were of a younger age than the worldwide average. Surprisingly our study showed diabetes to be more prevalent in the patients than hypertension. Most patients reached within the thrombolysis window. Attendants weren't aware that their patients had symptoms of stroke.
Keywords: Ischemic, stroke, demography, lahore.

Introduction

Stroke is a medical condition in which poor blood flow to the brain results in cell death.[1] Ischemic stroke occurs as a result of an obstruction within a blood vessel supplying blood to the brain. It accounts for 87 percent of all stroke cases.[2] Stroke accounts for 85.5% of mortality due to all stroke deaths worldwide.[3] The main neurological symptoms observed during or after stroke are sensory-motor disorders, cognitive impairment, visual impairments, speech disorders, coordination disorders, and swallowing problems.[4,5] Besides, the necessity of treatment strategies, rapid evaluation of stroke patient clinical clues, and results interpretation is equally important for emergency stroke management.[6,7] TPA can be given as the treatment of stroke upto 4.5 hours of symptom onset.[8] Mechanical Thrombolectomy by using a stent retriever device is strongly recommended within 6 hours of symptom onset.[9] The rationale of this study is to establish demographic characteristics of patients presenting with ischemic stroke presenting in one of the biggest tertiary care hospitals of Pakistan. Thus we can have an idea as to the risk factors, co-morbidities, history, symptoms on presentation and recognition of stroke in local patients. This can aid in rapid diagnosis of patients that is of utmost value in stroke patients.

Methods

This is a retrospective cross sectional study of 132 patients presenting in the emergency department of services hospital Lahore between February to May 2018. 132 patients included with simple random sampling technique and were those with new onset changes seen on CT scan confirmed as those of Ischemic Stroke by the radiologist.

Demographic characteristics, symptoms, risk factors and co-morbidities of patients were identified, enquired and noted. A 20 items stroke questionnaire was developed and filled by the doctors for every patient individually. Questions were asked from the patient directly or the closest relative available after taking proper informed consent. The responses were entered and analyzed using SPSS version 20.0 (IBM Co., Armonk, NY, USA).The quantitative data like age in years represented as mean standard deviations, whereas qualitative data like symptom recognition as frequency distribution. As the study was a cross sectional survey the requirement for ethical committee approval was waived.

Results

Out of our total 132 patients 74(56.06%) were male and 58(43.94) were female. The mean age of presentation was 62.1±12.3 years. The time duration from onset of symptoms to reaching services hospital was 2.3±2.87 hours. The patients travelled on average 53.5±31.25km to reach Services Hospital Lahore. The respondents on average had 6.75±2 family members.

120(90.91%) were married and 12(9.09%) were unmarried, divorced or widowed. As for the

education, 17(12.88%) received no formal education, 65(49.25%) were educated till primary, 34(25.76%) had done their Matriculation and 16(12.12%) were graduates.

37(28.03%) lived in a separate family whereas 95(71.97%) were from a joint family setup. A staggering 66.67% of patients were diabetic, 57.58% were hypertensive and 43.18% had ischemic heart disease, 71(53.78%) patients were smokers. Only 11(8.33%) were counseled that they may have a stroke whereas 121(91.67%) received no such counseling. Only 20(15.15%) of patients were previously taking medication for any condition. 24 patients (18.18%) had history of previous stroke/TIA. 24 patients (18.18%) had family history of stroke. 22 patients(16.67%) had stroke onset in morning, 38(28.79%) in evening and a majority 72(54.55%) had symptoms that started at night time. 103(78.03%) patients presented on an ambulance and only 27 (20.45%) chose to come on own transport. A vast majority, 118(89.39%) of patients presented with motor symptoms, 24 had altered state of consciousness (18.18%), Sensory symptoms were present in 17(12.88%) and speech impairment was present in 35(26.55) cases. Attendants of only 16 (12.12%) patients recognized they were having symptoms of stroke, whereas 116(87.88%) attendants had no idea that the symptoms were those of stroke.

Table-1:Risk factors.

Risk Factors	Present	Absent	Percentage
Diabetes	88	44	66.67%
Hypertension	76	56	57.6%
Ischemic Heart Disease	57	75	43.2%
Smoking	71	61	53.8%

Table-2:On previous medication.

On Medical	No. of Patients	Percentage
Yes	20	15.15%
No	112	84.85%

Table-3:Symptom of noset.

Symptom	No. of patients	Percentage
ASOC	24	18.88%
Speech	35	26.55%
Motor	118	89.39%
Sensory	17	12.88%

Table-4:Recognition as stroke.

Recognized as stroke by attendants	No. of Patients	Percentage
Yes	16	12.12%
No	116	87.88%

Discussion

Advancing age is a risk factor for stroke[10] and it is reflected in our study as the average age was 62 but as over 70% of all worldwide strokes occur after the age of 65,[11] among stroke victims, older adults have a higher mortality rate and increased risk of disability.[12-14] People in our study presented with stroke at an earlier age. The time between onset of symptoms and presentation was on average 2 hours 18 minutes, thus the majority of the patients could be thrombolised if facilities were provided. The patients traveled on average 53 km to reach services hospital so the majority of time spent between the onset of symptoms and presentation was in travailing. 66% of patients who presented were Diabetic. It is known that people with Diabetes are more likely to have a stroke.[15,16,17] Population based registries of stroke have reported a global prevalence of DM ranging from 9.5% to 20%[18,19,20] This is a huge difference and needs to be evaluated in further studies. 57.7% of patients were hypertensive. Hypertension is a known risk factor for Ischemic Stroke.[21] A majority of patients presented with motor symptoms which is consistent with study done by Kennedy Rl.[22] 78.03% of patients arrived in emergency on ambulances thus the system of ambulances is extremely vital in this time dependant management scenario and should be strengthened further. Only 12.12% attendants were aware that the patients had symptoms of stroke. This shows a lack of understanding and recognition of stroke and its symptoms by our common public.

Conclusion

Ischemic stroke is a major disease burden to our society. Majority of people are able to reach the emergency department within the thrombolysis window of 4 hours, thus emergency thrombolysis for patients of stroke would be common if started. Diabetes is a risk factor for stroke, and our study shows high prevalence of diabetes in patients presenting with stroke. While the degree of association might be less than our study has shown, this surely demands a more extensive research. Much needed is the education of our public about stroke and its symptoms, which will facilitate the urgent response needed in the management.

Department of Medicine Unit-IV
SIMS/Services Hospital, Lahore

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Original Article

Diagnostic Outcomes of the Females Presenting with Breast Lump in Surgical Department Services Hospital Lahore

Rohaba Shahid, Maryam Saghir, Haris Javed, Shabbar H Changazi, Mustansar Iqbal, Anam Zahra and Armghan Haider Ans

Objective: To identify the possible diagnostic outcomes of a breast lump in females.

Methods: It was a case series study design. It was carried out in the surgical departments of the Services Hospital Lahore from August 2017 to June 2018. Female patients aged above 15 years presenting to surgical outdoors with a breast lump were included in this study. Patients with a previous history of breast surgery, concurrent skin disease involving the breast, and non-cooperative patients were excluded from the study. Patients with a breast lump were then assessed through triple assessment, which included history and clinical examination, radiology and cytology or histopathology as required. All the data collected was entered and compiled using SPSS software. All the descriptive variables were analyzed in terms of frequency tables and percentages.

Results: The age of the patients ranged from 15 to 75 years with 60% of the patients were of 40 years or above and 40% were below 40 years of age. 40% of the patients were illiterate and 60% were literate while 88% were married and 12% were unmarried. Out of 200 patients, 104 (52%) had a mobile lump while 96 (48%) had a fixed lump, 186 (93%) had a hard lump whereas 14 (7%) had a soft lump, 134 (67%) had a painless lump while 66 (33%) had a painful lump, 32 (16%) patients with breast lump had a nipple discharge while 168 (84%) patients had no nipple discharge, and 45 (22.5%) patients with breast lump had skin changes while 155 (77.5%) had normal skin texture. Out of 200 patients, 84 (42%) were diagnosed with fibroadenoma, 106 (53%) were diagnosed with carcinoma, 4 (2%) with phyllodes tumor, 4 (2%) with simple breast cyst, 1 (0.5%) with sarcoma and 1 (0.5%) with tuberculosis of breast.

Conclusions: It was concluded that 57% of the patients presenting with breast lump had a malignant disease with breast carcinoma being the most common lesion and 43% of patients had a benign disease with fibroadenoma being the most prevalent disease.

Keywords: breast lump, breast cancer, benign, malignant.

Introduction

Patient's complaints of breast lumps are common, ranging from 40% to 70% in women seeking advice. A breast lump is usually a localized swelling, protuberance or mass in the breast. It is one of the prime indicators of breast disorders. Fortunately, most of the breast lumps are benign, but this does not deny the need for evaluation of any palpable breast lesion. Failure to diagnose breast cancer accounts for the most frequent and expensive claims brought against the physicians.[1] There are many causes of breast lumps, some of these causes are harmless while others can be painful or dangerous. Etiologies of breast lumps include infections, injuries, non-cancerous growths, and finally carcinoma. Most lumps are not cancerous as approximately 10% of breast lumps ultimately lead to a diagnosis of breast cancer.[3] There are several types of a benign breast lump, most of which are harmless and are caused by hormonal changes that occur during different times in a woman's life, such as during the menstrual cycle. There are several types of a benign breast lump. Fibroadenoma is a firm lump that moves around easily in the breast and is more common in younger women. Breast cyst is a smooth, firm fluid-filled lump most commonly seen in women aged 30 to 60. Breast abscess is a painful collection of pus that forms under the skin of the breast, usually as a result of bacterial infection. Other conditions include mastitis, fat necrosis, duct ectasia and lipoma. Most lumps of breast are benign, but breast cancer is the most common cancer and the second leading cause of cancer deaths in women. Malignant breast disease encompasses many histologic types that include infiltrating ductal or lobular carcinoma, in situ ductal or lobular carcinoma and inflammatory carcinoma.[4,5]

Researches on breast cancer risks have implicated hormonal status, both natural and by hormone Acement therapy (HRT). Increased breast density

being associated with an increased risk of breast cancer. Studies point the age of menarche and menopause, age of first pregnancy and number of full-term pregnancies as influential factors in the breast cancer risk. Other general risk factors include obesity, and excessive alcohol consumption. Ethnic and environmental factors may also play a role in breast cancer development.[6]

A patient presenting with a breast lump is evaluated with triple assessment with clinical, radiological and histological components. Radiological component included mammography or ultrasonography. Mammography is the first diagnostic test ordered in a woman over the age of 35 with a new breast complaint. Mammographic features suggestive of malignancy are asymmetry, clustered pleomorphic calcifications, increasing density of the breast tissue, or a new mass with irregular borders or spiculations. However, ultrasound is the first line of imaging in patient who is pregnant or less than 30 years old with focal breast symptoms. In addition, ultrasonography is also used to provide guidance for biopsies and other interventions.[7] Breast magnetic resonance imaging (MRI) is not indicated for the work-up of an undiagnosed mass. MRI is reserved for diagnostic dilemmas or to detect recurrence in patients with a breast implant.[8] Masses that are solid on radiology will require biopsy to exclude cancer and to provide a histological diagnosis. Fine needle aspiration and cytology or biopsy is the main stay of diagnosis in a suspicious breast mass.[9] Pakistan has peak incidence of breast carcinoma in Asia. Breast cancer is the most prevalent cancer in Pakistan as different studies show it kills nearly 40,000 women every year. According to the World Health Organization, breast cancer rates are getting worse and it is not even sparing younger age groups.[10]

The goal of this study was to evaluate the prevalence of different pathologies of breast lumps in female patients and its characteristics in our setup.

Methods

It was a case series study, which was conducted in the surgical units (I-IV) of the Services Hospital Lahore from Aug 2017 to June 2018. Services hospital is a tertiary level hospital with 31 departments, 27 major and 8 minor operation theatres and an outpatient attendance of 700 patients on average per day. An approval was taken from the ethical committee of the hospital. Sample size was estimated using WHO S-Size software by using the formula "Estimation of Population Proportion with specified relative precision at a confidence level of 90% and an anticipated population proportion of 0.65 with relative precision 0.15". The minimum sample size was 65. Total of 200 patients were recruited in the study which were fulfilling the inclusion criteria. Sampling technique was purposive sampling technique. Female patients aged above 15 years presenting to surgical outdoors with a breast lump were included in this study. Patients with previous history of breast surgery, concurrent skin disease involving the breast and non-cooperative patients were excluded from study. Patients with breast lump were then assessed through triple assessment which included history and clinical examination by the surgeon, radiological investigations and cytology or histopathology as required. After history and clinical examination, patients with age more than 35 years were subjected to mammogram and patients with 35 years or younger underwent ultrasonography of breast. Patients diagnosed with fibroadenoma (based on clinical examination and radiology) underwent excisional biopsy and patients suspected with malignant lesions underwent core needle biopsy. Patients diagnosed with breast cyst through ultrasound underwent aspiration and cytology of fluid. All the data collected was entered and compiled using SPSS software. All the descriptive variables were analyzed in terms of frequency tables and percentages. Questionnaires were filled after taking face to face interviews of the patients who came for evaluation. All the work performed in this study was in line with the PROCESS guidelines.[11]

Results

In this study, the age of patients ranged from 15 to 75 years with 60% of patients were of 40 years or above and 40% were below 40 years age. 40% of the patients were illiterate and 60% were literate while 88% were married and 12% were unmarried. Out of 200 patients, 104 (52%) had a mobile lump while 96 (48%) had a fixed lump with most fixed lumps being carcinoma. In this study out of 200 patients, 186 (93%) had a hard lump whereas 14 (7%) had a soft lump. This study showed that out of 200 patients 134 (67%) had a painless lump while 66 (33%) had a painful lump with the fibroadenoma being the most prevalent disease in painful lumps. In this study, 32 (16%) patients with breast lump had nipple discharge while 168 (84%) patients had no nipple discharge. Out of 200 patients, 45 (22.5%) patients with a breast lump had skin changes while 155(77.5%) had normal skin texture **(Table-1).** Out of 200 patients, 84 (42%) were diagnosed with fibroadenoma, 106 (53%) were

diagnosed with carcinoma, 4 (2%) with phyllodes tumor, 4 (2%) with simple breast cyst, 1 (0.5%) with sarcoma and 1 (0.5%) with the tuberculosis of breast **(Table-2).**

Table-1: Breast lump characteristics in benign and malignant breast diseases.

Mobility of lump	Mobile	55 (27.5)	49 (24.5)	104 (52)
Consistancy of lum	Soft	10 (5)	4 (2)	14 (7)
Pain in lum	Painful	46 (23)	20 (10)	66 (33)
Nipple dicharge	Present	1 (1)	30 (15)	32 (16)
Skin nodules or ulcers	Present	1 (0.5)	44 (22)	45 (22.5)

Table-2: Diagnostic outcomes according to the age groups.

Fibroadenoma	37 (18.5)	43 (21.5)	80 (40)
Phyllodestumour	3 (1.5)	1 (0.5)	4 (2)
Carcoma	1 (0.5)	0	1 (0.5)
Total	120 (60)	80 (40)	200 (100)

Discussion

This study was conducted to find out the diagnostic outcomes of a breast lump and the possible risk factors that result in breast conditions among female patients. A sample of 200 patients was selected for that purpose and study was conducted in the surgical departments of the Services Hospital Lahore.

In the present study, the age of patients ranged from 15 to 75 years with 60% of patients were of 40 years or above and 40% were below 40 years age. The age of the patients ranged from 6-72 years in the study on breast lumps conducted by Kumar R and between 17-56 years in the study carried out by Tiwari et. al.[12,13] In addition, fibroadenoma was a common lesion in age below 40 years of age and breast carcinoma was common in age 40 years or above. These results were in concordance with the study conducted by Walia BS et. al in 2017 which showed that the most common age group in patients with fibroadenoma was 21-30 years and in patients with breast carcinoma was 41 t0 50 years.[14] Similar results were also found in a study carried out by Yeole B et. Al.[15] In the study out of 200 patients, breast carcinoma was the most common lesion accounting for 53% (106) while fibroadenoma being the second common disease of breast involving 42% (84) of the total patients. Sadik AZ et. al in 2014 also illustrated that the breast carcinoma was the leading disease of the breast lump accounting for 46.15% of total cases and fibroadenoma being the second common lesion involving 40.16% of cases.[16] Similarly, Ahmed HG et. al in his study demonstrated that 34% of breast lesion to be carcinoma and 28% of cases to be fibroadenoma.[17] In the current study it was found that out 200 patients, 2% (4) patients had phyllodes tumor. In addition, 3 cases were benign and 1 case of phyllodes was malignant. In a study, Ahmed HG et. al showed that phyllodes tumor accounted for 1% of the total breast lump cases.[17] Similarly, Sadik AZ et also evinced that phyllodes tumor constituted only 1% of breast diseases.[16] In the study, 2% of the cases of breast lump were simple breast cysts. Ahmed HG et.al in their study found that 6% of cases of total patients presenting with breast lump had simple breast cyst.[17]

Breast sarcoma is an extremely rare and heterogeneous group of malignancies and constituting less than 1% of total breast malignancies.[18] In the present study, only 1 (0.5%) case of breast lump was diagnosed with the sarcoma of breast. Finally, Tuberculous Mastitis (TM) is a rare extrapulmonary presentation of tuberculosis accounting for less than 1% of all diseases of the breast in the industrialized world.[19] Incidence of this disease is higher in countries endemic for tuberculosis, like the Indian subcontinent, where it may be as high as 4%.[20] In the Arabian Gulf, the frequency of the disease is reported to be between 0.4% and 0.5%.[21] In this study, only 1 (0.5%) case of breast disease was discovered with tuberculous mastitis.

Conclusion

This study was conducted on female patients presenting with a breast lump to find out the possible diagnostic outcomes. The results indicated that 57% of the patients presenting with the breast lump had a malignant disease with breast carcinoma being the most common lesion and 43% of patients had a benign disease with fibroadenoma being the most prevalent condition.

Department of General Surgery
SIMS/Services Hospital, Lahore

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Original Article

Microbial Flora Analysis of Urinary Tract Infection in Patients Suffering from Nephrotic Syndrome in Lahore, Pakistan

Fiaz Ahmad and Saba Shamim

Objective: To find the microbial flora in urinary tract infection patients suffering from nephritic syndrome in tertiary care hospital, Lahore.

Methods: This cross sectional study was conducted in a tertiary care hospital Lahore from June 2014 June 2016. A total of 500 samples were collected from nephrotic syndrome patients suffered from UTI. The patients were divided in found age groups group 1 (15-25 years), group 2 (25-40 years), group 3 (40-60 years) and group 4 (above 60).Data was collected by using a predesigned questionnaire. Midstream urine was collected in sterile container and processed by standard microbiological methods. Frequency was determined by calculating the percentages.

Results: Out of 500 samples, females were found to be more affected i.e. 61 % (n=305) as compared to males, 39 % (n=195). Both genders were found to be most affected in age group 25-40 years (109 females: 92 males) and least was found in patients between 40 -60 years in females while above 60 years in male patients. E. coli showed the highest frequency (71 %) and found in all age groups, followed byKlebsiella (10%), S. aureus (10 %), Enterococcus (3 %), Streptococcus (3 %) and P. aeruginosa (3 %). Gram positive bacteria showed sensitivity to vancomycin, linzolid, ampicillin, nitrofurantoin, cephradin and penicillin. Gram negative bacteria showed sensitivity to imipenem, meropenem, gentamicin, amikacin, sulfzone, tazocin, cefruxime polymyxin B, colistin andnitrofurantoin.

Conclusions: Precautionary measures should be strictly followed to avoid infections and complications in urinary system by proper cleanliness and awareness of sex education in adults.

Keywords: nephrotic syndrome, urinary tract infection, bacteria, antibiotic sensitivity pattern.

Introduction

Nephrotic syndrome (NS) is a common renal disorder[1-6] characterized by hypercholesterolemia, hyperlipidaemia,[7] hypoalbuminaemia, proteinuria and generalized oedema.[8,9] The compromised immune system, includingdefective T-cell function and immunoglobulin loss, is responsible for bacterial invasion and colonization[8,10] which lead to UTI by hospital or community acquired microbial flora.[11,12] UTI is generally classified as lower and upper UTI. In lower UTI, bladder is infected (cystitis) whereas in upper UTI, one or both kidneys are infected (pyelonephritis).[11,12] As urine is formed in the body, it is immediately thrown out from bladder to urethra. Sometimes, urine remains in bladder and hence the microorganisms gain entry into bladder via urethra followed by colonization of urethral walls or bladder walls. Normally urine is sterile. But if somehow, bacteria gained entry into the urethra (its infection is called urethritis) and colonize it by overcoming host defense mechanisms, it results in UTI.[12] UTIs are common all over the world. It can be hospital acquired or community acquired.[11,13] The agents responsible for UTI include Staphylococcus, Enterococcus, and Klebsiella.[12]The causes of UTI in both genders include indwelling catheters, renal transplantation, renal failure, pregnancy, etc.[14] The women are more likely to be infected by UTI as compared to men[13] because of anatomy of female urinary and reproductive system.[12,15]The objectives of this study were microbial analysis of NS patients suffering from UTI. Both genders and all age patients were included in the study. The ratio of males, females and microorganism responsible for causing UTI in them, was determined. Antibiotic sensitivity pattern of bacterial isolates was established.

Methods

For this study, 500 samples were collected in sterile containers from a tertiary care hospital, Lahore. The study was carried from June 2014 - June 2016. The inclusion and exclusion criteria were kept in mind at time of samples collection.Patients of all age and both genders were considered who were suffered from both genders were considered who were

suffered from both UTI and renal failure (NS).Patients who were suffered from UTI but not renal failure (NS) were excluded from this study.Before sampling, the female patients were advised to clean the area around urethral opening with clean tap water and dry it. The urine samples from females were collected with labia apart in order to reduce the chances of commensal flora contamination. For male patients, it was advised to wash the hands before collecting the urine (middle of the urine flow) in sterile container. For isolation and identification of microorganisms from urine samples CLED agar and mannitol salt agar media were used. All bacterial isolates were identified on basis of cultural characteristics, colony morphology, Gram staining and biochemical tests.[16] The isolated and purified bacterial isolates were preserved by glycerol method.The antibiotic sensitivity was determined by disc diffusion Kirby Bauer methodon Mueller Hinton (MH) agar plates. The antibiotic discs were purchased from market. The zones of inhibition around discs were noted and reported.[17]To check the prevalence, percentages were calculated wherever required.

Results

For samples collection, patients of both genders were divided into four groups according to their ages **(Table-1)**. Female patients were observed more (305) as compared to male patients(195). In **Table II,** bacterial isolates according to different age groups are reported. E. coli was found in all age

Table-1: Gender ratio according to age group.

Group	Age (in years)	Genders	No. of Pts. (n=500)
Group-1	15-25	Male	35
		Female	101
Group-2	25-40	Male	92
		Female	109
Group-3	40-60	Male	42
		Female	41
Group-4	Above 60	Male	26
		Female	54
Total		Male	195
Total		Female	305

Groups. Klebsiella and S. aureus were present from 15 to 40 years of age. Streptococcus was observed in groups 2 and 3. Enterococcus and P. aeruginosa were resent only in group 3 **(Table-2)**. Among all isolates obtained in this study, E. Coli showed highest frequency (71 %) followed by S. aureus and Klebsiella i.e. 10 % each. Remaining other isolates including Streptococcus, Enterococcus and P. aeruginosa were present as 3 % **(Table-3)**. The antibiotic susceptibility pattern of all isolates is given in **Table-4**.

Table-2: Bacterial isolates in different age groups.

Group	Age (in years)	Bacterial isolates
Group-1	15-25	E. coli, Klebsiella, S. Aureus
Group-2	25-40	E. coli, Klebsiella, S. aureus, Streptococcus
Group-3	40-60	E. coli, Streptococcus, Enterococcus, P. Aeruginosa
Group-4	Above 60	E. Coli

Table-3: Prevalence of gram positive and gram negative bacterial isolates.

Gram Staining	Microorganisms	Frequency
Gram Positive	Streptococcus	3%
	Enterococcus	3%
	S. Aureus	10%
Gram Negative	E. Coli	71%
	Klebsiella	10%
	P. Aeruginosa	3%

Table-4: Antibiotic sensitivity of all bacterial isolates .

Microorganisms	Antibiotics Sensitivity
Streptococcus, Enterococcus, S. Aureus	Vancomycin,Linzolid, Nitrofurantoin, Cephradin, Penicillin, Ampicillin
E. Coli, Klebsiella, P. Aeruginosa	Imipenem, Nitrofurantoin, Gentamicin, Amikacin, Sulfzone, Tazocin, Meropenem, Cefuroxime, Polymyxin B, Colistin

Discussion

UTI is considered as one of the complication in patients suffering from nephrotic syndrome (NS). According to the present study, more females were found suffering from UTI as compared to males. Our finding is in agreement with previous work.[12,18] But in Baghdad, high ratio of males was observed.[19] The factors that contribute to high female ratio includes close existence of female urinary system (small urethral opening) and reproductive system (close proximity of vagina and anus), less awareness of sex

education regarding usage of contraceptive agents (spermicidal agents, diaphragm) and overall cleanliness of reproductive organ.[12] Although microbial flora varies with age but E. coli was found in all age groups from 15 years to above 60. In this study, E. coli contributed more, followed by Klebsiella and S. aureus. Our finding of E. coli confirmed Minardi et al.[18]who observed 80 % E.coli in patients under 50 years. E. coli was also observed in elder age woman of 90 years.[20] Here least observed bacterial isolates were Streptococcus, Enterococcus and P. aeruginosa which were found as 3 % each. In this study, only 3 % Enterococcus was found which is in contrast with the previous work conducted in China.[21]The frequencies of E.coli (20 %, 29 %), Klebsiella (8 %, 22 %), S. aureus (6 %, 14 %) were reported previously [12,22], respectively. Ezejiofor [12] also reported Pseudomonas (7 %) and Streptococcus (7%). E. coli, Klebsiella, S. aureus and Pseudomonas were also observed in Nigeria[10] and Bangladesh. [19]Pseudomonas was also reported in patients between 40-60 years of age.[10] Childhood E. coli and Klebsiella were reported from Colombia, South America. [23]NS is common in Pakistani and Nigerian children where bacterial invasion resulted in UTI.[8,24]

In last decades, E. coli was reported to be highest prevalent microorganism in UTI patients.[25] The bacterial flora of males consisted of E. coli, S. aureus, Klebsiella, Enterococcus and Streptococcus.[11] According to Sreeivasan et al.[22], UTI should be treated as soon as possible because if left untreated, the complications like hypertension, reflux nephropathy and chronic renal failure would likely to occur.

Adeleke and Asani[10] reported the resistance of S. aureus, Klebsiella and Pseudomonas to nalidixic aicd and ampicillin but sensitivity to cefotaxime, ceftriazone and ciprofloxacin. According to Echeverri et al,[23] childhood E. coli and Klebsiella showed resistant to most antibiotics but they were sensitive to amikacin. In our study, Gram positive bacteria were sensitive to vancomycin,[22] linzolid, ampicillin, nitrofurantoin, cephradin and penicillin which agrees with findings of Manhal et al.[22] who revealed sensitivity of amikacin, gentamicin, ceftazidime, cefoxitin and imipenem for isolated bacterial species E. coli, Klebseilla and Streptococcus. Similar sensitivity pattern were reported previously.[10,21] Sreenivasa et al.[22] he isolates sensitive to aminoglycosides and 3rd generation cephalosporins. In NS patients, UTI is caused by E. coli is common and major microorganism so far as it is.

Conclusion

In this study, it was concluded that females were more affected by NS and faced UTI as complication. Major microorganisms associated with such patients were E. coli, Klebsiella, S. aureus, Enterococcus, Streptococcus and P. Aeruginosa. These microorganisms were found to be sensitive to large range of antibiotics The awareness about cleanliness of reproductive system and sex education can help in decreasing the UTI in NS patients especially females.

Department of Biochemistry
Shalamar Medical and Dental College, Lahore
www.esculapio.pk

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Medical News

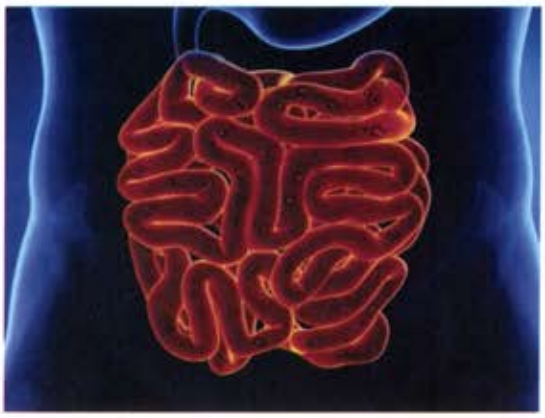
Irritable bowel syndrome (IBS)

Irritable bowel syndrome, or irritable bowel disease, is a long-term gastrointestinal disorder. It causes abdominal pain, bloating, mucous in stools, irregular bowel habits, and alternating diarrhea and constipation. Irritable bowel syndrome (IBS) or irritable bowel disease (IBD), is also known as spastic colitis, mucus colitis, and nervous colon. It is a chronic, or long-term, condition, but symptoms tend to change over the years.

IBS can cause persistent discomfort, but most people will not experience severe complications. Symptoms often improve as individuals learn to manage the condition. Severe and persistent severe symptoms are rare. IBS can lead to discomfort and abdominal pain. Symptoms often worsen after eating. A flare-up may last from 2 to 4 days, and then symptoms may either improve or go away completely.

Signs and symptoms vary considerably between individuals. They often resemble those of other diseases and conditions. Anxiety and depression may also occur, often because of the discomfort and embarrassment that can accompany the condition. Factors that may be involve dinclude. A person's mental and emotional state may have an impact. People who have had a traumatic experience have a higher risk of developing IBS. Hormonal changes can make symptoms worse. They are often more severe in women, for example, around the time of menstruation.

IBS can lead to discomfort and abdominal pain.



IBS causes discomfort in the gastrointestinal system.

Original Article

Protective Effect of Vitamin E on Phthalate Induced Toxicity on Diameter and Basement Membrane of Seminiferous Tubules

Nabeela Habib, Yasmeen Bashir and Ushna Habib

Objective: To investigate toxic effects on basement membrane and diameter of seminiferous tubules caused by phthalates and protection by vitamin E.

Methods: Twenty four male albino rats were divided into three groups of eight animals each. Group A was given 0.4 ml of corn oil daily for 15 days. Group B was given 0.15 ml of Dioctyl phthalate (DOP) dissolved in 0.4 ml of corn oil daily for 15 days. Group C was given 0.15 ml Dioctyl phthalate and 10 mg of vitamin E, each dissolved in 0.4 ml of corn oil respectively, daily for 15 days. The mode of administration was oral gavage.

Results: On histological examination the testes of animals of group B showed disrupted and ruffled basement membrane. The diameter of seminiferous tubules in different groups did not show much variation. Co-administration of vitamin E and DOP to group C showed that DOP in this group had less deleterious effect as it did in group B, where DOP was given alone.

Conclusions: Phthalate induced testicular toxicity, effect on basement membrane and diameter of seminiferous tubules was prevented by co-administration of vitamin E and DOP.

Keywords: phthalates, dioctyl phthalate (DOP), vitamin E.

Introduction

Phthalates are synthetic chemical esters of phthalic acid and serve multifunctional roles in a variety of consumer products resulting in ubiquitous daily exposures in adults and children.[1] DOP also known as di (2-ethylhexyl) phthalate (DEHP), is one of the commonly used compound. These compounds impart flexibility, transparency and durability to PVC plastics, which are then used in an extensive range of products including toys, clothing, building material, paints, curtains, wall papers, food packaging and plastic wraps. They are also used in cosmetics, including perfumes, soaps, shampoo, hairspray, nail polish and skin moisturizers.[2] Fast food may be a source of exposure to DEHP.[3] They are, therefore, an unavoidable part of contemporary living.[4,5] Phthalates are not chemically bound in the polymers. Therefore, migration or emission of phthalates from the products into the environment is likely to occur.[6] DEHP is also used in many medical devices including intravenous (IV) tubing, IV fluid bags, total parenteral nutrition bags/tubes, and catheters[7]. Certain chemical in personal care and consumer products, including low molecular weight phthalates, or their precursors, are associated with altered pubertal timing in animal studies.[8] Some phthalate exposures from personal care products are associated with menopausal hot flashes in women.[9] Thereafter, considerable concern was raised regarding toxic effects of all PAEs, especially DOP.

Plastic materials used in food processing and storage may also increase the phthalate content of some foods.[10] Aging disposable plastic food wraps and bottles particularly at high environmental temperatures lead to transfer of phthalates into the environment. Elevated temperatures of microwave oven used in many households may lead to transfer of phthalate compounds from plastic packaging and crockery into the food being warmed. After exposure the route of entry into the body can be ingestion, inhalation or dermal contact.

DOP is rapidly absorbed and converted to mono (2-ethylhexyl) phthalate (MEHP), which also leads to male reproductive organ damages in animals, chiefly the testes when administered orally to rats.[11,12,13] Di-ester phthalates are hydrolyzed into monoester phthalates in the intestine and parenchyma, i.e., phthalates are converted in the body to a metabolite, a break-down substance produced by metabolism.[14]

Phthalates have been linked to adverse reproductive effects in male pubertal and adult rodents exposed in utero and during lactation, such as reduction in the weights of reproductive organs and a reduction in sperm count.[15] Oral administration of DOP to rats has been reported to significantly increase the lipid peroxidation by generating ROS which in turn leads

to testicular degeneration and infertility.[16] Free radicals in the cell, such as hydroxyl radical, superoxide ion and hydrogen peroxide, attack lipids, sugars, proteins and DNA. Oxidative injury to these molecules may impair a range of biomolecular processes.[17,18] Since testicular physiology is impaired by reactive oxygen species (ROS)-dependent mechanism, suggestive of the fact that antioxidant enzymes are important in the testes. Considering the fact that phthalates also have a role in reducing the male fertility by causing seminiferous tubules atrophy and seminiferous epithelial cells disintegration, it is suggested that the mechanism behind it is oxidative stress in testes of adult rats.[19]

These studies suggest that antioxidant enzymes are customarily important in testes.[20] Antioxidants such as vitamins C and E have been shown to guard tissues against ROS[21]. Supplementation of vitamins with antioxidant effects enhanced the regeneration of damaged seminiferous epithelium in DOP treated animals, suggesting that these vitamins have a beneficial effect on DOP-induced spermatogenetic toxicity.[22] Cells are normally fortified with antioxidant defense system to counter the effect of ROS, but when the generation of ROS exceeds the capacity of cells to counteract these, additional help is required. Therefore, excess ROS generated in testicular tissues due to DOP require antioxidants such as vitamins C and E.

Methods

This study was carried out at the Experimental and Research Laboratories of University of Health Sciences, Lahore and rat was used as an experimental model, after approval from the ethical committee of the University. Twenty four healthy adult male Albino rats of Wistar strain, aged 6-8weeks and weighing 200-250 gm were used; housed in cages of appropriate size, kept in a controlled environment with room temperature of 23±2°C, and humidity of 55±5%, light and dark cycles were maintained for 12 hours each. They were fed on normal rat chow, given water ad libitum and allowed to acclimatize for a period of two weeks. The rats were divided into three groups of eight animals each. Each animal in every group was labelled with eosin stain on their back. **Group A** was given 0.4 ml of corn oil daily for 15 days by oral gavage. **Group B** was given 0.15 ml of Dioctyl phthalate dissolved in 0.4 ml of corn oil daily for 15 days by oral gavage. **Group C** was given 0.15 ml Dioctyl phthalate and 10 mg of vitamin E, each dissolved in 0.4 ml of corn oil respectively, daily for 15 days. Animals were sacrificed on the sixteenth day and testes were removed under anesthesia, cut into two pieces each and kept in Bouin's fixative for 48 hours. Each half was then washed with 70% alcohol for 72 hours to remove yellow color of Bouin's fixative; processing was done in an automatic tissue processor and paraffin blocks were prepared. Sections 4µm thick were obtained using rotary microtome. The slides were stained with hematoxylin and eosin and then examined under light microscope using X10 and X40 magnification. Diameter of seminiferous tubule was measured with the help of Leica, DM 1000 microscope with 10X objective lens and ocular micrometer; the method described by Culling, 1974 was used. The ocular micrometer was inserted into the eye piece of the microscope and calibrated using 10X objective lens, the eyepiece micro-metered and adjusted so that the scale on the linear micrometer seemed sharply focused. A stage micrometer was placed on the microscope stage and brought into focus. The area at which both ocular and stage micrometers exactly matched was observed. The factor calculated by calibration of ocular micrometer with the stage micrometer. The stage micrometer was then removed and both vertical and horizontal diameter of seminiferous tubules measured using ocular micrometer, and a mean diameter of each of these seminiferous tubules was calculated and was multiplied with the factor calculated;

100 stage divisions = 1mm =1000µm
1 stage division = 1000/100 =10 µm
1 division of ocular micrometer was = 1 stage division
1 division of ocular micrometer = 10 µm
The calibration factor =10µm

The cross sectional profiles of ten seminiferous tubules were identified in each section. The mean diameter of each seminiferous tubule was calculated by measuring the diameters twice at right angles to each other and calculating their mean. Six sections from every animal were observed and a total of 144 sections from 24 animals were examined; thus the diameter of 1440 seminiferous tubules were recorded. The basement membranes of seminiferous tubules in each PAS stained section of the Twenty four animals were observed regarding their thickness and regularity using 40X objective. The basement membranes showing irregularities were counted as ruffled and those showing breaks were counted as disrupted. SPSS 20 was used for statistical analysis. Mean±SD and Median with interquartile range was given for diameter of seminiferous tubules. Normality of the data was checked by Shapiro Wilk test. A comparison was done for the outcome, both in

qualitative and quantitative measurement, between the groups for differences. The difference in the quantitative measurement was tested by one way analysis of variance (ANOVA) and Kruskal Wallis test. Post Hoc Tukey test and Mann Whitney U test with Bonferroni correction were applied to evaluate the significance of individual variations between the control and treatment groups. Fisher's exact test was used to determine the association between groups regarding effect on basement membrane. p. value ≤ 0.05 was considered statistically significant.

Results

Histological examination revealed normal looking regular and thin basement membrane in control group A **(Fig-2).** However, group B showed disrupted and irregular basement membrane **(Fig-2).** Group C showed regular and thin basement membrane **(Fig.-2).** The diameter of seminiferous tubules in different groups did not show much variation. A few tubules in group B did show some atrophy. However, when the results were compared between different groups they were not statistically significant (p=0.200).

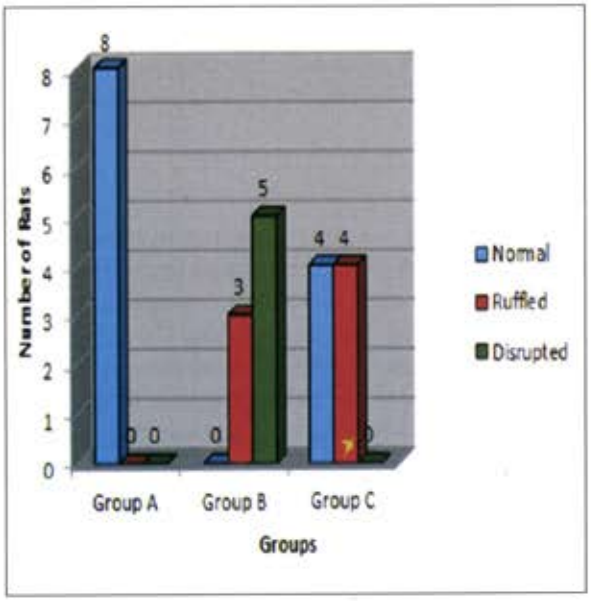


Fig-1: Bar chart showing number of rats with normal, ruffled and disrupted basement membranes in groups A, B, and C. In group A all the rats had normal basement membranes of the tubules, in group B, 3 rats had ruffled and 5 had disrupted basement membranes. In group C, 4 of the rats had normal and 4 had ruffled basement membranes. None of the rats in group C had disrupted basement membrane.

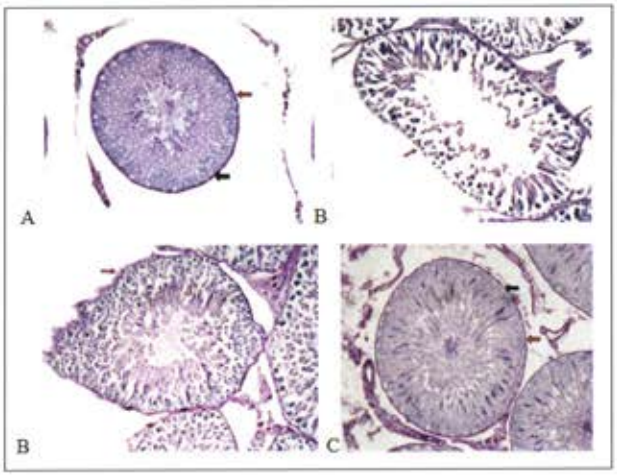


Fig-2: Photomicrographs of histological sections of testis from groups A illustrating regular (red arrow) and thin (black arrow) basement membrane, group B illustrating disrupted structure and basement membrane (red arrow) and ruffled basement membrane (red arrow), group C illustrating regular (red arrow) and thin (black arrow) basement membrane. PAS stain X400. **Diameter of Seminiferous Tubule:**

Table-1: Showing difference in the mean (with standard deviation) and median of the diameter of seminiferous tubules between control and experimental groups.

Groups	Mean ± SD	Frequency
Group A	Mean±SD	243.99±6.88
	Median (Q_1,Q_3)	14.55 (236.41-250.96)
Group B	Mean±SDI	241.42±11.45
	Median (Q_1,Q_3)	6.50 (241.20-247.50)
Group C	Mean± SD	236.10±1069
	Median (Q_1,Q_3)	7.78 (235.25-243.03)
p-value	0.200	

$p \leq 0.05$ is considered statistically significant.

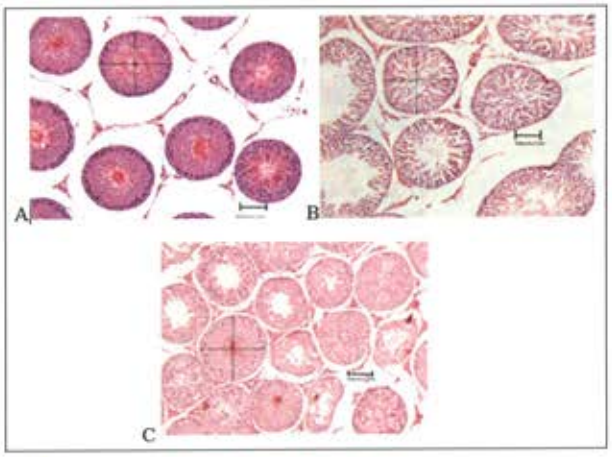


Fig-3: Photomicrograph of histological section of testis from group A showing several seminiferous

tubules; one with vertical and horizontal diameter of 247μm as measured in cross-sectional profile, from group B showing several seminiferous tubules; one with vertical and horizontal diameter of 245 μm as measured in cross-sectional profile and from group C showing several seminiferous tubules; one with vertical and horizontal diameter of 247 μm as measured in cross-sectional profile. Reference line measures 100 μm. H&E stain. X100.

Discussion

In the present study the rats of group A showed thin and regular basement membrane indicating a normal pattern. After 15 days of administration of DOP to the rats of group B,the basement membrane of the seminiferous tubules revealed the detrimental effect of DOP. Many tubules showed ruffled basement membrane, others showed disruption. The ruffled effect was seen due to the sloughing of the germinal epithelium which lead to the collapse of the tubule, resulting into ruffled appearance of the basement membranes. The disrupted basement membrane however was due to possibly the oxidative stress mechanism of the DOP which caused lipid peroxidation of the membranes.

There was not much variation in diameter of seminiferous tubules in different groups. A few tubules in groups B showing some atrophy is attributed to the sloughing of the germinal epithelium by the DOP. However, when the results were compared between different groups they were not statistically significant (p=0.200).

The results observed in the present study are in accord with the previous reports which revealed that Phthalate esters are associated with tissue damage,[23] which is responsible for the disruption of the basement membrane. In other areas atrophy of the seminiferous tubules was shown by decreased diameter of the tubules and ruffled basement membrane. However the rats in group C were given both DOP and vitamin E, it showed that DOP in this group did not have the same deleterious effect as it did in group B, where DOP was given alone. The basement membrane remained thin and regular indicating lesser or no damage to the cells in group C as compared to those in group B. This reveals a preventive effect of Vitamin E which is due to its antioxidant properties. These results of present study are in accordance with the previous study which suggests that one of the important mechanisms of testicular damage is oxidative stress caused by phthalates which dissociate easily from their compounds, particularly at high temperatures.[24] The increase in global warming, therefore poses a great threat to human health by causing the release of such chemicals into the environment. To reduce the oxidative stress, supplementation of antioxidant vitamin E is highly beneficial.[25]

It is evident from the discussion that phthalates are toxic to the normal health of testes and the use of antioxidants can forestall its deleterious effects. The facts that phthalates are being used widely in the manufactured goods;[26] the increasing utility of such items in the modern lifestyle[24]and that they are easily and constantly being ejected into the environment from the products they are used in, increase the problem many folds. The last and the most important fact is that they are a constant source of health hazard, affecting not only the present but the future generations also. Consequently this complex problem needs to be tackled elaborately at the environmental level.

Conclusion

It is concluded that our observations confirmed the previous findings on phthalate induced toxicity on rat testes. The results also show the vitamin E has a beneficial effect in preventing the histological changes in the testes of rats. Since vitamin is easily available and cheap, it can be employed in to reduce oxidative stress in the body produced by phthalates.

Department of Anotomy
SIMS/Services Hospital, Lahore

www.esculapio.pk

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Original Article

To Determine the Frequency of Concordance Between Duplex Ultrasound Scan and Ct Scan in Detection of Endo-leak in Patients Following EVAR

Muhammad Naeem Afzal, Shabbar Hussain Changazi, Muhammad Umar Warraich, Usman Ismat Butt, Samiullah Bhatti and Mustansar Iqbal

Objective: To determine the frequency of concordance between Duplex ultrasound scan and CT scan in detection of endo-leak in patients following EVAR.

Methods: This retrospective, descriptive study was conducted at Department of Vascular Surgery, Mater Misericordiae University Hospital Dublin, Ireland. The study was conducted from14thJuly, 2014 to13th July, 2016. Age range 50-70 years were included in the study. All patients who had Endovascular Aneurysm repair (EVAR) were followed up in six months' time using Duplex ultrasound scan and Computerized Tomography (CT). The detection of endo-leak on Duplex ultrasound scan and confirmed by Computerized Tomography (CT).The concordance between the two investigations was estimated by calculating the overall percentage of agreement (concordance) and the κ coefficient. The follow up imaging results were collected by using PACS (Picture archiving and communication system). All the data entered and analyzed using computer software SPSS version 17. Mean and standard deviation was calculated for quantitative variables like Age and BMI. Frequency and percentages were calculated for qualitative variables like gender, co morbidities like hypertension, DM, smoking status and concordance. Effect modifiers gender, BMI and co morbidities DM and HTN were controlled by stratification of data.

Results: Total 113 patients were enrolled in this study. In the study, mean age was 68 years with the standard deviation of 3.09. 70.8% of patients were males and 29.2% were females. 46.9% of patients had BMI of 26-30 BMI and 34.5% had BMI >30. Among the total patients, 64.6% patients were diabetic, 77% hypertensive and 88.5% patients were smokers. 70.8% of endo-leaks were diagnosed by Duplex ultra-sound scan, while 77.8% of endo-leaks were diagnosed by CT scan. Cohens kappa value is 0.91 which shows strong association. Concordance between Duplex ultra-sound scan and CT scan calculated as 95.6%.

Conclusions: This study concluded that Duplex ultra-sound scan can safely replace CT scan as a surveillance modality. Duplex ultra-sound scan can be used as a primary long-term surveillance imaging modality for patients with post EVAR and it will be more economical for patients without any loss of scan accuracy.

Keywords: endovascular aneurysm repair, endo-leak, concordance, comorbidities.

Introduction

Endovascular aneurysm repair (EVAR) is a type of endovascular surgery used to treat aneurysm of the aorta, most commonly an abdominal aortic aneurysm (AAA). The procedure involves the placement of an expandable stent within the aorta to correct aortic aneurysm without operating directly on the aorta. In 2003, EVAR bettered open aortic surgery as the most common technique for repair of AAA .[1,2] Studies that assign aneurysm patients to treatment with EVAR or traditional open surgery have demonstrated fewer early complications with the minimally-invasive approach. Some studies have also observed a lower mortality rate with EVAR .[3,4]

An endo-leak is the most prevalent and disastrous complication of EVAR and is found in 30-40% of patients intraoperatively (seen on the on-table angiogram after stent deployment), and in 20-40% during follow-up.[5] Endo-leaks are characterized by persistent blood flow within the aneurysm sac following endovascular aneurysm repair (EVAR). Normally the aortic stent-graft used for EVAR excludes the aneurysm from the circulation by providing a conduit for blood to bypass the sac.[6]Endoleak may become evident intra-operatively, years down the track, or anywhere in between. Thus, endovascular stent placement requires routine surveillance to enable detection of potential complications.

Computed tomograhic (CT) angiography is the most accepted investigative tool for monitoring patients with endografts as it yields comprehensive images that allows us to determine the diameter of the

aneurysm sac, endograft migration, and endoleak presence.[7] Nevertheless, there are two main concerns regarding CT angiographyradiation and contrast agent nephrotoxicity both of which are crucial in patients who will require lifelong surveillance.[8, 9, 10] Although magnetic resonance angiography can yield follow-up information but it must be used with caution in patients with a glomerular filtration of less than 30 mL/min because of the risk of nephrogenic systemic fibrosis, which is a complication that is also related to cumulative contrast agent exposure.[11] Color Doppler (CD) ultrasonography (US) is the noninvasivealternative for follow-up, but the reported sensitivity in endoleak detection ranges from 42% to 97%. First-generation US contrast agents did not improve the CD US results, and reported data did not support their use in EVAR follow-up.[12] Secondgeneration US contrast agents have an expanded diagnostic capability. These agents consist of gas microbubbles (perfluorcarbon or sulfur hexafluoride) encapsulated by a phospholipid shell that have nonlinear behavior when interrogated with a low-mechanical-index ultrasound beam, resulting in the emission of harmonics that can be detected with specific contrast software. The use of a low mechanical index causes minimal microbubble disruption, enabling real-time blood flow investigation over several minutes.[13] These US contrast agents can be used safely in patients with impaired renal function. The data reported at EVAR show good specificity and sensitivity, and they show that the technique can provide angiodynamic information.[14]

Methods

A retrospective, descriptive study carried out at Vascular Surgery Department Mater Misericordiae University Hospital, Dublin, Ireland from 14th July,2014 to 12th January,2015. Assuming concordance as 75% between duplex ultra-sound scan and CT Power 75%, confidence level 95%, margin of error 8%, total Sample Size(n) was calculated to be 113. Convenience sampling was done (all data available was be extracted from computerized records). All patients having aneurysm (non-rupture) and undergoing elective endovascular aneurysm repair between ages of 50-70 years were included in the study. However, patients who failed to get concurrent scans were excluded.

Data of all Patients fulfilling the inclusion criteria was included in this study. Hospital patient center data base is used to find out the patients. All patients who had Endovascular Aneurysm repair (EVAR) and followed up in six months' time using Duplex ultrasound scan and Computerized Tomography (CT). The detection of endo-leak on Duplex ultrasound scan and confirmed by Computerized Tomography (CT) as per operational definition was taken as concordance. The follow up imaging results was collected by using PACS (Picture archiving and communication system) and Patient center with the help of medical record number.

All the data entered and analyzed using computer software SPSS version 17. Mean and standard deviation were calculated for quantitative variables like Age and BMI. Frequency and percentage were calculated for qualitative variables like gender, co-morbidities like hypertension, DM, smoking status and concordance. Effect modifiers gender, BMI and co morbidities DM and HTNwere controlled by stratification of data. Post stratification chi square test were applied. A p value < 0.05 was considered statistically significant.

Results

There were total 113 cases that were enrolled in this study. Mean age found in the study was 68 years with the standard deviation of 3.09. There were 70.8% male patients (80) and remaining 29.2% were female (30). When BMI was checked most of the patients were overweight that is 46.9% cases fall in 26-30 BMI category and 34.5% were found obese that is BMI is >30. Among the total cases 64.6% patients were diabetic, 77% were hypertension, 88.5% patients were smokers. 70.8% endo-leaks were diagnosed by Duplex Ultra-Sound Scan while 29.2% were not. While 77.8% endo-leaks were diagnosed by CT scan. Cohen's kappa value was 0.91 that showed strong association. Sensitivity of Duplex ultrasound Scan was 100%,

Table-1: Distribution for endo-leak on duplex ultra sound.

Endo-leak	Frequency (%)
Yes	80 (70.8%)
No	33 (29.2%)
Total	113 (100)

Table-2: Distribution for endo-leak on CT.

Endo-leak	Frequency (%)
Yes	85 (75.2%)
No	28 (24.8%)
Total	113 (100)

while specificity 61.7%, PPV was found as 35%. Concordance between Duplex ultrasound scan and CT scan calculated as 70.8% for the presence of endo-leak and 24.8% for the absence of endo-leak between both radiological procedures.

Table-3: Endo-leak on Duplex Ulta-Sound scan.

Endo-leak on Duplex Ultra-Sound Scan	Endo-leak on CT Yes)	No	Total
Yes	80	0	80
No	05	28	33
Total	85	28	113

Table-4: Stratification with respect to gender, hypertension, smoking status and BMI for Duplex ultrasound scan.

Characteristic	Yes	No	Total	P-value
Gender	59	21	80	
	21	12	33	0.41
	80	33	113	
Hypertension	65	21	87	
	14	12	26	0.54
	80	33	113	
Smoking Status	73	33	100	
	07	27	13	0.60
	80	33	113	
BMI	O9	0	9	
	12	0	12	
	31	22	53	0.55
	28	11	39	
	82	33	113	

Discussion

Color Duplex Ultrasound (CDUS) is an inexpensive, harmless, non-invasive and widely available imaging modality which is the investigation of choice for the screening and surveillance of AAA prior to intervention. Aneurysm sac size and blood flow within the residual aneurysm sac can be determined using CDUS which could therefore be capable of replacing CT as the primary surveillance tool following EVAR. Recent guidelines from the European Society for Vascular Surgery state that CDUS is a safe and sensitive method of endo-leak detection, but caution that it should not be a standalone modality for follow up after EVAR. Although initial, reports comparing duplex ultra-sound scan with CT suggested that sensitivity and specificity were comparable. There were total 113 cases that were enrolled in this study. Mean age found in the study was 68 years with the standard deviation of 3.09. These results are inconsistent with research conducted by Greenhalghet al.,[1] illustrated the mean age of 70 years while most of the studies like Chahwan et al.,[15] showed the mean age in range of 65-75 years. In the study 70.8% cases were found as male and remaining 29.2% were female. Chahwanet al.[15] calculated 76.9% of patients as male while 23.1% patients as females.

In this study most of the patients were overweight, that is 46.9% cases fell in 26-30 BMI category and 34.5% were found obese with BMI >30. Park et al.[16] in their research evaluated that obesity was the one of the most important factor that leads to the procedures like EVAR. In this study, 64.6% patients were found diabetic. Committee (2005)[17] in a study showed 68% DM patients that underwent EVAR. 77% of participants were hypertensive, 88.5% patients were smokers and 11.5% patients were non-smokers. Gidlundet al.[18] showed significant association of hypertension with EVAR patients. In this study,70.8% endo-leaks were diagnosed by Duplex Ultra-Sound Scan while 29.2% were not. While 77.8% endo-leaks were diagnosedby CT scan. Cohen's kappa coefficient was 0.91 that shows strong association. Sensitivity of Duplex ultra-sound scan was 100%, while specificity was 61.7%. PPVwas found as 35%. Gray et al.[19] in a research showed that CDUS was found to have a sensitivity of 100% and a specificity of 85.7% in the detection of endo-leaks. The positive predictive value was 28.7% and negative predictive value 100%. In this study, there were no endo-leaks which were detected on CT but missed on CDUS. Manning and colleagues[20] in a series of 132 patients reported values similar to our own, documenting a 45% positive and 94% negative predictive value for CDUS when compared to CT for postoperative surveillance following EVAR. Specificity of CDUS for endo-leak detection was 67% when compared with CTA and sensitivity for CDUS was 86%. Their conclusions was broadly similar, suggesting CDUS as a first line screening tool which allowed selection of a smaller cohort of patients in whom CT was necessary.

Conclusion

It is concluded that Duplex ultra-sound scan safely replace CT scan and it can be considered as a primary long-term surveillance imaging modality for patients with post EVAR that may be economical for patients without any loss of scan accuracy. However, abnormalities that may result in Duplex ultra-sound scan can be further proceeded to CT scan in a very small group of patients.

Department of Surgery
SIMS/Services Hospital, Lahore

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Original Article

Frequency of Low Bone Mineral Density in Local Population at Rahim Yar Khan

Javed Iqbal, Tahir Bashir, Asif Mehmood, Tahira Liaquat, Shazia Shabnam and Mazhar Hussain

Objective: To determine the frequency of low bone mineral Density in different age groups and sex of local population at Sheikh Zayed Medical college, Rahim Yar Khan .

Methods: This cross sectional comparative study was carried out at the Outpatient Department of Medicine Sheikh Zayed Medical college Rahim Yar Khan from January 2016 to December 2016. Patients from both genders were recruited for the study. Three thousand fifty two patients were included in the study. Brief history was taken and height and weight were recorded and Bone Mineral Density (BMD) was calculated. Bone mineral density was measured in all patients by DXA scan.

Results: Out of 3052 patients, 37.1% belong to age less than 30 years and 47.9% belong to age between 31 to 50 years and 15% were more than 50 year of age. Out of 3052 patients, 42.5% were male and 57.5% were female. Out of these patients 1809 (59.3%) had normal BMD while 1243 (40.7%) had abnormal BMD. out of these, 1142 patients (37.4%) had osteopenia, while 101 patients (3.3%) had osteoporosis. The lowest BMD values were observed in the age group more than 50 years, where 47.1% had normal BMD, 40.5% had osteopenia and 8.1% had osteoporosis. While in the age group between 31-50 year, 58.3% had normal BMD, 38.7% had osteopenia and 2.9% had osteoporosis. While in age group less than 30 years 65.4% patients had normal BMD, 32.7% had osteopenia and 1.9% had osteoporosis. Regarding sex, out of 1297 male patients 57.2% had normal BMD. 39.2% had osteopenia and 3.6% had osteoporosis. Out of 3052 patient 1755 were female. About 60.8% had normal BMD, while 36.1% had osteopenia and 3.1% had osteoporosis.

Conclusions: The study showed high prevalence of low bone mineral Density in local population of Rahim Yar Khan in both females as well as males. This study showed that in comparison with female, male patients also need special attention to their bone health.

Keywords: bone mineral density, osteopenia, osteoporosis.

Introduction

Osteoporosis is a skeletal disorder characterized by a loss of bone osteoid that reduces bone integrity and bone strength, predisposing to and increase the risk of fractures.[1] The frequency of fracture varies with ethnicity, sex, and age.[2] Osteoporosis can be caused by a verity of factors, the most common causes are aging, sex hormone deficiency, alcoholism, smoking and high dose glucocorticoid administration. Salty food preference and coffee consumption is also associated with osteoporosis.[3,4] Greater Intake of Fruit and Vegetables Is associated with Greater Bone Mineral Density and Lower Osteoporosis Risk in Middle-Aged and Elderly Adults.[5] Certain diseases like rheumatoid arthritis, renal diseases and chronic obstructive pulmonary diseases.[3,6] Low level of vitamin D and heavy metal exposure is also considered risk factor for osteoporosis.[7,8] Low lean mass is associated with osteopenia and osteoporosis.[9] Smoking and chronic hepatitis is also associated with osteoporosis.[10,11] Bone mineral density is typically expressed in g/cm^2 per cm^2, for which there are different normal ranges for each bone and for each type of dual energy x-ray absorptiometry (DXA) measuring machine.[2,8] The T score is a simple way of reporting bone density in which the patient's bone mineral density is compared to the young normal mean and expressed as a standard deviation score.[1,2,12] The world health organization has established criteria for defining osteoporosis based upon the T score. Surveillance with DXA bone densitometry is recommended for postmenopausal woman and elderly men with a frequency according to their T score. DXA scan should be obtained every 5 years for T score -1.0 to -1.5, every 3-5 years for score -1.5 to -2.0,, and every 1-2 years for score under -2.0.

Methods

This cross sectional comparative study was carried out at the Outpatient Department of Medicine Sheikh Zayed Medical college Rahim Zayed Medical

college Rahim Yar Khan from January 2016 to December 2016. All the patients were included through non-probability purposive sampling. After informed consent, brief history was taken. Ethnicity was determined by asking the place of origin. Patients of both genders were recruited for the study. Height and weight were recorded in cm and kg respectively. BMD was calculated. Bone density was measured in all patients by DXA scan Pegasus smart serial no 0114 PG 2183. To cover technical aspects and errors we checked BMD by using same machine and same operator.

Data had been analyzed using SPSS version 20. Mean and standard deviation (SD) were calculated for qualitative variables while frequency and percentages were calculated for quantitative variables. Chi-square test was applied to study association of bone mass with gender. A p-value < 0.05 was considered as significant.

Results

Out of 3052 patients, 37.1% belong to age less than 30 years and 47.9% belong to age between 31 to 50 years and 15% were more than 50 year of age **(table 1).** Out of 3052 patients, 42.5% were male and 57.5% were female**(table 2).** Out of these patients 1809 (59.3%) had normal BMD (bone mineral density) while 1243 (40.7%) have abnormal BMD. out of these patients with abnormal bone mineral density, 1142 patients (37.4%) had osteopenia, while 101 patients (3.3%) had osteoporosis **(table 3).** The lowest BMD values were observed in the age group more than 50 years, where 47.1% had normal BMD, 40.5% had osteopenia and 8.1% had osteoporosis. While in the age group between 31- 50 year, 58.3% had normal BMD, 38.7% had osteopenia and 2.9% had osteoporosis **(table 4).** While in age group less than 30 years 65.4% patients had normal BMD, 32.7% had osteopenia and 1.9% had osteoporosis. Regarding sex, out of 1297 male patients 57.2% had normal BMD. 39.2% had osteopenia and 3.6% had osteoporosis. Out of 3052 patient 1755 were female. About 60.8% had normal BMD, while 36.1% had osteopenia and 3.1% had osteoporosis**(table 5).**

Table-1: Age distribution.

	Age	Frequency	Percent	Valid percent	Cumulative%
Valid	10-30 years	1131	37.1	37.1	37.1
	31-50 years	1462	47.9	47.1	85.0
	>50 years	459	15.0	15.0	100.0
	Total	3052	100.0	100.0	

Table-2: Sex distribution.

	Sex	Frequency	Percent	Valid percent	Cumulative%
Valid	Male	1297	42.5	42.5	42.5
	Female	1755	57.5	57.5	100.0
	Total	3052	100.0	100.0	

Table-3: Bone mineral density.

	BMD	Frequency	Percent	Valid percent	Cumulative%
Valid	Normal	1809	59.3	59.3	59.3
	Osteopenia	1142	37.4	37.4	96.7
	Osteoporosis	101	3.3	3.3	100.0
	Total	3052	100.0	100.0	

Table-4: Age/Bone Mineral Density (Crosstabulationcan.).

			Bone Mineral Density			
			Normal	Osteopenia	Osteoprorosis	Total
Age	10 - 30 yrs.	Count	740	370	21	1131
		% Within Age	65.4%	32.7%	1.9%	100.0%
		% Within Osteoporosis	40.9%	32.4%	20.8%	37.1%
		% of Total	24.2%	12.1%	0.7%	37.1%
	31- 50 yrs.	Count	853	566	43	1462
		% Within Age	58.3%	38.7%	2.9%	100.0%
		% within Osteoporosis	47.2%	49.6%	42.6%	47.9%
		% of Total	27.9%	18.5%	1.4%	47.9%
	> 50 yrs.	Count	216	206	37	459
		% Within Age	47.1%	44.9%	8.1%	100.0%
		% Within Osteoporosis	11.9%	18.0%	36.6%	15.0%
		% of Total	7.1%	6.7%	1.2%	15.0%
Total		Count	1809	1142	101	3052
		% Within Age	59.3%	37.4%	3.3%	100.0%
		% Within Osteoporosis	100.0%	100.0%	100.0%	100.0%
		% of Total	59.3%5	37.4%	3.3%	100.0%

Table-5: Sex/Bone Mineral Density (Cross tabulation)

			Bone Mineral Density		
		Normal	Osteopenia	Osteoprorosis	Total
Sex	Male	Count	742	508	471	1247
		% Within Age	57.2%	39.2%	3.6%	100.0%
		% Within Osteoporosis	41.0%	44.5%	46.5%	42.5%
		% of Total	24.3%	16.6%	1.5%	42.5%
	Female	Count	1067	634	54	1755
		% Within Age	60.8%	36.1%	3.1%	100.0%
		% within Osteoporosis	59.0%	55.5%	53.5%	57.5%
		% of Total	35.0%	20.8%	1.8%	57.5%
Total		Count	1809	1142	101	3052
		% Within Age	59.3%	37.4%	3.3%	100.0%
		% Within Osteoporosis	100.0%	100.0%	100.0%	100.0%
		% of Total	59.3%	37.4%	3.3%	100.0%

Discussion

Osteoporosis is a major problem of health care delivery services, both in the developed and developing countries. It is a common public health problem which has significant mortality and morbidity due to associated fracture risk. In a study, Bone mass density was lower in immigrant women from Somalia who were living in Sweden, in relation to both the American and the African-American populations. Vitamin D supplementation should be considered to prevent osteomalacia, osteoporosis and future fractures.[13] Evidence from one other trial of screening to prevent osteoporotic fractures suggests that treatments reduce the risk of hip, vertebral and non-vertebral fractures.[14] A study on osteoporosis in men shows that Osteoporosis in men remains under-diagnosed and less appreciated. After a minimal trauma and fracture, men usually do not seek evaluation and treatment. The lifetime risk for osteoporotic fracture in older men may range from 13 to 25%. Due to fear of side effects of treatments and other reasons management in men at risk for fracture is challenging.[15] So it is important to know about its prevalence in our population. After the initial observations and definitions of osteoporosis based on Caucasian populations, systematic research in Asian populations started in the 1980s. Significant variations between different ethnic groups with respect to the rate of osteoporotic fractures, bone mineral density and disease risk factors emerged from the data. Osteoporosis is therefore not a homogeneous disease across the world. There is very limited work done in Pakistan for measuring the frequency of this serious health problem.

Conclusion

The study showed high prevalence of low bone mineral density in local population of Rahim Yar Khan in females as well as in males. This study showed that in comparison with female, male patients also need special attention to their bone health. The results in various ethnic groups are comparable, however various factors are affecting bone health so, further multicentre studies at larger scale are recommended.

Department of Medicine
Sheikh Zaid Medical, Rahim Yar Khan Lahore

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Original Article

Indications, Findings and Complications of Upper Gastrointestinal Endoscopy Procedures in a Tertiary Care Hospital of Pakistan

Mamoona Ghias, Tazeen Nazar, Bilal Aziz, Ambren Butt, Aqsa Naseem, Shandana Tarique and Sajid Abaidullah

Objective: To determine the frequency of indications, findings and complications in patients undergoing upper gastrointestinal endoscopy.

Methods: After taking an informed consent, patients presenting for esophagogastroduodenoscopy (EGD) to the endoscopy suite of South Medical Ward were selected for the study using non probability consecutive sampling technique.Astructured questionnaire was used to collect the data. Data was analyzed using SPSS version 26.0.Results were presented in the form of mean and SD, figures and tables.

Results: Out of a total of 255 patients, mean age of the patients was 49.3 years out of which 137 (53.7%) were male and 118(46.7%) were female. Eighty seven (34.1%) patients underwent EGD due to upper gastrointestinal bleeding (UGIB). 57(22.4%) had follow up banding and 41(16.1 %) had screening for varices. 31(12.2%) patients had acid peptic disease. In 4 (1.6%) patients significant bleeding occurred and in 9(3.5%) hypotension was the complication. One patient had hypoxemia, five had minor bleeding and two had post procedure aspiration pneumonia.

Conclusions: Upper GI bleed followed by follow up banding was the main indicationin our patients,varicealhaemorrhage was the most common cause of UGIB.

Keywords: endoscopy, UGIB, Varicealhaemorrhage.

Introduction

Esophagogastroduodenoscopy (EGD) is the gold standard test for the investigation of upper gastrointestinal symptoms, like upper GI bleed, epigastric pain etc. It allows direct visualization of mucosa, and if required, diagnostic and therapeutic intervention. Mayo hospital being one of the largest hospitals in South-East Asia, receives around 5 hundred thousand patients in emergency room (ER) per year.[1]One of the commonest presentations in medical ER is upper GI bleed which requires EGD on urgent basis. So, this study was done to determine the frequency of indications, procedure findings and complications associated with EGD and limitations regarding endoscopy department in South medical Ward, Mayo Hospital, for future improvement.

Common indications for EGD include acute gastrointestinal bleeding originating in the upper gastrointestinal tract, gastroesophageal reflux, screening or surveillance of Barrett's oesophagus, peptic ulcer disease, portal hypertension, to take gastric and duodenal biopsy, isolated dysphagia and/or odynophagia, persistent isolated nausea or vomiting, dyspepsia , chronic anaemia and/or iron deficiency. [2]Acute upper gastrointestinal bleeding (AUGIB) is a common medical emergency, with an annual incidence of 133/100,000 [3] corresponding to approximately one presentation every 6 min in the UK [3]In a prospective series of 1000 cases of UGI bleeding, peptic ulcer was the most common cause (55%) followed by esophageal varices (14%)[4,5] In another data, peptic ulcer disease was responsible for only 21% of episodes of UGI bleeding and esophageal varices for 12% of episodes[6] Complications of upper gastrointestinal endoscopy are rare, but clinicians need to be able to recognize complications when they do occur so appropriate treatment can be undertaken. Sedation is the source of a large proportion of these adverse events, the majority of which are cardiopulmonary complications. Perforation is more common with dilation and endoscopic mucosal resection than with routine upper endoscopy, but overall is still rare. Infectious complications of upper endoscopy are especially uncommon. Bleeding is unlikely during routine upper endoscopy with and without biopsy. Patients taking antithrombotic agents should have the risks of stopping these medications weighed against the risk of the procedure.[3]A large case series report adverse effects 1 in 200 to 1 in 1000, and mortality ranging from 1 in 2000.

Despite advances in endoscopy, service provision, mortality following UGIB has remained high over the last two decades and currently stands at approximately 10%.[7] The purpose of this study is to establish the frequency of indications, findings and complications associated with upper GI endoscopy. It will also help to point out local disease pattern and the shortcomings that we have regarding our endoscopy unit.

Methods

This Cross-sectional Study was conducted in Mayo Hospital, Lahore from June, 2018 to December, 2018. 255 patients presenting to the endoscopy unit of South Medical Ward were selected using Non-probability Consecutive Sampling Technique. Patients of both genders in the age group of 13-80 years were enrolled in the study. Patients having a valid indication for EGD were referred from outpatient, in-patient and Accident and Emergency Department. Patients with hemoglobin <8g/dl, oxygen saturation <90% as assessed by finger pulse oximeter, having a blood pressure of <90/60 mm Hg were not included in the study. Also patients who were in hepatic encephalopathy, having active cardiac disease or psychiatric illness and those having cervical spine disease were excluded from the study. An informed consent was obtained from all the patients. Olympus GIF-240 Endoscope was used, all procedures were performed by experienced endoscopists. 4% Xylocaine solution was used for gargles for local anesthesia. Intravenous midazolam was given to non-cirrhotic and anxious patients. Esophageal varices were ligated using six-shooter multiple band ligator. Fundal varices were injected with Inj. Histoacryl. Diluted inj. Adrenaline was used as a vasoconstrictor agent. Parameters recorded were age, gender, viral serology for hepatitis B and C, complete blood count, indications for the procedure, procedure findings, complications and histopathology results. All the data was analyzed using computer software SPSS version 26.0. Quantitative data was recorded and presented in the form of Mean± SD. Qualitative data was presented as frequency and percentages.

Results

Out of 255 patients, minimum age was 13 years and maximum 90 years with mean±SD of 49.3± 13.39 years.137(53.7%) were male and 118(46.7%) were female. 87(34.1%) patients underwent EGD due to UGIB. 57(22.4%) had follow up banding and 41(16.1 %) had screening for varices. 31(12.2%) patients had APD (table 1). 242(94.9%) were HbsAg negative and 13(5.1%) were positive. 163(63.9%) were HCV positive out of which 100(61.3%) were newly diagnosed and 92(36.1%)patients were negative. 39(15.3%) were given sedation. 131(51.4%) patients had Esophageal varices on EGD. 39(15.3%) had gastropathy , 18(7.1%) had fundal varix, 16(6.3%) patients had hiatal hernia and 10(3.9%) had gastric or duodenal ulcers, 2 of which underwent endoclipping, 4underwent vasoconstrictor injection therapy and rest were managed medically(table 2). 31(12.2%) had non-specific gastritis on biopsy, 9(3.5%) had H pylori and 6(2.4%) had squamous cell carcinoma in rest of patients biopsy was not taken. Mean haemoglobin level was 9.7g/dl with SD of 1.39g/dl. In 4(1.6%) patients significant bleeding occurred and in 9(3.5%) hypotension was the complication .1 patient had hypoxemia, 5 had minor bleeding and 2 had post-procedure aspiration pneumonia. Non-availability of a recovery room, recovery drugs and location of the endoscopy suite far from the parent medical ward were the main limitations.

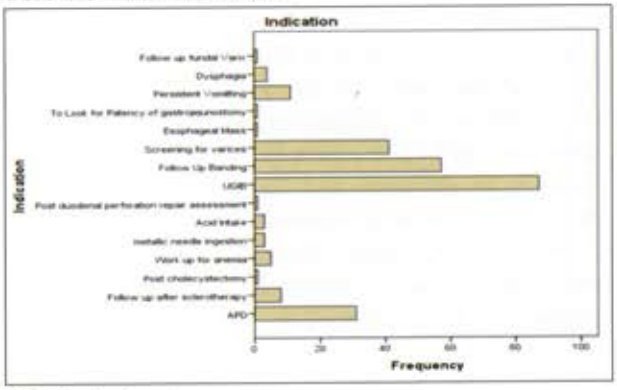

Fig-1: Indication.

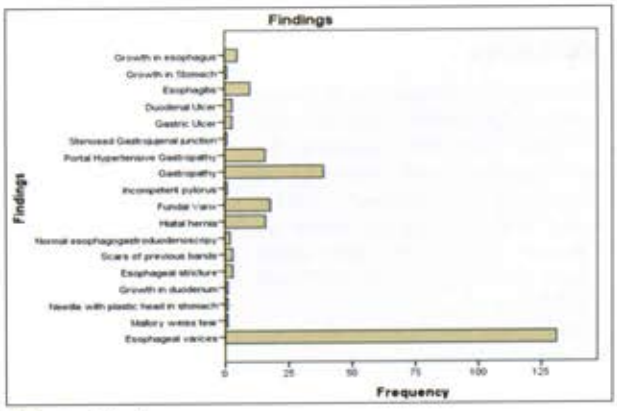

Fig-2: Findings.

Discussion

Real time assessment and interpretation of the findings encountered can be effectively done with

upper GI endoscopy that includes visualization of the oropharynx, esophagus, stomach, and proximal duodenum[8]. It is a widely used procedure in almost all parts of the world. In has an important diagnostic value for peptic ulcer disease, varices, malignancies, strictures etc. It is also used for surveillance of Barrett'soesophagus, variceal banding, injection sclerotherapy and malignancies etc. Diagnostic biopsies can be performed and hemostasis can be achieved via different techniques and dilation or stenting for significant strictures. A study from Netherlands reported that in a period of 20 years the diagnostic yield of upper GI endoscopy showed significant changes. Reflux disease increased in prevalence while peptic ulcer disease had decreased.[9] These results do not match the findings of our study as in our study upper GI bleed patients had the largest proportion. In a retrospective study done in Kenya, dyspepsia was the main reason for referral, but the majority of such patients had normal findings. In contrast in our study only a small number of patients had normal findings i.e., 0.8%, and majority had abnormal findings. This can be attributed to good pre-procedure assessment of indication.In patients with dysphagia, cancer of the oesophagus was the main diagnosis.[10] So referrals should be for alarm symptoms and with proper assessment of indication to decrease the health care burden especially in developing countries.

In another study from Tanzania, oesophageal varices were the most frequent cause of upper GI bleeding (51.3%) followed by peptic ulcers in 25.0% of cases.[11] In in our study also the main indication for upper GI endoscopy referral was upper GI bleed i.e. 34.1%. This may be attributed to low socioeconomic status, low literacy level, unawareness of preventive methods and common use of herbal treatments and over the counter drugs.All these factors result in late seeking of medical attention when the disease is already advance. Mean hemoglobin was also very low among our study patients that further indicate poor health status. Complications are rare but can be fatal at times. So an endoscopist must have proper knowledge and management skills of possible complications.

Quality indicators for EGD were followed to the best possible level according to American Society for Gastrointestinal Endoscopy (ASGE) guidelines.[12] Lack of trained anesthetist, shortage of recovery medications, lack of resuscitation area and recovery room were the main limitations. Living in a developing country with a large population and a very high doctor to patient ratio, proper pre-procedure assessment should be made to manage the burden in public sector hospitals. More equipped units and trained staff is needed to decrease mortality associated with emergencies that can be managed with EGD.

Conclusion

Upper GI bleeding due to variceal hemorrhage is the most common indication for EGD in our setup. We recommend mass screening for chronic hepatitis B and C to be done at nationallevel. Provision of trained staff, well-equipped endoscopy suites are the need of the hour to ensure decreased morbidity and mortality associated with upper GI bleeding irrespective of the etiology.

Department of Medicine
KEMU/Mayo Hospital, Lahore

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Original Article

Primary Repair of Oesophageal Perforation, An Experience of 64 Cases

Amer Bilal, Abdul Baseer and Muhammad Imran

Objective: To assess the outcome of primary repair of Oesophageal Perforation

Methods: Sixty four patients who underwent primary repair of Oesophageal perforation from June 2002 to May 2016 were retrospectively analyzed. Patients of all ages, both sexes and benign thoracic oesophageal perforation were included. Patients were admitted through emergency department as a referred case .Contrast study was done after stabilization. Right thoracotomy done for upper and mid level thoracic esophageal perforation whereas left thoracotomy was done for lower end thoracic esophageal perforation. Contrast study was done on 7thpost operative day. Six months follow- up was done in all cases. Variables measured were postoperative leakage, stricture formation, morbidity and mortality.

Results: Out of 64 patients, male to female ratio was 2:1, age ranges from12 to 65 years with a median age of 38 years. Perforation was caused by iatrogenic instrumentation in 49 patients, trauma in 9and ingested foreign bodies in 6. In all patients initial chest x ray was done, location of perforation was confirmed by gastrograffin study involving upper third thoracic esophagus in 14 cases , middle third 21 and lower third in 29 cases. Morbidity was 11/64 (17.18%) and mortality was 4/64 (6.25%). At 6 months follow-up, all 56 surviving patients were able to eat a normal diet.

Conclusions: Primary repair and tissue reinforcement of benign oesophageal perforation is safe in early cases and obviates the need for a second operation, while preserving the natural GI tract.

Keywords: esophageal perforation, thorax, benign, primary repair.

Introduction

Esophageal perforation causes significant morbidity and potential mortality. Determinants of morbidity and mortality are the cause of the injury, location of the injury along the esophagus, and delay in diagnosis and treatment. Spontaneous perforation, such as postemetic Boerhaave's syndrome, accounts for up to 36% of esophageal perforation, 19% of iatrogenic injuries, and 7% of external trauma.[1]

The frequency of perforation of the esophagus is 3 in 100000 in the United States.[2] A perforation is a hole through which the contents of the esophagus can move in the mediastinum, the area around the chest. Esophageal perforation can occur at any age and at any level depending upon the cause. Esophageal perforation presents as an emergency because treatment delay reduces survival. Iatrogenic perforation, spontaneous perforation, and trauma account for a large majority of esophageal perforation.[3,4] Endoscopic procedures are the most common cause of iatrogenic esophageal perforation. Perforation usually occur in the left posterior aspect of the lower esophagus and are five times more frequent in male.[2] Further more, diagnosis is frequently delayed, and the large number of possible interventions has made management controversial. Nontheless there is an increasing consensus that primary repair affords the patient the best likelihood of survival with minimal morbidity.[5,6,7] We have repaired primarily all non malignant thoracic esophageal perforations when the esophagus has been considered salvageable. In this report we review our results with 64 consecutive attempts at primary repair of non malignant thoracic esophageal perforation.

Methods

Computerized clinical record of 64patients who underwent primary repair of esophageal perforation from June 2002 to May 2016 was retrospectively analyzed carefully for surgical outcome. Patients of all ages, both sexes and diagnosed iatrogenic benign thoracic esophageal perforation were included. Malignant esophageal perforation and iatrogenic benign cervical and abdominal esophageal perforation were excluded from the study. All patients were admitted through emergency department as referred case. Immediate management was resuscitation and chest intubation for the pneumothorax or empyema; all patients were kept in ICU, contrast study was done in all cases after

stabilization.Perforations of the upper and middle third of the esophagus were approached from the right side through the fourth through sixth intercostal space, depending on location, while injuries to the distal third of the esophagus were managed from the left side of the chest, through the seventh intercostal space.

Procedure included primary repair of esophageal perforation including separate closure of mucosal and muscle layer by continuous suturing after refreshing the margins and buttressing the anastomotic area with intercostals muscle flap followed by Witzel feeding Jejunostomy. Feeding through jejunostomy tube was started on second postoperative day, while contrast study was done on seventh post operative day on all patients. Variable measures were postoperative leakage, stricture formation, morbidity and mortality of the primary repair.

Results

Out of 64 patients, 41 patients were males and 23 were females, ages ranged from 12 to 65 years with a mean age of 38 years **(Table-1).**Esophageal perforation was caused by instrumentation in 49patients , ingested foreign body in 6 and trauma in 9 **(Table-2).** Among the foreign bodies 3 patients had ingested batteries, 2 had coin ingestion whereas 1 had chicken bone. 20 patients had pre existing esophageal disease: achalasia in 16 hiatus hernia in 2, and reflux stricture in 2. All patients presented more than 12 hours after the perforation.

In all patients initial chest x ray was done, location of perforation was confirmed by gastrograffin study involving upper third thoracic esophagus in 14 cases , middle third 21 and lower third in 29 cases. 7 patients developed post operative leak which were managed conservatively and healed after 3 weeks. 3 patients developed wound infection and 1 patient developed stricture which responded well to dilatation. 3 patients died due to respiratory complications and one died due to myocardial infarction, others had complete recovery **(Table-3).** At 6 months follow-up all 64 surviving patients were able to eat a normal diet.

Table-1: Preoperative data of patients.

Variable		n=	% age
Sex	Male	41	64.0625
	Female	23	35.937
	Age rage (years)	12-65	12-65
	Mean age (years)	38	38

Table-2: Eitologyt.

Factors	n=	Percentage
Instrumental	49	76.56
Foreign Body	06	9.37
Trauma	09	14.06

Table-3: Complications.

Complication		n=	% age
Morbidity		11	17.18
	Post operative leak	7	10.93
	Postoperative stricture	1	1.56
	Wound infection	3	4.68
Mortality		4	6.25
	Respiratory complication	3	4.25
	Myocardial infection	1	1.56

Discussion

Esophageal perforations remain a challenging problem with significant morbidity and mortality[7]Recognition of the importance of early diagnosis and aggressive definitive surgical intervention has brought about a dramatic decline in mortality related to esophageal perforation.[8,9] Esophageal perforation is usually iatrogenic [10], the result of endoscopic procedures[11] such as esophageal dilatation for strictures and for achalasia in particular [12].In our study 83.34 % cases esophageal perforation was caused by the iatrogenic injury secondary to endoscopy.

Male predominance has been reported by Fry L C in series of 248 cases.[13] In our study male to female ratio was 2:1. In a review from Masssachusetts General Hospital, Wright et al, described the treatment of 28 patients with esophageal perforation.[14] Wright concluded that patients who present with sepsis have an increased risk of post-operative leak and therefore should have the repair buttressed. Wright had reported incidence of post operative leak in 11% of patients post operatively in patients who were operated with in 24 hours. In our study we have observed post operative leak in 10.93% cases (7/64).Whyte and Orringer described the management of 22 patients with esophageal perforations.[15] Both Wright and Whyte emphasized that in the absence of cancer or an irreversible distal obstruction, meticulous repair of the esophageal perforation with reinforcement by either fundoplication or revascularized pedicle of muscle or pleura is the preferred approach, in as much as primary healing is likely and the morbidity associated with prolong drainage or diversion may be avoided. According to various studies, primary repair can be carried out in most cases of thoracic esophageal

perforation, with a low mortality rate and esophagectomy should be reserved for patients with carcinoma or extensive necrosis of theesophagus.[16-25]

In our study we have used intercostals muscle flap to buttress the primary repair in all cases. In a study by Ayed AK at Kuwait University for esophageal perforation due to benign cause primary repair and tissue reinforcement is safe in early cases and obviates the need for a second operation.[26] In our study we did Witzel feeding Jejunostomy in all cases as a safety net as total parentralnutrition is very expensive and is not available in our setup. Feeding through jejunostomy tube was started on second postoperative day, while contrast study was done on seventh post operative day on all patients. Acute esophageal perforations of a functional esophagus are best treated with early primary closure with buttressing of the repair with intercostal muscle with nutritional support in the form of Feeding Jejunostomy. In our series this has resulted in very good result in that all 56 surviving patients were eating normally on 6 months follow up. A success rate of 56/64 (87.50%), with a morbidity and mortality of (17.18%, 6.25 %) respectively is not only acceptable but desirable in a condition which previously use to carry formidable morbidity and mortality of >20%&>30%)respectively.[9,27]

Conclusion

Esophageal perforation has high morbidity and mortality. Mostly are iatrogenic. Management option include primary repair with tissue flap buttress or esophageal diversion±resection. Primary repair is applicable to many nonmalignant intrathoracic esophageal perforations. Principle of surgery includes complete exposure of the limits of the mucosal injury, a meticulous 2 layer closure, tissue reinforcement from intercostals muscle and total elimination of distal obstruction are essential. Primary repair with tissue flapbuttress is required in late (>6hrs) esophageal perforation because of sepsis and possible post operative leak. Feeding jejunostomy is a useful adjunct for looking after the nutritional side in a cost effective manner. This approach of primary repair reinforced with intercostals muscle flap and adjunct feeding jejunostomy should be taken for all in trathoracic benign esophageal perforation. This result in very acceptable morbidity and mortality of17.18 %% & 6.25 % respectively and all survivors were eating normally at six months follow up.

Cardiothoracic Surgery Unit,
Medical Teaching Institution,
Lady Reading Hospital, Peshawar, Pakistan.

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Answer Picture Quiz

Answer:

The abnormality is in the sclerathe tough white outer coat of the globe. A large area of necrotic sclera can be seen extending around the superonasal side of the cornea. The abnormality is in the sclerathe tough white outer coat of the globe. A large area of necrotic sclera can be seen extending around the superonasal side of the cornea. Non-necrotising scleritis presents as a red sore eye, but the white avascular area of sclera seen here is indicative of necrotising disease. Necrotising scleritis can be associated with several connective tissue disorders, the most common being Wegener's granulomatosis. The combination of necrotising scleritis, upper airway symptoms, and constitutional symptoms strongly suggest this as the diagnosis. Necrotising scleritis is associated with a medical disorder in 39-50% of cases, particularly connective tissue disease or systemic vasculitis.1 2 History taking, examination, and investigations should centre on a differential diagnosis of systemic lupus erythematosus; rheumatoid.

Original Article

Frequency of Retinopathy in Patients With Newly Diagnosed Type II Diabets Mellitus Along with Microalbuminuria

Farrukh Maqsood, Hafiz Muhammad Tahir, Muhammad Adnan Hasham, Abida Pervaiz, Naz Akram and Sajid Nisar

Objective: To find the frequency of retinopathy in patients with recent onset of non-insulin dependent diabetes mellitus along with microalbuminuria.

Methods: It was conducted in Medical unit 4, Services Hospital, Lahore over a period of 6 months. It is a descriptive cross-sectional study.

Results: In our study, out of 85 cases, 25.88%(n=22) were between 18-50 years of age whereas 74.12%(n=63) were between the age range of 51-80 years, mean+sd was measured as 56.62+9.19 years, 56.47%(n=48) were male while 43.53%(n=37) were females. The presence of retinopathy in cases of type II diabetes mellitus of recent onset was recorded in 31.76% as a frequency(n=27).

Conclusions: We concluded that microalbuminuria is associated with diabetic retinopathy in cases with recent onset of type II diabetic patient and may be considered as a reliable marker of retinopathy.

Keywords: newly diagnosed type ii diabetes mellitus, microalbuminuria, retinopathy.

Introduction

Type 2 diabetes has been emerging a global problem and now the problem has been at its peak encasing many regions of the world. The individuals with diabetes mellitus are having greater risk of complications that occur as a result of this disease. One of the manifestations of diabetic eye involvement is in the form of retinopathy that leads to blindness, and this is preventable. However, incidence of retinopathy has been less prevalent in some Asian countries[1], but during the next decade the frequency and severity of diabetic retinopathy will hugely emerge as a result of increase in sedentary life style, the effect of urbanization, increasing obesity and longer lifespan. [2] Diabetic retinopathy is a markedly specific complication of vascular origin and is a vison-threatening problem seen in diabetes mellitus.[3] Patients having 30-40% risk of nephropathy with type 1 diabetes after 20 years in comparison with the individuals having type 2 diabetes mellitus. In these patients there is a relatively low prevalence, about 15%, of the cases having kidney related problems.[4] However the locally published data is scanty and does not tell us the relation of various complications particularly retinopathy risks in Pakistan.[5] A local study determined the frequency of diabetic retinopathy in newly diagnosed patients of type 2 diabetes mellitus with microalbuminuria as 21.66%.[6] An other recent local study recorded these findings in 51.61% of the cases.[7] The rationale of the study is that two recent local studies are showing a significantly difference regarding frequency of retinopathy in individuals with recent onset of type II diabetes mellitus along with microalbuminuria. We consider it necessary to record findings in our population so that the exact frequency may be determined which will be helpful for the patients and physicians.

Methods

The study was carried out in in-patient department of Medical unit 4, SHL. Eighty-five patients sampled with 95% confidence level, 9% margin of error taking expected %age of diabetic retinopathy i.e. 21.6%[6] in these individuals with recent onset of type II diabetes mellitus. It was a cross-sectional non-probability convenience sampling. Patients between age 18-80 years, of both genders (male/female) and newly diagnosed cases of type II diabetes mellitus as evidenced by raised venous glucose on 2 separate occasions i.e. fasting≥126mg/dl, or random >200mg/dl (any one of these on medical record) along-with ≥30 mg/24 hr microalbuminuria (confirmed by urine complete examination) were included in the study. All those cases were eliminated from our study that were under treatment of diabetic retinopathy (on history and medical record). Detailed history of the individuals for diabetes mellitus and microalbuminuria was recorded and these cases were followed through fundoscopy with the help of a single consultant ophthalmologist to diagnose retinopathy. The presence/absence of retinopathy was recorded by the researcher herself. Data was

entered and analyzed using SPSS version 18.0. Mean and standard deviation was calculated for quantitative variable like age and duration of diabetes mellitus. Frequencies and percentages were calculated for qualitative variables like gender and diabetic retinopathy. The data was stratified for age, gender, levels of HbAc1, duration of disease to control the effect modifiers. Post stratification chi square test was used as a test of significance by using p value <0.05 as significant.

Results

A total of 85 individuals were selected in the light of inclusion and exclusion criteria in order to find the frequency of retinopathy in patients with type II diabetes mellitus of recent onset along with microalbuminuria. Age distribution of the patient was done, it shows that 25.88%(n=22) were between 18-50 years of age whereas 74.12%(n=63) were between 51-80 years of age, mean±sd was calculated as 56.62+9.19 years. (**Table-1**) Gender distribution of the patients showed that 56.47%(n=48) were male while 43.53%(n=37) were females. (**Fig-1**) Mean duration of diabetes mellitus was calculated as 5.22±1.97. (**Table-2**) Frequency of retinopathy in cases with type II diabetes mellitus of recent onset was recorded in 31.76%(n=27) while 68.24%(n=58) had no findings of retinopathy. (**Fig-2**)

Table-1: Age distribution (n= 85)

Age (in Years)	No. of Patients	% age
18 - 50	22	25.88%
51 - 80	26	74.12%
Total	85	100%
Mean ± SD	56.62±9.19	

Table-2: Mean duration of DM(n=85)

	Mean	
Duration of DM (months)	5.22	1.97

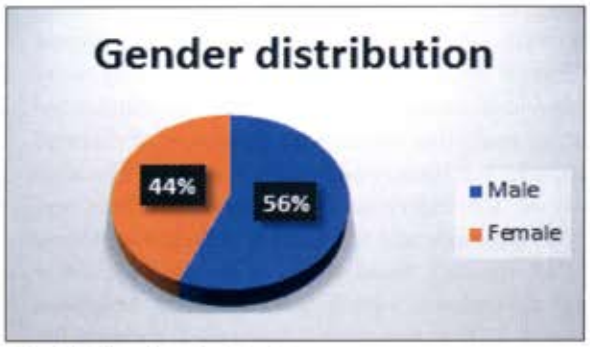

Fig-1: Gender distribution.

The data was stratified for age, gender, duration of diabetes mellitus, levels of HbAc1, duration of disease to control the effect modifiers. Post stratification chi square test was used as a test of significance by using p value <0.05 as significant. (**Table-3 &4**)

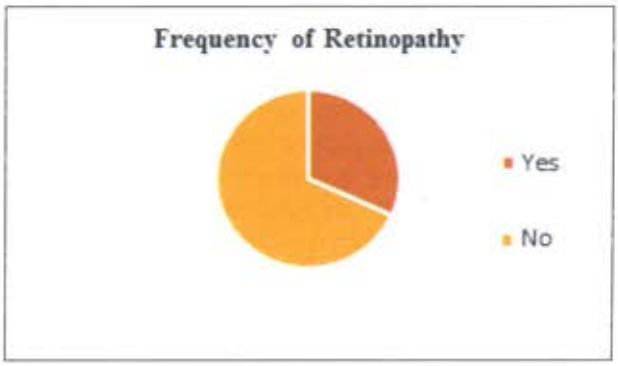

Fig-2: Frequency of retinopathy in patients with newly diagnosed type II DM along with microalbuminuria (n=85)

Table-3: Stratification for frequency of retinopathy in patients with newly diagnosed type II DM along with microalbuminuria with regards to durards to duration of diabetes (n=85.

Duration of DM (months)	Retinopathy Yes	No	p-value
1-6	11	52	0.000
>6	16	06	

Table-4: Stratification for frequency of retinopathy in patients with newly diagnosed type II DM along with microalbuminuria with regards to HbA1c levels (n=85).

HbA1c level	Retinopathy Yes	No	p-value
7 - 8	09	37	0.008
> 8	16	21	

Discussion

Diabetes mellitus still remains the commonest disorder of metabolism in which either there is less insulin that is secreted, or there is insensitivity to insulin effects. Diabetes mellitus has been posing a huge burden on health system because of its multiple complications involving various systems of the body. The visual symptoms in diabetic patients have been attributed to diabetic retinopathy that may be an associated maculopathy or proliferative complications of it. Multiple studies have been conducted in the past to find out the risk factors like the onset of diabetes, its duration, the blood glucose control, any stress related or hyperglycemic state of the body like gestation, family history, and microalbuminuria for the development of retinopathy.

This study was performed with the view that two recent local studies are showing a significantly difference regarding frequency of retinopathy in individuals with recent onset of type II diabetes mellitus along with microalbuminuria, however, we consider it necessary to record findings in our population so that the exact frequency may be determined which will be helpful for the patients and physicians. In our study, out of 85 cases, 25.88%(n=22) were between 18-50 years of age whereas 74.12%(n=63) were between 51-80 years of age, mean+sd was calculated as 56.62+9.19 years, 56.47%(n=48) were male while 43.53%(n=37) were females. Frequency of retinopathy in individuals with recent onset of type II diabetes mellitus was recorded in 31.76%(n=27). A previous local study determined the frequency of diabetic retinopathy in newly diagnosed patients of type 2 diabetes mellitus with microalbuminuria as 21.66%[6] which is near to our findings. Whereas another recent local study recorded these findings in 51.61% of the cases,[7] it shows higher frequency of the morbidity. Masoud R Manaviat and others[8] identified the correlation in cases having type II diabetes mellitus between the risk factors that leads to the development of complications like retinopathy and microal buminuria, however, it was found to be 39.3% (232 patients) as a frequency of retinopathy, 5.4% of among the total cases were having proliferative diabetic retinopathy (PDR). A reasonable work had been done to see the association between retinopathy and albuminuria in diabetes Type 2. There is a variation between the studies and according to them the frequency of retinopathy has been varied between 16 to 53.4%.[9-14] The prevalence rate is 31.76% according to the current study that is meeting in between the previously described ranges. This variability in the rate can be due to different analytical techniques used by those studies, variation in controlling the blood glucose levels, the cases under study and or the races involved. Lunetta reported the incidence rate of microalbuminuria of 15%.[9] There is a strong correlation between the stage of retinopathy and the extent of microalbuminuria in the aforementioned studies. The current study revealed that microalbuminuria is a major contributor for the development of retinopathy, in addition to the levels of HbA1c and the association of such complications has been observed by the same mechanism that leads to the damage of tissues.

Conclusion

Microalbuminuria is associated with diabetic retinopathy in cases having type II diabetes mellitus of recent onset and may be considered as a reliable marker of retinopathy.

Department of Medicine Unit-IV
SIMS/Services Hospital ,Lahore.

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Original Article

Choice of Technique for Repair of Obstructed Inguinal Hernia: A Comparison of Maloney's (Darn) Repair and Desarda Repair

Neelam Wajid,Sabih Nofal, Abdul Waheed Khan, Abdullah Zaka Cheema, Hira Butt and Nauman Akbar

Objective: To compare the outcomes of Malooney's (Darn's) Repair and Desarda Repair in cases of obstructed inguinal hernia.

Methods: A total of 68 patients (34 underwent Maloney's repair, 34 underwent Desarda's repair) were included in the study and were observed for early post operative pain, wound infection, hospital stay, chronic pain at 6 months and recurrence after 1 year.

Results: The results for acute pain, wound infection and hospital stay were comparable for the two groups. Desarda's repair was superior to Maloney's repair in terms of chronic pain and recurrence at 1 year.

Conclusions: The results for acute pain, wound infection and hospital stay were comparable for the two groups. Desarda's repair was superior to Maloney's repair in terms of chronic pain and recurrence at 1 year.

Keywords: Inguinal hernia , maloney'srepair , desarda repair , obstructed inguinal hernia.

Introduction

The field of hernia surgery has a rich and illustrious history with numerous great surgeons contributing to its development over the years. Different techniques have been advocated for the successful repair of inguinal hernia at various points in history. Over the last few decades, consensus amongst most surgeons has developed regarding the use of Lichenstein Mesh Hernioplasty technique as the most appropriate method.[1,2] However, in cases of obstructed hernia, surgeons usually avoid the use of mesh. In such cases the choice of technique of repair is usually very limited and often decided by experience of the surgeron. Maloney introduced Darn Repair in 1946.[8] His ideas were further promoted by Abrahamson in the 1970s.[9] This implies the use of Prolene Suture to form a woven mesh between the inguinal ligament and the conjoint tendon. Desarda repair was developed by Dr. M Desarda in 2001[10] involving tissue reinforcement of the posterior wall by using a strip of external oblique aponeurosis. Various studies have declared results of Desarda repair to be comparable with those of Lichenstein repair[11-20] in uncomplicated hernia's. However no study has yet been carried out which compares the two non mesh techniques, Malooneys (Darn's) Repair and Desarda Repair. By carrying out this study, we wish to examine the options available to the surgeon when not using a mesh.

Methods

From July 2016 to July 2018, all patients that presented to Accident and Emergency Department Lahore General Hospital, were screened for the presence of obstructed inguinal hernia on the basis of history and clinical examination. 68 patients were admitted through Emergency Department with Obstructed hernia and were divided randomly by lottery method into two groups (34 each). Group A: 'Maloney's Repair' and Group B: 'Desarda Repair'. ASA Grade I and II patients were selected for the study. Patients with co-morbidities and complicated hernias were excluded from the study. Maloney's repair was done by using a supra inguinal incision. Subcutaneous tissue was divided and external oblique aponeurosis incised open. Cord was lifted and the hernia sac was surgically reduced. Darn's repair with Prolene 0 suture was done by figure of 8 sutures between inguinal ligament and conjoint tendon. All layers were closed in reverse order. Desarda repair was performed by a supra inguinal incision. External Oblique aponeurosis was approached and incised open. The cord was lifted and the hernia sac reduced. Upper leaf of external oblique aponeurosis was sutured to the inguinal ligament with Viacryl 1, beginning from lacunar ligament to deep ring with a continuous suture.Sutured upper leaf was again incised I 2 cm above the suture line, extending from symphysis pubis to about 1 2 cm lateral to deep ring.Lower leaf was sutured to posterior wall fascia or conjoint tendon with continuous Viacryl 1.Then the upper leaf was sutured to lower leaf with Viacryl 1 in continuous fashion and the skin was closed.

Post operatively, acute pain assessment was done at

12, 24 and 36 hours with the help of Visual Analog Scale (VAS). Wound infection was assessed at 48 hours with the help of Southampton Wound Grading System. Post operative hospital stay was noted in both groups. On followup examination, chronic pain at 6 months was assessed. Hernia recurrence was evaluated in both groups at 1 year.

Results

During the first 24 hours Group A (Maloney's) 16 patients reported significant pain whereas 11 patients from Group B (Desarda's) reported pain in the first post operative day. At 36 hours 6 patients from Group A and 5 patients from Group B gave history of pain. Thus pain in the early post op period was comparable for the two techniques. Wound infection was assessed at 24 hours. Group-A (Maloney's) 4 patients showed Southam- pton Grade Ia or Ib infection whereas 3 patients from Group B (Desarda's) showed evidence of Southampton Grade Ia or Ib infection. All the patients in the study were mobilized out of bed within 6 hours of surgery. Most were discharged within 48 hours. Only 7 patients from Group A (Maloney's) and 5 patients from Group B (Desarda's) were discharged after 48 hours. After 06 months 4 patients from Group A (Maloney's) Repair reported chronic pain whereas 2 patients from Group B (Desarda's) reported Chronic Pain. On 01 year follow up examination, 2 patients who underwent Maloney's Repair reported recurrence of hernia (Group A). There were no recurrences in the Desarda's repair group (Group B). Thus the results for Group A (Darn's) and Group B (Desarda's) was comparable in terms of acute pain, wound infection and post operative hospital stay. Whereas according to our findings, Group B (Desarda'srepair) was superior to Group A (Darn's repair) in terms of Chronic pain and Recurrence at 01 year.

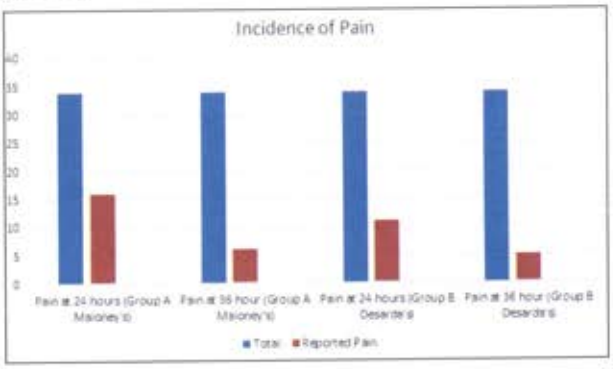

Fig-1: Incidence of pain.

Discussion

It has been observed by the writers that in a scenario when proceeding with a hernia repair without the use of Mesh, most surgeons opt for a Maloney's repair. Desarda repair is a newer alternative which is based on dynamic tissue repair. For some, it may be technically more challenging than a Maloney's repair, but it has shown to have comparable results to Lichenstein technique in'multiple studies. It can be completed without the use of Polypropylene suture. On the basis of the data presented, it is recommeneded that Desarda's Repair is a better option than Maloney's Repair when performing Surgery for Obstructed Inguinal Hernia.

Conclusions

The results for acute pain, wound infection and hospital stay were comparable for the two groups. Desarda's repair was superior to Maloney's repair in terms of chronic pain and recurrence at 1 year.

Department of General Surgery
Lahore General Hospital, Lahore.

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Original Article

Audit of Ahmad Glaucoma Valve Implantation in Childhood Refractory Glaucoma (A Prospective Study)

Khawaja Mohsin Ihsan, Amtul Mussawar Sami, Abdul Baqi, Saba Tauqeer and Farhana Mukhtar

Objective: To evaluate the long terms result of Ahmed glaucoma valve after implantation in pediatric refractory glaucoma.

Methods: This retrospective study was conducted in Eye unit 1, Services Hospital / Services Institute of Medical Sciences, Lahore from Dec 2007 to Dec 2018. Total number of patients were 12, out of these AGV was implanted unilaterally in 7 patients and bilaterally in 5 patients. Qualified success was defined as IOP less than 21 mm of Hg with anti glaucoma medication regardless of their number. Complete success was defined as IOP less than 21 mm of Hg without any anti glaucoma medications.

Results: This long term study shows that only one patient has controlled IOP without medications.

Conclusions: Despite of the small number of cases in this study Ahmad Glaucoma Valve seems to be effective in primary congenital glaucoma. Success rate declines over time, considering the need for further alternative medication and surgical procedure.

Keywords: goniotomy, trabeculectomy,. ahmad glaucoma valve. glaucoma drainage devices. Intra ocular pressure.

Introduction

The management of pediatric glaucoma is quite challenging due to poor response to anti glaucoma medications and different surgical techniques like goniotomy, trabeculotomy and trabeculectomy with or without anti metabolites, but still no gold standard treatment is available for refractory congenial glaucoma . The use of glaucoma drainage devices (GDDs) play important role in the management of congenital , complicated and intractable glaucomas. Aqueous drainage devices of various designs have become important tools in the care of glaucoma patients who are refractory to other conventional treatments. Glaucoma drainage implants reduce the IOP of the eye by directing the outflow of the aqueous humour through the shunt device. They create a pathway that completely bypasses the natural drainage system. Ahmed introduced the Ahmed glaucoma valve in 1993, which was pressure sensitive, unidirectional valve and was designed to open at intra-ocular pressure of 8mmHg.[1]

Methods

This retrospective study was conducted in Eye unit 1, Services Hospital / Services Institute of Medical Sciences, Lahore from Dec 2007 to Dec 2018 for the duration of 11 years. Total number of patients were 12, out of these AGV was implanted unilaterally in 7 patients and bilaterally in 5 patients. The Ahmad Glaucoma Valve implantation procedure was performed as follows; The superotemporal quadrant was preferred and use in all cases. A conjunctival flap was made . blunt dissection was carried out and a pocket was formed, the Ahmad glaucoma valve was implanted in this pocket after priming with 2 ml of balanced salt solution. The valve was secured with superficial sclera with two interrupted sutures, then the tube was trimmed and inserted into anterior chamber 2mm, and anterior chamber was formed, conjunctiva stitched .Subconjunctival injection of antibiotics and steroids was given and anti septic dressing was done. Qualified success was defined as IOP less than 21mm of Hg regardless of the number of glaucoma medications. Complete success was defined as IOP less than 21 mm of Hg without any anti glaucoma medications.

Results

1- Abid Ali, age 15years, Right Buphthalmos with AGV implanted twice in right eye, pressure controlled with adjunctive topical antiglaucoma medications, left phthisical eye due to multiple glaucoma surgeries in different hospitals.V/A is 6/36

and pressure is under controlled.

2. Yaseen 12 years V/A is counting finger at 1 feet Right AGV implanted ,pressure is controlled with adjunctive topical anti-glaucoma medications, cupped disc. Left phthisical eye due to multiple glaucoma surgeries in different hospitals.

3.Khadija 7 years V/A Counting fingers at 1 feet B/L AGV implanted and pressure controlled on adjunctive topical antiglaucoma medications, cupped disc.

4.Fatima 10 years of age .Right AGV ,6/36 in both eyes. She is on full anti glaucoma treatment for right eye, left eye is blind. B/L Cupped disc

5.Abdullah 3 years of age Bilateral AGV was implanted, now he has only PL positive Bilateral hyphaema in both eyes due to recurrent trauma.

6. Saman 5 years now 16 years, V/A 6/36 and 6/9 respectivelyRt. trab with MMC after removal of AGV due to hypotony and left AGV implanted No anti glaucoma medication treatment. IOP is controlled.

7. AGV also implanted in her brother's only eye, but he lost his eye due to hypotony inspite of treatment and removal of valve.

8.Asghar 2 years ,V/A Counting finger at one feet.
Bilateral AGV implanted
With adjunct anti glaucoma treatment

9.Kahinat, 2 years. Right aphakic glaucoma, AGV implanted with Full adjunct anti glaucoma treatment.

10. Ali, 3 years of age,cupped disc, 6/60 V/A Right AGV implant with adjunct anti glaucoma medications.

11. Umer AGV implanted bilaterally, removed from left eye due to intractable pain of unknown origin. AGV in right eye, patient is on full anti glaucoma treatment and has severe dry eye.V/A cf at half feet

12.Mahnoor had bilateral AGV on adjunct anti glaucoma treatment

1- Abid Ali,

2. Yaseen

3.Khadija

4.Fatima

5.Abdullah

6. Saman

7. AGV

8.Asghar

Discussion

The aim of this study was to share our experience of AGV implantation in pediatric refractory glaucoma for longer duration. Refractory congenital glaucoma is a challenging situation due to resistant to topical anti glaucoma medications and faulty/ dysgenesis of anterior chamber angle development which leads to poor drainage of aqueous humor. The most important complication in our study after implantation of AGV was hypotony in three patients, which lead to shallow anterior chamber followed by choroidal effusion or suprachoroidal hemorrhage. Shallow flat anterior chamber in these eyes permit the tube to touch the corneal endothelium leading to corneal decompensation.[4,5,6] Our all patients are on adjunctive topical anti glaucoma medication ,reason being excessive fibrosis and scarring at the place of surgery and other important factor was multiple previous filtration surgeries. Apart from this these patients need examination under anaesthesia which were not possible frequently, it was also noted that compliance and followup of our patients was very poor. In a long

term follow up in pediatric glaucoma Albis-Donado showed cumulative probability of survival at 6 months, one year, two year, three year and four year 96.65,82.4%,78.7%,70% and 41.65% respectively. This is consistent with our study that with passage of time the efficacy of Ahmad glaucoma valve decreases.

Conclusion

we have found certain limitation in our study which include retrospective design, small sample size and another drawback to include those patients who had previously failed multiple glaucoma surgeries which significantly effect our results, as this is a aggressive disorder and success rate decline over time .There is a need of factors for longer survival of valve in pediatric population ,alternative medications or surgical procedures for long term survival.

Department of Ophthalmology
SIMS/ Servieces Hospital, Lahore
www.esculapio.pk

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Original Article

The Histological Pattern of Glomerular Diseases on Renal Biopsies Of The Patients Presented to the OPD of S.H.L

Zahid Rafique, Hafiza Sumaira Rehman, Asmara Asrar, Imrana Hamid, Ajwar Tariq and M. Shahzad Hafeez

Objective: To review and identify the pattern of glomerular diseases on native kidney biopsies done in SHL.

Methods: Descriptive and analytical study. USG guided biopsies done in nephrology unit of SHL of the patients. Retrospective study on renal biopsies done from Jan 2008 to Jan 2018.Native kidney biopsies of 100 patients included in the study. Glomerular diseases are one of the commonest causes of chronic kidney disease& end-stage renal disease in developed countries and are equally important cause of renal failure in developing countries. Worldwide it is the most important cause of chronic kidney disease leading to end-stage renal disease after diabetes and hypertension. If it presents early and diagnosed well in time it is completely treatable in most of cases. So it is even more important to diagnose GN at an early stage so that patients can be prevented to reach end-stage renal disease, especially in third world countries which cannot bear the burden of cost of end-stage renal disease.

Results: The mean age of patients was 28.29±12.20years. There were 61 males and 39 females. Membranous GN was most common i.e. in 29 cases, FSGS in 20 cases, Membrano-Proliferative GN in 12 cases, Cresenteric GN in 6 cases, minimal changes disease in 6 cases, Lupus Nephritis in 6 cases, Mesangio-Proliferative in 5 cases, Diabetic Nephropathy in 4 cases, Amyloidosis in 4 cases, Interstitial Nephritis in 3 cases, Diffuse Proliferative in 2 cases, hypertensive Nephropathy in 1 case, Diffuse Sclerosing in 1 case, Rapidly Progressive in 1 case and Focal Mesengio-Proliferative in 1 case.

Conclusions: The current study indicates the most common GN in the patients presented to the Nephrology OPD of SHL was Membranous GN and the 2ndcommonest was the FSGS followed by Membrano Proliferative GN and the mean age was 28 years.

Keywords: glomerulonephritis, chronic kidney disease, end-stage renal disease.

Introduction

Glomerular diseases is one of the commonest cause of chronic kidney disease and end-stage renal disease in developing countries.[1] In most developing countries, the incidence and histological patterns of primary glomerulonephritis (GN) remains undetermined. Because patients present late with established end-stage renal disease. GN remains the most probable underlying etiology in this group labeled as having end-stage renal disease of uncertain etiology.[2] In the absence of a national or regional renal biopsy registry, we lack the essential epidemiological data to formulate a comprehensive plan to manage the glomerular diseases and their long-term sequelae. In our healthcare system of meagre resources and limited nephrology services, there is a dire need for ways and protocols whereby these diseases can be detected and managed early.[3]

The outcome of GN largely depends on the underlying medical cause clinical findings and histological appearance. In renal medicine examination of renal tissue lays the foundation of clinical diagnosis due to which kidney biopsy remains the chief diagnostic procedure in variety of renal diseases. Histological descriptions are used to name clinical diseases or syndromes. Accordingly we performed hospital based descriptive study, aiming to see the pattern of Glomerular Diseases amongst the patients presented to OPD of SHL.

Methods

The tetrospective study and Nephrology OPD of SH. The duration was JAN 2008 to JAN 2018. 100 cases was calculated with 95% confidence level, 5% margin of error and anticipated proportion i.e. 6.5% of diabetic nephropathy. Non-probability, consecutive sampling. Selection criteria: Inclusion: patients age 10-65years presented to nephrology OPD of SHL with suspected Glomerular diseases and already underwent native kidney biopsies will be included in the study. Kidney transplant patients, UTI and Obstructive nephropathy, renal mass biopsies and insufficient samples. Data Collection: 100patients fulfilled selection criteria presented to OPD with native kidneys were included. Informed

consent and demographics were taken. Then USG guided biopsies were done for light microscopy and immunofluorescence.Forlight microscopy samples were fixed in 10% formaldehyde solution and sections were stained with eosin and haematoxylin, periodic acid Schiff and silver methemmenamine, mason trichromatic and Congo red stain were used whenever required. Immunofluorescence microscopy panel included staining for IgA, IgG, IgM, C3, C1q and fibrinogen. Reports were assessed and findings were noted on proforma.Data is analysed through SPSS Version 20. Quantitative variables were calculated as mean and standard deviation while categorical were calculated as frequency and percentage.

RESULTS: In this sample, the mean age of patients was 28.29±12.20years. There were 61 males and 39 females. Table 1

Membranous GN was most common i.e. in 29 cases,FSGS in 20 cases,Membrano-Proliferative GN in 12cases,Cresenteric GN in 6 cases,minimal changes disease in 6 cases,Lupus Nephritis in 6 cases,Mesangio-Proliferative in 5 cases, Diabetic Nephropathy in 4 cases,Amyloidosis in 4 cases,Interstitial Nephritis in 3 cases,Diffuse Proliferative in 2 cases,hypertensive Nephropathy in 1 case, Diffuse Sclerosing in 1 case, Rapidly Progressive in 1 case and Focal Mesengio-Proliferative in 1 case. Fig 1 samples. Data Collection: 100patients fulfilled selection criteria presented to OPD with native kidneys were included. Informed consent and demographics were taken. Then USG guided biopsies were done for light microscopy and immunofluorescence. Forlight microscopy samples were fixed in 10% formaldehyde solution and sections were stained with eosin and haematoxylin, periodic acid Schiff and silver methemmenamine, mason trichromatic and Congo red stain were used whenever required. Immunofluorescence microscopy panel included staining for IgA, IgG, IgM, C3, C1q and fibrinogen. Reports were assessed and findings were noted on proforma. Data is analysed through SPSS Version 20. Quantitative variables were calculated as mean and standard deviation while categorical were calculated as frequency and percentage.

Results

In this sample, the mean age of patients was 28.29±12.20years. There were 61 males and 39 females. **(Table-1)** Membranous GN was most common i.e. in 29 cases, FSGS in 20 cases, Membrano-Proliferative GN in 12cases, Cresenteric GN in 6 cases, minimal changes disease in 6 cases, Lupus Nephritis in 6 cases, Mesangio-Proliferative in 5 cases, Diabetic Nephropathy in 4 cases, Amyloidosis in 4 cases, Interstitial Nephritis in 3 cases, Diffuse Proliferative in 2 cases, hypertensive.

Table-1: Demographics of patients.

N	100
Age in years	28.29±12.20
Male	61
Female	39

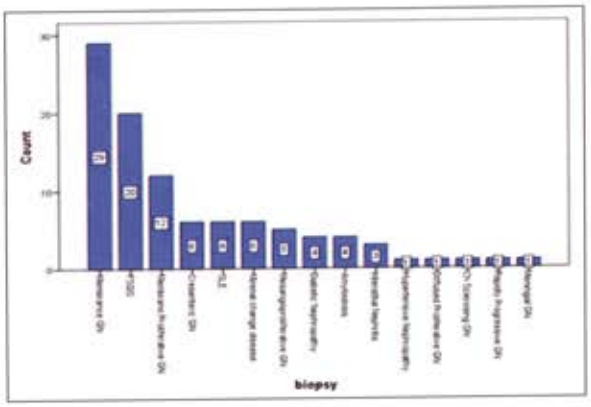

Fig 1: Distribution of biopsy findings Nephropathy in 1 case, Diffuse Sclerosing in 1 case, Rapidly Progressive in 1 case and Focal Mesengio-Proliferative in 1 case. **(Fig- 1)**

Discussion

Although the number of patients reaching end-stage kidney disease without a biopsy-proven diagnosis is increasing, the utility of renal biopsy is still an object of debate.Renal biopsy still remains a concrete approach for managing a substantial percentage of renal diseases.[8] Glomerulonephritis is not strictly a single disease but they are categorized into different pathological patterns.Diagnosing the pattern of GN is important because the outcome and treatment differ in different types.[9] In quest of elucidating the histological pattern of renal disease is the indication for renal biopsy and a number of observational analysis have been conducted worldwide.[10] But few nationwide studies are available on this topic in the literature.

The prevalence and incidence of GN varies widely in different parts of world. There are very few national registries for studies on glomerular diseases are available at mass level.Most of the studies on glomerular diseases are single center or multi center based.[11] Like the other few studies available nationwide the most common glomerulonephritis was membranous GN followed by FSGS. There may be a few influencing factors, such as most of our cases presented very late. The disease may be initially was

minimal change disease which converted to membranous GN and burnout disease converted to FSGS which is 2nd most common GN. Poverty can also be not neglected in our country for late presentation of patients and lack of awareness for renal disease and not willingness for renal biopsy. Moreover this part of the world is endemic for chronic infections such as Hepatitis B and C. Hepatitis B and C is associated with membranous GN and hepatitis B with FSGS. So our result differs from the worldwide results.

A study from North Pakistan showed Nephrotic syndrome was most common indication for renal biopsy in 50% of the cases, followed by renal insufficiency (26%) and steroid resistance (24%). In children with primary glomerulonephritis, minimal change disease was found to be the most common histological pattern (24.09%), followed by focal segmental glomerulosclerosis (FSGS), 18.30%; mesangioproliferative glomerulonephritis (GN), 17.83%; mesangiocapillary GN, 11.08%; post streptococcal proliferative GN (Post. strep GN), 10.60%; membranous GN, 4.82%; crescentic GN, 4.34%. Among children with secondary GN, chronic Sclerosing GN was found to be most common (1.93%), followed by chronic tubulo interstitial nephritis, 1.69% and hypertensive nephropathy, 1.69%; Renal Amyloidosis, 0.96% and Lupus Nephritis III, 0.96%; acute tubular necrosis, 0.72%; AL port's Syndrome (0.48%).[12]

As a study from SIUT Karachi a tertiary care center having the result that, a total of 316 adult patients were included. Of these, 201 (63.6%) were male and 115 (36.4%) were female. Mean age was 28.4 ± 10.51 years with a range of 1678 years. The spectrum of pathological lesions in the adult nephrotic population was wide and comprised focal segmental glomerulosclerosis (FSGS) (39.87%), followed by membranous GN (26.58%), minimal change disease (14.82%), mesangiocapillary GN (4.3%), mesangioproliferative GN (4.11%), post-infectious GN (2.84%), immunoglobulin A nephropathy (2.53%), and other rare lesions.[13]

Another study from DOW Medical College concluded that,the commonest primary disease was membranoprolifeartive and commonest secondary disease was lupus in adults.[14] In a study by Hashmi et al., out of 140 cases of GN, 70% were those of primary GN and 30% had secondary glomerulopathy. Membranous GN was the most common primary GN (33.6%) followed by FSGS (20.4%), whereas lupus nephritis is the most common secondary glomerulopathy (47.6%) followed by amyloidosis and diabetic glomerulosclerosis (16.6% each). They found a considerable high incidence of membranous glomerulonephritis and FSGS in our population that entails a need to investigate prevalence of associated factors like Hepatitis B and HIV infections in population at risk. Moreover, renal biopsy registry would be instrumental in this regard to record changing disease pattern in this part of the world.[15]

A study from Peshawar shows the pattern as, focal segmental glomerulosclerosis is the most common diagnosis (23%), while lupus nephritises the most common secondary glomerular disorder (7%). Other common glomerular disorders are membranous nephropathy (12%), immunoglobulin A nephropathy (9%), and post-infectious glomerulonephritis (6%).[4]

If we look on South Asian population, a study from India shows, Most frequent primary GN was membranous nephropathy constituting 35.8%, followed by minimal change disease at 16.7%.[16]

If we took a glimpse on international data, a study from Riyadh, Saudi Arabia shows the result as,most common histological lesion was focal segmental glomerulosclerosis (40.8%) associated with a high incidence of hypertension (86.7%), nephrotic syndrome (61.7%), hematuria (48.8%), and renal impairment (33.3%). Mesangioproliferative glomerulonephritis was the second most common lesion (21.1%), followed by membranous glomerulonephritis (13.6%), immunoglobulin A nephropathy (13.6%), membranoproliferative glomerulonephritis (9.5%), and minimal change disease (1.4%). Although not as common as in most other developed countries, immunoglobulin A nephropathy is being increasingly recognized in Saudis. Lupus nephritis remained the commonest cause of secondary glomerulonephritis (48.5%), whereas amyloidosis was conspicuously absent.[17]

A study from Korea having results as, the most common primary GN was immunoglobulin A nephropathy (28.3%), which was followed by minimal change disease (15.5%), membranous nephropathy (12.3%), FSGS (5.6%) and membranoproliferative GN (4.0%). The most common secondary GN was lupus nephritis (8.7%).[5]

The same results were found by Swami Nathan et al., evaluating the incidence of glomerular diseases in Olmest County, Minnesota. Immunoglobulin A nephropathy was the most frequent followed by FSGS, which was the leading cause of nephrotic syndrome in white adults, and then membranous nephropathy.In Brazil, as Polite et al., report in their paper, FSGS is the most frequent among primary glomerulonephritis, followed by membranous

nephropathy and immunoglobulin A nephropathy.[19] Lupus nephritis is the most common secondary form followed by post-infectious glomerulonephritis whose frequency is decreasing in most industrialized countries but remain high in some developing communities as shown by Kanjanabuch et al., primary glomerulonephritis represent approximately half of all native renal biopsies, similar to almost all databases.[20]

Conclusion

The study of Histological Pattern shows Membranous GN was the most common GN in our study followed by FSGS and Membranoproliferative GN.

Department of Nephrology
SIMS/Servoces Hospital ,Lahore.

www.esculapio.pk

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Original Article

Initial Experience of Multi-detector Computed Tomography Angiography for Cerebral Vascular Pathology in a Public Sector Hospital

Tahira Nishtar, Nosheen Noor, Tabish Ahmad, M. Aftab

Objective: To share the initial experience of using Computed Tomography Angiography (CTA) for detection of cerebral vascular pathologies.

Methods: This retrospective observational study was carried out in the Department of Radiology, MTI Lady Reading Hospital, Peshawar from 15th March 2017 to 31st January 2018. 68 consecutive patients referred for cerebral CTA to exclude cerebral vascular pathology were included in the study. Cerebral CTA was performed using standard protocol on 160 slice Toshiba Aquilion series CT scanner. Data obtained was analyzed using latest SPSS version.

Results: Out of 68 patients, 33 were males and 35 were females. Age range was from 9 to 67 years with median age of 41.5 years. Among 68 patients, 28 cases were reported abnormal, diagnoses being aneurysm (41.17%), followed by vascular occlusion (2.94 %) and arterio-venous malformation (2.94 %) while 34 cases turned out to be normal. Cerebral aneurysms presented as subarachnoid hemorrhage on initial NECT brain in 60.7% and as intra-cerebral hemorrhage in 14.28% while 25% patients had normal NECT brain.

Conclusions: Multidetector CT angiography (CTA) is no doubt the investigation of choice for detecting cerebral vascular pathologies.

Keywords: CT angiography, cerebral, vascular pathologies.

Introduction

Nowadays, multi-slice CT angiography has become the most important tool for diagnosis of vascular pathologies and is the most widely prescribed investigation for the evaluation of vascular morphology. Compared to catheter angiography, CT angiography is faster, non-invasive with fewer complications. It is a low cost examination compared to catheter angiography. It is a safe, fast and minimally invasive procedure which has improved tremendously with the advent of multi-slice CT scanner in the form of 4 to 64 slice and above spiral CT scanner with rapid acquisition of isotropic data sets with a huge range of techniques for post processing of images.[1]

For morphologic evaluation of intracranial vessels, CTA has been regarded as a reliable tool in recent years. Also, various studies have demonstrated the accuracy of CTA in detecting vascular diseases, even in the presence of acute SAH.The introduction of multisection CT systems has enabled faster acquisition and better reconstruction and hence has become superior to DSA in detecting small vascular diseases such as tiny aneurysms.[2,3] The neurovascular applications of CTA include vascular occlusion, vascular malformations, cerebral aneurysms and dural venous sinus thrombosis. Especially in an emergency scenario such as trauma, stroke and SAH, fast imaging techniques greatly facilitate quick therapeutic decision making.[4] The facility of CT angiography is recently established in Lady Reading Hospital which is a high volume public sector hospital and largest in the province. Aim of this study is to share the initial experience of cerebral CTA performed in our department and the spectrum of cerebral vascular pathologies reported in local community.

Methods

Theret68 consecutive patients who underwent multi-slice cerebral CT angiography in department of radiology, LRH-MTI Peshawar, from 15th March 2017 to 31st January 2018 were evaluated retrospectively. All patients had a simple non-enhanced CT (NECT) brain as a baseline investigation. Cerebral CT angiographies were evaluated and co-reported by two consultant radiologists who performed cerebral vascular pathology detection, quantification and characterization by 2D multi planar reconstruction, three dimension maximum intensity projection (3D MIP) and volume rendered techniques. The protocols used for all patients included; Multi slice CT Angiogram performed with a 160 slice multi detector CT scanner (Aquilion 160 Toshiba Japan). An 18-20

G intravenous (IV) cannula is inserted in the antecubital fossa. After taking a scout image, CT angiography is initiated after onset of IV infusion of non-ionic iodinated contrast material (Ultravist 320), using a power injector at the rate of 5ml / sec. Total scanning time is about 15 to 20 seconds with the use of power injector. Total volume of contrast material used is 50 - 70 ml. Scanning parameters include 120kV, 225mA, section thickness 0.5mm and reconstruction interval 1mm. Data achieved and 3D reconstruction done on Vitrea workstation by utilizing volume rendered and MIP algorithm. Diameter of each aneurysm measured and graded as small (<5mm), medium (5-15mm), large (16-25mm) or giant (>25mm). Presence/ absence, number of aneurysms, their locations, size of aneurysm and its neck, projection, presence or absence of thrombus were included in our standard report. Data obtained was analyzed using latest SPSS version.

Results

Out of 68 patients, 33 were males and 35 were females. Age range was from 9 to 67 years with median age of 41.5 years **(Table-1).** Among 68 patients, 28 cases were reported abnormal, diagnoses including aneurysm (41.17%) **(Table-2),** followed by vascular occlusion (2.94%) and arteriovenous malformation (2.94%) (Table-3), whereas, 34 screening cases turned out to be normal. Cerebral aneurysms presented as subarachnoid hemorrhage on initial NECT brain in 60.7% and as intra-cerebral hemorrhage in 14.28%. 25% patients with aneurysm had normal NECT brain, i.e. un-ruptured aneurysm was diagnosed on screening CTA. **(Table -4).**

Table-1: Data of patients.

	Variable	n=68
Sex	Male	33
	Female	35
	Age Range	09.67 years
	Mean Age	41.5 years
Total patients with pathological findins		28
	Male	12
	Females	16

Table-3: Other cerebral vascular pathologies

Pathology	n=68	%Age
Arteriovenous malformation	02	2.9
Thrombosis	14	1.47
Stenosis	01	1.47
Vasculitis	01	1.47
Hypoplastic vessel	01	1.47

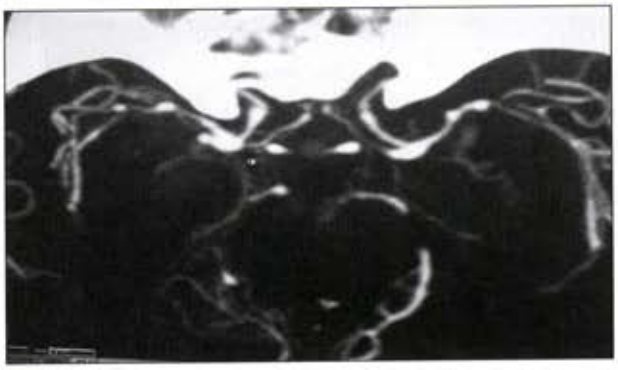


Fig-1: Axial MIP image demonstrating lobulated me-

Table-2: Cerebral aneurysms related to specific vessels

Vessel Involved	Total aneurysms n=28	SIZE OF ANEURYSM Small ((>5mm)	Medium (5-15mm)	Large (16-25mm)	Giant (>25mm)
Anterior cerebral artery	07 (25%)	01 (3.57%)	06 (21.43%)	00	00
Anterior communicating artery	05 (17.85%)	01 (3.57%)	03 (10.71%)	01 3.57%)	00
Middle cerebral Artery	08 (28.57%)	01 (3.57%)	07 (25%)	00	00
Posterior cerebral Artery	01 (3.57%)	00	01 (3.57%)	00	00
Basilar artery	02 (7.14%) (2.9%)	01 (3.57%)	01 (3.57%)	00	00
Posterior Communicating Artery	02 (7.14%)	00	02 (7.14%)	00	00
Females	03 (10.71%)	01 (3.57%)	01 (3.57%)	00	00
Total	**28 (100%)**	**28 (100%)**	**21 (75%)**	**2 (7.14%)**	**00**

Table-4: NECT brain findings in abnormal cerebral CTA.

CTA Pathologies	n=34	CORRESPONDING CT BRAIN FINDINGS Intracerebral hemorrhage	SAH	Normal CT	Cerebral infarcts
Aneurysms	28	4	17	7	-
AVM	02	-	1	1	-
Vascular thrombosis	02	-	-	-	2
Vasculitis	01	-	-	1	-
Hypoplastic vessel	01	1	-	-	-
Total	34	5	18	9	2

dium size aneurysm of right Middle Cerebral Artery and multiple small aneurysms involving M1 segments of bilateral MCA.

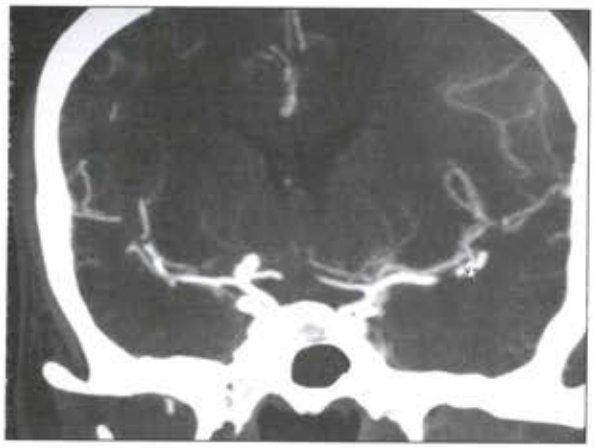
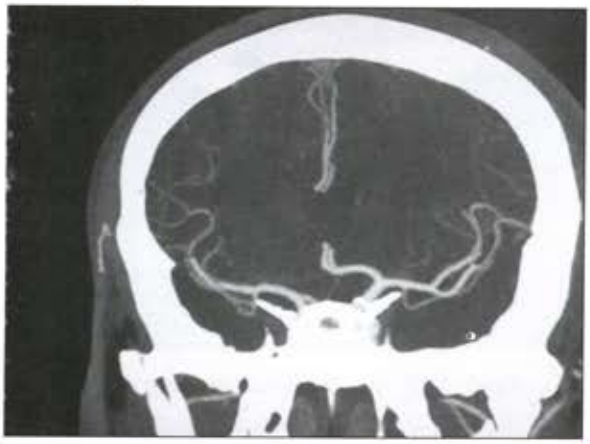


Fig-2: Coronal MIP image demonstrating a superiorly projecting medium size aneurysm of suraclinoid part of right Internal Carotid Artery



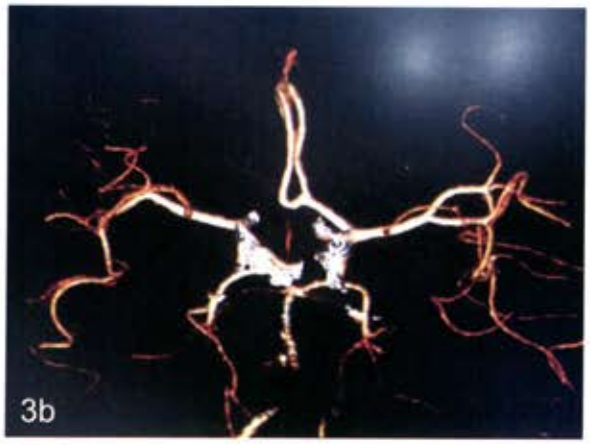


Fig-3: C3a (coronal MIP) & 3b (3D Volume Rendered) showing congenital hypoplastic A1 segment of right ACA, right A2 segment receiving supply from left ACA via anterior communicationg artery.

Discussion

CTA with a Multi detector 64 MDT or more system has been accepted as a proven method for detection of cerebral vascular pathologies and plays a role in screening asymptomatic patients by imaging un-ruptured aneurysms.[2] In our study we have used 160 slice CT scanner for performing cerebral CTA using various techniques including MPR (Multiplanar Reformation), thin-slab maximum intensity projection (MIP) and volume rendering (VR) followed by segmentation algorithms, and automatic lumen boundary definition alongside bone removal with subtraction algorithms. All the above provide quality of vessel analysis comparable to that achieved with 3D rotational conventional angiography.

Ruptured aneurysms can cause intra-cranial hemorrh age in the form of intra-cerebral hematoma or SAH which are the most alarming and catastrophic conditions especially subarachnoid hemorrhage, as it can cause significant morbidity and mortality and poses significant challenges both in the diagnosis and management. Intra-cerebral hematoma can lead to worsened patients clinical state requiring early decompression surgery.[1-5] In our study 60.7% ruptured aneurysm caused SAH and 14.28% caused intra-cerebral bleed. In 25% cases un-ruptured aneurysms were diagnosed where initial NECT brain was normal. Optimum image quality of CT cerebral angiography is dependent on 3 factors:1) Scan protocol, 2) Image reconstruction measures and 3) Image post processing. Besides limiting scanning area to area of interest, the equipment automatically adjusts the radiation dose accurately to the body thickness of patient. The data achieved is assessed in 2D and 3D reforms including rotational views.[6]

With the use of multi-slice CT the procedure of CTA is performed so rapidly that patient movements hardly affect the image quality. Furthermore, advanced post processing software improves morphological depiction of blood vessels. The anatomic relationship with surrounding structures is better elaborated, and three-dimensional image display allows better details in a rapid and easily reproducible fashion. Volume-renderin g reconstruction mode eliminates the difficulties imposed by the proximity of the bones at the base of the skull to the vessels imaged, as this may hinder post processing reconstruction of blood vessels in the posterior fossa. Therefore, volume rendering is the preferred and primary reconstruction mode that also enables the performance of curved MPR. Direct demonstration of the vascular walls on the sectional images achieved only with multi-slice CTA assists in differentiating atherosclerotic narrowing from

spasm. Multi-slice CTA also enables accurate measurements of luminal diameter, thereby providing quantitative data and to help select patients for endovascular or other treatments.[3] Based on size cerebral aneurysms can be classified as small (<5mm), medium (5-15mm), large (16-25mm) and giant (>25mm), supergiant aneurysms have also been reported (>50mm). [8] In our study the aneurysms were most commonly found involving middle cerebral artery, i.e. 8 out of 28 (28.57 %) followed by anterior cerebral (25%), anterior communicating (17.85%) and internal carotid arteries (10.71%) [Figure 1 & 2]. According to size the commonest aneurysms were medium sized (75%) followed by small (17.85%) and large (7.14%). No giant aneurysms were diagnosed in our study.

Cerebral AVM are congenital abnormal vascular connections within brain.[9] The most commonly associated complication is intracranial hemorrhage.[10] CTA is important for initial and follow up evaluation of AVM .The feeding arteries and draining vessels of AVM are demonstrated by CTA [11] which is important for management planning; operative/ embolization. In our study 2 patients were diagnosed as having AVM, one in MCA territory and other involving thalamo-striate vessels. The feeding and draining vessels were reported. No associated hemorrhage was reported. The patients presented with symptoms caused by mass effect of the AVM on surrounding structures.

Variation of cerebral circulation are common especially in circle of Willis. When assessing cerebral CT angiogram it is important to understand the appearance of these normal variants and their clinical relevance. Congenital hypoplasia of anterior cerebral artery A1 segment is reported to be present in 10% of autopsy and absence of A1 segment is seen in 1-2%.[12] Although it is a rare finding, we reported hypoplastic A1 segment of anterior cerebral artery in one out of sixty eight cases (1.47%). [Fig 3a & b]

Conclusion

Multidetector CT angiography (CTA) is no doubt the investigation of choice for detection and screening of cerebral vascular pathologies which include a wide spectrum ranging from congenital variants to aneurysms and complex arteriovenous anomalies.

Deportment of Radiology
MTI, Lady Reading Hospital, Peshawar, KPK
SIMS/Servoces Hospital ,Lahore.

www.esculapio.pk

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