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Editorial

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Editorial

Autism's Origin – Advanced Research

Mohsin Masud Jan
Editor

Autism — which impairs the ability to communicate, regulate behavior and relate to others — is thought to affect about 1 in 88 children in the United States. The mutations appear to come into play in mid-pregnancy. They interrupt the formation of specific cells that connect brain layers in a region that controls movement, sensory perception, conscious thought and language.

The changes appear to cause a sort of faulty wiring of the brain before birth, the researchers said. They also said their findings might explain why early intervention programs, which enroll kids as young as 1 year old, help children with autism. Since their brains are still developing, they might be capable of correcting or compensating for some of these bad connections. For both studies, researchers took advantage of BrainSpan atlas, an ambitious public project to catalog the gene makeup of the brain at many different ages. The brains used in the project are from 57 healthy, deceased males and females. Their ages ranged from six weeks after conception to 82 years old.

The work is groundbreaking, said one expert. "This is something we couldn't have done two years ago because we didn't have this dataset," said Jeremy Willsey, a graduate student in genetics at Yale University. Willsey led one of the studies, in which researchers focused on rare "lightning strike" mutations that caused a loss of function in nine genes. These mutations are changes to DNA that occur randomly, and aren't passed from parent to child. But previous studies have shown that individuals with autism often share these same random mutations.

Focusing on the actions of these nine genes, the researchers checked the BrainSpan atlas to see if any were working together at the same time. They found that those genes and others associated with autism worked together at only three distinct places and periods in development. Those corresponded to the deeper layers of the front of the brain between 10 and 24 weeks after conception. The gene mutations seem to interfere with the development of nerve cells that connect different brain regions. "We know there's a disruption in the cells' development, but we don't know much more than that," Willsey said. "That's sort of the next step that our lab is addressing. That's what's going to help you progress toward treatment."

For the other study, researchers at the University of California, Los Angeles, took a different approach. Using the BrainSpan data, they first looked at gene expression in normal brains from eight weeks after conception through 12 months of age. They then mapped hundreds of genes shared by individuals with autism and determined when and where those genes were active in the developing brain. Strikingly, although there were many autism risk genes, they all acted together at just a few points in brain development.

The researchers also compared the activity of autism risk genes to the genes involved in intellectual disability, or low I.Q. Although the conditions share many of the same risk genes, the study found that they were active in different ways at different times, adding more proof that the two conditions are distinct. Their findings also pointed to a disruption in the brain's wiring, probably because of an error in the development of the brain-connecting nerve cells.

The researchers stressed, however, that the findings probably don't explain all cases of autism. "These gene mutations definitely contribute to autism in some people," said Neelroop Parikshak, a graduate student at the University of California, Los Angeles, who led the second study. "[But] we don't know how much in a given individual." Willsey agreed. He said that for the first time, however, these studies show the genetics of autism in action, something that should speed the path to better treatments.

Original Article

Nephrotic Syndrome

Histopathological Patterns in Childhood Steroid Resistant Nephrotic Syndrome

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ABSTRACT

Objective: To determine the frequency of various histopathological lesions in children with steroid resistant nephrotic syndrome (SRNS) presenting to the Children's Hospital & the Institute of Child Health, Multan.

Study Design: Retrospective observational study

Place and Duration of Study: This study was conducted at the Department of Paediatric Nephrology, The Children's Hospital and The Institute of Child Health, Multan, Pakistan from October 2005 to December 2012.

Materials and Methods: Medical record of 152 children with SRNS, who were biopsied, was reviewed. All SRNS patients, both initial steroid resistant and late non-responders were included in the study.

Results: Out of the total 152 patients, 98 (64.5%) were males and 54 (35.5%) females, with a male to female ratio of 1.8: 1. Mean age and standard deviation of patients was μ 8.11 ± 3.58 years with age range of 1 to 15 years. Histopathological spectrum showed focal segmental glomerulosclerosis (FSGS) as the commonest (59; 38.81%) lesion followed by mesangioproliferative glomerulonephritis (MesPGN) (40; 26.31%), minimal change disease (MCD) (35; 23.02%) and mesangiocapillary glomerulonephritis (MCGN) (13; 08.55%). Four (2.63%) patients had membranous nephropathy. One patient of renal amyoidosis was also diagnosed on renal biopsy.

Conclusion: Overall FSGS was the commonest lesion followed by MesPGN, MCD, and MCGN. IgMN was an associated finding in 25% cases of MesPGN. FSGS was significantly more common among children >10 years. MCD was significantly more common among children 1-5 years. MesPGN and MCGN were significantly more common among children >5 years.

Key Words: Steroid resistant nephrotic syndrome, Renal biopsy, Histopathological pattern, Children

INTRODUCTION

Nephrotic syndrome is one of the most common renal diseases in children. It has an incidence of 2 to 7 per 100,000 population per year and a prevalence of 16 per 100,000 population.[1,2] The basic pathophysiology of all forms of nephrotic syndrome is an abnormal selective permeability barrier, leading to pathologic protein loss across the glomerular basement membrane. The hallmark of nephrotic syndrome is heavy proteinuria (>40 mg/m^2/hr), hypoalbuminemia (<2.5 g/dl), edema, and hyperlipidemia. [2,3]

It is predominantly idiopathic minimal change nephrotic syndrome (MCNS), responsible for approximately 85% of cases and characterized by its benign nature and steroid responsiveness. The majority of children will respond to steroid therapy within the first four weeks of treatment with prednisolone. Children, who do not achieve complete remission with adequate corticosteroid therapy, are considered steroid resistant (SRNS), and there is consensus about diagnostic renal biopsy in these children.[1,2,3] Observations show that about 10-20% of children with idiopathic nephrotic syndrome present with idiopathic steroid resistant nephrotic syndrome.[4,5]These children are much more likely to progress to chronic kidney disease.[6]

Various studies show an increasing trend of SRNS in children with preponderance of focal segmental glomerulosclerosis (FSGS). Azher et al in 2011, in a study in children with SRNS done in Pakistan, found that focal FSGS was the most common (28.8%) histopathological lesion, followed by IgM nephropathy (IgMN) in 17.7%, minimal change disease (MCD) and membranous nephropathy (MN) in 13.3% each, membranoproliferative glomerulonephritis (MPGN) in 11.1%, mesangial proliferative glomerulonephritis (MesPGN) in 8.8% and IgA nephropathy (IgAN) in 6.6% patients.[6] Studies done in India,[7] Nigeria[8] and Iran[9] in children with SRNS also show that FSGS was the most frequent histopathological lesion. The studies done at Sindh Institute of Urology and Transplantation (SIUT), Karachi showed an increasing prevalence of FSGS over the years in Pakistani population with higher prevalence of atypical features. This trend has immense therapeutic and prognostic significance. [10,11]

The children's Hospital and the Institute of Child Health, Multan is a tertiary care referral hospital draining a wide population area from southern Punjab, interior Sindh and Balochistan. Primary objective of this study was to find out the distribution pattern of underlying histopathological lesions in children with SRNS coming to this hospital.

MATERIALS AND METHODS

In this retrospective observational analysis, medical record of 152 children presenting with steroid resistant nephrotic syndrome, who were biopsied from October 2005 to December 2012 at the Nephrology department, the Children's Hospital and the Institute of Child Health, Multan was reviewed. All 1 to 15 years old patients from both gender, initial steroid resistant or late non-responders, were included in the study.

Patients were labeled steroid resistant if they failed to achieve complete remission (i.e three consecutive days of nil proteinuria on urinary dipstiks) after four weeks of prednisolone 60mg/m^2 plus three pulses of intravenous methylprednisolone infusions 1G / 1.73 m^2 /day on alternate days. Late non-responders were the patients who initially responded to the steroids but over a period of time became steroid resistant during a relapse.

In the prepared patients, ultrasound guided percutaneous renal biopsy was performed with Dr. J Fine Core Disposable Semiautomatic Biopsy Needle (size 16 G x 150 mm) under local anaesthesia. Two to three cores of renal tissue were taken. Biopsy specimen, preserved in formalin, were sent to the histopathologist at Dr. Zia-ud-Din University Hospital, Karachi for histopathological review by light microscopy (LM) and immunofluorescence (IF) study.

Patients name, age, date, registration number, presenting complaints, details of therapy and biopsy results were recorded by a careful review of the record and the actual biopsy reports. The outcome variable, that is histopathological lesions, was noted in the order of frequency.

Data was analyzed using statistical software SPSS-10. Descriptive statistics were applied to analyze the data. The quantitative variables were calculated by mean and standard deviation and qualitative variables by percentages and frequencies.

RESULTS

In the present study a total of 152 patients, having SRNS, who underwent ultrasound guided percutaneous RB were included. Mean (μ) age and standard deviation (±) of patients were μ 8.11, ± 3.58 years with age range of 1 to 15 years. Age at presentation was highest in the age group 6-10 years (n=62; 40.79%). There were 43 (28.28%) patients between 1-5 years and 47 (30.92%) between 11-15 years. There were 98 male (64.5%) and 54 (35.5%) female patients with a male to female ratio of 1.8:1.

Histopathological spectrum showed FSGS as the commonest (59; 38.81%) lesion the mesangio-proliferative group, followed by MesPGN (40; 26.31%), MCD (35; 23.02%) and MCGN (13; 08.55%). Amongst 10 patients (25%) had associated IgM nephropathy (IgMN), 2 patients (5%) each had IgA nephropathy (IgAN) and focal mesangial proliferation. Membranous nephropathy (MN) was detected in four patients (02.63%). One female patient of renal amyloidosis was also diagnosed on renal biopsy as shown in table I.

Table No.I: Histopathological Lesions in Patients with Steroid Resistant Nephrotic Syndrome

Lesion	No. of patients	Percentage
FSGS	59	38.81%
MesPGN	40	26.31%
MCD	35	23.02%
MCGN	13	8.55%
MN	04	2.63%
RA	01	0.66%
Total	152	100%

Key: FSGS= Focal Segmental Glomerusclerosis, MesPGN= Mesangioproliferative glomerulonephritis, MCD= Minimal Change Disease, MCGN= Mesangiocapillary Glomeulonephritis, MN= Membranous Nephropathy, RA= Renal Amyloidosis

Out of the total 43 patients between 1-5 years, 11 (25.58%) had FSGS; 21 (8.83%) had MCD and 11 (25.58%) had MesPGN. MCGN was not detected in this age group. Out of the total 62 patients between 6-10 years, 27 (43.54%) had FSGS, 10(16.12%) had MCD,19 (30.64%) had MesPGN, and 6 (09.67%) had MCGN.Four patients with MesPGN in this age group had associated IgMN and one patient had associated IgAN. Out of the 47 patients in the age group 11-15 years, 21(44.68%) had FSGS, 04 (08.51%) had MCD, 10 (21.27%) had MesPGN, 07 (14.89%) had MCGN, and 04 patients (08.51%) had IgMN. One patient had IgAN associated with MesPGN. Age wise breakup is shown in table 2.

Table No.2: Age Wise Distribution of Different Histopathological Lesions

Age (years)	No. of patients	No. of patients with FSGS	No. of patients with MesPGN	No of patients with MCD	No. of patients with MCGN	No. of patients with other lesions
1 – 5	43	11(25.58%)	11(25.58%)	21(48.83%)	Zero	Zero
6 – 10	62	27(43.54%)	19(30.64%)	10(16.12%)	06(09.67%)	Zero
11 – 15	47	21(44.68%)	10(21.27%)	04(08.51%)	07(14.89%)	05(10.64%)
Total	152	59(38.81%)	40(26.31%)	35(23.02%)	13(08.55%)	05(10.64%)

Table No.3: Sex Wise Distribution of Different Histopathological Lesions

Sex	Total No.of patients	No. of patients with FSGS	No. of patients with MesPGN	No. of patients with MCD	No. of patients with MCGN	No. of patients with other lesions
Males	98	36(36.73%)	30(30.61%)	24(24.48%)	6(6.12%)	2(2.04%)
Females	54	23(42.59%)	10(18.51%)	11(20.37%)	7(12.96%)	3(5.55%)
Total	152	59(38.81%)	40(26.31%)	35(23.02%)	13(08.55%)	5(3.29%)

FSGS was significantly more common among children > 10 years. MCD was significantly more common among children 1-5 years. MesPGN and MCGN were significantly more common among children > 5 years.

Out of the total 98 male patients, 36 (36.73%) had FSGS, 24 (24.48%) had MCD, 30 (30.61%) had MesPGN, and 6 (6.12%) had MCGN. Out of the total 54 female patients 23 (42.59%) had FSGS, 10 (18.51%) had MesPGN, 11 (20.37%) had MCD, and 7 (12.96%) had MCGN. Two males and 2 females had MN each. Sex wise breakup is shown in table 3.

DISCUSSION

Steroid resistant nephrotic syndrome is believed to be associated with a high risk of progressing to chronic kidney disease. The underlying histopathology usually affects the course of the disease as well as the response to treatment. Despite the absence of evidence based recommendations regarding the role of renal biopsy in these patients, the procedure provides important information on renal histology and outcome.[12] Present study is one of the largest series of patients over a span of 7 years from a single institution in Pakistan which describes the frequency of various histopathological lesions in children presenting with steroid resistant nephrotic syndrome at our hospital. FSGS, MesPGN, MCD and MCGN account for the majority of cases in decreasing order of frequency. IgMN is an associated finding in about a quarter of patients with MesPGN. In the landmark study by International Study of Kidney Disease in Children (ISKDC) MCD, FSGS, and MesPGN each accounted for about a quarter of children with SRNS.[13] Our study showed FSGS as the commonest lesion accounting for 38.81% of all patients followed by MesPGN which accounted for 26.31% cases. MCD was the third commonest (23.02%) lesion in our SRNS children. This is in accordance with most of the recent series reported in Pakistan and worldwide in children with SRNS.[14,15,16] Mubarak et al evaluated the spectrum of histopathological lesions in children with SRNS at a single centre in Pakistan. FSGS comprised 38.5% followed by MCD 23.2%, IgMN 13.6%, MesPGN 10.2%, MN 8.2% and MCGN 4.8%.[17] Amer et al in 2011, in a study on children with SRNS done in Peshawar, Pakistan found that FSGS was the most common histopathological lesion (28.8%), followed by IgMN in 17.7%, MCD and MN in 13.3% each, MPGN in 11.1%,MesPGN in 8.8% and IgAN in 6.6%. Safaei A and Maleknejad reported FSGS as the commonest (41%) lesion in Iranian children who underwent renal biopsy.[18] Jameela A Kari et al conducted a study in SRNS children in Kingdom of Saudi Arabia. FSGS comprised 39% of cases followed by IgMN in 28%, MesPGN in 17%, MCD and C1q nephropathy (C1qN) in 8% each and IgAN in 3%. Bonilla-Felix et al reported an increased incidence of FSGS in American children (23% before 1990 versus 47% after 1990).[19] Similarly, Srivastava et al found a higher incidence of FSGS in American children with reciprocal decline in the incidence of MCD in recent years.[20] Gulati et al found an increased incidence of FSGS in Northern and Eastern Indian populations from 20% between 1990 and 1992 to 47% between 1992 and 1996.[21] A few studies from Pakistan, Japan, France and Kuwait found a lower incidence of FSGS.[22,23,24] In our study MesPGN was the second commonest lesion after FSGS. Hafeez F et al in a study on SRNS in children in Lahore found MesPGN in 60% of cases.[25] The same histological lesion is prevalent in Chinese population.[26] A few studies found MCD as more common than FSGS in children with SRNS.[22,23,24] In our study MCD was the third most common lesion. The variable histopathologycal pattern may be related to environmental, genetic, or racial factors but the exact cause is unknown.[22] In our study IgMN was associated finding in 25 % cases with MesPGN. However, its existence as a separate entity is still controversial. Mubarak M et al published one of the largest studies of IgMN in children with idiopathic nephrotic syndrome and reported an incidence of 13.6% in children with SRNS.[27]

While evaluating clinicopathological spectrum of renal biopsies in children, our study showed a male predminance (M:F = 1.7) which is consistent with many series from around the world.[3,4,5] Age-wise break up showed a higher incidence of MCD in younger children less than 5 years age and a higher incidence of FSGS in older children more than 10 years age. MesPGN and MCGN were significantly more common in children older than 5 years. This disparity may be explained by the fact that some patients with MCD on a first biopsy may have FSGS if a biopsy is done later in the disease, especially if they are persistently steroid resistant or if they have developed secondary steroid resistance. Since it is only necessary to identify a single area of focal hyalinosis in a single glomerulus to diagnose FSGS, the question of whether FSGS was present all along but missed on the first biopsy because a representative lesion was not included in the biopsy, or whether "true"

MCD can evolve into FSGS, is unanswerable. There are grounds for believing that the lesions of FSGS arise as a consequence of unremitting heavy proteinuria, rather than being the cause of it. If this is true, it follows that steroid resistant cases are more likely to develop FSGS than steroid responsive cases, in whom proteinuria is intermittent.[28] Though, our study was a retrospective, observational analysis, it gives a good view of the underlying histopathological lesions prevailing in our SRNS patients. But prospectively designed, multicenter studies involving larger sample size would be the better representative. This would guide us to plan better management strategies for these patients.

CONCLUSION

The histopathological pattern in our children with SRNS shows FSGS as the commonest lesion followed by MesPGN and MCD. IgMN was associated with a quarter of patients with MesPGN.

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Original Article

Arterial Supply of Brain

Variable Arterial Supply of Motor Areas of Human Brain

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ABSTRACT

Objective: To study the arterial supply of motor areas of human brain regarding its variable source due to its significance in neurosurgical practice and angiography.

Study Design: It is prospective descriptive study on cadaveric human brains

Place and Duration of Study: This study was conducted on different cadaveric brains collected from anatomy and Forensic Departments of various teaching institutes during July2007-July2008

Materials and Methods: A total 100 brains were collected. skull cap was cut by electric saw meinges were saved, Skull cap was removed. Brain was removed through epidural space without any injury to blood vessels. After putting one week in 10 % formaline jar, dura was removed and branula No.24 was passed into each anterior and middle cerebral arteries separately at different times. Blue Indian ink was injected into anterior cerebral artery after ligating anterior communicating Artery. After injection branula was removed and ligature applied to the artery so that dye may not escape. Now branula was passed into middle cerebral Artery and the red Indian ink was injected so that contrasting colours clearly demarcate the blood vessels supplying the motor areas of brain. Arteries supplying from functional areas were divided in two groups A and B. Group A include primary motor cortex and group B include motor speed area or Broca's area. Each of this group is further subdivided into three sub groups A1, A2 , A3 and B1, B2, B3. Sub group A1 and B1 include area supplied by single artery, Sub group A2 and B2 include area supplied by multiple arteries whereas subgroup 3 include variant arteries supplying that area. Results were statistically evaluated. Sign test was used to test for presence of variant artery in each area and it was statistically significant.

Results: In group A out of 100 cases no case fell in such group A1 , 96 cases (96%) fell in such group A2, where middle cerebral Artery and anterior cerebral Artery supplying the area . The frontal branches of middle cerebral artery two to three in number and anterior parietal branch of middle cerebral Artery supply 80% of area while one to two branches of frontopolar Artery, branch of anterior cerebral Artery supply 1.0 to 1.5 cm strip on supero medial surface of motor area. The anterior cerebral Artery supply the leg area and middle cerebral Artery the face trunk and upper limb area. In sub group A3, 4 cases (4%) accessory middle cerebral Artery appeared as variant Artery.

In group B out of 100 cases 90 cases (90%) fell in sub group B1. 9 cases (9%) fell in sub group B2 where middle cerebral Artery through frontal branch and accessory middle cerebral Artery supply the area 1 case (1%) fell in such group B3. Where anterior temporal branch of inferior trank of middle cerebral Artery supply the area as variant Artery. 19 cases out of 100 (19%) showed variations among these 4 cases (4%) showed variations in arterial supply of primary motor cortex and 1 case (1%) showed variations in the arterial supply of motor speech area. Collateral vessels may modify the effects of cerebral ischaemia.

Conclusion: anatomical variations of the cerebral arteries are of immense importance in surgery , angiography and all non-invasive procedures to help in interpretation of cranial angiogram. The major variations include duplication segmental duplication, aplasia, hypoplasia and fenestration of the vessels.

Key Words: Primary motor area, motor speech area, Artery, variation, cerebral vessels.

INTRODUCTION

The brain is highly vascular organ. It has branching arterial network. It demands 15% of the cardiac output and utilizes 25% of the total oxygen. Arterial supply is from two sources, the corotid system with its two branches to brain, that is anterior and middle cerebral arteries whereas vertebral system terminate as basilar and posterior cerebral arteries. The functional areas under consideration derived their blood supply from anterior and middle cerebral arteries[1,2].

Anterior cerebral Artery is branch of internal carotid Artery which soon join with its opposite Artery by anterior communicating Artery. Artery enter the longitudnal fissure ascends on the medial surface of hemisphere and continue on the superior surface carpus callosum and ends by anastmosing with the posterior cerebral Artery. It gives medial striate Artery, orbital branches, the frentopolar Artery. It supplies medial parts of frontal lobe and extends on convexity of cerebral hemisphere. Occulsion of the trunk of one anterior cerebral, Artery may produce a contralateral hemiplegia which is greatest in lowerlimb[3,4].

Middle cerebral Artery enter between temporal lobe and insula emerges through leteral sulcus to be distributed on the supero lateral surface of hemisphere

to supply frontal parietal and temporal lobe. Its cortical branches include lanticulo striate, anterior temporal, orbito-frontal. Pre-Rolandic Rolandic anterior and posterior parietal branches, a posterior temporal branch and angular branch which is its terminal branch . Middle cerebral supply Broca's area, the motor and pre motor areas. Occulsion of the middle cerebral artery may produce a sever contralateral hemiplegia most marked in upper limb and face, sever aphasia occur when dominent hemisphere is involved[5,6,7].

Primary motor areas is situated in frontal lobe. It is bounded anteriorly by pre central and behind by central sulcus. It is located in pre central gyrus, the anterior wall central sulcus and anterior part of paracentral tobule. It controls voluntry movements of opposite side of body, the micturation and defecation reflexes. The human body is represented in an inverted form in this area. a frontopolar branch of the anterior cerebral Artery supply leg area. The frontal branches of the middle cerebral Artery supply remaining part of the motor area[8,9].

Motor speech area or Broca's area is situated in inferior frontal gyrus. It is centre for initiation of speech, movements of tongue lips and laryngeal musculature. A lesion of this area results in motor aphasia. The frontal branches of the middle cerebral Artery supply this area[10].

MATERIALS AND METHODS

It is Prospective Descriptive study on cadavaric brains. Study population is 100 human brains done in one year duration. It includes only healthy brains. Associated functional areas were excluded and brains with perforated and injured vessels were excluded. The brains were collected from various teaching institutes with permission. Skull cap was cut. Maringes were saved, brain was removed through epidural space without any injury to blood vessels. Each brain was put in 10% formaline jar for one week. After one week dura was removed and branula No.24 was passed into each anterior and middle cerebral arteries. Blue ink was injected by syringe into anterior cerebral artery after ligating anterior communicating artery. After injection branula was removed and ligature applied to artery so that dye may not escape. Now the branula was passed in the middle cerebral artery and red Indian ink was injected so that contrasting colours clearly demarcated the blood vessels supplying the motor areas of the brain. By this method all the branches of anterior and middle cerebral arteries were fully displayed. Statistical analysis included calculations of proportions of cases by type of blood supply for each functional area. Non parametric methods (sign) test, friedman test and mann whitrey u tests) were used for statistical significance. groups of blood vessels supplying the motor areas were divided into two groups A and group B. Each group was subdivided into three subgroups A1, A2, A3, B1, B2, B3.

Subgroup A1 and B1 include the area supplied by single artery. Subgroup A2 and B2 include the area supplied by multiple arteries. Subgroup A3 and B3 include the area supplied by variant arteries.

RESULTS

Table No.1. Number of single, multiple and variant arteries supplying motor areas.

Group	Motor area supplied	Subgroup	inference	Results of total 100 cases No. of cases found	%age
Group A	Primary motor cortex	A1	Single artery	0	0%
		A2	Multiple arteries	96	96%
		A3	Variant arteries	4	4%
Group B	Motor speech areas (Broca's arta)	B1	Single artery	90	90%
		B2	Mutiple arteries	9	9%
		B3	Variant arteries	1	1%

Statistically significant P value < 0.05 Sign test was used to test for presence of variant artery in each motor area and it was statistically significant (P -value < 0.05). To test for difference in presence of variant artery between two motor areas. friedman test was used which was significant table 2.

Table 2 Difference in presence of variant artery between two motor areas

Presence of variant Artery	Motor Area	
	A	B
Present	4	1
Absent	96	99

(Chi-square statistic=26.407, d.f =4, P value=0.000).

To determine which groups of motor area were different Mann whitrey U test was performed variant artery was found in significant number in area A as are compared area B. A and B=0.007 statistical significant P-value < 0.05.

These groups were treated as follows.

Group A: It includes arteries supplying to primary motor cortex. Subgroup A1, A2, A3 out of 100 cases no case fell in subgroup A1, 96 cases fell in subgroup A2, where middle cerebral and anterior cerebral artery supply the area. The frontal branches of middle cerebral

artery two to three in number and anterior parietal branch of the middle cerebral artery supply 80% of the area while one to two branches of the frontopolar artery branch of anterior cerebral artery supply 1 to 1.5 cm strip on the superomedial border of the motor area. Thus the anterior cerebral artery predominently supply the leg area and the middle cerebral artery, the face trunk and upper limb areas. These results are compareable to earlier studies. In such group A3. 4 cases (4%) accessory middle cerebral artery appeared as variant artery. (Figures 1 & 2).

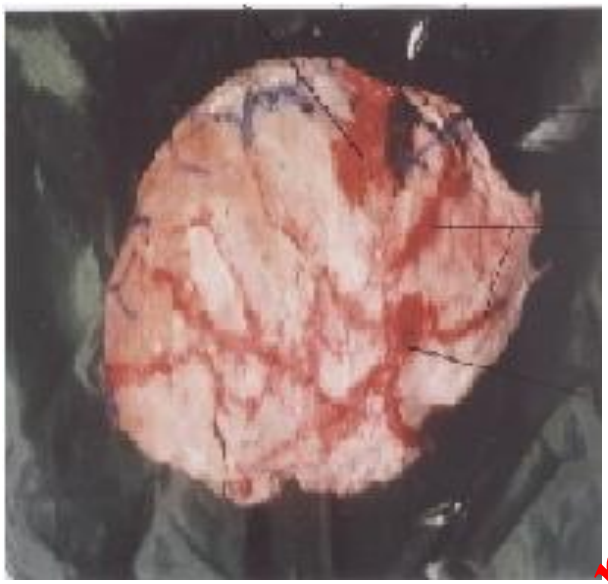

Figure No.1: Showing the branches of auterior and middle cerebral artery supplying the motor area.

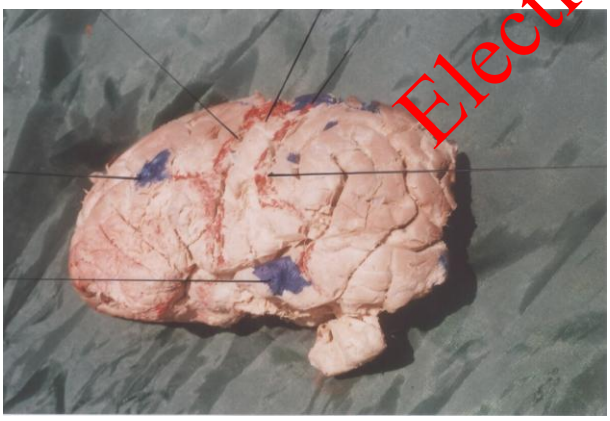

Figure No. 2: Showing accessory middle cerebral artery supplying the motor and sensory area

Group B: It includes arteries supplying to the primary motor speech area. Out of 100 cases (90%) fell in subgroup B1 superior trunk of the middle cerebral artery through one to two frontal branches supply this area. 9 cases (9%) fell in sub group B2 where middle cerebral artery through frontal branch and accessory middle cerebral artery supply the area. 1 case (1%) fell in such group B3 where anterior temporal branch of middle cerebral artery supply the area as variant artery (Figures 3 & 4).

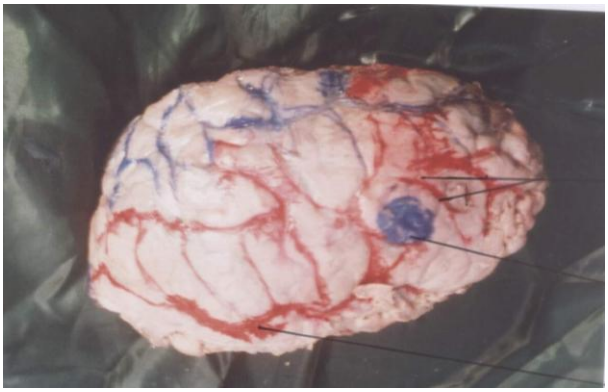

Figure No.3: Showing the frontal branch of middle cerebral artery and accessory cerebral artery supplying the motor speech area.

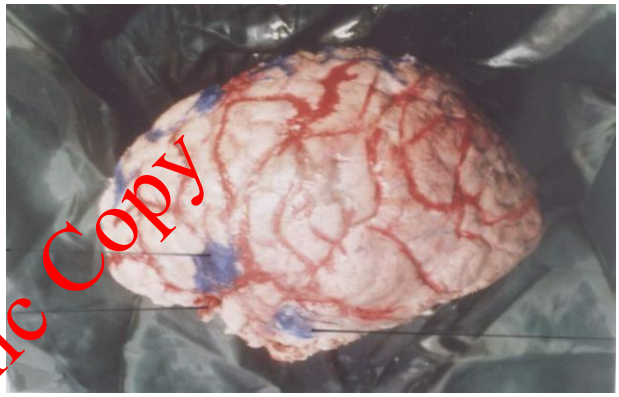

Figure No.4: Showing the anterior temporal branch of inferior trunk of cerebral artery supplying the motor speech area.

Anomilies of the cerebral circulation are not rare and have profound clinical implications 19 cases (19%) out of 100 cases showed variation. Among these 4 cases (4%) showed variations in arterial supply of primary motor area and 1 case (1%) showed variation in arterial supply of motor speech area Collateral vessels may modify the effects of cerebral Ischaemia.

DISCUSSION

Anomilies of cerebral circulation are not rare and have clinical implications. According to different studies, cerebral vascular diseases present one of the leading problem[11]. They are followed by the risk of high mortality rate and caused high level disability. This study has shown 19% variation in supply of anterior and middle cerebral arteries to motor areas of brain and superficial anastomosis between the cortical branches of these arteries are found to exist profoundly.

Different studies proved that one of duplication of middle cerebral artery and one of the accessory middle cerebral artery were studies in two cases and it was noted that the double vascularization of hemisphere can give rise to strokes with better progress despite the

Occlusion of one of the middle cerebral artery. In these studies, 4% of duplication of middle cerebral artery and 3% of accessory middle cerebral artery were noted.[12,5,7,]

In another study, proved by cerebral angiography images on M.R.I of 891 patients were examined and various variation of the anterior cerebral artery like unilateral A1, segment aphesia in 5.6% cases, three A2 segments in 3% cases and unpaired A2 segments in 2% cases and fenestration in 1.2% cases. In this study 4% cases showed hypoplesia of the A1 segment of anterior cerebral artery and duplication of the anterior communicating artery in 2% and fenestration in 8% cases.[13]

Two studies relating duplication of middle cerebral artery has been reported. In first study radiological images revealed presence of two branches of left middle cerebral artery. In second study the frequency of MCA duplication is reported to be 0.2 - 0.9%**.**[14,15]

In another study, anatomical variation of the anterior cerebral artery were observed. A singe ACA was plresent in one case and three in three cases.[16]

CONCLUSION

Anatomical variation of the cerebral arteries are of immense importance in surgery, angiography and all non-Invasine procedures. They may help in interpretation of the cranial angiograms. The data provided in the study may provide important information to the neuroanatomists operating in these areas as well as the teaching the vascular supply of the brain.

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Original Article

Myasthenia Gravis

Repetitive Nerve Stimulation Test, An Investigation that Helps in Confirming Diagnosis in Seronegative Myasthenia Gravis

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ABSTRACT

Objective: To assess the effectiveness of Repetitive Nerve Stimulation Test in the diagnosis of Seronegative Myasthenia Gravis.

Study Design: Descriptive Observational.

Place and Duration of Study: This study was conducted at Dow University of Health Sciences and Jinnah Postgraduate Medical Centre during the period of three years from 2010 to 2013.

Materials and Methods: A total 129 cases, both out patients as well as inpatients, who were diagnosed as a case of Myasthenia Gravis clinically and by other investigations including, Edrophonium Test, Chest Radiology, and Acetylcholine Receptor antibodies were studied.

Results: Out of 129 cases, of Myasthenia Gravis, who were admitted or came in outpatient department, 55 subjects are male. On Repetitive Nerve Stimulation study at 3Hz, significant decrement was found in trapezius in 16 (88%) patients who are seronegative and in 90 (81%) seropositive patients.

Conclusion: Repetitive Nerve Stimulation Test is a promising tool in the diagnosis of Myasthenia Gravis and should be a part of investigations used to diagnose this neuromuscular junction disorder especially in seronegative cases, for confirming the diagnosis.

Key Words: Nerve Stimulation Test, Seronegative Myasthenia Gravis, neuromuscular junction

INTRODUCTION

Myasthenia Gravis is a chronic autoimmune neuromuscular disease characterized by varying degrees of fatigue of the skeletal muscles of the body. The hallmark of this disease is muscle fatigue that increases during periods of activity and improves after periods of rest. As it is an autoimmune disorder the antibodies are either directed against the muscle nicotinic acetylcholine receptors (nAChR) itself or against other post synaptic targets such as the muscle specific kinase (MuSK) that indirectly reduce nAChR numbers. [1,2] Myasthenia Gravis can begin at any age, but onset in the first decade is relatively rare (10%). The peak age of onset is between 20 -30 years in female and between 50-60 years in male.[3] The incidence in female is higher under the age of 40 years whereas in later life it is higher in males. The initial symptoms or signs of Myasthenia Gravis are ptosis or extra ocular muscle weakness in up to 65% of patients. While increasing muscle fatigue, bulbar and proximal limb weakness occurs in generalized Myasthenia Gravis. Some patients may present with neuromuscular respiratory failure from the onset.[4] In addition to history and examination, various modalities are used for the diagnosis of Myasthenia Gravis including pharmacologic (Edrophonium Test)[5], electro diagnostic (Repetitive Nerve Stimulation & Single Fiber EMG)[6,7,8,9] and immunologic methods (Anti AChR Antibodies & Anti MuSK Antibodies).[10,11,12] The thymus has been implicated as having a central role in the pathogenesis of MG and thymic abnormalities such as thymic hyperplasia and thymoma are present in a large percentage of MG patients.[13,14] It has an association with thymic abnormalities, imaging (CT scan) of chest for detection of anterior mediastinum mass is also an important prelude especially when thymectomy is considered, in addition to pharmacological treatment both symptomatic and immune modulating.[15,16,17]

The term seronegative myasthenia gravis (SNMG) refers to the generalized disease without detectable anti-acetylcholine receptor (anti-AChR) antibodies. In these patients, 70 % cases have IgG antibodies against the muscle-specific kinase (MuSK) have been described[9,10].

MATERIALS AND METHODS

Hundred twenty nine consecutive patients (55 men and 74 women; mean age 40 years in seropositive and 33 years in seronegative patients) with generalized Myasthenia Gravis, seen at Dow University of Health Sciences and Jinnah Postgraduate Medical Centre, were studied during the period of 3 years from 2010 to 2013. For diagnosis of generalized Myasthenia Gravis, we required involvement of Neck and proximal muscles

weakness, Ocular symptoms for example Ptosis, Diplopia, Bulbar muscles involvement for example Dysphagia, Respiratory muscles weakness. With history of Episodic generalized body weakness and reduced exercise tolerance. These patients have positive response to edrophonium injection, electrophysiological evidence of a defect in neuromuscular transmission decrement on repetitive nerve stimulation test, or positive acetylcholine receptor or MuSK antibodies. Edrophonium was injected intravenously. Initially 2 mg was given as a test dose. If this was tolerated and no definite improvement in strength occurred after 30 seconds another 8 mg was injected. A positive test consisted of obvious improvement in blepharo-ptosis and/or muscle strength, and equivocal improvement was regarded as negative. Patients with Sensory symptoms, History of sphincter involvement, upper or lower motor neuron signs, with Pupillary Involvement and with Constant weakness, were excluded from the study.

Patients' clinical disabilities were evaluated using the Osserman's Scale[18] and Myasthenia Gravis Foundation of America (MGFA) clinical classification.[19] In patients receiving anticholinesterase medication, this medication was withdrawn 24 hours before the electrophysiological examination.

Electrophysiology: Repetitive nerve stimulation was performed in patients by using the Neuro-pack electro diagnostic machine by Nihon Kohdan. The recording was done on proximal, distal and facial muscles (in case of Ocular Myasthenia) on either side at 34 degree Celsius skin temperature. Repetitive nerve stimulation test was carried out at 3 Hz in abductor digiti minimi, trapezius, orbicularis oculi, and nasalis by stimulating ulnar nerve at wrist, spinal accessory at Erb's point and facial nerve respectively. Ten supramaximal stimuli were delivered at 3 Hz, at rest, 10 sec and the consecutively for 3 min after 1 minute of maximal voluntary contraction of the target muscle. A decrement exceeding 10% in the baseline to peak amplitudes in nasalis muscles and 15% or more in trapezius and abductor digiti minmi, between first and fifth response was considered significant (fig.1).

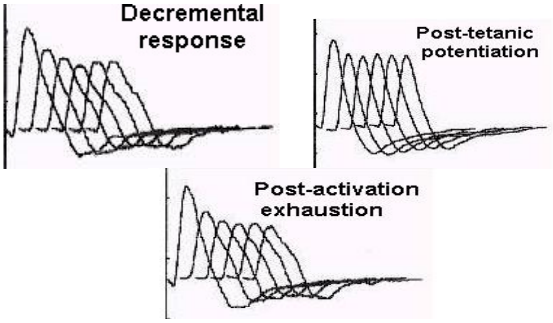

Figure No.1:

When no decrement was obtained from the muscle at rest, a one minute voluntary exercise was given and RNS repeated after two and four minute. The distal compound muscle action potential was recorded and when found to be ambiguous; a 10 sec post exercise response was recorded to rule out any increment due to a presynaptic neuromuscular defect.

Antibody Assays: AChR antibodies were measured by a standard radioimmunoprecipitation assay using human adult type AChR as antigen.

RESULTS

In this study the effectiveness of Repetitive nerve Stimulation study (RNS), in seropositive and seronegative myasthenia gravis is compared. The Seropositive and seronegative groups were compared with regard to significant decrement on repetitive nerve stimulation at 3 Hz. Out of 129 patients with Myasthenia Gravis, 18 appeared to be seronegative (13.9%).

Table No.1: Age Distribution (n=129)

Age in years	Frequency/Percent
Under 15	0
19-29	27
30-40	40
41-50	36
51-60	18
60 & above	08

Table No.2: Clinical and laboratory data of the patients with Myasthenia Gravis:

	Seropositive (n= 111)	**Seronegative (n = 18)**
Age in Years, (Mean)	19-64 (40.35)	22-48 (32.9)
Male:Female	48:63	7:11
Positive Edrophonium Test	90%	64%
Thymoma	1%	0%
Thymic Hyperplasia	10%	5%

Table No.3: Significant Decrement on Repetitive Nerve Stimulation Test in patients with Myasthenia Gravis:

	Seropositive (n= 111)	**Seronegative (n = 18)**
Nasalis	70 (63%)	13 (72%)
Trapezius	90 (81%)	16 (88%)
Abductor Digiti minimi	75 (67%)	14 (77%)

According to age distribution chart most common age of presentation of Myasthenia Gravis is between 30 to 40 years (Table 1). In seropositive patients it is about 40 years and in seronegative patient the mean age of onset in around 32 years.

Positive edrophonium test is found in 90 % of seropositive and 64 and 46% in seronegative. Thymoma is found in only 1 % seropositive patient. While 10% seropositive cases have thymic hyperplasia. Thymoma was not seen in Seronegative, patients, but 5% of them have thymic hyperplasia. (Table 2).

When comparing Repetitive Nerve Stimulation test with a frequency of 3 Hz in Trapezius muscle both in Seropositive and seronegative patients', it was found that 88% patients who were seronegative have significant decrement, which was nearest to the decrement response in seropositive patients. This response can also be seen in abductor digiti minimi muscle (Table 3), and it reflects the significance of Repetitive Nerve Stimulation test in confirming diagnosis of Seronegative Myasthenia gravis.

DISCUSSION

In this study, the effectiveness of Repetitive Nerve Stimulation Study in Seronegative as well as seropositive Myasthenia Gravis is evaluated. Myasthenia Gravis is a chronic autoimmune neuromuscular disease characterized by varying degrees of weakness of the skeletal muscles of the body. In more than 80% patients antibodies to acetylcholine receptor are detected by serology[2,10]. Approximately, 12% to 17% of patients with generalized Myasthenia Gravis lack demonstrable serum Acetylcholine receptor antibodies, and they are referred to as the seronegative myasthenia gravis[11,12]. In our study 13.9% patients were seronegative.

The change in muscle response to repetitive nerve stimulation has become the most commonly used test for the diagnosis of Myasthenia Gravis. It has shown to be a useful diagnostic technique provided it is used correctly and to its full capability. It has also given additional knowledge about Myasthenia gravis[7,8].

There is normally no change in size of the responses to paired or repetitive shocks delivered to the motor nerve at rates of up to 10 Hz or in the response to single shocks delivered before and after maximum voluntary activity or tetanic stimulation. In myasthenia gravis, a progressive decrement in the response may occur with repetitive stimulation (especially at 2 to 3 Hz), or an initial decrement may be followed by a leveling off of the response at a reduced size. Abnormalities are more likely to be found in proximal rather than distal limb muscles and in facial rather than limb muscles. Repetitive nerve stimulation at 3 Hz is positive in about 75% of patients with generalized Myasthenia Gravis.[20] Repetitive Nerve Stimulation Test is found in significantly higher number of Seronegative Myasthenic Patients[21].

In contrary to the study (D.E. Stickler) that conclude the insignificant electrophysiological results in seronegative patients, we have found a considerably good percentage of Seronegative patients who have significant decrement on Repetitively Nerve Stimulation Test [22].

One study suggests that, for individual patients with an atypical picture of Myasthenia Gravis by dissociation between a severe clinical pattern and no definite neurophysiological findings on conventional tests, repetitive nerve stimulation and/or stimulated single-fibre EMG with an increasing stimulation rate may be helpful[23].

Another study showed that Repetitive nerve stimulation (RNS) abnormalities were observed in 86% of Muscle Specific Kinase antibody-positive and 82% of Acetylcholine Receptor antibody positive patients[24].

In our study it is found that 77.7% patients with seronegative myasthenia gravis have significant decrement on repetitive nerve stimulation at 3Hz which is nearest to decrement found in seropositive patients.

CONCLUSION

This study reports the result of Repetitive Nerve Stimulation study in seronegative as well as seropositive myasthenia gravis. This brings about the usefulness of this simple diagnostic tool in the evaluation of patients with myasthenia. This test proved its effectiveness equally in seropositive as well as in seronegative myasthenia gravis and for the confirmation of Seronegative Myasthenia Gravis where the diagnosis is in doubt.

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Original Article

Lignocaine in Nasal Packs

Efficacy of 5 % Lignocaine Ointment in Reducing the Post-Operative Pain due to Intra-Nasal Packs

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ABSTRACT

Objective: To determine the efficacy of 5% lignocaine ointment in reducing the post-operative pain following nasal surgery with bilateral intra - nasal packs.
Study Design: Randomized, Prospective, Control study.
Place and Duration of Study: This study was conducted at the ENT Department, Benazir Bhutto Shaheed Teaching Hospital Abbottabad from July 2011 to June 2012.
Patients and Methods: A total of 120 patients , who underwent Septoplasty were included in the study .Patients were separated into Group A (n- 40), these patients were having intranasal packs soaked with Liquid paraffin. Group B (n- 40), these patients were packed with 5% lignocaine ointment ,and Group C, (n - 40),in this one side of the nasal cavity was packed with liquid paraffin (C1) and the other side with 5 % lignocaine ointment (C2) .In all three groups the intranasal packs were removed after 24 hrs. The severity of post operative pain and the amount of analgesics required by each group calculated.
Results : In group B (n- 40) the mean VAS was 5.60+-2.40 as compared to 7.27+-1.881 in group A and 7.40+-1.033 (C1), 6.62+-1.764(C2).in group C at 6hrs post operatively. The mean VAS at 24 hrs post operatively in group B was 6.63+-1.125, significantly lower than group A (7.15+-1.252) and group C1 (6.07+-1.023).,C2(4.90+-1.236).
The mean time to first request for rescue analgesia was significantly prolonged in group B, 220.53+-42.12 min as compared to 148.32+-32.45 min.(group A) , and 190.61+-35.45 min. (group C). The total analgesia (Diclo fenac sodium) required post-operatively was 175.32+-14.13mg in group B , as compared to 225.14+-25.73mg (group A) and 200.16+-41.89mg (group C).
Conclusion : Topical use of lignocaine ointment is safe and may have a significant role in the relief of pain due to post- operative nasal packing.
key Words: Septoplasty, Intranasal packs, Pain, Lignocaine ointment.

INTRODUCTION

Difficulty in nasal breathing is probably the most common complaint in rhino logic practice .About 80% of the general population has a deviated nasal septum (DNS) to some degree [1].

The Septoplasty surgery began in 19th century and it has been modified and enhanced ever since.[2]

Packing of the nasal cavity following intra nasal surgery is still widely practiced Post- operative complications ,while uncommon , are frequently pack related. Patients for whom the nasal packs are used may faced to some problems like naso-pulmonary reflex ,intractable pain, sleep disorder, post-operative infection and very dangerous complication like toxic –shock syndrome.[3]

The most frequent problem that Septoplasty patients worry about , is the pain and discomfort that they have to go through during nasal packing and its removal. This short period of discomfort stays clearly in patient's mind.

Wrapping the packs with gel foam , blocking the sphenopalatine ganglion[4], keeping packs for a shorter time [5], and moistening packs with topical anesthetics are some procedures to reduce pain.

The primary objective of this randomized double-blind controlled study is to determine the role of 5% lignocaine ointment soaked nasal packs in reducing post- operative pain.

MATERIALS AND METHODS

This study was conducted at Benazir Bhutto Shaheed Teaching Hospital from July 2011 to June 2012.120 patients who were due to undergo Septoplasty ,were enrolled in the study. Patients were selected based on their complaint of nasal obstruction and diagnosis was solely made on rhino logic findings. Patients undergoing other simultaneous surgical procedures e.g. turbinectomy, polypectomy or rhinoplasty were excluded. Patients with cardiac conduction problems, concurrent treatment with anti-arrhythmic drugs, history of recent local or systemic infection, reported allergy to lignocain and patients with history of use of analgesic medications in the three days before surgery were also excluded from the study.

After obtaining written informed consent , the study was conducted on 120 patients of either sex, aged 18-55 years .All surgeries were executed under general anesthesia , the naso septal access with Cottle ` s technique. Nasal splints were placed. The nose was packed for 24 hrs. The patients were randomly divided into 3 groups of 40 patients each.
Group A; Nasal packs with liquid paraffin
Group B ; Nasal packs with 5% lignocaine ointment
Group C; One side of the nasal cavity was packed with liquid para fin (C1) and the other nasal side was packed with 5% lignocaine ointment (C2), thereby acting as their own control.
Pain intensity was assessed post-operative by using visual analog score (VAS), (0,no pain, 10, excruciating pain).VAS was performed at 6 hrs post-operative and 24 hrs post-operative. Diclofenac sodium 50 mg oral was given BID and Diclofenac sodium 75 mg was given I/M if requested.
The total consumption of analgesic used in the first 24 hrs post-operative was calculated.

Statistical Analysis: The data were analyzed using SPSS. Paired t- test was used to compare VAS in each group. A p value < 0.05 was considered significant. Post –Hock tests and ANOVA test were applied to compare the VAS between different groups.

RESULTS

Table No l: Mean VAS at 6hrs and 24 hrs post-operatively

Group		Visual Analog Scale 6 hours	Visual Analog Scale 24 Hours
Group A	Mean	7.27	7.15
	N	40	40
	Std. Deviation	1.881	1.252
Group B	Mean	5.60	6.63
	N	40	40
	Std. Deviation	2.405	1.125
Group C1	Mean	7.40	6.07
	N	40	40
	Std. Deviation	1.033	1.023
Group C2	Mean	6.62	4.90
	N	40	40
	Std. Deviation	1.764	1.236
Total	Mean	6.72	6.19
	N	160	160
	Std. Deviation	1.955	1.424

A total of 120 patients who underwent the Septoplasty were studied . Out of 120, 63 (52.5%) were male and 57 (47.5 %) were female. The age range was from 18 years to 55 years.
Pain scores post-operative were significantly lower in group B,(5.60+-2.40) (p<0.000), compared to group A (Table I). The mean time to first request for analgesia was significantly prolonged in group B,(220.53+-42.12 min. p <0.005) ,much less than group A and group C (Table 2)
There was a clear difference in the VAS in patients having mixed nasal packs, the VAS was significantly lower on the lignocain side as compared to liquid paraffin packs.
The total consumption of analgesia post- operative was also less in group B (175.32+-14.13mg ,p<0.000) as compared to group A and group C (Table 3). No systemic complications were observed in any of the group.

Table No 2: Mean Time to request for Analgesia post-operatively

Group A	Group B	Group C
148.50+-32.45 min.	220.53+-24.12 min.	190.61+-36.45 min.

Table No 3: Mean Diclofenac sodium consumption in first 24 hrs post-operatively

Group A	Group B	Group C
225.14+-25.73 mg	175.32+-14.13 mg	200.16+-41.89 mg

DISCUSSION

Pain has been called the silent epidemic of our times. Topical anesthetics work by reversibly blocking sodium channels and preventing propagation of painful nerve impulses .It reduces post-operative pain, improves patient comfort and diminishes the need for further parenteral medications such as opioids and non-steroidal ant-inflammatory drugs.[6]Lignocaine is one of the most widely used local anesthetic agents.Lignocaine is a tertiary amine that is an amide derivative of diethylaminoacectic acid. Allergic reactions to amide group of anesthetic are extremely rare [7] .Lignocaine is variably and incompletely (less than 50 %) absorbed when administered by intra nasal route [8].
Recent studies indicate that nasal packs significantly contribute to post- surgical pain.[9] Topically applied 5% lignocaine ointment significantly improved post operative analgesia in the 1st 24 hrs after Septoplasty. Kuo et al have found that the post operatively applied lignocaine ointment packs caused less pain in Septoplasty patients compared to gauze packs alone .[10]
Pain scores were significantly lower in the 1st 6 hrs as compared to 24 hrs and this may be due to the short duration of action of lignoacine.

Several experimental studies demonstrated that various antinociceptive techniques applied before injuries are more effective in reducing post injury central sensitization phenomena compared to administration after injury.[11]

Absorption of lignocaine varies according to both the site and the mode of delivery and fluctuates with the use of vasoconstrictor or cholinergic drugs.[12] Hala and Ghaffar[13] has also confirmed that pre-emptive topical 2% lignocaine gel soaked pledget improves post operative analgesia.

Buchanan at el.[14] has also provided clinically based evidence for the use of bupivacaine as a local anesthetic in reducing pain following nasal surgery with packing.

CONCLUSION

Topical use of 5% lignocaine ointment is safe and may have a significant role in the relief of pain due to post operative nasal packing.

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Original Article

Role of Vit E on Kidney

Effects of Gentamicin on Renal Parenchyma and Prevention by Vitamin E in Young Albino Rats

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ABSTRACT

Objective: To determine the preventive role of Vitamin E on renal parenchyma after given of gentamicin in young albino rats.

Study Design: Experimental study

Place and Duration of Study: This study was carried out in the Department of Anatomy Baqai Medical University and Muhammad Medical College, Mirpurkhas from June 2011 to November 2011.

Methods and Material: 30 young albino rats were taken. They were divided into three groups ; A, B and C. The animals in group-A given normal saline 10 ml/kg/day intraperitoneal for 2 weeks. Group-B received gentamicin 100 mg/kg/day intraperitoneal for 2 weeks and group-C receives gentamicin 100mg/kg/day intraperitoneal with vitamin-E 2 mg/kg/day orally for 2 weeks. On day 15 all animals were sacrificed with deep ether anesthesia. Their kidneys were removed, fixed in 10 % formalin. Representative blocks were taken and embedded in liquid paraffin. For routine histological examination 5 µm thick section cut by microtome and stained with H&E, PAS and silver methenamine. Renal histology was done under light microscope to see the proximal and distal tubular diameter and count.

Results: No significant (P>0.05) changes were observed in the histopathology of kidney tissues of the groups A and C rats. The group B significantly (P<0.001) affected the histopathology of kidney.

Conclusion: It may be concluded that gentamicin produces changes in kidney, which may be attributed to ischaemia resulting in tubular necrosis in young albino rats simultaneous administration of vitamin-E partially protect the morphological and histological changes induced by gentamicin.

Key Words: Gentamicin, Vitamin-E, young albino rats, Kidneys.

INTRODUCTION

Gentamicin is an aminoglycoside bactericidal antibiotic that works by binding the 30S subunit of bacterial ribosome, interrupting protein synthesis, used to treat many types of bacterial infection, particularly those caused by gram negative organism.[1]

Gentamicin cause deleterious effects on kidney function, especially with respect to solute homeostasis, maintenance of renal perfusion and glomerular filtration. Renal toxicity can be a result of hemodynamic changes, direct injury to cells and tissue.[2] Studies that evaluated episodes of acute tubular necrosis (ATN) or Acute interstitial nephritis (AIN) due to antibiotics (e.g. aminoglycosides) has been reported to be upto 36%[3,4] Most episodes of drug-induced renal dysfunction are reversible, with function returning to baseline when the medication is discontinued. Chronic renal injury can however, be induced by some medications, leading to chronic tubulointerstitial inflammation, papillary necrosis.[5,6] Heightened physician awareness is necessary if renal injury and associated morbidity from renal failure are not to be prevented.

Vitamin E is the collective name for a set of 4 related α-, β-, γ-, and δ-tocopherols and the corresponding four tocotrienols α-, β-, γ-, and δ- which are fat-soluble vitamins with antioxidant properties[7,8]. The majar sources of Vitamin-E are avocado, nuts, such as almonds or hazelnuts, red palm oil, seeds, spinach, green leafy vegetables, vegetable oils (canola), corn, sunflower, soybean, cottonseed, olive oil, wheat germ, wholegrain foods, milk and asparagus[9]. The administration of vitamin E (antioxidant) has been shown to be beneficial in prevention and attenuation of renal scarring in numerous animal models of kidney diseases[10]. Antioxidative (tocopherol) therapies have been shown to prevent acute decrease in renal function induced by ischemia, contrast media and drugs like diclofenac sodium (NSAID) [11].

MATERIALS AND METHODS

This study was carried out during the period from June 2011 to November 2011, in the Department of Anatomy Baqai Medical University and Muhammad Medical College, Mirpurkhas. For this experimental study 30 young albino rats aged 2 weeks, weighing ranging from 20gm to 30gm were used. They were originally obtained from Charles River breeding laboratories, Brooklyn, Massachsetts, USA, and were cross bred at the animal house of Muhammad Medical College, Mirpurkhas. The animals were kept in the

animal house on a balanced diet. They were put under observation for one week prior to the experimental procedure for assessment of their state of health on basis of weight gain or loss.

The animals used in this study were divided into 3 groups: A,B and C. the animals in each group were kept in a separate cage and labeled. Each animal was weighed period to treatment.

Group-A (10 Animals): In this group each animal received normal saline 10 ml/kg/day intraperitoneal once daily for 2 weeks.

Group-B (10 Animals): In this group each animal received Gentamicin 100 mg/kg/day intraperitoneal once daily for 2 weeks.

Group-C (10 Animals): In this group each animal received Gentamicin 100 mg/kg/day intraperitoneal and vitamin-E (α-tocopherol acetate) 2 mg/kg/day dissolved in olive oil given orally by feeding tube once daily for 2 weeks.

On day 15 the animals were sacrificed kidneys were removed, bisected in two halves, one half fixed in 10% formalin and second in alcoholic formalin. The tissues were sectioned and mounted on slides. They were stained by Haematoxylin & Eosin, silver methamine and periodic acid Schiff stain.

The morphological changes in renal parenchyma were observed under light microscope. Five observations for each parameter were recorded in each animal. Proximal and distal tubular counts were made under 8x ocular and 40x objective with counting reticule in randomly selected five fields in the cortex of the kidney and proximal and distal tubular diameter was measurd with th help of ocular micrometer. The data was subjected to statistical analysis Student 't' test was employed to see the significance of the results.

RESULTS

Observations in Group-A (Control): In H&E stained sections the histological structure in the cortical and medullary portion appeared absolutely normal without any change in either glomeruli or tubules as shown in Figure 1.

In PAS stained sections the bursh border on the apical surface of proximal tubular epithelial cells stained magenta in colour and almost filled the tubule. The glycogen content of the cytoplasm of proximal tubular cells was quite normal. The basement membrane of proximal and distal tubules also stained magenta, which was distinct and regular.

Silver methenamine stained sections revealed basement membrane of glomeruli, Bowman's capsule and proximal and distal tubules which was faint in outline, and unmeasurable by light microscopy.

The mean values of number of proximal convoluted tubules per unit area as noted in group-A was 24.0 ± 0.49. when group-A compared with group-B highly significant increase (P<0.001) was noted in group-A, however, when group-A compared with group-C statistically non-significant difference (P>0.05) was observed.

The mean values of diameter of proximal tubules measured in unit area in group-A was 50.9 ± 0.74 µm, which when compared with group-B, statistically significant decrease (P<0.05) was noted in group-A, however, when compared with group-C, no significant difference (P>0.05) was observed.

The mean values of number of distal tubules per unit area, as observed in Group-A was 22.7 ± 0.56, which when compared with that in group-B , a highly significant increase (P<0.001) was observed in group-A, however, when compared with group-C, no significant change was noticed.

The mean values of diameter of distal tubules per unit area in group-A was 38.4 ± 0.37 µm, which when compared with group-B, a highly significant decrease (P<0.001) was noted in group-A, however, when compared with group-C, no significant change occurred.

Observations in Group-B: In H&E stained sections the interstitium of renal cortical area was sparse with few inflammatory cells but no marked oedema, many dilated and congested blood vessels were observed as shown in Figure 2.

In PAS stained sections the bursh border at the luminal surface appeared scanty and indistinct and at some places it was completely absent. The intracellular glycogen content of the proximal as well as distal tubules was moderately depleted. However, the basement membrane of proximal and intact..

In silver methenamine stained sections the basement basement membrane was visible as intensely stained black line around proximal and distal tubules which was quite thickened in some tubules but still not measurable by light microscopy.

The mean values of number of proximal convoluted tubule per unit area observed in group-B was 16.1 ± 0.66, which when compared with that in group-C, a highly significant decrease (P<0.001) was noted in group-B.

The mean values of diameter of proximal tubules per unit area in group-B was 54.3 ± 0.97 µm, which when compared with group-C, highly significant increase (P<0.001) occurred in group-B.

Mean values of distal tubular count per unit area as observed under high magnification in group-B was 14.5 ± 0.34, which when compared with group-C, highly significant decrease (P<0.001) was observed in group-B.

Mean values of diameter of distal tubules per unit area in group-B was 54.5 ± 0.59 µm, which when compared with that in group-C, highly significant increase (P<0.001) was noticed in group-B.

Observation in Group-C: In H&E stained sections the histological structure in the cortical and medullary

portion appeared absolutely normal without any change in either glomeruli or tubules as shown in Figure 3.

In PAS stained sections showing normal bursh borders at the apical surface of proximal tubules cells. It was well defined and almost filled the lumen of proximal tubules. The intracellular cytoplasm had normal glycogen content, basement membrane also appeared a regular outline.

The basement membrane of proximal and distal tubules was observed in silver methenamine stained sections. These sections showed uniformly continuous black stained basement membrane in both ttubules.

The mean values of the number of proximal convoluted tubules per unit area as observed under high magnification in group-C was 22.9 ± 0.66, which when compared with that in group-A, no significant change was observed. However, when compared with group-B statistically highly significant increase (P<0.001) was noted in group-C.

The mean values of diameter of proximal tubules per unit area in group-C was 51.6 ± 0.90 µm, which when compared with that in group-A, statistically no change was noticed. However when compared with group-B statistically significant decrease (P<0.01) was noted in Group-C.

Table No. 1: Comparison of Proximal and distal tubular counts and diameters per unit area between groups A and B.

	Group A Controls (n=10)	Group B Gentamicin (n=10)	
	Mean ± S.D ± SEM	Mean ± S.D ± SEM	P value
Proximal Tubular Count per unit area (Under Reticule)	24.0 ± 1.56 ± 0.49	16.1 ± 2.08 ± 0.66 **	0.001
Mean Diameter of Proximal Tubules (Under Ocular Micrometer)	50.9 ± 2.33 ± 0.74	54.3 ± 3.07 ± 0.97 *	0.030
Mean Distal Tubular Count (Under Reticule)	22.7 ± 1.77 ± 0.56	14.5 ± 1.08 ± 0.34 **	0.001
Mean Diameter of Distal Tubules (under Ocular Micrometer)	38.4 ± 1.16 ± 0.37	54.5 ± 1.85 ± 0.59 **	0.001

The mean values of the number of distal tubules per unit area as observed under high magnification in group-C was 20.7 ± 0.67, which when compared with that in group-A, no significant change was observed. However when compared with group-B statistically highly significant increase (P<0.001) was noted in Group-C.

The mean values of diameter of distal tubules per unit area in group-C was 39.8 ± 0.32 µm , which when compared with that in group-A , statistically no change was noticed. However when compared with group-B statistically highly significant decrease (P<0.001) was noted in Group-C.

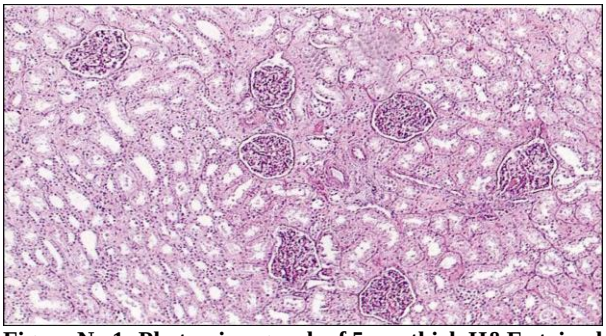

Figure No.1: Photomicrograph of 5 µm thick H&E stained paraffin section of rat kidney from group-A (control), showing normal architecture of renal cortex under low magnification. x101.

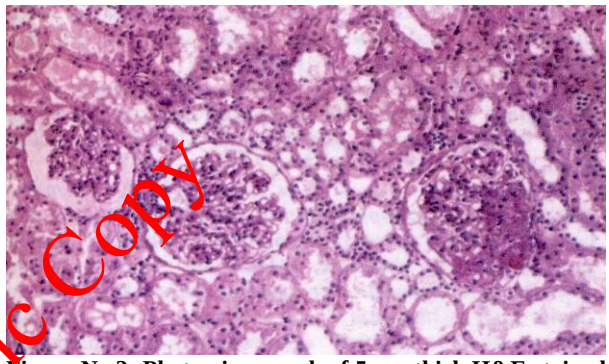

Figure No.2: Photomicrograph of 5 µm thick H&E stained paraffin section of rat kidney from group-B treated with gentamicin, showing dilated blood vessels with marked infiltration of inflammatory cells and damaged tubules. x205.

Table No.2: Comparison of Proximal and distal tubular counts and diameters per unit area between groups A and C.

	Group A Controls (n=10)	Group C Gentamicin with Vitamin E (n=10)	P-value
	Mean ± S.D ± SEM	Mean ± S.D±SEM	
Proximal Tubular Count per unit area (Under Reticule)	24.0 ± 1.56 ± 0.49	22.9 ± 2.08 ± 0.66	0.419
Mean Diameter of Proximal Tubules (Under Ocular Micrometer)	50.9 ± 2.33 ± 0.74	51.6 ± 2.85 ± 0.90	0.856
Mean Distal Tubular Count (Under Reticule)	22.7 ± 1.77 ± 0.56	20.7 ± 2.11 ± 0.67	0.067
Mean Diameter of Distal Tubules (under Ocular Micrometer)	38.4 ± 1.16 ± 0.37	39.8 ± 1.01 ± 0.32	0.079

Table No.3: Comparison of Proximal and distal tubular counts and diameters per unit area between groups B and C.

	Group B Gentamicin (n=10)	Group C Gentamicin with Vitamin E (n=10)	P-value
	Mean ± S.D ± SEM	Mean ± S.D ± SEM	
Proximal Tubular Count per unit area (Under Reticule)	16.1 ± 2.08 ± 0.66 **	22.9 ± 2.08 ± 0.66	0.001
Mean Diameter of Proximal Tubules (Under Ocular Micrometer)	54.3 ± 3.07 ± 0.97 *	51.6 ± 2.85 ± 0.90	0.01
Mean Distal Tubular Count (Under Reticule)	14.5 ± 1.08 ± 0.34 **	20.7 ± 2.11 ± 0.67	0.001
Mean Diameter of Distal Tubules (under Ocular Micrometer)	54.5 ± 1.85 ± 0.59 **	39.8 ± 1.01 ± 0.32	0.001

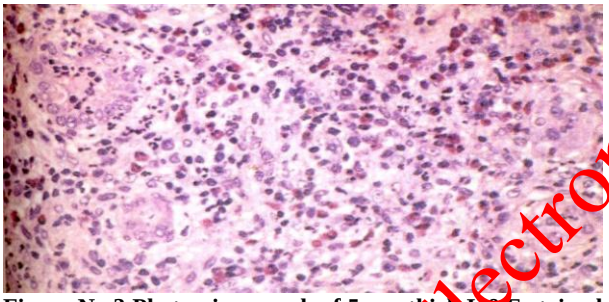

Figure No.3 Photomicrograph of 5 µm thick H&E stained paraffin section of rat kidney from group-C treated with gentamicin, and vitamin-E, showing almost normal proximal convoluted tubules (PT) and distal convoluted tubules (DT) x416.

DISCUSSION

Nephrotoxicity induced by Gentamicin has been found even in therapeutic doses.

Vitamin-E, an antioxidant is known to be a potent scavenger of free radicals which have been implicated in over hundred conditions in humans including ischaemia of many organs[12].

Studies on the Gentamicin have shown that prolonged administration of this drug should be considered as a risk for nephrotoxicity[13]. In the present study three groups of animals were used group-A acted as control, group-B received Gentamicin while group-C received gentamicin and vitamin-E.

The effect of both these drugs were observed including number and diameter of proximal and distal convoluted tubules.

The proximal tubular count was not changed significantly in group-C, when compared with control group-A, whereas a significant decrease in number of tubules per unit area in group-B occurred which may be attributed to damage to the tubular epithelial cells by ischaemia[14].

The highly significant increase observed in the diameter of proximal tubules in group-B as compared to groups A and C, may be attributed to degeneration of cells in proximal tubules resulting in apparent increase in their diameter[15].

The total number of distal tubules in group-B was significantly lower when compared with group A and C. The decrease in number of tubules may be attributed tofocal ischaemic necrosis of some of the tubules resulting in their numbers[16].

The diameter of distal tubules in group-B showed highly significant increase as compared to that in groups A and C, which may be attributed to vacuolar degeneration of cells which fill the lumen of damaged tubules resulting in increase in diameter[16].

CONCLUSION

It may be concluded that gentamicin produces changes in kidney, which may be attributed to ischaemia resulting in tubular necrosis in albino rats and simultaneous administration of vitamin E partially protect the morphological and histological changes induced by gentamicin.

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Original Article

Effects of Anti-Hypertension Drug

Efficacy & Biochemical Evaluation of Pharmaceutical Optimized Valsartan 80mg (F-3) with Essential Hypertension

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ABSTRACT

Objective: The objective of this double-blind, comparative study evaluating efficacy and biochemical effects of optimized Valsartan 80mg (F-3) as monotherapy in adult patient with essential hypertension.

Study Design. Double-blind, comparative study

Place and Duration of Study: This study was conducted at the Department of Biochemistry, University of Karachi from January 2011 to September 2011.

Materials and Methods: This was multicenter randomized, double-blind, comparative study. Patients were randomized to receive once Valsartan (F-3) daily for 8 weeks and at the end of study efficacy and biochemical evaluation was done.

Results: The patients treated with optimized Valsartan 80mg (F-3) alone, blood pressure reduction was lower, although significant; reaching values of 140.9 ± 11.3 / m88.9 ± 5.5 mmHg ($p < 0.05$ versus Placebo) by the end of eight weeks of treatment. . No significant variation of blood glucose was observed and different parameters of lipid profile were also observed during the eight weeks of treatment with antihypertensive regimen used. Thus, the drug regimens used may be considered neutral as regards glucose and plasma lipid metabolism profile because drug used at low doses.

Conclusion: We can suggest that the high antihypertensive efficacy, good tolerability and no biochemical effects of the optimized Valsartan 80mg (F-3) it is an excellent option for the treatment of hypertension in a wide range of hypertensive patients, with a high potential to reduce cardiovascular risks.

Key Words: Hypertension, Valsartan, Biochemical effects

INTRODUCTION

Hypertension is one of the strongest modifiable risk factors for cardiovascular and kidney disease and has been identified as the leading risk factor for mortality[1].In European countries the prevalence of hypertension in adults is estimated to be approximately 44%.[2] Current guidelines for the management of hypertension recommend a target blood pressure of 140/90 mmHg, with a stricter target for patients who have a high risk of cardiovascular events (< 130/80 mmHg).[3,4] Valsartan can control blood pressure for 24h,[5] probably because of its highly selective blockade of the AT1 receptor. In addition, when the AT1 receptor is blocked by an ARB and unbound Ang II can bind the AT2 receptor, the stimulation of the AT2 receptor may be involved in the effects of the ARB. The stimulation of AT2 receptors mediates natriuresis, which may contribute to the antihypertensive effect[6]. Interestingly, the local application of valsartan by means of valsartan-eluting stents inhibits neointima formation and increases AT2 receptor mRNA expression after vascular injury in a rabbit model, suggesting that up-regulation of the AT2 receptor by valsartan plays an important role through its antiproliferative effect.[7]Comparative safety and efficacy trials indicate that angiotensin receptor blockers like olmesartan medoxomil have superior tolerability and antihypertensive efficacy[8]. Similar investigation using olmesartan, medoxomil and amlodipine besylate showed great effectiveness and tolerance in patient with hypertension[9]. Combination therapies reduced B.P to a greater extent than with amlodipine besylate alone as indicated with benazepril hydrochloride with valsartan and with perindopril[10,,11.] The angiotensin-receptor blocker (ARB) valsartan and the calcium-channel blocker (CCB) amlodipine have proven to be safe and effective antihypertensive agents when used as monotherapy.[12–15] Therefore, the objective of this comparative study evaluating the efficacy and biochemical effects of optimized Valsartan 80mg (F-3**)** with placebo in the treatment of patients with essential hypertension.

MATERIALS AND METHODS

This was multicenter, randomized, placebo-controlled, comparative study. Patient was randomized to receive optimized Valsartan 80mg (F-3) once daily and Placebo once daily for 8 weeks. The study was conducted in Department of Biochemistry, University of Karachi from January 2011 to September 2011, Patients were selected from four different hospitals of orange Town and 80 patients were selected for the study. Therefore 80patients were effectively analyzed for efficacy and

tolerability the analysis of antihypertensive efficacy and biochemical effects of a therapeutic regimen in the long term becomes important. The primary efficacy variable was change from baseline in MSDP at the end of study. Secondary variable was change in mean sitting systolic blood pressure from baseline. Safety biochemical parameters (complete blood count, renal function, liver function, electrolytes, protein profile, and enzymes) and electrocardiogram at rest were also determined in all patients at the baseline (week O) and at the 8th week of antihypertensive treatment. At the same time points, glucose metabolism parameter values and plasma lipids (total cholesterol, HDL-cholesterol, LDL-cholesterol, and triglycerides) were also recorded. Biochemical parameters were determined using an automated method.

RESULTS

The patients treated with optimized Valsartan 80mg (F-3) alone, blood pressure reduction was lower, although significant; reaching values of 140.9 ± 11.3 / m88.9 ± 5.5 mmHg ($p < 0.05$ versus Placebo) by the end of eight weeks of treatment. Variations in blood pressure measurement in the standing position during treatment were similar to those recorded in the sitting position, and no episode of orthostatic hypotension was reported in either of the therapeutic regimen.

Table No.1: Baseline characteristics

	Valsartan (F-3) (n=60)	Placebo (n=20)
Age (years)	50.2 ± 9.3	51.5 ± 9.8
Male / Female (%)	43.4 / 56.6	35.0 / 65.0
Body weight (Kg)	68.9 ± 13.5	71.2 ± 12.2
BMI (kg/m2)	27.5 ± 3.8	27.8 ± 3.4
SBP sitting (mmHg)	149.5 ± 11.5	148.8 ± 10.9
DBP sitting (mmHg)	95.7 ± 7.4	94.9 ± 7.8

Table No.2: Ambulatory blood pressure monitoring. Mean values of blood pressure

	Valsartan (F-3) (n=60)	Placebo (n=20)	P-value
Systolic BP - 24 hours (mmHg)			
Baseline	149.8 ± 11.2	149.2 ± 11.5	NS
Week 8	140.9 ± 11.3	148.9 ± 11.2	0.0074
Diastolic BP - 24 hours (mmHg)			
Baseline	97.6 ± 7.4	95.4 ± 8.8	NS
Week 8	88.9 ± 5.5	94.9 ± 7.9	0.0003

NS: Non significant, p: probability

No significant variation in leg volume measurement was observed among the both groups studied during the eight weeks of treatment. No significant variations of blood glucose were observed and different parameters of lipid profile were also observed during the eight weeks of treatment with antihypertensive regimen used. Thus, the drug regimens used may be considered neutral as regards glucose and plasma lipid metabolism profile because drug used at low doses.

Table No.3: Baseline Biochemical characteristics

	Valsartan (F-3) (n=60)	Placebo (n=20)
Fasting Blood Glucose (mg/dl)		
Baseline	97.4 ± 11.5	99.1 ± 8.8
Week 8	95.5 ± 11.9	98.9 ± 9.2
	Total Cholesterol (mg/dl)	
Baseline	197.2 ± 43.2	195.2 ± 33.3
Week 8	199.7 ± 43.5	193.9 ± 34.1
	LDL - Cholesterol (mg\dl)	
Baseline	114.4 ± 34.1	117.9 ± 25.9
Week 8	114.9 ± 34.5	116.8 + 24.7
	HDL - Cholesterol (mg\dl)	
Baseline	52.9 ± 13.1	48.9 ± 11.7
Week 8	51.8 ± 12.8	48.7 ± 11.5
	Triglycerides (mg\dl)	
Baseline	137.2 ± 88.5	145.5 ± 88.1
Week 8	136.1 ± 89.3	144.2 ± 88.9

DISCUSSION

The baseline characteristics of the population included in the study are shown in Table No 1. We can observe that the groups were not different in relation to age, body mass index and weight, heart rate, and systolic and diastolic pressure values. No significant variations of blood glucose and different parameters of lipid profile were observed during the eight-week of treatment with any of the three antihypertensive regimens used. Thus, the drug regimens used may be considered neutral as regards glucose, plasma lipid metabolism. The results of this study showed that the optimized product Valsartan 80mg (F-3) as a high antihypertensive efficacy that is sustained in the long term with a quite reduced percentage of loss of blood pressure control in table No.2 We observed that more than 71.8% of the patients treated with optimized product of Valsartan 80mg (F-3) remained with diastolic blood pressure levels equal to or lower than 90 mmHg, thus achieving the goals for the treatment of hypertension. The difficulty to achieve the goal of controlling systolic blood pressure explains why the international guidelines for studies on antihypertensive drugs still use criteria based on diastolic blood pressure to describe the antihypertensive efficacy of a drug, in spite of the fact that guidelines indicate the real need to control systolic blood pressure as well. It is important to point out that blood pressure reduction provided by the treatment with optimized product of Valsartan 80mg (F-3) did not cause any secondary Increase in sympathetic activity, since no significant variations of heart rate occurred. In addition to a high efficacy in reducing blood pressure, keeping it at controlled levels,

an antihypertensive drug should also have a good biochemical profile, since the presence of adverse effects may decrease the degree of compliance of the patient to the therapeutic regimen, thus ultimately leading to treatment dropout. Our results showed that the optimized product of Valsartan 80mg (F-3) at low doses has a very good biochemical profile with a low incidence of adverse events. The good biochemical profile of the optimized Valsartan 80mg (F-3) may be explained by the use of lower doses of each of the hypotensive drugs, since the existence of a strong relation between the dose of the hypotensive drug and the frequency of adverse events is known. However, some drugs used in the treatment of hypertension, such as diuretics and beta-blockers, are known to be able to promote harmful alterations in lipid metabolism, especially in glucose metabolism. In our study we observed that the use of the optimized Valsartan 80mg (F-3) did not change parameters of either glucose metabolism or plasma lipids, thus having a neutral biochemical profile even when used for 8 weeks. Table.No.3 Based on these results we can suggest that the optimized product Valsartan 80mg (F-3) is safe and adequate for the treatment of hypertension in patients with metabolic syndrome, diabetes mellitus and dyslipidemias. Because alterations in these parameters are very frequently observed in hypertensive patients. Incidentally, hypertension is frequently associated to the metabolic syndrome; also, the frequency of this association increases with age. However, some drugs used in the treatment of hypertension, such as diuretics and beta blockers, are known to be able to promote harmful alterations in lipid metabolism, especially in glucose metabolism. Based on these results we can suggest that this therapeutic modality is safe and adequate for the treatment of hypertension in patients with metabolic syndrome, diabetes mellitus and dyslipidemia.

CONCLUSION

In brief, the results of this multicenter study demonstrated that the optimized Valsartan 80mg (F-3) has a high antihypertensive efficacy, allowing approximately 71.8% of the patients treated to achieve and maintain for eight weeks. We can suggest that the high antihypertensive efficacy, good tolerability and no biochemical effects of the optimized Valsartan 80mg (F-3) it is an excellent option for the treatment of hypertension.

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Original Article

Hepatitis E

Frequency of Hepatitis E among Patients Visiting Rural Health Centre Ranipur Sindh

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ABSTRACT

Objective: To determine frequency of Hepatitis E among patients visiting rural health centre Ranipur Sindh.
Study Design : Retrospective study
Place and Duration of Study: The study was conducted in patients visiting OPD at rural Health Centre Ranipur from June 2011 To February 2012.
Materials & Methods: The study was conducted in patients visiting OPD with the complaints of gastrointestinal symptoms and jaundice. A designed, structural Performa was filled with the consent of the patients after taking permission from hospital administration. A sample random technique was used to get blood sample and sent to the local laboratory for screening Hepatitis E through Immunochromatography method. 10 to 50 years aged male and female patients were included in the study. The data was analyzed using SPSS 16.
Results: Total 2118 patients were screened. 98 (4.27%) cases were positive for Hepatitis E. Among them, the frequency of HEV was highest in children (10-15 years), followed by young adults (16-30) and older adults (31-50). In all patients, females were 58% and males were 42%.
Conclusion: In this study we found significant number of HEV cases, among whom the larger number was from children. In all age groups, females were more affected. Further research should be done for making plans and designed strategies to prevent the epidemic of HEV.
Key Words: Hepatitis E, Prevalence, Epidemics

INTRODUCTION

Hepatitis E is an inflammatory disease of the liver, caused by a virus called Hepatitis E virus (HEV). It is estimated that HEV causes 271000 deaths per year globally[1]. The virus is transmitted through oro-fecal route, mainly through contaminated water and food. It can also be acquired through ingestion of infected meat. HEV Infected Blood transfusion and products are additional routes of transmission[2,3]. It affects most commonly the young and middle aged adults of 15-40 years[4,5]. The disease generally presents with acute illness. Clinical features include flu like symptoms, lethargy, loss of appetite, abdominal pain, fever, jaundice and hepatomegaly. The disease has no specific treatment but symptomatic only. The disease can be prevented by proper hygienic measures. Proper disposal of waste, clean water supply, self hygiene and the use of hygienic food prevent this disease[6,7].

The disease is generally self-limited within few weeks and generally does not progress to the chronic disease. However, two recent reports have shown the evidence of chronic HEV infection in transplanted patients[8,9]. Hepatitis E has a mortality rate of 0.2–1% in the general population[2]. HEV results in increased mortality in the patients, suffering from chronic liver disease[10]. It is diagnosed by detection of antibodies against HEV and HEV nucleic acids in serum through Immuno chromatography (ICT) or ELISA and Polymerase chain reaction (PCR), respectively[11,12,13]. There are two types of antibodies, i.e., immunoglobulin M (IgM) and immunoglobulin G (IgG). During acute phase, IgM is elevated, which then declines to base line within 3 to 6 months. IgG is also raised during acute phase and can be detected for two years. Other studies have shown that IgG for HEV can be detected till 13 years post infection[14,15]. Hence, presence of IgM indicates acute infection. IgG is more valuable in studies for detection of HEV seroprevalence[11]. These antibodies can be detected in the patients' serm by using commercial kits of various international companies[14]. As in most of the cases, HEV has a self-limiting outcome, therefore the patients are ignored regarding the management of the disease, which results in fulminant hepatic failure and death of few patients. Hence in the presented study, we investigated the frequency of HEV in our region to help the proper management and prevention of the disease outbreak.

MATERIALS AND METHODS

Retrospective study was conducted in OPD of Rural Health Centre Ranipur Sindh from June 2011 To February 2012. Total 2118 patients of 10 to 50 years age, both male and female, presenting with signs and symptoms of hepatitis such as, jaundice, right hypochondrial or epigastric pain, loss of appetite, nausea, vomiting, lethargy, muscle ach and fever were included in the study. A designed structural Performa was filled with the consent of the patients after taking permission from the hospital administration. A sample

random technique was used to get blood sample (2 to 3 ml) and sent to the local laboratory, where the serum was isolated for HEV screening. HEV test was performed by using EIA (enzyme linked immunosorbent assay) method, which detects antibodies against hepatitis E virus. The data was collected and analyzed using SPSS version 16.

RESULTS

Out of 2118 patients, 98 (4.27%) were positive for HEV infection. Maximum number of affected patients was from children (10-15 years). Overall, females were more affected than males. Further details for gender and frequency of HEV in various age groups are listed in table 1.

Table No.1: Frequency of Hepatitis E

Gender	Male n = (%)	Female n = (%)	Total n = (%)
Gender	41 (41.8)	57 (58.2)	98 (100)
Age	Male n = (%)	Female n = (%)	Total n = (%)
10 to 15yrs	17 (41.5)	24 (58.5)	41 (41.8)
15 to 30yrs	14 (41.2)	20 (58.8)	34 (34.7)
> 30 yrs	10 (43.5)	13 (56.5)	23 (23.5)
Total	41 (41.8)	57 (58.2)	98 (100)

n: number

DISCUSSION

In the presented study, the frequency of hepatitis E infection was determined, which was 98 (4.67%) among 2118 patients, presenting with symptoms of suspected hepatitis. This is the first time study in our region regarding HEV infection. Very few studies have been conducted in other parts of our country in which HEV prevalence was found to be 12.5%[24]. Our results correlate with the other studies conducted in Turkey and Israel where HEV frequency was found to be around 4% and 2%, respectively[16]. There are multiple studies conducted on the prevalence of HEV worldwide. Various results have been shown by various groups. In our neighbouring countries such as Iran, it was 7.4%[25], in India 35%[17] and in Bangladesh 22.5%[18]. Literature review shows variations in the incidence of hepatitis E in the same country, for example, another study in India showed the frequency of HEV infection to be 18%[18]. Prevalence of HEV infection in school children of Chennai India was previously described to be 16%[19]. The variation depends upon the outbreak of the virus, which can be due to epidemiological factors, including weather changes, water and food supplies, and social hygienic conditions. It has already been shown that these factors affect the out breaks of hepatitis E[20,21]. Our findings regarding the HEV infection to be commonest among females correlate with the other studies[22,23]. Another important finding of our study was that the children group (10-15 years old) was most commonly affected, which variates from the other studies conducted in other countries which show the young adults to be the most common group affected. However, another study conducted in Egypt showed that HEV infection was most common in age group of 10-20 years. As in our region, children of 10-15 years are school going and belong to poor families. Lack of awareness of health and the poverty are the major factors to cause outbreaks of various infectious diseases including hepatitis E among children.

Therefore, further studies are required to know the frequency and causative factors of HEV infection in our region at various time points so that the disease can be prevented and the awareness programs regarding personal hygiene, hygienic food and water supply, and the social sanitation could be launched.

CONCLUSION

Hepatitis E is a common health issue in our region affecting more commonly children and females. More attention and awareness programs for the people are needed to prevent this disease and increase the quality of life with a good health.

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Original Article

Correlation Between Clinical Severity and Eosinophillic Count in Asthmatic Patients

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ABSTRACT

Objective: To determine the correlation between the blood eosinophil count and the severity of symptoms in asthmatic patients.

Study Design: Prospective observational study

Place and Duration of Study: This study was carried out in Dow General Hospital, Dow University of Heath Sciences from 1st January 2011 to 31st December 2011

Materials and Methods: Asthmatic patients who were admitted in Dow General Hospital, Dow University of Heath Sciences, and those who fulfilled the inclusion criteria were enrolled in the study. Physical examination was carried out and the severity of the symptoms was gauged by using Peak Expiratory flow meter and absolute eosinophil count. The data thus collected was analyzed using SPSS Version 15.

Results: Among 56 patients who were enrolled in the study 29(51.8%) were male and 27(48.2%) were female. Ages were between 13 and 70 years. The absolute eosinophil count ranged between 70/mm^3 and 1400/mm^3. Based on the definition of asthma severity, 20 patients (35.7%) had mild asthma, 17(30.4%) had moderate and 19(33.9%) patients had severe asthma.

Conclusion: Statistical analysis showed that no relationship exist between blood eosinophil count and the severity of asthma. ($p < 0.003$).

Key Words: Asthma, Bronchial asthma,Absolute eosinophil count

INTRODUCTION

Asthma has emerged as a common cause of disability[1,2]. It is defined as a chronic disease involving inflammation of airways along with the increased response resulting in reversible lower airway obstruction.[3] Its etiology is multifactorial.[4] IgE, mast cells, basophils, and eosinophils are essential components of allergic inflammation [5.]

According to WHO it is the most common chronic disease, affecting around 235 million people currently, worldwide. It has more than 10% prevalence worldwide[6.] The worldwide ISAAC study showed that the prevalence of asthma among Pakistani children is 8%. [7] The patho-physiology of asthma runs a gamut of multi-facet dimensions. It is clinically heterogeneous with several factors mediating its onset.[8]

MATERIALS AND METHODS

This was a prospective observational study was carried out with patients presenting with asthmatic symptoms to Dow General Hospital, Dow University of Health Sciences between the period of one year from 1st January 2011 to 31st December 2011.The study included 56 patients with asthma who were admitted in Department of Medicine, Dow General Hospital, DUHS. Inclusion criteria was Symptom resolution with bronchodilator therapy confirms the diagnosis,Peak Expiratory Flow (PEF) demonstrate reversibility and any Alternative diagnosis are excluded. Exclusion criteria were Upper respiratory disease, Foreign body in trachea or bronchus, Vocal cord paralysis, Mechanical obstruction of the airways. (Foreign body or tumor lymph nodes), Heartdisease, Chronic Obstructed Pulmonary disease, Pulmonaryembolism, Pulmonary infiltrations with eosinophilia and cough secondary to drugs. Patients were included with their clinical history fulfilling the criteria for the asthma and previous episodes of asthma their History, clinical examination and the therapeutics regime was noted. Physical examination and hematological assessment was carried out in every case according to Performa attached. Patients having asthma were observed using their Peak Expiratory Flow. Mild Asthma PEF value ≥80% of the predicted value, Need for inhaled β-agonist short acting every 8 hours or more and no Night times symptoms. Moderate Asthma; PEF value 60 – 80% of the predicted value, Need for inhaled β-agonist short acting every 4 – 8 hours with mild Night times symptoms. Severe Asthma; PEF value <60% of the predicted value, Need for inhaled β-agonist short acting every 2 – 4 hours And severe Night times symptoms .Blood eosinophil count was recorded and the severity of the asthma was evaluated according to the definition of severity. Eosinophil count has been divided in three categories: Group I i.e. < 500/mm^3,

Group II i.e. 501-1000/mm^3 and Group III i.e. >1000/mm^3. Both the count and the severity were analyzed using Chi- square using SPSS (version 10.0) software.

RESULTS

56 (Fifty six) patients with asthma were included in the study. Among those who were enrolled in the study 29(51.8%) were male and 27(48.2%) were female.The subjects included in the study aged between 13 years and 70 years with the mean age of 42.75 years .The severity of asthma was gauged on clinical examination and Peak Expiratory Flow (PEF). The absolute count of eosinophil was also sent. The absolute count of eosinophil ranged between 70/mm^3 and 1400/mm^3 with a mean count of 436.73/mm^3 (Table 1). 20 patients (35.7%) had mild asthma, 17(30.4%) had moderate and 19(33.9%) patients had severe asthma (Table 2). As the objective of the study was to evaluate absolute eosinophil count as a marker of severity, it was found that the relationship between the two parameters was not significant (Table 3).

Table No.1: Range of Absolute Eosinophilic Counts I Study Subjects

Maximum	Mean	Std. Deviation	N	Minimum
1400.00	436.7321	225.7487	56	70.00

Table No.2: Severity of asthma in study subjects

	Frequency	Percent
Mild	20	35.7
Moderate	17	30.4
Severe	19	33.9
Total	56	100.0

Table No.3: Cosinophil distribution along with asthma findings on the basis of severity.

Eosinophil distribution	Asthma findings			Total
	Severe	Moderate	Mild	
< 500	2 3.6%	0 0%	0 0%	2 3.6%
501-1000	7 12.5%	11 19.6%	19 33.9%	37 66.1%
> 1000	10 17.9%	6 10.7%	1 1.8%	17 30.4%
Total	19 33.9%	17 30.4%	20 35.7%	56 100.0%

χ^2 = 16.37, d.f = 4, p < 0.003, Statistically significant difference

The data revealed independence between both findings at P < 0.05

Graph 4: Age Distribution

N	Mean	Minimum	Maximum
56	42.7500	13.00	70.00

DISCUSSION

Asthma is a chronic inflammatory disease of airway. It affects 14 to 15 million people in United States, and affected 4.5 million children. In Pakistan in a study conducted in 2007, prevalence of asthma in school going children between the ages of 3-15 years was found to be 15.8%[9]. The increasing prevalence of asthma and recognition of burden it imposes, has led to extensive research into its cause, pathophysiology and management.[10]

This study was conducted to evaluate absolute eosinophil count as marker of severity of asthma in patients.

In this study conducted over a period of six months, 56 patients diagnosed with asthma were enrolled. 20 patients (35.7%) had mild, 17 (30.4%) and 19 (33.9%) patients were found to have severe asthma. When their absolute eosinophil count as marker of severity of asthma was evaluated, no significant relationship was found between the two parameters.

In a study conducted by Barry showed total eosinophil count to be related with asthma activity and for early detection of exacerbations and also found it to be useful in regulating in steroid dosage[11]. Similar results were concluded in another study by Christoph Walker, where they found close correlation between severity of asthma and serum eosinophil count and T cell activation.[12]

In another research conducted in 2009-2010 in Sweden on 12,406 subjects,[13] also found blood eosinophil counts and exhaled nitric oxide levels to be independently associated with wheeze and asthma events in patients, although only intermediate or high blood eosinophil counts were found to be associated with emergency department visits. Also another study conducted in 2006 concluded that there is a direct relation between late phase asthmatic reactions and blood eosinophil count.[14]

In a study published in 2012 studiedvariability of blood eosinophils count in patients with moderate asthma during 24 hour[15], found significant variability among the levels of eosinophil count, putting the utility of single eosinophil count in question. Similarly another study conducted in London in 2013 showed blood eosinophil count to be not a reliable marker of inflammatory process in children with severe asthma[16], as 86% patients with severe asthma had normal blood eosinophil count.

These observations suggest that there may be a direct association between eosinophils and airway reactivity in subjects who develop late-phase

CONCLUSION

This study was conducted to evaluate the relationship of eosinophil count in the blood and the severity of the

condition. However, the study did not show any relationship between these two variables and it seems that both peripheral eosinophil count and the severity of asthma are independent of each other. The limitation of study is that differentiation between intrinsic and extrinsic asthma is not clearly made as extrinsic asthma have predisposition to form IgE antibodies and intrinsic asthma may form IgEantibodies. Secondly the starting age of study group in thirteen years and above when atopic asthma tend to diminish. Thirdly sample size is small so larger scale study is needed to support this conclusion.

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Original Article

Oral Maxillofacial Surgery

Anxiety Levels in Dental Patients

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ABSTRACT

Objective: The aims of the study were to describe the level of dental anxiety in a representative sample population.
Study Design: Experimental study
Place and Duration of Study: This study was conducted at the Fatima Jinnah Dental College, Karachi. The study was conducted 1st to 31st of March 2013
Material and Methods: All patients coming to the dental OPD for different dental procedures during the month of March 2013 were included in the study. Study sample comprised of 213 patients 135 Females and 78 Males. The age of the patients ranged from 5 to 75 years. The study sample was divided into three groups: 1) 5-24 years 2) 25-39 years and 3) 40-75 years According to the performed dental procedures the sample was divided into two groups; 1) undergoing invasive procedures 2) undergoing non-invasive procedures Measurement of anxiety levels were recorded on the proforma using Norman Corah's anxiety scale data was entered on Microsoft Excel work sheet and was analyzed using SPSS 14.
Results: The results of this study showed women having higher DAS values as compared to men both in educated and non-educated strata regardless of the nature of the procedure being performed invasive or non-invasive. In the study 40% males and 25.5% females were relaxed when asked for their anxiety levels when visiting for a dental checkup and considered it as an enjoyable experience. 49.1% Males and 47.3% Females were relaxed waiting in the dental office. When asked regarding the noise of a drill 3.6% Males and 8.2% Females felt very anxious. For question relating to tooth cleaning and instrument preparation 5.5% Males and 8.2% Females were very anxious.
Conclusion: This study has shown that educated individuals in both the genders have more anxiety as compared to uneducated individuals. Government funding should be directed towards awareness programs for population regarding dental treatments. Training of dental practitioners in patient counseling should be emphasized in the management of anxious patient.
Key Words: Anxiety level, Dental treatment

INTRODUCTION

Anxiety related to dental treatment is very common and it is potentially distressing, both for the patient and for the dental practitioners. Anxiety can be defined as a feeling of worry, nervousness, or unease about something with an uncertain outcome[1]. Anxiety is one the biggest factors in the avoidance of dental care.[2,3]
Dental anxiety is associated with a number of different factors like; pain, discomfort or previous bad experience during dental treatment. Patient's anxiety makes it harder to provide treatment, treatments becomes more time consuming and can also affect the quality of dental care. Understanding the behavior of an anxious patient will aid to improve patient care. The intensity of dental anxiety is different among certain groups in the population.[4] Neverlien in his study has shown that younger people, people with low income or low socioeconomic status, and people with lower levels of education tend to have more severe dental anxiety than people who are elderly, more affluent, or better educated.[5]
Only a few studies concerning dental anxiety are published in Pakistan. This study is done at the Fatima Jinnah Dental College, Karachi. Measurement of anxiety levels were recorded on the proforma using Norman Corah's anxiety scale[6,7] data was entered on Microsoft Excel work sheet and was analyzed using SPSS 14.

MATERIALS AND METHODS

This study was conducted at the Fatima Jinnah Dental College, Karachi. All patients coming to the dental OPD for different dental procedures during the month of March 2013 were included in the study. Study sample comprised of 213 patients 135 Females and 78 Males.
The age of the patients ranged from 5 to 75 years. The study sample was divided into three groups:
1) 5-24 years
2) 25-39 years and
3) 40-75 years
According to the performed dental procedures the sample was divided into two groups;
Group 1: undergoing invasive procedures like simple extraction, impaction, fillings and root canal treatment
Group 2: undergoing non-invasive procedures like consultation, scaling, polishing and orthodontic treatment.
Dental anxiety was estimated using the Corah's Dental

Anxiety Scale (DAS). (Table 1) This scale measures reactions to four different dental treatment situations:
1) before attending the dental surgery;
2) waiting in the dental operatory;
3) sitting in the dental chair; and
4) undergoing treatment.
Each question has five pre-structured answers evaluated on a scale from one to five;
a = 1, b = 2, c = 3, d = 4, e = 5. The maximum possible total can be 20

Table No.1: Norman Corah's Dental Questionnaire

1. If you had to go to the dentist tomorrow for a check-up, how would you feel about it?
a. I would look forward to it as a reasonably enjoyable experience.
b. I wouldn't care one way or the other.
c. I would be a little uneasy about it.
d. I would be afraid that it would be unpleasant and painful.
e. I would be very frightened of what the dentist would do.
2. When you are waiting in the dentist's office for your turn in the chair, how do you feel?
a. Relaxed.
b. A little uneasy.
c. Tense.
d. Anxious.
e. So anxious that I sometimes break out in a sweat or almost feel physically sick.
3. When you are in the dentist's chair waiting while the dentist gets the drill ready to begin working on your teeth, how do you feel?
a. Relaxed.
b. A little uneasy.
c. Tense.
d. Anxious.
e. So anxious that I sometimes break out in a sweat or almost feel physically sick.
4. Imagine you are in the dentist's chair to have your teeth cleaned. While you are waiting and the dentist or hygienist is getting out the instruments which will be used to scrape your teeth around the gums, how do you feel?
a. Relaxed.
b. A little uneasy.
c. Tense.
d. Anxious.
e. So anxious that I sometimes break out in a sweat or almost feel physically sick.
SCORING THE DENTAL ANXIETY SCALE (DAS)
a = 1, b = 2, c = 3, d = 4, e = 5 Total possible = 20
Anxiety rating:
5 - 8 = mild anxiety
9 - 12 = moderate anxiety but have specific stressors that should be discussed and managed
13 - 14 = high anxiety
15 - 20 = severe anxiety (or phobia). May be manageable with the Dental Concerns Assessment but might require the help of a mental health therapist.

Anxiety was rated as;
5 - 8 = mild anxiety
9 - 12 = moderate anxiety
13 - 14 = high anxiety and
15 - 20 = severe anxiety (or phobia).
Data was entered on Microsoft Excel work sheet and was analyzed using SPSS 14

RESULTS

A total of 213 patients completed the questionnaire regarding their anxiety level and were included as a part of this study. The study group was **41%** of the patients belonged to age group of 5-24 years, **37%** of the patients belonged to age group of 25-39 years, **22%** of the patients belonged to age group of 40-75 years According to Corah's questionnaire:

1. Relating to a visit for a dental checkup 40% Males and 25.5% Females were looking to it as an enjoyable experience.
2. Question relating to waiting in the dental office approx. 49.1% Males and 47.3% Females were relaxed.
3. Question regarding the noise of a drill 36.4% Males and 30.9% Females were relaxed while 36.4% Males and 27.3% Males Females felt a little uneasy and approx. 3.6% Males and 8.2% Females felt very anxious.
4. Question relating to tooth cleaning and instrument preparation 27.3% Males and 26.4% Females were relaxed, 34.5% Males and 28.2% Females felt a little uneasy, 20% Males and 25.5% Females were tense and 5.5% Males and 8.2% Females were very anxious.

Population undergoing invasive procedures including extraction, impaction removal, fillings and root canal treatment comprised of 83 individuals (approx. 50%popuplation). In educated strata 30 Males and 78 Females had Mild anxiety levels followed by 15 Males and 30 Females with Moderate anxiety levels, 6 Males and 15 Females with High anxiety levels and 3 Male and Females with Severe anxiety levels. In uneducated strata 3 Male and 9 Females with Mild anxiety levels followed by 12 Males and 33 Females with Moderate anxiety levels 3 Female with Severe anxiety levels.

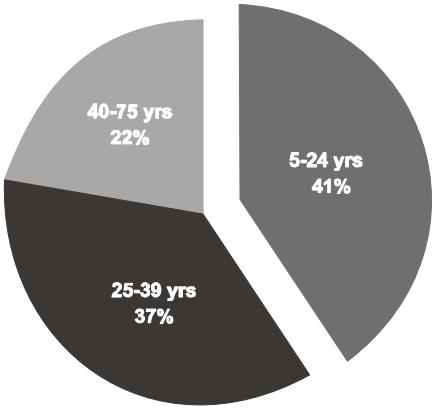

Figure No. 1: Age group distribution

Population undergoing non-invasive procedures including routine consultation, scaling and orthodontic treatment in educated strata 54 Males and 63 Females had Mild anxiety levels followed by 15 Males and 42 Females with Moderate anxiety levels, 9 Males and 15 Females with High anxiety levels and 6 Males and 18 Females with Severe anxiety levels. In uneducated strata 6 Males and Mild anxiety levels followed by 6 Males and 6 Females with Moderate anxiety levels and 6 Females with Severe anxiety levels.

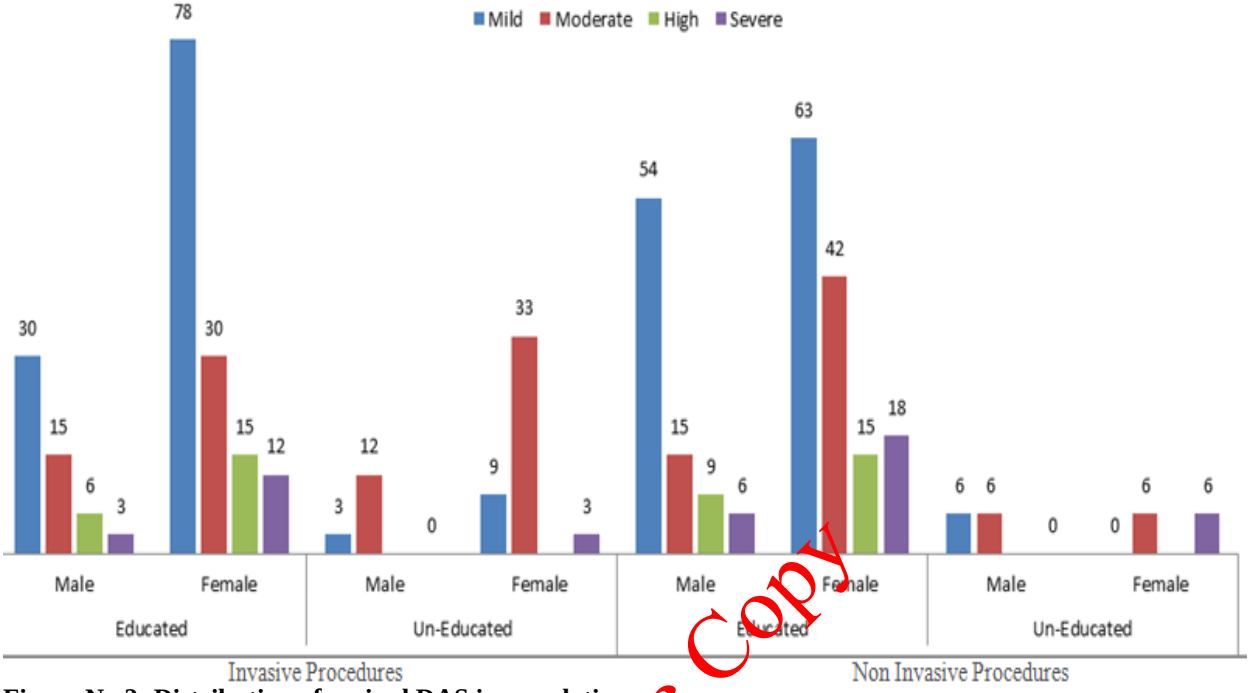

Figure No.2: Distribution of revised DAS in population group

DISCUSSION

Research on human responses to pain stimulus has generally found that women report higher levels of anxiety and exhibit less tolerance to pain at a given stimulus as compared to men.[8] The results of this study also showed similar results women showing higher DAS values as compared to men both in educated and non-educated strata regardless of the nature of the procedure being performed invasive or non-invasive. (Fig. 1 & 2) These results are most likely due to real differences in anxiety levels between genders or a greater readiness among females to acknowledge feelings of anxiety to perhaps both factors acting in combination. Stabholz also had similar finding in his study.[9]

In our study 40% males and 25.5% females were relaxed when asked for their anxiety levels when visiting for a dental checkup and considered it as an enjoyable experience. 49.1% Males and 47.3% Females were relaxed waiting in the dental office. When asked regarding the noise of a drill 3.6% Males and 8.2% Females felt very anxious. For question relating to tooth cleaning and instrument preparation 5.5% Males and 8.2% Females were very anxious. Similar findings were shown in the study conducted in Nigeria.[10,11] This study showed significantly higher anxiety levels in both the genders undergoing invasive procedure as compared to non-invasive procedures. The level of education also had an effect on anxiety levels[12] this study has shown that educated individuals in both the genders have more anxiety as compared to uneducated individuals. Perhaps this may be because of the increase in awareness related to experience and education.

CONCLUSION

There is a high prevalence of fear and anxiety in female population in respect of dental procedures. Invasive procedures create more anxiety as compared to non-invasive procedures. Government funding should be directed towards awareness programs for population regarding dental treatments. Training of dental practitioners in patient counseling should be emphasized in the management of anxious patient.

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Original Article

Learning via MCQs

Effective learning through Multiple Choice Questions against short Essay type of assessment in Medical Physiology students of Lahore

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ABSTRACT

Objective: The present study was carried out to evaluate the advantages of Multiple Choice Questions (MCQ) against short Essay type (SEQ).

Study Design: longitudinal study

Place and Duration of Study: This study was conducted Rashid Latif Medical College, Lahore from December 2011 to March 2013.

Materials and Methods: A total of 200 second year students were involved in the study and their scores in SEQ and MCQ papers were analyzed. Out of them 100 students were girls and 100 were boys. The students were informed that they are going to be accessed via three SEQ examinations and three MCQ examinations and then a survey and viva was conducted. Gender differences in performances were also studied.

Results: The result of this study shows that those students who were kept on MCQ type of assessment emerges to be weak students at the end of the session as compared to others who were assessed by SEQs

Conclusion: The SEQ type of assessment was established as a better method of assessment to strengthen student`s learning process and helped students to exert and retain more knowledge.

Key Words: multiple choice questions, short essay type, assessment

INTRODUCTION

Learning is obtaining new knowledge besides amending and enhancing previous one. Deep learning engages long term memory through analysis of new knowledge and thoughts as well as in-depth understanding of the newly acquired information, it also associate these to prior knowledge. In learning assessment plays important role. Assessments and evaluation encourages students to exert more and the methods of assessment play important role in their learning process [1].

The choice of best method of assessment in Medical college curriculum of Physiology is debatable topic from last few years in Lahore. In last decade there was a swift transfer of the assessment methodology from essay question towards MCQs[1, 2]. Innovations are fine and are required in every system after passage of time .The necessity of bring up innovations arises due to the modern era and its upcoming requirements which also leads to quick examination system and quicker results. Other reasons can be enormous rise in medical students quantity internationally and the need of highest quality and standardized medical education. There can also be a desire to revolutionize which mirrors the hasty life style of current generation which leads to the development of multiple choice questions as an assessment tool [1-3].

Multiple choice examinations are those type of assessment in which students opt for the best probable answer from alternatives given. They consist of a main statement and a set of choices. The main statement is referred as stem and the correct reply is defined as the key but the other incorrect answers are referred as distracters. There are several advantages to multiple choice examinations. It can be a very successful evaluation technique depending upon the expertise level of question maker. They usually involve less time and results in an additional complete assessment of the knowledge as they usually test precise knowledge. They have twisted knowledge into a kind of puzzle, mystery or a crossword according to some critics. According to them it do not let examiner assess the students' knowledge properly. Others say that with these tests students can neither put up and prove their own perception nor they can give irrelevant details. However, in spite of all the criticism multiple choice tests are still accepted because they are standardized. Essay types also has there disadvantages including the individual behavior and perception of the examiners for marking same question and many more along with the issue of scribbled handwriting and time consumption etc. It has also been noticed that female students constantly were far better students then male's worldwide [3-7].

It was hypothesized that if students are asked to prepare MCQ there learning ability and deep learning is reduced as compared to informed SEQ test.

MATERIALS AND METHODS

A total of 200 second year students were involved in the study and their scores in SEQ and MCQ papers were analyzed for the period of less than two years. Out of them 100 students were girls and 100 were boys. The

students were informed that they are going to be accessed by means of three SEQ examinations and three MCQ examinations and then a survey and viva was conducted.

The study was conducted by selection of students who scored 60% marks in the general IQ test and were also of top merit in Fsc. Premedical. After the selection of students they were divided

into two groups 100 each, having equal students of both genders. One group was put into SEQ examination and the other group gone through MCQ examination. Three tests of three different topics were conducted among both groups. Then on same syllabus a verbal examination was conducted for both groups and a survey was also conducted asking students about merits and demerits of SEQs versus MCQs.

Statistical analysis: Statistical analysis was carried out with the SPSS. The data was expressed as mean ± standard deviation. The significance of differences between two groups of data was done by applying student`s t- test after verification of normality of data and equality of variance.

RESULTS

Results of the present study were presented as follow:-

The SEQ and MCQ results of students of whole year (three test / year) were depicted in Table no 1 and were plotted in figure 1.It compared the average of three SEQ test results of group one with the results of MCQ`s test (three test / year) of other group , having 100 students of equally both genders. The results of the two groups were almost more or less similar and p-value is non- significant reflecting that the difference among two groups is not noticeable.

Table No.1: SEQ and MCQ results of students of whole year (three test / year)

Groups	SEQ/NCQ Examination results Mean 1 standard deviation	p-value
SEQ students group (n=100)	79.5±1.0%	0.324
MEQ students group (n=100)	81.0±1.5%	

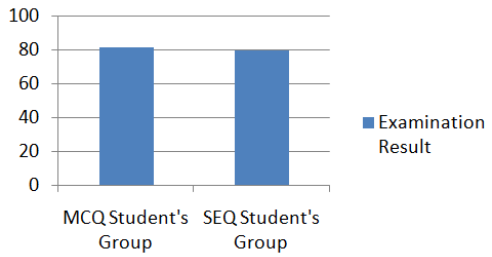

Figure No.1: Examination Result

The Viva results of students of both groups were represented in Table no 2 and are plotted in Figure 2 showing the comparision of verbal performance when both groups were having 100 students of equally both genders. The comparative results of the two groups were highly significantly different as estimated by the p-value. The result of this study shows that those students who were kept on MCQ type of assessment emerges to be weak students at the end of the session as compared to others who were assessed by SEQs.

Table No.2: Viva results of students of both groups

Groups	Viva results Mean ± standard deviation	p-value
SEQ students group (n=100)	85.5±2.0%	0.000*
MEQ students group (n=100)	62.0±3.5%	

*** significant (p-value < 0.05)**
Non significant (p-value > 0.05)

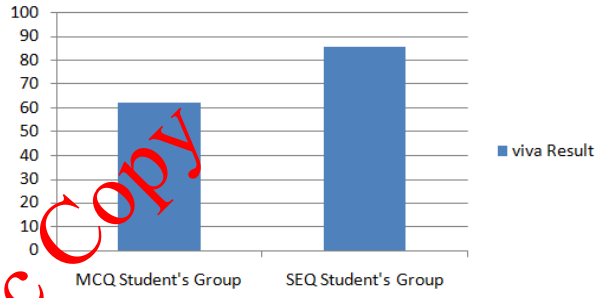

Figure No.2: Viva result

In survey report the students said that while preparing for MCQ examination, they just failed to retain the memorizing part and were unable to develop a clear concept besides whatever they read was not retaining and it was really easy to attempt MCQ without actually preparing for it

DISCUSSION

Assessment works as an incentive for learner and educator. The constant internal assessment system is a form of teaching learning activity.[8] This helps the students to prepare their studies and syllabus on time and also maintain and develop them more disciplined, perceptive and improves their result. The concluding assessment in any subject should supposed to be made upon the result of a large number of periodical tests and assignments.[9] In 2010 a research was conducted in subject of pharmacology which put side by side the performance of medical students in MCQ as well as SEQ and revealed that student performance and result was independent of examination format. [10]

The noteworthy finding of this study was that there was a no statistically significant difference between student performance on MCQ and SEQ as noted by Mujeeb and Dagogo also[10, 11] in their similar researches, but there was remarkable difference of student scores in viva voce examination in this research which was not

considered in methodology of above mentioned researches. This research indicated that, in general, students who performed well in the SEQ were also likely to do well in the MCQs but there depth of concept and practical life implementation of the bookish knowledge which was judged by multiple examiners in viva was far less in those students who belong to MCQ group.

CONCLUSION

The SEQ type of assessment was established as a better method of assessment to strengthen student`s learning process and helped students to exert and retain more knowledge. The result of this research goes in favor of SEQ type of assessment as assessment methods guide to fabricate better learning among students.

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Original Article

Low Backache in Pregnancy

Prevention of Low Backache in Pregnancy

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ABSTRACT

Objective: To document the effect of back care advice on the frequency and severity of low backache in pregnancy.
Study Design: Comparative cross sectional study
Place and duration of Study: This study was conducted in Antenatal Outpatient department of Obstetrics & Gynecology, Khyber Teaching Hospital, Peshawar from Jan 2012 to Jun 2012.
Materials and Methods: Advice on back care was made available to a group of primigravidae women as early in their pregnancy as possible. For comparison another group of primigravidae women for which no such advice was given was recruited. Both groups were followed throughout pregnancy for the occurrence of low back pain and its severity.
Results: The study comprised of 200 primigravidae with 100 women each in study group and control group. Seventy eight women in study group and 65 in the control group reached term. Among the study group 28.2 % experienced low backache in contrast to control group in which 56.9% developed back pain during pregnancy. In the study group 68.1% were having mild, 27.2 % moderate and only 4.5% severe pain. In the control group majority of women experienced moderate to severe pain. Furthermore the study group had pain much later in gestation as compared to control group.
Conclusion: Low backache was less common inprimigravidae women who receive advice on back care early in pregnancy. Low back pain, if present was less troublesome and severe than pregnant women for whom no such advice was available.
Key words: Low backache, Pregnancy, back care

INTRODUCTION

Low back pain represents a common pathophysiological process of pregnancy. A 9-month prevalence rate of approximately 50% is widely quoted in the literature.[1,2,3] The classical hypothesis of low back pain postulates that weight gain experienced during pregnancy results in postural changes that produce pain. Due to the anterior displacement of the center of gravity of the trunk and abdomen, women may unconsciously shift their head and upper body posteriorly over their pelvis, inducing hyperlordosis of the lumbar spine.[4] The belief is that this shift in load distribution generates stress on intervertebral disks, facet joints, and ligaments, promoting joint inflammation.[4,5]

While postural changes may not be clinically significant, the short time frame in which one's weight increases may play a role, albeit secondary, in the development of low back pain.[6,7] Weight gain may exceed the capability of trunk and pelvic musculature compensation and thus contribute to pain.[4,7] The weight of the gravid uterus may also directly compress on the base of the pelvis and lumbosacral plexus, and cause pain radiation to the buttocks and legs.[4,5,6]

Occupational factors may engender real and perceived changes in the levels of stress on the back. In fact, the rising prevalence of low back pain may be attributed to a rising trend among women to work throughout pregnancy in certain populations.[8,9] Vocational risk factors include sitting or constrained work posture; prolonged periods of standing, lifting, twisting, bending forward; inability to take breaks at will; and post-work fatigue. However, advising complete inactivity, such as prolonged bed rest, for low back pain is not recommended because of associated muscle weakness.[9,10]

Prevention of low back pain in pregnancy is possible with simple strategies like advice on back care. Type of work, physical demands, degree of monotony, and body posture when seated are some of the factors that require evaluation. Studies reveal amelioration of low back pain in pregnancy with improvement of these work conditions.[9,10,11] Back care includes: [12,13,14]

(1) Adopting good postural practices like: Standing up straight, Using a comfortably wide stance while standing up, resting one foot on a low step stool while standing for long periods of time, taking frequent breaks during work, sitting with care by using a chair that supports back and/or placing a small pillow behind lower back
(2) Wearing low heeled shoes with good arch support
(3) Avoiding bending at the waist to lift a small object and avoid lifting heavy objects.
(4) Sleeping on one side rather than on back and while sleeping on back, keeping the back straight.
(5) Bending one or both knees while sleeping. It might also help to place one pillow between knees and

other under one side to decrease pressure of gravid uterus on the back.

(6) Maintaining regular physical activity like walking.

This study aims to illustrate the effect of advice on back care during antenatal visits on the frequency and severity of low backache.

MATERIALS AND METHODS

Over a period of six months, 200 primigravidae with period of gestation less than 12 weeks and presented for antenatal care to Outpatient obstetrics & gynecology department were recruited to the study. They were randomly assigned to study and control groups with 100 women in each group. Women with existing low bachache were excluded from the study. Written informed consent was taken from all patients. Women in study group were given detailed advice regarding back care during pregnancy. Special emphasis was placed on teaching women to observe good postural practices, avoiding heavy weight lifting and taking rest during prolonged standing. Advice was facilitated by providing women with written advice and pictorial handouts for better understanding. Help was taken from second author in this respect. Control group was not given such an advice. Both groups were followed up at each antenatal visit at monthly intervals. Back pain was assessed at each visit and back care advice was further augmented. Severity of backache if present was documented by using "Dallas Pain Questionnaire", which is a 16-item visual analog scale. It evaluates in percentage the functional and emotional aspects of low back pain. Pain was categorized into mild, moderate and severe. Mean gestational age at which pain first developed was noted for both control group and study group.

RESULTS

There were 200 primigravidae,100 in each study group and control group. Mean age was 28 years with a range of 18 to 32 years. Mean period of gestation was 10 weeks with a range of 8.2 to 11.5 weeks. Among the study group 5 were lost to follow up while 78 reached term. In the control group 65 reached term and 6 were lost to follow up.

In the study group 28.2% (n=22) women experienced low backache during pregnancy. The mean gestational age at which back pain was first experienced was 32.2 weeks. Intensity of pain as assessed with "Dallas questionnaire" was mild in 15 women (68.1%) cases. In 6(27.2%) women pain was graded as moderate. It was severe in only one (4.5%) of woman.

In the control group 37(56.9%) developed pain, which was mild in 6 (16.2%) women. It was moderate in 22(59.4 %), while 9 (24.3%) women experienced severe pain. Mean gestational age at which pain first developed was 26.4 weeks.

Table No. 1: Characteristics of Study group and Control group

Variables	Study group	Control group
	n= 100	n=100
Age(years)	27.2	28.1
Period of gestation(weeks)	9.6	10.5
Weight(kg)	62.2	64.2
Height(inches)	63.2	64.1
Occupation: Working House wives	n= 15 n= 75	n= 11 n= 89
Gestational age at which backache first experienced (weeks)	32.2	26.4

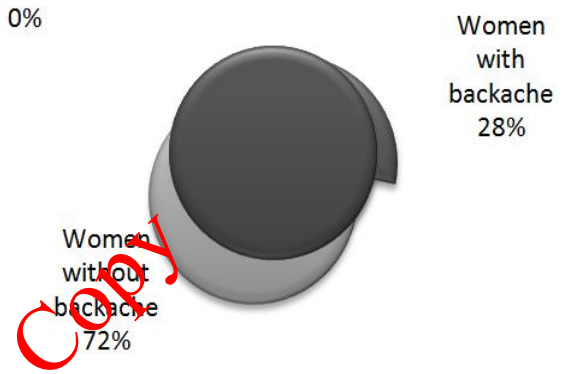

Figure No. 1: Frequency of Backache in Study group

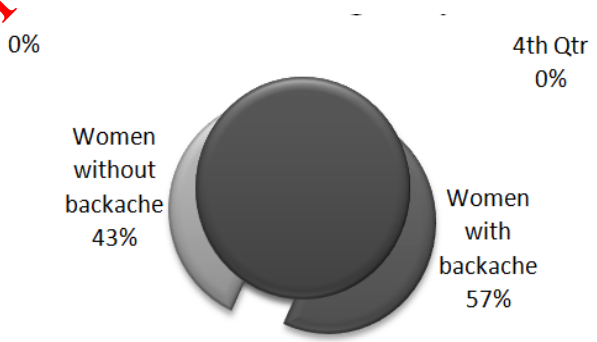

Figure No.2: Frequency of Backache in Control group

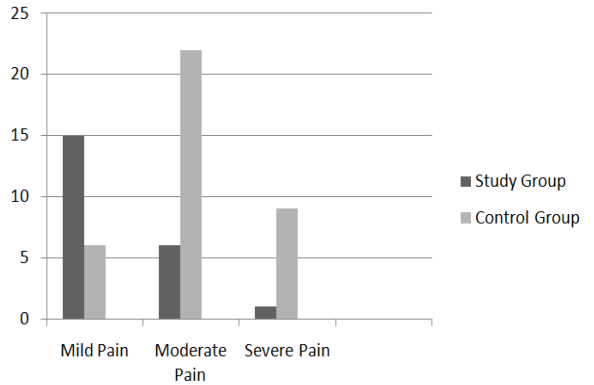

Figure No. 3: Comparison of Severity of Backache in study group and control group

DISCUSSION

An enduring debate in pregnancy care is whether low back pain is an inevitable or perhaps even essential component of a healthy pregnancy. Some have suggested that low back pain may perform a functional role as a protective agent by focusing women's attention on the physical stresses their bodies are undergoing, thereby making them more cautious during pregnancy.[15] Regardless, prevention, diagnosis and treatment of low back pain present formidable challenges to patients and their health care providers.

Low back pain and posterior pelvic pain previously were considered one entity, and past research has grouped these two conditions under the single classification of "low back pain." More recently, they have been discretely described and measured, and it is now evident that they require individual consideration for diagnosis and management.[16,17]

While no correlation has been demonstrated between low back pain and the health of a pregnancy, its onset has been reported to dramatically affect a patient's life. Brynhildsen et al[18] found that 19% of women with severe low back pain during pregnancy elected not to have another pregnancy due to their fear of low back pain recurrence. Low back pain may present a constant obstacle during pregnancy when performing activities of daily living. It reportedly results in sick leave from work in as many as 30% of pregnant women, persists >6 months in 6% of cases, and disturbs sleep in over one-third.[19,20]

Low backache in pregnancy can be prevented by adopting a number of strategies. In our study we studied the effect of a simple strategy, back care advice on the development of backache in pregnancy. We had specifically chosen primigravidae as most of the multigravidae have preexisting backache or due to poor back care in previous pregnancies they are already predisposed to back pain. Although they can still prevent aggravation of their pain by paying attention to back care. Brynhildsen et al[18] concluded from a long-term follow-up study that 94% of women who suffer from low back pain during pregnancy will develop low back pain in the subsequent pregnancy. Ostgaard et al[20] found that women with any history of back pain are 50% more likely to experience low back pain during pregnancy than women with no prior back pain and that pain will persist for a longer duration. Back care advice given to women in their first pregnancy, if properly followed is beneficial in prevention of backache right from the start.

The role of exercise has been studied in the prevention of backache in pregnancy. However we did not incorporate advice on exercise in our study. Majority of our population belong to low socioeconomic strata. Most are uneducated and it is very hard to make them understand proper exercises for back care. Back strengthening exercises if not done properly may do more harm than good. Furthermore, it is rather impossible for pregnant women to perform such exercises while living in a joint family system with small congested homes.

Our study showed that majority of women were unaware of what constitutes proper back care. They did not know the proper posture to adopt during sitting, standing, picking up and lifting things from the ground, lying down and sleeping. Adopting a proper posture is not only important in preventing backache in pregnancy but it is helpful in prevention of back pain in the long run even out of pregnancy. It is surely a part of healthy living practices.

The results of our study showed that back care advice played its part in preventing the development of back pain in pregnancy. Women who were ignorant of back care and were not given health education about back care, more than half of those experienced back pain during pregnancy. This is consistent with study done by Mantle MJ et al.[14] In contrast among those who receive such an advice only 28.2 % experienced pain which was mild in majority of cases. Ostgaard et al[20] applied the objective measurement of sick leave to determine the relative success of back education and training classes once back pain set in during pregnancy. This study reported a 12% decrease in sick leave time among pregnant women enrolled in an individualized back education and training program.

In Pakistan, so far no back care advice is given in the antenatal period to pregnant women coming to antenatal OPD. It is an effective and simple strategy to prevent backache in pregnancy. Incorporating such an advice as a part of standard antenatal care not only at the level of tertiary care but also at primary care level is the need of the day. Primary health care workers need to be trained about delivering such an advice and pictorial leaflets in simple language need to be provided to the pregnant women.

CONCLUSION

Back care advice constitutes a primary strategy in the prevention of backache in pregnancy. It is simple and easy to adopt. Making the women to understand proper back care will not only benefit them but will also be helpful in the health education of community in the long run. We recommend that the orthopedic and obstetric communities jointly engage in formulating strategies to prevent this problem. It seems naïve to conclude that low back pain is an inevitable component of pregnancy and is not preventable.

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Original Article

Fingerprint Pattern

Fingerprint Pattern in the population of Wah Cantt

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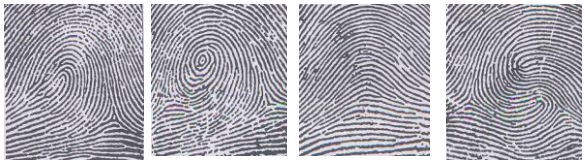
ABSTRACT

Introduction: Fingerprinting is the surest method of human identification and identification is the big problem with particular reference to growing terrorism and crime rate in our country.
Objective: To study the fingerprint pattern in the population of Wah Cantt. in connection with the role of fingerprints in identification.
Study Design: Cross sectional and observational study.
Place and Duration of Study: The study was conducted in the population of Wah Cantt. Total duration of study was three months from 01-09-2013 to 30-11-2013.
Material and Methods:
A group of 6 Lecturers were trained to take finger prints from different walks of population of Wah Cantt. The fingerprints were taken on unglazed paper with help of ink pad. The data was scrutinized regarding type of fingerprints. The collected data was analyzed by SPSS version 10.
Results: A total sample of 1000 persons were taken. Among 596 were male and 404 females. The most common type of finger prints remained loops 56.7 % followed by whorls 27.6 %, Arches 8.4% and composites type of fingerprints were detected in 7.3 % persons.
Conclusion: Statistically variations are present in the finger prints as in the population of the whole world.
Key Words: identification, Finger print pattern, Population

INTRODUCTION

Personal Identification means determination of individuality of a person[1]. Identification is the most common problem worldwide with particular reference to terrorism and other crimes. Fingerprint Identification is the method of identification using the impressions made by the minute ridges present on the balls of the fingers. No two persons have exactly the same finger prints in the world. There is absolutely no change in this pattern throughout life. It is a surest method of identification of a person[2]. Other personal characteristics are usually changed with the passage of time but finger prints never. It has been calculated that chances of there being an identical finger prints in two persons is about one in 64 billions [3]. Identification may be complete (absolute fixation of personality) or incomplete (like determination of age, race, sex, and stature etc) [4].



Loop **Whorl** **Arch** **Composite**

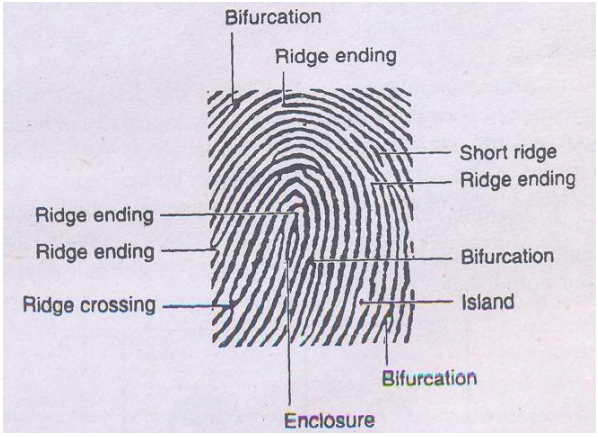
Figure No.1: 4-types of finger print pattern

Every contact leaves a trace[5]. Finger prints present on the weapon of offence offer a definite help to identify the culprit. The most valuable evidence that an investigator can obtain from the crime scene is the finger prints of suspects [6]. In criminal cases fingerprints of all 10 fingers are taken [7]. These skin ridges may be obliterated when skin is removed, damaged or putrefied. According to history of fingerprints, in 1892 the 1st case of murder was resolved with help of finger prints[8].

Finger prints are broadly divided into four types [9].

1. Loops
2. Arches
3. Whorls
4. Composites

These broad groups are further subdivided according to difference in pattern of ridges. The following finger prints shows points to be noted during study of finger prints.



Fingerprint Ridge characteristics

To determine the similarities between fingerprints recovered and fingerprints of suspects general pattern of friction ridges along with core, delta ridge ending, bifurcating, length, breadth crossing, branching and presence/absence of islands are analyzed. There are as many as 150 individual ridge characteristics on the average fingerprint[10]. 16 points of similarity required before declaring finger prints to be identical. Same number of points of similarities are used by Scotland yard London and FBI (Federal Bureau of Investigation) in USA[11]. The process of personal identification by studying the pattern of fingerprints is the job of fingerprint Expert.

MATERIALS AND METHODS

A group of 6 lecturers (comprising 3 males and 3 females) belonging to Wah Cantt were trained to get fingerprints from the people belonging to different walks of life. The full fingerprints plain and rolled were taken on the unglazed paper with help of ink pad. Fingerprints of total 1000 persons (males=596 & females= 404) of age 18years and above were taken. The analysis was done regarding type of finger prints (loop, arch, whorl and composite) present in the population of Wah Cantt. The collected data was analyzed by SPSS version 10.

RESULTS

Overwhelming majority belong to loops group of fingerprints present in 567 persons. Among the other groups 276 individuals belong to whorls & 84 finger prints are of arches type. While least common group of fingerprints remained composites present in only 73 individuals. As for as gender is concerned among the out of total 404 females, 219 (54.2 %) belongs to Loops, while 118 (29.21%) females have Whorls type, 41 (10.15 %) females belongs to Arches and only 26 (6.44%) belong to composites type of fingerprints. The fingerprint study conducted at Lahore also shows almost the similar results[12].

Table No.1: Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	4.538[a]	3	.209
Likelihood Ratio	4.506	3	.212
N of Valid Cases	1000		

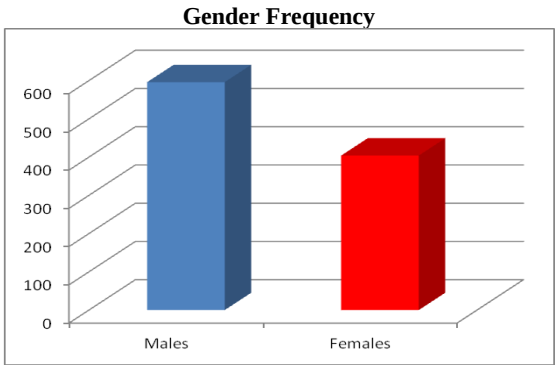
a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 29.49

p-value is 0.209 which is insignificant

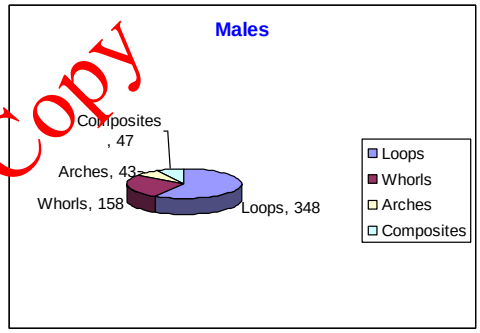
Table No.2: Total percentage of fingerprints:

Pattern	**Total Numbers**	**percentage**
Loops	567	56.7
Whorls	276	27.6
Arches	84	8.4
Composites	73	7.3

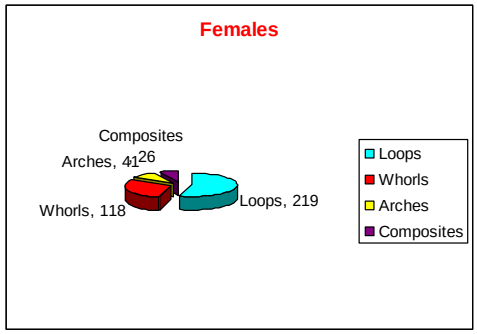
Gender	Male	Female
Total	596	404
Loops	348	219
Whorls	158	118
Arches	43	41
Composites	47	26
Percentage	59.6	40.4



A



B



C

Figures A, B, & c: Male & female pattern of fingerprints

DISCUSSION

The Study of fingerprints, the surest methods of identification, is also called dactylography[13]. Finger prints are complicated pattern of hills and valleys, called ridges and furrows respectively[14]. Proliferation of cells in the stratum germinativum forms epidermal ridges which extends into the developing dermis are fingerprints. Theses ridges appear in the embryo at 10th week and are prominently established by 17th week of

intrauterine life[15]. The two features of fingerprints most important for their use as means of personal identification are

1. Every finger print is unique to an individual
2. Finger prints don't change throughout life.

Among the 4 major patterns of fingerprints, the average distribution of pattern of finger prints is as loops about 65%, whorls about 25 % arches about 7 % and composites about 2-3 %.

These patterns of fingerprints are so unique that even identical twins don't have identical finger prints [19]. According to presence of fingerprints anywhere, these are divided into three categories.

1. Visible fingerprints
2. Latent fingerprints
3. Plastic fingerprints

Unintentionally we leave our fingerprints on multiple places daily called chance fingerprints. These latent prints are made visible by dusting process or chemicals. Plastic prints are impression of finger prints on gum, newly painted areas, wax, tick dust, soap or clay etc.

A medical person have to work with the collaboration of police. It is the duty of the police to protect the fingerprints of the offender left on scene of crime or weapon. In Scotland fingerprints may be taken as soon as a person is under arrest, but in England they may not be taken before conviction unless with permission or on authority from a Magistrate to whom a Police inspector may apply. This method of identification is also very useful in case of unidentified dead bodies of victims and terrorists etc. Nobody may be allowed to touch any weapon, glass, telephone, furniture, door-knob or handle etc. at the scene of crime before the fingerprints are preserved. However identification of a person may not be possible even with the help of a perfect fingerprint, if the person has never been fingerprinted or his fingerprints are not present in the centralized database; as there is nothing to compare with. The FBI maintains fingerprint data of more than 20 million persons[16].

Finder-II (fingerprint reader) is a computerized automatic fingerprint reader system used by FBI of USA which can record each fingerprint data in ½ second. Today fingerprints are used to prevent forged signatures, identify accident victims, verify job applications and provide personalized access everything from ATMs to computer networks and mobile phones[17].

CONCLUSION

Study of pattern of fingerprints needs boarder study to generate exact figures at national level.

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Original Article

Effects of Drugs in Keratoconjunctivitis

Efficacy of Lodoxamide Versus Sodium Cromoglycate in Vernal Keratoconjunctivitis

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ABSTRACT

Objective: To determine efficacy of lodoxamide as compared to that of sodium cromoglycate when used for the treatment of vernal keratoconjunctivitis.

Study Design: Prospective comparative clinical trial.

Place and Duration of Study: This study was carried out at the Department of Pharmacology and Therapeutics Basic Medical Sciences Institute (BMSI) in collaboration with Department of Ophthalmology Jinnah Postgraduate Medical Center (JPMC) Karachi from April 2010 to October 2010.

Materials and Methods: A total of untreated 80 cases with clinical diagnosis of vernal keratoconjunctivitis (VKC) of 5-29 years of age and of both sexes were included in this study. Patients of other types of allergic conjunctivitis and of VKC already on medication were not included in this study. Follow up visits were carried out at fortnightly intervals for the period of at least three (03) months to rule out comparative efficacy of the two drugs.

Results: We studied a total of 80 cases, 56 males (70%) and 24 females (30%) with diagnosis of VKC. All cases were divided in two groups; group A and group B. Group A comprised of 40 patients who used lodoxamide whereas; Group B comprised 40 patients who used sodium cromoglycate. No significant difference in demographic features was found in two groups ($p>0.05$). The results showed significant improvement in all symptoms and signs in 60 days of study in group A (lodoxamide) and in group B (sodium cromoglycate) improvement was observed in 90 days of the study ($p<0.05$).

Conclusion: Improvement in all the symptoms and signs was earlier (within 30 days of study) in group A than in group B.

Key Words: Efficacy Lodoxamide, Sodium cromoglycate, VKC.

INTRODUCTION

Vernal keratoconjunctivitis (VKC) is a chronic, bilateral, asymmetrical seasonally exacerbated allergic inflammation of cornea (-kerato) and of bulbar or tarsal conjunctiva (-conjunctivitis). It is more common in children and young adults having atopic history and living in hot climates[1, 2]. Atopic individuals often develop asthma and eczema in childhood[3]. Its incidence in males is twice as compared to females at pre-pubertal age and incidence is equal at puberty[4, 5]. This male preponderance is demonstrated in different studies in Pakistan[6].

The disease is an immunologically mediated type I hypersensitivity reaction to environmental allergens like pollens, animal dander, mites and molds[7]. Clinical types of disease are palpebral, limbal and mixed types. Presenting symptoms are severe itching, photophobia and lacrimation accompanied by ocular discomfort and lacrimation[8, 9]. Signs are ropy mucous discharge, edema of eyelids, chemosis and cobblestone papillae, the hallmark of disease[10]. Diagnosis of disease is based on clinical signs and symptoms. The disease is more prevalent in hot climates like Sub Saharan and Middle East and less common in temperate and almost non-existent in cold climate countries[11]. Severity of disease increases in spring and summer and decreases in fall winter in Mediterranean and other temperate regions[12] while large number of cases reported from subtropical areas like Pakistan[7]. Therapeutic measures are required to alleviate signs and symptoms and to avoid long-standing permanent damage to vision[13]. Lodoxamide and sodium cromoglycate are the two mast cell stabilizer drugs commonly used for treatment of VKC. Both the drugs act by preventing calcium influx in mast cell membrane which prevents its degranulation hence; inflammatory mediators are prevented from being released[14, 15]. Although severe and resistant cases are also treated with topical steroids but these may cause unwanted elevation of intraocular pressure and risk of corneal infections through local immunosuppression[16].

MATERIALS AND METHODS

This prospective study was conducted on eighty (80) patients at Department of Pharmacology and Therapeutics Basic Medical Sciences Institute (BMSI) in collaboration with Department of Ophthalmology Jinnah Postgraduate Medical Center (JPMC) Karachi during April 2010 to October 2010.

Lodoxamide and Sodium cromoglycate were instilled topically four times daily in each eye, in both treatment groups A and B of 40 patients separately. Severity of signs & symptoms was assessed at baseline visit day 0, then evaluation of improvement in all parameters i.e. cobblestone papillae, ropy mucous discharge, photophobia, itching and lacrimation, was carried out at fortnightly follow-up visits at day 15, 30, 45, 60, 75 and 90 with the help of slit-lamp examination.

Statistical Analysis: A comparative trial (Lodoxamide vs. Sodium cromoglycate) was conducted and samples of 80 diagnosed patients (40 from each group) with vernal keratoconjunctivitis were enrolled for this study after taking written consent. Statistical software SPSS version 11.5 was used for data analysis. The results were given in numbers and percentages for qualitative variables and mean and standard deviation for quantitative variable (age). Chi-square test was used for comparison of two treatment groups and p-value of < 0.05 was considered as statistically significant.

RESULTS

The demographic features are shown in **Table.1** which reveals that all patients ranged in ages between 5-29 years of age. Males were 70% (56 patients) and females were 30% (24patients) in both treatment groups. Mean value in group A was14.7 ± 0.96 whereas; in group B it was14.4 ± 0.91. There was no statistically significant difference in gender and age distribution in both treatment groups (p>0.05).

Table No.1: Demographic Features in Two Treatment Groups

	Treatment group	
	Lodoxamide (n=40)	Sod. Cromoglycate (n=40)
Gender		
Male	28 (70%)	28 (70%)
Female	12 (30%)	12 (30%)
Age (years)		
5 – 14	23 (57.5%)	21 (52.5%)
15 – 19	8 (20.0%)	10 (25.0%)
20 – 24	5 (12.5%)	7 (17.5%)
25 – 29	4 (10.0%)	2 (5.0%)
Mean ± SEM	14.7 ± 0.96	14.4 ± 0.91

No significant difference in two treatment groups (p >0.05)

Table No.2: Improvement in different symptoms and signs in two treatment groups from day 0 to day 90

	Lodoxamide (n=40)		Sod. Cromoglycate (n=40)		P-value
	No.	%	No.	%	
Cobblestone papillae					
Day 0	40	100.0	39	97.5	-
Day 15	29	72.5	39	97.5	0.002
Day 30	6	15.0	31	77.5	0.001
Day 60	1	2.5	16	40.0	0.001
Day 90	1	2.5	2	5.0	-
Ropy mucous discharge					
Day 0	30	75.0	32	80.0	0.592
Day 15	11	27.5	29	72.5	0.001
Day 30	1	2.5	18	45.0	0.001
Day 60	-	-	2	5.0	-
Day 90	-	-	-	-	-
Itching					
Day 0	40	100.0	40	100.0	1.000
Day 15	39	97.5	39	97.5	0.812
Day 30	21	52.5	38	95.0	0.001
Day 60	1	2.5	21	52.5	-
Day 90	-	-	3	7.9	-
Photophobia					
Day 0	37	92.5	35	87.5	0.709
Day 15	36	90.0	35	87.5	1.000
Day 30	20	50.0	34	85.0	0.001
Day 60	1	2.5	22	55.0	0.001
Day 90	-	-	2	5.0	-
Lacrimation					
Day 0	40	100.0	38	95.0	0.473
Day 15	28	70.0	36	90.0	0.025
Day 30	8	20.0	30	75.0	0.001

Day 60	1	2.5	18	45.0	0.001
Day 90	-	-	2	5.0	-

Table.2 reveals the improvement along with the comparison of percentage decrease in all symptoms and signs in both treatment groups from day 0 to day 90. A total of eighty (80) patients enrolled in both groups (40 patients in each group). All patients were followed up fortnightly. There was a highly significant improvement in all symptoms and signs in group A (lodoxamide) at day 30 and 60 of the study ($p<0.001$) whereas; improvement in symptoms and signs in group B (sodium cromoglycate) was observed at day 90 of study ($p<0.05$).

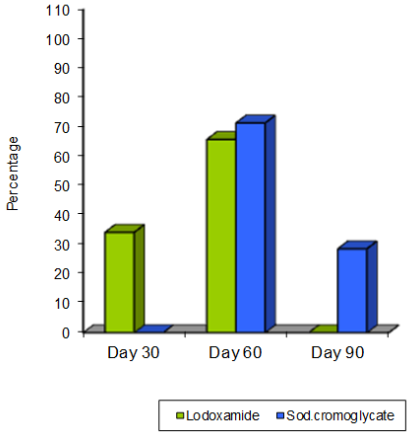

Figure No.1: Comparison of improvement rate in both treatment groups (day-30 to day 90)

Figure 1 reveals that the improvement in symptoms and signs was seen within 30 days of study in 34.2% (13) cases in group A whereas; in group B improvement was not seen. Within 60 days, 65.8% (25) cases were improved in group A and 71.4% (25) cases in group B. Within 90 days remaining of 28.6% (10) cases in group B were improved. The overall improvement rate in group A (Lodoxamide) was 97.4% (38 out of 39 cases) whereas; in group B (Sodium cromoglycate) it was 92.1% (35 out of 38 cases). The improvement was declared when patients became free from symptoms and signs.

Clinically Lodoxamide shown to have faster mode of action on all parameters as compared to Sodium cromoglycate as shown in table 2.

DISCUSSION

The VKC is a common ocular allergy prevailing in our society due to allergens (like pollens, animal dander, industry fumes) and hot weather also adds intensification of the disease. Topical steroids are widely used in controlling the severe distressing symptoms and signs of the VKC e.g. intense itching, photophobia and lacrimation, giant papillary conjunctivitis, corneal shield ulcers and limbitis. But the injudicious and prolonged use of topical steroids carries a high risk of steroid-induced cataract, glaucoma and corneal ulcer with superadded-infections of fungi, viruses and bacteria[17, 18]. Keeping in view all these aspects this study was conducted to evaluate efficacy of two commonly used topical mast cell stabilizers; lodoxamide and sodium cromoglycate. Lodoxamide has been used topically as an ophthalmic solution since late 1990s[19]. The study to assess the safety and efficacy of lodoxamide in vernal keratoconjunctivitis was conducted by the principal author in 2011 and that also revealed very promising effects in improving symptoms and signs of VKC[20]. Sodium cromoglycate also known as 'Cromolyn sodium' was approved by Food and Drug Adminstraion (FDA) America, in 1973[21, 22]. Both the drugs proved to be effective in controlling the early phase inflammation of VKC. But the lodoxamide controlled signs and symptoms of disease i.e. itching, photophobia, lacrimation, ropy mucous discharge and cobblestone papillae, more effectively and earlier than sodium cromoglycate as the results of our study revealed. Bonini et al reported in1997[23] in their study that lodoxamide controlled significantly the ocular itching as compared with placebo. Though the lodoxamide is used in controlling the symptoms and signs of VKC but sodium cromoglycate can also be used for the same purpose and itching is especially controlled within a week after commencement of therapy[24].

CONCLUSION

Our study revealed that between the two mast cell stabilizers used during this study, the lodoxamide is clinically fast effective than Sodium cromoglycate in relieving symptoms and signs of VKC.

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Original Article

Syphilis in Pregnancy

Analysis of Syphilis and Associated Risk Factors in Pregnant Women Belongs to Remote Areas of Sukkur

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ABSTRACT

Objective: To determine and analysis of Syphilis and Associated Risk Factors in Pregnant Women Belongs to Remote Areas of Sukkur.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted on women belongs to peripheral areas of sukkur over a period of fifteen months, which beginning in May, 2012.

Materials and Methods: Patient's 5ml whole blood was collected through venepuncture technique. Data were collected by all women answered a questionnaire and by investigating Blood Sample VDRL test and FTA-ABS test. The study was conducted in a confidential manner and numbers were used to identify the participant.

Results: Total 200 Pregnant women were included in the present study. Mean age of women was 25.4 years while range was 18 to 39 years. Out of the 200 samples, 6 (3.0%) were positive for active syphilis. Majority was belonging to low socioeconomic group of population.

Conclusion: Active syphilis infection in pregnant women belongs to remote areas with low socioeconomic level were significantly disquieting. Alarming results of this study suggestive that seropositive status is often discovered in routine serological studies during pregnancy at health centers and efficient prolonged treatment of mother were available.

Key Words: Syphilis, Treponema Pallidum infection, Pregnant women, VDRL, FTA-ABS.

INTRODUCTION

During the last two decades much attention been drawn to pathogens have been associated with sporadic pregnancy loss. These include toxoplasma, human immune deficiency virous, mycoplasma, treponema pallidum, herpes and chlymadia[1]. The prevalence of seropositivity of syphilis in pregnancy is rare in northern europe and united states. Syphilis continues to be a major cause of pregnancy loss and adverse pregnancy outcome among women who do not receive antenatal syphilis screening and treatment[2,3]. Screening and treatment for syphilis in pregnant women have been recommended as a potentially feasible and cost-effective intervention to reduce fetal and prenatal mortality and other adverse outcomes[4]. Maternal syphilis has been associated with prenatal morbidity and mortality in many parts of the country5. As in most resource- limited countries, widespread screening is not conducted in Pakistan for many important infections and metabolic disease during pregnancy, including syphilis, HIV, gonorrhea, Chlamydia and inborn error of metabolism[6]. In addition, Pakistan has one of the highest fertility rates of any country in the world, estimated by UNICEF to be 3.6 per women. Syphilis in pregnant women is associated with low birth weight, prematurity, and intrauterine death[7].

Active syphilis infection in developed counties is rare. But in part of the world where the traditional venereal disease has not been controlled, such as peripheral areas of Pakistan, the magnitude of the problems associated with congenital syphilis such as saddlenose and cleft palate has been still prevalent[8,9].

Syphilis is caused by the spirochaete treponema pallidum. This organism is transmitted during sexual activity from a mucocutaneous lesion. The cervical changes, such hyperemia, eversion, and friability, which occur during pregnancy may facilitate the entry and lead to spirochaetaemia[10]. The fundamental histological changes both congenital and acquired syphilis are vasculitis and its consequences, necrosis and fibrosis. Pregnancy has no known effect on the clinical course of syphilis[11]. In acquired infection, after an initial incubation period of 3-90 days, a solitary papule with central ulceration, teeming with spirochaets, erupts at the site of inoculation, which is often found on the genitalia, and less frequently on the rectal and the oral mucosa[12]. This popular lesion is known as the chancre of syphilis and marks the primary stages of the diseases. The mother can transmit the infection transplacentally to the fetus or during passage through the birth canals by contact of the newborn with a genital lesion. Breast feeding does not result in the

transmission of syphilis, unless an infections lesion is present on the breast[13].

However, certain risk factors associated with a high prevalence of syphilis included maternal, age husband's occupation, income, late antenatal care, illiteracy, unemployed, habitual drug use, husband's habitual drug use, husband's extramarital reaction, and blood transfusion[14].

The true burden of syphilis in our country is unknown. The main reasons are that the mothers are mostly asymptomatic or have non-specific symptoms, lack of awareness about such diseases, inadequate facilities for screening tests or their high cost, poor access to a health facility and nonexistence of surveillance systems[15]. The present study was designed to estimate the prevalence and associated risk factors for syphilis in pregnant women residing to periphery of sukkur.

MATERIALS AND METHODS

Study design and site: A cross-sectional study on the analysis and associated risk factors for syphilis in pregnant women. The woman belongs to peripheral areas of sukkur, Pakistan. Many of all women were illiterate and even many of them were not properly guided of their basic ethics of their religions.

Enrolment of patients: Women attending local health clinics were enrolled in this study after taking their informed consent.

Duration of study: The study was conduct over a period of fifteen months, which beginning in May, 2012.

Data collection: The patients were interviewed by using a structured questionnaire to collect the bio data and history of patients.

Blood sample: Approximately 5 ml Blood sample were draw by using disposable syringe through vein puncture technique from cubital vein and transferred into a plain tube for biochemical analysis. Samples were taken to the laboratory as soon as possible. The plain tubes were centrifuged at 3000 rpm for 10 min to obtain the serum which were tested for syphilis using both VDRL and FTA-ABS assay.

Syphilis serology testing and case definition: The serum was tested for syphilis, using Venereal Disease Research Laboratory (VDRL) test and Fluorescent Treponemal Antibody – Absorption (FTA-ABS) assay.

RESULTS

Syphilis serological results: Total 200 women were enrolled and tested in this study, Out of 200 women, 06 (3.0 %) has serological results that were consistent with active syphilis (VDRL test reactive and reactive FTA-ABS assay). 05 (2.5%) women were reactive with VDRL only and considered as false-positive or very early infection (VDRL test reactive and a non- reactive FTA-ABS assay).

Multivariate analysis: Risk factors were included in multivariable analysis based on the strength of association criteria.

Table No. 1: Serological results of syphilis

Results	No. of women (n = 200)	Interpretation
VDRL and FTA-ABS Non-reactive	189 (94.5 %)	No evidence of syphilis
VDRL reactive and FTA-ABS Non-reactive	05 (2.5 %)	False – positive or very early infection
VDRL and FTR-ABS Reactive	06 (3.0 %)	Active syphilis

Table No. 2: Frequency and percentage of syphilis by socio-demographic risk factors in a population of pregnant women of rural Sukkur

Socio-demographic risk factors	Frequency (%) (n=06)
Maternal age < 18 years	4 (66.6%)
No school / primary education only	5 (83.3%)
Unemployed (housewife)	6 (100%)
Husband with no school / primary education only	2 (33.3%)
Husband self-employed	2 (33.3%)
Monthly income (Pak Rupees) ≤ 7000	6 (100%)

Table No. 3: Frequency and percentage of syphilis by clinical and behavioral risk factors in a population of pregnant women of rural Sukkur

Clinical and behavioral risk factors	Frequency (%) (n=06)
Gravidity > 1	5 (83.3%)
≥ 1 live children	4 (66.6%)
History of previous low birth weight delivery	3 (50.0%)
History of previous congenital anomaly	1 (16.6%)
No contraceptive use before current pregnancy	3 (50.0%)
5 + years of marriage	3 (50.0%)
Presence of genitourinary symptoms	2 (33.3%)
Presence of genitourinary symptoms in husband	1 (16.6%)
Habitual drug use	4 (66.6%)
Husband's habitual drug use	3 (50.0%)
History of blood transfusion	1 (16.6%)

DISCUSSION

The active syphilis observed in this study was .3.0 %. This is significantly high as compared to rate in USA. Mediterranean, pacific, and in European countries. The

definition of active syphilis used in the study was based on the serological finding expected for the various stage of disease[16]. Women who had both a non-reactive VDRL test and a non-reactive FAT-ABS assay were considered to be negative for syphilis. Those who were reactive with VDRL test and non-reactive FTA-ABS were considered to be false-positive. And those who were reactive with FTA-ABS and non-reactive with VDRL were considered as old treated or untreated (syphilis resolved).

In a study conducted in Tanzania, 59 cases of untreated maternal syphilis is a significant cause of adverse pregnancy outcomes women who fail to receive antenatal syphilis screening[17]. Another study reveals effective syphilis screening program would reduce stillbirths by 51% and preterm births by 24% in an unscreened population that satisfies the study's inclusion criteria and with similar syphilis prevalence to that of Mwanza Region[17,18].

Antenatal syphilis screening is a highly cost-effective intervention and should be prioritized as an essential part of antenatal care throughout sub-Saharan Africa. Health education massages for pregnant women should continue to reinforce the message that untreated maternal syphilis is a danger to the unborn infant, that it can be diagnosed and treated, and that women should attend an ANC that can perform syphilis screening as soon as they suspect that they are pregnant[19].

It is true that several studies have found few or no case of syphilis among general population. A study conducted in similar group from Dhaka Bangladesh among 284 pregnant women found prevalence of 3%[20]. Another cross sectional clinic based study conducted in Bangladesh in two urban primary health care level clinics among 1105 women found 1.5% prevalence of syphilis[21]. And a study in Bulgaria had shown 0.9% prevalence of syphilis. But a study from china was seroprevalence was 0.5 % which is very low as compared to this study[22]. A piece of research work among blood donors at Lahore found 0.78% seropositive for syphilis[23]. Another study conducted in Lahore in men presenting with dermatological complaint, showed 31.6 % men positive for syphilis[16]. In addition should be noted that in neighboring India, the prevalence of syphilis ranges between 2.0-4.8% among women of reproductive age[23].

Differences in the prevalence of syphilis according to race and sex have been reported. It was reported that man 20-29 years old had consistently higher rate of infection compared to age matched women with male to female ratio of 5.2:1[24]. Epidemiologically data on prevalence of syphilis among women in Pakistan are not available, however according to world Bank report the total burden of disease was about 350 Disability Adjusted life Years per 1000 population per year. Sexually transmitted infection formed 2.2% of Disability Adjusted life years of which syphilis was 0.50%in Pakistan. In our study out of 06 positive women with active syphilis. Results of this study have shown significantly. Sexual contact is the primary mode of transmission of syphilis and all the women denied extramarital sex. As the information was collected from women and not from their husbands therefore it was possible that the men might have had risky behavior unknown to their spouses.

Significant association of syphilis with travel of sex partner in past one year such as among distance truck driving and drug abusers has been reported. The risk of transmission through blood was negligible due to improved donor's serologic testing and of refrigerated blood components[18].

In this study also blood transfusion history was not significantly related to infection. To increase the percentage of screening for syphilis during pregnancy for women a risk, collaborative efforts would be needed among health care providers, health insurances, policymakers and public [23, 24].

CONCLUSION

Public health strategies to prevent maternal and fetal syphilis are similar to those of that focus on syphilis and other STDs in general population. These include early identification of infected individuals and high risk populations. Identification of the partners and their treatment should be ensuring. Promoting the accessibility and the use of health care are needed.

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Original Article

Epidemiology of Suicide in Multan

Suicide

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ABSTRACT

Objectives: Since suicide is increasing in Pakistan and has become a major Public problem, the objective of our study is Analysis of the different methods used for suicide, most vulnerable persons from point of view of factors responsible for suicide ideation and commission. Finally to suggest remedial measure for prevention of suicide.

Study Design: Retrospective study.

Place and Duration of study: This study was carried out at the Department of Forensic Medicine, NMC Multan from 01-01-2007 to 31-12-2011

Materials and Methods: The study consisted of 90 cases of suicidal deaths declared as suicideon the information retrieved through psychological Autopsy belonging to both genders and different age groups, whose autopsy was conducted in the mortuary of department of Forensic Medicine, NMC Multan. Findings were recorded on the Performa and the results statistically analysed.

Results: The study disclosed that suicidal rate was 1.22/100000 with male dominance. The most vulnerable age for suicide in male was 21-30 years and that for females was between 11-20 years. Hanging was the commonest method employed.

Conclusion: The suicide is increasing in Multan and all over Pakistan and demands immediate intervention and remedial measures for its prevention.

Key Words: Suicide, Hanging, Socio-economic status.

INTRODUCTION

Killing of self is called suicide. It is an act of taking one's own life voluntarily and intentionally. The term attempted-suicide is used when a person attempts to take or has a tendency to take his own life. Suicide can be classified into six degrees depending upon the circumstances while attempting suicide[1]. Legal position in Pakistan is that attempted suicide is crime according to Qisas and Diyat act 1997 vide section 325 which states that whoever attempts to commit suicide and does any act toward the commission of such offence, shall be punished with simple imprisonment for a term which may extend to one year, or with fine , or with both[2] where as it is no more a crime in U.K since 1961and also in U.S.A with exception of some states. The incidence and pattern of suicide vary from country to country. Cultural, religious and social values play some role in this regard[3]. According to the W.H.O, every year; almost onemillionpeople die from suicide, a "global" mortality rate of 16 per100, 000 or one death every 40 seconds. .On World Suicide Prevention Day 2008, WHO claimed that Japan, China and India might account for about 40% of the world suicides. Most people who commit suicide in India (37.8%) are below 30 years of age. The percentage of suicides committed by those below 44 years is 71%. Experts claim that 60% of these suicides have not occurred if proper intervention was undertaken. Mental disorders (particularly depression and alcohol use disorders) are a major risk factor for suicide in Europe and North America; however, in Asian countries, impulsiveness plays an important role. Suicide is complex with psychological, social, biological, cultural and environmental factors involved[4]. A study conducted in Pakistan negates the widely held belief that suicide is a rare phenomenon in an Islamic country like Pakistan, and underscores the need for more culture specific research on this important public health problem[5].

There are no official statistics on suicide from Pakistan. Suicide deaths are not included in the national annual mortality statistics. National rates are neither known nor reported to the World Health Organization[6]. Information on suicide in Pakistan comes from a number of sources including newspapers and reports of Non-Governmental Organizations (NGO).

MATERIALS AND METHODS

A total numberof 90 dead bodies were received in mortuary of NMC, Multan whose death was declared as suicidal on the basis of information retrieved from the police inquest, observations/findings during the conduction of the autopsy on these cases and psychological autopsy (questions with the relatives, old/new friends and neighbours of the victim) were segregated from all the autopsies conducted at the department of Nishtar Medical College Multan during the period of five years with effect from 01-01-2007 to 31-12-2011. These cases were divided on the basis of age, gender, method of commission of suicide, socio economic status and the weather during which the suicide occurred.

RESULTS

On the analysis of data recorded, our study revealed as under; the total number of autopsies conducted during

the period of study w.e.f. 01-01-2007 to 31-12-2011 were 1652 and the cases of suicides were 90, which is 5.45% of the total number of autopsies. The highest incidence of suicide occurrence was during 2007 (24 cases) at the rate of 2.0/month and the lowest was during 2010 (14 cases) at the rate of 1.16/month.

Table No.1: Year wise distribution of autopsies on suicidal/total number of autopsies

Year	No of autopsies conducted on suicide cases.	Total no. of autopsies conducted.	%age	Per month incidences of cases of suicide.
2007	24	392	6.12%	2.0
2008	20	336	5.95%	1.66
2009	16	370	4.32%	1.33
2010	14	290	4.82%	1.16
2011	16	264	6.06%	1.33
Totals:	90	1652	5.45%	1.49

Table No.2: Deaths due to suicides in various age groups

Age (yrs)	Male	Female	Combined
11 – 20	10	14	24
21 – 30	32	08	40
31 – 40	08	08	16
41 – 50	02	-	02
51 – 60	06	-	06
Above 60 Yrs	02	-	02
Totals:	60	30	90

Keeping in view the average midyear population of Multan and the average suicide rate in the five years, the rate of the suicide comes out to be 1.22/100000 in the city of Multan. The most vulnerable age for suicide in the male was between 21-30 years (32 cases) followed by the age between 11-20 years (10 cases), where as in female, the most vulnerable age for suicide was 11-20 years (14 cases) followed by the age between 21-30 years (8 cases).

The most common method adopted for committing suicide was hanging which was utilized by 53.33% of the victims followed by flame burning (13.33%). This was followed by firearm (12.22%) and then poisoning (11.11%). There was male preponderance, who resorted the method of hanging to commit suicide (66.6%) as compared to females (33.4%) who hung themselves for committing suicide. Our study revealed that female preferential method was flame burning to commit suicide, with the significantly higher percentage (66.6%) as compared to males (33.4%).

It was also disclosed by our study that the highest number of the persons 80 (88.9%)who committed suicide belonged to low socio-economic status followed by middle socio economic status, which was only 6.7%. The minimum number of persons who committed suicide belonged to upper socio-economic status with the lowest of 4.4% which is an agreement with the study conducted in India[7].

Table No.3: Different Methods used for Commission of Suicides

Modes of suicide		11 – 20	21 – 30	31 – 40	41 – 50	51 – 60	Above 60 Yrs	Totals
Hanging	M	06	16	08	-	-	02	32
	F	06	06	02	-	02	-	16
Poisoning	M	-	02	-	02	-	-	04
	F	02	02	02	-	-	-	06
Flame	M	-	-	04	-	-	-	04
	F	02	02	04	-	-	-	08
Drowning	M	04	02	-	-	02	01	09
	F	-	-	-	-	-	-	-
Firearm	M	-	10	-	-	-	-	10
	F	-	01	-	-	-	-	01
Sharp weapons	M	-	-	-	-	-	-	-
	F	-	-	-	-	-	-	-
Misc	M	-	-	-	-	-	-	-
	F	-	-	-	-	-	-	-
Totals:	M	10	30	12	01	02	04	59
	F	10	11	08	-	02	-	31

Table No.4: Socio-economic status of suicide

Status	Total No of cases	Percentage
Low socio-economic status	80	88.9 %
High socio-economic status	06	6.7 %
Upper socio-economic status	04	4.4 %

DISCUSSION

Suicide is one of the ten leading causes of death in the world, accounting for more than a million deaths annually.[7]However incidence and pattern of suicide varies from country to country depending on social, cultural and religious values[3]

Suicide rates are highest in Europe's Baltic states, where around 40 people per 100,000 die by suicide each year, second inline is the Sub-Saharan Africa where 32 people per 100,000 die by suicide each year. The lowest rates are found mainly in Latin America and few countries in Asia[8].

Our study showed that hanging is the most common method used by 53.33% of the suicide which is consistent with the other studies conducted in Pakistan and other countries. The reason for hanging to be resorted for majority of suicide might be easy and is certain lethal method[7, 9, 11, 12, 13, 14, 15], followed by poisoning[3, 6,7,9,10,19] and firearm[3, 9, 17, 23, 24].

Our study disclosed that male to female ratio of the victim of the suicide is 2:1 with male preponderance and coincides with the reports of the studies conducted in Pakistan and abroad.[3, 5, 9, 10]

According to our study, about 71 % of the suicides were committed by the persons between the ages of 11-30, declining toward the advancing age whereas only 8.8% cases of the suicide were found to be above 50 years of age,which is in contrast with the western countries where the number of the suicide in elderly subject is greater[16].

The trend of suicide is increasing day by day in Pakistan. The common causative factors are unemployment, homelessness, socio-economic problems, social injustice, marital disharmony, difficulty in inter personal relationships, and extreme poverty[17].Extreme poverty has evolved a new method of jumping into the water of the mother along with the children, the reason might be that her children may not suffer socio-economical and socio-cultural problems after her death. This phenomenon is very alarming for the authorities engaged in the prevention of suicide in Pakistan.

Murad M Khan (2007) reported that while official rate of suicides are lacking it has been possible to calculate the rates of suicides in six cities of the Pakistan. The crude rates vary from a low of 0.43/100,000 per year (average for 1991-2000) in Peshawar to a high of 2.86/100,000 for Rawalpindi (in 2006), with other cities falling in between: Karachi, 2.1/100,000 (1995-2001); Lahore, 1.08/100,000 (1993-95); Faisalabad, 1.12/100,000 (1998-2001) and Larkana, 2.6/100,000 (2003-2004)[18], which is agreementwith our study and other studies conducted in Pakistan which also shows low rate of suicide in Pakistan.

M. S. Reddy reported in 2010 that 90% of the suicides can be traced finally to the hopelessness leading to depression, so all the major psychiatric disorders carry an increased risk of suicide, and also commented that people on antidepressant therapy have tendency to commit suicide after 10-14 days of commencement of antidepressant therapy[19].

Bertolote and Fleischmann, 2002, observed that Suicide rates in Islamic countries are considerably lower than other countries[20]. Simpson and Conklin (1989) carried out a 71 nation cross-national analysis and showed when factors such as social, economic and demographic modernity are controlled; Islam has an independent effect on lowering suicide rates[21].The major deterrent effect of Islam toward the commission of the suicide is perhaps the firm belief in the life herein after and suicide has been declared as "Haram" according to the teachings of the Islam.

It has been observed in our study that most of the suicide incidents took place in hot/ rainy weather i.e. months of April, May, June and July which has also been reported in many studies conducted worldwide[3, 7,17, 22].

CONCLUSION

In Pakistan, the suicide DSH (Deliberate Self Harm) rate has increased very speedily in the recent years. The most powerful factor towards depression & suicidal ideation and commission, should be alleviated by the hectic efforts of the Government and NGOs. Crisis intervention centres& suicidal prevention hot line should be established on the pattern of Sri Lanka and other western countries. As mentioned earlier, attempted suicide is a crime in Pakistan, suicide in most other countries is thought as less as a crime and more as ill-fated outcome of the hopelessness/depression resultant from social disorganization. It is therefore suggested that the person who attempts suicide should be provided treatment in psychiatric institution rather than to be subjected to punitive action for his rehabilitation in the society.

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Original Article

Anaemia in Pregnancy

Prevalence and Proportion of Anemia in Pregnant Women Suffering from Malaria

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ABSTRACT

Objective: To find out the prevalence and proportion of anemia in pregnant women suffering from malaria. The aims & objectives of our study were to evaluate prevalence & proportion of anemia in pregnant women with malaria among the patients visiting the tertiary hospital PUMHS Hospital, Nawabshah, Shaheed Benazirabad so as to give awareness of these complications to doctors to ensure early diagnosis, prevention & prompt treatment of such cases.
Study Design: Descriptive observational study.
Place and Duration of Study: This study was conducted at Outpatient Department of MMCH Hospital & Department of Pathology from April 2012 to February 2013.
Materials and Methods: Study includes total 120 cases of malaria, diagnosed on the basis of clinical & laboratory findings. The hematological complications like anemia, leukocytosis & thrombocytopenia were studied in these patients.
Results: Out of 120, 64 patients were anemic. We divided pregnant women into 5 groups, 40 patients were in 16 – 20 years age group and amongst them 55% patients were anemic, 34 patients were in 21 – 25 years age group and amongst them 50% were suffering from anemia, 22 patients were in age group 26-30 & amongst them 22 % anemic, 15 cases were in age group 31 – 35 & out of them 46% were anemic and in age group 36 – 40 years 46 percent were anemic. Overall there were 53% anemic patients in total of 120. According to the occupation status majority were daily wages laborers and farmers and other were housewives. Out of 120 patients most of them were Multigravida. Most of the patients were suffering from anemia, 76% patients had Leucocytosis with Neutrophillia, 74 percent patients had complication of Lymphocytosis, 80 percent of patients had decreased level of monocytes and 60 percent had decreased level of platelets. All the patients were suffering from fever and associated symptoms of chills, sweating, feeling of hotness and coldness, 63 percent had back pain, 45 percent had headache and 23 percent had complication of Spleenomegaly. The diagnosis of malaria was made on clinical grounds & confirmed by laboratory findings. The problems of hematological complications as anemia, leukocytosis & thrombocytopenia were detected among the patient of malaria by determining hemoglobin concentration, complete blood picture & urine examination report.
Conclusions: P.vivax malaria is most prevalent variety. Anemia, leukocytosis & thrombocytopenia are the most common hematological complications in these patients. It is suggested to ensure
i. Effective malaria control program in country, specially interior Sindh.
ii. Effective measures for prevention, diagnosis & treatment of patients.
iii. Effective health education through electronic & print media.
Key Words: Anemia, Pregnant Women, Malaria

INTRODUCTION

Malaria remains a global health problem with an estimate of 3 billion people at risk of infection in 109 malaria endemic countries. Approximately 250 million cases occur annually leading to approximately one million deaths. 1.2 billion people live in areas with a high risk of malaria (more than 1 reported case per 1000 population per year). There were an estimated 247 million malaria cases among 3.3 billion people at risk in 2006, causing nearly a million deaths, mostly of children under 5 years[1]. In human the sprozoites are transmitted into body by mosquito bite & they first infect the liver cells, then red blood cells & releasing merozoites that mature in male & female gametocyte in human body. When a healthy female mosquito bites a malaria infected human these gametocytes reach in mosquito's stomach unite together to form zygotes that develop into Oocysts which grow & rupture to release sporozytes & cycle starts again[5].

According to world malaria report 2011, there were 225 million cases of malaria worldwide & malarial mortality rate reduced by 5% with overall 20-23% throughout world, as an estimated 655000 deaths in 2011 & 781000 deaths in 2010[2]. Although infection due to Plasmodium falciparum is responsible for the greatest overall morbidity and mortality, P.vivax contributes seventy to eighty million new cases to the annual worldwide burden of disease, especially in

temperate regions[3]. Over 40% of world population lives in malaria endemic area including South Asia, India, Pakistan, Bangladesh, Africa, areas of Middle East, Central and South America[4].

As for hematological complications of malaria are concerned, the anemia, leucocytosis, leucopenia & thrombocytopenia are well recognized complications. The pathogenic mechanisms that cause these complications include haemolysis of parasitized & non-parasitized red blood cells, depression of erythropoiesis, megakaryopoiesis & bone marrow depression, so also immune mediate destruction of thrombocytes caused by releasing of inflammatory cytokines such as tumor necrosis factor & interleukine 1,6 & 10 from the activated macrophages in malaria[6].

The factors contributing to the severity of hematological complication are malaria immunity, endemicity, hyperparacytemia, hemoglobenopathies, G6PD deficiency nutritional status & co-morbidity of HIV & dengue fever[7].

The clinical presentation of malaria caused by all species of malaria parasite resembles & includes fever, headache, body ache, joint pain, chills, sweating & vomiting. These symptoms appear within 1 – 2 weeks after bite of infective mosquito[8].

Pl. falciparum originally was discovered in gorillas caused sever malaria especially among the children producing anemia, respiratory distress, hepato-splenomagaly & finally renal failure or black water fever & cerebral malaria with retinal changes (whitening) which may be a useful clinical sign that distinguish malaria from other causes of fever[9,10].

Although blood is most frequently used to make a diagnosis of malaria by microscopic examination of Giemsa stained blood films but saliva & urine have been investigated as an alternative non invasive techniques[11]. The rapid malaria diagnosis test & polymerase chain reaction have been discovered recently to be used for diagnosis of malaria. These tests are not implemented in poor country like Mozambique due to their high cost. Often the history of fever is taken as the indication to treat malaria in these countries[13,14,15].

MATERIALS AND METHODS

This Observational descriptive study was conducted at outpatient department of MMCH Hospital & Department of Pathology from Apr 2012 to Feb 2013. Total 120 pregnant patients visiting OPD were included in the study and patient having any morbidity were excluded from the study. The prevalence of malaria with reference to age, sex, area of residence & clinical findings were recorded. For the laboratory diagnosis of malaria blood samples in test tube containing EDTA were sent to pathology department. Thick & thin blood smears were made on the clean glass slides from the EDTA mixed blood, & examined under microscope for detection of various developmental stages of malaria parasites after staining with Giemsa stains. The Hb concentration, CBC including RBC, TLC, DLC & platelet counts were determined by a hematological analyzer (Sysmac). The ESR & ICT were also done from the same blood sample.

RESULTS

Out of 120 pregnant patients, 40 were from urban and 80 pregnant women were from rural life. Out of 40, 19 patients were anemic and 21 were non-anemic while out of 80 rural patients 50% were anemic (Table No. 1) . We divided pregnant women into 5 groups, 40 patients were from 16-20 year (anaemic patient were 22), 34 patients were from 21-25 year (50 percent women were suffering from anemia), 20 patients were in age group 26-30 years (11 patients were anaemic), 15 patients were between 31-35 (7 patients were anaemic) and 11 were in 36-40 years group (7 were anaemic). Overall 64 patients were anemic in total 120 cases (Table No.2). Regarding occupational status, majority were daily-wages laborers and farmers and rest were housewives (Table No.3). Out of 120 patients majority were multigravida (Table No.4). All patients were suffering from anemia but 76% had Leucocytosis with Neutrophilia, 74 percent patient had complication of Lymphocytosis, 80 percent of patient had decreased level of monocytes and 60 percent had decreased level of platelet (Table No. 5). All the patients were suffering from fever and associated symptoms of chills, sweating, feeling of hotness and coldness, 63 percent had body pain, 45 percent had headache and 23 percent had complication of Spleenomegaly (Table No. 6).

Table No. 1: Distribution of case with reference to residence

Place of residence	Anemic	Non – Anemic
Urban 40	19 (47.5%)	21 (52.5%)
Rural 80	45 (56.25%)	35 (43.75%)
Total 120	64(53.33)	56(46.67)

Table No. 2: Distribution of case with reference to age

Age related group	Total case	Anemic	Non – Anemic
16-20 yrs	40	22 (55%)	18 (45%)
21-25 yrs	34	17 (50%)	17 (50%)
26-30 yrs	20	11 (55%)	9 (45%)
31-35 yrs	15	7 (46.66%)	8 (53.33%)
36-40 yrs	11	7 (46.66%)	4 (36.66%)
Total	120	64(53.33)	56(46.67)

Table No. 3: Distribution of case with reference to occupation

Sr. No.	Occupation group	Total case	Anemic	Non – Anemic
1	Housewife	15	10 (66.66%)	5 (33.33%)
2	Farmer	30	17 (56.66%)	13 (43.3%)
3	Daily-wages worker	75	60 (80%)	15 (20%)

Table No. 4: Distribution of case with reference to parity

S. No.	Parity	Total case	Anemic	Non – Anemic
1	Primigravida	35	18 (51.42%)	17 (48.57%)
2	Multigravida	58	40 (68.96%)	18 (31.04%)
3	Third trimester	27	18 (66.66%)	9 (33.33%)

Table No. 5: Distribution of case with reference to haematological complications

Sr. No.	Haematological Complications	No. of patients	Percentage
1	Anemia	120	100.00
2	Leucocytosis with Neutrophilia	92	76.60
3	Lymphocytosis	89	74.16
4	Decrese in Monocytes	95	80.00
5	Thrombocytopenia	72	60.00

Table No. 6: Distribution of case with reference to clinical findings

Sr. No	Clinical Findings	No. of Patient	Percentage
1	Fever	120	100%
2	Associated Symptoms like Chills, Sweating, feeling of Coldness and hotness.	120	100%
3	Bodyache	76	63.33%
4	Headache	55	45.83%
5	Pallor	80	66.66%
6	Spleenomegaly	28	23.33%

Table No.7: Distribution of cases with reference to haematological parameters(Hb & ESR)

Sr. No.	Haematological parameters	No. of Patient	Percentage
1	HB 5.5 – 11.5 g/dl 8.5 ± 3	88	73.30
2	ESR 40 – 110mm 37.5 – 72.5	120	100.00

Table No. 8: Distribution of cases with reference to hematological parameters determined by haematological analyser (Sysmac)

Sr. No.	Haematological parameters	No. of patients	Percentage
1	TLC: 6500-25000/cumm Mean=8750 ± 1625	90	75%
2	RBCs: 2.4-4.5m Mean=3.5±1.0	67	55.8%
3	DLC: Eutrophils 67-85% Mean=80.5 ± 5.5	92	76.6%
4	Lymphocytes 10-14% Mean=11±3	87	72.5%
5	Monocytes: 10-18% Mean=14±4	96	80.0%
6	Eosinophils: 2-4% Mean=3±1	120	100%

DISCUSSION

The malaria mortality rate in 2010 was 50, 56 & 86 persons per 100,000 populations in 3 Africans countries as reported by Guardian news London[16]. On the celebration of malaria day on 25 April 2011, the map of Plasmodium falciparum malaria & endemicity in 2010 & several other maps related to malaria were published in Asia, Africa & America as noted by Gething et al[17].

Malaria was endemic in broadband around the equator, in areas of America, many part of Asia and much of Africa, & 85 – 90% of malaria mortality due to the P. falciparum occurred among the children & pregnant women in Sub-Saharan Africa[18].

Malaria was prevalent throughout the human history & one in every two people had been died due to malaria & its complications. Atlas projects founded by Wellcome UK Trust to rectify malaria mapping providing more contemporary & robust means by which the current & future malaria disease burden was assessed as reported by Hay et al[19].

The malaria superimposed with HIV infection is increasing a person's susceptibility to malaria infection as stated by Abu Redid et al[20].

The female anopheles mosquitoes such as A.culicifacies & A.sephenisi were common in Pakistan that transmitted malaria as recorded by national Malaria control program 2006[21]. While prevalent rate of P. Vivax malaria was two times higher than P. falciparum in interior Sindh as well as in Baluchistan Pakistan, Mehmood et al[22], Nizamani et al[23] & Yasin Zai et al[24].

The hematological complications in malaria such as anemia, Leucocytosis with Neutrophilia & thrombocytopenia were stated by Khalid et al[25] & age as a risk factor for thrombocytopenia & anemia in children treated for acute uncomplicated falciparum malaria was found by Adedapo et al[26]. The high

concentration of interleukin-10 associated with thrombocytopenia in falciparum malaria was demonstrated by Casal-Pascual et al[27]. The hemozoin containing leukocytes (HCL) such as monocytes & neutophils seen in blood films on patients with malaria were negatively correlated with severity of malaria in Ugandan children as stated by Mujuzi et al in his study[28].

In contrast to this study, Hunched et al studies stated that presence of HCL in blood films of patients with malaria were used as reliable diagnostic but less prognostic tools[29]. Both studies stated that hemozoin is brownish black malaria pigment that digests product of hemoglobin produced by phagocytosis of parasitized & none parasitized RBCs by monocytes & neutophils. Casal – Pascual el al demonstrated that suppression of erythropoises produced severe malarial anemia that is associated with hemozoin containing leukocytes in peripheral blood[30].

The hematological complications of malaria evaluated by hematological parameters to differentiate malaria from other acute febrile illness were studied by Danish et al[31]. They stated that severe anemia & thrombocytopenia determined by hemoglobin & platelets counts less than 5g/dl & 5000/cumm respectively in these patients had more specific, sensitive & predictive values to diagnose malaria.

CONCLUSION

P.vivax malaria is most prevalent variety. Anemia, leukocytosis & thrombocytopenia are the most common hematological complications in these patients. It is suggested to ensure

i. Effective malaria control program in country, specially interior Sindh.
ii. Effective measures for prevention, diagnosis & treatment of patients.
iii. Effective health education through electronic & print media.

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Original Article

Risk Factors and Management of Birth Related Femoral Fracture

Femoral Fracture due to Birth Trauma

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ABSTRACT

Objective: To evaluate the risk factors and management of femoral fractures related to birth trauma.
Study Design: Descriptive Case series Study
Place and Duration of Study: This study was conducted in Department of Orthopaedics& Traumatologyand Department of Obstetrics & Gynecology of Khyber Teaching Hospital, Peshawar from April 2008 to March 2013.
Materials and Methods: Over a period of 5 years,cases of femoral fractures in newborns due to birth trauma presenting to Orthopaedic&Taumatologydepartment or occurring in Obstetrics & GynecologyDepartment of Khyber Teaching Hospital Peshawar were recruited to the study. Birth histories of the cases were explored with respect to period of gestation, birth weight, presentation at birth and mode of delivery.Type of fracture and management used was documented. Cases were followed till recovery.
Results: Mean gestational age was 38.1 weeks and mean time to diagnose was 3 days. Presentation of baby was breech and mode of delivery was Caesarean section in majority of cases.Mid shaft fracture was present in ten cases and three had subtrochanteric fracture. All patients showed complete union at a mean duration of 3.2 weeks.
Conclusion: Femoral fracture due to birth trauma in newborn is a rare injury. It is more common in cases of Caesarean section done for breech presentation. Risk is high in preterm and/or low birth weight babies. Fracture mostly involves shaft of femur.These fractures have very good prognosis and show complete healing following immobilization.
Key Words: Femoral Fracture, Birth Trauma, Risk Factors, Management

INTRODUCTION

Fractures may occur due to significant mechanical forces at any point of time in the series of events in childbirth.[1] The most common fracture usually encountered is that of clavicle.[2] Fracture of femur is considered rare in newborns and has been described with difficult deliveries.[3]The reported incidence varies between 0.13 and 0.077 per 1,000 deliveries[3,4]. The earliest case of femoral shaft fracture in a newborn was reported in 1922 following a difficult breech delivery.[5]Since then, much literature has been published regarding the possible aetiology, risk factors and management of this injury.[3,4,6]

The mechanisms of injury to femur have been well described with vaginal delivery. It may happen in the context of malpresentation, low birth weight, macrosomic baby and difficult or precipitous delivery.[2,4,7] Caesarean section is presumed to reduce the risk of fractures. This consideration has been catechized in many reports in the literature.[8,9,10] The prevalent use of low segment vertical incision to reduce maternal morbidity compounded by difficult indications such as breech presentation or obstructed labour may increase the incidence of neonatal injuries in Caesarean section.[9,11,12,13,14]Other risk factors associated with this injury include osteogenesisimperfecta and osteopaenia of prematurity.[15,16]

Several treatment modalities areused for treatment. The basic principle underlying these is strict immobilization of the femoral shaft.[14,17,18] The proximal fragment is flexed, abducted and externally rotated in case of subtrochanteric fracture of femur. Simple strapping of the thigh to the trunk in the same way as a Pavlik harness to achieve reduction by bringing the distal fragment in alignment with the proximal one is effective.[14,17,19]Fractures of the shaft of femur are usually encountered with minimal angulation and are best managed with toe–groin cast or hip spika until the fracture becomes sticky.[17,19,20]

MATERIALS AND METHODS

The study included a cohort of all newborn babies with age less than one week, with femoral fracture due to birth trauma presented to the Orthopaedic& Traumatology Department or Obstetrics &Gynaecology Department of Khyber Teaching Hospital from April 2008 to March 2013. Written informed consent was taken from the parents of all newborns. A detailed history with particular emphasis on birth history was taken from all parents. Birth records from the concerned Obstetrics department were obtained. The help of second author was taken in this regard. Details of obstetrical history of the mother with respect to any illness during pregnancy like diabetes were sought. Period of gestation at the time of delivery, mode of delivery and any complications during birth were recorded. A note was made of birth weight of the baby. A thorough clinical examination was carried out. Presence of other birth injuries, fractures, nerve palsies

and/or stigmata of other musculoskeletal, metabolic and/or genetic disorders like presence of blue sclera and hypermobile joints(osteogenesisimperfecta) was documented. Type and extent of femoral fracture was recorded.Treatment modality was decided depending on the site of fracture and angulation at the site. Femoral fractures in the subtrochanteric region were managedwith pavlik harness, while fractures of the shaft were managed in a spica cast. All patients were followed on a weekly basis in the outpatient department. All of them were pain free by 4 weeks, and healing had occurred by then.Pavlik harness and spica cast both were removed at the end of 4th week.

RESULTS

There were 13 newborns with femoral fractures due to birth trauma. There were 9 males and 4 female neonates. Mean gestational age was 38.1 weeks (range 34 to 41 weeks) with 3 preterm neonates. The mean birth weight was 2.6 kg (range 2.1 to 3.5 kg). Mean age was 4 days. All neonates were born in our hospital obstetric department.

Table No. 1: Characteristics of Neonates with birth related femoral fractures (n=13)

Gender	Males=9 Females=4
Gestational age at birth(weeks)	Mean= 38.1
Preterm	n= 3
Birth weight(kg)	2.6 kg
Age at presentation(days)	Mean=4

Table No. 2: Characteristics of Femur fracture

Laterality	Right: n=8 Left: n= 5
Time to diagnosis(days)	Mean= 3
Type of fracture	Subtrochanteric:n= 3 Mid shaft of femur: n= 10
Time to heal(weeks)	Mean= 3.1

Three neonates were born to mothers with diabetes. Eight mothers were primigravidae and 5 were multigravidae. Mean age of mothers was 30 years (range 25 to 39 years).

Mode of delivery was vaginal in 5 and Caesarean section in 8 cases. In the cases delivered vaginally presentation was cephalic in 2 and breech in 3. There was one case of outlet forceps delivery. Among the group delivered by caesarean section 6 were breech presentation, one cephalic and one neglected transverse lie. Neonate with cephalic presentation was a case of obstructed labour. There were 7 emergency and only one elective caesarean section.

Mean duration to diagnosis of fracture was 3 days(range 1 to 5 days). Right femur was involved in 8 and left in 5 cases. One neonate had fracture humerus along with femur. That neonate had features suggestive of osteogenesisimperfecta.Midshaft of femur was fractured in 10 cases. There were 3 cases of subtrochanteric fracture.No neonate had any dysmorphic features.

Mean time of fracture healing was 3.1 weeks. No non union was recorded. All fractures showed satisfactory union by 4 weeks.

DISCUSSION

The differential diagnosis of femoral fracture in a newborn includes osteomyelitis, osteogenesisim perfecta, child abuse, and metabolic bone diseases.Eherenfest[5], in 1922 ,was the first to report a femoral fracture during caesarean section.He described a midshaft fracture during caesarean section delivery in amother with diabetes and a uterine myoma. Similarly, Denesand Weil[21] reported three infants with femoral fracturesduring caesarean section due to traumatic separation of theproximal femoral epiphyses.

The mechanism of injury has been postulated to be most commonly torsional injury leading to spiral fracture of the shaft of femur [4]. Most of the fractures in our series were of the same type. In the case of vaginal breech delivery, excessive traction on the leg when the breech is fixed at the pelvis can lead to fracture of the femoral shaft.[2]Morris et al [3], reporting in 2001 on their experiencewith femoral fractures occurring during delivery, found an incidence of 7 infants/52,296 deliveries, or 0.13 per 1000. In our study the incidence of femoral fractures was 0.077 per 1000 deliveries in our hospital.

In our study mode of delivery was caesarean section in 8/13 cases (61.5%) which correlates with the findings of Kancherla R et al[14]who reported it in 6/10 (60%) cases. Though Caesarean section was postulated initially to decrease this pattern of injury, many contrary reports have shown a reverse incidence [3, 10].Givon and collaborators[17]assessed the treatment of neonates with femoral fractures. They too noted the increased risk for femoral fracture during caesarean section (73% of fractures occurred during caesarean section).One reason could be the decreased space for maneuverability of obstetric procedures in these patients.Other causes may include poor relaxation, poor delivery techniques and small incision.[7]In majority of cases presentation of the baby was breech which required traction on the legs to deliver the baby through a small transverse uterine incision.Most of the caesarean sections were done in emergency when senior staff was not available and surgery was done by junior doctors. Furthermore most of the women presented in advancedlabour where the breech was already engaged or with the foot descended into the vaginaand thus excessive traction was used to disimpact the breech to deliver the baby.

The role of gender in fracture risk has not been assessed in the published literature. In the study of 11 cases published by Givon et al [17], most of the neonates were female (n = 7). However, we had more males (n = 9) than females (n = 4). Therefore, we could not draw any conclusions on the possible role of gender on fracture risk.

The mean gestational age at diagnosis in our patients was 38.1 weeks. We had two pre-term babies, the rest being full term. The mean birth weight of the babies was 2.6 kg. Of the thirteen, four of them were <2.5 kg, considered to be low birth weight. Thus, earlier speculated risk factors such as macrosomic post-term or pre-term babies might have less bearing whereas low birth weight in full-term pregnancies might prove to be influential in our country.

Diagnosis of femoral fracture was made after a mean period of 3 days (range 1–5 days) in our study. This is similar to the time period observed by Kancherlaet al.[14]The recommended modes of treatment for a fractured femur in neonates is conservative and includes a spica cast, the Pavlic harness, and Bryanttraction. In our study we used spica cast for shaft of femur fracture and Pavlik harness for subtrochantericfracture. We did not use Bryant traction because it requires inpatient care and keeping the neonate in this position is cumbersome. Moreover skin complications are more considering the fragile and delicate skin of small neonates.

Our study does have some limitations. Most of our cases were diagnosed only when a referral was sent to us by the neonatologists or obstetrician based on suspicion, leading to a possibility of missing an occult fracture. A thorough screening protocol by the neonatologist in the event of a difficult delivery would be quite helpful. Considering our small patient sample size, our findings may not be generalized.

CONCLUSION

Femoral fractures following delivery, though rare on presentation, should be looked out for, especially in difficult caesarean sections. When encountering a difficult labor, which started as a breech and ended as a caesarean section,obstetricians should bear in mind that the risk for femoral fractures is higher than in vaginal delivery.Thorough clinical examination and proper orthopaedic consult in the event of doubtful presentation would help. These fractures have very good prognosis and show complete healing following immobilization.

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Original Article

Tetanus Toxoid

Tetanus Toxoid (TT-2) Coverage & its Associated Socio-demographic Factors among Married Women of Reproductive Age in Urban & Slum Areas of Hyderabad

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ABSTRACT

Background: Neonatal tetanus is vaccine preventable infection & a cause of neonatal mortality in our country. TT-vaccination of women at child bearing age can safeguard women & reduce neonatal mortality.

Objectives: To assess the TT-2 coverage among women at reproductive age in Hyderabad urban & slum areas. To determine the socio-demographic risk factors influencing the TT-vaccination coverage.

Study Design: A community based cross sectional study

Place and Duration of Study: This study was conducted in Hyderabad city areas (Gari Khata, Noorani Basti), Latifabad Unit No: 5, 11, 12 & Qasimabad (Phase I, Sehrish Nagar, Nasim Nagar) from 15th June-15th August 2014.

Materials and Methods: 220 women of child bearing age were approached through convenience sampling. Questionnaire based interviews & examining the vaccination cards were study tools. Data comprised of categorical & continuous variables & was analyzed by SPSS Version 16. Categorical variables were analyzed by chi-square test; mean & standard deviation was calculated for continuous variables & were analyzed by applying student t-test. The p-value ≤ 0.05 was taken as level of significance for associations.

Results: TT-2+ coverage was 40.9 percent; 29.1% women were not ever TT-vaccinated. Significant associations were observed between TT-2 coverage & ante-natal visits (p=0.04), educational level (p=0.05); socio-economic class (p=0.02) & women's working status (p=0.01); Age & parity were not associated (p= 0.09 & 0.31 respectively). Most common reason for non-vaccination was unawareness about TT-vaccination schedule (30.5%).

Conclusions: Low TT-2 coverage in slum areas of Hyderabad demands attention of health care providers to help improve the situation.

Key Words: Tetanus toxoid, child-bearing age, antenatal visits, parity, urban, slum areas.

INTRODUCTION

Tetanus is a vaccine-preventable disease. It is a deadly infectious disease for which immunization is available in EPI at infant level and for females of reproductive age[1]. In 1989, the World Health Assembly called for the elimination of neonatal tetanus by year1995, and since then considerable progress has been made using the strategies of clean delivery practices, routine tetanus toxoid (TT) immunization of pregnant women, and immunization of all women of childbearing age with three doses of TT vaccine in high-risk areas during supplementary immunization campaigns[2]. A review of the literature found that TT vaccination coverage in Pakistan ranged from 60% to 74% over the last decade. Worldwide tetanus accounts for 5% of maternal deaths and 14% of all neonates deaths annually [3]. Low vaccination coverage, the main driver for neonatal tetanus in Pakistan, is due to many factors, including lack of awareness among public[1]. Large reductions in deaths due to neonatal tetanus have been reported following major increases in the coverage of tetanus toxoid immunization to the women at child bearing age[4]. World Health Organization (WHO) observes that for the woman to be protected during pregnancy, the last dose of tetanus toxoid must be given at least two weeks prior delivery[5]. The purpose of this study was to estimate the coverage of TT-2 among women of reproductive age and to sort out associated risk factors in target population in Hyderabad.

MATERIALS AND METHODS

It was a community based study conducted in Hyderabad city areas (Gari Khata, Noorani Basti), Latifabad Unit No: 5, 11, 12 & Qasimabad (Phase I, Sehrish Nagar, Nasim Nagar). These areas were selected in order to get mixed population sample. The duration of study was two months i.e from 15th June-15th August 2014.

Study population, Sample size & Sampling technique: Two hundred & twenty subjects were selected for the study through convenience sampling.

Inclusion & Exclusion Criteria: Married women at reproductive age (15-49 years) were approached & were interviewed with reference to the most recent pregnancy. Those who did not consent were dropped from the study. In case of joint families, a single

woman per family was selected in order to get broader representation of the target population.

Data Collection Tool & Analysis: After informed consent, the data was recorded on a questionnaire including demographic & social information likely to affect tetanus toxoid coverage. Women themselves were the respondents. Verbal history of TT-vaccination was taken & was confirmed by examining the vaccination card. To explore reasons of non-vaccination or partial vaccination, we included few open-ended inquiries in the questionnaire. The variables of interest were woman's age, parity, educational level, socio-economic & working status, TT-1, TT-2 & TT-2 + coverage; number of ante-natal visits undertaken during recent pregnancy, source of information for TT-vaccination & reasons for not being vaccinated. The data was analyzed by using SPSS Version 16. The categorical variables were analyzed by chi-square test; continuous variables were analyzed by student t-test. The p-value ≤ 0.05 was taken as level of significance for associations.

RESULTS

Two hundred & twenty women of reproductive age were approached for the interview. Regarding TT-vaccination, there were 40.9% women who had received two or more doses of tetanus toxoid; 30.0% had received only single dose of this vaccine & 29.1% were those who had never received tetanus toxoid vaccine (Chart I). There were 70% women who showed vaccination card; while remaining 30% did not have any record of vaccination against tetanus. The minimum age recorded was 18 years & maximum age was 46 years. The mean age was 32 years with standard deviation of ± 6.8 years. Age of women did not show any association with TT vaccination status of women (p=0.09). There was rural-urban imbalance regarding tetanus toxoid coverage (22.2% in rural as against 59.5% in urban areas) (Chart II).There were more than 70% women who were between para 2-3 (Chart III). No association of parity with TT vaccination was observed (p=0.31). 39.5% of women had undergone not a single ante-natal visit during recent pregnancy, 31.8% had only one such visit; while remaining 28.7% were those who had gone through two or more ante-natal check up. A statistically significant association was observed between total number of ante-natal check up & TT-2 vaccination coverage (p=0.04). Tetanus vaccination status was also related to educational level of women (p=0.05); but its strong association was seen with socio-economic class (p=0.02) & her working status (p=0.01). There were 4.1% women who gave past history of fits suggestive of neonatal tetanus in although there was no documentary evidence available. Regarding knowledge about TT-vaccine, 84.6% were aware about it; majority of them (73.8%) got information from some health care personnel (Chart IV). The most common reason for not being vaccinated was women's unawareness about the schedule of TT-vaccination & the place from where to get vaccinated (30.5%) (Table I).

Table No.1: Reasons for non-vaccination

Reasons as stated by respondents	%age
Don't know about place & time of receiving TT-vaccine	30.50%
Not allowed by husband/family	22.60%
Thought TT-vaccine was a contraceptive	16.30%
Found no time from household work	14.40%
Health center away from house	6.40%
Miscellaneous reasons	9.80%
Total	100.00%

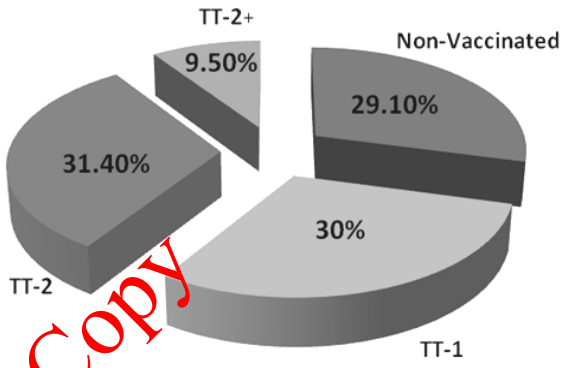

Chart No.1: Tetanus Toxiod coverage among study population (n=220)

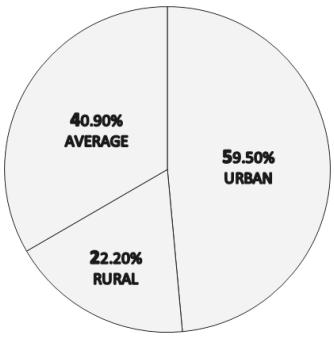

Chart No.2: Area wise TT-2 coverage

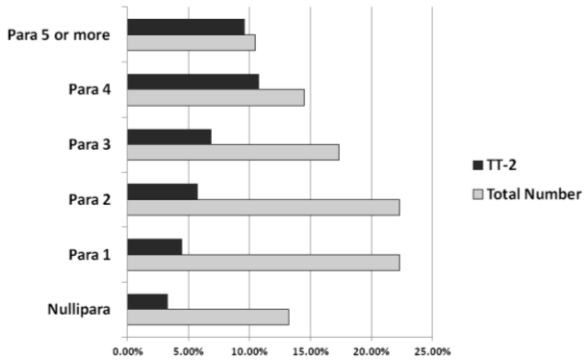

Chart No.3: Relation of parity & Tetanus Toxoid vaccination

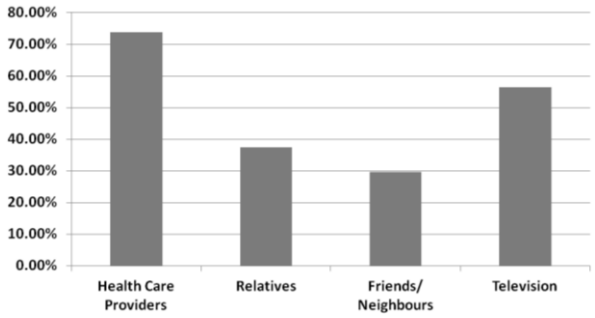

Chart No.4: Source of information about Tetanus Toxoid vaccination

DISCUSSION

The study on two hundred & twenty women revealed TT-2 coverage of 40.9 %.World Health Organization reported TT coverage of 56% in developing countries[6]. Afridi et al reported TT coverage of 65% among women of reproductive age in Peshawar[7]. Similar were the findings of Mansuri FA et al[8]. The lowered rate of vaccination coverage in our study may be due to small sample size or because slum population was over represented in our study resulting in incorporating less privileged women in our study. Our sample of two hundred & twenty included 78 women belonging to urban areas & 142 from slum areas. Siddiqui S et al highlighted in their study the extremely wide rural-urban disparity in TT vaccination coverage; the slum areas were most affected regarding missed opportunities[9]. Another reason could be that we excluded those women who could not show the vaccination card. Surprisingly, our study did not show association with age & parity of women (p= 0.09 & 0.31 respectively). Our findings were endorsed by another research in India showing no association of TT vaccination coverage with woman's age[10]. Abebe DS et al however argue that as parity increases, the coverage of TT-vaccine also increases[11]. The number of the ante-natal visits during recent pregnancy revealed significant association to vaccine coverage (p= 0.04); Hasnain S also concluded that the TT2 coverage was greater among the respondents who had antenatal care as compared to those who did not[12]. The antenatal visits provide an opportunity to women to come in contact with health care providers thus increasing the chances for women to get vaccinated. This was endorsed by Gitta SN et all, too[13]. Aboud S et al proved that the more the numbers of ante-natal visits are done, the lesser were the chances of missed opportunities for TT-vaccination[14]. The ante natal care coverage in Pakistan has increased from 61% in year 2007 to 87% in year 2010; still there is room for improvement[15].

One of the major factors responsible for under coverage of women for ante natal care is lack of awareness due to lack of education in our community. Lack of women educational was associated to under coverage of TT-vaccination (p=0.05) besides low socio-economic status (p=0.02) & working status (p=0.01). Nisar N et al concluded that education was significantly associated with utilization of maternal health services as 22% of illiterate women received antenatal care while 85% of literate women did so[16]. Unawareness, being less educated, poverty were reported to indirectly affect TT vaccine coverage through their effect on lowering antenatal visits[17]. Basher MS revealed illiteracy as one of the known important factors that stand in the way of vaccination[18]. As the female's level of education increases, the awareness among them regarding their health also increases and thus more females get themselves vaccinated[19]. The ante- natal visits provide direct interaction of women to health professionals & enhance the communication between them. An indirect evidence of this was revealed from our study by finding that 84.6% of the women we approached, were aware about it & majority of them (73.8%) got information from some health care personnel thus suggesting strong association with TT-2 coverage (p=0.04). Alam AY et al showed that tetanus toxoid coverage was higher among women utilizing antenatal care (92%) compared to those who were not (8%)[20]. In our study, women quoted various sources of information for vaccination including family friends, relatives, through television but majority of them came to know about it through health providers. The most common reason for not being vaccinated was that women were not aware about the schedule of TT-vaccination & the place from where to get vaccinated (30.5%). The same were the findings of Naeem M et al[21] & Rahman M et al[22] too.

CONCLUSION

We concluded that tetanus toxoid (TT-2) coverage of Hyderabad slum areas is quite low. The findings point to the need for a broad-based campaign to promote access to TT immunization as well as to promote the completion of all five TT doses in Hyderabad especially in remote & slum areas of the city. Based on these findings, we recommend community awareness programs in order to improve utilization status of preventive programs including vaccination.

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Original Article

Combination Therapy of DM

In vitro Evaluation of Mutagenicity of Metformin and Aspartame alone and in Combination

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ABSTRACT

Objective: To assess the Mutagenicity of Metformin and Aspartame in vitro.
Study Design: Observational / Analytical study
Place and Duration of Study; This study was carried out at Department of Pharmacology and Toxicology, University of Veterinary and Animal Sciences Lahore from 1st Jan 2011 to Dec 2011.
Materials and Methods: Ames Salmonella/ Microsome Mutagenicity Assay was used to check the mutagenic potential of test chemicals & control. The data was analyzed by using Statistical Package of Social Sciences.
Results: Metformin was found to be highly mutagenic against TA100 and TA98 both in the presence and absence of metabolic activation system. The results were significant because there was 2 fold rise in number of revertants as compared to the negative control. Overall metformin exhibited more mutagenicity against TA 100 as compared to TA 98 strain of Salmonella Typhimurium. Aspartame showed significant rise in mutagenicity at 100µg/plate and 250µg/plate in dose dependant manner against TA 100 in presence of metabolic activation system. When combination doses of aspartame and metformin were studied, even those doses became mutagenic which were not mutagenic alone. The data advocates that combination doses showed significant additive effect ($p < 0.05$) in the intensity of mutagenic index as compared to the mutagenic index of metformin and aspartame alone.
Conclusion: Both of these products alone & together may cause significant damage to the cells of body as well. Combination therapy of these products should be monitored closely.
Key Words: Diabetes Mellitus, Metformin, Aspartame, Ames Assay, Mutagenicity, S-9.

INTRODUCTION

Diabetes Mellitus (DM) is a chronic disease characterized by high levels of blood sugar. Different oral antidiabetic drugs are being utilized as single as well as combination therapy. Among them Metformin is the most common one. Moreover diabetic patients utilize various low calorie sweeteners to decrease their sugar consumption per day. Aspartame is most widely used artificial sweetener used by diabetic as well as non- diabetic population.

Diabetes Mellitus is a progressive disease and about 6% population in Westernized countries is currently being affected with Diabetes. The ratio is expected to be doubled by 2020[1]. Pakistan stands amongst the highly predominant region, presently having 6.9 million affected people, probably expected to be increased twofold by 2025 and will have an effect on 11.5 million people[2]. Recently Pakistan is ranked at 7th position in the list of countries with problem of DM and it may exceed to 4th position if same circumstances prevail throughout[3]. Mostly the patients of Diabetes are obese at the time of diagnosis and it will be difficult for them to achieve normal glucose level without using oral antidiabetic agents. Metformin prevents obesity and also has advantageous effects on various cardiovascular risk factors. Therefore, Metformin is extensively prescribed as the drug of choice for type 2 Diabetes Mellitus[4]. Metformin is also known to be used to induce and maintain pregnancy in Polycystic Ovary Syndrome[5]. According to a study it is assumed that metformin is associated with the production of oxidative stress in cells leading to DNA fragmentation[6]. In another study it is concluded that metformin is responsible for oxidative stress in white adipocytes, by increasing the levels of reactive oxygen species[7].

Epidemic rates of obesity and type II DM are taking place in the United States and even other areas of the world. Basically this outbreak of obesity have come into view by modification in our dietary habits and decreased physical activities. An important yet not well-supported dietary change is the gradual rise in the quantity of various sweeteners which are used in the food industry[8].

Among these low calorie sweeteners Aspartame is the most widely used sweetener almost capturing 50% of the consumer market in the world. It was discovered in 1965 and now it is easily available in more than 5000 commercial products in not less than 90 countries. Since 1988 almost 80% complaints about various food additives submitted to FDA belong to aspartame[9].

After approval from FDA Aspartame consumption as low calorie sweetener and sugar substitute is being controversial because of its ill effects on health such as carcinomas of brain[10].

MATERIALS AND METHODS

Chemicals: Test chemicals i.e., Aspartame and Metformin were provided by Popular Laboratories, Lahore Pakistan. Metabolic Activation System (S9) was obtained from Environmental Biodetection Products Inc. (EBPI, Canada) in lyophilized form along with its co factors. All other chemicals and media used were of analytical grade.

Mutagenicity Assay: Ames Salmonella/ Microsome Mutagenicity Assay was used to check the mutagenic potential of test chemicals. Standard pour plate incorporation assay and Pre incubation Assay were performed according to the method illustrated by Mortelmans and Zeiger[11]. Standard pour plate incorporation assay was performed to check the mutagenic potential of test drugs without addition of metabolic activation system S9 mix, while Pre incubation assay was used to evaluate the mutagenicity in presence of S9 mix. Two mutant strains of Salmonella Typhimurium TA 100 and TA 98 were used to check reversion caused by test drugs. TA 100 is sensitive to the Base pair substitution mutation whereas TA 98 is used to evaluate the test chemicals which are responsible for Frame shift mutation. Both the strains were cryopreserved at -80°C in nitrogen cylinder according to the protocol described in Mortelmans and Zeiger[11].

Evaluation of mutagenicity was performed by using glucose minimal (GM) agar plate containing glucose minimal medium, Vogel Bonner Salts, Top agar supplemented with 0.5mM Histidine/biotin 2ml, test chemical dilution, 0.05-0.1ml bacterial culture and 0.5ml S9 mix was poured onto the GM agar plate and allowed to solidify for 3 -5 minutes. Now the plates were inverted and incubated at 37°C for 48 hours. In each experiment negative control plate containing top agar supplemented with 0.5mM Histidine/biotin and bacterial culture was poured on GM agar plate without addition of any test chemical. Positive control used to check mutagenicity against TA 100 was sodium azide (5µg/plate) whereas against TA 98 the positive control was 2 nitroflourene (1µg/plate). After the given period of incubation the number of revertant colonies per plate were counted and compared with the number of revertants in negative control plate.

Mutagenic Index of Test Chemicals: Mutagenic Index was measured by applying following formula:

$$\text{Mutagenic Index (M.I.)} = \frac{\text{Number of Revertant Colonies per Plate with Test Chemical Dose}}{\text{Number of Natural Revertant Colonies of Negative Control Plate}}$$

If Mutagenic Index is greater than 2, it means the test concentration will be mutagenic.

Mutagenic response was considered positive when number of colonies in test chemical plate were more than or equal to two fold than the natural revertants of –ve control or background colonies[12].

Statistical Analysis: The data was analyzed by using Statistical Package of Social Sciences SPSS for windows (version 16; SPSS Inc; Chicago IL; USA) and student t-test was applied. The value of $p<0.05$ was considered significant.

RESULTS

10 different concentrations of Metformin in range of 10µg/plate to 400µg/plate were checked for mutagenic response. Similarly 10 different concentrations of Aspartame ranging from 12.5µg/plate to 8000µg/plate were checked for mutagenicity. 10 combination doses of Aspartame: Metformin in range of 12.5:10 µg/plate to 8000:400 µg/plate were checked for their mutagenic potential. In case of Metformin, mutagenicity was observed only when the test concentration ranging from 80µg/plate, 100µg/plate and 150µg/plate were evaluated in Pre Incubation Assay using metabolic activation system S9 mix using TA 100 strain. Whereas the concentrations of 100µg/plate and 150 µg/plate were also found mutagenic while assaying with the same TA 100 strain but without metabolic activation system. Results were considered significant because the revertant colonies showed two fold rise in number of revertant colonies as compared to the negative control plates.

Mutagenicity was observed only when the test concentrations 80µg/plate and 100µg/ plate were evaluated in Pre Incubation Assay using metabolic activation system S9 mix against TA 98 strain. Whereas the concentration of 100µg/plate was also found mutagenic while assaying with the same TA 98 strain but without metabolic activation system (Table 1).

In case of Aspartame Mutagenicity was observed only when the test concentrations of 100µg/plate and 250µg/plate were evaluated in Pre Incubation Assay using metabolic activation system S9 mix with TA 100. Whereas same doses were proved to be non-mutagenic when evaluated in Standard Plate Assay without S9 mix with TA 100. All the 10 doses of Aspartame were found to be non mutagenic in both Pre Incubation Assay and Standard Plate Assay with TA 98 as number of revertants were insignificant because no two fold rise in number of revertant colonies were found as compared to the negative control plates (Table 2).

The concentrations of combination doses of 25:20, 50:80, 100:100 and 250:150µg/plate were found mutagenic with S-9 Mix while assaying with TA 100. Whereas the concentrations of the combination 50:80, 100:100 and 250:150µg/plate were found to be mutagenic while checking the combination without S9

Table No.1: Mutagenic Potential of Metformin

Metformin									
Sr. No	Conc.µg per plate	Revertant Colonies Per Plate							
		TA 100				TA 98			
		+ S-9	M.I.	-S-9	M.I.	+S-9	M.I.	-S-9	M.I.
1	10	122	0.67	61	0.64	65	0.81	36	0.72
2	20	157	0.94	75	0.79	80	1.001	43	0.86
3	80	392	2.35*	99	1.03	184	2.30*	49	0.97
4	100	479	2.85*	265	2.79*	224	2.80**	105	2.09*
5	150	618	3.69**	341	3.54**	148	1.85	77	1.54
6	200	330	1.81	171	1.78	112	1.40	67	1.33
7	250	278	1.53	142	1.48	85	1.06	52	1.01
8	300	174	1.043	96	1	75	0.93	42	0.84
9	350	141	0.85	74	0.78	53	0.66	28	0.58
10	400	83	0.49	44	0.46	39	0.49	16	0.33
-Control	0	182		96		80		51	
+Control	5	1928	10.57	936	9.75	410	5.13	200	3.94

-control × 2*, -control × 3**, -control × 4 and above***

Table No.2: Mutagenic Potential of Aspartame

Aspartame									
Sr. No.	Conc. µg/plate	Revertant Colonies per Plate							
		TA 100				TA 98			
		+S-9	M.I.	-S-9	M.I.	+S-9	M.I.	-S-9	M.I.
1-	12.5	185	0.71	66	0.68	55	0.69	31	0.62
2-	25	212	1.16	87	0.90	66	0.82	36	0.71
3-	50	248	1.36	110	1.17	68	0.85	39	0.76
4-	100	389	2.14*	115	1.21	82	1.025	41	0.83
5-	250	546	3**	140	1.48	95	1.19	44	0.88
6-	500	289	1.59	149	1.55	107	1.32	48	0.93
7-	1000	244	1.34	122	1.28	87	1.09	38	0.73
8-	2000	207	1.14	105	1.10	77	0.97	29	0.55
9-	4000	179	0.98	87	0.93	52	0.65	26	0.50
10-	8000	108	0.595	55	0.58	48	0.60	19	0.37
-ve	0	182		96		80		51	
+ve control	5	1928	10.57	936	9.75	410	5.13	200	3.94

-control × 2*, -control × 3**, -control × 4 and above***

Table No.3: Mutagenic Potential of Combination of Aspartame and Metformin

Aspartame : Metformin									
Sr. No.	Conc. µg per plate	Revertant Colonies Per Plate							
		TA 100				TA 98			
		+ S-9	M.I.	-S-9	M.I.	+S-9	M.I.	-S-9	M.I.
1	12.5:10	189	1.04	85	0.89	66	0.82	35	0.74
2	25:20	395	2.17*	102	1.07	164	2.05*	45	0.89
3	50:80	587	3.22**	190	2.04*	250	3.13**	119	2.24*
4	100:100	814	4.47***	288	3.03**	329	4.12***	185	3.72**
5	250:150	915	5.03***	340	3.58**	154	1.93	90	1.78
6	500:200	346	1.90	165	1.72	139	1.74	69	1.35
7	1000:250	315	1.73	133	1.39	118	1.47	58	1.14
8	2000:300	279	1.53	108	1.14	95	1.13	53	1.05
9	4000:350	185	1.02	82	0.86	64	0.79	37	0.74
10	8000:400	150	0.83	67	0.71	43	0.54	25	0.49
-Control	0	182		96		80		51	
+Control	5	1928	10.57	936	9.75	410	5.13	200	3.94

-control × 2*, -control × 3**, -control × 4 and above***

mix using TA 100 strain as significant difference ($p < 0.05$) was found in no. of colonies of revertants as compared to the negative control. The concentrations of combination doses of 25:20, 50:80 and 100:100µg/plate were mutagenic with TA 98 using metabolic activation system whereas 50:80 and 100:100µg/plate were also mutagenic using TA 98 strain without metabolic activation system i.e. S-9 mix (Table 3).

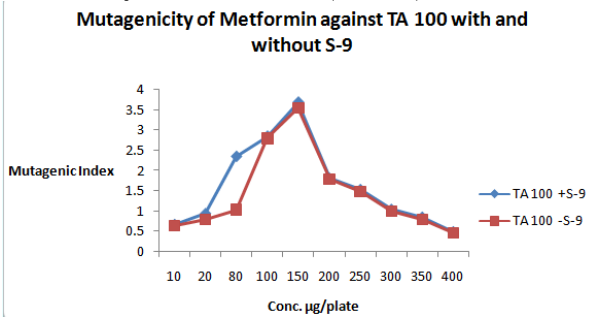

Figure No.1: Mutagenic Potential of Metformin against TA 100 with and without S-9

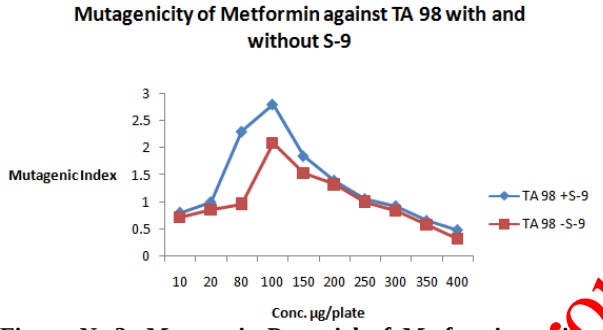

Figure No.2: Mutagenic Potential of Metformin against TA 98 with and without S-9

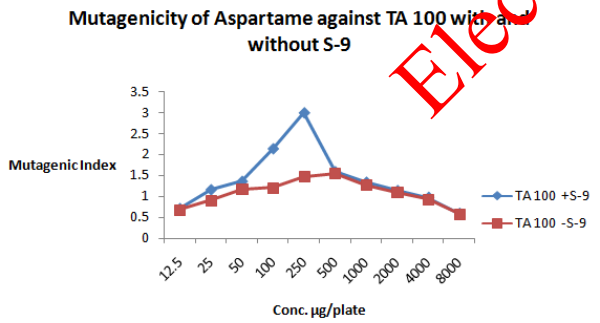

Figure No.3: Mutagenic potential of Aspartame against TA 100 with and without S-9

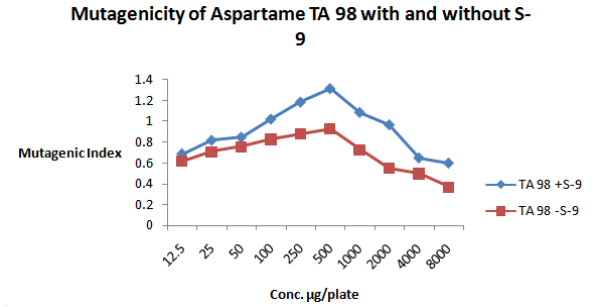

Figure No.4: Mutagenic Potential of Aspartame against TA 98 with and without S-9

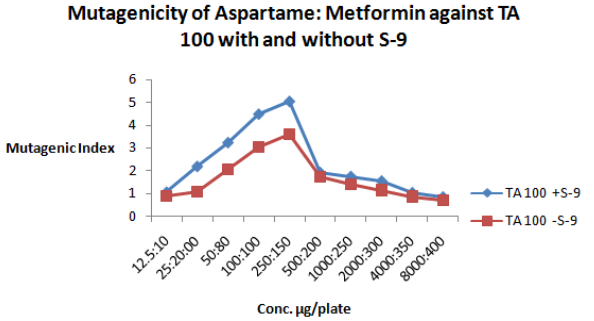

Figure No.5: Mutagenic Potential of ASP: MET against TA 100 with and without S-9

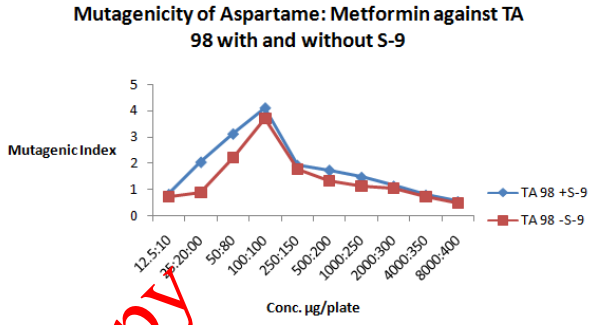

Figure No.6: Mutagenic Potential of ASP: MET against TA 98 with and without S-9

DISCUSSION

Diabetes mellitus Type 2 is a progressive disorder and incidence of this disease is rising rapidly. In the US alone, 41 million individuals of the total population have symptoms of prediabetes, posing them at elevated risk for the established disease of diabetes. The pathological symptoms of type 2 diabetes include insufficient insulin discharge and resistance to the action of insulin[13]. High rates of type 2 Diabetes Mellitus in Pakistan are affecting the quality of life socially as well as financially. This may be due to the poor monitoring criteria as well as high rates of complications associated with the patients of Diabetes Mellitus[14]. A survey conducted in Pakistan concluded that newly diagnosed DM patients were 5.0% in men and 4.8% in women in rural areas 5.1% in men and 6.8% in women in urban areas[15].

This frightening situation may lead to severe consequences. So to treat this progressive disease effective oral antidiabetic agents must be prescribed to deal with the challenge of Diabetes Mellitus. Metformin is the most commonly prescribed drug against DM as it can help to decrease various secondary disorders associated with Diabetes Mellitus such as obesity. Metformin reduces blood glucose level and also cause reduction in obesity. Diabetic population routinely utilizes some low calorie sweetener to reduce their daily intake of sugar. Aspartame is the most common artificial sweetener utilized by diabetic population in

their daily diet schemes. So it is important to determine the toxicological data associated with Metformin and Aspartame. Current study was an attempt to provide the toxicological Index of metformin alone and in combination with aspartame by performing Ames mutagenicity assay to evaluate their mutagenic potential.

Results of Ames test revealed that both metformin and aspartame were mutagenic at different concentrations and the combination doses exhibited significantly high ($p<0.05$) mutagenic index as compared to the metformin and aspartame alone. Among metformin and aspartame, metformin proved to be more mutagenic. A significant ($p<0.05$) dose dependent rise in the mutagenicity against TA 100 and TA 98 was exhibited at 100 and 150µg/plate as compared to the negative control plate. While the dose of 80µg/plate was mutagenic only in presence of metabolic activation system S-9 mix. Maximum mutagenicity was observed at 150 µg/plate against TA 100 both in the presence and absence of S9 mix. Whereas in case of TA 98 maximum mutagenicity was observed at 100 µg/plate both in presence and absence of S9 mix. The results were in accordance with the study results revealed that metformin may have a significant mutagenic potential in pregnant females and their embryos[16]. Moreover metformin may cause DNA damage to Chinese Hamster Ovary cells which supports the hypothesis that metformin may cause DNA damage both directly and indirectly via various unforeseen mechanisms[17]. These studies are in line with the fact that metformin may inhibit the phenomenon of mitochondrial respiration[18]. This fact supports the Warburg theory of cancer that the key factor for tumorogenesis is an inadequate cellular respiration caused by insult to mitochondria[19].

Aspartame caused significant mutagenic response against TA 100 with metabolic activation system having maximum mutagenicity at 250µg/plate. Over all mutagenic potential of aspartame was relatively high against TA 100 as compared to TA 98 strain of Salmonella typhimurium. These results are in accordance with the study in which aspartame and saccharin were checked for their mutagenic potential and aspartame was proved to be more mutagenic as compared to saccharin. Moreover the mutagenic potential was more profound when drug was assayed with TA 100 in presence of metabolic activation system[20]. Similarly aspartame treatment resulted in dose dependant chromosomal aberrations at all concentrations whereas it did not cause Sister Chromatid Exchange[21]. However the data is also available which contradicts the result of this research work such as Ames assay was conducted on aspartame, acesulfame-K and sucralose with and without metabolic activation system and the results revealed that these sweeteners were non mutagenic[22]. The reason for the mutagenic response of aspartame may be credited to the fact that aspartame is mainly composed of 3 components 50% aspartic acid, 40% phenylalanine and 10% methanol. The last component, methanol, is the most dangerous as it is converted to formaldehyde and formic acid[23]. Formaldehyde is a known carcinogen causing severe damage to DNA affecting the process of DNA replication. If the linkages between formaldehyde and DNA become permanent, it may hinder DNA replication resulting in gene mutations[24].

When the combination doses were subjected to Mutagenicity Assay, the results revealed significantly high mutagenic index as compared to metformin and aspartame alone. The order of mutagenicity was same in all 3 assays as large number of revertants were found in case of TA 100 as compared to TA 98. Moreover the mutagenic potential was high in the presence of metabolic activation system S9 mix during Pre incubation Assay as compared to Standard Pour Plate Incorporation Assay.

When combination doses of Aspartame and Metformin were administered, mutagenicity was revealed at 50:80 and 100:100 µg/plate against both mutant strains of Salmonella typhimurium. Relatively large number of revertant colonies was found when assay was performed in presence of S9 mix. The dose ratio of 25:20 µg/plate was only found mutagenic in Pre incubation assay against TA 100 as well TA 98. The results of this study reveal that the threshold level of mutagenicity caused by metformin, aspartame and their combination was same. But the intensity of mutagenic index with combination doses was relatively high as compared to the individual drugs. The reason for this significantly high mutagenicity as compared to aspartame and metformin might lay in the fact that metformin is responsible for increased production eNOS and NO in endothelial cells[25]. On the other hand it was reported that when aspartame was nitrosated for 30 minutes, tremendous rise in mutagenicity in both TA 100 and TA 98 strains of Salmonella typhimurium was observed. So care must be taken by taking into account the risk posed by endogenous nitrosation of foods in human stomach[26].

CONCLUSION

It can be concluded from the present study that metformin is causing more mutagenicity to both strains of Salmonella Typhimurium as compared to aspartame. When combination of aspartame and metformin were exposed to check their mutagenic potential, the results showed significantly high ($p < 0.05$) mutagenicity as compared to metformin and aspartame individually. Most of the diabetic patients utilize aspartame as an artificial sweetener along with their daily regimen of antidiabetic drug metformin. So care must be taken while using both these products together as it may cause significant damage to the cells of body.

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Original Article

PIVD

The use of Mechanical and Manual lumbar Traction in the Management of Prolapsed Inter-vertebral Disc (PIVD). A Survey of Physical Therapists in Pakistan

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ABSTRACT

Objective: To evaluate the use of mechanical and manual traction in the management of lumbar spine prolapsed inter-vertebral disc and its time and cost effectiveness.

Study Design: Observational / Analytical study

Place and duration of study: Alain physiotherapy clinic Karachi and musculoskeletal outpatient Physiotherapy departments (public sector and non public sectors) across Karachi, Lahore, Rawalpindi and Peshawar between October 2012 and January 2013.

Materials and Methods: Participants were selected from Alain physiotherapy clinic Karachi and various physiotherapy departments who offer musculoskeletal assessment and treatment services across Pakistan. Information were gathered on the use of mechanical and manual traction with their effectiveness and its cost and time effectiveness. Descriptive data analysis of information on the use of mechanical and manual traction was done with its time and cost effectiveness in clinical practice.

Results: The overall response rate of 82% in which 79% use mechanical and manual lumbar traction in Patients with prolapsed inter vertebral disc and nerve root symptoms. The effectiveness of traction was reported by 98% of physical therapists. Time effectiveness was reported by 78% and overall the physical therapists reported that both mechanical and manual tractions were cost effective treatments.

Conclusions: Study results show that traction continued to be used in prolapsed inter-vertebral disc of the lumbar spine. The results also clarify the clinical, time and cost effectiveness of the traction treatment.

Key Words: Low back pain; Physical therapy techniques; traction, prolapsed inter-vertebral disc.

INTRODUCTION

Back pain is a very common problem which has serious impact on people working capacity and life style. There are many causes of back pain amongst which lumbar spine vertebral disc bulge is very common. In disc bulge annulus fibrosis becomes weakened and nuclear fluid bulges into the annulus postero-laterally or laterally. This causes a split between annulus fibrosis and nucleus palposus squeezing into vertebral canal commonly known as Prolapsed inter-vertebral disc (PIVD). [1,2] The causes of this bulge are herniation of inter-vertebral disc, degeneration of the disc, obesity, sudden jerk, sprain, trauma to spine and heavy weight lifting. The nucleus can extrude out in three directions i.e. centrally, posterio-laterally and upward into the vertebral body. The posterior longitudinal ligament is narrowest over L4-5 and L5-S1 level in the central backward direction which is the most common site of PIVD. Pain is the primary symptom of PIVD which can radiate to the lower back, buttocks, thighs and anal/genital regions. Pain may also radiate into the foot and can be dull, poorly defined or sharp shooting pain. [3,4,5] The femoral and sciatic nerves are mostly affected, causing thigh pain, numbness and symptoms of sciatica in one or both legs [5]. Due to compression of nerve roots muscular weakness, abnormal tendon reflexes leading to postural changes, scoliosis, antalgic gait and limited spinal movement especially flexion in later stages. [6,7] Physical Therapists use variety of conservative treatment methods in the management of PIVD. These include patient education on proper body mechanics, mobilization and manipulation of lumbar spine, electrotherapy modalities, traction (mechanical or manual). Other treatments applied are lumbosacral supports and the medications example Non-steroidal anti-inflammatory drugs (NSAIDs), steroids and Epidural injection and life style changes like weight control, tobacco cessation etc. [8,9]

In severe nerve compression and disc bulges surgical interventions such as laminectomy and discectomy could be applied for immediate relive of pressure on nerves. [10]

Amongst all these interventions lumbar traction is a commonly used treatment applied by Physical Therapists in clinical practice. Several studies have reported favorable results using traction to treat herniated disc and radiculopathy in lumbar spine. In

most of these studies traction was applied in combination with an extension-oriented treatment approach in patients with nerve root compression.[11,12,13] When the aim is to separate vertebrae for the therapeutic purpose, a relatively high force (40-50% of the body weight) and low treatment time (8-12 minutes) are recommended.[14,15] In contrast the literature does not support the continued use of mechanical and manual traction in the treatment of PIVD. [16,17] Despite little evidence, still many studies have revealed its continuous use with back pain patients: United Kingdom and Republic of Ireland 7%,[18] Northern Ireland 13.7, [19] Netherlands 7% [20],United States 21%, [21] and in Canada up to 30%. [22] Other studies have concluded that methodologic quality of trials on the use of traction is poor. [23,24] therefore, clinical guidelines for traction has not been produced[25]. The literature did not recommended mode of traction (mechanical and manual) and other important clinical parameters. There is a gap in the area to guide type of traction, it is necessary to explore which traction method (mechanical or manual) has been used in clinical practice. This descriptive cross sectional survey of physical therapists in Pakistan was conducted to look at the use of traction modality in the treatment of PIVD. This study explored the type of traction (mechanical or manual) used by physical therapists.(2) Experience of use of manual and mechanical traction and (3) The effects of manual and mechanical traction.

MATERIALS AND METHODS

Survey Design: The study design was a cross-sectional (self-reported) postal questionnaire survey of qualified Physical herapists in various cities of Pakistan including Karachi, Lahore, Rawalpindi and Peshawar.

Sampling Frame: A random selection of physiotherapy departments who offer musculoskeletal physiotherapy assessment and treatment services (40 departments) in Pakistan were identified. The managers and head of departments were contacted for consent to conduct this survey in their departments and provision of qualified physiotherapists list. Sample (N = 153) physiotherapists working in musculoskeletal physiotherapy were identified. The study was done between October 2012 and January 2013.

Questionnaire Design: The contents of the questionnaire were discussed with expert manual physiotherapists and were based on lumbar traction literature. Before the distribution of questionnaire feedback of 3 physical therapists specialized in manual therapy was collected, questions were modified according to feedback. The modified version of questionnaire consists of 5 closed questions, with a comment section for each question and seeking information about experience of using traction techniques in disc problem, type of traction applied (manual or mechanical), time and cost effectiveness of traction techniques and response of traction techniques. A self addressed prepaid envelop, covering letter and questionnaire were sent to the participants. A postcard and reminder letter was sent to all non respondents after 4 and weeks 8 weeks of the first distribution, asking the therapists to indicate the reason for non response by ticking the appropriate box on the postcard. Options available were "I do not work with LBP patients," "I do not use traction with LBP patients. "I am not interested to participate."

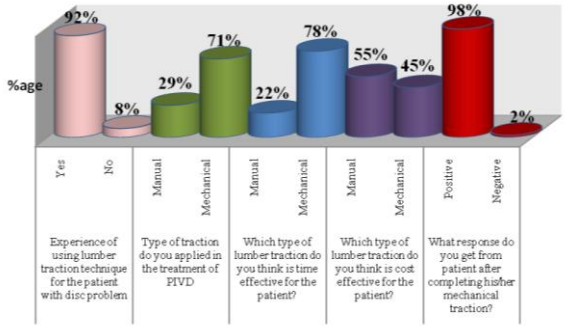
Statistical Analysis: Data was analyzed using statistical package for social sciences (SPSS) version 11by collated response of close questions. Descriptive analysis of each question was done and expressed in the form of table and graph.

RESULTS

Survey response: Questionnaires received back were 126 of the 153 questionnaire sent; the response rate was 82.2%. Of respondents, 79% (n=100) returned fully completed questionnaires, 14.2% (n =18) did not use traction with low back pain patients. A further 6.3 % (N=8) returned the questionnaire and were not interested to participate. Overall 17.8% (N=27) physiotherapists not responded without mentioning any reason, this may not affect this study results as the overall response rate was 82.2%. See table 1.

Table No.1: Survey Response

Questionnaires sent out	153	%age
Questionnaires received back	126	82.2%
Non Respondents	27	17.8%
Questionnaire included in the study and fully completed	100	79%
Respondents did not use traction	18	14.2%
Respondents did not want to participate	8	6.3%



Graph 1: Analysis of various parameters.

Experience of using traction: The responses showed 92% Physical therapists had experience of using lumber traction technique for the patients with disc problem

and 8% had no experience but have used traction in supervision. Graph 1.

Type of traction: In the treatment of PIVD 71% Physical therapists had used mechanical lumber traction while only 29% used manual traction.

Time and cost effectiveness of traction: Overall 78% (78 out of 100) Physical therapists believed that mechanical lumber traction was time effective. At the first session patient were treated for less than 15mins. Overall 55% Physical therapists who fully filled and returned the questionnaire believed that manual lumber traction was cost effective for PIVD treatment as compared to 45% who thought mechanical lumber traction was more cost effective for patient.

Response to traction use: In terms of effectiveness of traction 98% Physical therapists reported positive response from traction in PIVD patients while only 2% reported no response from traction use.

DISCUSSION

To our knowledge this survey was the first in Pakistan looking at the use of traction in current physical Therapy clinical practice to treat patients with PIVD. The collected information contains clinician experiences of using traction, types of traction applied in PIVD patients, time and cost effectiveness of mechanical and manual traction and response from traction use. No survey has been found exploring the specific use of mechanical and manual traction in clinical practice and results of this study provides clinically relevant information on the use of mechanical and manual traction in the treatment of lumbar PIVD. Previous studies produced inconclusive results for the use of traction because of poor quality trials. [24] This study could be used to guide the clinicians in selection of appropriate traction method especially in today's health care services where time and cost has been considered as an important factors.

The results revealed that 79% of Physical Therapists still use mechanical and manual traction in the treatment of PIVD. This is consistent with the findings of a study conducted in the United Kingdom which showed that 76% of Physical Therapists used traction for low back pain patients[26]. Several other studies conducted in the United Kingdom and Ireland. [18,19] have indicated traction is still commonly used despite poor evidence for its use and widespread promotion of guidelines. [16,17] Another survey conducted in Canada revealed that 30% of low back patients were treated with traction by the physical therapists. The reason for not using traction was lack of knowledge of the Physical Therapists and limited post graduate training in manual therapy [27]. This survey showed that 98% of the respondents believed that tractions has positive outcome with PIVD patients. This is in agreement with another study revealed that the traction is still commonly used because "it seemed to work clinically," and only 5% of the respondents reported that there is poor quality research in this area. [26] The author has concluded that in Pakistan like other developed countries physical therapists are reluctant to follow guidelines and still using traction despite poor evidence. For Guideline production it is important to consider high quality research which may improve compliance with the Guidelines.

In the treatment of PIVD 71% Physical therapists had used mechanical lumber traction while only 29% used manual traction. This could be explained by the fact that only small number of Physical Therapists are trained to perform manual spinal traction in Pakistan. The author did not collect the data about participants trainings which is an area where physical therapy practice can improve in the future. This is supported by another study in which 79% respondents used mechanical traction and 53% preferred to use manual traction.[26] In this study 92% of the respondents reported they have experience to use traction while 8% reported they had no experience. This is interesting to note that despite having no experience they still preferred to use traction under supervision which shows strong believe in traction use for pain management.

Further 74% Physical therapists gave first preference to traction use for pain relief in sciatica, 15% to decrease size of herniation, 8% to muscle spasm and 4 % gave opinion that lumber traction decrease recurrence of prolapsed disc. This is in agreement with another survey where nerve root pain was treated with traction modality by 77.5% Physical Therapists. [2] Overall 78% (78 out of 100) Physical therapists believed that mechanical lumber traction was time effective. At the first session patient were treated for less than 15mins. A study conducted in the UK reported that on the first session patients were treated for less than 10 minutes with "nerve root" irritation or "pain" whereas 11 to 20 minutes session was applied for stiffness. [26]

This statement is supported by study of Saunders et al,[28] suggested that 8-10 minutes treatment session is required in treating disc protrusion whereas Hickling [29] advocates 20-40 minutes. Both of these authors recommended shorter treatment duration and force in the initial treatment session. Several other studies have suggested that for first traction treatment, or painful conditions, it is recommended to start at less than 50% of the body weight and gradually increase the force over several sessions.[30,31,32] This survey does not explore the time period for subsequent therapy sessions and in future trials this could be explored further. In addition this survey did not include questions about frequency of traction treatments sessions.

Another study explored this further and concluded that patients with "nerve root" pain were likely to receive treatment two or three times per week whereas patients with stiffness and pain were commonly treated 2 time per week. [26] Further, 55% Physical therapists who fully

filled and returned the questionnaire believed that manual lumber traction was cost effective for PIVD treatment as compared to 45% who thought mechanical lumber traction was more cost effective for patient. This could be explained by the fact that mechanical traction machines involved cost and not all smaller scale departments can afford to provide the facility of mechanical traction.

CONCLUSION

The results of this survey showed that Mechanical and Manual traction widely continued to be used in Pakistan despite limited evidence. In addition, the results clarify that majority of physical Therapists believed that traction is an effective treatment technique for lumbar nerve root pain. Furthermore traction was reported to be time and cost effective modality for patients with prolapsed inter-vertebral Disc (PIVD) in lumbar spine.

Limitations of the study: In this survey Physical Therapists of selected departments in Pakistan were included without randomization. This survey was more focused on mechanical and manual traction treatment methods therefore; the results may not be applicable to other countries where various types of traction (auto-traction, positional traction) could be applied. This survey contained only five closed ended questions limited to time and cost effectiveness information gathering along with response the therapist get from traction. However, it does not explore other important parameters such as Respondents profile, traction modalities, patient selection for traction, traction position, frequency traction treatment, selection of traction weights and training of therapists who applied traction. Further studies with inclusion of all these parameters and random sampling with a larger sample size is required in future trials.

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Original Article

Arthroscopy

Correlation of the Findings of Clinical Examination and Arthroscopy of Knee Joint under Local Anesthesia

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ABSTRACT

Objective: To study the correlation of the findings of clinical examination and arthroscopy of knee joint under local anesthesia

Study Design: Descriptive study

Place and Duration of Study: This study was conducted in the Orthopaedic Department, Railway Hospital Islamabad and Ibn e Siena Hospital & Research Institute Multan from March 2008 to March 2010.

Materials and Methods: This study was conducted in 50 patients with some type of problems in the knee since March 2008 to March 2010. 40 (80%) patients were diagnosed clinically, but clinically diagnosis was totally correct in 25 (50%) patients while 15 (30%) patients had additional arthroscopic findings besides those diagnosed clinically.

Results: With the help of arthroscopy the diagnosis was improved to 94% that is near the international study of 90%. The clinical diagnosis was entirely incorrect in 7 (14%) cases. In these cases the clinical diagnosis was wrong but correct diagnosis was apparent at arthroscopy. So arthroscopy should be considered as a diagnostic aid to use in conjunction with a good history, complete physical examination and appropriate roentgenograms. A high degree of accuracy combined with low morbidity, has encouraged the use of arthroscopy to assist in diagnosis, to determine prognosis and to provide treatment.

Conclusion: Arthroscopy under local anesthesia is highly economical, having good patient's acceptability and can be performed as a day case procedure. Meanwhile it is reliable, safe and well-tolerated alternative to conventional techniques to improve the diagnostic accuracy.

Key Words: Arthroscopy, Knee Joint, Anesthesia, Local

INTRODUCTION

The knee is one of the most commonly injured joint because of its anatomic structure, its exposure to external forces and its functional demands.[1] The use of an optical instrument as a diagnostic aid came later in orthopaedic discipline as compared to other discipline such as Eye, ENT, Urology and Gynecology. Endoscopy was first introduced in orthopaedic surgery in japan and it became possible to examine cadaver knee with optical instrument.[2] Arthroscopy did not come in practical usage in western world until 1970. As the first half of the seventh decade past, it became apparent that arthroscopy has been accepted as a valuable aid in the diagnosis and treatment of knee derangement. It has become a routine procedure in many centers of the world to evaluate and treat the knee problems.[3] It is well established that arthroscopy provide useful information in chronic knee problems in which diagnosis and treatment is in doubt.[4]

The diagnosis of lesions of the knee joint has been based largely on recognition of the typical history and findings on the clinical examination. One of the causes of difficulty in diagnosing lesions of the knee joint lies in the fact that different lesions can produce identical findings and standard roentgenograms are non-diagnostic. Even at arthrotomy, it can be difficult to be certain that all etiological causes are being properly visualized. For these reasons, diagnostic aid have long been sought and arthrography had been widely used as a mean to improve the diagnostic accuracy.

Arthroscopy in the beginning was added to the diagnostic technique for the evaluation of the knee problems. Improvements in instrumentation and advances in diagnostic techniques acquired simultaneously to make procedures more widely applicable. Arthroscopy does not decrease the importance of a thorough history and careful physical examination nor does it replace the need for sound clinical judgment.

Every patient must have clinical evaluation before any invasive procedure is performed. Such evaluation must include a thorough history, complete physical examination, appropriate laboratory studies and roentgengraphic studies. When thorough arthroscopic examination is done to establish diagnosis, it substantially reduces hospitalization, post-operative morbidity and inflammatory response and provides improved follow up evaluation.[5]

The conventional way of arthroscopy of knee for diagnostic and surgical purposes is performed either under general anesthesia, spinal or epidural anesthesia.

For simple diagnostic arthroscopy, one had to admit the patient, carry out all investigations and needs the anesthetist and main operation table. Patients with knee problem had to wait long as more serious patients took most of the operating time. Now we are accommodating more patients than we use to do in previous years. Patients usually walk the theatre from preoperative room and after procedure walk out without going to the recovery room. Only few surgeons have reported the use of local anesthesia for arthroscopy.[6]

Diagnostic arthroscopy can be performed safely and reliably as an outpatient or day case procedure if the surgeon is experienced.[7] Even in the best hands, the accuracy of the knee examination is 71% but by the diagnostic arthroscopy accuracy increase to 97%.[8] This study will act as an improved guideline for the arthroscopy of knee joint along with comparative analysis with other studies and its correlation with clinical examination.

MATERIALS AND METHODS

This study was conducted in the Orthopaedic Department, Railway Hospital Islamabad and Ibn e Siena Hospital & Research Institute Multan, from March 2008 to March 2010. A total number of 50 patients with age between 15 to 60 years were included in the study. Patients having medical problems and those who did not gave consent of arthroscopy were excluded from the study. Their history was taken & examination was done to make provisional diagnosis which was confirmed arthroscopically.

The arthroscopy of all 50 patients was performed under local anesthesia without tourniquet as an outpatient procedure. All the patients were evaluated thoroughly by history, clinical examination and radiographically. Routine investigations like plane x-ray knee joint and blood complete with ESR, pre-anesthetic assessment and consent of the patient were obtained. The duration of arthroscopy was one to one and half hours.

The 20ml mixture of 2% lidocaine and 0.5% bupivacaine with ratio of 1:1 was used. 10ml of mixture was injected intra-articularly, 4ml into antero-lateral portal, 4ml into the antero-medial portal and the remaining 2ml into the supero-lateral portal for irrigation needle.

All operations were carried out under prophylactic antibiotics. First generation cephalosporin 1gm intra-venously was used per-operatively and was followed by 500mg TDS orally for four days and oral diclofenac 50mg TDS was used for pain relief. The patient was advised to have complete rest for at least 24 hours. Early static quadriceps exercise were started and stitches were removed on 12 to 14th postoperative day.

RESULTS

Our study included 50 patients having some sort of knee problems. Each patient had clinical diagnosis on the basis of sufficient signs and symptoms before the arthroscopy was done.

The patients included in the study had age ranging between 15 to 60 years (average 35.5 years) and having no significant medical problems like chronic cardiovascular or respiratory disease. Male patients were 41 (82%) and female patients were 9 (18%). Male to female ratio was being 4:1. In 25 patients (50%) right knee was involved while in another 25 patients (50%) left knee was involved. (Table No.1)

The mechanism of injury in most of the cases was trauma (26 patients) including road traffic accident, twisting sport injury or fall on the ground. In our study of 50 cases, 24 patients had no history of trauma. 11 patients gave history of fall, 11 patients had history of twisting injury, 3 patients had blunt trauma while 1 patient had valgus strain. (Table No. 1)

Out of 50 patients, 39 patients were having pain and swelling of the knee and difficulty in walking. Swelling was mild in 17, moderate in 9 and severe in 3 patients. 7 patients had instability or giving way of the knee joint. 10 patients had history of locking of knee joint. History of fever associated with knee symptoms was present in 7 patients. Gait was normal in 27 patients, limping in 22 and one patient was unable to walk. Quadriceps atrophy was present in 43 patients. (Table No. 2)

Abduction or valgus stress test was positive in 3 and adduction or varus stress test positive was positive in 2 cases. Anterior drawer's test was positive in 6 cases. Pivot shift phenomenon was positive in 3 and jerk test was positive in 2 cases. McMurray test was positive in 18 cases (6 on medial rotation of foot and 12 on lateral rotation of foot). Appley's grinding test was positive in 13 cases and apprehension test was negative in all the patients. (Table No. 3)

Clinical diagnosis was based on history and thorough physical examination and then evaluated radiographically. Clinically 11 patients were found to have lateral meniscus tear or degeneration and 13 had medial meniscus tear or degeneration. Anterior cruciate ligament tear in 5, non-specific synovitis in 15, osteoarthritis in 15 cases were diagnosed. 4 patients were having established acute pyogenic arthritis that we had to lavage and biopsied in emergency. Radiological examination was normal in 38 patients. Osteoarthritic changes were seen in nine, soft tissue swelling in one, old chip fracture of lower pole of patella in one and haziness of the knee joint in one patient.

On arthroscopic examination, 8 patients were shown to have lateral meniscus tear or degeneration showing the accuracy of Mcmurrary's test on medial rotation of foot to be 75% and 20 patients were seen to have medial meniscus tear or degeneration with accuracy of Mcmurray's test on lateral rotation of the foot to be 60%. (Table No. 3)

In 4 patients there was complete tear of anterior cruciate ligament while in one patient there was partial tear showing the accuracy of Anterior Drawer's test to be 82%. No posterior cruciate ligament tear was seen. (Table No. 3)

There was roughening of the articular cartilage of lateral and medial femoral and tibial condyles having degenerative joint changes in 19 cases and in 10 cases patello-femoral joint was involved.

Non-specific synovitis was seen in 20 cases and was confirmed later on histopathologically on arthroscopic biopsy. One patient not diagnosed clinically was seen to have villonoduler synovitis and was confirmed on histopathological examination of the biopsy specimen. Chondrmalacia patellae was seen in 2 cases.

Table No 1. The characteristics of patients with knee problems

Characteristics		No. of Patients (%)
Age	15 – 30 yrs	22 (44%)
	31 – 45 yrs	18 (36%)
	46 – 60 yrs	10 (20%)
Gender	Male	41 (82%)
	Female	09 (18%)
Side Involved	Right	25 (50%)
	Left	25 (50%)
Mechanism of Injury	Twisted Injury	11 (22%)
	Blunt Trauma	03 (06%)
	Valgus	01 (02%)
	Fall on ground	11 (22%)

Table No 2: Associated signs & symptoms of patients with knee problems

Clinical Signs & Symptoms		No. of Patients (%)
Swelling	Mild	17 (34%)
	Moderate	09 (18%)
	Severe	03 (06%)
Instability		07 (14%)
Locking		10 (20%)
Crepitation		15 (30%)
Fever		07 (14%)
Other Joint Involvement		01 (02%)
Limping Gait		22 (44%)
Quadriceps atrophy		43 (86%)

One patient was having discoid lateral meniscus and one other patient was suspected of having medial meniscus tear on arthroscopy but could not be confirmed. Two cases, one suspected of medial meniscus tear and another of having intra-articular loose body was shown on arthroscopy to be the normal knee joints.

Clinical versus arthroscopic diagnosis was correct in 25 cases and incomplete or with additional arthroscopic findings in 15 cases. So the accuracy of clinical diagnosis that was judged by arthroscopic findings and histopathology reports was up to 80%. Diagnosis was totally incorrect in 7 patients and in only 3 cases the interpretational of arthroscopic examination was nonconclusive. So the accuracy of our arthroscopic diagnosis was up to 94%. (Table No. 4).

Table No 3: Percentage accuracy of the clinical tests in knee examination

Clinical Tests		No. of Patients
Stress Test		
	Clinically Positive Test	05
	Arthroscopically Collateral Ligament Tear	03
	Percentage Accuracy	60%
Anterior Drawer Test		
	Clinically Positive Test	06
	Arthroscopically ACL Tear (Complete)	04
	Arthroscopically ACL Tear (Partial)	01
	Percentage Accuracy	83%
McMurray Test		
	Clinically Positive Test on Medial Rotation of Foot	06
	Arthroscopically Lateral Meniscus Tear	08
	Percentage Accuracy	75%
	Clinically Positive Test on Lateral Rotation of Foot	12
	Arthroscopically Medial Meniscus Tear	20
	Percentage Accuracy	60%
	Aggregate Percentage	67.5%

Table No 4: Correlation of the clinical and arthroscopic diagnosis of knee

	No. of Patients
Correct Diagnosis	25
Incomplete Diagnosis	15
Incorrect Diagnosis	07
Suspected Arthroscopic Diagnosis	03
Correct Clinical Diagnosis	80%
Correct Arthroscopic Diagnosis	94%

DISCUSSION

This study was conducted on patients having knee problems. Out of 50 patients, youngest patient was 15 years old with synovitis of the supra-patellar pouch of left knee joint while the oldest patient was 60 years old having tuberculous synovitis with secondary osteoarthritis of left knee joint. Maximum number of patients belong to the age group was between 21 to 30 years.

Above 40 years, the incidence of the traumatic knee problems due to road traffic accident or sport injury falls. These patients mostly presents as cases of

osteoarthritis of the knee secondary to old untreated or improperly treated knee derangements. It is only in the late teen that some youngsters present with sign and symptoms of knee problems especially after some sports injury.

In fact there is no age group in which arthroscopy of the knee joint has no place. Thus in our study of 50 cases with age of the patients ranges from 15 to 60 years, with mean age of 35.52 years and the peak age of 21 to 30 years. Male to female ratio was about 4:1. In our society there is less exposure of ladies to traffic, industrial, sports and other type of hazards because most of the time our women stay at home and perform domestic work as compared to western women life style.

In our study of 50 cases, 22 patients gave history of trauma to knee joint after fall in road traffic accident or during sports injury, 3 patient sustained blunt trauma to the knee joint while 1 patient had valgus strain of the knee joint while walking. Over all in our study, the incidence of trauma related to knee problems as compare to western countries was quite low. The reason was that a wide variety of conditions effecting the synovium, such as tuberculous synovitis, synovial chondromatosis, and pigmented villonodular synovitis rarely presents with any history of trauma. It was only in the younger patients with torn menisci, cruciate ligament insufficiency, chondral fracture who gave history of preceding trauma in almost all the cases. Older patients with a long history of knee problem may or may not remember the incidence of trauma as the initiating cause of their problem. In 40 out of 50 cases there was full positive correlation between the clinical diagnosis and findings at the arthroscopy. In other words the clinical diagnosis was correct in about 80% of the cases.

Out of 40 cases in which the clinical diagnosis was correct, in 25 cases arthroscopy served to confirm the diagnosis but did not directly influence surgical management. In 15 cases the clinical diagnosis was incomplete and the additional diagnosis was made with the help of arthroscopy.

It is a clinical practice to diagnose a single condition which gives most striking features while knee may have other lesions masked by sign and symptoms of a one. For example one case diagnosed clinically as anterior cruciate ligament deficiency, was subjected to diagnostic arthroscopy. Arthroscopic examination revealed, besides a tear of the anterior cruciate ligament, a lateral ligament injury. In one patient with a palpable intra-articular loose body in the supra-patellar pouch, when examined arthroscopically revealed multiple loose bodies in the joint and were removed by mini arthrotomy. Diagnostic arthroscopy improved the clinical diagnosis in these cases and as a result a better planning could be made for arthrotomy incision.

The clinical diagnosis was entirely incorrect in 7 cases. In these cases the clinical diagnosis was wrong, but the correct diagnosis was apparent at arthroscopy. In 3 cases, the arthroscopic examination was non-conclusive. In one case due to mild intra-articular bleeding, structures could not be visualized in spite of joint lavage. Arthroscopic biopsy was taken which showed traumatic synovitis on histological examination. In another case, there was slight discoloration of the femoral condoyle but diagnosis was doubtful. Another patient had suspected medial meniscus tear on arthroscopy but the result was not conclusive. In theses 3 cases, we were unable to diagnose or treat the condition arthroscopically.

Many different techniques of local anesthesia have been described. We have used half the recommended dose of local anesthetics, so that the serum level of lignocaine and bupivacaine remain well below the limit of toxicity.[6]

The problem of poor visibility was controlled with frequent wash out with normal saline. A 23G infusion set needle was used as an irrigation needle so that the joint remains distended and the temponade effect of normal saline prevented the bleeding in the knee. Furthermore the use of adrenaline in lignocaine prevented troublesome bleeding in the knee joint. Arthroscopy under local anesthesia is economical and save manpower and time. It requires no special equipment, per-operative investigations, postoperative care and hospitalization. Meanwhile it is reliable, safe and well-tolerated alternative to conventional techniques.[5]

An arthroscopy routinely is performed like an operation that is to stay in an operating theater under aseptic precautions as we practice during other major surgical procedures. The general anesthesia ensures adequate muscle relaxation so that varus and valgus stress can be applied to the knee during examination without giving the patient discomfort. But during arthroscopy under local anesthesia, all patients may have some discomfort while manipulating the joint. In co-operative patients, local anesthesia can be used.

Proper irrigation with a physiological saline solution is important in order to ensure and unobscure the image. Even minute quantity of blood that could obscure the image should be washed away. The instrument is preferably inserted on the anterolateral side. To make the various structures visible, manipulation is necessary. If the proper instruments are used, the technique of arthroscopy can be learned without too much difficulty but interpretation of the observation requires experience.

In this study of 50 cases, the role of arthroscopy was assessed both in the diagnosis and treatment of these cases in our set up. Arthroscopy is mandatory for accurate and complete diagnosis of the knee joint. In our series of 50 cases, arthroscopy was done for diagnostic purposes. The efficacy and patient

acceptability of arthroscopy of the knee joint under local anesthesia was assessed. The accuracy of arthroscopic diagnosis in our series came to be about 94%, which is little lower than reported in international studies (97% in study of Curran & Woodward and above 90% in study of Oberlander M A, Shalvoy R M, Hughstone J C).[8,9] This is because we have recently established arthroscopy units and our experience is much less than the developed centers of the western world.

The accuracy of clinical diagnosis is 80% less than that of arthroscopic diagnosis. This shows superior role of arthroscopy in the diagnosis of the knee problems.[10] The only difficulty with the use of arthroscope was the high skill of triangulation required in more complicated arthroscopic procedures.[11] This is definitely a matter of experience which comes with regular use of the technique for a long time. We feel therefore that arthroscopy is probably the most normative special examination now available for the diagnosis of the "Knee problem", we would stress that the technique, while relatively simple, requires time and patience to learn.[12,13] Accuracy comes only with experience and the occasional arthroscopies might well become discouraged. For this reason we advocate that the technique must be put into the hands of more individuals in a medical community.

In case of arthroscopy under local anesthesia, the patient was called for arthroscopy on the day of operation and was discharged after the completion of the procedure. The short stay reduced the hospital cost which is beneficial both for the patient and economy of the country. Diagnostic arthroscopy performed on outpatient basis results in rapid turnover of patients. Arthroscopy was found to be associated with low morbidity. Most of the patients after arthroscopy were able to stand and walk on the same night. This is because of smaller incision and less inflammatory response. This result in fast rehabilitation of the patients.[14,15]

Arthroscopy performed under local anesthesia was found to be having good efficacy and patient's acceptability. It is highly economical and safe, saving manpower and time. It requires no special pre-operative investigations, post-operative care and hospitalization.[16]

CONCLUSION

Arthroscopy under local anesthesia is highly economical, having good patient's acceptability and can be performed as a day case procedure. Meanwhile it is reliable, safe and well-tolerated alternative to conventional techniques to improve the diagnostic accuracy.

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Original Article

Bladder Stones

Evaluation of Dietary and Biochemical Risk Factors Involved in the Pathogenesis of Bladder Stones in Children of Below Ten Years Age at Hyderabad Sindh

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ABSTRACT

Background: Bladder stones in children of below ten years age continue as a major pediatric health problem in Hyderabad-Sindh.

Objective: To investigate dietary and metabolic risk factors involved in the pathogenesis of bladder stones in children of below ten years age.

Study Design: Case control study

Place and Duration of Study: This study was conducted at the Biochemistry and Surgery Departments, Isra University, Hyderabad from January 2011 to December 2011.

Materials and Methods: Thirty four children with bladder stones admitted for treatment in the pediatric surgery unit, Liaquat Medical College Hospital Jamshoro during 6 months and 30 normal controls were examined. Information regarding diet and dietary habits of the subjects were obtained through standard questionnaire developed for that purpose. Biochemical aspect of bladder stone disease was studied by measuring creatinine, urea, uric acid, sodium, potassium, calcium, magnesium, phosphate, chloride and bicarbonate levels in serum samples of bladder stone patients and control subjects.

Results: The results of present study show that although, average intake of water and milk by patients and control subjects were comparable, majority (73.5%) of the bladder stone patients admitted to drink water when they felt thirsty, contrary to control subjects who used to take water at regular intervals.

The mean tea intake by bladder stone patients was significantly ($P<0.05$) greater than that of the control subjects. Same was true for the intake of green leafy and seedy vegetables ($P<0.05$).

From the blood parameters measured in bladder stone patients and control subjects, the levels for potassium, magnesium and phosphate were found to be significantly ($P<0.05$) higher in bladder stone patients compared to control subjects, whereas reverse was true for creatinine, chloride and bicarbonate levels.

Conclusion: Children with bladder stones were noted to have serum creatinine levels significantly lower than the control subjects. Their dietary and fluid intake habits were also found to be quite different from that of the control subjects. These observations suggest that malnutrition and poor dietary habits are the major risk factors involved in the pathogenesis of childhood vesicallithiasis at Hyderabad-Sindh.

Key Words: Vesicallithiasis, Bladder stones, Dietary risk factors, Metabolic risk factors

INTRODUCTION

The urinary stones are composed of crystalline constituents and organic matrix.[1,2] Childhood vesicallithiasis is a very common urological finding in Hyderabad (Sindh) and adjoining areas[1-3,16,17]. From antiquity to the early twentieth century American and European children were also prone to develop endemic bladder stones[4,5,16]. However, at the turn of the twentieth century these stones become nihilistic in European children. The disappearance of endemic bladder stones in European children had been linked with improvement in the diet and hygenic conditions of the population[6, 7]. However, this observation lacked biochemical proof of its precise nature. One thing which is quite obvious is that genesis of the endemic bladder stones in children in Pakistan could be prevented if dietary and metabolic causes of their formation are ascertained. Thus by properly addressing the risk factors involved in the causation of endemic bladder stones in children, this disease can also be effectively eradicated from Pakistan.

MATERIALS AND METHODS

Thirty four bladder stone patients (26 males and 8 females) with ages ranging from 1-10 years age and thirty controls (21 males and 9 females) matched for age and gender and with no personal or family history of bladder stones were included in the study, after getting informed consent in Urdu/Sindhi from one of their parents.

The ethical approval of the study was granted by the ethical committee of Isra University. Information regarding diet and dietary habits of bladder stone

patients and control subjects were obtained through standard questionnaire developed for that purpose. Serum creatinine, uric acid and calcium levels were determined by using MERCK micro lab 300LX; Inorganic phosphate and urea levels by Automatic analyzer A25; potassium, sodium, chloride and bicarbonate levels by Electrolyte 4 Analyzer (Nova Biomedical); while magnesium by Perkin Elmer Analyst 700 atomic absorption spectrophotometer.

RESULTS

Table 1 shows comparison of age and weight between children with bladder stones and controls. The age range for both cases and controls were 1-10 years. The mean age for cases (4.48 ± 2.69) and controls (5.23 ± 2.95) were comparable. Similarly no significant difference (P>0.05) was seen in the mean body weights of bladder stone patients and control subjects.

Table No.1: Comparison of age & weight between bladder stone patients and control subjects.

Characteristics	Bladder stone patients (n=34 26 ♂& 8♀	Control subjects (n=30 21 ♂& 9♀	P. Value
	Mean ± S.D	Mean ± S.D	
Age (years)	4.48 ± 2.69	5.23 ± 2.95	0.35
Weight (Kg)	13.23 ± 5.66	15.72 ± 7.04	0.15

Table 2 shows comparison of serum variables between bladder stone patients and controls. Bladder stone patients in comparison to control subjects had significantly higher (P<0.05) serum potassium, magnesium and phosphate levels, whereas reverse was true for serum creatinine, chloride and bicarbonate levels. Interestingly, the mean serum creatinine concentration in bladder stone patients was found to be lower than the lower normal limits for creatinine.

Comparison of socioeconomic status and of average fluid intake between bladder stone patients and control subjects are shown in Tables 3 and 4 respectively. Although, the subjects of the two groups were comparable with respect to socio-economic status, they were considerably different in their dietary and fluid intake habits. Bladder stone patients in comparison to control subjects had high intake of tea, green leafy and seedy vegetable and less intake of animal protein.

Water drinking habits of bladder stone patients and control subjects (Table 5) disclosed that majority (73.5%) of the bladder stone patients admitted that do not drink water at regular intervals, and only take water when they feel thirsty. On the contrary, control subjects used to drink water at regular intervals.

Table No.2: Comparison of serum variables between bladder stone patients and control subjects.

Variables in serum	Bladder stone patients (n=34)	Control subjects (n=30)	P. Value
	Mean ± S.D	Mean ± S.D	
Creatinine (0.7-0.9 mg/dl)	0.59 ± 0.21	0.89 ± 0.38	0.001
Urea (11-36 mg/dl)	24.27 ± 8.44	21.50 ± 5.93	0.07
Uric acid (2-7 mg/dl)	3.21± 0.91	3.74 ± 1.59	0.06
Sodium (135-148 mmol/L)	141.53 ± 5.00	142.37± 5.97	0.28
Potassium (3.5-5.8 mmol/L	5.60 ± 1.40	4.75 ± 1.24	0.006
Calcium (1.2-1.4mmol/L)	1.99 ± 0.36	2.09 ± 0.19	0.08
Magnesium (0.7-1.00 mmol/L)	1.26 ± 0.59	0.89 ± 0.35	0.001
Phosphate (1.16–1.81mmol/L)	1.94 ± 1.20	1.27 ± 0.44	0.02
Chloride (98-105 mmol/L)	100.53 ± 6.02	102.73 ± 4.39	0.05
Bicarbonate (18-25 mmol/L)	18.07 ± 3.25	19.47 ± 2.99	0.04

*P value is calculated by using Students "t" test.
P<0.05 is considered statistically significant

Table No.3: Comparison of socio-economic status between bladder stone patients and control subjects.

Socio-economic	Bladder stone patients (n=34)	Control Subjects (n=30)	P. Value
Poor	31 (91.2%)	27 (90.0%)	0.60
Affordable	03 (8.8%)	03 (10.0%)	

*Chi-square test applied to calculate P. Value

Table No.4: Comparison of average fluid intake between bladder stone patients and control subjects

Fluid intake	Bladder stone patients (n=34)	Control subjects (n=30)	P. Value
	Mean ± S.D	Mean ± S.D	
Average water intake (ml)	590.62± 280.75	648.75 ± 272.21	0.40
Average tea intake (ml)	430.00± 200.34	240.38 ± 142.14	0.05
Average milk intake (ml)	120.59 ± 108.09	123.33 ± 131.78	0.926

*P. Value is calculated by using Students "t" test.

Table No.5: Comparison of frequency of water drinking habits between bladder stone patients and control subjects.

Frequency of water drinking	Bladder stone patients (n=34)	Control subjects (n=30)	*P-value
Regular interval	9 (26.5%)	18 (60%)	0.004
When feel thirsty	25 (73.5%)	12 (40%)	

*Chi-square test applied to calculate P. Value.

DISCUSSION

The majority of the bladder stone patients in present study were males. This observation is in agreement with the published reports for Pakistan and other developing countries where this disease is endemic[8-11]. The examination of various organic and inorganic constituents in serum samples of bladder stone patients and control subjects disclosed that bladder stone patients had significantly higher levels for potassium, magnesium, and phosphate and lower levels for creatinine, chloride and bicarbonate than did the control subjects. The mean values for creatinine in bladder stone patients were even lower than the lower normal limits for creatinine. This suggests that the kidneys of the bladder stone patients are functioning normally and that the only reason for their low levels of creatinine could be their lower muscle mass. This is also supported by the finding that bladder stone patients had lower body weights as compared to control subjects. This situation is closely related to a diet poor in animal protein. However, animal protein deficiency may not be the only dietary risk factor. This is suggested because of the absence of bladder stones in communities living in equally poor economic circumstances and presumably as short of animal protein. Thus, it has been proposed that a diet low in animal protein, calcium and phosphate and high in oxalate is associated with the development of bladder stones in children[12-14].

Present study has demonstrated that increased intake of tea (a rich source of oxalates) during early ages is one of the most important risk factors identified in bladder stone patients. The other variables which differed between cases and controls were drinking water habits of the two groups. Bladder stone patients used to drink water most often when they felt thirsty. On the contrary, control subjects used to take water at regular intervals. This is important for voiding of crystals that form in the urinary system.

Thus, a dietary advice to increase the intake of both animal protein and milk, and decrease the intake of oxalate rich foods including tea along with regular frequent intake of water is hoped to decrease the chances of occurrence as well as recurrence of bladder stones in children in this area.

CONCLUSION

In the light of above discussion, it can be concluded that a dietary advice to increase the intake of milk and animal protein and decrease the intake of tea and seedy and leafy vegetable diet along with regular intake of fluids (to avoid dehydration or over-saturation of urine) might provide a good protection against the bladder stone disease in children in this area.

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CORREGENDUM

Captions of figures of article titled "The Effects of Monosodium Glutamate on the Histology of Fallopian Tube in Female Rats" published in Med Forum Volume 25 No.1, January 2014 at Pages 76-79 have been printed wrongly due to typographical mistake which may be read as under:-

Figure No. 1: Micrograph of cross section of fallopian tubes of control group (Group A) Hematoxylin & Eosin staining. (Magnification at x400).

Figure No. 2: Micrograph shows the cross section of the fallopian tubes of treatment group (Group B) that received 1.5mg/kg Hematoxylin & Eosin staining. (Magnification at x400). Atrophic and degenerative changes, cellular hypertrophy and cellular vacuolation are visible.

Figure No. 3: Micrograph shows the cross section of the fallopian tubes of treatment group (Group C) that received 3mg/kg Hematoxylin & Eosin staining. (Magnification at x400). Atrophic and degenerative changes, cellular hypertrophy and cellular vacuolation seen. Lysed red blood cells are visible

Editor