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Editorial

Adulterated Milk: Increases Susceptibility to Disease

Mohsin Masud Jan

Editor

Milk, one the most nutritious of human food, is being converted into injurious substance through different types of adulteration, making the consumers vulnerable to cancer, kidney failures, abnormal growth and diseases of joints and high blood pressure.

Pakistan produces 41 billion litres of milk annually and is ranked fourth largest global milk producer after India, United States and China. Only six percent of this milk is processed by documented producers and around 10 percent is sold after pasteurisation by non-documented producers. The rest is distributed by milkmen that bring it from far way places to the urban centres.

Since milk has a shelf life of less than six hours, it has to be preserved, while transporting it to the cities.

Its shelf life could be increased through pasteurisation to 72 hours or through ultra heat treatment to three months. The ordinary milkmen do not pass the milk through these processes and as an alternative add chemical preservatives such as penicillin, streptopenicillin, formaldehyde, hydrogen peroxide, sodium bi-carbonate, urea, hair removing chemicals, etc to prolong its shelf life.

All these adulterants have severe health implications on the consumers. The oldest and simplest method of adulterating milk is by dilution with water. If the water used is pure it does no harm other than to defraud the consumer but if it is impure, as it often is when drawn from wells near manure heaps, in barnyards, or country privies, it may prove fatal.

The adulterants / preservatives assume the proportion of health hazards for end consumers, particularly infants, the experts said, adding that formaldehyde is the substance most commonly used for preserving milk and is rarely, if ever, added to any other food. Its use is inexcusable and especially objectionable in milk served to infants and invalids.

District administrations across the country are aware of the malpractice in milk sales. In all the cities, the period samples taken by them reveal adulteration of injurious substances but have been unable to eliminate or reduce

this menace. Abnormal growth, nervous disorder in babies, diseases of joints, kidneys and high blood pressure stem from adulterated milk.

Melamine, in particular in combination with cyanuric acid, causes deposition and precipitation of bi-refrangent (double refraction) crystals, thereby causing renal failure.

In cases where antibiotics or formalin are used to preserve milk it would not be possible to break the milk in to curd by adding lemon juice or a spoon of curd.

A more dangerous trend developed in recent years among the dairy farmers is to inject growth hormone (rBGH) to dairy cows or buffaloes to increase milk production.

It has now been established that growth hormones induce prolonged negative energy balance for at least eight weeks during which increased milk production is paralleled by reduced total body fat, excessive tissue loss and hypertrophy of foregut tissue.

The traces of this hormone are found in the milk consumed by human beings, adding that this milk contains higher quantity of fat with long chain fatty acids.

Besides, this milk induces premature growth stimulation in infants, gynecomastia (excessive development of the breasts in males) in young children and breast cancer in women.

This unethical practice should be curbed through stern administrative action.

A worker of a milk processing plant said that when a cream separator at a creamery is cleaned it is often found to contain a residue of manure, hairs, dirt, and perhaps pus and blood from inflamed udders. This speaks volumes about the way we collect and sell milk.

It is a general perception that officials from the police and civic bodies collect bribes from dairies and adulterators and allow the racket to continue.

Milk is a complete food, readily digested and absorbed. It is a sole natural food for infants for the first few months of life and is chiefly valuable as a source of good quality nutrients.

Evaluation of Naked Eye Single Tube Red Cell Osmotic Fragility Test for Screening of Beta Thalassemia Trait

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ABSTRACT

Objective: The study aimed to evaluate the validity and significance of Naked Eye Single Tube Red cell Osmotic Fragility Test (NESTROFT) for screening of beta thalassemia trait (BTT) to reduce the incidence of birth of thalassemic child in community.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at Diagnostic and Research Lab in Pathology Department of Peoples University of Medical Health Sciences (PUMHSW) at Shaheed Benazirabad from January 2013 to December, 2013.

Materials and Methods: Total 504 subjects comprising 303 (60.3%) females and 201(39.7%) males with age ranging between 5 and 48 years and male to female ratio 1:1.5 were selected for this study. The family history of thalassemia and history of cousin marriages were noted. EDTA anti-coagulated whole blood samples were collected for on-site NESTROFT testing, and later tested for Complete Blood Count (CBC) and serum Ferritin concentration at Diagnostic and Research Laboratory of Pathology Deptt. PUMHS. Screening for BTT was done on Naked Eye Single Tube Red cell Osmotic Fragility Test (NESTROFT) with 0.36% freshly prepared saline. The diagnosis of BTT was confirmed on automated Hemoglobin Electrophoresis at cellulose acetate alkaline pH. Red cell indices (automated Hematology cell counter cell-tac alpha) were assessed along with peripheral smear morphology (Leishman's stained slides) as enhanced tool for BTT case finding.

Results: Out of total 504 subjects 201 married women and 101 married men with their mean age (26.5 ± 21.5) years were selected. In this study, female to male ratio was 1.5:1 and among the total 302 married subjects, ratio of cousin marriages (60.4%) was noted. Neither any women were pregnant nor there was history of thalassemia in their families. The laboratory parameters such as the mean values of hemoglobin g/dl, RBC count millions/cmm, PCV %, MCV fl, MCH pg, MCHC g/dl among these subjects respectively were 11.9 g/dl, 4.5 millions/cmm, 82 fl, 38.7%, 26.9 pg, 33.2 g/dl. Out of 504 samples, NESTROFT was positive in 21 (4.1%) and negative in 483 (95.9%). Out of all NESTROFT positive cases 15 (71.4%) were true positive confirmed on the hemoglobin electrophoresis with increased hemoglobin A2 level above 3.5 and remaining 6(28.6%) were false positive. Only 4 (1%) cases were false negative, then sensitivity, specificity, positive and negative predictive values and efficiency of NESTROFT were calculated 87%, 86%, 71%, 99% and 99.9 respectively.

Conclusion: The NESTROFT is a valuable, cost effective screening test for beta thalassemia trait.

Key Words: Beta thalassemia trait (BTT), Naked eye single tube red cell osmotic fragility test (Nestroft), Screening.

INTRODUCTION

The two types of thalassemia such as alpha and beta are autosomal recessive disorder of hemoglobin molecule caused by genetic defects like mutation or deletion leading to either complete lack of or decrease synthesis of either beta or alpha chains, if affected individuals carries abnormal beta gene from both parents they are called homozygous while individuals carrying abnormal beta gene from their mother or father they are called heterozygous carriers¹. The patients with beta thalassemia major or homozygous state present with severe type of anemia that appear at 06 month of age when fetal hemoglobin changes into the adult hemoglobin, hepatosplenomegaly, bone deformities while the patients with beta thalassemia minor or

heterozygous carriers are asymptomatic and the diagnosis depends upon estimation of hemoglobin, red blood cell indices, examination of peripheral blood and bone marrow smears and detection of adult hemoglobin, hemoglobin A2 as well as fetal hemoglobin by hemoglobin electrophoresis². The expenses of treatment of beta thalassemia major are quite high amounting \$2100 or 100000 per year for one thalassemic child involving regular blood transfusion to correct anemia, iron chelation therapy to prevent iron overloading of vital organs and endocrine glands, splenectomy to reduce need of blood transfusion, bone marrow transplantation, gene therapy, recent advanced chemotherapy. As the monitoring & treatment of this disorder is expensive, it puts a socioeconomic burden on the families and ultimately on the state, therefore

when planning health facilities it is preferably needed to prevent the thalassaemia in developing countries like Pakistan and India rather than to treat³. The prevention of thalassaemia include awareness about the thalassaemia, education, premarital screening and genetic counseling, prenatal diagnosis, mass screening of population in rural areas of resources limited countries have great importance in highly prevalent regions including Greece, Italy, Saudi Arabia and Turkey⁴. For mass screening of beta thalassaemia trait in our rural areas of resource limited country, a valid and effective test is needed such as naked eye red cell osmotic fragility test (NESTROFT) initially described by Kattamis et al and this test is inexpensive, requires a small amount of blood, does not require sophisticated equipment as compared to the expensive, time consuming and difficult laboratory technique for the detection of beta thalassaemia trait not suitable for rural areas⁵. The diagnosis of beta thalassaemia is important not only for screening of beta thalassaemia major but it could be differentiated from iron deficiency anemia to prevent iron loading by giving iron supplementation in the beta thalassaemia trait, the useful laboratory test that differentiate the BTT from iron deficiency anemia are estimation of the hemoglobin concentration, RBC count and mean corpuscular volume along with hemoglobin A2 and serum ferritin levels and also NESTROFT could be used to differentiate these two types⁶ due to the cousin marriages in our country, the couples refuse to testing for the screening of beta thalassaemia during pregnancy because of danger of occurrence of beta thalassaemia major in their coming children due to the un-education and un-awareness, hence premarital screening is important among the couples who are planning to marriage than the screening of couples during pregnancy. The aim of our study is to evaluate the validity and effectiveness of NESTROFT test among the peoples living in the rural areas of districts Shaheed Benazirabad, Sanghar and Naushero Feroze for the screening of beta thalassaemia in rural setup. We also determine the importance of cousin marriages among the married couples.

MATERIALS AND METHODS

A. Inclusion criteria

1. An analytical and cross sectional study was conducted at diagnostic and research laboratory in pathology department of PUMHS from January 2013 to December 2013 on a samples of 504 subjects coming from rural areas of districts Shaheed Benazirabad and other neighboring districts. Total 504 subjects including 151 married couples and remaining 200 subjects were selected for this study. Out of 504 subjects, 293 were females and 211 were males, hence females to males ratio was 1.4:1 and among the married couples, 81 couples were present with cousin marriages.

2. The awareness regarding the thalassaemia was created by distributing pamphlets to the each people and detailed history was filled by each people about the any family member present with beta thalassaemia major as well as history of cousin marriages and any woman who was pregnant should be noted.

B. Exclusion criteria: The liver diseases, other type of hemoglobinopathies and pregnant women were excluded from this study because of limitation of naked eye single tube red cell osmotic fragility test (Nestroft) in this study.

The Five ml of venous blood was taken from all these subjects, 3 ml of blood out of 5 ml was well mixed in quantity of 1.5 ± 0.2 mg/ml anticoagulant such as Ethylene Diamine Tetracetic acid from these and remaining 2ml blood was allowed to clot in separate tube. All the coagulated and anti coagulated samples of blood were send to the diagnostic and research laboratory in pathology department of PUMHS for the screening of beta thalassaemia trait. The Nestroft was done using 0.36% buffered saline and hematological parameters such as hemoglobin g/dl, RBC indices (PCV, MCV, MCH & MCHC) were analyzed by Nihon kohden, estimation of hemoglobin A2 level in NESTROFT positive cases was carried out by hemoglobin electrophoresis on cellulose acetate membrane using TEB buffer, pH 8.6. Hb A2 estimation was done following elution after electrophoresis on cellulose acetate, TEB buffer, pH 8.9 for this test in these subjects within two hours of collection of anti clotted blood samples. Two to three peripheral blood smears were also made and stained by Leishman's stain in each case. Serum ferritin was done by the principle of microplate immunoenzymometric assay using ACCUBIND ELISA Microwells (Monobind Inc. Product Code: 2825-300) in suspected cases of heterozygous state of beta-thalassaemias from the clotted blood samples. A cut off Hb A2 level of $\geq 3.6\%$ was used for diagnosing thalassaemia trait and serum ferritin level of $<10\mu\text{g/dl}$ was taken as cut off of iron deficiency. The results were analyzed statistically by using SPSS version 16.0.

The NESTROFT was done with freshly prepared 0.36% buffered saline from stock solution that was prepared in the form of 10% buffer saline at pH 7.4 with NaCl 90g, anhydrous Na_2HPO_4 13.65G and NaH_2PO_4 2.43g (can be stored in well stoppered bottle in refrigerator for 6 months). Working buffer was prepared fresh by putting 3.6ml of stock solution for 100 ml buffer (by adding distilled water). For NESTROFT testing, 20uL volume of EDTA anti-coagulated whole blood was pipetted out into a clean glass test tube (10x100mm) containing 4 mL of 0.36% freshly prepared buffered saline solution. Contents of tubes were mixed and left at room temperature for 20 minutes. After mixing again, tubes were read in a standardized light against sharp black lines drawn behind the tube at a standardized distance.

The results were recorded as "Negative" with clearly visible lines and "Positive" when lines were not visible and "Doubtful" when partially visible lines seen. The doubtful cases were also interpreted as positive result. The preliminary NESTROFT test result cards were issued to all participating subjects. Subjects with positive NESTROFT were counseled for follow up confirmation of BTT on Hb Electrophoresis at 8.6 Ph (HbA₂ > 3.5 %).

RESULTS

The socio demographic characteristic of 504 subjects enrolled for study were showed in table 1. The mean age 26.5 ± 21.5 years of these subjects composed of 202 unmarried and 302 /151 married couples including 293 (58.1%) females, 211 (41.9%) males with female to male 1.4:1 ratio was observed. Out of total 151 married couples, 81 couples were consanguineous marriages (53.6%) and 71 couples were non consanguineous.

Table No. 1: The socio demographic characteristic among all the subjects (n=504)

S.No.	Characteristics	Total Subject
1	Mean age	26.5 ± 21.5 years
2	Sex	293 (58.1%)
	Females	211 (41.9%)
	Males	Female to male ratio 1.4:1
3	Marital status	
	Married	302 (59.9%)
	Unmarried	202 (40.1%)
4	Married couple	151 / 302
	Consanguineous	81 / 162 (53.6%)
	Non Consanguineous	70 / 140 (46.4%)
5	Education	
	Illiterate	391 (75.2%)
	Literate	113 (24.8%)
6	Occupation	
	Housewives and Labors	472 (87.8%)
	Government Servants	32 (12.2%)
7	Socio economic status	
	Upper middle class	12 (5.4%)
	Poor and lower middle class	492 (94.6%)

The significance difference of values of hematological parameters such as mean values of hemoglobin g/dl, Red Blood Count millions / cmm, Packed Cell Volume %, Mean Cell Volume fl, Mean Cell Hemoglobin pg, Mean Cell Hemoglobin Concentration g/dl, Red Cell Distribution width %, NESTROFT positivity and microscopic examination of peripheral blood smears revealed a fairly hypochromic microcytic red cell picture with presence of target cells among the 21, 182 subjects with BTT, iron deficiency anemia (IDA)

respectively and normocytic normochromatic picture in 301 subjects with non BTT and Non IDA out of total 504 subjects were showed in table 2. Serum Ferritin level <15ug/dl was taken as cut off for IDA. Ferritin levels were found normal in BTT cases. Peripheral bloods smear morphology in BTT positive case. Out of 504 samples, Nestroft was positive in 21 (4.3%) and negative in 483 (95.70%) samples. Out of all nestroft positive cases 15 (3.3%) were true positive (HbA₂ > 3.5) while remaining 6 were false positive and false negative were observed in 4 (1%) subjects only. Sensitivity 89%, specificity 98%, positive predictive value 71% and negative predictive value 99% while efficiency of test was calculated to be 97.2%.

Table No. 2: Hematological parameters and NESTROFT positivity among the subjects with the BTT and iron deficiency anemia as well as non BTT and non iron deficiency anemia (n=504)

Laboratory parameters	Iron deficiency anemia n=182	Beta Thalassaemia Trait n=21	Non BTT and Non Iron deficiency anemia n=301
Hemoglobin g/dl	10.7 ± 2.6	11.2 ± 2.4	11.9 ± 2.7
PCV %	31.3 ± 8.1	31.1 ± 6.7	35.1 ± 8.5
RBC count million/cmm	4.2 ± 0.3	5.5 ± 0.8	5.5 ± 0.9
MC fl	68.2 ± 7.5	66.3 ± 6.8	82 ± 7.5
MCH pg	22.5 ± 3.1	21.2 ± 2.9	24.3 ± 1.9
MCHC g/dl	29.8 ± 3.4	31.5 ± 3.5	33.8 ± 2.1
RDW %	15.9 ± 2.8	14.1 ± 0.4	14.2 ± 0.3
PBS	Microcytic hypochromic Red Blood Cells (RBC) with presence of target cells.	Microcytic hypochromic Red Blood Cells (RBC) with presence of target cells.	Normocytic normochromic Red Blood Cells
NESTROFT	09 cases (4.9%) positive out of 182 (95.1%) cases	15 cases (71.4%) positive out of 21 cases	Negative in 474 (94%)

Table No. 3: Nestroft result hemoglobin A2 and serum ferritin levels among the subject with BTT and iron deficiency anemia. (n=203)

Types	Nestroft	Hemoglobin A2 %	Serum Ferritin (ug/dl)
BTT	Positive True 15 False 6 Negative True 483 False 4	4.8 ± 1.5 < 3.5	15 ± 2.1
IDA	Positive 9 (4.9%) Negative 173 ()	2.1 ± 0.9	10.2 ± 1.9

< = less than

BTT = Beta Thalassaemia Trait

IDA = Iron Deficiency Anemia

SD=Standard Deviation

Table No.4: Sensitivity, Specificity, positive and negative predictive values and efficiency of nestroft in prediction of BTT.

Sensitivity (%)	Specificity (%)	Positive predictive values (%)	Negative predictive values (%)	Efficiency of test (%)
78.8%	98.3%	71.0%	99.0%	98.9%

DISCUSSION

World Health Organization⁸ reported that thalassaemias were significant health problem throughout the world including Mediterranean countries, Indian sub continent, Middle East and in Pakistan 5 – 8 % prevalent rate of beta thalassaemia trait with 8-10 million carriers as well as 6,000 children's were born each year, the frequency of thalassaemia increased due to the high ratio of cousin marriages. Abdullah⁹ KN, et al reported that risk factors such as poverty, the high ratio of cousin marriages, poor health facilities and lack of education and thalassaemia control program in Pakistan, the frequency of beta thalassaemia was increased, hence bill about thalassaemia control program in our country has been put forward in the national assembly because treatment of thalassaemic child remained source of miseries including socio economic burden on the family and state. Due to the heterogeneity of beta thalassaemia trait because of increased ratio of cousin marriages in Pakistan, therefore prevention of beta thalassaemia major is not difficult task due to the simple, cheap required two rupees per head, easy to perform and adaptable for mass screening, coming close to an ideal screening test called NESTROFT testing in which exposure of RBC with 0.36% saline of subjects of BTT remained sensitive solution and provides accurate results compared to other concentrations of saline, in contrast to difficult laboratory tests that are time consuming and expensive as well as not suitable for mass screening of BTT required for screening as reported by Singh et al¹⁰. Recently published data concludes that NESTROFT can be effectively used as screening marker for detection of 96-100% β -Thalassaemia trait observed by Rakholia et al¹¹ and Mamtani et al¹². According to a recent study conducted at PNS Shifa Hospital, Karachi, Pakistan, NESTROFT had a Positive Predictive Value of 85.38%, Negative Predictive Value of 97.66% and the diagnostic accuracy of NESTROFT was 94.6% correlating to internationally published data and Red Cell Osmotic Fragility Test could be used as a potential screening test for thalassaemia because microcytic red cells in thalassaemia have a low surface area to volume ratio and therefore resist lysis when placed in a hypotonic saline solution reported by Yazdani et al¹³.

Other studies such as Niazi et al¹⁴ and Eijaz et al¹⁵ had proved that useful laboratory tests such as hematological parameters are utilized for the differentiation of beta thalassaemia trait from the iron deficiency anemia and the individuals with Hb A2 >3.5% were labelled beta thalassaemia trait while serum ferritin below 15.0 μ g/l indicated iron deficiency. In our study with ratio of cousin marriage (53.6%), the diagnostic accuracy of Nestroft among the subjects with BTT were proved and sensitivity, specificity, positive and negative predictive values as well as efficiency of NESTROFT were 78.8%, 98.3%, 71.0%, 99.0% and 98.9% respectively. Our study were correlated with International as well as Pakistani study.

CONCLUSION

One tube Osmotic Fragility test is a cost effective and simple test that can be done in the field without any equipment or expertise. It is very sensitive for the screening of Beta thalassaemia carriers. The test has a high negative predictive value and OTOFT negative individuals can safely be declared free of thalassaemia.

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Effects of Electromagnetic Radiations from Cell Phones on the Concentration of Sperm in Albino Rats

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ABSTRACT

Objectives: To observe the changes in the number of sperms in semen in response to exposure to the electromagnetic radiation (EMR) from cell phones.

Study Design: Experimental comparative study.

Place and Duration of Study: The study was conducted in Institute of Basic Medical Sciences (IBMS), Animal house of Dow University of Health Sciences (DUHS) and Dow Diagnostic Research and Reference laboratory, Ojha campus, Karachi from February 2011 to October 2011.

Materials and Methods: Seventy male Albino rats obtained from the animal house of IBMS, DUHS, Karachi, were divided into two main groups. Group A (control) and Group B (exposed), each containing 35 rats. Both groups were subdivided in five subgroups A1, A2, A3, A4, A5 for control group A and B1, B2, B3, B4, B5 for exposed group B, each consisting of 7 rats. The EMR was given by cell phones to exposed group for 3 hours/day and were sacrificed on 30, 50, 70, 90 and 110 days of exposure. Mean values of concentration of sperm in group A were compared with exposed group B. Statistical analysis was performed by SPSS using One Way Analysis Of Variance to find significance among groups. T-test was used to compare mean differences between groups.

Results: The concentration of sperm was found to be significantly decreased in exposed groups.

Conclusion: This study concluded that exposure to EMR from cell phones affects the semen quality by producing significant decrease in concentration of sperm.

Key Words: Cell phones, electromagnetic radiation, male infertility, sperm concentration, neubauer chamber.

INTRODUCTION

Reproduction is necessary for the survival. More than 4.5 million couples experience infertility each year.¹ Currently, there is a great scientific discussion about data suggesting that male fertility is going to decline markedly as a result of modern lifestyle.² Life style risk factors include cigarette smoking, alcohol consumption, chronic stress and nutritional deficiencies. Recent studies suggest, environmental reasons also produce adverse effects on sperm quality, in addition to factors such as occupational exposure to chemicals, heat, radiation and heavy metals.³

Infertility is a major health issue; many couples of reproductive age in human population suffer from this problem. Irrespective of cause of infertility, whether it is primary or secondary, infertile couples suffer from severe psychological as well as emotional stress.⁴ It is therefore, not only a medical problem but also a psychological stress on the relationship of couples. Various psychological consequences of infertility include anxiety, depression and problems in marital relationship.⁵ Parenthood is no doubt one of the most universally accepted aspiration in adulthood. According to the WHO, infertility is to be considered as a public health issue.^{6, 7}

It is a major problem that affects families instead of individual. When considering causes of infertility

approximately half of them involving male partner. When these couples seek options to resolve their problem and do not become successful, suffer from mild to severe depression, anxiety and disappointment. It can be a major crisis in the lives of many couples.⁴

Besides life style, infertility or subfertility is caused by some environmental factors, like smoking that can affect the normal development of gamete and embryo.⁸ Apart from many other causes affecting the fertility, environmental factors like exposure to EMR play a vital role in development of infertility to some extent. Cellular phones give off low levels of radiofrequency (RF) in microwave range in their active mode.⁹

EMR is a self-propagating wave in space or through matter. EMR has an electric and a magnetic field component which oscillate in phase perpendicular to each other and to the direction of energy propagation. EMR is classified into different types according to frequency of wave, (in order of increasing frequency): radio waves, microwaves, infra red radiation, visible light, u v radiation, x- rays and gamma rays have the highest frequency wave. Energy and momentum is carried by EM radiation which can be transferred when it interacts with matter.¹⁰

Behaviour of EM radiation depends on its wavelength. Higher frequencies have shorter wavelength and lower frequencies have longer wave lengths.^{10, 11, 12, 13}

Research on EMR is being conducted worldwide and is continuing to find adverse effects on health.¹⁴

Among different networks linking societies worldwide, cellular phone technology network form a major part of this. Radiofrequency electromagnetic waves have been used for a long time for different types of wireless broadcast like radio and television.¹⁵

Due to advancement in the field of science and technology the chances for Electromagnetic fields (EMFs) exposure are increased. Commonly used appliances like hair dryers, microwaves and vacuum cleaner have been known to produce EMFs and levels are high enough to produce adverse health effects. The laboratory equipment like incubators and centrifuge mostly used in laboratories for processing sperm for assisted reproductive procedures are supposed to produce EMFs that eventually lead to cause adverse effects on sperm.¹⁶

MATERIALS AND METHODS

This experimental comparative study was conducted at the Department of Anatomy, Institute of Basic Medical sciences (IBMS), Animal house of Dow University of Health Sciences (DUHS) and Dow Diagnostic Research and Reference laboratory (DDRL), Ojha campus, Karachi from February 2011 to October 2011.

Seventy adult male albino rats were selected for study. The rats were divided into 2 groups, control group (A) and exposed group (B), each comprising 35 rats. Both the groups were subdivided into five subgroups A1, A2, A3, A4 and A5 (control) and B1, B2, B3, B4 and B5 (exposed) respectively with seven rats in each group. Each subgroup of exposed group "B", was exposed to EMR emitted from conventional GSM (global system for mobile communication) cellular phones (1835 to 1850 MHZ) for 3 hours daily for a period of 30, 50, 70, 90 and 110 days. Each cage was provided with 8 cell phone sets in active silent mode. The small cages which were specially designed to keep 8 sets of cell phones were then placed inside the plastic cages of rats for 3 hours for the purpose of exposure to EMR emitted from cell phones.

After the exposure to EMR from cell phones for 30, 50, 70, 90 and 110 days to the subgroup B1, B2, B3, B4 and B5 respectively, rats were sacrificed. The scrotal sac was exposed and testes along with the spermatic cord were identified. The testes along with epididymis, ductus deferens and blood vessels were excised. Epididymis was cleared from all tissues, tail of epididymis was identified. A small nick was given to cauda epididymis with the help of sharp scalpel and was cut longitudinally and placed in Petri dish containing 5 ml of normal saline. The cut epididymis were left for few minutes in Petri dish so that the sperms from epididymis could swim out of epididymis and collected in saline. The transparent normal saline changed into turbid grayish white color.¹⁷

The number of sperms were counted with the help of Neubauer ruling method.¹⁸ A small drop of fluid from Petri dish was taken with the help of hemoglobin pipette and charged the Neubauer chamber. Out of 9 squares counting was done in large 5 squares. The numbers of sperms were counted in four outer large squares and one large central square at magnification power of 10 under light microscope.

Formula for counting cells in Neubauer chamber:

Ocular counting reticule was used for counting sperm in a specified area. In present study, reticule was placed in eye piece of light microscope. The counting reticule had 20 squares in both axes.¹⁹ Statistical analysis was performed by SPSS version 16 using One Way Analysis Of Variance (ANOVA) to find the significance difference among groups. Independent sample T-test was used to compare the mean differences between the groups. Statistically significant p value of ≤ 0.05 is taken as significant.

RESULTS

Intergroup comparisons were done between subgroups of control Group A and Exposed Group B at different time intervals. Intragroup comparisons were done between subgroups of exposed Group B to evaluate changes in the concentration of sperm after being exposed to EMR from cell phones. The changes in concentration of sperm were measured in million/ml of semen.

Intra group comparisons: Mean $\pm$ SD values of exposed subgroups B1, B2, B3, B4 and B5 were 7.02 ± 0.81 , 5.55 ± 0.57 , 4.52 ± 0.56 , and 4.12 ± 0.52 and 2.92 ± 0.23 million/ml respectively as shown in Table 1.

Table No.1: Mean number of sperm (Neubauer chamber) million/ml $\pm$ S.D in different groups at variable time interval:

Animal Subgroups (n=7)	Control group A (n=35) A1-A5	Exposed Group B (n=35) B1-B5	P- value
30 Days	7.28 ± 0.79	7.02 ± 0.81	0.55
50 Days	7.79 ± 0.63	5.55 ± 0.57	0.000***
70 Days	7.97 ± 0.70	4.52 ± 0.56	0.000***
90 Days	7.84 ± 0.68	4.12 ± 0.52	0.000***
110 Days	7.27 ± 0.65	2.92 ± 0.23	0.000***
Mean $\pm$ S.D	$7.63 \pm .72$	4.83 ± 1.50	0.000***

P Value: ≤ 0.05 = Significant *
 ≤ 0.005 = moderately Significant **
 ≤ 0.0005 = highly Significant ***
 ≥ 0.05 = Insignificant

Statistically significant decrease in concentration of sperm was observed while comparing Group B1 and B2 (P-value 0.000), B2 and B3 (P-value 0.01), B3 and B4

(P-value 0.68), B4 and B5 (P-value 0.004) at C.I of 95% as shown in Table 1.

Intergroup comparisons: When the mean $\pm$ SD values of concentration of sperm in control subgroup was compared with respective exposed subgroup, a highly significant (P-value 0.000) decrease was observed in concentration of sperm in exposed subgroups at C.I of 95% as shown in Table 1.

DISCUSSION

Male reproductive functions recently more focused due to reports and data showing time related decline in semen quality. Retrospective data analysis indicated that there may be decline in sperm count in some part of the world. In occupational studies, only a few types of exposure were found to have an impact on male reproductive function. Lifestyle and general environmental factor might play a crucial role.²⁰

Attention of scientific community and public have been attracted over global decline in semen quality. Numerous studies have been published showing a compromise in sperm quality. The reason for decline in semen quality is possibly due to environmental, nutritional, socioeconomic or other unknown causes.²¹

Present study identified a highly significant reduction in number of sperm in exposed group when compared with controls. Decrease in the number of sperm was more significant in groups exposed to EMR for longer duration. This was also observed in a study by Salama N (2010). In this study 24 rabbits divided into 3 groups, exposed to radiation for 8 hours per day for 12 weeks in specially designed cages. A drop in sperm concentration was noticed at week 6 which was statistically more significant at 8 weeks.²²

Recent studies on human semen by Agarwal A et al (2008) and De luliis GN (2009) demonstrated that there was an increased production of ROS in human semen due to radiation from cell phones. It was suggested that RF-EMW may cause disturbance of ROS metabolism either by causing increase production of ROS or by decreased activity of antioxidant enzymes.^{23, 24}

Specific absorption rate (SAR), is the amount of radiofrequency (RF) energy absorbed from cellular phones into the local tissue. SAR is the most useful quantitative measure for determining exposure from transmitters or source that is kept close to the body. SAR of cell phones is differing from cell phones to cell phones. But it usually ranges from 0.12 to 1.6 watt /kg body weight depending on the model. According to Federal Communication Commission, 1999; the accepted upper limit of SAR in USA is 1.6 watt/kg. The higher the SAR of cell phones the more harmful would be the effects on exposed tissue.^{25, 26} In their studies Erogul O et al (2006), Agarwal et al (2008), Davoudi M

et al (2002) and Kilgallon SJ et al (2005) also suggested that EMW emitted from cell phones can reduce the fertilization capacity of men.^{10, 23, 27, 28}

A review by Deepinder F (2007) also in agreement with current study which demonstrated the type and the degree of adverse effects that have known to be produced due to the EMR emitted from cell phones.²⁵

Several studies with limitations in study design, suggest a possible link between cell phone use and infertility. The current study is in accordance with a study by Lahdetie (1995) found that use of cell phone causes adverse effect on the quality of semen by decreasing sperm counts, mobility, viability and morphology.³

These findings were also observe in a human study by Agarwal A et al (2008), including 361 men attending an infertility clinic indicated that the use of cellular phones has adverse effects on semen quality, resulting in decrease in sperm count, motility, viability and morphology. These four sperm parameters decreased in the population of study who were in habit of using cell phones for long hours. These hazardous effects on semen quality might result in male infertility.²⁹

A study performed by Kilgallon et al (2005) also supported this finding, suggested that cellular phones when stored close to testis had significant negative impact on concentration of sperm as well as on the percentage of motile sperms.²⁸

CONCLUSION

The present study indicated that EMR from cell phones has adverse effects on testes of albino rats. EMR decreases the quality of semen by affecting the concentration of sperm. It is observed that human exposed to EMR might suffer from subfertility or even infertility, depending on the duration of exposure to EMR.

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Protective Effect of Vitamin E (α Tocopherol Acetate) on Diclofenac-Induced Nephrotoxicity in Young Albino Rats

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ABSTRACT

Objective: To determine the preventive role of Vitamin E on renal parenchyma after given of Diclofenac Sodium 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 per day. Group-B received diclofenac sodium 2 mg/kg per day and group-C receives diclofenac sodium 2mg/kg/day dissolved in distilled water with vitamin-E 2 mg/kg/day dissolved in olive oil administered half an hour before the diclofenac sodium by feeding tube per day 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 μ m 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 diclofenac sodium produces changes in kidney, which may be attributed to ischaemia induced by inhibition of prostaglandin synthesis resulting in tubular necrosis in young albino rats simultaneous administration of vitamin-E partially protect the morphological and histological changes induced by diclofenac sodium.

Key Words: Diclofenac sodium, Vitamin-E, Young albino rats, Kidneys.

INTRODUCTION

Diclofenac sodium is a non-steroidal anti-inflammatory drug (NSAID) having analgesic, antipyretic and anti-inflammatory activities¹. Diclofenac Sodium completely absorbed after oral administration reaches a peak concentration in plasma within 2-3 hours after single dose. The elimination half life ($t_{1/2}$) of diclofenac sodium is about 3 times longer in synovial fluid compared to plasma².

The diclofenac sodium is metabolized in the liver by cytochrome P450 isozyme of the CYP2C sub family and undergoes hydroxylation during phase 1 and conjugation with glucuronic acid to form metabolites either as conjugates or sulfates during phase 2. Up to 60-70% of metabolites are excreted in the urine and up to 30% excreted in the bile.

Evidence from clinical and pharmacological studies imply that diclofenac sodium exerts its actions by inhibiting cyclooxygenase (COX) enzyme³.

Diclofenac sodium cause deleterious effects on kidney function, especially with respect to solute homeostasis and maintenance of renal perfusion and glomerular filtration. It acts by reducing prostaglandin biosynthesis through inhibition of cyclooxygenase (COX)⁴.

The scarring of the small blood vessels, called capillary

sclerosis due to ischemia is the initial lesion of analgesic nephropathy⁵. Capillary sclerosis is leads to renal papillary necrosis and in turn, chronic nephritis⁶.

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 major 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 asparagus⁹. 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 diseases¹⁰. 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, Massachusetts, 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 body weight orally once daily for 2 weeks.

Group-B (10 Animals): In this group each animal received diclofenac sodium by feeding tube at a dose of 2 mg/kg/day dissolved in distilled water, once daily for 2 weeks.

Group-C (10 Animals): In this group each animal received diclofenac sodium 2mg/kg/day dissolved in distilled water by feeding tube once daily for 2 weeks. These animals also received vitamin-E (α -tocopherol acetate) 2 mg/kg/day dissolved in olive oil administered half an hour before the diclofenac sodium 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 measured with the 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 brush 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 $50.9 \pm 0.74 \mu\text{m}$, 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 $38.4 \pm 0.37 \mu\text{m}$, 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 brush 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 distal tubules was intact.

In silver methenamine stained sections the 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 $54.3 \pm 0.97 \mu\text{m}$, 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 $54.5 \pm 0.59 \mu\text{m}$, 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 brush 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 tubules.

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 $51.6 \pm 0.90 \mu\text{m}$, 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.

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 $39.8 \pm 0.32 \mu\text{m}$, 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.

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

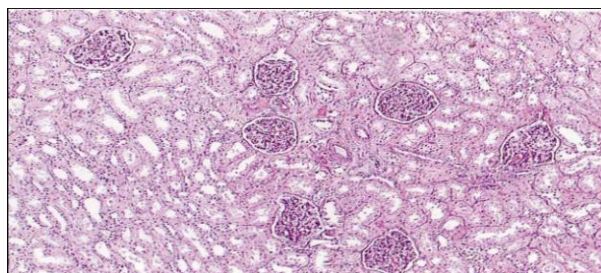
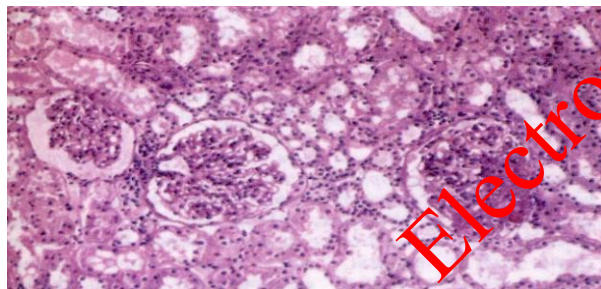
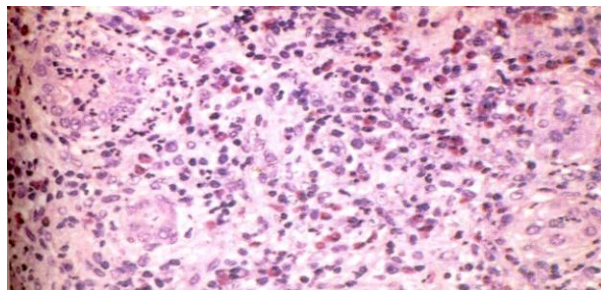
	Group A Controls (n=10)	Group B Diclofenac Sodium (n=10)	P-value
	Mean $\pm$ S.D $\pm$ SEM	Mean $\pm$ S.D $\pm$ SEM	
Proximal Tubular Count per unit area (Under Reticule)	$24.0 \pm 1.56 \pm 0.49$	$16.1 \pm 2.08 \pm 0.66^{**}$	0.001
Mean Diameter of Proximal Tubules (Under Ocular Micrometer)	$50.9 \pm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

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

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

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

**Figure No.1: Photomicrograph of 5 μ m 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 μ m thick H&E stained paraffin section of rat kidney from group-B treated with diclofenac sodium, showing dilated blood vessels with marked infiltration of inflammatory cells and damaged tubules. x205.****Figure No.3: Photomicrograph of 5 μ m thick H&E stained paraffin section of rat kidney from group-C treated with diclofenac sodium, and vitamin-E, showing almost normal proximal convoluted tubules (PT) and distal convoluted tubules (DT) x416.**

DISCUSSION

Non-steroidal anti-inflammatory drug (NSAID), are the known nephrotoxic drugs, 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 organs¹¹.

Studies on the diclofenac sodium have shown that prolonged administration of this drug should be considered as a risk for nephrotoxicity¹³. In the present study three groups of animals were used group-A acted as control, group-B received diclofenac sodium while group-C received diclofenac sodium 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 produced by inhibition of prostaglandin in renal arterioles resulting in constriction¹⁴.

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 diameter¹⁵.

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 to focal ischaemic necrosis of some of the tubules resulting in their numbers¹⁶.

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 diameter¹⁶.

CONCLUSION

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

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A Comparative Assessment of Root Canal Preparation, Employing Manual and Rotary Instrumentation Technique - An in Vitro Study

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ABSTRACT

Objectives: To determine changes in root canal curvature after preparation with manual or rotary instrumentation technique and to determine maintenance of working length by either manual or rotary instrumentation technique.

Study Design: Experimental study

Place and Duration of Study: This study was carried out at Aga Khan University Hospital over a period of six months.

Materials and Methods: Mandibular molars, extracted due to caries or periodontal reasons and mesiobuccal canals, with curvature between 20- 40° were included. In Group A preparation was carried out with ProTaper instruments and in group B with manual NiTi files. An ISO #15 NiTi file was placed in the canal and radiograph taken to determine working length, radiograph was scanned, print made and canal curvature determined. Upon completion of preparation, radiograph with #30 NiTi file was taken and working length assessed. Same radiograph was scanned, and changes in curvature were assessed by comparing preoperative and postoperative prints. Data analysis was done with SPSS version 14.0 and Paired and Independent sample t tests.

Results: Difference in Pre and Post operative root canal curvature was lower in ProTaper group, but not satisfactorily significant. Working length was better maintained in ProTaper group as compared to group prepared with Manual Ni-Ti instruments.

Conclusion: ProTaper instrumentation technique maintained working length better than manual instrumentation technique. No difference in operative curvature was observed, although difference was smaller in ProTaper group.

Key Words: Pulpotomy, Rotary NiTi, Working length determination, Canal curvature, Apical Preparation.

INTRODUCTION

Root canal preparation of curved root canals is associated with many procedural difficulties such as maintaining the shape of the curved canals. Instrumentation of curved canals is very difficult because conventional instruments are stiff and result in straightening of the canal which is associated with ledges, perforations, zips and elbows.^{1,2} In order to eliminate some of the short comings of these traditional endodontic instruments, nickel titanium instruments have been developed.

Purpose of root canal filing is the achievement of a conical configuration, allowing a more effective filling and establishment of accurate length of the tooth during root canal treatment.³⁻⁶

Traditional stainless steel instruments, when used in severely curved canals, often fail to achieve the tapered root canal shape.^{1,7,8} Enlargement of curved root canals with stainless steel (SS) files may result in instrumentation accidents.⁹

Nickel Titanium (NiTi) endodontic instruments have been shown to be more flexible than stainless steel instruments. NiTi-alloy has several advantages over stainless steel such as greater flexibility, shape memory effect and a better resistance to torsional fracture, the elastic limit for NiTi files has been shown to be two to three times that of stainless steel.¹⁰

During the last decade, several new nickel–titanium (Ni–Ti) instruments for rotary endodontic treatment have extended the endodontic armamentarium. Several investigations have shown the ability of some new rotary Ni–Ti systems to maintain the original root canal curvature well.¹¹⁻¹³

The purpose of this study was to determine which instrumentation technique was better in maintaining root canal curvature and working length. Although many reports on root canal preparation can be found in the literature, definitive scientific evidence on the quality and clinical appropriateness of different instruments and techniques remains elusive. To a large extent this is because of methodological problems, making comparisons among different investigations difficult if not impossible.¹⁴ Not many studies have compared manual and rotary instrumentation techniques and the results are still very contradicting regarding choice of the instrumentation technique. In addition, very few studies have been done in developing countries so far, therefore it was important to carry out a study which could help us in determining an instrumentation technique which was more beneficial in achieving the objectives of root canal treatment.

MATERIALS AND METHODS

This In Vitro Quasi experimental study was carried over a period of six months at The Aga Khan University Hospital, Karachi. Total sample size was sixty extracted molar teeth. The inclusion criteria for the study were human mandibular molars, extracted due to caries or periodontal reasons and mesiobuccal canal of mandibular molars, with curvature between 20-40 degrees as measured by Schneider's method.^{15,16}

Teeth with calcified canals, internal or external resorption and with less than 20° curvature or severely curved canals with more than 40° curvature as measured by Schneider's method were excluded from the study. Teeth were randomly distributed into two boxes thirty teeth in each box, labeled 'A' and 'B'. Each group was assigned an instrumentation technique. This was done by a draw performed by a colleague, who was not related to the study. Group A: Prepared with rotary (ProTaper/ Dentsply) instruments. Group B: Prepared with manual instruments (Ni-Ti Files/ Dentsply).

Ethical Clearance: Ethical clearance from University Research Council of The Aga Khan University Hospital was obtained along with grant for conducting this study URC Project ID: 052024SUR.

Access cavities were prepared and occlusal surfaces reduced to solid flat reference points in both the groups. An ISO #15 Ni-Ti file was placed in the canal and radiograph was taken to determine working length 1.0 mm short of the radiographic apex and recorded for each canal. Radiographs were taken with the help of standardized XCP (Henry Schein) in mesiodistal direction using paralleling technique. For preoperative canal curvature assessment the same radiograph with #15 Ni-Ti file in the canal, was scanned and image transferred to computer, the image was magnified ten times (Adobe Photoshop 6.0), a print made and canal curvature measured and determined by Schneider's method. In group A instrumentation with rotary instruments was carried out according to

manufacturer's instructions. In group B instrumentation with manual technique was carried out with NiTi files using step back technique. Upon completion of root canal preparation in both the groups, post interventional radiograph with #30 NiTi master apical file was taken in order to assess changes in working length. The post interventional radiograph was scanned and transferred to computer, the image magnified ten times (Adobe Photoshop 6.0), a print made and canal curvature measured and determined by Schneider's method.

Deviation in canal curvature (degrees) was determined by comparing postoperative curvature measurements with preoperative values and changes in working length (mm) were determined by subtracting the final working length from original working length.

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 14.0. The difference in the pre and post operative readings of canal curvature and working length was compared using Paired samples t-test (within the group comparison) for the two procedures. Independent samples t-test (between the groups comparison) was used to compare the canal curvature and working length in the two groups. A p-value less than 0.05 were taken as statistically significant. Error graphs (Mean with 95% confidence intervals for mean) were also made for type of procedures, pre operative and post operative root canal curvature and working length.

RESULTS

Root Canal Curvature in group A prepared with Rotary instruments was better maintained as compared to group B prepared with Manual instruments (Table 1). No significant difference was also observed between the two groups before procedure for root canal curvature. The average difference of the curvature in pre and post operation was found to be lower among Rotary technique when compared with manual technique (p-value=0.119) (Table 2).

Table No.1: Mean Distribution of Manual and Rotary (ProTaper) Instrumentation Techniques with 95 percent Confidence Interval for the Difference

Manual or Rotary(Protaper)	Pre-operation	Post-operation	95% Confidence Interval for the difference	p-value
	Mean (SD)	Mean (SD)		
Manual Working Length	17.2 (2.07)	16.3 (1.97)	0.9 (0.47, 1.33)	<0.001
Rotary Working Length	16.9 (2.49)	16.6 (2.65)	0.3 (0.02, 0.45)	0.032
Manual Curvature	25.9 (5.35)	21.6 (5.31)	4.3 (3.2, 5.34)	<0.001
Rotary Curvature	26.0 (5.19)	22.9 (4.53)	3.1 (2.04, 4.16)	<0.001

Table No.2: Mean Difference (Pre – Post) Distribution of Manual and Rotary (Protaper) Instrumentation Techniques with 95 percent Confidence Interval for the Difference

Working Length or Curvature	Difference in pre-post Manual	Difference in pre-post Rotary (Protaper)	95% Confidence Interval for the difference	p-value
	Mean (SD)	Mean (SD)		
Working Length	-0.90 (1.15)	-0.23 (0.57)	-0.67 (-1.14, -0.19)	0.007
Curvature	-4.27 (2.86)	-3.10 (2.84)	-1.17 (-2.64, 0.31)	0.119

Working length in group A prepared with Rotary instruments was better maintained as compared to the group B prepared with Manual instrument (Table I). No significant difference was observed between the two groups before procedure for working length. The average difference of the working length in pre and post operation was found to be significantly lower among Rotary technique when compared with manual technique (p -value=0.007) (Table 2).

DISCUSSION

During instrumentation of root canal, development of a continuously tapered form and the maintenance of the original shape and position of the apical foramen are important objectives. Ledge formation, blockages, perforations and apical transportation are undesirable accidents observed following the preparation of curved root canals. Flexible nickel-titanium instruments have been effective in minimizing complications in narrow and curved canals.¹⁷⁻¹⁹ To deal with the complex problem of preparing curved root canals, several instrumentation techniques have been introduced.²⁰

Working length and canal curvature maintenance are two very important objectives to be obtained in root canal therapy by any instrumentation technique; therefore in order to achieve these objectives the author used Nickel Titanium files in both the groups. Several studies²¹⁻²⁶ have been carried out and have shown that that preparation with nickel-titanium files was more effective and produced more appropriate canal shapes than stainless steel files. They found that rotary instruments were able to maintain working length better. They concluded that ProTaper rotary instruments prepared curved root canals effectively and safely were able to maintain working length better than manual instruments ($P < 0.05$),

In developing countries this area of endodontics needs to be evaluated, this system is used widely, there fore we felt a need to conduct a study in order to assess the capabilities of this system in maintaining working length and canal curvature and our results statistically prove that this system maintains working length and canal curvature better than manual Nickel Titanium instruments.

Following are the limitations of our study.

1. Can not generalize the results as they were performed by one operator.
2. Inter examiner reliability cannot be measured, since it was performed by one operator.
3. Bias: Due to single person examination, personal bias might be introduced, although precautions were made.

CONCLUSION

Within the limits of this study, following conclusions were drawn:

- Rotary (ProTaper) instrumentation technique maintained working length better than manual instrumentation technique. On the other hand, no difference in the operative curvature was observed, although the difference was smaller in ProTaper group.
- ProTaper instruments prepared canals in extracted human mandibular molars without obvious procedural errors to a smooth tapered shape of appropriate sizes

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The Use of Vaginal Misoprostol to terminate the Pregnancy in Second Trimester

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ABSTRACT

Objective: To determine the effectiveness of vaginal Misoprostol for the second trimester termination of pregnancy.

Study Design: Prospective randomized trial.

Place & Duration of Study: This study was carried out in the Unit of Post Graduate Medical Institution Peshawar / Lady Reading Hospital Peshawar from 1st January till 31st December 2006.

Materials and Methods: A total of 100 patients were included in this study. Misoprostol 400 microgram, was administered intra-vaginally and repeated after every 4 hours up to a maximum of five doses or until the termination of pregnancy, which ever was earlier. The exclusion criteria were as allergy to prostaglandin, a previous classic caesarean section or Hysterectomy, active vaginal bleeding, severe asthma and epilepsy.

Results: Period of gestation ranged from 12 to 20 weeks. Indications for 2nd trimester termination of pregnancy were chromosomal or structural fetal anomalies (anencephaly) whether dead or alive, missed abortion intrauterine fetal death. Success rate at 48 hours was 90%. The median induction to termination interval was 16 hours. Few women suffered gastrointestinal side effects such as nausea (6%), vomiting (3%) and diarrhea (1%).

Conclusion: 400 Microgram of Vaginal Misoprostol is highly effective way of cervical ripening and termination of second trimester pregnancy.

Key Words: Second trimester termination, Misoprostol.

INTRODUCTION

Misoprostol is being investigated for its role in the management of post partum hemorrhage, induction of labour, cervical ripening and termination of pregnancy. Initially this drug was approved by the US food and Drug Administration (FDA) in 1988 for oral administration for the prevention and treatment of peptic ulcer associated with the use of non-steroidal anti-inflammatory drugs. Since the early 1990s however, Misoprostol has been viewed with increasing interest by obstetricians and gynecologists because of its uterotonic and cervical ripening activity^{1,2}. Prostaglandin analogue is commonly used for termination of pregnancy in the second trimester, as it is cheaper and stable at room temperature. Although it can be used orally but vaginal administration was used in most studies because it has been shown to be more effective^{3,4}. Misoprostol is manufactured as oral tablets of 200 micrograms scored and 100 microgram unscored. It has stability in ambient temperature, long shelf life and low cost and rapidly absorbed via the oral route and although not formulated for parental use, can also be administered sublingually, recently and vaginally. Misoprostol is extensively absorbed and undergone rapid desertification to Misoprostol acid. The objective of this study was to assess the efficacy of 400 microgram Misoprostol intra-vaginally and its side effects.

MATERIALS AND METHODS

This descriptive study was carried out in Gynae – A unit of Postgraduate Medical Institute / Lady Reading

Hospital Peshawar from 1st January 2006 to 31st December 2006. Data was collected on prescribed Proforma regarding maternal age, parity, gestational age, maternal complications and cervical ripening and hospital stay. All the parameters analyzed for descriptive statistical data was calculated on SPSS version 10. A total of 100 women between 12-20 weeks gestation were recruited for this study. Ethical approval for the study was obtained from the hospital institutional review board. An informed written consent was obtained from all patients. All these women were admitted through Out Patient department (OPD). A medical and Gynecological history was taken and the gestational age was determined by menstrual history, pelvic examination and Ultra Sonography report. Blood was taken for measurement of hemoglobin and blood grouping, random blood sugar level a coagulation profile (PT/APTT, FDP) in case of fetal demise. Rhesus negative women were given anti-D immunoglobulin following the treatment prior to discharge from hospital. Misoprostol, 400 mg was administered intravaginal and repeated 4 hourly up to a maximum of 5 doses or until the termination of pregnancy which ever was earlier. The procedure was repeated if the patient failed to abort within 24 hours. Vital signs of the patients including temperature, pulse rate and blood pressure were monitored 4 hourly. Following abortion of the fetus, all patients received 5 units of oxytocin and 0.4mg of ergometrine maleate. The primary outcome measure in the study was the induction to abortion interval. Induction to abortion interval was defined as the duration between initiation of intervention and the

abortion of fetus. The secondary outcome measure were the success rates at 24 hours and 48 hours, the need for repeat course of medications, the need for evacuation of the uterus and adverse effects like nausea, vomiting, fever, diarrhea and shivering. Product of conception was examined and evacuation of the uterus was performed if it was incomplete. The indications for termination of pregnancy in second trimester were chromosomal or structural fetal anomalies (anencephaly), missed abortion and maternal disease. The exclusion criteria were an allergy to prostaglandins, a previous classic caesarean section or hysterectomy, active bleeding. Severe asthma and epilepsy etc.

RESULTS

A total of 100 women with period of gestation ranged from 12-20 weeks. Age of patients was between 20 – 40 years. Primigravidae were 20, hours. The indications for termination of pregnancy in second trimester were chromosomal or structural anomalies (anencephaly) 20% missed absorption 70% and maternal disease 10% (Table). Ten patients failed to abort after 48 hours and they subsequently aborted after receiving extra amniotic PGF2 alpha. The success rate at all 48 hours was 90%. The medium induction to abortion interval was 16 hours. Twenty women and two for retained placentae. Few women suffering gastrointestinal side effects such as nausea (6%), vomiting (3%), and diarrhea (1%) Table 2.

Table No.1: Indications for Termination of Pregnancy

Indications	Percentage
Fetal Anomalies	23 %
Missed Abortion	69 %
Maternal Disease	08 %

Table No.2: Adverse effects of Misoprostol

Adverse Effects	Number
Nausea	6
Vomiting	3
Diarrhea	1

DISCUSSION

Misoprostol has been studied extensively as it is cheap and stable at room temperature. In a study by Wong KS et al. Vaginal Misoprostol 400 micro gram every 3 has achieved a success rate of 90% in 48 hours. The median induction – to – abortion interval was 15.2 hours^(1-4, 17). In a study by Lurie et al. mean induction – to – abortion interval for vaginal Misoprostol was 14 hours. In a comparative study by Oi Shan Tang both vaginal and sublingual groups achieved a success rate of 90% in 48 hours. The median induction-to-abortion interval was comparable for the two routes of administration 10-12 hours. While in our study success rate was over 90% in 48 hours and median induction-to-abortion interval was

16 hours. However, significantly more women aborted in 24 hours. While in a study by Dickinson J. et al. success rate within 24 hours was 76% after administration of 400 mg vaginal Misoprostol and mean induction-to-abortion interval was 18.2 hours⁽¹⁵⁾. A similar study done by Tang OS et al. clinical efficacy of vaginal Misoprostol was also higher in 24 hours^(3,8). However it was observed that the Misoprostol tablets took a long time to dissolve in vagina and achieved a sustained and long lasting effect. Misoprostol in the dose of 400mg every 4 hourly were more effective in terms of a significantly shorter drug administration – to – abortion interval and a higher percentage of successful abortion within 48 hours. The significantly lower cost of vaginal Misoprostol has important financial implications for both the individual and the health care system, and it's of particular relevance to the developing countries. Ferguson et al. reported that the induction-to-abortion intervals correlated inversely with gestational age, whereas Ashok and Templeton suggested longer induction-to- abortion intervals at increased gestation. Our study showed no correlation between gestational age and induction-to-abortion interval^(13,16). Induction for termination of pregnancy in the second trimester includes chromosomal and structural abnormalities. In a study by Lin-lin Su, the induction for termination of pregnancy was fetal anomalies, social reasons, and maternal disease. They account 33.6%, 65.6% and 0.8% of the inductions respectively, while in our study indication for terminations of pregnancy were fetal anomalies (20%) missed abortion (70%) and maternal disease 10%^(1, 2,4). Intravaginal Misoprostol in the dose of 400mg is effective and associated with fewer side effects. Side effects of prostaglandins are mainly due to their effects on smooth muscles and are dose related. Following vaginal administration of Misoprostol, the plasma concentration remains raised for longer but the peak levels are lower after oral administration. In a study by Julia, women reported less nausea, vomiting and diarrhea with the use of vaginal Misoprostol. One limitation of vaginal Misoprostol is the need for repeated 3 hour or 4 hour dosing and the higher likelihood of fever and shivering⁽⁷⁾. In our study 10 patients failed to abort within 48 hours and they subsequently aborted after receiving extra amniotic PGF2 alpha. Twenty women required surgical evacuation of the uterus, eighteen for retained pieces of trophoblastic and two for retained placenta while in study by Julia evacuation was required in 10⁽⁶⁾. Misoprostol has been evaluated in randomized controlled trails (RCTs) in women pre-treated with mifepristone or gemeprost. These studies that a higher dose of Misoprostol and the vaginal route of administration may be associated with higher success rate. A recent RCT of 3 regimens for vaginal Misoprostol which included both dead and live fetuses

concluded that Misoprostol 400mg every 6 hours was the preferred regimens for STPT. The interval of vaginal Misoprostol administration, 6 verses 12 hours, was examined in 2 studies with inconsistent results^(6,7). While in our study Misoprostol 400mg every 4 hourly was associated with higher successful rate and less side effects, like nausea, vomiting and diarrhea.

CONCLUSION

Vaginal Misoprostol is safe and cost effective. It should be the intervention of choice for mid-trimester termination of pregnancy, particularly for multiparous women in the early second trimester.

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Quantitative and Morphometric Study of Adipose Tissue from Abdomen in Adult Women of Hyderabad

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ABSTRACT

Objective: To determine adipocytes count per unit area in the superficial subcutaneous layer of the abdomen of an adult woman.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at Department of Anatomy, Isra University Hospital Hyderabad from July 2011 to December 2011.

Materials and method: 80 adult women including 40 obese and 40 non obese for different abdominal surgeries visited in the Isra university hospital Hyderabad. Superficial subcutaneous layer of the abdominal adipose tissue were obtained during surgery. Tissues were processed for routine H&E staining. After processing, the number of adipocytes was counted through ocular grid microscopy method.

Results: In obese, the mean number of adipocytes was 119.02 ± 5.81 with range of 100-140 and in non-obese, the mean number of adipocytes was 79.02 ± 6.02 with range of 50-98. The result showed a significant ($p < 0.05$) increase number of adipocytes in obese women as compare to non obese women.

Conclusion: From this study it was conclude that in obese women there is increased number of adipocytes as compare to non obese women. As increased number of adipocytes enhance the cardiovascular as well as metabolic diseases and producing fatal health risks. Therefore there is need to elaborate the cause of disorder and its proper diagnosis through counting or assessment of adipocytes which helpful for management of diseases.

Key Words: Adipose tissue, subcutaneous tissue. Abdomen

INTRODUCTION

Adipose tissue is a supporting tissue which is derived from primitive mesenchyme. It is found in clumps throughout the loose supporting tissue. Two type of adipose tissue are present, white adipose tissue and brown adipose tissue¹. Adipose tissue is present below the skin and around the internal organs. It accumulates in the deepest level of skin which provides insulation from heat and cold². Two main compartments of subcutaneous abdominal adipose tissue are present, superficial subcutaneous adipose tissue and deep subcutaneous adipose tissue³. These compartments are anatomically and morphologically are different. Fat in different parts of the body grows differently, and despite the prevailing belief that the number of fat cell in the body remain constant in an adult study that found the number of fat cells in the lower body actually increases with weight gain, while weight gain in the abdomen causes to fat cells grow in size⁴. The total number of fat cells and the size of the fat cells are the components determining total fat mass accumulated in adipose tissue. In lean and obese individuals the number of adipocytes is set during childhood and adolescence. The number of adipocytes shows little variation during adulthood, but annually 10% of the fat cells are renewed⁵. In order to study and examine the clinical relationship of common metabolic factors

related to obesity, the fat cell size and fat cell number is important and these factors are related to obesity⁶. Since at present no baseline data in the population of our region (sindh) with unique metabolic demography is available. Hence the attempt is to be made to count the number of cells per unit area in adipose tissue from abdomen in adult women, i.e of subcutaneous tissue of both obese and non obese women for comparison and measurement of disease.

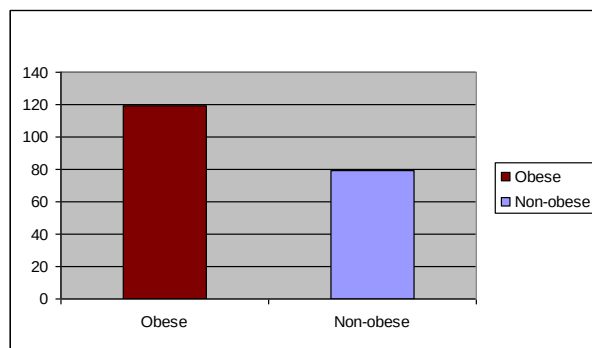
MATERIALS AND METHODS

This cross sectional study was conducted at department of Anatomy, Isra University Hospital Hyderabad. Practical laboratory work was carried out in postgraduate Laboratory Isra University Hospital. 80 adult women including 40 obese and 40 non obese presented for different surgeries. Superficial subcutaneous layer of the abdominal adipose tissue were obtained during surgery. Tissue was processed for routine H&E staining. After processing, counting the number of cells per unit area was carried out through ocular grid microscopy method. Data was analyzed by using SPSS version 16.0.

RESULTS

In Obese, the mean number of adipocytes was 119.02 ± 5.81 with range of 100-140 and in non-obese,

the mean number of adipocytes was 79.02 ± 6.02 with range of 50-98. The mean of number of adipocytes of obese and non- obese is shown in Graph 1. When we correlate the value of number of adipocytes per unit area the (P value <0.05) was found significant .



Graph No. 1. Comparison of Number of Adipocytes in Obese and Non-obese Patients

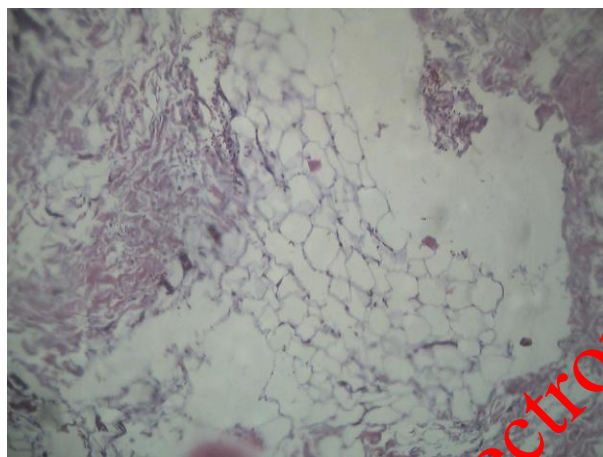


Figure No. 1: Photomicrograph of 4μm thick H & E stained section of superficial layer of subcutaneous layer of adipose tissue from abdomen in non obese showing decrease number of adipocytes at power X 100.

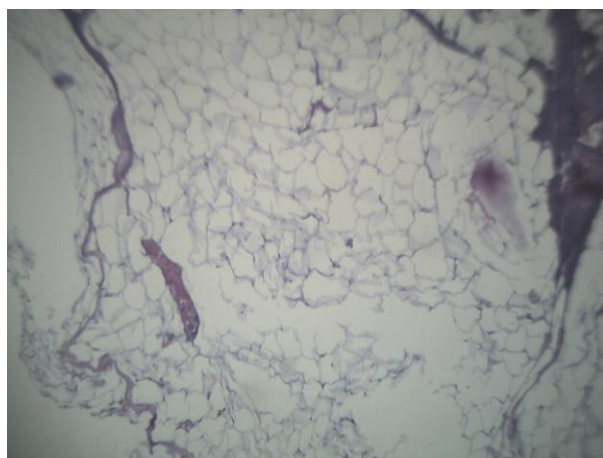


Figure No. 2: Photomicrograph of 4μm thick H & E stained section of superficial layer of subcutaneous layer of adipose tissue from abdomen of obese showing increase number of adipocytes at power X 100.

Superficial layer of subcutaneous layer of adipose tissue from abdomen in non obese showing decrease number of adipocytes Figure 1, while there was increased number of adipocytes observed in superficial layer of subcutaneous layer of adipose tissue from abdomen of obese women Figure 2. These findings correlate the differences between obese and non obese women.

DISCUSSION

The association of adipocytes size and number regulated by factors independent of variations in body fat distribution. Mean adipocyte size and number of adipocytes has been positively correlated with normal and obese adults 7. The study of Lester B et al 8 said that cell number is greatest with omental cell size (in non obese was $23-65 \times 10^9$ and in obese was $37-237 \times 10^9$) and smallest with gluteal (in non obese was $20 - 41 \times 10^9$ and in obese was $28 - 128 \times 10^9$) but in our study we only compared superficial subcutaneous layer of abdomen in obese and non obese. So our results show the mean of number of adipocytes was 119.02 ± 5.81 in obese but the mean of number of adipocytes was 79.02 ± 6.02 . Also Yourka D et al 9 reported that mean number of subcutaneous abdominal adipocytes in non obese was 11.6 ± 5.5 and in obese was 15.7 ± 4.4 as our study also in agreement with such study shows the mean number of subcutaneous abdominal adipocytes in non obese was 79.02 ± 6.02 but in obese was 119.02 ± 5.81 . The study of swati et al 10 supported our finding that his study reported the mean number of subcutaneous abdominal adipocytes per unit area was 116 ± 6.5 that is inline of our study shows that the mean number of subcutaneous abdominal adipocytes was 128.03 ± 5.81 in obese.

CONCLUSION

From this study it was conclude that in obese women there is increased number of adipocytes as compare to non obese women. This increased number of adipocytes enhances the cardiovascular as well as metabolic diseases and producing fatal health risks. Therefore need to elaborate the cause of disorder and its proper diagnosis through counting or assessment of adipocytes which will be helpful for management of diseases.

Recommendations

- In our study, we have examined the superficial subcutaneous layer of abdomen in adult woman of Hyderabad population. Same study can be replicated in other area of country.
- Further work should be carried out by using deeper layers of abdominal tissue.
- Comparison between different layers of abdominal tissue and genders can be carried out as well.

- Comparison of abdominal adipose tissue between disease and non disease patient's can be carried out.

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Outcome of Early Management of Club Foot by Ponseti Technique

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ABSTRACT

Objective: The Objective of this study is to assess the anatomical correction, cosmetic and functional outcome of the Ponseti method in idiopathic congenital Talipes Equino Varus (CTEV).

Study Design: Experimental and case series study

Place and Duration of Study: The study was carried out in the Department of Orthopaedic Surgery and Traumatology (DOST) Liaquat University of Medical & Health Sciences Jamshoro for a period of two years from 21-01-2009 to 20-01-2011.

Materials and Methods: This study was contains 50 cases of congenital talipes equino varus "CTEV". In this study all the case were selected with age of one year from the birth with congenital "talipes Equino Varus". All the cases with Acquired "Talipes Equino Varus", atypical foot, "talipes Equino Varus" with Arthrogryposis Multiplex Congenital, "talipes Equino Varus" previously treated by method other than ponseti technique were excluded from the study.

Results: Total 50 cases of congenital Telipase Equino Varus (CTEV) having 77 feet were analyzed in this study with (male female ratio 1:7). Out of 50 cases, 27 (54.0%, n = 50) had bilateral (54 feet) deformities and 23 (46.0%, n = 50) cases were unilateral deformities. Severity was assessed according to Pirani Scoring system. 48 (62.0%) had severe foot deformity while 29(37.60%, n = 77) patients had moderate foot deformity. Out of 77 feet, rocker bottom foot deformity developed in 03 (3.8%) feet, increased stiffness of ligaments and joints occurred in 1(1.2%, n =77) foot while vascular complications like skin ulceration and necrosis was observed in 1(1.2%, n =77) feet. At the end of 2 to 3 years follow-up period, in 72 (94.0%, n = 77) patients congenital clubfoot deformities were corrected successfully by using Ponseti method while 05 (6.0%, n = 77) patients were not fully corrected due to other complications.

Conclusion: The Ponseti method is a fast, safe and effective treatment for congenital idiopathic clubfoot and radically decreases the need for extensive corrective surgery.

Key Words: Ponseti method, idiopathic congenital Club feet, 12 months age.

INTRODUCTION

Idiopathic congenital talipes equinovarus (CTEV) is a relatively common complex three dimensional deformity of the foot affecting approximately 1–2/1,000 newborns¹ and about 1.2 per 10000 births among Caucasians, with approximately 50% of cases are bilateral.² Clubfoot deformity in children is difficult to treat because of the complex pathological anatomy of the growing foot.³ The clubfoot is not a single bone deformity but it is varying combination of four basic deformities including hind-foot equines, varus, forefoot adduction and medial subluxation of navicular bone.⁴ CTEV may occur as an isolated birth defect i.e. idiopathic or may be associated with other congenital deformities e.g. Edward syndrome, Spina bifida, Arthrogryphosis, Meningomyelocoele and Cerebral palsy.⁵ The deformity consist of four components including equinus, hind foot varus, fore foot adduction and cavus or medial subluxation of navicular bones.^{5,6}

In Ponseti's technique, the first two casts are applied with the forefoot supinated so as to bring it into alignment with the hind foot.⁷ The third cast is applied with the forefoot abducted and simultaneous counter pressure over the head of talus. In the fourth cast, the forefoot is further abducted. Prior to the fifth cast, the degree of dorsiflexion is assessed and if dorsiflexion is not possible beyond neutral, then a percutaneous Achilles tenotomy is required. Congenital Talipes Equino Varus is a matter of concern for the parents as well as to treating doctors because clubfoot needs early treatment and strict follow-up⁸ to achieve satisfactory end results at adolescent. The goal of treatment is to reduce or eliminate these four deformities so that the patient has a functional, pain free, plantigrade foot, with good mobility and without calluses, and does not need to wear modified shoes.⁸ The Ponseti technique is based on a thorough understanding of the anatomy and pathology of Congenital Idiopathic Clubfoot it involves a fairly small number of manipulations (between five and seven) and usually requires performing an Achilles

tendon tenotomy under local anaesthesia⁹, later on Denis Brown shoes were advise. Looking at the local and international literature which shows Ponseti's method is safe and effective mode of treatment and radically decrease the need for extensive corrective surgery.¹⁰ Study conducted by Sharma has showed effectiveness of Ponseti method in congenital club foot to be 95%.⁴ A local study by Iqbal J has evaluated effectiveness of Ponseti method in congenital club feet children under one month.⁷ We designed this study to save the time by reducing the number of casts as advised by Ponseti and money of this resource deprived country and prevent the long term sufferings and complications of the morbidity and other methods. In comparing the conservative and operative methods of treatment, literature reveals that the conservative method i.e. Manipulation and serial casting produces lower or no complication, less pain and better function.^{11,12} The conservative method is found to have impressive short and long term results to the tune of 90%.¹³ This study aims to assess the anatomical correction with cosmetic and functional outcome of the Ponseti method in Congenital "Talipes Equino Varus" under 12 months of the age.

MATERIALS AND METHODS

This experimental study was contains 50 cases of congenital talipes equino varus "CTEV" and was carried out in the department of Orthopaedic and Traumatology of Liaquat University of Medical and Health Sciences Jamshoro/Hyderabad, with the duration of two years from 21-01-2009 to 20-01-2011. In this study all the case were selected with age of one year from the birth with congenital "talipes Equino Varus". All the cases with Acquired "Talipes Equino Varus", atypical foot, "talipes Equino Varus" with Arthrogryposis Multiplex Congenital, talipes Equino Varus" previously treated by method other than ponseti technique were excluded from the study. The Data was entered and analyzed in statistical program SPSS version 16.0. Simple frequencies and percentages of categorical variables such as gender, estimated growth, placental localization, medical disorders, any addiction, hospitals, place of delivery, mode of delivery, deformities, severity of clubfoot, procedures, complications, final outcome, were calculated. No statistical test was applied for any comparison.

RESULTS

Total 50 cases of congenital Telipase Equino Varus (CTEV) having 77 feet were analyzed in this study based on inclusion criteria. Out of 50 cases, 32(64.0%) were males and 18(36.0%) were females (male female ratio 1:7). Out of 50 cases, 27 (54.0%, n = 50) had bilateral (54 feet) deformities and 23 (46.0%, n = 50) cases were unilateral deformities. Of these, 13 were on left side and 10 on right side. The parents of the patients

with unilateral deformity were informed about possible foot length differences and atrophy in leg muscles. Table No.1

Severity was assessed according to Pirani Scoring system. In the present study, out of total 77 feet, 48 (62.0%) had severe foot deformity while 29(37.60%, n = 77) patients had moderate foot deformity. Chart No. 1.

All the cases were initially treated by POP casting. Percutaneous Achilles tenotomy was performed in 53(68.8%, n = 77) patients. Chart No.2.

Out of 77 feet, rocker bottom foot deformity developed in 03 (3.8%) feet, increased stiffness of ligaments and joints occurred in 1(1.2%, n =77) foot while vascular complications like skin ulceration and necrosis was observed in 1(1.2%, n =77) feet. At the end of 2 to 3 years follow-up period, in 72 (94.0%, n = 77) patients congenital clubfoot deformities were corrected successfully by using Ponseti method while 05 (6.0%, n = 77) patients were not fully corrected due to other complications. Table No. 2.

Table No. 1 base line charecteristics of the patients (n = 50)

	Number	Percentage
Gender Distribution		
Male	32	64.0%
Female	18	36.0%
Frequency of Deformities		
Bilateral	27	54.0%
Unilateral:	23	46.0%
- Left	13	43.5%, (n = 23)
- Right	10	56.5%, (n = 23)

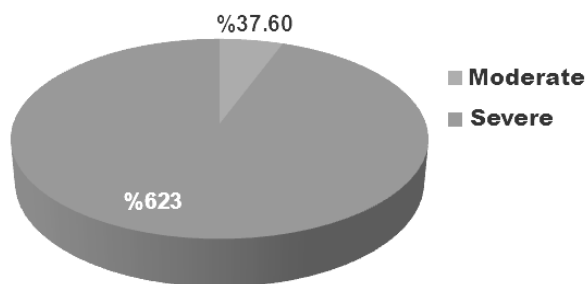
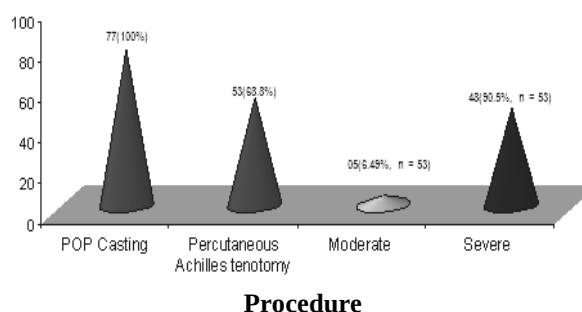


Chart No. 1: Severity of clubfoot (n = 77)



Case No.2: Details of Procedure Performed (n = 77)

Table No. 2: Complications and Outcome of Treatment (n = 77)

	Number	Percentage
Complications		
Rocker bottom feet	03	3.8%
Increased stiffness of ligaments and joints	01	1.2%
Vascular complications	01	1.2%
OUTCOME		
Corrected	72	94.0%
Failure	05	6.0%

DISCUSSION

Clubfoot or congenital talipes equinovarus is a complex deformity of foot that requires meticulous and dedicated efforts on the part of the treating physician and parents for the correction of the deformity. Idiopathic clubfoot has been documented as a hard and frustrating deformity to treat.¹⁴ Ponseti treatment for clubfoot has been gaining popularity due to the good results demonstrated by Ponseti and other institutions.¹⁵ In this series, 64.0% were male and 36% were female. The male to female ratio is high (male: female, 1:7) in comparison to the series of Gupta A et al.¹⁶ who showed the slightly higher frequency of gender in his study i.e. 81% male and 19% female while Khan NU et al.¹⁷ reported the 60.3% male and 39.7% female which is similar to this study. In a local study conducted by Arif M. et al.¹⁸ described 53.3% male and 46.7% female out of 30 cases of congenital talipes equinovarus (clubfoot), this difference is because of small sample size. Palmer¹⁹ explained this by suggesting that females require a greater number of predisposing factors than males to produce a clubfoot deformity. Social bias and increased attention towards males in our region can account for the higher incidence in males in our study. The order of birth also seemed to have an influence on the occurrence of clubfoot, with 65% of cases in the first-born child, which is in accordance with various other studies.^{20,21}

In the present study, out of 50 children, 54.0% had bilateral clubfoot and 46.0% had unilateral clubfoot (13 on left side and 10 on right side). Khan NU et al.¹⁷ involved 48.9% children having bilateral clubfoot and 51.0% had unilateral clubfoot out of 141 patients, this less difference is due to large sample size of the study. Gupta et al.¹⁶ showed similar results i.e. 60% children had Bilateral clubfoot while 40% had unilateral clubfoot in his study on 96 patients.

The Ponseti method of conservative clubfoot treatment is an excellent method of club foot treatment, of which there have been successful results in western countries.^{21, 22, 23, 24}

In this study reporting early results of the Ponseti treatment, 92% of the deformities were corrected without need for extensive surgery. This recovery rate is consistent with the results, reported by Herzenberg et al.²¹, whose study included similar population and follow-up. Another study by Goksan SB et al.²⁷ recovery rate was 95% which is similar to this study.

The duration of casts in this study for more than 70% of feet was five weeks or (3 to 8). The duration decreased over time as we mastered the technique and started getting faster correction. Ponseti et al.²⁵ reported five–12 weeks' duration of casts (average, 9.5 weeks). In another study by Laaveg et al.²⁰, the average duration was 8.6 weeks whereas Gupta A et al.¹⁵² also observed that the duration of casts for more than 85% of feet was five weeks or less which correlate to this study. The duration decreased over time as we mastered the technique and started getting faster correction. These findings correlate well to the study of Gupta A et al.¹⁶ Ponseti et al.²⁵ reported five–12 weeks' duration of casts (average, 9.5 weeks). In another study by Laaveg et al.²⁰, the average duration was 8.6 weeks. Morcuende et al.²³ reported an average time from the first cast to tenotomy as 16 days for one group and 24 days for another group in the same study.

The Ponseti method²⁶ of correction of clubfoot deformity requires serial corrective casts with long-term brace maintenance of the correction. In this study reporting early results of the Ponseti treatment, 92% of the deformities were corrected without need for extensive surgery. This recovery rate is consistent with the results, reported by Herzenberg et al.²¹, whose study included similar population and follow-up. An other study by Goksan SB et al.²⁷ recovery rate was 95% which is similar to this study.

CONCLUSION

In conclusion, the Ponseti method is a very safe, efficient treatment for the correction of clubfoot that radically decreases the need for extensive corrective surgery. Furthermore, it can be used successfully in children especially when no previous surgical treatment has been attempted. The decline in extensive clubfoot surgery should encourage national efforts to make this method the gold standard in the treatment of congenital idiopathic clubfoot. Educational programs should be targeted to primary care physicians, pediatricians, gynaecologists and lady health workers to increase awareness of the Ponseti method and its excellent results, so that they can advise families accordingly. It is advised that the treatment of club foot should be started within few days of birth to achieve best results. Orthopedicians who adopt the Ponseti method will feel rewarded by the satisfaction of successfully correcting what traditionally has been a very frustrating deformity to treat.

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To Observe the Role of Angiotension Receptor Blocker Losartan in Treating Prehypertension

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ABSTRACT

Objective: The primary objective of the present study was to determine whether in patients with prehypertension six months of treatment with an angiotensin II, type 1 receptor antagonist (at a dose of 8mg once a day) reduces the incidence of hypertension in borderline patients

Study Design: Randomized, open-labeled, prospective study.

Place and Duration of Study: This study was conducted in the department of pharmacology and therapeutics, Basic Medical Sciences Institute (BMSI), Jinnah Post Graduate Medical Centre (JPMC), Karachi, from July 2007 to January 2008.

Materials and Methods: This study involved eighty untreated participants between 30 to 60 years of age of either sex with blood pressure on study entry in high-normal range i.e. systolic blood pressure of 130 to 139 mmHg and diastolic blood pressure of 85 to 89 mmHg, according to the classification developed by Joint National Committee on prevention, Detection, Evaluation, and Treatment of high blood pressure (JNC-VI). All participants were randomized and enrolled in study after baseline investigations and informed written consent.

Results: All values have been expressed in standard error of mean ($\pm$ SEM). Forty patients were treated with DR1 and DR2 from day 0 to day 90th of study period respectively. In DR1 group the mean systolic B.P was decreased from 138 mmHg to 125.8 mmHg from day 0 to day 90th. In DR2 group an increase was observed in systolic B.P from 128 mmHg to 136 mmHg from day 0 to day 90th. An average percentage decrease of 8.21 % in case of DR1 while, 5.52 % was increased in DR2 group. In same way a decrease of 11.82 % in DR1 group, while, an increase of 11.5 % was observed in case of DR2 group in mean diastolic blood pressure respectively from day 0 to day 90th of study duration.

Conclusion: Treatment of prehypertension with an angiotension receptor antagonist May decreases incident hypertension. Additional studies will be needed to ascertain whether this or other strategies involving early pharmacological treatment of prehypertension would positively affect clinical outcomes.

Key Words: Prehypertension, Candesartan Cilexetil, Systolic blood pressure, Diastolic blood pressure.

INTRODUCTION

Regardless of terminology, Prehypertension is considered as a precursor of hypertension¹ and is associated with excess morbidity and deaths from cardiovascular cause². The name of the range of blood pressure between what is clearly normal and what is definitely hypertensive changed from transient hypertension in the 1940s³ to borderline hypertension in the 1970s⁴ high- normal blood pressure in the 1990s⁵ and most recently prehypertension in 2003⁶. Furthermore, an association of prehypertension with other cardiovascular risk factors has been established. We justified our study of pharmacological intervention with the use of an angiotensin-receptor blocker in prehypertension is based on following three grounds. One, in prehypertension, blood pressure remains a strong predictor of cardiovascular events after a statistical adjustment for other risk factors⁷ suggesting

that lowering blood pressure might be beneficial. Hypertension is a self-accelerating condition. The transition from prehypertension to established hypertension reflects in part ongoing changes such as arterial hypertrophy⁸ and endothelial dysfunction⁹. Increased vasoconstriction and diminished vasodilatation, consistent with these structural and functional findings have been described in prehypertension¹⁰. Two, Growth factors mediated by stimulation of the sympathetic nervous system¹¹ and excess activity of the renin-angiotensin system¹² tend to promote vascular hypertrophy by direct as well as hemodynamic effects. Third, present guidelines recommend that prehypertension be managed with changes in the participants lifestyle, weight loss¹³, salt restriction, exercise, and dietary modifications have been shown to reduce blood pressure in clinics specializing in lifestyle modifications.¹⁴ Despite

intensive community efforts to promote healthful lifestyles, however, the prevalence of prehypertension in the United States is increasing¹⁵

MATERIALS AND METHODS

This study was conducted in the department of pharmacology and therapeutics, Basic Medical Sciences Institute (BMSI), in collaboration with the department of medicine, Jinnah Post-graduate Medical Centre, Karachi, from July 2007 to January 2008. This six months, randomized study involved eighty untreated participants between 30 to 60 years of age of either sex with blood pressure on study entry in high-normal range i.e. systolic blood pressure of 130 to 139 mmHg and diastolic blood pressure of 85 to 89 mmHg, according to the classification developed by Joint National Committee on prevention, Detection, Evaluation, and Treatment of high blood pressure (JNC-VI). All participants were randomized and enrolled in study after baseline investigations and informed written consent.

The study period was consisted of 24 weeks with weekly follow-up visits of participants; but the observations of the parameters were recorded on day 0, day 45 and day 90 of the study period. The selected participants were divided into two groups. DR1 (losartan) and DR2 (Placebo). The DR1 group received Tab. losartan 50 mg once a day for 90 days, while DR2 group received Placebo once a day for 90 days. Following parameters were observed in the present study.

- Systolic blood pressure
- Diastolic blood pressure

RESULTS

The results have been expressed as mean $\pm$ SEM (standard error of mean). Forty participants were treated with DR1 and DR2 from day 0 to day 90th of study duration respectively. In DR1 group the mean systolic blood pressure was decreased from 138 mmHg on day 0 to 125.8 mmHg on day 90th. This reduction was found statistically highly significant ($p < 0.001$). The average percentage reduction in systolic B.P was 8.21 % from day 0 to day 90th of the treatment as shown in table 1A and figure 1A. In DR2 group 40 study participants were treated from day 0 till day 90th of study duration. The mean systolic blood pressure was increased from 128 mmHg on day 0 to 136 mmHg on day 90th of the treatment. This increase was also observed statistically significant. The average percentage increase in systolic blood pressure was observed 5.52 % from day 0 to day 90th of treatment as depicted in table 1.

In DR1 group, the mean diastolic blood pressure on day 0 was 87 mmHg which decreased to 75.8 mmHg on day 90th. This decrease in diastolic blood pressure was found statistically significant with a p-value ($p < 0.001$),

while in case of DR2 group the mean diastolic blood pressure was increased from 74 mmHg on day 0 to 85 mmHg on day 90th of study period. This increase in mean diastolic blood pressure was found statistically significant. The mean diastolic changes have been depicted in Table 2.

Table No.1: Changes in mean systolic B.P from Day 0 – Day 90th, of the treatment with DR1, DR2 groups

Groups	Day -0 B.P (mm Hg)	Day-90 B.P (mm Hg)	% change from day 0 – day 90 th
DR1	138 $\pm$ 0.07 (40)	125.8 $\pm$ 0.6 (38)	↓8.21 %
DR2	128 $\pm$ 0.41 (40)	136 $\pm$ 0.2 (36)	↑5.52 %

Key:

- DR1 (losartan)
- DR 2 (Placebo)
- Values are in (mean $\pm$ SEM)
- All observations are in mmHg
- ↓ shows decrease in percentage in B.P
- ↑ shows increase percentage in B.P

Table No.2: Changes in mean diastolic B.P from Day 0 – Day 90th, of the treatment with DR1, DR2 Groups

Groups	Day -0 B.P (mm Hg)	Day -90 B.P (mm Hg)	% change from day 0 – day 90 th
DR1	87 $\pm$ 0.2 (40)	75.5 $\pm$ 8.33 (38)	↓11.82 %
DR2	74 $\pm$ 0.58 (40)	85 $\pm$ 0.24 (36)	↑11.5 %

Key

- DR1 (Losartan)
- DR 2 (Placebo)
- Values are in (mean $\pm$ SEM)
- All observations are in mmHg
- ↓ shows decrease in B.P
- ↑ shows increase percentage in B.P

DISCUSSION

Untreated hypertension is a self-accelerating condition; evolving arteriolar hypertrophy and endothelial dysfunction facilitate the later increase of blood pressure and contribute to the transition from prehypertension to established hypertension. Abnormalities in cardiovascular structure and function and in neuroendocrine control occur in young adults with a predisposition to hypertension¹⁶. Therefore, we hypothesized that an intervention in humans with prehypertension might alter the natural history and prevent or delay the onset of established hypertension¹⁷. The results of our study are in accordance with clinical trials of Julius et al 2006¹⁸ and Whelton PK et al 2002.¹⁹ The main objective of the present study was to

realize and recognize the importance of prehypertension and its intervention at its initial stages. The current international guidelines recommend lifestyle modifications for the management of prehypertension. The findings of our study can also be correlated with the findings of the Trial of Hypertension preventions.

CONCLUSION

Treatment of prehypertension with an angiotension receptor antagonist May decreases incident hypertension. Additional studies will be needed to ascertain whether this or other strategies involving early pharmacological treatment of prehypertension would positively affect clinical outcomes.

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Factors Associated with Tuberculosis Treatment Default

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ABSTRACT

Objective: This study analyzed tuberculosis treatment default determinants in the Muzaffaraabad Azad Kashmir in order to plan the effective interventional tuberculosis control program.

Study Design: Prospective cross sectional cohort study

Place and duration of Study: This study was carried out at Azad Kashmir Combined Military Hospital (AK CMH)/Sheik Khalifa Bin Ziad (SKBZ) Muzaffaraabad (MZD) designed for patients defaulting from tuberculosis treatment from 1.1.2013 to 31.12.2013.

Material and Method: This study included 110 adults with diagnosis of TB treatment default. The study protocol incorporated structured questionnaire, physical examinations, radiological, laboratory investigations and potential factors for TB treatment defaults. The statistical analysis was performed using SPSS-20. The chi square test was done and $p < 0.05$ was considered as statistical significance.

Results: PLUM-Ordinal regression analysis revealed that many clinical variables have statistical significant association with tuberculosis treatment defaults. Factors identified to be associated with treatment default were; male gender ($p < 0.007$), distance from the health post ($p < 0.007$), displacement ($p < 0.024$), financial Constraints ($p < 0.001$), no body at home to bring medicine or take patients to hospital ($p = 0.001$), route closed in winters ($p = 0.001$), improvement from symptoms (0.009) and went abroad (0.001).

Conclusion: Determinants of treatment defaults and associated factors should be considered in treatments plan and policy actions to tuberculosis control programs. Information on disease, treatment plan and education of the individual along with population should be done in order to minimize treatment default and spread of multi drug resistance to anti-TB drugs.

Key Words: TB, Anti TB Drugs, TB Control Programme

INTRODUCTION

Tuberculosis (TB) and treatment default is a major public health problem in our country. The endemic of TB increased the need for effective strategies for its control. The prevalence account for 80% of cases of TB worldwide.¹ and Pakistan is eighth among 22 high burden countries of TB in the World.² The default rates of TB have been increasing day by day. Treatment default is a dangerous problem in TB control and can lead to persistence of infectious, increased relapse rates and emergence of resistant strains.³⁻⁴ Mortality rates are high among TB patients who discontinue treatment and also associated with comorbidities ei. HIV infection.⁵⁻⁷ A treatment default result in multidrug-resistant tuberculosis (MDR-TB) is defined as resistance of the TB bacillus to at least isoniazid and rifampicin. The World Health Organization (WHO) recommends the adoption of the Directly Observed Treatment Short-Course strategy (DOTS)⁸ in order to avoid MDR-TB. Although treatments default reduces by DOTS⁸, other studies did not support it.⁹

Factors identified to be associated with treatment default are: lack of knowledge about the disease, distance from the health post, partial or complete regression of symptoms in the first two months of treatment, the side effects associated with the

medication, male gender, age, the use of toxic substances and hospitalization during treatment, pre-existing pulmonary disease, previous default, TB/HIV co-infection, absence of supervised treatment and poor quality of patient care at the Health Unit and poor interventional strategy to control the disease.¹⁰⁻¹⁴

MATERIALS AND METHODS

This study was carried out at department of medicine SKBZ/AKCMH Muzaffaraabad. All adults with clinical diagnosis of TB, based on history, clinical examination and laboratory investigations were admitted to hospital. The data was obtained on standardized forms and entered in SPSS 20. TB defaulters were patients who interrupted treatment for two consecutive months or more as defined by WHO.¹⁵ Variables studied were: age, sex, treatment performed, type of treatment, clinical form, sputum smear microscopy, diabetes, other co-morbidities. The association of potential risk factors with defaulting was initially studied. The ethical committee approved the study.

RESULTS

The table shows the frequency of total of 110 TB patients who were enrolled in the study. From the total study population 74.6% (82/110) were males and

25.4% (28/110) were females. The mean age of the study population was 44.94 ± 21.37 (Mean $\pm$ SD).

Risk factors for default: Results of assessment on risk factors associated to default from TB treatment are shown in table.

Age and Gender: The statistical analysis of males showed a greater risk of default as compared to females and this difference was also statistically significant. The Analysis also revealed that the age has the significant association with TB treatment default in adults.

Living (distance, route closed, displacement) and treatment: There was statistically significant association between treatment defaults receiving treatment in a health unit related to patient's location away in rural area, displacement and also when routes closed in winter (table).

Clinical forms: Treatment default according to clinical form (types of TB) of the patient were observed with pulmonary 86(78.2%), pleural 5(4.5%), abdominal

5(4.5%), lymphadenopathy 6(5.5%), TBM 3(2.7%) skin TB 3(2.7%), disseminated TB 1(0.9%) and bone TB 1(0.9%) cases. This difference was statistically non significant.

Improvement to treatment: There was significant association between improvement to treatment and TB treatment default.

Associated Conditions related factors: Associated (Co-infection) with diabetes mellitus and corticosteroids showed no statistically significant risk for defaults ($p < 0.296$).

Type of treatment entrance numbers of default: There was no significant association between Numbers of default and TB treatment default.

Influence of duration of treatment: Duration of treatment in weeks and treatments default in relative had no significant association with treatment default. Treatment default in months ($p = 0.05$) has statistical significant for TB treatment default.

Table No.1: Risk factors for TB treatment default

Main reasons for default	Total	Percentage	P-Value
N (%)	110		
Age (mean $\pm$ SD)	44.94 ± 21.37		.007
Male	82	74.6	.522
Female	28	25.4	.323
Distance	12	10.9	.007
Displacement	6	5.5	.024
Financial Constraint	5	4.5	.001
Nobody at home to bring medicine or take patient to hospital	10	9.1	.001
Route closed in winters	18	16.4	.009*
Side effect for drugs	26	23.6	.005*
Improvement	31	28.2	.009*
Went abroad	2	1.8	.001*
Type of TB first time	110	100.0	.910*
Contact of relation			.534*
Duration of treatment default (weeks)	9.33 ± 6.65		.445*
Duration of treatment default (months)	19.34 ± 32.97		.05*
Associated condition	15	13.7	.296
Default relative TB	40	36.3	.663
Reporting back	40	36.3	.05
Default No,	110	100.0	.872
Condition of arrival			.041
Mortality	10	9.0	.765

*PLUM-Ordinal Regression; Chi-Square

DISCUSSION

High treatment default rate and low cure rates are most significant factors for the maintenance of disease transmission, the development of multiple drug resistance (MDR-TB) and high mortality.¹⁶ These factors are observed as an increase in the number of cases of primary and acquired multidrug resistance.

Patients with TB are predominantly urban. The large territory of the Muzaffaraabad AK with thick population favors the transmission of the disease. The distant periphery makes it difficult to control TB because traveling from far away and road mostly closed during winters season makes difficult treatment follow-up. Therefore, understanding the factors leading to

treatment default is of extreme importance to plan effective strategies for TB treatment control programs. Living in the city appeared to be associated with non compliance. TB patients groups having DOT'S coverage was higher in city than in the remote district .Our results were similar to those for previous study with respect to sex which was identified as a risk factors. Study in India showed sex as well as noncompliance as a risk factor for treatment default. Our study has shown similar result.¹⁷We observed that the adults 44.94 ± 21.37 (Mean $\pm$ SD) years of age were at risk of abandoning treatment. Our study showed that treatment default occurred mainly in this age group due to poor socioeconomic conditions. TB/HIV co infected / disseminated TB patients that tend to develop-infection were not evaluated for treatment default in our study. TB accelerates the evolution of HIV infection to AIDS by decreasing the patients survival.¹⁸Alcoholism has been identified as risk factor for treatment default worldwide and along with anti tuberculosis drugs increases the risk of liver damage¹⁹but not evaluated by us per se. Diabetic patients had no increased risk of noncompliance although it is associated with older age which also lowered the risk of treatment default.²⁰ Studies have shown prior noncompliance was because of poor information of TB patient about the disease and treatment. The poor quality of TB service, large population, sub-optimal implementation of public health facilities, inadequate knowledge, insufficient explanation on disease were also important risk factors for low adherence to treatment.

The statistically significant similarity of the results obtained with and without DOT in Asia, raises many issues related to quality and cost benefits of anti TB programs. The uniform strategy should be investigated to deal with this issue. A good relationship between patient and health professional can improve treatment adherence. There are several factors related to health care that may negatively affect adherence. They include negative attitudes of health professionals, lack of credibility and negative attitude of the patient in relation to services, lack of proper medicines and poor access to health services.²¹The association of factors related to the health system studied above, predictors of abandonment should be considered when planning the TB control activities. Others significant factors associated with treatment default are poor education, the occurrence of default in the previous treatment, TB/HIV co-infection, alcoholism and other co-morbidities. Patients who have these conditions should be considered as targets for individualized attention and priority by health professionals, with emphasis on conducting DOTS.

The limitation of the our study was non evaluation of TB/HIV co-infection, alcoholism, negative attitudes of health professionals and patient, sub-optimal

implementation of public health facilities and other co-morbidities.

CONCLUSION

Factors identified to be associated with treatment default were; male gender, distance from the health post, displacement, financial Constraints, no body at home to bring medicine or take patients to hospital, route closed in winters, improvement from symptoms and went abroad. These factors should be considered in addressing health care policy against tuberculosis in TB control programming. Ensuring these patients should receive DOTS under strict provision. Information about the disease and treatments should be available both to healthcare provider as well as patients in order to promote adherence to treatment and avoid the spread of MDR-TB.

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Estimation of Monocytes in Patients with Coronary Artery Disease

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ABSTRACT

Objective: To evaluate the role of monocyte count in patients presenting for coronary artery heart disease and to assess its significance as a risk factor.

Design: Cross sectional study.

Place and Duration of Study: This study was carried on the patients taken from Coronary Care Unit (CCU) Department of Isra University Hospital, Dewan-e-Mushtaque CCU and from Red Crescent Hospital CCU from May 2011 to October 2011.

Materials and Methods: In this study 140 individuals were enrolled to observe the monocyte count in patients with coronary artery disease. In control group 42, Stable Coronary Artery Disease (CAD) 34 and Acute Myocardial Infarction (AMI) 64 individuals were taken. Three ml of blood was collected in EDTA bottles for differential leukocyte count (DLC) from each patient presenting with chest pain in coronary care unit. The total leukocyte count (TLC) and other parameters were determined by different automatic analyzers in the clinical laboratory.

Results: In all three groups male predominance with 70%, 64% and 64% in Stable CAD, control, and AMI group was seen respectively. In stable CAD group highest percentage (53%) of patients were seen in 56 to 65 years age followed by 50% of patients of 35-45 years and 42% of patients of 46-55 years in control and AMI group respectively. Both in stable CAD and AMI groups; monocyte count was highly significant in diabetic patients however in individuals with higher BMI; monocyte count was significantly increased in AMI group than stable CAD and control groups.

Conclusion: It is concluded from the present study that monocyte count has significant relationship between clinical stages of CAD and diabetic patients. However individuals with higher BMI showed significant high levels of monocyte count in AMI group only.

Key Words: Atherosclerosis, monocytes, Coronary artery disease, Acute myocardial infarction.

INTRODUCTION

Multiple factors including dyslipidemia, dysglycemia, smoking, and genetic predisposition all contribute to the coronary artery disease¹. Pathogenesis of atherosclerosis is mainly supposed due to endothelial injury. This results in the inflammatory reactions and activation of immune system.^{2,3}

Multi-centric studies have reported decreased fibrinolytic response in patients presenting for coronary artery disease having increased count of WBC and ultimately leads to higher mortality². Coronary artery heart disease is the most frequent cause of mortality worldwide and these patients urgently require medical services to manage and for evaluation of acute-onset chest pain in emergency department⁴.

As it is categorized under inflammatory disease, some inflammatory markers have been used / proposed for evaluation of cardiovascular risk⁵. From all those markers suggested the total leukocyte count (TLC) has been the most productive and clinically applicable and also being practiced¹, due to its low cost and easy and wide availability⁵. Pathogenesis of atherosclerosis involves important cells of inflammation however very

little literature is available about the role of these inflammatory cells particularly monocytes in CAD. Some studies also highlighted the role of peripheral monocyte count in patients with variant angina⁶.

Monocytes/macrophage plays very crucial role in development of atherosclerosis. The circulating monocytes are named as lipid laden foam cells when they engulf the fatty acids and reach inside the vessel wall. Hence this event is the earliest in the atherosclerotic plaque formation. Later these lipid laden foam cells secrete several proteolytic enzymes causing rupture of the plaque and plaque instability. Subsequent sequence of changes leads to unstable angina or acute myocardial infarction (MI). Also in the infarcted area monocytes are recruited rapidly, where they enhance the wound healing, damage to the extracellular matrix and reperfusion injury⁷. Monocyte potentiates the inflammatory process in atherosclerosis by plaque formation and rupturing the fibrous cap thus their role could be taken as a risk factor for coronary artery heart disease. Some studies have also shown that increased number of leukocytes during coronary artery disease is linked with decreased epicardial blood flow in myocardium following reperfusion, thrombo- resistance

and adverse outcome⁸. Some of the studies have reported the association of left sided heart function recovery with monocyte count with high predictive value. Also the ST segment elevation was related with monocyte count^{9,10}.

Although the current available data has shown that monocyte count is predictive for long term cardiovascular risk but sufficient documented data is not yet available for its role in coronary heart disease. The present study was designed to evaluate the role of monocyte count in patients who are admitted with angina and acute myocardial infarction and to assess its significance as a risk factor.

MATERIALS AND METHODS

A total number of 140 patients selected were divided into three groups for this study according to criteria mentioned below. The study was carried out from May 2011 to October 2011. All the patients included in this study; presented in Coronary Care Unit (CCU) Department of Isra University Hospital, Dewan-e-Mushtaque CCU and from Red Crescent Hospital CCU Hyderabad. All patients were interviewed and detailed information regarding the disease was recorded on a printed Performa. A prior permission was obtained from the respective CCU Incharge and consent was obtained from attendants before interview.

140 patients selected for this study were divided into

1. **Control Group:** Consisted of 42 individuals with chest pain with normal electrocardiogram (ECG).
2. **Stable-CAD Group:** Consisted of 34 patients with angina pectoris typical at mild to moderate exertions. With no previous myocardial infarction or any electrocardiogram findings.
3. **Acute Myocardial Infarction Group:** Consisted of 64 patients of acute myocardial infarction (AMI).

The diagnosis of AMI was based on the presence of at least two of the following criteria:

- A. Typical pain with duration of more than 20 minutes; increased CK-MB or increase in Trop-T levels.
- B. An elevation of the ST segment ≥ 1 mm for at least two frontal leads or ≥ 2 mm for at least two precordial leads on the electrocardiogram at rest or appearance of new Q waves on the electrocardiogram at rest.

Inclusion Criteria: All the patients of either gender (male and female) with age over 18 years, presenting at emergency department / CCU with acute chest pain.

Exclusion Criteria:

- Patients under 18 years of age.
- Patients of chronic renal failure (serum Creatinine ≥ 2.0 mg/dl)

- Patients with a history of trauma, surgery, neoplasia & infectious diseases in the 30 days prior to admission.
- Patients using immune-suppressive therapy.
- Clinically significant endocrine, hematologic or respiratory disease.

Samples Collection Procedure

- Three ml of blood was collected in EDTA bottles for differential leukocyte count (DLC) from each patient presenting with chest pain in coronary care unit. The TLC and other markers were determined by different automatic analyzers in the clinical laboratory.
- The slides stained with Leishmann's stain were used for counting DLC manually.

RESULTS

In this study 140 individuals were enrolled to observe the monocytes count in patients of coronary artery disease. In control group (n=42), Stable CAD (n=34) and AMI (n=64) individuals were taken. In all three groups the number of male patients was found to be higher 64% in control, 70% in Stable CAD and 64% in AMI group respectively. (Figure: 01)

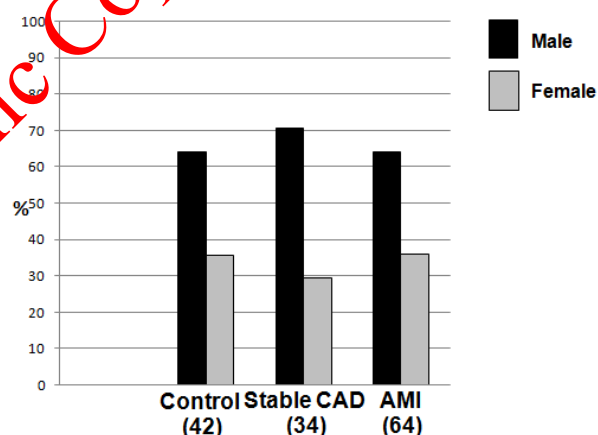


Figure No.1: Gender distribution between cases and controls

Table No.1: Age distribution (years) between cases and controls

Age (Years)	Control Group	Stable-CAD Group	AMI Group	Total
35-45	21	2	12	35
46-55	14	10	27	51
56-65	7	18	21	46
>65	---	4	4	8
TOTAL	42	34	64	140

Among the AMI group highest proportion of the patients were recorded between the ages 46-55 years

(27 out of 64). In control group highest recorded patients were between ages 35-45 years i-e: 21 individuals out of 42. In stable CAD group 18 patients out of 34 were between 56 to 65 years of age (Table: 1).

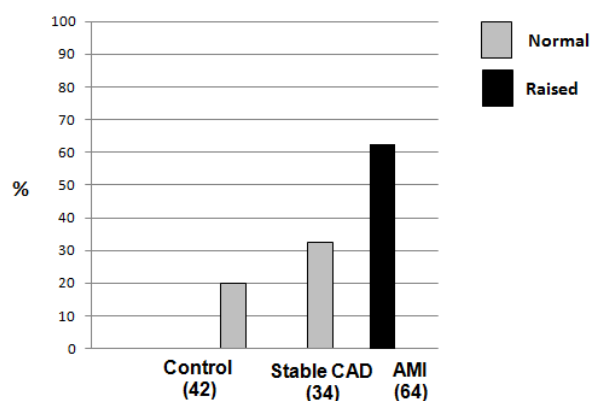


Figure No.2: Comparison of cardiac marker (Trop-T) between cases & controls

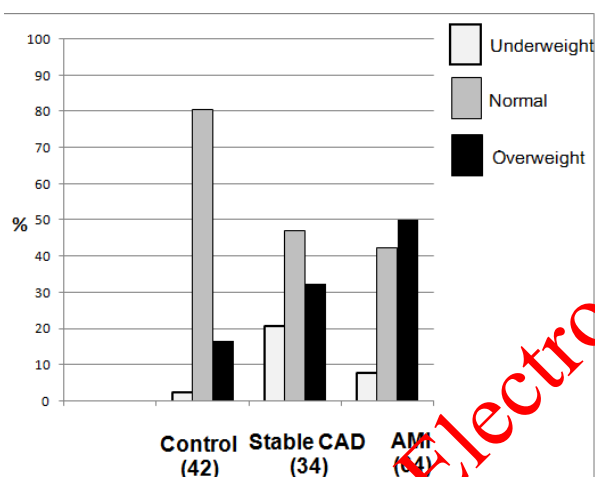


Figure No.3: Comparison of BMI between cases & controls

Table No.2: Association of BMI with Monocyte Count in cases and controls

	BMI		
	Over Weight	Normal	Under Weight
Control	17%	81 %	2%
Monocyte Count / mm ²	(600-800)	(400-600)	(200-400)
Stable CAD	32%	47%	21%
Monocyte Count / mm ²	(800-1000)*	(400-800)	(200-600)
AMI	50%	42%	8%
Monocyte Count / mm ²	(800-1000)**	(800-1000)*	(800-1000)*

* = Significant (p < 0.05) ** = Highly significant (p < 0.04)

Trop-T was measured in all three groups (control, stable CAD and AMI). In control group, levels of Trop-T was investigated in only in 20% of the individuals and results showed normal levels, in remaining 80% of control group individuals, the Trop-T were not investigated on the basis of clinical findings. In stable CAD Trop-T levels were noted in 33% and were found normal, the rest of the individuals were not preferred for Trop-T. However in AMI group Trop-T levels were significantly increased in about 63% of individuals (p= 0.005) (Figure: 2).

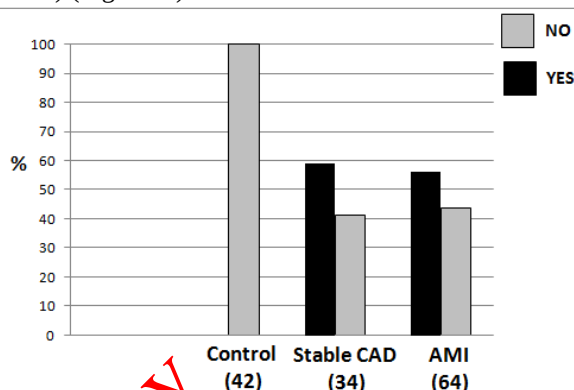


Figure No.4: Comparison of Diabetes Mellitus between cases & controls

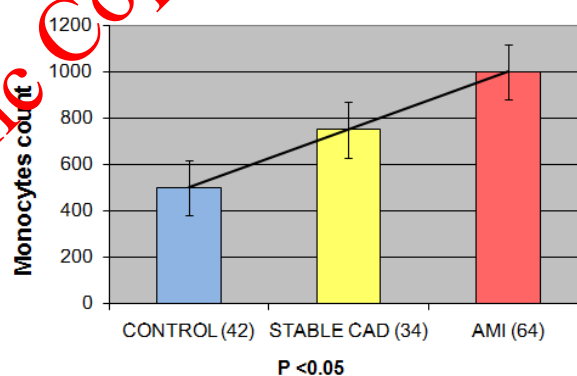


Figure No.5: Comparison of monocyte count between cases & controls

Table No.3: Association of diabetes with monocyte count

	Diabetes Mellitus	
	Diabetic	Non Diabetic
Control	NIL	100%
Monocyte Count / mm ²	(200-800)	(200-800)
Stable CAD	59%	41%
Monocyte Count / mm ²	(800-1000)**	(800-1000)
AMI	57%	43%
Monocyte Count / mm ²	(800-1000)**	(800-1000)

** = Highly significant (p < 0.01)

BMI analysis results revealed that in control group, BMI was normal in 81% individuals, 2% were underweight and around 17% individuals were overweight. In stable CAD about 47% individuals were having normal BMI while 21% of the individuals were underweight and 32% were overweight. In AMI 42% individuals were of normal weight, 8% of individuals were underweight and 50% of individuals were overweight (Figure 3).

In control group individuals who were overweight monocyte count were found to be in normal range and similar results were noted in normal and underweight individuals. In stable CAD group, the monocyte count was significantly increased in overweight individuals while it was normal in underweight and normal group individuals. In AMI group, in overweight individual monocyte count was highly significant with $p < 0.04$. Similarly significant results were also found in normal and underweight individuals where p value turns out to be $p < 0.05$ (Table: 2).

The ratios of diabetic patients were also noticed in study individuals. In control group all 42 individuals were non diabetic while in stable CAD about 59% of individuals were diabetic while 41% of individuals were non diabetic. In AMI group about 57% of individuals were having diabetes and 43% of individuals were non diabetic (Figure: 4).

In control group, consisting of all non diabetic individuals; the monocyte count was found normal. Both in stable CAD and AMI groups, monocyte count was highly significant in diabetic and in non diabetic patients it showed significant values with P value ($p < 0.01$ and $p < 0.05$ respectively) (Table: 3).

After revealing and analyzing all the risk parameters it was found that monocyte count is significantly and greatly increasing from control to stable CAD and the AMI group respectively ($p < 0.05$) (Figure: 5).

DISCUSSION

The aim of the present research is that increase in the levels of monocyte count is directly associated with poor prognosis and vaso-occlusive events in patient of coronary artery disease, the experimental data suggest a direct role of monocyte count in micro vascular obstruction. The only way to test whether monocyte count contribute directly to poor outcome in ischemic cardiovascular disease is to assess its levels in blood in patients who presented with chest pain secondary to coronary artery disease. The increase in monocyte count will correlate with the patient clinical stage and underlying risk factors of CAD. Hence, it turns out to be one of the prognostic tools for the prediction of an increased risk of CAD due to atherosclerosis. This view was also proposed by Pamukcu B, et al.

In present study it is also discovered that monocytosis is an independent risk marker for severity of atherosclerosis which is totally consistent with the work done by Burkhard L, et al.

In the present study, the monocytes were found to be (one of the most important components of the inflammatory process) an independent marker for the prognosis of stable CAD and AMI. These results are in agreement with Abrahão Afiune Neto, et al who also states that the increases in the number of monocyte count are related to the CAD and AMI.

Another study by Furman MI et al, showed a higher incidence of congestive heart failure and higher intra-hospital mortality rate in both men and women was observed with leukocytosis ($\geq 10,000/\text{mm}^3$). This correlates with our present study that, monocytosis is strongly associated with CAD which in turns is the common cause of congestive heart failure.

Hung MJ et al reported that, peripheral monocyte count is increased in the patients with variant Angina. The study is consistent with our present study, in which we also observed that levels of monocytes are elevated in patients of stable angina comparatively to the control group of individuals.

This research has also discovered that a very high incidence of monocytosis was visible in patients with Stable CAD and AMI group and these results are consistent with the studies done by Sposito AC, et al, who reported that leukocytosis is more severe in patients with stable CAD that have had a prior AMI; than those with just stable CAD.

As in this study, gradual increase in monocyte count was noted in a comparison between the control group and the stable CAD and AMI groups, which correlate with the study of Barron HV et al, indicating a gradual increase in the level of monocyte count which is associated with level of severity of atherosclerosis, the coronary blood flow, and high mortality in patients of CAD.

The study of Mariani et al, also highlighted the importance of monocytes count independently related to the recovery of left ventricular function at six months following AMI which strongly associate with this present study indicating monocytosis is strongly associated with AMI and it's a independent risk marker for CAD.

Simcha R. Meise et al observed a significant increase in monocyte count 2–3 days following acute myocardial infarction (AMI); the study is consistent with our present study.

Findings of Panutsopoulos D et al display a statistically significant association of the increased in the levels of endothelial growth factor (VEGF) and transforming growth factor $\beta 1$ (TGF- $\beta 1$) levels in peripheral monocytes, with stable angina and diabetes in coronary artery disease. The study is consistent with our present study which shows association between monocyte count and diabetes in Stable CAD group and AMI group of individuals.

Grau AJ et al reported that Neutrophilia is an independent risk variable for cardiovascular disease; however this study have shown that the monocytosis works better prognostic tool for Cardiovascular disease than any other isolated subtypes of leukocytes.

CONCLUSION

It is thus concluded from the present study that monocyte count has important role, which is directly related to the clinical stages of CAD, accounting for the slightly higher values of AMI group in comparison with the stable CAD group and also between the stable CAD group compared with the control group.

Hence it is recommended that in the rural areas of underdeveloped countries where best diagnostic methods are not readily available, the TLC and DLC being simple, inexpensive, and widely could be made available even at remote areas. Thus it may be tuned into an additional parameter for the preliminary approach of patients with suspicion of CAD.

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Frequency of Hypodontia in a Tertiary Care Hospital of Karachi

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ABSTRACT

Objective: To compare frequency of missing teeth in samples of population from Karachi.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted in Department of Orthodontics, Karachi Medical & Dental College from October 2011 to October 2012.

Materials and Methods: During the study period, 465 panoramic radiographs were evaluated and according to exclusion and inclusion criteria 309 panoramic radiographs were selected, out of which 109 (35.27%) were males and 200 (64.73%) were females. The patients were 12-25 years old. Data were collected and entered into the SPSS software (version 18; Chicago) to calculate frequencies, percentages and mean $\pm$ SD.

Results: 02 males were found with hypodontia (1.83%) while 10 females were found with hypodontia (5%). Few teeth like maxillary central incisors, 1st premolar & 1st molar in both arches show no congenital absence. A total of 17 teeth, (males = 3, females = 14) in 12 patients were congenitally missing. The most common congenitally missing teeth were maxillary left 2 incisor 23.52% followed by mandibular left 2 pre-molar 17.64%.

Conclusion: By early detection of missing teeth, alternative treatment modalities can be planned and minimize the complications of CMT. In this study it has been observed that among the population of Karachi threshold for agenesis of maxillary left 2nd incisors is the most commonly missing, followed by mandibular 2nd premolars.

Key Words: Hypodontia, Congenitally missing teeth.

INTRODUCTION

Congenitally missing teeth (CMT) refers to teeth whose germ did not develop sufficiently to allow the differentiation of the dental tissues. It is defined as missing of one or more teeth.¹ It can be seen sporadic or in hereditary syndromes. This anomaly occurs in three categories:

1. Hypodontia (Agenesis of less than 6 teeth, occurred without syndrome).²
2. Oligodontia (six or more teeth are missed).³
3. Anodontia: (absence of all of the teeth, usually seen with ectodermal dysplasia).⁴

Etiology of tooth agenesis is not clear but some probable factors are: Heredity (mutations of the genes PAX9 and MSX1),⁵ Ectodermal dysplasia, localized inflammation, trauma, radiation, and systemic conditions such as rickets, syphilis, etc.⁶ CMT causes problems in chewing, speech and aesthetics.² Knowledge of the condition may help to develop more effective treatments.¹ By considering and completion information from studies of Silva MR and Sisman Y, *et al* the prevalence of CMT varies in different populations from 0.3% to 34.3%.^{1,7} CMT was reported 10% by McDonald.⁴ The objective of this study was to compare frequency of missing teeth in samples of population from Karachi.

MATERIALS AND METHODS

This cross-sectional study was conducted in Department of Orthodontics, Karachi Medical & Dental College from October 2011 to October 2012. During the study period, 465 panoramic radiographs were evaluated and according to exclusion and inclusion criteria 309 panoramic radiographs were selected, out of which 109 (35.27%) were males and 200 (64.73%) were females. The patients were 12-25 years old. Inclusion criteria were: Having no specific syndrome Ectodermal dysplasia, no lip/palate cleft, age more than 12 years old. Exclusion criteria were: Missing 3rd molar, history of tooth extraction or tooth loss due to trauma, caries, periodontal disease or orthodontic extraction, not enough radiographic quality to accurately diagnose the CMT. A tooth was considered congenitally missing when the absence of crown mineralization was confirmed in the panoramic radiographs. Data were collected and entered into the Statistical Package of Social Sciences (SPSS version 18; Chicago) to calculate frequencies, percentages and mean $\pm$ SD.

RESULTS

Table No.1: Frequency of Congenitally Missing Teeth by Tooth Type

Tooth Type	Frequency (%)	Tooth Type	Frequency (%)
Lower Right Canine	11.76	Upper Right Canine	5.88
Lower Left Canine	11.76	Upper Left Canine	5.88
Lower Left 2 Incisor	5.88	Upper Right 2 Incisor	11.76
Lower Right 2 Pre-Molar	5.88	Upper Left 2 Incisor	23.52
Lower Left 2 Pre-Molar	17.64		

A total of 309 panoramic radiographs, which fulfilled the inclusion criteria were selected in the Department of Orthodontics, Karachi Medical & Dental College, from October 2011 to October 2012. Among 309 panoramic radiographs, 109 (35.27%) were males and 200 (64.73%) were females. The patients were 12 to 24 years of age (19.5 ± 4.2). Among 109 male panoramic radiographs, 02 males were found with hypodontia (1.83%) while among 200 female panoramic

radiographs 10 females were found with hypodontia (5%), as shown in Figure # 1. Few teeth like maxillary central incisors, 1st premolar & 1st molar in both arches show no congenital absence. A total of 17 teeth, (males = 3, females = 14) in 12 patients were congenitally missing, with an average of 1.42 ± 0.66 teeth per patient. The most common congenitally missing teeth were maxillary left 2 incisor 23.52% followed by mandible left 2 pre-molar 17.64% (Table # 1). Bilateral missing tooth in maxilla (66.6%) was more than mandible (33.33%), as shown in Table # 2. Frequency of CMT in mandible (52.95%) was greater than maxilla (47.05%), as shown in table # 3. In this study, 64.70% were in the left side of jaws and 35.30% of CMT were in the right side of jaw (Table # 4).



Figure No.1: Frequency of Hypodontia among Genders

Table No. 2: Distribution of Unilateral and Bilateral Congenitally Missing Teeth in Various Types of Teeth

Absent Tooth	Upper Lateral	Upper Canine	Upper 1 Pre-Molar	Upper 2 Pre-Molar	Lower Lateral	Lower Canine	Lower 1 Pre-Molar	Lower 2 Pre-Molar	Total
Unilateral Missing	2 (22.2%)	0	0	0	1 (11.1%)	2 (22.2%)	0	4 (44.4%)	9 (100%)
Bilateral Missing	2 (50%)	1 (25%)	0	0	0	1 (25%)	0	0	4 (100%)

Table No. 3: Distribution of Congenital Missing Teeth by Jaw

Jaw	Male	Female	Total
Maxilla	2 (66.66%)	6 (42.85%)	8 (47.05%)
Mandible	1 (33.33%)	8 (57.15%)	9 (52.95%)
Total	3 (17.64%)	14 (82.36%)	17 (100%)

Table No. 4: Distribution of Congenital Missing Teeth by Sides

Side	Male	Female	Total
Right	1 (33.33%)	5 (35.71%)	6 (35.29%)
Left	2 (66.66%)	9 (64.29%)	11 (64.71%)
Total	3 (17.64%)	14 (82.36%)	17 (100%)

DISCUSSION

CMT is the most common developmental abnormality of teeth.¹ Several factors are proposed as etiology of

CMT such as radiation, chemotherapy, some syndromes (such as Down syndrome, etc), infection and local inflammation, specific pattern of innervations, some systemic diseases, the changes resulting from human developmental and genetic factors, etc.; however the main cause is still unknown.¹⁻² Although CMT occurs in many syndromes, the incidence of non-syndromic and familial form is more.⁸ Some studies believe that it has been happening more commonly in recent decades.⁷ We had taken the cases of age in between 12 to 25 years. Michael Behr, et al believed that after age of 10 differences in results are negligible.⁹ Endo, et al reported that calcification of premolars could be delayed until ages 9-12 years.¹⁰

In the present study, frequency of CMT was 5% in females and 1.8% in males. This result is similar to many studies, where the average frequencies of CMT in males were also less than females.^{2,7,10-11} Silva, et al⁵ in

Mexico, Chung, *et al*¹² in Korea and Behr, *et al*⁹ in Germany concluded that CMT in females and males were almost equal with no significant differences of genders. Only Polder, *et al*¹¹ concluded that CMT in females were are 1.3 times more probable than males with significant differences. We suggest the fact that women are more anxious than men about dental visits, leads to higher prevalence of CMT for them.

In this study, we had included present orthodontic treatment candidates with excluding 3rd molar, the importance of this is so much that Polder, *et al*¹¹ in their meta-analysis study, excluded studies including only orthodontic patients. However, selection of orthodontic patients for CMT assessment is for easier access and sufficient number of their records like panoramic radiographs and some studies discussed that this approach neither causes overestimation of CMT,^{1,12} nor differs in missing patterns.^{7,11} i.e., Sisman, *et al*⁷ reported the prevalence of CMT in orthodontic patients was the same as general population.

In our study, frequency of CMT was 3.88%. This value was lower than most of the European studies as mentioned in studies of Silva MR and Sisman Y, *et al*^{1,7} and higher than the frequency of Altug-Atac AT, *et al*,¹³ this can be due to racial differences and different oral hygiene in Iran's society.

In our study, 47.1% of CMT were in maxilla and 52.9% in mandible, therefore frequency of CMT in mandible was more than maxilla. Our findings were similar to the Backman, *et al*² in Sweden while differ from many previous studies.^{1,7,9,12-14} Polder, *et al*¹¹ reported that the prevalence of CMT in both jaws was almost equal. Pattern of tooth innervations may be one of the risk factors of CMT in the maxilla.¹⁵

In all of the assessed radiographs, number of individuals with unilateral CMT was more than those with bilateral CMT. In study of Chung, *et al*¹² in South Korea and Polder, *et al*¹¹ in Europe, Australia and North America revealed same results and unilateral CMT was significantly more than bilateral. In the present study, bilateral CMT in maxilla (75%) was significantly higher than mandible (25%). This was due to the relatively high frequency of bilateral CMT in maxillary lateral incisors. Like our finding, Polder, *et al*¹¹ stated in their meta-analysis study that bilateral missing of maxillary lateral incisors was much more than unilateral and for other teeth unilateral CMT was more frequent. Our findings were in contrast with findings of Silva, *et al*¹ in Mexico and Endo, *et al*¹⁰ in Japan, probably due to racial differences of assessed communities.

The present study discloses that the least frequency of CMT belongs to first and second molars of both jaws (0.0%), followed by mandibular canine (1.29%). These results agree with studies conducted by Endo, *et al*¹⁰ in Japanese, Chung, *et al*¹² in Korea and Peker, *et al*⁸ in Turkey. Albeit in Sisman, *et al*'s study, in Turkey and

Backman, *et al*'s study in Sweden the least frequency was pertaining to upper and lower canines.^{2,7}

The most common form of CMT was single tooth missing (2.91%), and double teeth (1.29%). Therefore, our study supports other studies; however the percentages were relatively different.^{7,10-12}

In this study, 64.70% were in the left side of jaws while 35.30% of CMT were in the right side of jaws and the difference was significant. These results disagree with result of Sisman, *et al*⁷ in Turkey and in contrast with the findings of Fekonja, *et al*¹⁶ in Slovenia and O'Dowling IB, *et al*¹⁷ in Ireland, while Silva, *et al*¹ in Mexico, Endo, *et al*¹⁰ in Japan and Al-Mehrat, *et al*¹⁸ in Jordan concluded that the incidence of CMT was equal in both sides. Of course they did not find any significant relationship in this regard.

The role of heredity in the incidence of CMT has been identified and even several involved genes have been introduced.¹⁹ Behr, *et al*⁹ studied on two different races in South of Germany and found that not only was CMT observed more in some races, but also type of prevalent missing teeth could be different among them.

CONCLUSION

The importance of diagnosis and management of CMT is most important. By early detection of missing teeth, alternative treatment modalities can be planned and minimize the complications of CMT. In this study it has been observed that among the population of Karachi threshold for agenesis of maxillary left 2nd incisors is the most commonly missing, followed by mandibular 2nd premolars.

Recommendations: We suggest selecting equal number of males and females for more accurate evaluation of sex ratio. We also recommend taking diagnostic radiographs after the eruption of permanent teeth to evaluate the presence or missing of them, predict feasible use of space retainer and other supportive therapies to reduce the esthetic as well as functional concerns of CMT, as Hakan Tuna, *et al*²⁰ emphasized in their clinical report. Limitation of the present study is inaccessibility of the whole society. Due to ethical considerations, one cannot prescribe panoramic radiographies for the patients randomly. Therefore, we had to select the cases from subjects referring to the Orthodontics Department of KMDC. We suggest designing studies to assess familial history aspects of CMT in retrospective or prospective approach to provide better estimation and evaluation of role of genetic in CMT.

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Health, Marital Status and Mode of Living: An Anthropological Study of Ageing Community in Rawalpindi City

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ABSTRACT

Background: Culture is a learned behavior. It is a community's knowledge and set of practices that evolves out of continuous interactions with the outer environment feedback either positive or negative. In a strict sense culture is a man-made nature opposite to physical nature to survive.

Objective: The objective of the study was to investigate the interrelationship of older persons' (OPs) marital status and mode of living with their medical history.

Study Design: Cross Sectional Study

Place and Duration of the Study: The study was conducted on behalf of Help Age Pakistan. The data collection was done in various union councils of Rawalpindi city. The study duration was three months and lasted from Sep-2013 to Dec-2013.

Materials and Methods: Structured questionnaire was developed to collect information on Older Persons' health, economic and psychological status. In this regard, an extensive questionnaire was designed and pre-tested vigorously. Questionnaires were filled by the graduates of PMAS-Arid Agriculture University.

Results: The respondents who were single were mostly heart patients (n=14, 21.4%). The married respondents reported other diseases that included mental health, skin problems, paralysis, eye and hearing impairments and TB etc (n=704, 20.7%). Widows and widowers were in the third category with the same problems reported in second category (n=274, 20.1%). Results in the category of hypertension explain that elder peoples living in their own houses reported 9.1% hypertension, OPs living in rented houses suffering from hypertension were 10.3%, in case of hired residence percentage recorded was 0.0% and in the other category of living like living with relatives, friends or any other, 14.3% OPs were fighting with hypertension in their lives.

Conclusion: The data reveal that OPs living single are likely to catch heart problems, the married OPs were suffering from mental illnesses, dermatological problems, paralysis as well as hearing and visual impairments. The results show that OPs living in their own houses were better off than the ones living in other mode of living. Rented houses reported high percentiles of hypertensions, heart problems, and diabetes.

Key Words: Older Persons, Mode of Living, Marital Status, Diabetes, Heart Problems, Hypertension, Skin Problems

INTRODUCTION

It is widely accepted that some of the new attitudes and ways of life that are spreading rapidly around the world as a result of faster communication and transportation have the possibility of endangering healthy local practices. New technology, leisure, and wealth also carry an element of danger. Anthropology offers a powerful, systematic way of understanding what factors are affecting people's health, and how to evaluate public health plans that affect people's behavior.¹

Medical anthropology is the primary discipline addressing the interfaces of medicine, culture, and health behavior and incorporating cultural perspectives into clinical settings and public health programs. Health professionals need knowledge of culture and cross-cultural relationship skills because health services are

more effective when responsive to cultural needs. Cross-cultural skills also are important in relationships among providers of different cultures when, for example, African American and Filipino nurses interact with each other or with Anglo, Hispanic, or Hindu physicians. Knowledge of culture is also necessary for work in community settings, such as collaborating with diverse groups and organizations to develop culturally relevant public health programs. Health care providers and patients are more effective in managing their health and care with cultural awareness and the ability to manage the numerous factors that affect well-being.²

Ethnomedical studies (see Bannerman, Burton, and Wen-Chieh, 1983) reveal that health problems and treatments are conceptualized within cultural frameworks. Culture directly affects the manifestations of conditions, their assessment and social implications,

and processes of treatment. Ethnomedical analyses show the importance of understanding healing from the cultural perspective of the group, their social dynamics, the social roles of healers, and the conceptual and cosmological systems^{3,4}.

Gerontology is the study of old age and ageing. Although everyone has an intuitive sense of what 'old age' and 'ageing' are, providing a watertight objective definition is surprisingly difficult. *Ageing* could be said simply to be the process of growing older⁵.

Falling on custom and practice, we can state that *old age* is defined as the final segment of the lifespan, and for those who must have a number to attach to this, it is further defined as beginning at around 60 years of age. Different gerontologists have different threshold ages for the onset, but 60 is a reasonable compromise figure. In fact, it has been accepted by the mainstream literature for nearly 200 years⁶.

Inadequate social support is associated not only with lower overall general health and wellbeing, but also with higher levels of emotional distress, more illness and higher mortality rates⁷.

There is a wide consensus that participation in social networks is highly beneficial and connected with ageing that is comfortable, secure and productive. Such participation, to the extent that it means feeling valued and appreciated, is regarded as a significant component of wellbeing⁸.

Ageing is a sociologically interesting phenomenon because although it is a virtually universal experience – almost all of us will get old before we die – it occurs within very diverse and complex social and power dynamic contexts, including socio-economic grouping, health status, and access to financial resources, gender, ethnicity and geographical location. It is paradoxical that, on the one hand, we congratulate ourselves that in our society more people live longer than at any other time in history, but on the other hand, old people are demonized for the caring and/or financial burden they impose on their family, the community and the state⁹.

Most research on older people has been grounded in problem assessing and addressing, and as such has pathologized the experience of ageing. It is only comparatively recently that gerontology has attempted to develop theoretical frameworks that seek to make sense of the social experience of ageing¹⁰.

Reflection on ageing is as old as intellectual thought itself – from ancient times, philosophers, scientists, theologians, economists, artists and writers have pondered the meanings and experiences of growing and being old. What is definitely not a phenomenon of the twentieth and twenty-first centuries is the heartfelt cry of older people that they are not treated with the respect they consider their due from younger generations – certainly not the way they respected their elders in their youth. Note the following quotation from a thirteenth-century sermon (popularly ascribed to St Peter

Celestine; this sermon is sometimes ascribed to the eleventh century Peter the Hermit). The young people of today think of nothing but themselves. They have no reverence for parents or old age. They are impatient of all restraint. As for girls; they are forward, immodest and unwomanly in speech, behavior and dress¹¹.

Older men are married, have children and grandchildren, and enjoy better health and greater wealth than previous cohorts or never married peers¹².

The many different areas of medical anthropology reflect a growing trend of applying cultural knowledge to resolve health problems; a variety of aspects are listed below in "Applications: Areas of Medical Anthropology." Cultural knowledge and intercultural perspectives help facilitate relations among provider cultures, patient cultures, and institutional cultures. Cultural perspectives inform providers regarding how patients, families, and significant others conceptualize health problems and will respond to proposed care. Cultural perspectives enhance effectiveness in clinical practice and community health by enabling changes in professional style, institutional practices, and community behaviors where appropriate. Understanding a patient's personal and social life in relationship to the treatment plan helps ensure effective communication, appropriate resource utilization, and the success of treatments. Culturally sensitive approaches also help patients by helping providers accommodate to patients' concerns with alienation, powerlessness, distress, and despair¹³.

The World Health Organization (WHO) characterized health as complete physical, mental, and social well-being and the capability to function in the face of changing circumstances. The WHO also emphasized the "highest possible level of health" that allows people to participate in social life and work productively¹⁴. Health involves social and personal resources in addition to physical conditions; a sense of overall well-being derived from work, family, and community; and other relations, including psychosocial and spiritual¹⁵.

Cultural effects on health are part of a system linking the physical environment, social institutions, and biology. Although they also include the physical environment, I refer to these systems as cultural systems models out of recognition that culture shapes our understandings of and interactions with the physical environment, including having effects on the physical environment. Similar cultural systems models have been proposed by physicians, nurses, and public and community health practitioners (Brody, 1973; Engel, 1977, 1980; Blum, 1983; Leininger, 1991, 1995; Baer, Singer, and Johnsen, 1986; Sallis and Owen, 1998), who use cultural systems approaches as conceptual frameworks for addressing health, disease, and care in relationship to the ecology, the total physical and social environment. These models also incorporate demographic, technological, economic, political, and

other social conditions that affect the physical environment¹⁶⁻²¹.

MATERIALS AND METHODS

For data gathering a structured tool was developed on Older Persons' health, economic and psychological status. An extensive questionnaire was designed and pre-tested vigorously. Questionnaire contained bio-informatics including demographic information of clients and the second part covered base-line information, Third part contained information on economic status, fourth part was about the medical histories of the older persons, fifth section comprised information on Social and Psychological profile of OPs, and the last and sixth part consisted information about legal and social protection issues of OPs. Questionnaires were administered with the help of a research team that comprised the graduates of department of Anthropology of PMAS-Arid Agriculture University along with professionals of Regional Development Network (RDN) as well as field staff of Pakistan National Center on Ageing (PNCA).

RESULTS

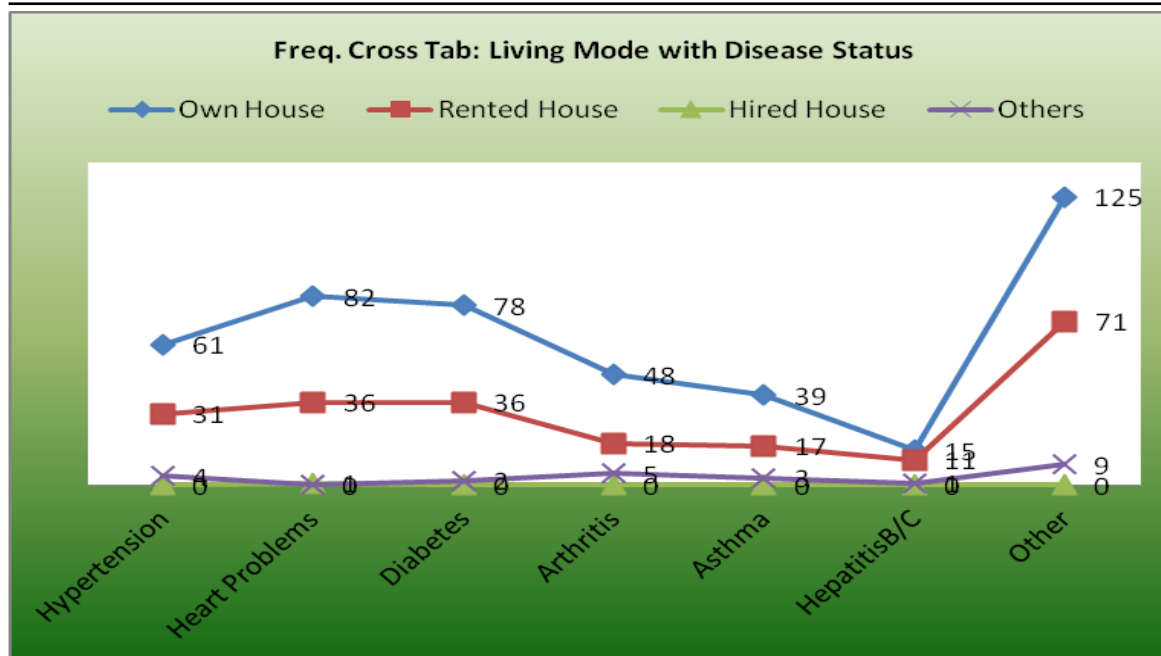
Marital Status with Disease Status: The table educates that correlation of diseases with the marital status of the respondents. The respondents who were single were mostly heart patients (n=14, 21.4%). The married respondents reported other diseases that included mental health, skin problems, paralysis, eye and hearing impairments and TB etc (n=704, 20.7%). Widows and widowers were in the third category with

the same problems reported in second category (n=274, 20.1%). The divorced OPs revealed a different trend in which an equal percentile of 33.3% was recorded in Hypertension, Heart problems and other diseases. The respondents living separately from the spouses scored equally in three categories those were heart problems, arthritis and other diseases.

Living Mode with Disease Status: Mode of Living is very imperative especially for elders it is always an important factor when discussed in terms of health status and other problems. Results in the category of hypertension explain that elder peoples living in their own houses reported 9.1% hypertension, OPs living in rented houses suffering from hypertension were 10.3%, in case of hired residence percentage recorded was 0% and in the other category of living like living with relatives, friends or any other, 14.3% OPs were fighting with hypertension in their lives. Highest rate of Heart ailments recorded in the category of hired houses. Diabetes was more prominent among the elders living in rented houses, the category of 'others' depicted the highest percentage of arthritis and asthma among respondents. The table also contends that living mode is directly related with the health status. As stated earlier in the study that living conditions of the families on a general level was not satisfactory at all. This situation goes more severe in terms of studying the livings of OPs. Mostly the families were found to living in accommodations ranging from one to two room dark and damp apartments with serious compromises on privacy issues.

Table No.1: Comparison of Marital Status with Diseases

Marital Status	Do you have any of the following								Total
	Hypertension	Heart Problems	Diabetes	Arthritis	Asthma	Hepatitis B/C	Other	NA/ No disease	
Single	0	3	0	2	1	0	2	6	14
	.0%	21.4%	.0%	14.3%	7.1%	.0%	14.3%	42.9%	100.0%
Married	60	83	81	38	39	18	146	239	704
	8.5%	11.8%	11.5%	5.4%	5.5%	2.6%	20.7%	33.9%	100.0%
Widow/ widower	35	31	35	30	19	9	55	60	274
	12.8%	11.3%	12.8%	10.9%	6.9%	3.3%	20.1%	21.9%	100.0%
Divorced	1	1	0	0	0	0	1	0	3
	33.3%	33.3%	.0%	.0%	.0%	.0%	33.3%	.0%	100.0%
Separated	0	1	0	1	0	0	1	2	5
	.0%	20.0%	.0%	20.0%	.0%	.0%	20.0%	40.0%	100.0%
Total	96	119	116	71	59	27	205	307	1000
	9.6%	11.9%	11.6%	7.1%	5.9%	2.7%	20.5%	30.7%	100.0%



Graph: Living Mode & Diseases

DISCUSSION

The data reveals that marital status is strongly related to the OPs' medical history. Pakistan being a third world country always finds its cultural roots in the ancient Indus river civilization. The social institution of family has always been very influential and only recognized social support network existing for the last many centuries. Family is the socio-cultural bond that lays out the foundations of identity as well as the social reference. Family is not only a natal bond rather it also acts as building social support networks that are operational to provide social and psychological support to its members in the larger context of society. Marriage institution is the cultural arrangement of extending social ties and enhancing the alliances to other non-familial layers of society to in order to bring them in familial brethren and thus ensuring survival against hard outer-external hostile environment. The individuals not practicing marital options are more prone to contract ailments which put them at the mercy of their peer groups or extended family ties for look after and medical attentions. Marital partners and offsprings are the only support group that play important role in caring for OPs. The data reveal that heart problems being the most important are higher among the OPs who remained single throughout their lives. It is not to say that the married OPs did not face any medical issues rather it is to say that the severity of medical issues goes higher among unmarried OPs as compared to the married OPs who usually suffer less intensity medical ailments including neurosis, dermatological problems and hearing and visual impairments.

The mode of living also affects the disease status of OPs. The data show that the socio-economic status of OPs is strongly correlated with the medical history of the respondents. Mode of living can not only be taken as a mere living pattern rather it is directly associated with the economic stability of the respondents. Generally, it was observed that the respondents' economic stability liberates them from fear of getting displaced. The genuine human wish of owning a shelter frees the respondents from many mental stresses and thus positively saves them from many psychological and pathological issues. The OPs living in their own homes are less likely to be affected from hypertension, heart problems, diabetes and arthritis. The vital statistical details also bring forth the fact that the quality of living also affects the health status of OPs. For example, health status among OPs goes better if there is a separate room for them that ensures their privacy. Residential apartments ranging from one to two rooms usually scored poor in case of OPs where they are not enjoying their privacy as well as those rooms were found to be darker and damper.

CONCLUSION

The aim of paper was study two important variables regarding the general welfare of older persons in Rawalpindi city. The first variable that was studied was to see the marital status of OPs with their medical history. The second variable highlighted the relationship of mode of living with the medical problems. On the basis of the information collected it can be safely concluded that marital status positively affects the health of older persons which means that in case of being married the health status of older persons is generally found to be more satisfactory. The underlying fact is that the older persons are being taken

care of by their marital partners as well as their offsprings. The marital status also provides an opportunity for psychological care by the rest of the family members. On the other hand, the mode of living is directly related to the economic stability of older persons which directly affects the health status of them. The respondents living in their homes owned by them bring a mental satisfaction from the fear of being at the mercy of others. The further details reveal that houses ranging from two to three rooms also positively affect the medical status of OPs as they enjoy their privacy. Houses from one to two rooms report that OPs usually are given place in darker and damper rooms which negatively affects their health.

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Profile of Unnatural Deaths; in Faisalabad

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ABSTRACT

Objectives: To find out the magnitude, manner and modalities of unnatural deaths among all cases brought to the Forensic Medicine Department (PMC) Faisalabad for post mortem examination.

Study Design: Retrospective study.

Place and Duration of Study: The study was conducted in the Department of Forensic Medicine, Punjab Medical College Faisalabad from 1st January, 2012 to 31st December, 2012.

Materials and Methods: Study material has been collected from mortuary of (PMC) Faisalabad including police inquest reports, postmortem reports and hospital record / treatment history of the victims. A total of 397 cases of Medico legal deaths were brought for postmortem examination in the Department of Forensic Medicine, Punjab Medical College Faisalabad during one year study period. All these cases were grouped according to age, gender, manners and modalities of medico legal / unnatural deaths. The data collected, & analyzed.

Results: The commonest manner of death in overall age groups was homicide followed by accident, suicide & natural deaths, whereas; 59 cases remained undetermined. Among 228 homicidal deaths, Firearms were the predominant weapons of infliction (70.17%). A total of 64 (85.33%) persons lost their lives in Road Traffic Accidents (RTA) among 75 accidental deaths.

Out of total 397 cases, Males were (74.82%) and females (25.18%). The age group most commonly involved was 20-29 years (29.97%) followed by 30-39 years (21.41%) & 40-49 years (15.61%), whereas; the victims belonging to age group of 10-19 years contributed for (12.09%).

Conclusion: Our study concludes that Homicide was the most dominant manner of death among the unnatural deaths. Fatalities caused by Firearms were the commonest form of homicide; Road Traffic Accident was the commonest modality among accidental deaths whereas; the suicide was found as rare manner of death.

Key Words: Medico Legal Deaths, Homicide, Suicide, Accidents, Unnatural Deaths

INTRODUCTION

Death is a tragedy in whatever form, at whatever time and in whatever way it comes¹. The death is natural when it is due to any pathology (disease) or ageing and is unnatural when caused prematurely against order of the nature by injury, poison or other means of violence. Unnatural deaths may be accidental, suicidal, homicidal or undetermined. The data of unnatural deaths may reflect the law and order situation in a particular area of jurisdiction². It is our firm belief being Muslims that time & place of death is fixed which is not known to anyone except Allah; the Almighty, but in case of death which is premature, unexpected and resulting from violence causes harassment / depression not only among the relatives of deceased but also have certain impacts all over the society³.

Every Human being is blessed with the gift of life for the purpose of being happy & to bring peace for all but the purpose is ignored when human pursuit of wealth and power, satisfaction of physical appetites, and passions terrorize their fellow human beings. The crime and violence exist in the society since long over the centuries but in this modern era there is an extreme aggravation of these problems⁴. The Type & Magnitude

of violence leading to injuries, disabilities and death, has been pointed out by various authors in their studies. In Pakistan, attempts have been made by the researchers to find out the magnitude, cause and manner of death as well as the sociodemographic background of the victims of unnatural deaths, at different centers from province of Baluchistan,⁴ Punjab,⁵⁻⁹ Sindh,¹¹⁻¹² KPK,¹³⁻¹⁷ and AJK¹⁸.

Profile of the cause & manner of death forms the cornerstone of the Health Management Information System (HMIS). Drawing public attention and awareness towards casualties is important to prevent unnatural deaths; this possibly could reduce the incidence of such cases.

This paper will not only find out the magnitude of unnatural deaths but also provide a snapshot of the demographic profile, manners and modalities involved in medico legal deaths, presented to the Department of Forensic Medicine Punjab Medical College, Faisalabad for post mortem examination. The finding of this study will create awareness among the people about deaths related to violence which is the important public health concern in the society. It will also be helpful for law enforcement agencies to make the strategies for prevention of such incidences.

MATERIALS AND METHODS

This study was performed on 397 cases of medico legal deaths reported from the urban and rural areas of Faisalabad brought to Department of Forensic Medicine (PMC) Faisalabad during the calendar year 2012; (1st January 2012 to 31st December, 2012). There were 297 males and 100 females belonging to the ages from 0 to 90 years.

As regards the data of age, gender, hospital notes / treatment history, Medico legal certificates is concerned; that was obtained from post mortem unit of (PMC) Faisalabad, whereas the record about circumstances of death was sought from the police inquest reports / FIRs. The relatives and friends of the victims were also interviewed in suspected cases of suicidal deaths. The data entered on a Performa, statistically analyzed and the results were summarized in tables and charts.

Ethical Considerations: Permission was obtained from Head of the Department of Forensic Medicine (PMC) Faisalabad, for examining the relevant data required for this study.

RESULTS

Out of the total 397 victims of Medico legal deaths, 228 (57.43%) cases were of homicides and 75 (18.89%) of accidents while 23 cases (5.80%) were involved in suicidal deaths. In 12 (3.02%) cases, the manner of death was natural, whereas manner of death in 59 (14.86%) cases was undetermined. The detail is shown in Table (1) below:

Table No.1: Showing distribution of manner of death in Medico legal fatalities (n397)

Manner	Number of cases	% age
Homicide	228	57.43%
Accidental	75	18.89%
Suicidal	23	5.80%
Natural	12	3.02%
Undetermined	59	14.86%
Total	397	100%

Age wise distribution of the victims revealed that majority of the deaths 119 (29.98%) were in the age group of 20-29 years, followed by 85 (21.41%), 62 (15.61%) and 48 (12.09%) cases involving age groups of 30-39 years, 40-49 years & 10-19 years respectively. Both extremes of age were least presented. The detailed distribution of age & gender is shown in Table (2).

Among 228 cases of homicidal death, firearms were the weapon of choice used by the assailants in 160 (70.17%) cases followed by 30 (13.15%) deaths by sharp edged and pointed weapons, whereas blunt weapons contributed to cause the death of 17 (7.45%) victims. Manual strangulation was responsible to kill 09 (3.95%) victims; while death occurred by asphyxia due

to throttling / smothering in 08 (3.50%) cases. Burning contributed in 02 (0.87%) victims while another 02 (0.87%) victims died of hanging. Details are shown in Table 3.

Table No.2: Showing age and sex wise distribution of Medico legal deaths (n397)

Age group (Years)	Male	Female	Total	% age
0-9	14	07	21	5.28%
10-19	35	13	48	12.09%
20-29	88	31	119	29.98%
30-39	66	19	85	21.41%
40-49	44	18	62	15.61%
50-59	22	05	27	6.80%
60-69	21	01	22	5.56%
70-79	05	05	10	2.52%
80-89	02	01	03	0.75%
Total	297 (74.82%)	100 (25.18%)	397	100%

Table No.3: Showing distribution of Homicidal death cases (n=228)

Types	Male	Female	No. of cases	% age
Firearms	129	31	160	70.17%
Sharp Force	18	12	30	13.15%
Blunt Force	12	05	17	7.45%
Strangulation	05	04	09	3.95%
Smothering / Throttling	06	02	08	3.50%
Hanging	01	01	02	0.87%
Burning	Nil	02	02	0.87%
Total	171 (75 %)	57 (25 %)	228	100%

Among a total of 75 accidental deaths, 64 (85.34%) persons lost their lives in Road Traffic Accidents. Death due to Railway track accidents occurred in 02 (2.66%) victims, Accidental Burns took the life of 08 (8.01%) victims whereas 01 (1.33%) case died of accidental electrocution. The detail of distribution among accidental fatalities is shown in Table (4)

Table No.4: Showing distribution of accidental death modalities (n=75)

Modalities	Male	Females	No. of cases	% age
Road Traffic Accidents (RTA)	52	12	64	85.34%
Accidental Flame Burns	04	04	08	8.01%
Railway track accidents	02	Nil	02	2.66%
Electrocution	01	Nil	01	1.33%
Total	59 (78.66%)	16 (21.34%)	75	100%

Among total 23 suicidal deaths, hanging had higher incidence 13 (56.52%) cases followed by firearms in 08 (34.78%) cases. There was 01 (4.35%) case of self destruction by flame burn while 01 male ended his life by jumping from height. Details shown in Table (5).

Table No.5: Showing distribution of modalities in suicidal deaths (n=23)

Modalities	Male	Females	Total cases	% age
Hanging	05	08	13	56.52%
Firearm Injuries	05	03	08	34.78%
Burning	01	Nil	01	4.35%
Jumping from height	01	Nil	01	4.35%
Total	12 (52.17%)	11 (47.83%)	23	100%

DISCUSSION

Faisalabad is thickly populated / industrial city, known as Manchester of Pakistan, with modern and traditional ways of living. According to the Economic survey conducted in 2009-10, Faisalabad had the population of 2,912,269 being the 3rd largest city of Pakistan¹⁹. Faisalabad city being hub of the textile industry, with a busy dry port and famous educational institutions, is situated at the junction of roads leading to different cities of the province & majority of the people travel on roads of this region for the purpose of trade & their personal matters.

We have tried to find out the manners and modalities of deaths which were brought for medico legal autopsies in the mortuary of Forensic Medicine Department Punjab Medical College, Faisalabad during the study period i.e. 1st January 2012 to 31st December, 2012. Results of our study showed that the most dominant manner of death was homicide followed by accidents. Out of total 397 deaths, 228 (57.43%) were homicidal, 75 (18.90%) accidental and 23 (5.80%) committed suicide. In 12 (3.02%) cases, the death occurred due to natural causes whereas in 59 (14.86%) cases the manner of death remained undetermined. (Table No.1). This finding of present study is in agreement with studies conducted at Peshawar¹³ and Dera Ismail Khan¹⁴, which showed homicidal deaths predominance in all unnatural deaths. Whereas; the finding of our study are in contrast with the studies conducted at Dacca^{20,28}, Hyderabad¹⁰ and Nigeria²¹ which showed the accidental deaths as dominant manner in all Medico legal deaths.

Our results illustrate that during the period under study, 228 (57.43%) cases were labeled as homicidal deaths. These finding are consistent with the studies conducted in Lahore⁶, and Nawabshah¹¹ but is less than the percentage found in Bahawalpur⁷, and Peshawar¹³.

The most vulnerable age group in our study was 20-29 years involving 119 (29.97%) fatalities, followed by 85 (21.41%) victims in the age group of 30-39 years, 62 (15.61%) cases of 40-49 year and 48 (12.09%) cases of

10-19 years. The cases belonging to both extremes of age were least involved.

Our results are similar with the studies in different centers of Pakistan^{8,9,12,15} and other countries²²⁻²⁶ reporting highest incidence of medico legal deaths in this age group. This is due to the fact that persons belonging to this age group are active, mobile & energetic. The young individuals are short tempered & easily become emotional which result in violence.

Deaths among males were predominant 297 (74.81%), while female number was 100 (25.19%) & this male to female ratio is similar to the findings of other authors^{17,20, 23}.

Road Traffic Accident victims among accidental deaths were mostly vehicular occupants than the pedestrians. The main reasons for RTAs in this area are overcrowded roads with different type of vehicles used for transportation of goods, including heavy vehicles, animal carts, tractor trolley & auto rickshaw, etc. The situation is versed due to defects in vehicles and lack of observance of traffic rules.

Suicide was a rare manner of death contributed in 23 (5.79%) cases and out of those, 12 males committed suicide as compared to 11 females. Hanging was adopted for committing suicide in 13 cases which outnumbered as compared to other methods. Among them, 5 were males and 8 female.

It has been observed that firearms as weapon of assault (70.17%) outnumbered all other weapons used among 228 cases of homicidal deaths. This finding is in similarity with the fact that guns are the method of choice for committing intentional deaths. The United Nations global study on homicide statistics; "On trends and patterns in homicide" estimated 468000 homicidal deaths in the year 2010 and firearms was involved in 42 percent of global homicides²⁷. Similar pattern has been reported by some authors in their studies^{14,16} conducted at different centers of Pakistan indicating the firearms as weapons of choice to be used for killing as compared to other modalities.

CONCLUSION

Our study showed that homicide was the commonest & dominant manner of death as compared to others. Accidental deaths were the next to homicide. Fatalities due to Firearms were on the top of homicidal injuries and deaths during the period of our study. The males belonging to 2nd & 3rd decade of life were commonly involved in violence. Among accidental deaths, majority of the victims lost their lives in Road Traffic Accidents.

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Mortality Pattern in Children in General Pediatric Ward of Abbasi Shaheed Hospital Karachi

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ABSTRACT

Objective: To determine the different causes of mortality in children and to identify the risk factors associated with mortality.

Study Design: Descriptive Study.

Place and Duration of Study: This study was conducted in Department of Pediatric unit- I Abbasi Shaheed Hospital from April 2010 to March 2011.

Materials and Methods: All those infants and children who expired in unit I of Abbasi Shaheed Hospital were included. A previously prepared Performa was filled. The indicators studied were age, sex, total duration of hospitalization, total duration of illness and diagnosis of each infant and child, nutritional status and immunization status of all the children

Results: Out of 3420 patients 157 children expired out of 3420 admitted patients 1789 were males and 1631 were females. Most of the children admitted were below the age of five years. 64 children expired within first 24 hours of admission. 56% were malnourished and 63% were either not immunized or had received only partial immunization. Infectious diseases were responsible for 67 % of all deaths. Malnutrition, non-immunization, late referrals were the risk factors identified.

Conclusion: In this study mortality was found to be 4.59 % and the risk factors identified were similar to other studies conducted in Pakistan and other third world countries. For the good management of patients and to decrease mortality it is suggested that awareness should be made in General practitioners, other health workers and general public for early referrals. Vaccination and malnutrition were major risk factors contributing to death effective strategies are recommended like community based health education campaigns.

Key Words: Mortality in Children, Risk factors, Nutritional status and immunization

INTRODUCTION

Since UNICEF was founded, there has been a major change in global mortality. By far the greatest emergency facing the world's children today is the silent emergency of frequent infections and wide spread under nutrition. No Major Emergency, such as famine, drought or flood has ever killed 280,000 children in a week¹. Yet that is what this silent emergency is now doing every week. More than 14 million children under five years of age die annually in third world². In Pakistan about 3.5 million children are born every year. There are over 20 million children below five year of age. They are very vulnerable to disease and death, contributing to almost half of the mortality and bearing 3/5th of morbidity load in the community³. In Pakistan, 78 infants out of 1,000 live births die every year while under-five mortality is 94 deaths per 1,000 live births⁴. Nearly 8 million children died in 2010 before reaching the age of 5, largely due to pneumonia, diarrhea and birth complications⁵. Mortality rate especially infant mortality rate (IMR) are useful indicators of population health. High infant mortality suggests poor socioeconomic status but more specific information is

needed as to leading causes and major risk factor involved. This information is essential for determining effective action and preventive measures. The present study was conducted with aim to determine the risk factors in relation with infant and child mortality in the developing country like Pakistan.

MATERIALS AND METHODS

This study was conducted over a period of one year from April 2010 to March 2011 in Department of Pediatrics Abbasi Shaheed Hospital Karachi. ASH is a tertiary care hospital. It was a descriptive study. The study has included infant and children who expired in pediatric ward during the study period. Sample technique was non probability convenience sampling. The Inclusion criteria was children from one month to fourteen years of age who were admitted through OPD or emergency in pediatric ward of ASH and expired during their stay in the ward during the study period of one year. Exclusion criteria includes children less than one month of age, children who were shifted to oncology ward and PICU and children suffering from gastroenteritis because children suffering from gastroenteritis are either treated in emergency or shifted

to Gastroenterology ward. In this study information regarding infant and children who died during the stay in ward were gathered. The detailed information was recorded on pre-designed proformas.

RESULTS

A total of 3420 children were admitted in pediatric ward of AbbasiShaheed Hospital Karachi. The children were between the ages of one month to thirteen years. 1789(47.7%) were male and 1631(52.3%) were female. 2451(74.3%) of the admitted patient were below the age of five years and only 879 (25.7%) were above the age of five years.

Among the children below the five years of age 899 (26.3%) children were one month to six month of age, 498(14.5%) were six month to one year of age and (37.1%) were one year to five year of age. Of these 3420 admitted patients 3198(93.5%) were discharged after treatment. 157(4.6%) patient expired during their stay in ward. The outcome of 65(1.9%) patients is not known as they left against medical advice.

Out of these 157 expired patients, 40 patients were between ages of one month to six months, 29 were between six months to twelve months of age, 71 were between one year to five years of age and 17 were above five years of age. Table 1

Among the 157 expired patients 85 (53.69%) were males and 72 (46.3%) were females with an overall male to female ratio of 1.2:1. It was observed that almost twice number of male children expired compared to female in the age group one to six months. Beyond that age period no noticeable difference in mortality could be observed between male and female children.

Majority 99 (63%) were brought to the children emergency in critical state. Of these 51 (52%) died within first 24 hours of their admission. 38 (39 %) patient expired between 1 to 7 days, while 10 (9%) had duration of hospitalization of more than seven days (Range 8 -30 days before death.)

Duration of illness prior to admission was prolonged in majority of the children. There were 107 (68.4) who had 3 to more than 30 days of illness. Only 50 (31.6%) had duration less than 48 hours before admission.

It was observed that 72 (46%) of the children were referred by general practitioners GP's. Other mode of referrals are shown in Table 3.

Mild to severe malnutrition was noted in 58.6% of the children who expired. Most of these children were below two years of age, indicating the malnutrition is an important risk factor, especially in children below two years of age.

Among the 58.6% malnourished children, 16.8 % had first degree, 21.4% had 2nd degree, while 61.4% were having in 3rd degree malnutrition.

Immunization status of 118 (75.3%) of 157 expired patients were either not immunized or had received only partial immunization. Only .8 % of children had vaccination record. Table 2

In this study it was noted that 65% of all deaths were due to infectious diseases namely diarrhea respiratory CNS measles and sepsis.

Respiratory tract were the leading cause of mortality in our study, the death figure being 45 Fig 1

CNS infection (Meningitis, Encephalitis and Tuberculosis - Meningitis) were second in the line killing 41 (20%) children. Among these CNS infections, meningitis took the lives of 24 patients. Encephalitis claimed 10 lives, while TBM was responsible for 7 deaths, Figure 1

Sepsis still remains one of the major causes of death especially in children below 6 months of age; it is responsible for killing 22 (11%) children, mostly below 6 months of age. Fig 1

Our evaluation revealed that out of 157 total death 12.7% were due to two major complications of measles that is, measles pneumonia and measles encephalitis, claiming 13 and 7 lives respectively. Fig 1

Eleven (3.8%) children died due to Hepatic disease Mortality in children due to accidental poisoning was 7 (3.5%) Kerosene oil poisoning was the commonest infant followed by insecticides.

Hence malnutrition, late referrals and non – immunization were observed as the most common risk factors in all those children who expired.

Table No. 1: Age and sex distribution of expired patient

Age (Months)	Male	Female	Total	M/F Ratio
1 – 6	26	14	40	1.8 : 1
7 – 12	16	13	29	1.2 : 1
13 – 59	37	34	71	1.0 : 1
More than 60 Months	9	8	17	1.1 : 1
Total	88	69	157	1.2: 1

Table No. 2: Immunization Status of Expired Children

Vaccination Status	Total	Percentages
Completely vaccinated	58	37 %
Unvaccinated	31	20 %
Partially Vaccinated	68	43 %
Total	157	100

Table No.3: Modes of Referral

Modes of Referral	Total Number of Patients	Percentages
Brought Directly to ASH	38	24 %
By General Practitioners	72	46 %
By other Hospital and Centers	29	18 %
Others (Hakims, Homopaths, etc)	18	12 %
Total	157	100

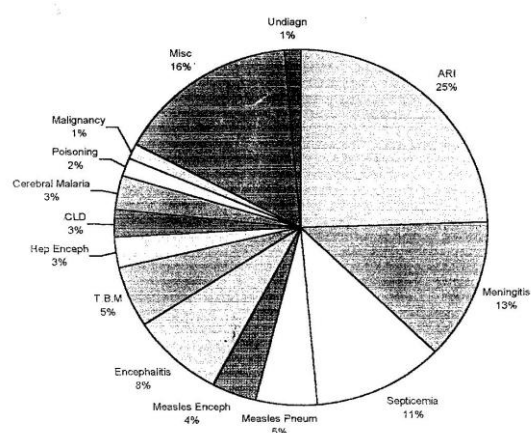


Figure No.1: Frequency of different diseases

DISCUSSION

In this study 157 number of patients expired during one year duration and the total number of admitted patients were 3420 accounting for a total mortality of 4.56%. Other studies which were conducted in Pakistan and in other South East Asian countries were high compared to this study. A study conducted in civil hospital where Mehnaz and Billoo found mortality of 16 %⁶. The logical reason for high mortality in other studies could be the inclusion of neonates and diarrheal mortality which were not included in our study.

High mortality was observed in children who were below five years of age. These findings are consistent with majority of studies conducted in developing countries⁷.

A survey was conducted by World Fertility Survey in 29 countries and they found most of the children died before reaching five years of age especially in countries like Pakistan, Nepal and Bangladesh⁸.

A male to female ratio of 1.2 : 1 was found in this study. WHO states that in most populations, female infants have lower mortality than their counterparts⁹.

This is in contrast to a study published in India. Khanna R, Kumar and Pulyel noted that mean infant mortality was 1.3 times higher in females than in males¹⁰.

Khalique N, Sinha SN, Yunus N and Malik AE. Reported similar result¹¹.

The study shows that acute respiratory tract infection was the leading cause of death in infants and children. About 25% patients expired due to respiratory infections.

A study conducted in Pakistan shows ARI was the leading cause of mortality among children.¹²

Khan M, A Rehman, G N and Qaazi S. A reported similar results¹³. Robert M. Douglas and Rennie M. Dsouza, also reported that acute respiratory infections are the leading cause of death in countries where mortality is high¹⁴.

ARI mainly pneumonia accounts for more than 18% of deaths in developing countries^{15,16}.

WHO reports that ARI kill more children under five than any other infectious disease accounting for almost 2 million deaths a year among this age group¹⁷.

In 80% to 90% of cases the problem is bacterial pneumonia which can be controlled by proper use of antibiotics. Parents can be educated to recognize the first danger signs, and community health workers can be trained to diagnose pneumonia, prescribing correct antibiotics and early referrals. In addition about 20% of acute respiratory infections could still be prevented by immunization¹⁸.

CNS infections are also one of the leading causes of mortality after ARI. CNS infections were the second main cause of mortality after ARI. Trevor Duke reported an incidence of 38 to 110 cases each year per 100,000 of population age less than five years and case fatality of 22% to 45¹⁹.

In this study sepsis took the life of 11% children, most children were between one to six months of age.

Today more than 200,000 cases of sepsis occur in United States with a mortality ranging 20 to 50% each year²⁰.

Most of us are aware of the risk posed by measles to children's health. In this study majority of children who were suffering from measles die due to measles pneumonia.

Iqbal H and Jamil T from Lahore reported 18 % mortality from measles complications, in which respiratory complications were the most common^{19,21}.

Some important observations regarding measles were noted. First, that most cases of measles were reported during the first three months i.e. from January to March. The second, that most of children who were admitted with the diagnosis of measles were vaccinated. Salahudin, Qadir M and Shah MZ also reported higher incidence of measles in winter as compared to summer¹⁹.

Poisoning although accidental, but still important cause mortality in children. In this study poisoning contributes for about 3% of mortality.

Kerosene oil poisoning was on the top followed by organophosphate poisoning but most children expired due to organophosphate poisoning.

Baloch GR, Hussain W, Malik A and Haider A in a study from Shikhan Zayed Hospital reported 8% mortality²².

Malnutrition is a major problem in children, especially of the third world. In this study 58% children were having some degree of malnutrition.

Of the nearly 12 million children under five who die each year in developing countries mainly from preventable causes, the death of over 6 million or 55% are either directly or indirectly attributable to malnutrition²³.

A study conducted in Lahore by M. Akbar²⁴ which showed more than 60% children were malnourished who expired during their study.

Delay in seeking early medical care is an important detrimental factor resulting in high mortality. It is suggested that awareness should be created among general public so they can use simple and effective e

treatments for minor illness, seek care early and to persist with treatment.

Around 2.5 million under-five deaths are averted annually by immunization against diphtheria, pertussis and tetanus (DPT) and measles²⁵.

In 2010, over 19 million children did not get all three primary doses of DPT vaccination.²⁵

All the health workers in developing countries are aware of the importance of immunization. So it is emphasized to improve immunization status of children through EPI programme.

CONCLUSION

In this study mortality was found to be 4.59% and the risk factors identified were similar to other studies conducted in Pakistan and other third world countries. For the good management of patients and to decrease mortality it is suggested that awareness should be made in general public. General practitioners and other health workers should be trained for correct diagnosis, proper treatment and early referrals.

Vaccination and malnutrition were major risk factors contributing to death effective strategies are recommended like community based health education campaigns.

To reduce the mortality we third world countries have to follow the simple inexpensive, and acceptable methods, the European countries have adopted 50 years ago and achieve sticking decreases in their mortality.

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Practices and Perceptions of Dental Surgeons to Patients on Blood Thinners

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ABSTRACT

Objective: This article focuses on the mixed perceptions of the dentists in treating patients on blood thinners and the awareness amongst them regarding protocol and management of such patients.

Study Design: Cross-sectional descriptive and analytical study

Place and Duration of Study: This study was conducted at Jinnah Medical and Dental College from August 2013 to December 2013. The data was collected from three dental colleges of Karachi.

Material and Methods: The study was conducted at Jinnah Medical and Dental College. A 17-item questionnaire was used to collect the data. The data was collected from three dental colleges of Karachi to evaluate the dentist's perception and protocols put into practice related to patients on blood thinners. The study included 92 dentists. The data was stored in excel worksheet and was analyzed using SPSS.

Results: Amongst the 92 dental practitioners evaluated in the research 50% advised their patients to stop antiplatelet therapy prior to a dental procedure. 64.13% of the dentists were of the opinion that antiplatelet therapy be stopped before performing any treatment 94.56% of the dentists said they are aware of the reasons why patients are kept on anticoagulant drugs. Based on the data collected 67.39% of the dental practitioners delayed the treatment for patients taking blood thinners 95.65% referred the patients to their cardiologist prior to an invasive treatment. The optimal range of INR was known by 84.78% of practitioners.

Conclusion: Dental practitioners in this study population display a wide range of practice in their approach to patients on blood thinners. A trend towards overly conservative management is seen in the former. In contrast, the approach to the patients appeared to be haphazard, with about 20% of those never checking the INR pre-operatively. There is a clear need for greater awareness of an evidence-based approach to the dental management of this unique patient group to avoid unnecessary and preventable complications. There is an acute need for creating awareness and adherence to the new guidelines for safe and effective practice.

Key Words: Blood thinners, Latest guidelines, Dental management.

INTRODUCTION

Blood Thinners are being widely prescribed for various medical conditions such as atrial fibrillation, multiple venous thromboembolism and other valvular-dysfunctions, such patients undergo dental procedures in a routine.¹ Although bleeding or hemorrhage can occur in such patients there still remains controversy regarding the anticoagulation protocol that should be followed when considering patients who have to undergo extensive dental treatment.^{2,3}

A group of dentists believe that the anticoagulation protocol should not be altered while others are of the opinion that anticoagulation therapy should be stopped for some period of time before any surgical procedure be carried out.⁴ Currently it remains a question whether the dental treatment should be carried out whilst the patient is on anticoagulation therapy or should it be stopped prior to a dental invasive procedure.⁵

This article focuses on the mixed perceptions of the dentists in treating patients on blood thinners and the awareness amongst them regarding protocol and management of such patients.

MATERIALS AND METHODS

The study was conducted at Jinnah Medical and Dental College. A 17-item questionnaire was used to collect the

data. The data was collected from three dental colleges of Karachi to evaluate the dentist's perception and protocols put into practice related to patients on blood thinners. The study included 92 dentists. The data was stored in excel worksheet and was analyzed using SPSS.

RESULTS

Amongst the 92 dental practitioners evaluated in the research 45.65% of them were into dental practice for less than 3 years while the other 23.91 % had been working for less than 5 years, 15.21% for more than 5 years and 13% percent for more than 10 years. 31.52% of them belong to the operative/endodontics specialty and the same ratio of general practitioners while 7.60% ,6.52% 2.17% and 8.69% belong to orthodontics, prosthodontics, periodontology and surgery respectively. Amongst the 92 dental practitioners that were evaluated 50% advised their patients to stop antiplatelet therapy prior to a dental procedure. 64.13% of the dentists were of opinion that antiplatelet therapy be stopped before performing any treatment that comes under surgery e.g. extractions, while 1.08% and 2.17% of the dentists recommend that the therapy be stopped before any treatment involving operative and periodontal problems respectively. None of the dentist was of the opinion of stopping an antiplatelet therapy prior to orthodontic or prosthodontic treatment.

94.56% of the dentists said they are aware of the reasons why patients are kept on anticoagulant drugs. Based on the data collected 67.39% of the dental practitioners delayed the treatment for patients taking blood thinners while the remaining 29.34% did not delay any treatment amongst them 95.65% referred the patients to their cardiologist for a consent prior to an invasive treatment. 95.65 % of the dentists were aware of the consequences of stopping an antiplatelet therapy, 93.47% had knowledge about the precautions taken while treating patients on blood thinners. Amongst these dentists 42.39% of them had encountered patients with severe bleeding. The optimal range of INR was known by 84.78% of practitioners. 35.86% of the dentist say that bleeding is best managed by pressure pack, 29.34% think it is managed best by sutures, Surgicel (7.60%), transamine (20.65%), electrocautery (3.25%) & FFPs (1.08%). A high ratio 80 % of dentists encounter patients who are hypertensive or have

coronary artery disease while only a few 15.21% do not experience patients with similar conditions.

Table No.1: Recommendations for the management of patients on anti-platelet agents.

Patients on a single anti-platelet agent

Do not stop for dental procedures

Patients on concurrent aspirin and dipyridamole

Do not stop for dental procedures

Patients on concurrent aspirin and clopidogrel

Consult with the patient's cardiologist

Patient may need referral to the dental hospital for the invasive dental procedure

Adapted from: **Randall, C., (ed.).** Surgical management of the primary care dental patient on antiplatelet medication. 2007. A guideline revision is due in late 2009 and will be available at:

<http://www.ukmi.nhs.uk/activities/specialistServices>

Table No.2: Percentage wise opinion of dentists about different dental problems

No	Question	Result	
1	Do you advise to stop antiplatelet drugs before a dental treatment?	Yes	No
		50%	50%
2	If yes which dental treatment / s will require stopping antiplatelet therapy a) Oral surgery b) Operative dentistry c) Periodontics d) Endodontic e) Orthodontic f) Prosthodontic	a) 64.13% c) 2.17% e) 0%	b) 1.08% d) 0% f) 0%
3	Are you aware of reasons for antiplatelet therapy?	Yes	No
		94.56%	5.43%
4	Do you know any common blood thinners?	Yes	No
		100%	0%
5	According to you should treatment be delayed for patients receiving antiplatelet therapy?	Yes	No
		67.39%	29.34%
6	Is it important to consult a cardiologist before interrupting antiplatelet medication(s)?	Yes	No
		95.65%	4.34%
7	Do you know the consequences of interrupting treatment with blood thinners?	Yes	No
		95.65%	3.26%
8	Are you familiar with the precautions taken while treating patient receiving antiplatelet therapy?	Yes	No
		93.47%	5.43%
9	Have you ever encountered a patient with severe bleeding during dental treatment, who was under antiplatelet therapy?	Yes	No
		42.39%	56.52%
10	Do you know the optimal INR for Dental surgical procedures?	Yes	No
		84.78%	14.13 %
11	Post -op bleeding in a patient taking anti-platelet therapy is best managed by a) pressure pack b) sutures c) surgicel d) transamine e) electrocautery f) FFPs	a) 35.86% c) 7.60% e) 3.26%	b) 29.34% d) 20.65% f) 1.08%
12	Do you usually experience patients taking blood thinners who are hypertensive or have any coronary artery disease?	Yes	No
		80.43%	15.21%
13	How long have you been into dental practice? a) <3yrs b) <5yrs c) >5yrs d) >10yrs	a) 45.65% c) 15.21%	b) 23.91% d) 13.04%
14	What is your specialty? a) operative / endo b) G.P c) orthodontics d) prosthodontics e) periodontics f) oral surgery	a) 31.52% c) 7.60% e) 2.17%	b) 31.52% d) 6.52% f) 8.69%
15	The best remedy usually adopted for managing post dental treatment bleeding at home a) pressure pack b) applying ice c) biting on teabag d) eating ice-cream	a) 50% c) 19.56%	b) 10.86% d) 14.13%
16	For how long will you stop the antiplatelet therapy prior treatment a) 2days b) 3days c) 4days d) 5days e) 6days f) 7days	a) 21.17% c) 2.17% e) 2.17%	b) 23.91% d) 9.78% f) 8.69%
17	Do you know normal values of CT, BT, PT and INR	Yes	No
		82.60%	17.39%

78.26% of the practitioners said that patients undergoing antiplatelet therapy are best managed at hospital. Dentist who believe that the antiplatelet therapy should be stopped for 2 days are 27.17% while 23.91%, 2.17%, 9.78%, 2.17% 8.69% advice that the antiplatelet therapy should be discontinued for 3, 4, 5, 6 and 7 days respectively prior to an invasive dental procedure. Results are shown in table 2.

DISCUSSION

Every year it is estimated that about 800,000 people worldwide undergo a non-surgical coronary artery interventional procedure and most patients with stents are maintained on an anti-platelet regimen.⁶ It is therefore extremely likely that dental practitioners will encounter these patients on a regular basis. The management of patients on anti-platelet agents dental care may be both inappropriate and inconsistent, as demonstrated by our limited study. The majority of respondents prefer to stop patients' anti-platelet agents prior to extraction. This practice is at variance with the current literature, which argues that the interruption of therapy may expose such patients to an increased risk of developing adverse cardiovascular events.⁷

This study showed that of those dentists who stop anti-platelet agents, 95% do so in conjunction with the patient's medical practitioner. It is proposed that the study population's practice of withdrawing therapy is based on evidence other than current guidelines from the dental literature. Furthermore, the practice of withholding anti-platelet agents in the post-operative period has no foundation in the current literature and should be strongly discouraged.⁸

Recommendations for the management of dental patients on anti-platelet agents are seen in Table 1. In 2007, the British Committee for Standards in Haematology (BCSH) Task Force on Haemostasis and Thrombosis, together with the British Dental Association and the National Patient Safety Agency, developed evidence-based guidelines for managing patients on warfarin.⁹

The guidelines clearly state that the risk of significant bleeding in patients taking warfarin and with a stable INR of <4 is very small. The guidelines stress that the risk of thrombosis may be increased in patients whose warfarin is stopped prior to dental surgery. Indeed, fatalities due to thrombo-embolic events have been documented as a result of stopping warfarin prior to invasive dental surgery.¹⁰ The guidelines unambiguously state that the patient should have his or her INR measured within the 72 hours preceding the procedure and ideally within 24 hours.¹¹

This study revealed that this guideline was not adhered to by 20% of respondents. This study had several weaknesses. One was the small sample size, which

always limits the value of reporting the means in a descriptive analysis.

CONCLUSION

Dental practitioners in this study population display a wide range of practice in their approach to patients on blood thinners. A trend towards overly conservative management is seen in the former. In contrast, the approach to the patients appeared to be haphazard, with about 20% of those never checking the INR pre-operatively. There is a clear need for greater awareness of an evidence-based approach to the dental management of this unique patient group to avoid unnecessary and preventable complications. There is an acute need for creating awareness and adherence to the new guideline for safe and effective practice.

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Effect of H Pylori on Iron and Serum Ferritin

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ABSTRACT

Background: *Helicobacter pylori* produce gastric inflammation and interfere with iron by producing extragastric complications. The deficiency of iron in patients with gastritis or peptic ulcer leads to iron deficiency anemia.

Objective: The objective of this study was to elucidate the effects of *Helicobacter pylori* infection on red serum iron and ferritin levels.

Study Design: Cross sectional analytical study

Place and Duration of Study: This study was conducted at the University of Health Sciences, Lahore from March 2009 to September 2009.

Materials and Methods: A total number of 90 subjects were included in the study. They were divided into group A (30 subjects with gastric symptoms and *H. pylori* infection), group B (30 subjects with gastric symptoms but without *H. pylori* infection), and group C (30 normal healthy age and sex matched subjects). *H. pylori* infection was considered positive on the basis of positive serology, rapid urease test and histopathological examination. Serum ferritin was estimated by chemiluminescence technique while serum iron was measured by endpoint colorimetric method.

Results: The results of this study did not show any significant effect on serum ferritin and serum iron (p value > 0.05) within the individual groups nor when compared with each other.

Conclusion: *H. pylori* infection did not affect the serum ferritin and serum iron levels.

Key Words: Ferritin, Iron, *Helicobacter Pylori*

INTRODUCTION

Many studies in the late 19th and in the early years of 20th century revealed the presence of *Helicobacter pylori* in the animal gastric mucosa. Later, it was identified and isolated by doing culture from the human gastric mucosa by Warren and Marshall in 1982 and upon this historic discovery; they were awarded Nobel Prize in Physiology/Medicine in 2005.¹ *Helicobacter pylori* are a spiral shaped microaerophilic gram negative bacteria. *Helicobacter pylori* are about 3 μ m in length and 0.5 μ m in diameter. *Helicobacter pylori* have the capability that it can change its shape from spiral to non-culturable form, i.e. coccoid.² Human stomach is reported to be the primary reservoir for *Helicobacter pylori*. In the human stomach, *Helicobacter pylori* are usually found in the gastric antrum. Greatest amount of the bacterium is reported under the mucus layer in gastric pits where it is reported to bind with Lewis b antigen on the surface of gastric epithelial cells with the help of Bab A adhesion molecules.^{3,4} After ingestion, *Helicobacter pylori* first reside in the stomach by neutralizing the gastric acidity. For neutralization, *Helicobacter pylori* secretes urease enzyme that produces ammonia from urea present in the stomach lumen by the process of hydrolysis. Ammonia being alkaline in nature neutralizes the gastric acidity.⁵⁻⁷ *Helicobacter pylori* produces gastric diseases by secreting Cag A and Vac A toxins.⁸ *Helicobacter pylori* associated gastritis is reported to result in many extra

gastric complications like iron deficiency and iron deficiency anemia, vitamin B₁₂ deficiency and megaloblastic anemia, and ischemic heart disease.⁹ The exact mechanism of iron deficiency and anemia due to iron deficiency is not clear. The proposed mechanisms are that *H. pylori* first produces alkaline media in the stomach by secreting urease enzyme that neutralizes gastric acidity by producing ammonia, thus decreasing the gastric power to dissolve the dietary content of iron.^{10, 11} Second, *H. pylori* decreases the vitamin C content of the gastric juice which is required for the formation of soluble complexes with iron, and also required as a cofactor for the reduction of ferric to ferrous form.¹² Third, it utilizes dietary iron for its own use.¹³ The present study is planned to see the effects of *H. pylori* on iron physiology as literature reveals controversial picture.

MATERIALS AND METHODS

It was a cross sectional analytical study conducted at the University of Health Sciences, Lahore. Subjects with *Helicobacter pylori* infection and subjects having gastric symptoms only were selected from the Services Hospital, Lahore. Ninety subjects including both male and female were selected for the study. The subjects were between 15-60 years of age. Subjects were divided into three groups. Group 1 was comprised of thirty subjects with *Helicobacter pylori* infection. Group 2 was composed of thirty subjects with history of gastric symptoms without *Helicobacter pylori*

infection. In the group 3, age and sex matched healthy subjects without gastric symptoms and *Helicobacter pylori* infection were included.

An informed consent was taken from all the subjects after explaining the study purpose and procedure. Detailed clinical history was obtained from all the subjects. Diagnosis of *Helicobacter pylori* infection was made by performing ELISA for *H. pylori* IgG antibodies, rapid urease test and histopathological examination.

5 milliliter of blood was taken in a plain tube and was centrifuged at 5000 rpm for 10 minutes. Serum was separated and stored at -80 °C for estimation of serum *H. pylori* IgG antibodies, serum ferritin and serum iron. Serum ferritin was estimated by chemiluminescence technique. Serum ferritin kit by Ortho-Clinical Diagnostics (Lot no. 1070) was used. Serum iron was measured by endpoint colorimetric method. The kit used for the measurement of iron was manufactured by Randox Laboratories Ltd., Ardmore, Diamond Road, Crumlin, Co. Antrim, United Kingdom (Cat No. S1257).

Statistical Analysis: The data was analyzed using SPSS 16.0. Mean $\pm$ SD are given for quantitative variables. Frequencies, percentages and graphs are given for qualitative variables. Arithmetic mean and standard deviation of all the quantitative variables like iron and ferritin was determined.

Two –Independent sample t-test was applied to observe group-mean differences between two groups (males and females in each group like A, B and C).

One way ANOVA was applied to determine the difference between groups and association between qualitative variables. The p value of less than 0.05 was considered statistically significant.

RESULTS

The age of subjects was found to be 32.87 ± 12.31 years in group A, 33.27 ± 11.64 years in group B, and 33.60 ± 11.12 years in group C. The difference of Mean $\pm$ SD age in three groups was non-significant ($p > 0.05$; Table 1).

There was no significant difference in serum iron concentration between males (116.1 ± 87.8 $\mu\text{g/dl}$) and females (95.9 ± 58.8 $\mu\text{g/dl}$) in group A. The serum ferritin values in males (64.4 ± 55.3 ng/ml) and females (63.8 ± 36.6 ng/ml) of group A were significantly not different ($p > 0.05$; Table 2).

There was no significant difference in serum iron concentration between males (88.0 ± 44.3 $\mu\text{g/dl}$) and females (84.4 ± 51.7 $\mu\text{g/dl}$) in group B. The serum ferritin values in males (63.6 ± 49.0 ng/ml) and females (59.8 ± 33.9 ng/ml) of group B were significantly not different ($p > 0.05$; Table 3).

No significant difference in serum iron concentration between males (112.1 ± 38.8 $\mu\text{g/dl}$) and females (106.9 ± 62.6 $\mu\text{g/dl}$) was found in group C. The serum ferritin

values in males (62.4 ± 22.7 ng/ml) and females (59.3 ± 33.2 ng/ml) of group C were significantly not different ($p > 0.05$; Table 4).

The difference in serum iron concentration (Fig. 1) between groups A (102.04 ± 87.81 $\mu\text{g/dl}$), group B (104.91 ± 34.93 $\mu\text{g/dl}$), and group C (108.93 ± 52.13 $\mu\text{g/dl}$) was not significant ($p > 0.05$). The serum ferritin values in group A (65.13 ± 48.03 ng/ml), group B (60.55 ± 42.07 ng/ml), and group C (68.96 ± 18.44 ng/ml) were significantly not different ($p > 0.05$; Fig. 2).

Table No.1: Age distribution of subjects in groups A, B and C

Parameter	Group A (n=30) (H.pylori +ve patients)	Group B (n=30) (H.pylori -ve patients)	Group C (n=30) (Healthy control)
Age (Years)	32.9 ± 12.3	33.3 ± 11.6	33.6 ± 11.1

The values are as Mean $\pm$ SD and statistically non significant

Table No.2 Comparison of serum ferritin and serum iron between males and females in group A

Parameter	Male (n=18)	Female (n=12)	p value
Serum ferritin (ng/ml)	64.4 ± 55.3	63.8 ± 36.6	0.92*
Serum iron ($\mu\text{g/dl}$)	116.1 ± 87.8	95.9 ± 58.8	0.27*

The values are as Mean $\pm$ SD

* The values are statistically non significant

Table No.3: Comparison of serum ferritin and serum iron between males and females in group B

Parameter	Male (n=16)	Female (n=14)	p value
Serum ferritin (ng/ml)	63.6 ± 49.0	59.8 ± 33.9	0.67*
Serum iron ($\mu\text{g/dl}$)	88.0 ± 44.3	84.4 ± 51.7	0.71*

The values are as Mean $\pm$ SD

* The values are statistically non significant

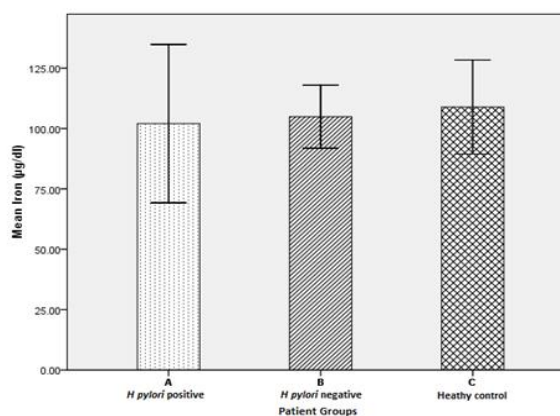


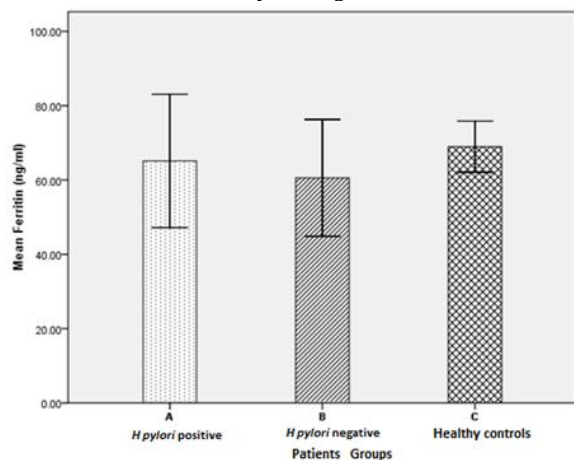
Figure No.1: Serum iron in groups A, B and C

Table No.4: Comparison of serum ferritin and serum iron between males and females in group C

Parameter	Male (n =14)	Female (n = 16)	p value
Serum ferritin (ng/ml)	62.4 ± 22.7	59.3 ± 33.2	0.47*
Serum iron (µg/dl)	112.1± 38.8	106.9± 62.6	0.82*

The values are as Mean ± SD

* The values are statistically non significant

**Figure No..2 Serum ferritin in groups A, B and C**

DISCUSSION

Literature review shows controversial picture about the association of *Helicobacter pylori* infection and iron deficiency anemia. A study carried out in the United States has revealed the association of *Helicobacter pylori* infection with iron deficiency both in the presence or absence of peptic ulcer disease.¹⁴ It has been also reported that iron deficiency anemia in patients with asymptomatic gastritis was corrected successfully when they were given eradication therapy for *Helicobacter pylori*.¹⁵ A study carried out in Turkish subjects also showed association of iron deficiency with *Helicobacter pylori* infection.¹⁶ Another study conducted in Korean children had documented decreased serum ferritin levels in patients with *Helicobacter pylori* infection.¹⁷ Low hemoglobin, ferritin, and B₁₂ levels with *Helicobacter pylori* infection also have been reported in Pakistani population.¹⁸

While on the other hand, no anemia or iron deficiency was revealed in *Helicobacter pylori* infected patients.¹⁹ In the same way, a large sample survey conducted in Denmark revealed only iron deficiency but no effect on the hemoglobin; mean corpuscular volume that could indicate iron deficiency anemia.²⁰ All the parameters of iron deficiency anemia like hemoglobin and mean corpuscular volume showed improvement after eradication therapy for *Helicobacter pylori* infection except the serum ferritin levels.²¹ Asymptomatic *Helicobacter pylori* infection was not found to be

associated with anemia or iron deficiency.²² No significant difference was observed in hemodialysis patients with or without *Helicobacter pylori* infection regarding iron deficiency anemia.²³ Our findings coincide with recently published studies. This study did not show any association of *Helicobacter pylori* infection with ferritin, transferrin receptors, and hemoglobin in these Latin American countries.²⁴ In a low socioeconomic country like Bangladesh, *Helicobacter pylori* infection was not proved as a cause of neither iron deficiency anemia nor resulted in failure to iron therapy or supplementation in young children.²⁵ In older subjects living either at home or in nursing homes, no association was observed between *Helicobacter pylori* infection and low serum iron, ferritin, transferrin, vitamin B₁₂ level.²⁶ Similarly, no association was observed between *Helicobacter pylori* infection and hemoglobin level in *Helicobacter pylori* positive and negative groups.²⁷ In children of Alaska, no difference was found between the patients and control subjects and eradication therapy for *Helicobacter pylori* infection failed to resolve iron deficiency anemia and isolated iron deficiency in a subset of 219 children.²⁸

CONCLUSION

This study concludes that *Helicobacter pylori* has no significant effect on serum iron, and serum ferritin levels.

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Frequency of Urinary Symptoms in Post Menopausal Women with Uterovaginal Prolapse

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ABSTRACT

Objective: To determine the frequency of urinary symptoms in postmenopausal women with Uterovaginal Prolapse

Study Design: Descriptive study

Place and Duration of Study: This study was conducted in Department of Obstetrics & Gynecology Unit II, Dow University of Health Sciences & Civil Hospital Karachi Pakistan from July 2006 to June 2007/

Materials and Methods: 60 (sixty) Consecutive pts were included in the study through structural Proforma from the outpatient, ward or emergency. Informed consent was obtained. A detailed history and related examinations and investigations were done. These include Urine DR, Urine C/S and Urodynamics like cystometry in selected patients.

Results: Majority of Women found have symptoms were at the age of 60 yr (36.66%) While urinary symptoms less seen at the age of 80 yr (6.66%) while Parity 6-10 was higher in Postmenopausal women to have urinary symptoms (63.33%). The urinary symptoms found in Postmenopausal women were frequent urine passing (33.33%), Nocturia (83.33%), Retention of urine (20.0%), Dysuria (26.66%), Voiding difficulty (53.35%), Urge incontinence (20.0%) and Stress incontinence (53.33%).

Conclusion: Pelvic organ Prolapse and urinary symptoms like incontinence are prevalent in older women and are associated with age. Large studies are required to assess the relationship of urinary symptoms with Uterovaginal Prolapse. Because these urinary symptoms effect over quality of life of women so it is recommended to reduce genital prolapsed and associated urinary symptoms by implementing some measures such as health education of women and weight control.

Key Words: Postmenopausal, Uterovaginal Prolapse, urinary symptoms

INTRODUCTION

Urogenital Prolapse also called Pelvic Organ Prolapse (POP), is the downward descent of the pelvic organs (bladder, uterus and rectum) that results in their protrusion through the vagina¹.

Urogenital prolapse occurs when there is a weakness in the supporting structures of the pelvic floor allowing the pelvic viscera to descend and ultimately fall through the anatomical defect, while usually not life threatening prolapsed is often symptomatic and is associated with a deterioration in quality of life and may be the cause of bladder and bowel dysfunction².

In a healthy women in whom the levator ani has normal tone and the vagina has adequate depth, the upper vagina lies nearly horizontal when she is upright. The result in a 'flap valve' in which the upper vagina presses against the levator plate when there is an increase in intra abdominal pressure, when the levator ani loses tone, it moves from a horizontal to a semi-vertical position, creating a widened genital hiatus (i.e the distance between the external urethral meatus and the posterior midline hymen) that forces the pelvic structures to rely on connective tissue for support, when the connective tissue support also fails, as a result of

possible collagen decrease and tearing, prolapse may occur¹.

The female genital organ are maintained in their normal anatomical position by a number of fascia condensation (endo pelvic fascia) referred to as ligaments, especially the transverse cervical (cardinal) and uterosacral ligaments, weakness in any of these supportive structures leads to uterine descent, particularly around the period of menopause when oestrogen withdrawal causes a second insult to the integrity of the pelvic supports already weakened by repeated vaginal deliveries. Hence child birth and ageing constitute the most important associated factors of female genital prolapse³.

The true incidence is uncertain due to the fact that a number of women with Uterovaginal prolapse may not present for management due to the privacy attached to the affection of the sexual / reproductive organs coupled with the stigmatization accorded associated clinical entities such as urinary and fecal incontinence. However, existing data suggest that about 50% of parous women suffer some form of genital tract prolapse and only 10-20% of them seek medical care⁴. Though not a life threatening condition it is a source of severe morbidity and psychological upheaval to the patient who is often socially withdrawn and

stigmatized. It is one of the common indications for major pelvic reconstructive gynecological surgeries, only recently, the World Health Organization (WHO) alerted all nations including developing countries of the need for greater recognition of the health of ageing women, since the number of ageing women appear to be increasing in proportion to the increasing life expectancy of each population⁴.

In the Women's Health Initiative Study, investigators found a 41.1% prevalence of pelvic organ prolapse at a standard physical assessment in postmenopausal women older than 60 yrs who had not had a hysterectomy. Poor conduct of labour, as in bearing down before full cervical dilatation, prolonged traction from high forceps delivery, and downward pressure on the fundus during attempts to deliver the placenta (Crede's manoeuvre) are all obstetric factors which predispose to U V prolapse. It is also common in conditions of chronically raised intra abdominal pressure which include COAD (Chronic Obstructive Airway disease), obesity, abdominal tumour, straining during defaecation and heavy physical exertion. Very rarely it could be due to the congenital weakness of the pelvic floor muscles (as in Spina bifida) joint hypermobility (as in connective tissue abnormalities) and altered collagen metabolism³.

The process of ageing can result in loss collagen, weakness of fascia and connective tissue.

These effects are noted particularly of during the postmenopause as a consequence of oestrogen deficiency. Women usually present with non specific & specific symptoms. The non specific symptoms are lump, local discomfort, backache, bleeding / infection if ulcerated, dyspareunia or apareunia, rarely in extremely severe cystourethrocele, uv prolapsed or vault prolapse, renal failure may occur as a result of ureteric kinking. While the specific symptoms are in case of cystourethrocele, urinary frequency and urgency, voiding difficulty, UTI and stress incontinence⁵.

The urinary incontinence can be categorized into 4 main types: Stress, Urge, Overflow and Functional incontinence, although most patients present with a mixed picture. Urinary Incontinence can restrict the social, family, professional and sexual activities of women and lower their quality of life by generating social isolation and emotional stress, often combined with a feeling of inferiority and depression. Along with these physical and social consequences, there is also a financial burden which is substantial and growing⁶.

Urinary urge incontinence and overactive bladder in age related and its prevalence rate is found to be similar among western and asian women. Stress and urge urinary incontinence are common in postmenopausal women and have different risk factors suggesting that approaches to risk factors modification and prevention might differ and should be specific to types of

incontinence. There is a special need for conducting studies among our population as risk factors for incontinence such as grand multiparity and obesity are common in our community. Urinary frequency and incontinence also have religious significance for our population. According to Islamic tradition, women must wash after every void or episode of urine leakage. This can be very troublesome at the time of Hajj or pilgrimage when frequent prayers are performed⁷.

The global prevalence of urinary incontinence is about 49% for stress urinary incontinence, 22% for urge urinary incontinence and 29% mixed incontinence. Urinary urge incontinence and overactive bladder is age related while stress and urge urinary incontinence is common in postmenopausal women⁸.

Approximately 1 in 3 women over the age of 65 yr have some degree of incontinence. By the age of 80 yrs 15% to 40% of community dwelling elderly have experienced incontinence⁷.

It is estimated that 50% to 70% of incontinence persons do not seek help for their problems and in a survey of Primary Care Physicians most enquired about incontinence in 25% or fewer of their patients. For these reasons, it is essential that questions about incontinence be included in the routine assessment of every older patient⁹.

Despite the high prevalence of urinary symptoms in the elderly and its profound impact on quality of life, these urinary symptoms continues to be under reported and under diagnosed due to reluctance of pts as well as providers to have the false belief that it is an unavoidable consequence of aging.

The aim of our study is to determine the frequency of urinary symptoms in postmenopausal women with Uterovaginal prolapse.

MATERIALS AND METHODS

The study was carried out in the department of obstetrics and Gynecology unit II, Dow University of Health Sciences and Civil Hospital Karachi Pakistan. This was a Descriptive Study from July 2006 to January 2007. Sixty patients were included in the study through structured proforma by purposive sampling technique from the outpatient, ward or emergency. Informed consent was obtained. The inclusion criteria were patients with all degree of uterovaginal prolapse, postmenopausal women, married & unmarried women. Inclusion criteria were women with diagnosed renal pathology, recurrent UTI, pregnant women and medical disorder such as Diabetes Mellitus.

A detailed history and related examination and investigations were done. These include urine DR, Urine C/S, and urodynamics like cystometry in selected patients. (Frequency was defined as the passage of urine seven or more times a day, or being awoken from sleep more than once a night to void which is also known as Nocturia. Urgency means a sudden desire to

void, while dysuria defined as urethral pain during micturation. Retention of urine means failure to empty the bladder totally. Voiding problems include hesitancy, a poor stream straining to void incomplete bladder and also frequency, urgency and dysuria. Stress incontinence means loss of urine on physical effort which urgeincontinence is an involuntary loss of urine associated with a strong desire to void).

RESULTS

In this study the frequency of urinary symptoms found in postmenopausal women were like frequent urine passing (33.33%), Nocturia (83.33%), Retention of urine (20.0%), Dysuria (26.66%), Voiding difficulty (53.33%), Urge incontinence(20.0%), while stress incontinence (53.33%).

Table No.1: Clinical presentations / symptoms of Pt: in frequency of urinary symptoms in postmenopausal women with uv prolapse

Table No 1 A N=60				
Symptoms	YES	%	NO	%
Frequent urine Passing	20	33.33%	40	66.66%

Table No 1 B N=60				
Symptoms	YES	%	NO	%
Nocturia	50	83.33%	10	16.66%

Table No 1 C N=60				
Symptoms	YES	%	NO	%
Retention of urine	12	20%	48	80%

Table No 1 D N=60				
Symptoms	YES	%	NO	%
Dysuria	16	26.66%	44	73.33%

Table No 1 E N=60				
Symptoms	YES	%	NO	%
voiding difficulty	32	53.35%	28	46.66%

Table No 1 F N=120				
Incontinence of urine	Yes	%	No	%
Urge incontinence	12	20%	48	80%
Stress incontinence	32	53.33%	28	46.66%

Table No.2: Age Distribution n=60

Age (yr)	Frequency	Percentage
40	2.0	3.33%
45	4	6.66%
50	12	20.00%
55	6	10.00%
60	22	36.66%
65	2	3.33%
70	6	10.00%
75	2	3.33%
80	4	6.66%

Majority of women found have symptoms were at the age of 60 yr (i.e 36.66%) while urinary symptoms less seen at the age of 40 yr (i.e 3.33%) and the age of 80 yr (6.66%), while Parity 6-10 was higher in postmenopausal women to have urinary symptoms (i.e 63.33%).

Table No.3: Parity n=60

Parity	Frequency	Percentage
0-1	0	0%
2-5	22	36.66%
6-10.	38	63.33%

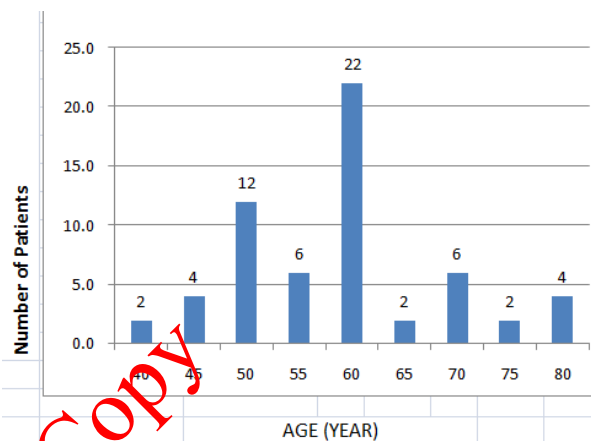


Figure No.1: Age Distribution: Frequency of urinary symptoms in post menopausal women with uv prolapse N=60

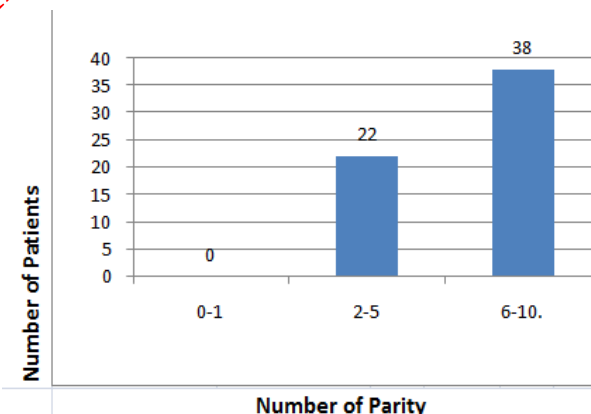


Figure No.2: Frequency of urinary symptoms in post menopausal women with uv prolapse to parity N=60

DISCUSSION

Menopause is the permanent cessation of menstruation resulting from the loss of ovarian and follicular activity. It usually occurs when women reach their early 50's but it can vary between 40 & 58 yr of age. The incidence of certain conditions (eg: Diabetes, breast cancer, cervical carcinoma) increases after menopause, Female pelvic organ prolapse is a common condition in Parous women.

According to one study conducted at Liaquat National Hospital Karachi 27.8% women who had urinary incontinence were postmenopausal⁹.

In our study majority of women found have symptoms less seen at the age of 40 yr (i.e. 3.33%) and at the age of 80 yr (i.e. 6.66%).

According to one study UI was more in women with high parity 9, while in this study parity 6-10 was higher in postmenopausal women to have urinary symptoms (i.e. 63.33%).

One study conducted at AKU Hospital Karachi Pakistan which states that the frequent urine passing symptoms occur in 44 (23.7%) of respondent and 74 (39.8%) experienced nocturia 6.

In our study the frequent urine passing symptoms found in postmenopausal women with Uterovaginal Prolapse is (33.33%) while nocturia found (83.33%)

Urinary urgency with or without incontinence effects one in four adults over the age of 65 yr while stress.

A Postal Study from US in more than 3,500 women reported UI in 45% of women including one quarter of those between the age of 30 & 39 yrs and half of those between the ages of 50 & 90 yrs¹⁰, while in our study urge incontinence reported 20.0% while stress incontinence reported 53.33%

According to one study dysuria occurred 18 (42.9%) of the with UV Prolapse 4. While in our study Dysuria found 26.66%, Voiding difficulty 53.35% found and Retention of urine found 20.0%.

CONCLUSION

Pelvic organ prolapsed and urinary symptoms like incontinence are prevalent in older women and are associated with age, Menopause and no hormone therapy. Large studies are required to assess the relationship of urinary symptoms with Uterovaginal Prolapse. Because these urinary symptoms effect over quality of life of women so it is recommended to reduce genital prolapsed and associated urinary symptoms by implementing some measure such as health education of women and weight control.

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Efficacy & Biochemical Evaluation of Pharmaceutical Optimized Felodipine 10mg (F-7) with Essential Hypertension

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ABSTRACT

Objective: The objective of this double-blind, comparative study evaluating efficacy and biochemical effects of optimized felodipine 10mg (F-7) as monotherapy with comparison to placebo 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 March 2011 to October 2011.

Materials and Methods: This was multicenter randomized, double-blind, comparative study. Patients were randomized to receive once Felodipine (F-7) daily for 8 weeks and at the end of study efficacy and biochemical evaluation was done

Results: The patients treated with optimized Felodipine 10mg (F-7) alone, blood pressure reduction was lower, although significant; reaching values of $140.2 \pm 11.3 / 87.9 \pm 5.5$ 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 Felodipine 10mg (F-7) 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, Felodipine, 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 mortality¹. 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}

Felodipine is a dihydropyridine calcium antagonist which is characterized by high vascular selectivity-that is, it is much more potent in its inhibition of contractile activity in vascular smooth muscle than in the myocardium. The in vitro ratio of vascular and myocardial potency for felodipine is greater than 118:1⁵ and felodipine plasma concentrations resulting in pronounced reductions in total peripheral resistance in patients produce no negative inotropic effects⁶ and no effects on cardiac conduction⁷. The efficacy and tolerability of felodipine in patients with congestive heart failure have been studied in several open⁸⁻¹⁰ and double blind placebo controlled phase II studies.¹¹⁻¹³ Thus Dunselman et al.¹² and Timmis et al.¹⁴ demonstrated improved exercise capacity with felodipine in patients with heart failure, while Tan et

al.¹¹ found no such improvement. Comparative safety and efficacy trials indicate that angiotensin receptor blockers like olmesartan medoxomil have superior tolerability and antihypertensive efficacy¹⁵. Similar investigation using olmesartan, medoxomil and amlodipine besylate showed great effectiveness and tolerance in patient with hypertension¹⁶. Combination therapies reduced B.P to a greater extent than with amlodipine besylate alone as indicated with benazepril hydrochloride with valsartan and with perindopril^{17,18}. Therefore, the objective of this comparative study evaluating the efficacy and biochemical effects of optimized felodipine 10mg (F-7) 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 Felodipine 10mg (F-7) once daily and Placebo once daily for 8 weeks. The study was conducted in Department of Biochemistry, University of Karachi from March 2011 to October 2011. Patients were selected from four different hospitals of orange Town and 80 patients were selected for the study. Therefore 80 patients 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 0) 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 Felodipine 10mg (F-7) alone, blood pressure reduction was lower, although significant; reaching values of 140.2 ± 11.3 / 87.9 ± 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

	Felodipine (F-7) (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/m ²)	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

	Felodipine (F-7) (n=60)	Placebo (n=20)	P-value
	Systolic BP - 24 hours (mmHg)		
Baseline	149.7 ± 11.2	149.4 ± 11.4	NS
Week 8	140.2 ± 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	87.9 ± 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

	Felodipine (F-7) (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	198.2 ± 43.1	195.2 ± 33.3
Week 8	199.7 ± 43.2	193.9 ± 34.1
	LDL - Cholesterol (mg/dl)	
Baseline	114.5 ± 34.2	117.8 ± 25.8
Week 8	114.9 ± 34.3	116.7 ± 24.7
	HDL - Cholesterol (mg/dl)	
Baseline	53.2 ± 13.1	48.8 ± 11.7
Week 8	51.8 ± 12.8	48.7 ± 11.5
	Triglycerides (mg/dl)	
Baseline	136.2 ± 88.2	145.5 ± 88.1
Week 8	126.1 ± 89.3	144.2 ± 88.9

DISCUSSION

The baseline characteristics of the population included in the study are shown in Table no1. 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 Felodipine 10mg (F-7) 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 Felodipine 10mg (F-7) 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 Felodipine 10mg (F-7) 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 Felodipine 10mg (F-7) at low doses has a very good biochemical profile with a low incidence of adverse events. The good biochemical profile of the optimized Felodipine 10mg (F-7) 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 Felodipine 10mg (F-7) 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 Atenolol 10mg (F-7) is safe and adequate for the treatment of hypertension in patients with metabolic syndrome, diabetes mellitus and dyslipidemia. 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 Felodipine 10mg (F-7) has a high antihypertensive efficacy, allowing approximately 72.3% 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 Felodipine 10mg (F-7) it is an excellent option for the treatment of hypertension.

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Three Years Audit of Maxillofacial Trauma at Abbasi Shaheed Hospital, Karachi

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ABSTRACT

Objective: The purpose of this retrospective study was to analyze the maxillofacial fractures treated during three years period with special attention to the age, causes, fractures pattern, clinical management and treatment modalities.

Study Design: Retrospective study

Place and Duration of Study: This study was carried out Oral & Maxillofacial Surgery Department of Abbasi Shaheed Hospital during the period of January 2008 to December 2010

Materials and Methods: 236 Patients data compiled. The data were reviewed and analyzed in terms of age, gender, aetiology, anatomical site and treatment methods.

Results: A total of 236 patients were included in this study presenting with maxillofacial trauma out of these 93.6% were males and 6.4 % female .Overall male to female ratio was 15:1.The most common age involved was second decade. The most common cause was RTA (82%)followed by fall (7.2%) and then assault (5.5 %). The fracture of the mandible was the most common constituting about (72.5%) of the maxillofacial fractures followed by Zygomaticomaxillary complex (ZMC) fracture (14.4%) and then Maxilla (5.9%). Regarding treatment more than 50 % patients received ORIF (Open reduction Internal fixation) via bone plates while remaining received MMF (Maxillo-mandibular fixation).In ZMC Fracture ,Gillies Temporal approach alone is the most common approach accounting 67% of cases while in Le-forte fracture ORIF constitute the most common treatment method.

Conclusion: The causes and pattern of maxillofacial fractures reflect trauma patterns within the community and, as such, can provide a guide for the design of programs geared towards prevention and treatment.

Key Words: Maxillofacial fractures, Mandible fractures, mandibles fixation,

INTRODUCTION

The Maxillofacial region occupies the most prominent position in the human body and rendering it vulnerable to injuries quite commonly. Injuries of the maxillofacial region may result varying degree of physical, functional and cosmetic disfigurement and it can occur as isolated injury or may be associated with multiple injuries.¹⁻³

The incidence and aetiology of maxillofacial fractures vary widely between different countries and even within the same country as a result of various contributing factors such as age, gender, the environment and the socioeconomic status and culture of the patients.⁴⁻⁶

Road traffic accident (RTA) is reported the leading cause of maxillofacial fractures in developing countries while interpersonal violence is the leading cause in developed countries. The other aetiological factors are firearm injury, sports injury, falls and industrial trauma.^{7,8-9} Most of the studies reported high frequency of fracture among males and young age group between the ages of 21-30 years.^{4,5,7-10}

The purpose of this retrospective study was to analyze the maxillofacial fractures treated during three years period with special attention to the age, causes, fracture pattern, clinical management and treatment modalities. In addition this study will evidence for recommendation

of possible preventive measures to be taken to reduce the incidence of maxillofacial fractures.

MATERIALS AND METHODS

This was a retrospective study which review the data of 236 patients sustaining maxillofacial fractures and who were attended between January 2008 to December 2010 at the Oral & Maxillofacial surgery Department, Abbasi Shaheed Hospital, Karachi Pakistan.

The data were reviewed and analyzed in terms of age, gender, aetiology, anatomical site and treatment methods. Age above 60 and isolated nasal and Nasoorbital ethmoid fractures were excluded in this study. The data was then computerized and subjected to statistical analysis using SPSS version 16

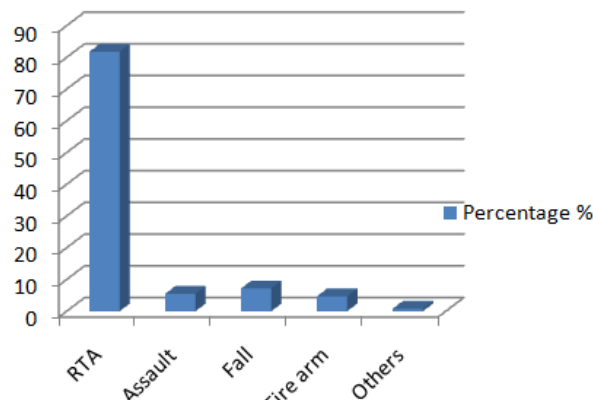
RESULTS

A total of 236 patients were included in this study presenting with maxillofacial trauma out of these 93.6% were males and 6.4 % female. Overall male to female ratio was 15:1.The age range from 13-40 years. The most common age involved was second decade (93%) followed by first decade (53%).

The most common cause of maxillofacial fracture was RTA (n=193, 82%), followed by fall (n=17, 7.2%) and then assault (n=13, 5.5 %) (Graph 1).

The fracture of the mandible was the most common constituting about (n=171, 72.5%) of the maxillofacial fractures followed by Zygomaticomaxillary complex (ZMC) fracture (n=34, 14.4%) and then Maxilla (n=14, 5.9%). (Table 1)

In Mandible the most common site involved was Parasymphysis (n=82, 27%) followed by Body (n=77, 26%) and then Angle (n=41, 14%). (Table 2)



Graph 1: Causes of Injury

Table No.1: Distribution of Fracture Site

Site of Fracture	Frequency(n)	Percentage %
Mandible	171	72.5
ZMC	34	14.4
Maxilla	14	5.9
Panfacial	17	7.2
Total	236	100

Table No.2: Distribution of site of Mandible Fracture

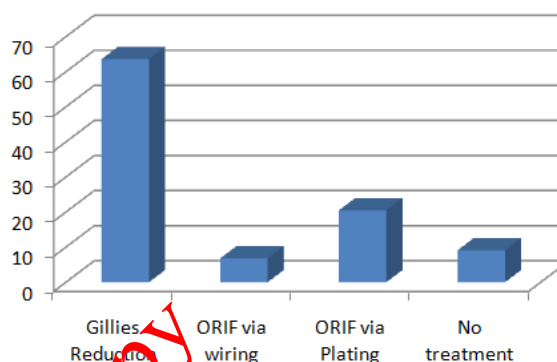
Fracture Site	Frequency(n)	Percentage %
Symphysis	18	6
Parasymphysis	82	27
Body	77	26
Angle	41	14
Ramus	8	3
Coronoid	6	2
Condyle	67	22

Table No. 3: Treatment of mandible fracture

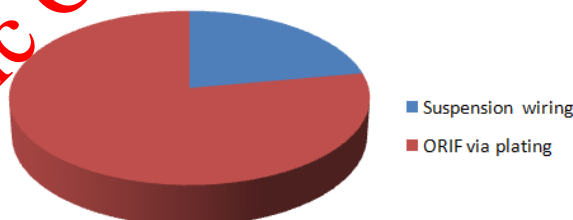
Method of Treatment	Frequency (n)	Percentage %
MMF via Arch bar	42	22
MMF via eyelet wiring	38	20
Circum-mandibular wiring	4	2
Bridal wiring	2	1
Occlusal splint	2	1
ORIF via wiring	16	9
ORIF via plating	82	44
No treatment	2	1
Total	188	100

In Maxilla the most common fracture was Le-Fort II (n=14, 67%) followed by Le-Fort I fracture (n=8, 38%) while In ZMC fracture the left site was most commonly involved (n=25, 41%) while 8% bilateral involvement. ZMC arch was involved in 16 % of cases.

Regarding treatment of Mandible fractures more than 50 % patients received ORIF via bone plates while remaining received MMF (Table 3). In ZMC Fracture, Gillies Temporal approach alone is the most common approach accounting 67% of cases while in Le-forte fracture ORIF constitute the most common treatment method. (Graph 2 & 3)



Graph No.2: Treatment of ZMC Fracture



Graph No.3: Treatment of Le-Fort Fracture

DISCUSSION

In the present study there is male preponderance. The male to female ratio is 15:1 which is very high compare to most of the studies even though it is higher than other cities of Pakistan.^{6,7,11} However the results are similar to those studies from Iran (12:1) and Nigeria (17:1).^{10,12} The preponderance of male subjects could be attributed to the fact that males are the main earner of the family and work outdoor and most of them have motorbikes. They do not wear helmet and drive recklessly. This will be attributed in the present study where 2nd decade male commonly involved in maxillofacial trauma. The result is consistent with most of the studies.^{10, 13, 14 & 15}

In the present study RTAs (82%) constituted the most common cause of injury. The studies done in various cities of Pakistan other than Karachi showing 40-50 % of RTA involvement in maxillofacial trauma however similar percentage showed in studies conducted in India (80%)¹⁵, Iran (91%)¹⁰ and Nigeria (83%).¹²

In contrast, studies conducted in Australia, Europe and North America found Assault to be the leading cause of maxillofacial trauma (30-40%) while in the present study assault contributed only 5.5 %.^{16,17}

Mandible is the bone most frequently involved in maxillofacial fractures. The frequency of mandible fracture in our population was 72.5% followed by ZMC (14.4%) and then Maxilla (5.9%). The result is similar with most of the studies^{4, 6, 7, 8,11} while in contrast few studies reported maxilla to be the most common site for midfacial fracture^{18, 19}.

In this study Parasymphysis fractures of mandible were the most common followed by Body fractures. This result is consistent with the studies done in other cities of Pakistan^{6,7}. Studies done by Subodh S et al.²⁰ in India, Ozkaya O⁴ in Turkey, Elgehani RA²¹ in Libya reported the same site of fracture. In contrast few studies refracted condyle is the most common site of mandible fracture^{22, 23}.

In ZMC, Left Zygoma fracture was most commonly involved while in maxillary fracture Le-Fort II was most commonly involved.

There are many treatment regimen in maxillofacial fracture but the selection may change according to the type & location of the fracture, patient characteristics and the surgeon's preference and experience. In the past most of the Mandible fractures operated by closed reduction only where the miniplate system was not popular. From last two decades ORIF (Open reduction internal fixation) via miniplates is very common because it is very comfortable to the patients and the patient recovered earlier but he has to face the cost of implant and hospital stay. In this study more than 59% cases operated by ORIF via miniplates while 40% cases operated via closed reduction either with arch bar or eyelet wirings

CONCLUSION

As this study revealed the most common cause of maxillofacial trauma is road traffic accident and mainly young adults are involved so strict traffic rules and regulations should be enforced and use of helmet with chin cap should be mandatory. The Government should adds few chapter regarding cause and consequences of head and maxillofacial trauma in text books so the young generation will alert for safe driving and follow the road crossing safety.

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Electronic Copy

Head: The Most Common Targeted Area in Murders

Targeted Body
Area in
Murders

1. Azhar Masud Bhatti 2. Babur Rashid Chughtai 3. Muhammad Iqbal

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ABSTRACT

Objectives: To identify the most targeted area in homicidal injuries which may be helpful in crime control in society.

Study Design: Retrospective and observational study.

Place and Duration of study: This study was carried out on 5 years autopsies reports collected from THQ Hospital Taxila from 2009 to 2013 and analysis was done with emphasis on most common targeted area of the body during this period.

Materials and Methods: Autopsy registers containing reports from 2009 to 2013, along with police papers and treatment notes were taken from THQ Hospital Taxila and analyzed with reference to most targeted area, kind of weapon used, age, sex, injury pattern and nature of injuries

Results: During total 5 year tenure total 279 autopsies were conducted. Among total 279 autopsies 234 (83.87%) dead bodies were of males while only 45 (16.13%) were belonged to females. 138 (49.46%) dead bodies were of adult age between 20-40 years, among these 112 (81.16%) belonged to males and 26 (18.84%) to females. In 88 (31.54%) cases head was targeted. The 2nd most common area of target was the chest, 76 (27.24%) persons were hit on the chest. In 33 (11.83%) persons abdomen was the target while 28 (10.04%) bodies were with neck injuries. Firearm was the most common weapon causing 177 (63.44%) deaths. Blunt weapon remained the 2nd mostly used weapon claiming 22 (7.88%) lives. Use of sharp edged weapon was restricted only to 7 (2.5%) persons. In total 40 cases (14.34%) no cause of death could be found.

Conclusion: The analysis may offer some help to bring the crimes under control.

Key Words: Head, Chest, Target.

INTRODUCTION

The word autopsy is derived from Greek and is translated as "to see with one's own eye"¹. Autopsy is mandatory in all cases of un-natural deaths. A Forensic autopsy is performed to determine the cause and the manner of death in people dying sudden, unexpected, violent, drug related, or otherwise suspicious deaths². The only thing worse than no autopsy is the partial autopsy, in every case the autopsy must be complete³. Analysis of autopsies performed in an area may be helpful to make certain amendments in the laws to control the crimes. Homicide means purposeful killing undertaken with the intension of causing the death of the victim. Common motives for homicide include trivial altercations, jealousy, revenge, romantic triangle, robbery, sexual assault, burglary and dispute in drug transactions⁴.

Head injury is defined as morbid state resulting from gross or subtle structural changes in the intracranial contents of the skull with or without involvement of skull or extra cranial structures, due to direct or indirect mechanical force⁵. There are three main components of the head; the scalp, skull and brain⁶. Skull has three tables, outer table the strongest and inner table (weakest) and in between two, there is dipole⁷. Of all the regional injuries those of head are most common and accounts for 25% of all deaths due to violence⁸. It

is also true that when a victim is pushed or knocked to the ground, he often strike the head⁹.

Globally head injury is a major problem for health services, not only in industrialized but also in developing world. Every year in UK about one million patients are admitted to the hospitals with head injuries of varying severity¹⁰. Approximately 300 per 100000 of the population per year require hospital admission in connection with head injury in Britain¹¹. Head injury is classified as coup injury and contre-coup injury. Injury at the site of impact is coup and opposite to the site of impact is contre-coup injury¹².

The firearms remained the most common used weapons in cases of homicides as in other studies also¹³. There is something happening new every day¹⁴, as modernization of firearm weapons increases their lethal power many times. On the skull a special phenomenon occurs on entry and exit wound, a making sloping surface or edge caused by firearm weapons called beveling. Beveling will occur on inner table of the skull on entry and on outer table of skull on exit wound¹⁵.

MATERIALS AND METHODS

The autopsy reports of duration from 2009 to 2013 along with police papers and treatment notes were collected from THQ Hospital Taxila. Complete analysis regarding age, gender, manner of death, opinion of the Authorized Medical Officers, kind of weapon used,

with particular emphasis on area wise distribution of injuries was made. Total 279 autopsies were carried out during tenure of 5 calendar years.

RESULTS

Total 279 postmortem examinations were carried out at THQ Hospital Taxila during 5 years (2009-2013) duration. Year wise distribution is given in Chart No.1.

Age and gender analysis: Regarding age of the victims, overwhelming majority 49.46% (138) belonged to adult age (20-40Years) group, among them 81.16% (112) dead bodies were of males and only 18.84% (26) of females. Age above 40 years remained the 2nd most common age group involved, as out of total 77 autopsies 89.61 % (69) remained of males and 10.39 % (8) of females. 53 bodies were belonged to young age between 12-20 years, 84.91 % (45) males and 15.09% (8) of females. Age between 0-12 years remained the least common age group being the innocent age as total out of 11 postmortems 72.73%(8) bodies were of males and 27.27(3) of females. Gender wise distribution is mentioned in Chart No.2.

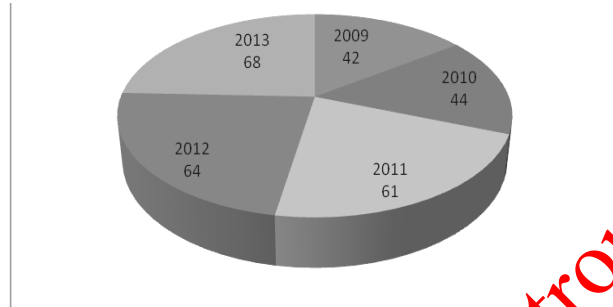


Chart No.1 Yearwise distribution of autopsies

Regional Distribution of injuries: Head remained the most common targeted area, as out of 279 persons 88 (31.54%) were hit on the head. 2nd most targeted area

Table No.1: Regional distribution of homicidal injuries

Year	No.	Head	%	Neck	%	Chest	%	Abdomen	%
2009	42	14	33.33	4	9.52	13	30.95	5	11.90
2010	44	19	43.18	3	6.82	14	31.82	4	9.09
2011	61	24	39.34	4	6.56	14	22.95	4	6.56
2012	64	17	26.56	9	14.06	17	26.56	3	4.69
2013	68	14	20.59	8	11.76	18	26.47	17	25.00
GT	279	88	31.54	28	10.04	76	27.24	33	11.83

Table No.2: Homicidal deaths due to poison, drown and burns

Year	No.	Poison	%	Drown	%	Burns	%	Nil	%
2009	42	1	2.38	-		2	4.76	3	7.14
2010	44	1	2.27	-		-	-	3	6.82
2011	61	3	4.92	-		-	-	12	19.67
2012	64	-	-	3	4.69	-	-	15	23.44
2013	68	2	2.94	1	1.47	1	1.47	7	10.29
GT	279	7	2.51	4	1.43	3	1.07	40	14.34

was chest, as 76 (27.24%) person died due to chest injuries. Overall head and chest injuries claimed 164 (58.78%) lives. Abdomen was at No. 3 as with involvement of 33(11.83%) cases. In 40 (14.34%) autopsies no cause of death could be ascertained. The detail of regional distribution of injuries found, are given in Table No. 1 & 2.

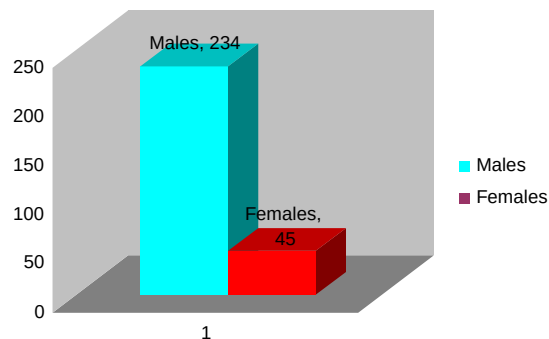


Chart No. 2: Gender wise distribution of autopsies

Manner of death: As for as the manner of death is concerned, most common 199 (71.33%) cases remained of homicide. The other detail is given in the following table No.4.

Kind of weapon used: Firearms remained the most commonly used weapon causing 177(63.44%) deaths. In 22 (7.88%) persons assault was committed with blunt weapon. 7 (6.81%) injuries were caused by sharp edged weapons. Hanging was responsible for causing 19(6.81%) deaths. In 7(2.51%) persons use of poison, in 4 drowning and in 3, burns remained the cause of death. 40 (14.34%) cases remained undiagnosed being negative autopsy.

Table No.3: Manners of deaths

Year	No.	Homicide	%	Suicide	%	Accident	%	Nil	%
2009	42	32	76.19	5	11.90	2	4.76	3	7.14
2010	44	35	79.55	3	6.82	3	6.82	3	6.82
2011	61	41	67.21	5	8.2	3	4.92	12	19.67
2012	64	41	64.06	-	-	8	12.5	15	23.44
2013	68	50	73.53	9	13.24	2	2.94	7	10.29
GT	279	199	71.33	22	7.88	18	6.45	40	14.34

DISCUSSION

An evil is almost always in a society, there could hardly any society in the world which can be considered absolutely crime free. It is generally the un-justice, delay in dispensation of justice, along with deteriorating moral values in a community results in rapid rise of crimes. The population in our country is rapidly developing into two major economic classes, very rich and very poor families with progressively declining middle class, is another cause of crimes.

In present days all over the world, dispensation of justice through legal system has become much dependent on medical science¹⁶. The victim is taken to medical facility for an examination and collection of existing evidence¹⁷. Forensic evidence is physical or trace evidence that can be significantly matched with a known individual or item. Every criminal could be linked to the crime she or he committed by examination of transferred trace evidence¹⁸, facts or circumstances that tend to implicate a person in a crime. It is very much unfortunate that medico-legal investigations in our country are of much low standard as compared with developed countries.

Though the murder is least common of all crimes but this offense receives the greatest attention from the law enforcement agencies and media¹⁹. Forensic autopsy is primarily conducted to know the cause of death, meaning disease or injury that initiated the lethal chain of events that led to death²⁰. In the past it was assumed that the murderer must have been a man of physical strength, great courage and daring. But with the modernization of weapons with particular reference to the firearms these qualities are no more required to commit a murder, Just press the trigger and life is over. Homicidal manner of killing remains on the top as in every society²¹. Number of persons committed suicide remained at minimum as suicide is prohibited not only in our religion but under our law also²².

In our study the Head remained the most common target, almost similar results in other studies conducted²³⁻²⁴. Of all injuries those of head and neck are the most common and most important in forensic practice²⁵. The incidence of head injuries is going up with the speeding mechanization of modern life²⁶. There is 33.5 % increase in head injury admission in UK in the last decade²⁷. Traumatic brain injury,

according to the World Health Organization, will surpass many diseases as the major cause of death and disability by the year 2020. With an estimated 10 million people affected annually by head injury, the burden of mortality and morbidity that this condition imposes on society, makes the traumatic brain injury, a pressing public health and medical problem²⁸.

Although the brain is well protected within strong, bony skull but it is not well restrained within this compartment and injuries to the brain result from differences between the motion of the skull and brain. Severe injury to the brain may occur without any external visible injury to the skull and scalp.

The firearms remained the most common used weapons for homicide is also indicated in other studies²⁹. Free availability, frequent use of these lethal weapons, constantly deteriorating law and order situation in the country have make us a gun culture state of society. Possession of firearms by males is much more common in our country as compared with females, being the male dominant society. But Possession of firearms in USA is more common in females than in males. Mostly adult persons (20-40 years) are the victims of homicide, is consistent with other studies also³⁰.

CONCLUSION

Strict statutory control over fatal weapons and rapid dispensation of justice are required to minimize the offence of homicide from our country.

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Incidence of Gestation Diabetes and Viral Hepatitis in Pregnant Women

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ABSTRACT

Objective: To study the incidence of gestational diabetes and viral hepatitis in pregnant women presenting in Islam Central Hospital Sialkot

Study Design: Cross sectional study based on patients attending Islam Central Hospital, Sialkot

Place and Duration of study: This study was carried out at Islam Central Hospital, Sialkot from 1st January 2012 to 30 November 2013.

Material & methods: Two hundred pregnant women were selected randomly attending Islam Central Hospital, Sialkot. The data was collected on proforma. The written informed consent was obtained on the consent form and permission was taken from the hospital committees. Blood samples were taken for diagnoses of hepatitis and second sample was taken for fasting blood glucose and then 75gm glucose in one glass of water was given to the patients. After 2 hours, another plasma glucose test was taken. Gestational diabetes was diagnosed on the basis of fasting plasma glucose level >126mg/dl, 2 hours post prandial plasma glucose level >199.8mg/dl and hepatitis was diagnosed by its kits.

Results: The age variation of pregnant women included in this study was as follows. 20 patients (10%) were of age 16-20 years, 102(51%) of age 21-30 years, 54(27%) of age 31-40 years and 24(12%) of age 41-50 years. 70 patients(35%) included in this study had undergone major surgery e.g., caesarean section while 130(65%) had not undergone any major surgery. 54(27%) pregnant women had history of blood transfusion and 146(73%) pregnant women had no history of blood transfusion. 158(79%) of the pregnant women had undergone minor procedure e.g., tooth extraction or ear piercing and 42(21%) had not undergone any minor procedure. 30(15%) of the pregnant women had history of miscarriage conducted by Dai and 170(85%) had no history of dai handling. The incidence of overweight/obesity was 138 (69%) in case of pregnant women and 62(31%) had no evidence of being overweight/obese. The incidence of gestational diabetes was 34(17%) in pregnant women and 166(83%) had no history of gestational diabetes. The incidence of viral hepatitis was 18 (9%) in pregnant women and 182 (91%) had no evidence of viral hepatitis. In this study, out of 9 cases, 3 cases (33.33%) were suffering from hepatitis A, 2 cases (22.22%) from hepatitis B and 4 cases (44.44%) were suffering from hepatitis C.

Conclusion: As the hygienic conditions in our country are very poor and dietary habits include eating food containing high carbohydrates and fatty contents so the incidence of metabolic diseases is increasing. The sedentary life style is also becoming common in pregnant women in our country therefore the incidence of gestational diabetes and hepatitis is increasing day by day in pregnant women irrespective of age, occupation, socioeconomic status, residential area and gravidity status.

Key Words: Gestational Diabetes Mellitus, Hepatitis, Pregnant Women

INTRODUCTION

Gestational diabetes mellitus is defined by American Diabetes Association as any degree of glucose intolerance with onset or first recognition during pregnancy¹.

Obesity is a common disorder which has become prevalent in whole world over the past 10 years². Body Mass Index (BMI) is the most widely accepted measure of obesity in adults³. BMI of more than 30kg/m² is considered as obesity⁴. It is well recognized that maternal obesity is associated with an increased risk of maternal, peripartum and neonatal complications⁵. Obesity increases the risk of gestational Diabetes, pre-eclampsia, macrosomia and caesarean delivery⁶.

The association of obesity, insulin resistance, glucose intolerance, hypertension and characteristic

dyslipidemia is called metabolic syndrome. All of the features of metabolic syndrome are closely related to elevated BMI⁷.

Overweight is a risk factor for impairment of carbohydrate tolerance in non-pregnant state and during pregnancy. Fasting and postabsorptive plasma insulin concentrations are higher in obese pregnant women than in non-obese pregnant women. Weight excess clearly increases the risk of overt impairment of carbohydrate tolerance in pregnant women. Even in moderately over weight subjects (BMI 25-30) or weight 120-150% of ideal body weight the incidence of gestational diabetes is 1.8 to 6.5 times greater than that in normal weight subject⁸. Gestational diabetes is found in 17% of women with obesity, in a study conducted in obesity unit, Hudding University Hospital, Sweden⁹. Findings of Ghu et al also indicate that high maternal

weight is associated with a substantially high risk of gestational diabetes mellitus¹⁰.

There is a strong correlation between obesity and gestational diabetes mellitus; therefore, it is pertinent to identify women at risk of developing gestational diabetes in relation with elevated BMI as gestational diabetes mellitus increases the risk of hypertensive disorders, chromosomal defects, macrosomia, caesarean delivery and high risk of developing type 2 diabetes mellitus.

The aim of the study was to determine the incidence of gestational diabetes and hepatitis in pregnant women to help in early diagnosis of gestational diabetes, hepatitis and its management to prevent maternal and fetal complications. Viral hepatitis is an inflammation of the liver due to viral infection¹¹. Major causes include specific hepatitis viruses, alcohol and drugs while less common causes include other viral infections and leptospirosis. Hepatitis A & hepatitis E virus are primarily transmitted via the fecal oral route and are most commonly acquired via ingestion of contaminated food. Hepatitis B & Hepatitis C are transmitted by blood transfusion, reused syringe, non-sterilized surgical instruments etc¹².

Viral hepatitis may result in fulminant hepatitis and death in only a small proportion of patients. However, it is a significant cause of morbidity and socio-economic losses in many parts of the world¹⁴. Because a good deal of patients have infections may be asymptomatic or may go unreported, the CDC estimated that the actual number of new hepatitis infections in 2007 was about 25,000^{15,16}.

MATERIALS AND METHODS

Two hundred pregnant women were selected randomly attending Islam Central Hospital, Sialkot. The data was collected on proforma. The written informed consent was taken on the consent form and permission was taken from the hospital committee. Blood sample was taken for diagnoses of hepatitis and second sample was taken for fasting blood glucose and then 75gm glucose in one glass water was given to the patients. After 2 hours, another plasma glucose test was obtained. Gestational diabetes was diagnosed on the basis of fasting plasma glucose level >126mg/dl, 2 hours post prandial plasma glucose level >199.8mg/dl and hepatitis was diagnosed by its kits.

RESULTS

The age variation of pregnant women included in this study was 20(10%) cases of age 16-20 years, 102(51%) of age 21-30 years, 54(27%) of age 31-40 years and 24(12%) of age 41-50 years (Table 1). The 70(35%) of pregnant women included in this study had undergone major surgery e.g., cesarean section and 130(65%) had not undergone any major surgery (Table 2). 54(27%)

pregnant women had taken blood transfusion and 146(73%) pregnant women had not taken blood transfusion (Table 3). 158(79%) of the pregnant women had undergone minor procedure e.g., tooth extraction or ear piercing and 42(21%) had not undergone any minor procedure (Table 4). 30(15%) of the pregnant women had miscarriage conducted by Dai and 170(85%) had not conducted any miscarriage conducted by Dai (Table 5). The incidence of overweight/obesity was 138(69%) as in case of pregnant women and 62(31%) without overweight/obesity (Table 6). The incidence of gestational diabetes was 34(17%) in pregnant women and 166(83%) had no gestational diabetes (Table 7). The incidence of viral hepatitis was 18(9%) in pregnant women attending the hospitals of our study and 182(91%) were without any viral hepatitis (Table 8). In this study out of total 9 cases, 3 cases (33.33%) were of hepatitis A, 2 cases (22.22%) were of hepatitis B and 4 cases (44.44%) were of hepatitis C were found (Table 9)

Table No.1: Age distributions of pregnant women (200)

Age in years	N	%age
16-20	20	10
21-30	102	51
31-40	54	27
41-50	24	12

Table No.2: Previous surgery cases distributions of pregnant women (n=200)

Previous surgery	n	%age
Yes	70	35
No	130	65

Table No.3: Blood transfusion cases distributions of pregnant women (n=200)

Previous blood transfusion	N	%age
Yes	54	27
No	146	73

Table No.4: Previous minor procedures Distribution in pregnant women (n=200)

Minor procedure	N	%age
Yes	158	79
No	42	21

Table No.5: Previous miscarriage conducted by Dai, Distribution in pregnant women (200)

Mis carriage conducted by Dai	n	%age
Yes	30	15
No	170	85

Table No.6: Incidence of overweight/obesity in pregnant women (n=200)

Overweight/obesity	n	%age
Yes	62	31
No	138	69

Table 7: Incidence of viral hepatitis in pregnant women (n=200)

Viral hepatitis	n	%age
Yes	18	9
No	182	91

Table No.8: Incidence of gestations diabetes in pregnant women (n=200)

Gestational diabetes	n	%age
Yes	34	17
No	166	83

Table No.9: Etiology of hepatitis in pregnant women (n=200)

Type of viral hepatitis	n	%age
A	6	33.33
B	4	22.22
C	8	44.44

DISCUSSION

Obesity is a global health problem that is increasing in prevalence. The WHO characterizes obesity as a pandemic issue with increased prevalence in females than males. Obesity during pregnancy is considered as a high risk state because it is associated with many complications¹⁶. Obesity has implications for all aspects of maternal/foetal health and outcome during pregnancy with short and long term effects¹⁷.

Obesity is an established risk factor for gestational diabetes. It is not known whether this risk might be reduced through weight loss between pregnancies. We tried to determine whether weight loss during pregnancies reduced the risk of gestational diabetes among obese women¹⁸. In current study, gestational diabetes was developing in 17% of obese women.

In a study conducted by Gulzar et al, 82% of women lost weight between pregnancies, with a mean weight loss of 23lbs. Women who lost at least 10lbs between pregnancies had a decreased risk of gestational diabetes relative to women whose weight changes by less than 10lbs (relative risk=0.63; 95% confidence interval=0.38-1.02) adjusted for age and weight gain was 22lbs. Women who gained at least 10lbs had an increased risk of gestational diabetes¹⁹.

Based on meta-analysis of the literature, it is estimated that the risk of developing gestational diabetes mellitus (GDM) is about two, four and eight times higher among overweight, obese and severely obese women, respectively, compared with normal weight pregnant women. The public health implications for the U.S. are significant because of the high prevalence of GDM and the potential adverse consequences associated with obesity and GDM including higher risk of adverse infant outcomes, higher risk of diabetes for the mother later in life and higher risk of diabetes and overweight for the offspring²⁰.

Thorpe and Howard suggest that GDM risk increases substantially with increasing maternal BMI. The increasing prevalence of obesity and related conditions such as GDM and type 2 diabetes are already changing predictors of the cost of medical care in the future²¹.

Foetal macrosomia is a common adverse infant outcome related to GDM, especially if GDM is unrecognized and untreated^{22, 23}.

Maternal obesity is associated with an increased risk of diabetes both pre gestational diabetes and GDM²⁴. Compared with normal weight women (BMI < 25kg/m²), a recent meta-analysis of 20 studies demonstrated that the OR of developing GDM was 2.14 (95% CI, 1.82-2.53), 3.56 (95% CI, 3.05-4.21) AND 8.56 (95% CI, 5.07-16.04) among overweight (BMI 25-30kg/m²), obese (BMI > 30kg/m²) and severely obese women (BMI > 40kg/m²) respectively²⁵.

A recent study found that weight gain in the 5 years prior to becoming pregnant, even at a rate of 1.1 to 2.2kg per year, increases the risk of developing GDM and that this was especially true for women who were not initially overweight²⁶.

In addition to pre-pregnancy BMI, a number of other demographic factors affect the incidence of GDM. Hedderson and colleagues found that GDM was more likely in women who were older than 35 years of age and who were of Hispanic or Asian ethnicity²⁷.

Majority of the above mentioned studies support findings of present study. Worldwide viral hepatitis is responsible for an estimated 1.4 million infections annually with variable course of illness²⁸.

Several studies have reported that viral hepatitis is responsible for major outbreaks as well as sporadic cases of acute hepatitis in Pakistan and other developing countries²⁹. In the present study 6(3%) cases were of HAV infection, 4(2%) cases were of HBV and 8(4%) were of HCV.

Vaccination is recommended for persons at increased risk for the disease including international travelers, non-injection and injection drug users and children living in communities with high rates of disease^{32, 33}.

CONCLUSION

As the hygienic conditions in our country are very poor and dietary habits include eating food containing high carbohydrates and fatty contents so the incidence of metabolic diseases is increasing. The sedentary life style is also becoming common in pregnant women in our country therefore the incidence of gestational diabetes and hepatitis is increasing day by day in pregnant women irrespective of age, occupation, socioeconomic status, residential area and gravidity status.

Suggestions

1. The diet containing high carbohydrates and fats should be avoided during pregnancy
2. The routine work in the home should be continued during pregnancy.
3. The hygienic conditions should be improved in the society.

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Therapeutic Effect of Carnitine on Atorvastatin induced Mechanical Myotoxicity of Gastrocnemius Muscles of Rats

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ABSTRACT

Objective: To Study Therapeutic Effect of Carnitine on Atorvastatin-induced Mechanical Myotoxicity of Gastrocnemius Muscles of Rats.

Study Design: Observational study

Place and Duration of Study: This study was conducted at Department of Physiology, University of Karachi, from 21st January 2012 to 30th December 2013.

Materials and Methods: Present study showed that effect of statin on mechanical properties of gastrocnemius muscle of rats and use of carnitine as prevention of statin induced myopathies. Animals were injected statin for 6 weeks in one group and carnitine to another group along with statin to study the possible therapeutic effect. After treatment period, animals were decapitated and gastrocnemius muscles were isolated. Twitch and tetanus of muscles were recorded in each group.

Results: Our results showed that treatment of statin reduced the body weight of animals and increased the resting length (106%) of isolated gastrocnemius muscles. We also observed that force of contraction of both twitch and tetanus in statin treated group were significantly reduced ($P > 0.0001$). This negative effect of statin on twitch and tetanus parameters of muscle was partially decreased by an additive treatment of carnitine.

Conclusion: Thus, carnitine plays a vital role in improving muscle contractile ability caused by statins. Our study demonstrated the potential preventive measure of atorvastatin-induced myopathy using carnitine and its impacts on mechanical function of muscles.

Key Words: Hypercholesterolemia, Skeletal muscles, Statin, Carnitine, Muscle twitch, and Muscle tetanus

INTRODUCTION

Statins are the most preferred and widely used drugs for the treatment of hypercholesterolemia and prevention of various cardiovascular diseases due to their efficacy and tolerance¹. Despite their life saving advantages, these drugs are reported to cause serious side effects in skeletal muscles. The chronic use of atorvastatin leads to adverse effects ranging from myalgias, myopathies and muscle cramps to fatal condition like rhabdomyolysis^{2,3,4}. A number of mechanisms of damage have been proposed including deleterious effects on mitochondrial respiratory chain, energy production by skeletal muscle, membrane cholesterol⁵ and degenerative changes in skeletal muscle⁶. Insufficient cholesterol in the muscle membrane due to statin treatment may alter membrane fluidity⁷ and makes it vulnerable to acidosis, because leakage of ions and mitochondrial dysfunction respectively. Both these negative effects ultimately damage the contractile properties of skeletal muscles.

Statin induced side effects could be prevented as well as treated by giving a combination therapy of statins with L-carnitine⁸. Carnitine is a quaternary ammonium compound essential for the breakdown of fats into energy in the body⁹. However, possible protective

effect of carnitine on mechanical properties of skeletal muscles is yet not well known. Therefore, the purpose of the present study was to determine the therapeutic effect of carnitine on contractile properties of gastrocnemius muscle for statin-induced myotoxicity. Physiological profile of statin induced muscle damage can be measured by mechanical parameters that are valid indicators of myopathy.

MATERIALS AND METHODS

Chemicals and Drugs: Commercially available statin (Lescol, Novartis) in the vehicle methylcellulose (CMC) suspension were used for the chronic dosing of rats in vivo. All chemicals used in the study were purchased from Sigma Aldrich until otherwise stated.

Grouping and Treatment of Animals: Albino rats of 250 to 300 grams were housed in different cages with 5 rats in each cage and the cages were labeled. The animals were randomly divided into three groups as follows:

Group I: the control group consisting of normal untreated animals

Group II: statin treated group to see the adverse effects of statins

Group III: statin + carnitine treated group, to see the prevention from adverse effects of statin.

After habituation process, statin was given at a dose of 10 mg/kg/day by rat feeding needle for 6 weeks. In parallel, control group was given 1 ml 0.5% of CMC (10) and 1 ml of carnitine 300mg/kg¹¹ with statin was administered to group III. After 6 weeks, animals were weighted again and dissection of animals followed by recording of mechanical properties of gastrocnemius muscle.

Muscles Dissection and Fixation: Gastrocnemius muscle from both the limbs was dissected out and isolated muscle was kept in oxygenated Krebs solution at 37⁰ C in the recording chamber. Composition of Krebs's solution (in mM): NaCl 119, KCl 4.8, CaCl₂ 3.2, MgSO₄ 1.2, NaHCO₃ 24, NaH₂PO₄ 1.2, EDTA 0.02 and glucose 11¹². Solutions were continuously gassed with 95% O₂ and 5% CO₂. 1mM tetrodotoxin was added to the solutions to avoid spontaneous contraction of muscle. The pH of solutions was maintained between 7.2 and 7.3 during each experiment.

The gastrocnemius muscle was fixed in the chamber and connected to the force transducer that was finally connected to the power lab. The stimulating electrodes were connected via lead with the stimulator and were placed under the muscle belly.

Mechanical Parameters Recording: Before recording of mechanical parameters, resting length was determined. Muscle was fixed in the organ bath and was kept flaccid. This flaccidity was tightened by mm and the muscle was stimulated at Frequency 1 Hz. This procedure was continued until maximum tension was developed in the muscle. At this point, length of the muscle was measured and was denoted as resting length.

In order to record the simple muscle twitch, the power lab was kept at 50V strength and 0.5m.Sec duration with frequency of 1 Hz. Tetanus was recorded by giving continuous stimulation for a short period of time. Low frequency tetanus was recorded at a frequency of 1 Hz while high frequency tetanus was recorded at frequency 80 Hz.

Statistics: SPSS software version 17 was used for the analysis of data. The results were expressed as mean $\pm$ SE. Student independent t test were performed for the determination of difference between group means. The significance level were set as P<0.05.

RESULTS

1) Effect on Body Weight: Body weights of animals of each group are shown in the table 1 on first day and last day of treatment. Values clearly indicated that chronic statin treatment was the main cause of profound decrease in body weight of the animals.

2) Resting Length: In the present experiments using gastrocnemius muscles of rat, the contraction properties

were studied in both control and treated muscles. In the first step, the resting length of muscles was determined to obtain maximum muscle contractions. The **resting length** of the muscles was significantly increased (106.6%) in statin treated muscles (control 3.0 $\pm$ 0.006, statin 3.2 $\pm$ 0.03; P<0.0001). However, use of statin along with the carnitine significantly reduced the resting length back to the range of control muscles (control 3.0 $\pm$ 0.006, Statin + carnitine 3.03 $\pm$ 0.01; P=0.037, Figure 1)

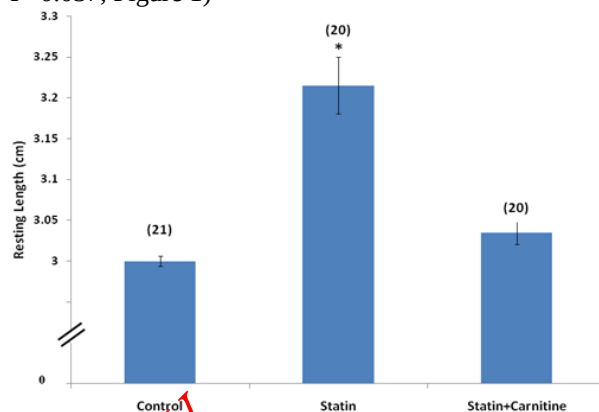


Figure No.1: Effect of Statin and Statin + Carnitine on the Resting Length of Gastrocnemius Muscles of Rats

Figure 1: Resting length of gastrocnemius muscle of rats chronically treated with atorvastatin (5 mg/kg/day) and from control rats. Each bar is represent Mean $\pm$ SE * represents a significant change (P < 0.01) when compared with control. ϕ represents a significant change when a comparison was made between statin treated and statin + carnitine treated groups. Values in parentheses indicate number of experiments.

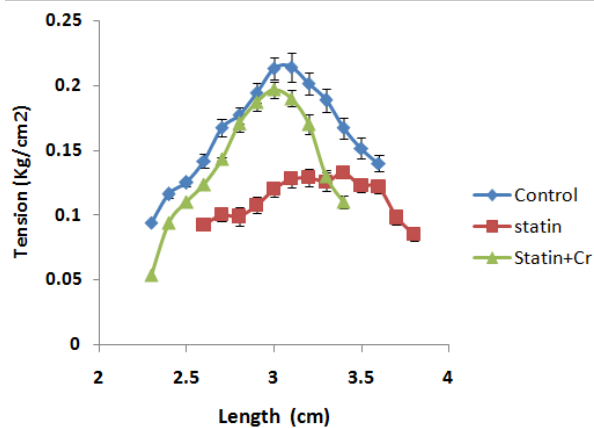


Figure No.2: Statin and Statin + Carnitine induced Length tension relationship of gastrocnemius muscles

Figure 2: Length-tension relationship of rat gastrocnemius muscles from statin and statin + carnitine group. Tension was plotted vs. muscles length during the twitch recording. The data were obtained from 20 muscles. Each data point indicated values in mean $\pm$ SEM.

3) Twitch parameters: Force of contraction (FOC) and contraction time (CT) were significantly reduced

by statin treatment. (FOC control 0.24 ± 0.005 , statin 0.14 ± 0.004 ; $P < 0.0001$) and (CT control 19.0 ± 0.17 , statin 17.3 ± 0.48 ; $P < 0.002$). This was regained near to normal when given along with carnitine. Similarly **rates of rise and relaxation** of twitch tension were significantly reduced ($P < 0.001$) with chronic statin treatment but carnitine could not reverse this effect significantly (Table 2).

Table No.1: Effect of Statin on body weight

	Before treatment	After Treatment
Control (21)	275 ± 5.1	265 ± 6.5
Statin (20)	270 ± 4.2	$240 \pm 5.5^*$
Statin + Carnitine (20)	283 ± 5.5	290 ± 5.2

The values represent Mean $\pm$ SE. * shows a significant change (P value < 0.01) when compare with control. Values in parentheses indicate number of experiments. The values represent Mean $\pm$ SE * shows a significant change (P value < 0.01) when compare with control. ϕ shows a significant change when a comparison was made between statin treatment and statin + carnitine treated groups. Values in parentheses indicate number of experiments.

Peak Duration and **Total Twitch Duration** were significantly increased by statin treatment ($P < 0.0001$ and $P < 0.005$ respectively), however only Peak Duration could be brought back to normal by carnitine while no improvement was seen in Total Twitch Duration. In

contrast, no effect of statin treatments was observed on **Half Relaxation Time** of the skeletal muscle. (Table 2)

Table No.2: Effect of Statin and Stain + Carnitine on Twitch Parameters of Rat Gastrocnemius Muscles

Parameters	Control (21)	Statin (20)	Statin + Carnitine (20)
Force of Contraction (Kg/cm^2)	0.24 ± 0.005	$0.14 \pm 0.004^*$	$0.25 \pm 0.012 \phi$
Rate of Rise of Tension (g/sec)	26.1 ± 0.7	$16.0 \pm 0.6^*$	$14.7 \pm 0.96^*$
Rate of Relaxation (g/sec)	17.2 ± 1.1	$11.8 \pm 0.8^*$	13.5 ± 0.8
Contraction Time (mS)	19.0 ± 0.17	$17.3 \pm 0.48^*$	$19.0 \pm 0.34 \phi$
Half Relaxation Time (mS)	9.0 ± 0.55	10.0 ± 0.55	$13.5 \pm 1.1^* \phi$
Peak Duration (mS)	4.1 ± 0.14	$7.15 \pm 0.29^*$	$3.5 \pm 0.13^* \phi$
Total Twitch Duration (mS)	32.0 ± 0.54	$35.3 \pm 0.91^*$	$36.4 \pm 0.75^*$

Table No.3: Effect of Statin and Statin + Carnitine on Tetanus of Rat Gastrocnemius Muscle

Parameters	Control	Statin	Statin + Carnitine	Control	Statin	Statin + Carnitine
	At Low Frequency			At High Frequency		
Force of Contraction (Kg/cm^2)	0.22 ± 0.006 (21)	$0.15 \pm 0.004^*$ (20)	$0.21 \pm 0.009 \phi$ (20)	0.91 ± 0.038 (21)	$0.55 \pm 0.02^*$ (20)	$1.0 \pm 0.06 \phi$ (20)
Half Relaxation Time (mS)	9.7 ± 0.35 (18)	10.8 ± 0.56 (18)	$12.7 \pm 0.76^*$ (20)	71.0 ± 2.8 (18)	$52.0 \pm 1.76^*$ (18)	$51.0 \pm 1.5^*$ (20)
Rate of Rise of Tetanus (g/sec)	21.7 ± 0.84 (21)	$15.5 \pm 0.54^*$ (20)	$18.5 \pm 0.5^* \phi$ (20)	10.7 ± 0.52 (21)	$7.8 \pm 0.35^*$ (20)	$11.7 \pm 0.39 \phi$ (20)
Rate of Relaxation (g/sec)	16.7 ± 1 (18)	$8.6 \pm 0.56^*$ (20)	$10.69 \pm 0.77^*$ (15)	2.0 ± 0.16 (18)	2.4 ± 0.18 (20)	$4.3 \pm 0.255^* \phi$ (15)

The values represent Mean $\pm$ SE. * shows a significant change (P value < 0.01) when compare with control. ϕ shows a significant change when a comparison was made between statin treatment and statin + carnitine treated groups. Values in parentheses indicate number of experiments

3) Length Tension Relationship: We plotted muscle tension against its length to see the relationship between these parameters. Graph shows that with increase in length of muscle, force of contraction was also increased up to a certain point and then started to decline with further increase in the length of muscle

(Figure 2). Stain significantly reduced the force of contraction by each cm increase in length of muscle and reached to a maximum strength on 3.2 ± 0.03 cm, in contrast to 3.0 ± 0.006 cm in control. Force of contraction in the carnitine group reversed this effect back to the control group in the initial lengths of muscle

and also showed resting length very close to control. While the force of contractions of carnitine group after resting length was declined more rapidly than control.

4) Tetanus Parameters: Force of Contraction of tetanus at low frequency was decreased by statin treatment upto 59% (control 0.22 ± 0.006 , statin 0.13 ± 0.004 ; $P < 0.0001$) while treatment of carnitine along with statin reversed this effect. Rates of rise and relaxation of Tetanus were also markedly reduced by Statin treatment up to level of significance ($P < 0.0001$). Improvement by carnitine was brought only in rate of rise of tetanus (Table 3)

At high frequency, force of contraction, half relaxation time and rate of rise of tetanus were significantly decreased by statin treatment ($P < 0.0001$). Carnitine also showed similar effect as was observed in low frequency. However, carnitine treatment had no effect on half relaxation time (Table 3).

We also calculated twitch-tetanus ratio of each group at both low and high frequency. We observed no significant change in the ratio of force of contraction of single twitch to tetanus at both low and high frequency. (Table 4)

Table No.4: Effect of Statin and Statin + Carnitine on Twitch-Tetanus Ratio of Rat Gastrocnemius Muscle

Parameters	Control	Statin	Statin + Carnitine
Ratio with low frequency	1.089 ± 0.013 (21)	1.10 ± 0.042 (20)	1.16 ± 0.016 (20)
Ratio with high frequency	0.272 ± 0.009 (21)	0.0277 ± 0.012 (20)	0.246 ± 0.0093 (20)

The values represent Mean $\pm$ SE. * shows a significant change (P value < 0.01) when compare with control. ϕ shows a significant change when a comparison was made between statin treatment and statin + carnitine treated groups. Values in parentheses indicate number of experiments

DISCUSSION

We assessed the effects of chronic statin treatment on the mechanical properties of rat gastrocnemius muscles and use of carnitine along with statin to judge its preventive effect. For this purpose, we chose lipophilic atorvastatin because it is the most widely used drug all over the world. Other lipophilic statin simvastatin is already withdrawn from the market due to its deleterious effects like rhabdomyolysis¹³.

Atorvastatin treatment resulted in a marked reduction in the amplitude of force of contraction during twitch and tetanus stimulation. Possible mechanism of muscle damage including mitochondrial dysfunction associated with the generation of oxidative stress, calcium

imbalance¹⁴ and enhanced energy metabolism¹⁵ have been reported previously. Mechanical properties of skeletal muscle are directly related to electrical properties. In our study electrical properties were also found to be altered (unpublished results).

Structural and functional modifications in skeletal muscle by statins are more prominent in fast twitch muscle¹⁶. We used gastrocnemius muscle which is a combination of fast and slow twitch fibers.

In our study, we observed that carnitine prevented this adverse effect of atorvastatin and increased the amplitude of force of contraction. Similar protective results were seen by carnitine in which tetanic contraction of soleus muscles was increased after ischemic reperfusion¹⁷. In another study, contractile functions of muscles were decreased at high frequency stimulation in the type 2 diabetic animal models and detected reduced level of carnitine¹⁸. This suggests that statin might have decreased carnitine level in the muscle and serum that led to altered contractile properties of skeletal muscle. Sufficient level of carnitine in the plasma prevented the generation of free radicals¹⁹. It has also been established that availability of carnitine limits the rate of fat oxidation. In addition, carnitine also prevents cytotoxicity by reducing mitochondrial permeability²⁰.

CONCLUSION

In conclusion, adverse effects of atorvastatin on contractile properties of skeletal muscle can be reduced with the use of carnitine.

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Frequency of Category 1 and Category 2 Tuberculosis in District Kotli Azad Kashmir

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ABSTRACT

Objective: To estimate the frequency of Category 1 and 2 Tuberculosis in area of research.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted in District Kotli Azad Kashmir from January 2009 to December 2009.

Material and Methods: This study was conducted with a population of 750,000. Data was collected from all the eight national TB centres in the District Kotli. It included every patient registered there with the diagnosis of tuberculosis including pulmonary and extra pulmonary tuberculosis and sputum smear positive and negative patients. They were classified as category 1 and category 2 according to the standard definitions. Results were given in tabulated form.

Results: From a total of 752 patients, 579 (76.99%) were pulmonary and 173 (23%) were extra pulmonary. In pulmonary TB cases, 259 (44.78%) were sputum smear positive [235 (90.73%) of them were category 1 and 24 (9.24%) were category 2]. In 320 (55.26%) sputum smear negative patients, 300 (93.75%) were category 1 and 20 (6.25%) were category 2. All of the extra pulmonary TB cases were category 1 (100%). As a whole 708 (94.15%) were category 1 and 44 (5.85%) were category 2.

Conclusion: In our study frequency of category 2 patients was found to be relatively low. It indicates that the problem of drug resistant tuberculosis is probably low in the area. It also shows the effectiveness of local TB control programme.

Key words: Category 1 and category 2 tuberculosis; MDR tuberculosis; Azad Kashmir

INTRODUCTION

Tuberculosis (TB) is highly prevalent in Pakistan. Pakistan is included in top five countries with highest burden of the disease. It is second most common cause of death among the infectious diseases.¹ Treatment of TB poses a special problem especially for poor countries like Pakistan. Due to peculiar structure of mycobacterial cell wall, most of the common antibiotics are not effective. There are limited numbers of antibiotics which must be given in combination for a prolonged period of time. Although with treatment TB is a curable disease in almost all the cases of drug sensitive tuberculosis, but without treatment 50-65% of patients die within five years.² Treatment regimens are costly and prolonged and are associated with many side effects which makes the compliance difficult. So there are quite high chances that patients may leave the treatment before it is complete. Lack of health education compounds the problem further. This is dangerous because it leads to emergence of drug resistant tuberculosis which is very difficult to treat. A report from Delhi, India clearly demonstrated that primary resistance was responsible for only 1.4% cases

of MDR (Multi Drug Resistant) TB, the rest being due to improper treatment.³

TB is a highly contagious disease and can easily spread by droplet infection to the close contacts of the patient. All over the world approximately two billion people are infected but most of them are asymptomatic.⁴ There were approximately 8.7 million new cases of TB throughout the world during the year 2011.¹ Millennium Development Goal (MDG) target was set by WHO to stop the progression and reduce the incidence of tuberculosis epidemic by 2015 and to eliminate the TB as public health problem by 2050.¹ One of the best ways of preventing the disease is to detect and treat the patients as early as possible before they can transmit the infection to others. So the efficient and appropriate treatment of TB is essential. But achieving this goal is not easy because of the problems related to the treatment of TB mentioned earlier. In practice most of the patients may start the treatment but many of them default before the completion. Today we know that MDR TB is a man made problem because of improper treatment of tuberculous cases.⁵

In a study from India the incidence of MDR TB in Delhi was found to be 14%.³ These patients are very dangerous to the community and their treatment is

really challenging. The success rate for MDR TB was 60-80% and for XDR (Extensive Drug Resistance) TB 44-60%.⁵ They cannot be treated with routine anti TB regimens and need second line drugs which may be more expensive and cause more side effects.⁶ Although the treatment is possible with currently available drugs but the chances of treatment failure are high with a higher mortality.⁷

There are a number of factors responsible for development of drug resistant TB. One of the most important factors is the previous history of treatment with anti TB drugs.⁸ Considering the importance of this factor, TB cases have been divided into two groups as following:

Category 1: Newly diagnosed cases of tuberculosis who never received the anti TB treatment before. Chances for them to be drug resistant are quite minimal and they can be started on the routine standard treatment of TB i.e. 2(R, H, Z, E) and 4(R, H).

Category 2: Patients presenting with tuberculosis who have previously received anti TB treatment. These include treatment failure cases, relapsed cases or those who defaulted without completing the treatment and now returned after treatment interruption.⁹

Chances of category 2 patients to have drug resistant tuberculosis are so high that they are treated with special intensive anti TB regimens which include five drugs in first two months, four drugs for next one month and then three drugs for subsequent five months e.g. 2(S, R, H, Z, E), 1(R, H, Z, E) and 5(R, H, Z). Rise in incidence of drug resistant tuberculosis along with the pandemic of HIV and increased population movement are a big obstacle to the effective control of TB all over the world.¹⁰ Constant provision of funds to implement the regional and global action plans against tuberculosis are needed for control of MDR and XDR TB and it needs the committed political leadership which can understand and foresee the magnitude of the problem.¹⁰

It is clear that treatment of category 2 patients is very difficult due to obvious reasons. If these patients are not recognized at the onset and not started on appropriate treatment, chances of their cure are minimal. This is dangerous for themselves as well as for the community. Furthermore inappropriate treatment may lead to XDR TB which is extremely difficult to treat. Keeping in mind all these factors we have tried to determine the frequency of category 1 and category 2 patients in district Kotli Azad Kashmir, a remote area towards north of Pakistan. This will indirectly assess the problem of drug resistant tuberculosis in the area. It will also throw light on the success and effectiveness of TB control programme. The data may be used for proper planning and appropriately targeting the efforts and resources of anti TB control programmes. The data may also be helpful for further research to determine the actual incidence of drug resistant tuberculosis in category 2 patients by doing culture and sensitivity of their sputum samples.

MATERIALS AND METHODS

This was a cross sectional study conducted in District Kotli Azad Kashmir which is an area towards north of Pakistan with a population of 750, 000. Data was collected from all the eight national TB centres in the District Kotli. It included every patient registered there with the diagnosis of tuberculosis from January 2009 to December 2009. All the patients of tuberculosis including pulmonary TB, sputum smear positive and negative patients and extra pulmonary cases were classified as category 1 and category 2 according to the standard definitions mentioned earlier in the introduction. Results were given in tabulated form.

RESULTS

Total of 752 patients were registered as tuberculous during the study period. Among them 579 (76.99%) were pulmonary and 173 (23%) were extra pulmonary tuberculosis. In pulmonary TB cases, 259 (44.78%) were sputum smear positive of whom 235 (90.73%) were category 1 and 24 (9.24%) were category 2. In 320 (55.26%) sputum smear negative patients, 300 (93.75%) were category 1 and 20 (6.25%) were category 2. All of the extra pulmonary TB cases (100%) were category 1. As a whole from total of 752 patients, 708 (94.15%) were category 1 and 44 (5.85%) were category 2. (See Table 1 and Figure 1)

Table No.1: Category of TB cases in various types of tuberculosis

Type of tuberculosis		Category of cases		Total
		Category 1	Category 2	
Pulmonary	Sputum smear positive	235 (90.73%)	24 (9.24%)	259
	Sputum smear negative	300 (93.75%)	20 (6.25%)	320
Extra pulmonary		173 (100%)	0	173
Total		708 (94.15%)	44 (5.85%)	752

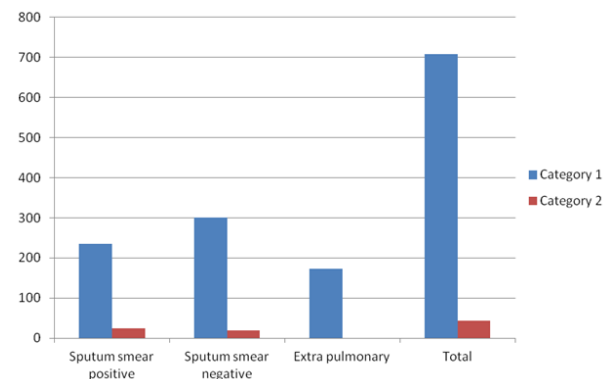


Figure No.1: Number of category 1 and category 2 cases in various types of tuberculosis

DISCUSSION

Tuberculosis is one of the oldest infectious diseases in the human history. Its treatment and control has always remained a challenge. With the development of anti TB drugs it was felt that the time of tuberculosis was over. But from the very beginning it was associated with multiple problems. We had only limited number of anti TB drugs. Streptomycin (S), Rifampicin (R), isoniazid (H), Pyrazinamide (Z) and Ethambutol (E) were the first line anti TB drugs. Most of the countries with highest disease burden were poor with very low economic resources to implement the proper TB control programmes and to provide complex and costly anti TB regimens. On top of that many of them were affected by political and social unrest, conflicts and corruption. Emergence of HIV epidemic in 1980s dramatically increased the incidence of TB throughout the world. Pakistan was amongst those with highest disease burden. WHO survey has indicated that incidence and prevalence of TB in Pakistan is 230 and 310 per hundred thousand respectively while the mortality is estimated to be 39/100,000.¹¹ With the consideration of poverty, poor socioeconomic conditions and lack of proper health facilities, it is extremely difficult to treat such an enormous number of patients adequately. Currently the world is facing another great problem in the control of TB i.e. the emergence of multi drug resistance (MDR) and extensive drug resistance (XDR) tuberculosis. MDR is defined as resistance against at least two drugs Rifampicin and Isoniazid, which are very important first line anti TB drugs. XDR is characterized by development of resistance, apart from rifampicin and INH, against one of the fluoroquinolones and one or more of the second line injectable drugs like Kanamycin, Capreomycin or Amikacin.^{5,2} This is a very dangerous development. Treatment of MDR and XDR TB is extremely difficult. It needs addition of more drugs including second line drugs which increases the cost and toxicity of the regimens.⁶ According to recommendations at least four drugs should be given to which mycobacterial isolates are sensitive. The drugs are chosen from five groups in a stepwise fashion on the basis of their efficacy, safety and cost.¹³ Previous treatment with second line drugs has increased the risk of resistance to these drugs leading to development of XDR TB.¹⁴ MDR TB is a major hurdle to TB control especially in certain areas of the world like some provinces of China and countries from former Soviet Union.^{15,16}

Drug resistance can develop in category 1 patients due to random genetic mutations in the mycobacteria but its frequency is very low. Exposure to anti TB drugs leads to selection pressure with predominant survival of drug resistant strains over susceptible strains. According to fourth report of global anti TB drug resistance, the prevalence of MDR TB in category 1 was 1.6% and in

category 2 it was 11.7%. During 2006 there were half a million MDR TB cases and 50% of them were in China and India.¹⁷ In 2008, 440,000 cases of MDR TB were found globally and it led to death of 150,000 patients. Among MDR TB, 5.4% were found to be XDR. All this is a man made problem which can be prevented by effective and prompt first line anti TB therapy of category 1 patients.¹⁸

A study from India found that prevalence of MDR TB was 20.4% among patients of category 2 pulmonary TB. Various other studies from India showed the prevalence of MDR TB to vary between 14 to 49% in patients who previously had received anti TB treatment. Such findings suggest that all category 2 patients should be screened for MDR TB. [9] On the other hand prevalence of MDR TB is low in category 1 pulmonary TB cases. A study from India showed the prevalence in such cases to be 1.1%. In various studies from India it varied between 0.14% to 5.3%.¹⁹ In a study from Gujarat state of India, MDR TB was found to be very low in category 1 patients (2.4%) but it was quite high in category 2 patients (17.4%). Among MDR cases there was very high resistance rate against Ofloxacin (24%) which can hamper the treatment and control of MDR TB.²⁰

It is of utmost importance to detect MDR and XDR TB cases early and start them on appropriate treatment. This can be done by high quality culture and sensitivity tests. But it is difficult and expensive. History of previous treatment with anti TB drugs is reliably associated with the risk of drug resistance and detection of category 2 patients can recognize those at risk of drug resistant tuberculosis. They can then be started on more intensive treatment regimens. In our study overall less than 10% patients were category 2. This is rather welcoming news because frequency of drug resistant TB is much higher in many parts of the world. Incidence of MDR tuberculosis in Delhi was 14% most which was due to improper previous treatment.³ According to WHO data from Pakistan, during 2012 frequency of MDR TB in retreatment cases was 32% while it was only 3.5% in newly diagnosed cases.²¹ More than 510,000 cases of MDR TB occur annually.²² According to a survey report from America, 20% of the isolates were MDR and 2% were XDR.²³

Treatment and control of MDR and XDR TB is cumbersome and its cost can be so high that it can drain all the money from the insufficient resources of the poor countries. It can destroy all our efforts for the control of TB globally.⁵ Stop-TB Drug-Resistance Programme was started to ensure optimal delivery of appropriate anti TB regimens. Its key components include strong political commitment, quality-assured drug susceptibility testing, reliable supply of good quality drugs, directly observed therapy settings, and strict monitoring of the individual treatment outcome and overall performance of the TB control programme.

[6] MDR TB is more common in poor and developing countries and more funds should be allocated for them to provide its quick and effective treatment. It is now possible through the Global Fund to Fight AIDS, TB, and Malaria, and the Green Light Committee for Access to Second-line Anti-tuberculosis Drugs.²⁴ To control tuberculosis it is essential to involve all the public and private practitioners and train them properly in the diagnosis and treatment.²⁵

In their study, Dr Mercedes C Becerra et al found that the households contacts of drug resistant tuberculosis patients, who developed active TB and who were tested for drug resistance, had very high frequency of MDR TB (90.9%).²⁶ According to these results, the chances of drug resistant TB in the household contacts of MDR and XDR TB patients are so high that if they are found to have active TB, they should be considered as category 2 patients and started on category 2 regimens although they may not have previous history of partial or complete anti TB treatment.

Low frequency of category 2 patients in our study indicates that the risk of MDR and XDR is probably low in the area. Further studies are needed to estimate the exact frequency of drug resistant tuberculosis in these category 2 patients. To minimize the risk of drug resistance we must implement all the preventive strategies like early diagnosis and treatment of category 1 patients, proper follow up and surveillance, inclusion and training of both private and public practitioners in the TB control programmes and efficient detection and appropriate treatment of category 2 cases. This needs a strong political will and constant supply of necessary funds.

CONCLUSION

MDR and XDR TB is an emerging problem throughout the world which can destroy all our efforts to control tuberculosis and eliminate it as a public health problem. Diagnosis of MDR and XDR TB needs costly investigations which are difficult to afford by a poor countries like Pakistan. Measuring the incidence of category 2 patients can give an indirect estimate of drug resistant TB. In our study frequency of category 2 patients was found to be relatively low. It indicates that problem of drug resistance is probably low in the area. It also shows the effectiveness of local TB control programme.

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Frequency of Chemotherapy Induced Neutropenia in Patients of Non Hodgkin's Lymphoma

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ABSTRACT

Objective: The aim of the study is to see the frequency and severity of neutropenia after first or subsequent cycles of chemotherapy in patients of Non Hodgkin's lymphoma (NHL).

Study Design: Descriptive cross sectional study.

Place and Duration of Study: This study was carried in the Radiotherapy & Oncology Department, Bolan Medical Complex Hospital, Quetta, from March 2010 to February 2012.

Patients and Methods: Forty two patients of different types of NHL diagnosed on lymph node biopsy presenting for the first time at Radiotherapy & Oncology Department in collaboration with Haematology Section (Pathology Deptt:), Bolan Medical Complex Hospital, Quetta, were included. They were admitted in the ward and evaluated with history, physical examination and for staging investigations. Patients were then planned for chemotherapy comprising cyclophosphamide, doxorubicin, and vincristine with prednisolone (CHOP) and with rituximab (R-CHOP). After the first cycle of chemotherapy they were monitored for expected neutropenia in the ward. The neutrophil counts were repeated on days 7 and 10 following chemotherapy. Neutropenia was graded as defined in the operational definition and all the data were entered on a designed data sheet.

Results: Forty two patients of NHL were included in this study, of which 34 patients received CHOP, and 08 patients R-CHOP, from march, 2010 to February, 2012. According to WHO classification, 24(57.1%) patients were of Diffuse large B-cell lymphoma (DLBCL), 08(19.0%) were follicular lymphoma (FL) and 04(9.5%) patients were Mantle cell lymphoma (MCL) and remaining 06(14.3%) are other types of NHL's. 2(4.7%) of patients suffered from grade IV neutropenia (absolute neutrophil count of $<0.5 \times 10^9/L$), 3(7.1%) had grade III Neutropenia (absolute Neutrophil count of $0.5 \times 10^9/L - 0.9 \times 10^9/L$), 3(7.1%) had Grade II neutropenia (absolute neutrophil count $1.5 \times 10^9/L - 1.4 \times 10^9/L$) and 5(11.9%) had Grad I neutropenia (absolute neutrophil count $1.5 \times 10^9/L - 1.9 \times 10^9/L$). Other risk factors noted, i.e., cardiac, Liver and Renal comorbidities in 3(7.1%), 5(11.9%) and 4(9.5%) of patients respectively.

Conclusion: Overall 30.8% of patients of NHL's suffered from neutropenia of all grades post first cycle of chemotherapy comprising CHOP and R-CHOP.

Key Words: Non Hodgkin's lymphoma, Neutropenia

INTRODUCTION

Chemotherapy induced neutropenia (CIN), is serious doselimiting toxicities that occur frequently during the first or subsequent cycles of chemotherapy. Identifying patients most at risk of developing CIN might help physicians to target prophylactic treatment with Granulocyte Colony-stimulating factor (G-CSF), in order to decrease the incidence, or duration of myelosuppression and facilitate delivery of chemotherapy as planned.

Myelosuppression represents a major toxicity of systemic cancer chemotherapy associated with considerable morbidity, mortality, and costs.¹ Such complications also result in dose reductions or treatment delays, which may compromise clinical outcomes.^{2,3} Previous studies have demonstrated that the risk of an initial episode of chemotherapy induced febrile neutropenia (FN) is greatest during the first

cycle of treatment when most patients are receiving full dose intensity often without prophylactic measures.^{4,5} The standard CHOP chemotherapy may produce severe neutropenia in first cycle which may compel for dose modification and early termination of therapy.⁶ While several studies have suggested that standard therapy may improve the outcome of patients, the requirement for dose reductions (from any cause) has been associated with lower response and survival rates.⁷ The addition of rituximab to the CHOP regimen (R-CHOP) has further improved patient outcomes.^{8,9}

CIN is a frequent and potentially serious adverse effect of cancer treatment¹⁰. Lymphoma patients with CIN who develop febrile neutropenia are typically hospitalized and treated with intravenous antibiotics^{11,12,13}. A common response to CIN is to reduce or delay delivery of chemotherapy treatment¹⁰. National Comprehensive Cancer Network Inc, 2008a, confirmed R-CHOP the current standard of care^[14].

CHOP-like chemotherapy carries a significant risk of FN (17-50%)^{15,16,17}. In addition to the risk associated with the chemotherapy regimen, other risk factors should be considered in order to determine the patient's overall FN risk^{14,15}. Several retrospective studies have identified potential risk factors for FN in lymphoma patients, including older age, low baseline blood cell counts, low serum albumin, anaemia, abnormal bone marrow, increased lactate dehydrogenase (LDH), co-morbid renal, cardiovascular or hepatic disease, full or high-risk planned chemotherapy regimen, and lack of G-CSF prophylaxis^{18,19}.

CIN is an important reason for not maintaining the desired dose intensity of CHOP therapy. A large percentage of neutropenia related deaths occurring within the initial (first 2) cycles of therapy has been described in several studies which emphasize the importance and severity of these events²⁰. Patients surviving these initial events may experience repeated events during their future course of treatment. This early neutropenic complication may impact the total length of hospitalization and thus influence not only economic factor but also the patients compliance to further chemotherapy²¹.

The present study was planned with a view to determine the frequency and severity of neutropenia in patients with NHL. These studies may help to target high-risk patients for prophylactic treatment in order to decrease the incidence of myelosuppression and enable full-dose chemotherapy to be delivered on schedule.

MATERIALS AND METHODS

This was a descriptive cross sectional study, conducted at Radiotherapy & Oncology Department in collaboration with Haematology Section (Pathology Deptt:), Bolan Medical Complex Hospital, Quetta, from march 2010 to February 2012.

42 patients of NHL diagnosed on lymph node biopsy presenting for the first time were studied. Convenience (non probability) sampling technique was used. All new patients of NHL diagnosed on lymph node biopsy who have not received any chemotherapy previously and age between 26-62 years were included. Patients with diabetes mellitus or on steroid therapy for any other reason were excluded. Patients with ischemic heart disease and cardiac dysfunction with an ejection fraction of less than 50% were also excluded.

RESULTS

On presentation the patients were admitted and a detailed history was recorded, followed by thorough physical examination especially emphasizing on evidence of lymphadenopathy and hepatosplenomegaly recording the size of each. Patients height and weight were recorded and body surface area was calculated using standard tables. This was followed by the base line investigations and staging investigations

including Blood complete picture and platelets counts, serum urea and creatinine, Liver function tests, chest X-Ray PA view/CT scan, Ultrasound abdomen/CT scan, Bone marrow aspiration and trephine examination, Blood sugar random, serum uric acid, electrocardiogram (ECG) and echocardiogram in case of any ECG abnormality showing a suspicion of ischemic heart disease. Patients were then planned for first cycle of chemotherapy comprising CHOP or R-CHOP the doses of chemotherapy were calculated using the body surface area as Inj.

Table No.1: Patients and Baseline Disease Characteristics (n=42)

Age (years), mean $\pm$ SD (range)	38 $\pm$ 15 (26-62)
Gender, n(%)	
Male	36 (85.7)
Female	06 (14.2)
Height (cm), mean $\pm$ SD (range)	169.9 $\pm$ 9(145-194)
Weight(kg), mean $\pm$ SD(range)	75 $\pm$ 16(41-176)
BSA m ² , mean $\pm$ SD (range)	1.8 $\pm$ 0.2(1.3-2.4)
WHO classification, n(%)	
Diffuse large Cell	24 (57.1)
Follicular	08 (19.0)
Mantle Cell	04 (9.5)
Others	06 (14.2)
Ann Arbor Staging, n(%)	
I	04 (9.5)
II	08 (19.0)
III	12 (28.5)
IV	18 (42.8)
Regimen, n(%)	
CHOP	34 (80.9)
CHOP-R	08 (19.0)
Neutropenia Grading, n (%)	
Grade I	05 (11.9)
Grade II	03 (7.1)
Grade III	03 (7.1)
Grade IV	02 (4.7)
No of comorbidities, Mean $\pm$ SD (range)	2.1 $\pm$ 2.1(0-11)
Cardiac Comorbidity n(%)	03 (7.1)
Liver comorbidity n(%)	5 (11.9)
Renal Comorbidity n(%)	04 (9.5)
Baseline albumin<3.5g/dl, n(%)	06 (14.2)
LDH>1000mg/dL, n(%)	7 (16.6)
BSA Body surface area, WHO World health organization, SD Standard deviation	

Cyclophosphamide 750 mg/m², injection Doxorubicin 50 mg/m², and Inj. Vincristine 1.4 mg/m² (maximum

dose 2.0 mg). all of these drugs were given slowly intravenously via the wide bore canula on day 1 of therapy together with Tablets Prednisolon 60-100 mg/m² orally from day 1 to day 5. After the first cycle of chemotherapy the patients were monitored for expected bone marrow suppression for next 10 days. Colony-stimulating factors were not given prophylactically. The neutrophil counts were repeated on days 7 and 10 following chemotherapy. All the blood samples were sent to the Haematology laboratory where these sample were analysed on Hematology Analyzer (Medonic 20) through standard protocol. The reports showing neutropenia were also assessed by haematopathologist to reduce the chances of error.

All data were entered on the data entry sheet. The data was analysed using SPSS. Neutrophil count (ANC) was noted after first and subsequent cycles of chemotherapy. Fig 1: shows that 2(4.7%) of patients suffered from grade IV.

Neutropenia (absolute neutrophil count of $<0.5 \times 10^9/L$), 3(7.1%) had grade III neutropenia (absolute neutrophil count of $0.5 \times 10^9/L - 1.4 \times 10^9/L$) (Table-1). Overall 30.8% of patients suffered from neutropenia of all grades post 1st and second cycles of chemotherapy. LDH was high in 7(16.6%) of patients, other risk factors noted, i.e., are cardiac, liver and renal comorbidities in 3(7.1%), 5(11.9%) and 4(9.5%) of patients respectively.

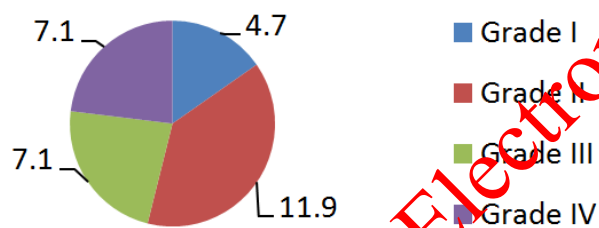


Figure No. 1: Grading of Neutropenia

DISCUSSION

The use of chemotherapy may improve tumor response rates in cancer patients, the prognosis for patients may be compromised by myelosuppression and its complications, including neutropenia and subsequent infective complications, often resulting in reduced chemotherapy dose intensity due to dose delays or reductions.

In this present study we treated NHL patients with standard chemotherapy regimens CHOP and R-CHOP and we observed the severity of neutropenia, found that overall 30.8% of patients suffered from all grades of neutropenia after first and second cycle of chemotherapy. The management of this neutropenia and its associated fever/infection costs are substantial and are likely to be an important cost driver especially in under developed countries. This fact was shown in a study from Germany by Herold et al²². Moreover in the

management of NHL with CHOP or R-CHOP chemotherapy, neutropenia after first and subsequent cycles may compel for dose modification and early termination of therapy. In this study several risk factors were found to be associated with febrile neutropenia among patients with NHL who were treated with CHOP-R-CHOP. The greatest risk of febrile neutropenia occurred during chemotherapy cycles 1 and 2 an increased risk was significantly associated with factors. i.e, age 56 years or older, baseline serum albumin level less than or equal to 3.5g/dL, ANC less than 1.5×10^9 at the time of presentation, and the presence of hepatic disease. The finding that the majority of initial hospitalizations for FN occur within the first 2 cycles of chemotherapy is consistent with a previous study in which 83% of these events occurred by cycle 3²³. The early time of onset is important because of the potential impact of resulting treatment delays or dose reductions on the overall dose intensity in patients with responsive and potentially curable. Malignancies such as NHL^{24,25,26}. These concerns are further confirmed by recent data, suggesting that patients hospitalized for FN in cycle 1 were 4.4 times more likely to prematurely discontinue CHOP chemotherapy, 19. Moreover in the management of NHL with CHOP, neutropenia after first cycle may compel for dose modification and early termination of therapy. This has an impact on survival also. As shown in a study by elizabeth at al the first-cycle FN hospitalisation and age ≥ 60 years were associated with premature termination of CHOP therapy and thus compromising survival²⁷. Abnormal bone marrow, BSA less than 1.9 m², serum albumin level less than 3.5g/dL, and LDH level greater than 1000/dL have all been identified as predictors of an increased risk for neutropenia in this patient population^{28,29}.

In another study from James P Wilmot Cancer centre, out of 577 patients receiving CHOP chemotherapy 160 patients experienced neutropenic events, i.e., 27% which was significantly associated with age more than or equal to 65 years^{30,31}. They further observed that first febrile neutropenic event occurred by day 14 of cycle 1 in one half of patients experiencing FN. In these studies the slightly higher percentage of patients experiencing the FN events may have occurred due to the relatively higher age group population³². However these events did affect the plan of chemotherapy that is early termination of chemotherapy. Longer lengths of stay and increased mortality rates have been associated with hospitalizations for older patients, possible because of comorbidities that are more common among the elderly^{33,34}.

CONCLUSION

The current study suggests that patients with NHL receiving CHOP or R-CHOP chemotherapy regimens who are at increased risk of hospitalization for febrile

neutropenia can be indentified. This may permit a more rational-targeted application of supportive care measures, such as the hamatopoietic growth factors, toward the patients at greatest risk and most likely to benefit.

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Frequency of Chemotherapy Induced Neutropenia in Patients of Non Hodgkin's Lymphoma

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ABSTRACT

Objective: The aim of the study is to see the frequency and severity of neutropenia after first or subsequent cycles of chemotherapy in patients of Non Hodgkin's lymphoma (NHL).

Study Design: Descriptive cross sectional study.

Place and Duration of Study: This study was carried in the Radiotherapy & Oncology Department, Bolan Medical Complex Hospital, Quetta, from March 2010 to February 2012.

Patients and Methods: Forty two patients of different types of NHL diagnosed on lymph node biopsy presenting for the first time at Radiotherapy & Oncology Department in collaboration with Haematology Section (Pathology Deptt:), Bolan Medical Complex Hospital, Quetta, were included. They were admitted in the ward and evaluated with history, physical examination and for staging investigations. Patients were then planned for chemotherapy comprising cyclophosphamide, doxorubicin, and vincristine with prednisolone (CHOP) and with rituximab (R-CHOP). After the first cycle of chemotherapy they were monitored for expected neutropenia in the ward. The neutrophil counts were repeated on days 7 and 10 following chemotherapy. Neutropenia was graded as defined in the operational definition and all the data were entered on a designed data sheet.

Results: Forty two patients of NHL were included in this study, of which 34 patients received CHOP, and 08 patients R-CHOP, from march, 2010 to February, 2012. According to WHO classification, 24(57.1%) patients were of Diffuse large B-cell lymphoma (DLBCL), 08(19.0%) were follicular lymphoma (FL) and 04(9.5%) patients were Mantle cell lymphoma (MCL) and remaining 06(14.3%) are other types of NHL's. 2(4.7%) of patients suffered from grade IV neutropenia (absolute neutrophil count of $<0.5 \times 10^9/L$), 3(7.1%) had grade III Neutropenia (absolute Neutrophil count of $0.5 \times 10^9/L - 0.9 \times 10^9/L$), 3(7.1%) had Grade II neutropenia (absolute neutrophil count $1.5 \times 10^9/L - 1.4 \times 10^9/L$) and 5(11.9%) had Grad I neutropenia (absolute neutrophil count $1.5 \times 10^9/L - 1.9 \times 10^9/L$). Other risk factors noted, i.e., cardiac, Liver and Renal comorbidities in 3(7.1%), 5(11.9%) and 4(9.5%) of patients respectively.

Conclusion: Overall 30.8% of patients of NHL's suffered from neutropenia of all grades post first cycle of chemotherapy comprising CHOP and R-CHOP.

Key Words: Non Hodgkin's lymphoma, Neutropenia

INTRODUCTION

Chemotherapy induced neutropenia (CIN), is serious doselimiting toxicities that occur frequently during the first or subsequent cycles of chemotherapy. Identifying patients most at risk of developing CIN might help physicians to target prophylactic treatment with Granulocyte Colony-stimulating factor (G-CSF), in order to decrease the incidence, or duration of myelosuppression and facilitate delivery of chemotherapy as planned.

Myelosuppression represents a major toxicity of systemic cancer chemotherapy associated with considerable morbidity, mortality, and costs.¹ Such complications also result in dose reductions or treatment delays, which may compromise clinical outcomes.^{2,3} Previous studies have demonstrated that the risk of an initial episode of chemotherapy induced febrile neutropenia (FN) is greatest during the first

cycle of treatment when most patients are receiving full dose intensity often without prophylactic measures.^{4,5} The standard CHOP chemotherapy may produce severe neutropenia in first cycle which may compel for dose modification and early termination of therapy.⁶ While several studies have suggested that standard therapy may improve the outcome of patients, the requirement for dose reductions (from any cause) has been associated with lower response and survival rates.⁷ The addition of rituximab to the CHOP regimen (R-CHOP) has further improved patient outcomes.^{8,9}

CIN is a frequent and potentially serious adverse effect of cancer treatment¹⁰. Lymphoma patients with CIN who develop febrile neutropenia are typically hospitalized and treated with intravenous antibiotics^{11,12,13}. A common response to CIN is to reduce or delay delivery of chemotherapy treatment¹⁰. National Comprehensive Cancer Network Inc, 2008a, confirmed R-CHOP the current standard of care^[14].

CHOP-like chemotherapy carries a significant risk of FN (17-50%)^{15,16,17}. In addition to the risk associated with the chemotherapy regimen, other risk factors should be considered in order to determine the patient's overall FN risk^{14,15}. Several retrospective studies have identified potential risk factors for FN in lymphoma patients, including older age, low baseline blood cell counts, low serum albumin, anaemia, abnormal bone marrow, increased lactate dehydrogenase (LDH), co-morbid renal, cardiovascular or hepatic disease, full or high-risk planned chemotherapy regimen, and lack of G-CSF prophylaxis^{18,19}.

CIN is an important reason for not maintaining the desired dose intensity of CHOP therapy. A large percentage of neutropenia related deaths occurring within the initial (first 2) cycles of therapy has been described in several studies which emphasize the importance and severity of these events²⁰. Patients surviving these initial events may experience repeated events during their future course of treatment. This early neutropenic complication may impact the total length of hospitalization and thus influence not only economic factor but also the patients compliance to further chemotherapy²¹.

The present study was planned with a view to determine the frequency and severity of neutropenia in patients with NHL. These studies may help to target high-risk patients for prophylactic treatment in order to decrease the incidence of myelosuppression and enable full-dose chemotherapy to be delivered on schedule.

MATERIALS AND METHODS

This was a descriptive cross sectional study, conducted at Radiotherapy & Oncology Department in collaboration with Haematology Section (Pathology Deptt:), Bolan Medical Complex Hospital, Quetta, from march 2010 to February 2012.

42 patients of NHL diagnosed on lymph node biopsy presenting for the first time were studied. Convenience (non probability) sampling technique was used. All new patients of NHL diagnosed on lymph node biopsy who have not received any chemotherapy previously and age between 26-62 years were included. Patients with diabetes mellitus or on steroid therapy for any other reason were excluded. Patients with ischemic heart disease and cardiac dysfunction with an ejection fraction of less than 50% were also excluded.

RESULTS

On presentation the patients were admitted and a detailed history was recorded, followed by thorough physical examination especially emphasizing on evidence of lymphadenopathy and hepatosplenomegaly recording the size of each. Patients height and weight were recorded and body surface area was calculated using standard tables. This was followed by the base line investigations and staging investigations

including Blood complete picture and platelets counts, serum urea and creatinine, Liver function tests, chest X-Ray PA view/CT scan, Ultrasound abdomen/CT scan, Bone marrow aspiration and trephine examination, Blood sugar random, serum uric acid, electrocardiogram (ECG) and echocardiogram in case of any ECG abnormality showing a suspicion of ischemic heart disease. Patients were then planned for first cycle of chemotherapy comprising CHOP or R-CHOP the doses of chemotherapy were calculated using the body surface area as Inj.

Table No.1: Patients and Baseline Disease Characteristics (n=42)

Age (years), mean $\pm$ SD (range)	38 $\pm$ 15 (26-62)
Gender, n(%)	
Male	36 (85.7)
Female	06 (14.2)
Height (cm), mean $\pm$ SD (range)	169.9 $\pm$ 9(145-194)
Weight(kg), mean $\pm$ SD(range)	75 $\pm$ 16(41-176)
BSA m ² , mean $\pm$ SD (range)	1.8 $\pm$ 0.2(1.3-2.4)
WHO classification, n(%)	
Diffuse large Cell	24 (57.1)
Follicular	08 (19.0)
Mantle Cell	04 (9.5)
Others	06 (14.2)
Ann Arbor Staging, n(%)	
I	04 (9.5)
II	08 (19.0)
III	12 (28.5)
IV	18 (42.8)
Regimen, n(%)	
CHOP	34 (80.9)
CHOP-R	08 (19.0)
Neutropenia Grading, n (%)	
Grade I	05 (11.9)
Grade II	03 (7.1)
Grade III	03 (7.1)
Grade IV	02 (4.7)
No of comorbidities, Mean $\pm$ SD (range)	2.1 $\pm$ 2.1(0-11)
Cardiac Comorbidity n(%)	03 (7.1)
Liver comorbidity n(%)	5 (11.9)
Renal Comorbidity n(%)	04 (9.5)
Baseline albumin<3.5g/dl, n(%)	06 (14.2)
LDH>1000mg/dL, n(%)	7 (16.6)
BSA Body surface area, WHO World health organization, SD Standard deviation	

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