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General Principles:

Authors should submit the manuscript typed in MS Word. Manuscripts should be written in English in British style/format in past tense and third person form of address. Sentence should not start with a number or figure. The manuscript should be typed in double spacing as a single column on A4, with white bond paper with one inch (2.5cm) margin on one side in Times New Roman style (12 font). Pages should be numbered consecutively through the last page of type written material. The material submitted for publication may be in the form of an original article, a review article, a case report or letter to the editor. Original articles should report original research with about 2000 words with not more than three tables or illustrations. References should not exceed 40 in number. Short communications should be of 250 words approximately. Letter should not exceed 150 words.

Components of manuscript should be in the following sequence:

TITLE PAGE: It should include the following: article title, abstract word count, manuscript word count, and the number of tables and figures.

- The title of the article. Authors should include all information in the title that will make electronic retrieval of the article both sensitive and specific. The title should be clear and concise. The title length should not exceed more than 14 words. Do not capitalize the first letter of each word in the title unless it is a proper noun. Do not use abbreviations in the title.
- Name of authors with highest academic degrees of each, their postal addresses, fax, phone number and mobile numbers.
- The name of the department(s) and institution(s) to which the work should be attributed.
- Disclaimers, if any.

- Corresponding authors. The name, mailing address, telephone and fax numbers, and e-mail address of the author responsible for correspondence about the manuscript.

ABSTRACT: It should be structured, not more than 250 words, briefly mentioning under following sub- headings Objectives, Design, Place and duration of study, Methods, Results and Conclusion. Abstracts should be followed by 3-5 MeSH (Medical Subject Headings) words. Use appropriate terms to increase searchability of your study.

MANUSCRIPT FORMAT:

INTRODUCTION: Present a background for the study. Include global, regional and local reports where appropriate. Cite only strictly pertinent references. State the purpose or objective of the study without sub- headings. Explain the hypothesis and the rationale of the research. Do not include data or conclusions from the current study.

MATERIAL AND METHODS: Methodology should be written including study design, ethical review statement, description of the selection of the observational or experimental subjects, study setting, study duration, sampling method, sample size calculations with references, follow-up period, inclusion and exclusion criteria, operational definitions, variables(independent and dependent), identification of the methods and apparatus (provide the manufacturer's name and address in parenthesis) and identification of all drugs and chemicals in paragraph/s form.

The source of the study subjects should be included and clearly described. The inclusion and exclusion criteria need to be elaborated. Any equipment used in the study should give the manufacturer's name and address. Procedures should be clearly described so as to facilitate others to reproduce them easily. References are necessary for to established methods, statistical methods, for already published methods not well-known, substantially modified methods with the reasons for using them, along with their limitations. All drugs and chemicals used should be stated in generic name(s), dose(s), and route(s) of administration. State the statistical software package used along with the version. Exact p-values and 95%confidence interval (CI) limits must be mentioned instead of only stating greater or less than level of significance. State the statistical software package used along with the version.

RESULTS: Emphasize or summarize only the most important observations. Give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical significance attached to them giving degree of freedom, test of significance value and p-value (in brackets) if any. Do not duplicate data in graphs and tables if already mentioned in text.

DISCUSSION: The discussion should begin with a summary of the main results. These are then discussed

with results of other published studies either supporting or refuting your results. Any new findings of the research should be emphasized and the relevance should be stated. These can be used for future research or clinical practice. Details of methodology or introduction should not be included in the discussion. Do not repeat in detail data or other information given in other parts of the manuscript, such as in the introduction or the results section. Limitations of the study should be stated at the end of the discussion in a separate paragraph.

CONCLUSION: It should be provided under separate headings and highlight new aspects arising from the study. It should be in accordance with the objectives.

REFERENCES: Vancouver style is essential for publication in Journal of Allama Iqbal Medical College. References should be cited in consecutive numerical order as first mentioned in the text and designated by the reference number in superscript. References appearing in a table or figure should be numbered sequentially with those in text.

The Journal follows Index Medicus style for references and abbreviated journal names according to the list of Journals indexed in Index Medicus: http://www.ncbi.nlm.nih.gov/nlmcatalog/

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Tables: Data should be placed clearly and concisely to enable the reader to comprehend easily. Do not repeat the results stated in tables in the text. Tables should be numbered consecutively and cited in the results. Arabic numerals should be used. The title should be short and explanatory and written on top of the table. The columns of the table should have a short heading. Footnotes should elaborate on the abbreviations. If any data or table has been included from a published article, the source should be cited.

Illustrations: Figures and pictures should clarify and augment the text. The selection of sharp, high-quality illustrations is of paramount importance. Figures of inferior quality will be returned to the author for correction or replacement. For x-ray films, scans, and other diagnostic images, pictures of pathology specimens or photomicrographs, high-resolution photographic image files are recommended. Legend should be placed below the figure and detailed explanations should be given as legends and not on the illustrations. Photomicrographs should have internal scale markers. Symbols, arrows, or letters used in photomicrographs should stand out on the background. Figures should have consecutive numbers and should be cited in the results accordingly in the text and written as "Figure". Arabic numerals should be used. Any symbols, arrows, numbers, or letters used to identify parts of the illustration should be explained clearly in the legend. Original illustrations should be submitted; previously published illustrations are not preferred. If a figure is taken from a previous publication, the source should be given as a reference. Written permission from the publisher should be provided by the author on submission of the manuscript.

HEALTH PROBLEMS IN FEMALES TAKING HORMONE BASED GROWTH PROMOTED POULTRY (HBGPP) FOOD IN VARIOUS CITIES OF PUNJAB

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House Officers, Jinnah Hospital Lahore

ABSTRACT

Background and objectives: In this study we are trying to assess Health Problems in Females taking Hormone Based Growth promoted Poultry (HBGPP) Food in various cities of Punjab, in the era of elite class with high grade Hormone Based Growth Based Poultry consumption. Study was conducted in various cities of Punjab including Lahore, Gujarat and Jhang. Objective of study was to explore Health Problems in Females taking Hormone Based Growth promoted Poultry (HBGPP) Food and assessing relationship between low and high grade chicken intake and corresponding health problems in females.

Material and Methods: This is Descriptive Cross sectional type of study conducted at various cities of Punjab including "Gujarat, Jhang and Lahore" during April – June, 2014 (03 months) with sample size of 150 subjects. Consecutive non-probability sampling technique was used to recruit the patients.

Data Collection and analysis: 150 subject those fulfilling the inclusion criteria were recruited for study from subjects of various cities of Punjab. After approval from ethical committee and informed consent from subjects detail demographic information collected. All the information entered in a structured questionnaire. Data analyzed in SPSS Version: 17.0. Mean and standard deviation calculated for numerical variables like age, parity and gravidity. Frequency and percentages calculated for nominal variables.

Result: In our study analysis, regarding age of respondents, 82.7% were between 18 to 26 years of age. 76% were unmarried.86% had professional education degree while 82% were student and 12.7 were house wives. 78. 7% were belonging with middle class families. 81.81% respondents got menstrual problems due to high grade chicken intake as compared to 67.12% respondents with low grade intake. 61% respondents with high grade chicken intake got abnormal hair growth as compared to 42.46% with low grade intake. 15.58% respondents got heaviness of voice with high grade chicken intake in comparison with 5.48% with low grade intake. 31% of respondents got hair fall with high grade chicken intake as compared to 13.69% with low grade intake. 68.80% respondents with high grade chicken intake got skin problems in comparison with 54.79% with low grade intake. While 74% respondents got other health problems like hypertension, Diabetes etc due to high grade chicken intake.

Conclusion: The results showed that frequency of certain problems like early menarche, menstrual complaints, hirsutism, male pattern baldness, heaviness of voice; skin changes and other problems (obesity, depression, breast lump, hypertension, and diabetes) are higher among those females who are taking high intake of HBGPP foods. These problems are more in younger females.

Recommendations: Public health education to be provided regarding safe and healthy poultry intake. Legislation to be formed at government level to ensure proper check and control on chicken feed. Inspection on regular basis to prevent any illegal hormone administration. Only licensed fast food companies should be allowed to advertise and sale their products.

Keywords: hormone based growth promoted poultry (HBGPP), high grade poultry consumption, problems of new era

According to the[1] European Union's Scientific Committee on Veterinary Measures Relating to Public Health, the use of six natural and artificial growth hormones in beef production poses a

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potential risk to human health. These six hormones include three which are naturally occurring — Oestradiol, Progesterone and Testosterone—and three which are synthetic—Zeranol, Trenbolone, and Melengestrol. The present broiler's diet consists of these hormones and that too in quantities much higher than allowed by FDA. The Committee also questioned whether hormone residues in the meat of "growth enhanced" animals can disrupt human hormone balance, causing developmental problems, interfering with the reproductive system.

The European Union's Committee reported that as of 1999, no comprehensive studies had been conducted to determine whether hormone residues in meat can be cancer-causing.[2] According to another study steroid hormones are added to some chicken feeds, specifically those fed to chickens that need to grow faster for more mature muscle content before butchering. This helps chicken farmers raise and sell chickens ready for slaughtering faster and with less cost to their operation due to a reduction in feed costs. However, these hormones are still present in chicken meat even after slaughtering and cooking, which means humans are getting this extra dose of steroid hormones too. Some international studies indicate precocious puberty directly related to hormone loaded foods [3,4,5,6,7,and8]

[9] Fast food consumption: predictor of weight gain from adolescence to adulthood in a nationally representative sample. Fast food consumption increased during the transition to adulthood, and is associated with increased weight gain from adolescence to adulthood. This behavior may be appropriate target for intervention during this important transition. The prevailing hormonal health issues of females in this era have motivated us to conduct this study. No completely similar study has been carried out as per our information in our region. With this study we wanted to identify problems faced by females so that the higher authorities could take measures for control of this issue.

OBJECTIVES OF THE STUDY

Major Objective:

"To identify Health Problems in a section of female population taking Hormone Based Growth promoted Poultry (HBGPP) Food in various cities of Punjab.

Sub-Objective:

"To determine the Health Problems in a section a section of female population according to frequency of Hormone Based Growth promoted Poultry (HBGPP) Food in various cities of Punjab.

Operational definitions

1. **Health Problems:**

In this study the Health problems are defined as symptoms presented by females taking the HBGPP Diet.

2. **Hormone based Growth promoted (HBGP) Poultry Food:**

I. Poultry farming is the raising of domesticated birds such as chickens for the purpose of farming meat or eggs for food.

ii. Hormone based Growth Promotion means use of steroid and growth hormones to increase the production of meat and eggs. The anabolic steroids (Hormones) use to promote growth includes estradiol, testosterone, progesterone and synthetic zeranol and trebalone.

3. **Grades HBGP-Poultry food intake**

i. Low grade Intake: Once / Twice a week

MATERIAL AND METHODS:

This is Descriptive Cross sectional type of study conducted at various cities of Punjab including "Gujarat, Jhang and Lahore" during April – June, 2014 (03 months) with sample size of 150 subjects. Consecutive non-probability sampling technique was used to recruit the patients.

Data Collection and analysis:

150 subject those fulfilling the inclusion criteria were recruited for study from subjects of various cities of Punjab. After approval from ethical committee and informed consent from subjects

detail demographic information collected. All the information entered in a structured questionnaire. Data analyzed in SPSS Version: 17.0. Mean and standard deviation calculated for numerical variables like age, parity and gravidity. Frequency and percentages calculated for nominal variables.

- **INCLUSION CRITERIA:**
– Females (16-35 yrs) who are apparently normal, having no diagnosed case of hormonal imbalance.
– Female taking HBGPP food e.g. Broiler Chicken.

- **EXCLUSION CRITERIA:**
– Females suffering from established reproductive diseases known to them.
– Female taking desi chicken.

Fig.03 **Educational Status of Study Subjects (n=150) percentage**
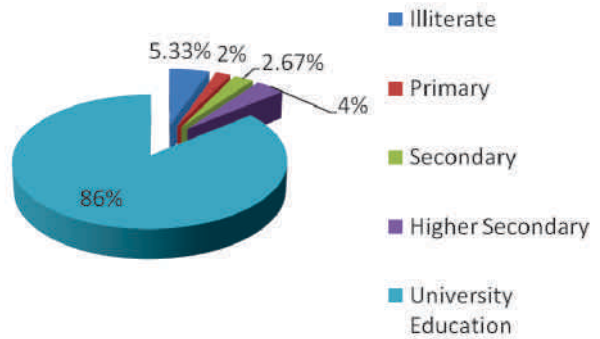
Fig.04 **Profession of Study subjects (n=150) percentage**
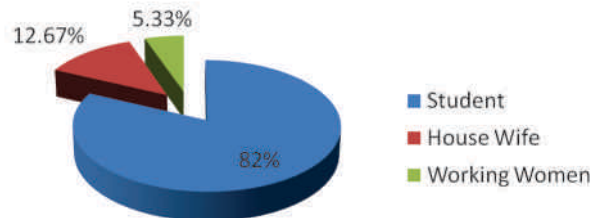
Fig.05 **Economic Status of Study Subjects (n=150) percentage**

Fig.01 **Age of Study Subject (n=150) percentage.**

Fig.02 **Marital Status of Study Subject (n=150) percentage.**
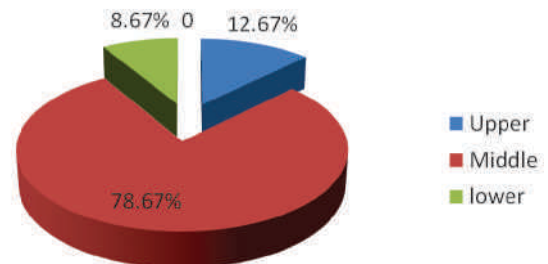
Fig.06 Relationship between the **Frequency of Chicken Intake** and **Onset of Period** in Study Subject (n=150) percentage
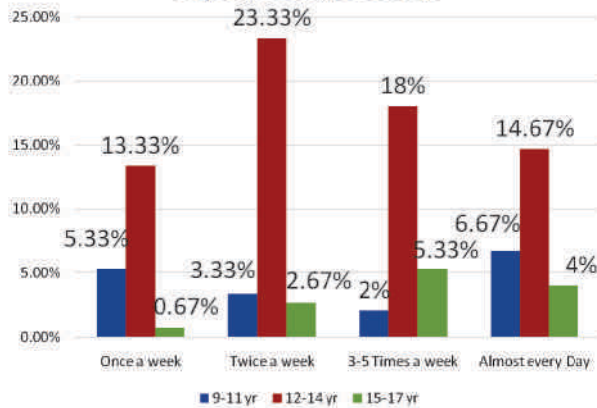
Fig.09 Relationship between Frequency of Chicken Intake and Heaviness of Voice in Study Subjects (n=150) percentage
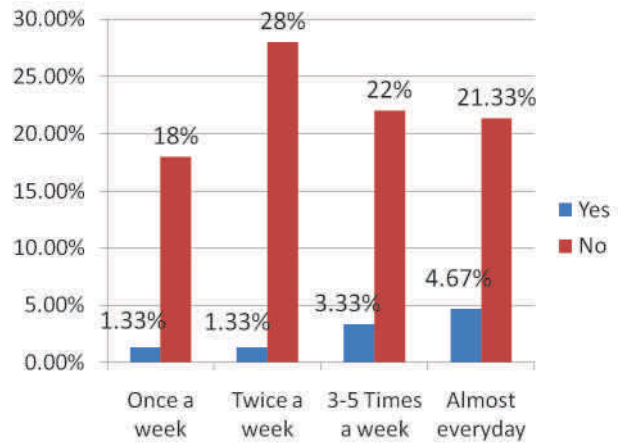
Fig.07 Relationship between the Frequency of Chicken Intake and Menstrual complaints in Study Subject (n=150) percentage
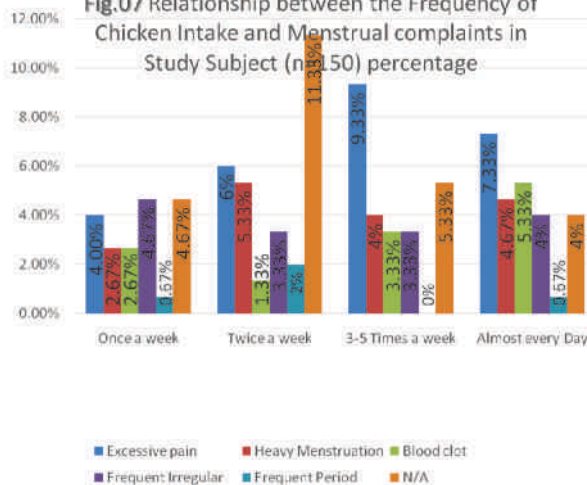
Fig 10 Relationship between the **Frequency of Chicken Intake** and **Hair fall** in Study Subject (n=150) percentage
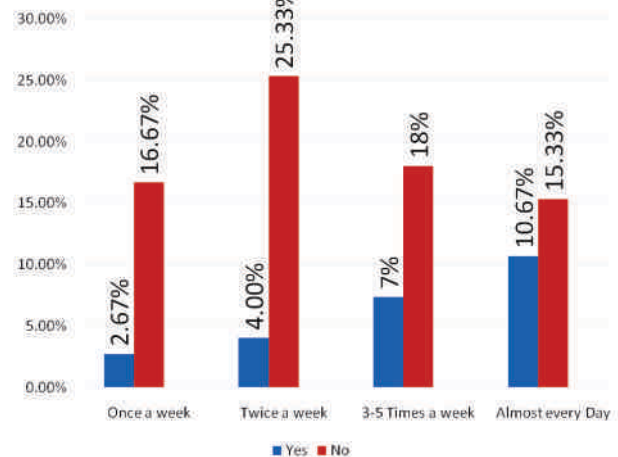
Fig 08 Relationship between the **Frequency of Chicken Intake** and **Hair Growth** in Study Subject (n=150) percentage
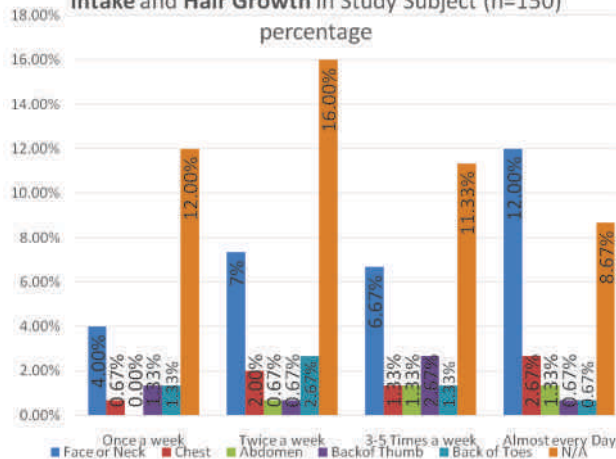
Fig 11 Relationship between the **Frequency of Chicken Intake** and **Skin Problem** in Study Subject (n=150) percentage
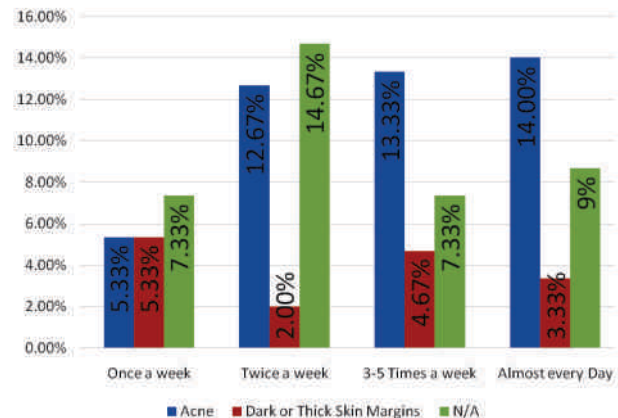
Fig 12 Relationship between the **Frequency of Chicken Intake** and **Other Health Problems** in Study Subject (n=150) percentage
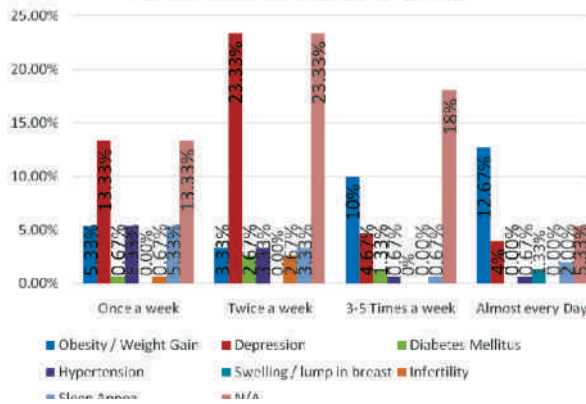
Occurrence of Health Problem in relation to frequency of Chicken Intake after the Results was pooled.

Fig 13 Menstrual Problems in relation to frequency of Chicken Intake (n=150) %
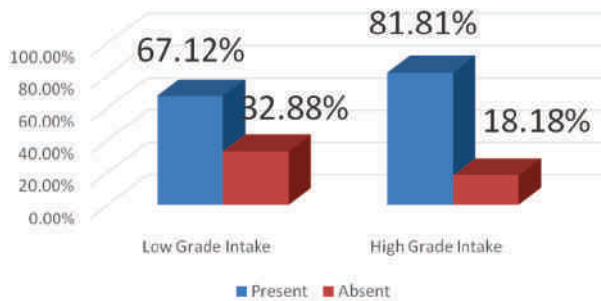
$X^2_{cal} = 4.276$

As p value is less than 0.05 (0.02) , so it is statistically significant . It means that risk of menstrual problem is higher among than those who are taking high intake of HBGPP food.

Fig 14 Abnormal Hair Growth in relation to frequency of Chicken Intake (n=150) %
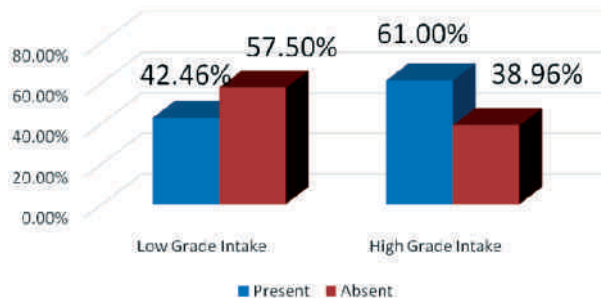
$X^2_{cal} = 5.178$

As p value is less than 0.05 (0.02) , so it is statistically significant . It means that risk of abnormal hair growth is higher among than those who are taking high intake of HBGPP food.

Fig 15 Heaviness of voice in relation to frequency of Chicken Intake (n=150) %
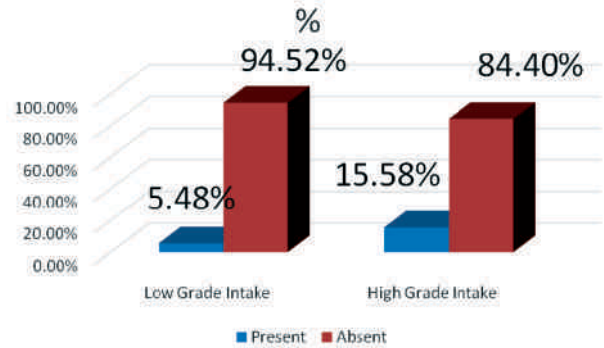
$X^2_{cal} = 4.017$

As p value is less than 0.05 (0.02) , so it is statistically significant . It means that risk of Heaviness of Voice is higher among than those who are taking high intake of HBGPP food

Fig.16 Hair Fall in relation to frequency of Chicken Intake (n=150) %
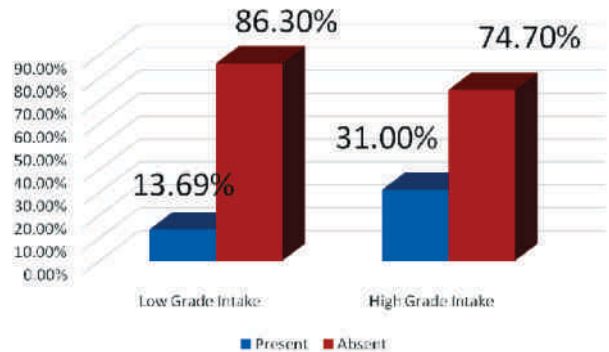
As p value is less than 0.05 (0.01), so it is statistically significant. It means that risk of Hair Fall from front are higher among than those who are taking high intake of HBGPP food.

Fig 17 Skin Changes in relation to frequency of Chicken Intake (n=150) %
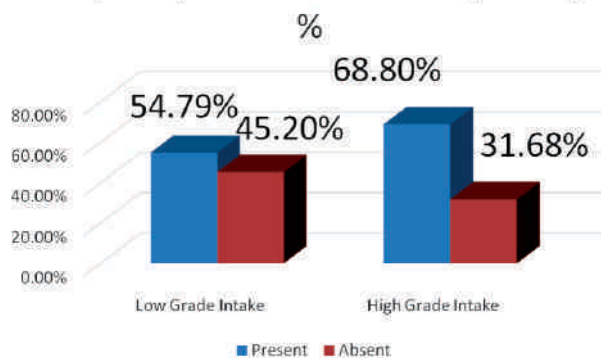
X^2_{cal} = 3.134

As p value is equal to 0.05, so it is statistically significant . It means that risk of Skin Changes is higher among than those who are taking high intake of HBGPP food.

Fig 18 Other Health Problems in relation to frequency of Chicken Intake (n=150) %
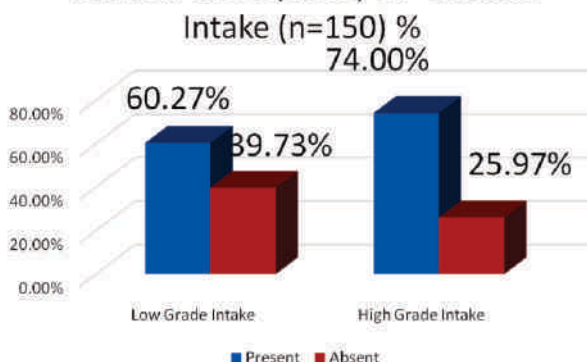
X^2_{cal} = 3.219

As p value is equal to 0.05, so it is statistically significant. It means that risk of certain Health Problems is higher among than those who are taking high intake of HBGPP food.

RESULTS

In our study analysis, regarding age of respondents, 82.7% were between 18 to 26 years of age. 76% were unmarried.86% had professional education degree while 82% were student and 12.7 were house wives. 78.7% were belonging with middle class families. Regarding relationship between Frequency of chicken intake and onset of periods, among those having chicken intake almost every day 14.67% got onset of periods during age of

12 to 14 years as compared to among those having intake once a week 13.3% got period onset during this age. Similarly among those having chicken intake almost every day 4% got onset of periods during age of 15 to 17 years as compared to among those having intake once a week 0.67% got period onset during this age. While comparing relationship between Frequency of chicken intake and menstruation complaints, among those having chicken intake almost every day 7.33%: Excessive pain, 5.33%: Blood clots,4.67%: Heavy menstruation, 4%: Frequent Irregular menstruation in comparison with among those having chicken intake once a week 4%: Excessive pain, 2.67%: Blood clots,2.67%: Heavy menstruation,4.67%:Frequent Irregular menstruation. Regarding relationship between Frequency of chicken intake and hair growth, among those having chicken intake almost every day , 12%:Face& Neck while 2.67% on chest as compared to among those having chicken intake once a week, 4% Face & Neck and 0.67% on chest hair growth. During comparing relationship between Frequency of chicken intake and heaviness of voice among those having chicken intake daily 4.67% had heaviness of voice as compared to 1.33% among having chicken intake only once a week. Regarding relationship between Frequency of chicken intake and Hair fall, among those having daily chicken intake 10.67% had history of hair fall comparing with 2.67% among those having once a week chicken intake.

In our study while comparing relationship between Frequency of chicken intake and skin problems, among those having daily chicken intake,14% got acne as compared to 5.33% among those having chicken intake once a week. Regarding relationship between Frequency of chicken intake and other health problems, among those having chicken intake daily, 12.67%: Obesity, 4%: Depression, 2%: Sleep apnea, 1.33%: Breast lump. 81.81% respondents got menstrual problems due to high grade chicken intake as compared to 67.12% respondents with low grade intake. 61% respondents

with high grade chicken intake got abnormal hair growth as compared to 42.46% with low grade intake. 15.58% respondents got heaviness of voice with high grade chicken intake in comparison with 5.48% with low grade intake. 31% of respondents got hair fall with high grade chicken intake as compared to 13.69% with low grade intake. 68.80% respondents with high grade chicken intake got skin problems in comparison with 54.79% with low grade intake. While 74% respondents got other health problems like hypertension, Diabetes etc due to high grade chicken intake.

DISCUSSION

According to our study the frequency of health related problems are higher in those females having high intake of HBGPPF contrary to those having low intake of HBGPPF.In European Journal of Dermatology[10], a study conducted on Korean subjects, those taking frequent fried chicken and broiler products (P<0.02) reported to have developed acne vulgaris . This correlates with our study (P=0.05) in which those having chicken intake once a week; 6.67% , twice a week ;12.67% , 3 to 5 times a week;13.33% and those with intake almost every day 14% of study subjects developed acne. This shows a relative increase. According to international Journal of Obesity (2005)[11], there is a positive association between consumption of hormone loaded chicken and meet products; and BMI, waist circumference and central obesity. According to UK based study published in Journal of Public Health Nutrition[12], the amount of fat in over bred chicken in modern diet may be 5 to 10 times more than what it used to be .According to our research (P=0.05), among those having chicken intake once a week;4%, twice;8%, 3 to 5 times ;10% and those with almost every day intake 12.67 % were reported obese. Thus correlating the facts with international research.

Excess body fats alter the level of hormones including insulin, leptinand estrogen; these accelerate the pubertal timing by causing obesity as mentioned in 'The Huffington Post.' "Today in US about 16% of girls enter puberty by the age 7 , 30% by the age of 8. A recent study determined that number of girls entering puberty at these early ages increased markedly between 1997 to 201013. According to our study; in age group of 9 to 11 years, those with once a week intake 5.33%, twice a week 3.33%, 3 to 5 times 2%, almost daily intake 6.67% had early puberty. According to Dr. Micheal (Lam MPH MD) ,it takes only 6 weeks now to grow a chicken to full size (down from 4 months in 1940),these are due to estrogen like hormones. Estrogen dominance occurs that is manifested as premenstrual syndrome, irregular menses, obesity, breast lump/swelling [14,15].

As estrogens increase, vitamin B6 decreases. Boosting of vitamin B6 helps reduce hair growth.According to Pakistan Journal of Medical Research[16], a research conducted in October, 2012 consumption of red meat and broiler chicken was more in females with hirsuitism and excessive hair growth. Similar results were reported in an article published in British Medical Journal (International Edition)[17]. According to our study (P=0.02) 12% females taking chicken almost every day demonstrated hair growth on face and neck contrary to only 4% of those taking only once a week. According to our study(P=0.01) out of those subjects having once a week intake 2.67%, twice a week 4%, 3 to 5 times a week 7.33% and almost daily intake 10.67% reported frontal hair fall.

CONCLUSION

The results showed that frequency of certain problems like early menarche, menstrual comp-laints, hirsutism, male pattern baldness, heaviness of voice; skin changes and other problems (obesity, depression, breast lump, hypertension, and diabetes) are higher among those females who are taking high intake of HBGPP foods. These problems are more in younger females.

Recommendations

- Public health education to be provided

regarding safe and healthy poultry intake.

- Legislation to be formed at government level to ensure proper check and control on chicken feed.

- Inspection on regular basis to prevent any illegal hormone administration.

- Only licensed fast food companies should be allowed to advertise and sale their products.

LIMITATIONS OF STUDY

1. Time constraints

2. Budget constraints, as increasing the sample size would have meant more expenses in the form of questionnaires.

3. Unequal participation of the students from different classes, so the results are not predictive of the entire student body of the college.

4. As some of the females were hesitant to disclose their health problems, so we were not able to get information appropriately which led to a limitation to our study .

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MATERNAL EDUCATION ABOUT NUTRITION AND ITS ASSOCIATION WITH THE CHILD NUTRITIONAL STATUS (2-5 YEARS OF AGE) VISITING PEDIATRICS OPD OF VARIOUS PUBLIC SECTOR HOSPITALS OF LAHORE

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House Officers, Jinnah Hospital Lahore

ABSTRACT

Background and Objectives: To determine the prevalence and risk factors of under-nutrition among children aged 2-5 years visiting pediatrics Outpatient Departments of Various Public sector hospitals of Lahore (Jinnah Hospital, Mayo Hospital, and Services Hospital), a cross-sectional survey of 200 randomly selected children was carried out. The study demonstrates the risk factors for childhood malnutrition and association of maternal education with the nutritional status of children. The objective of the study is to investigate the association of nutritional status of children with maternal educational status.

Material and Methods: It is a cross-sectional quantitative descriptive study, was conducted in Pediatric Outpatient Departments of Various Public sector hospitals of Lahore (Jinnah Hospital, Mayo Hospital, Services Hospital) during a period of 3 months from 1 April to 30 June 2014. Data from 200 mothers were collected with Non probability / purposive sampling technique.

Data Collection and analysis: A questionnaire was designed and pretested before start of study. After taking consent, both, from hospital administration and mothers of children, the questionnaire were filled by mothers. Nutritional status of children was assessed using their BMI. Data was analyzed with SPSS 17. The deviation of these values from age specific median values in reference population was conducted.

Results: Mothers of 39.4% (26 out of 66) of underweight children were illiterate. Mothers of 12.1% (8 out of 66) of underweight children had primary education. Mothers of 48.5% (32 out of 66) of underweight children had secondary education or higher. Mothers of 31.3% (42 out of 134) of normal children were illiterate. Mothers of 12.7% (17 out of 134) of normal children had primary education. Mothers of 56% (75 out 134) of normal children had secondary education or higher. 33% (66 out of 200) children were underweight while 67% (134 out of 200) were of normal weight. 19.50% (39 out of 200) of underweight children were males. 13.50% (27 out Of 200) of underweight children were females.

Conclusions: The present study shows significant levels of under nutrition in children aged 2-5 years from households with low earnings, low parental education or households in rural areas. The result also indicated that by improving nutrition, children's growth and development is increased and maternal education status plays pivotal role in increasing children's growth and prevent complications due to malnutrition through continuous training of parents. The training must be strong, scientific and based on reason that meats nutritional problem caused by cultural, social, superstitious and other interventions. In order to achieve this matter, a comprehensive cooperation of media, cultural groups, ministry of Health and government policies are required.

Key words: Maternal education, child nutrition, socioeconomic status, children 2-5 years old

Socioeconomic development and quality of life of masses living in any country is determined through child health and infant mortality rate. Development is not obtained only with physical capital in form of bricks, wheels, computers rather the actual capital is human itself. A healthy, intelligent and honest human force is the ardent energy to utilize the bricks and run the wheels. This is the reason that every developing country is striving hard to convert its population into human

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capital. It is one of Millennium Development Goals (MDGs) to reduce infant mortality rate by two-third till 2015.[3]

Nourished children not only perform better in education rather grow into healthier adults, become active labor force and hence are able to give their own children a better life. The nutritional status of children influences their health status, which is a key determinant of human development. Malnutrition is associated with about 60% of under-five mortality in sub-Saharan Africa (UNICEF, 1998)[6]. Therefore, improvement of children nutritional status increases the chances of child survival and is considered as a precondition for their contribution to community as well as human development (UNICEF, 1998)[6].

In parallel, it is well established that mothers' education has a positive effect on child health in developing countries (Caldwell, 1979)[5] though findings from existing studies have shown mixed results. Indeed, depending on the unit of analysis, the socio-economic and cultural context, some studies have shown significant maternal education difference in child nutritional status (Caldwell, 1979; Baraigi, 1980; Solon et al., 1996)[5,6,8] while other studies did not (pongouet al., 2006)[7]. Nevertheless, investing in women's education is widely advocated as a key intervention strategy for promoting child health. Socioeconomic status is one of the most important pathways explaining the link between maternal education and child nutritional status (Frost et al., 2005; Desai and Alva 1998; Caldwell, 1994)[5, 9, 10]. Education and socioeconomic status not only improves mothers' knowledge relating to health but also changes their attitude and behavior, which in turn positively affects the nutritional status of their children (Cleland, 1990)[2]. Children health depends upon educational attainment of mothers and their capacity to purchase those goods and services which are necessary for maintaining better health status of their children (Fros et al., 2005; Defo, 1997; Cleland and Ginneken, 1988)[11,12,14].

Education not only has direct and significant effect rather can shift negative attitude, traditional practices and beliefs related to health towards the adoption of modern ideas and medicated practices (Benta, et al., 2011; Frost et al., 2005; Defo 1997; Barrette and Brown 1996)[11,12,16]. Therefore, it is believed that educated mothers are less likely to believe in the supernatural reasoning of their child disease rather use modern medicine and preventive measures for the cure of disease (Heaton et al., 2005). Educated mothers can take decision regarding the health problem of their children (frost et al., 2005; Jejeebhoy, 1995) and their family size and birth interval (Benta et al., 2011)

Women having greater control on family income can improve the nutritional status of children particularly female child (Saraswathi, 1992) and children survival rate (Kishor, 1995).

This study provides the answer of the question; whether maternal education significantly affects child nutritional status.

OBJECTIVES:

The objective of the study is to investigate the association of nutritional status of children with maternal educational status

OPERATIONAL DEFINITION:
NUTRITIONAL STATUS:

Nutritional status of children was assessed using their BMI. The deviation of these values from age specific median values in reference population was conducted.

MATERIAL AND METHODS:

It is a cross-sectional quantitative descriptive study, was conducted in Pediatric Outpatient Departments of Various Public sector hospitals of Lahore (Jinnah Hospital, Mayo Hospital, Services Hospital) during a period of 3 months from 1 April to 30 June 2014. Data from 200 mothers were collected with Non probability / purposive sampling technique.

Data Collection and analysis:

A questionnaire was designed and pretested

before start of study. After taking consent, both, from hospital administration and mothers of children, the questionnaire were filled by mothers. Nutritional status of children was assessed using their BMI. Data was analyzed with SPSS 17. The deviation of these values from age specific median values in reference population was conducted.

Table: *Body Mass Index*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Underweight (BMI < 14.0)	66	33.0	33.0	33.0
	Normal (BMI 13.5 - 17.0)	134	67.0	67.0	100.0
	Total	200	100.0	100.0	

RESULTS AND MAIN FINDINGS
RESULTS:

Education of Mothers

The mean age of mother was 29.46 SD 4.89 with minimum age of 22 years and maximum age of 29 years. From 200 respondents 34% (68 out of 200) were illiterate, 12.50% (25 out of 200) were primary and 53.50% (107 out of 200) got secondary

or higher educated. Regarding occupational status of
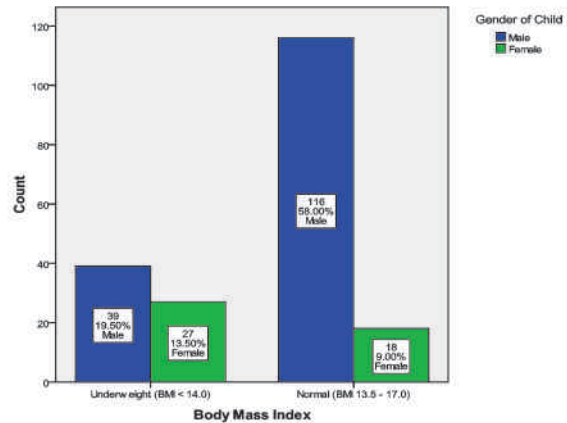
Table: *Education of Mothers vs. Body Mass index Cross tabulation*

			Body Mass Index		Total
			Underweight (BMI < 14.0)	Normal (BMI 13.5 - 17.0)	
Education of Mother	Illiterate	Count	26	42	68
		% within Body Mass Index	39.4%	31.3%	34.0%
	Primary	Count	8	17	25
		% within Body Mass Index	12.1%	12.7%	12.5%
	Secondary or higher	Count	32	75	107
		% within Body Mass Index	48.5%	56.0%	53.5%
Total		Count	66	134	200
		% within Body Mass Index	100.0%	100.0%	100.0%

Residential Status of Mothers

Table 1: *Age of child (Month)*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	24 - 35 months	36	18.0	18.0	18.0
	36 - 47 months	79	39.5	39.5	57.5
	48 - 60 months	85	42.5	42.5	100.0
	Total	200	100.0	100.0	

mothers, 91.50% (183 out of 200) were housewives and 8.50% (17 out of 200) were working women. While comparing socioeconomic status of mothers, 71% (142 out of 200) were middle class and the remaining 29% (58 out of 200) were poor class people. According to residential status of mothers, urban dwellers were 70.5% (141 out of 200) and

rural dwellers were 29.5% (59 out of 200). Regarding age of children's, 18% (36 out of 200) were in range of 24-35 months, 39.5% (79 out of 200) in range of 36-47 months and 42.5% (85 out of 200) were in range of 48-60 months. Comparison of gender of children showed, 77.5% (155 out of 200) were male and 22.5% (45 out of 200) were females. Regarding vaccination status of children, 96% (192 out of 200) did not have vaccination card and the remaining 4% had got it.

Statistically the mean of weight of child is 10.8960 with minimum value of 4.5 and maximum of 17.30. SD of weight of child of weight of child 3.76966 with minimum value of 4.5 and maximum of 17.30 the mean of health card availability was 1.9600.SD with minimum value of 1 and maximum of 2. The mean of BMI 14.5540, SD 1.11019 with minimum value of 13.20 and maximum of 17.20. 33% (66 out of 200) children were underweight while 67% (134 out of 200) were of normal weight. 19.50% (39 out of 200) of underweight children were males. 13.50% (27 out Of 200) of underweight children were females. 58% (116 out of 200) of normal children were males. 9% (18 out of 200) of normal children were females.

Mothers of 39.4% (26 out of 66) of underweight children were illiterate. Mothers of 12.1% (8 out of 66) of underweight children had primary education. Mothers of 48.5% (32 out of 66) of underweight children had secondary Education or higher. Mothers of 31.3% (42 out of 134) of normal children were illiterate. Mothers of 12.7% (17 out of 134) of normal children had primary education. Mothers of 56% (75 out 134) of normal children had secondary education or higher. Chi-square test was used to assess any statistical significance between BMI of children and educational status of women and was non-significant. (Chi-square = 1.317a P = .518).

DISCUSSION:

The present study reports on the level of malnutrition and impact of socio-economic status and maternal education on the nutritional status of children aged 2-5 years in Punjab. 200 mothers, representing different health regions of Punjab participated in the study; hence the study may be regarded as reasonable reflection of nutritional status of children countrywide. The study reveals that malnutrition is a serious problem in the country. If the awareness of mother in relation to child nutritional need is improved, the quality of children nutrition is also improved and this leads to increase in growth indices such as weight and height etc. The study also showed that educated mothers can nourish their child in better way according to hygiene principles without any additional cost of medicines. If nutrition is improved then all the dimensions of life are improved. Most of literate mothers were well aware of this fact.

It was alarming to know that approximately 33% children were malnourished. According to our study maternal education attainment level was not satisfactory. About 34% of mothers were illiterate, 12.50% were having primary education and 53.50% of mothers attained secondary education or higher. As the attainment level of education increases, the likelihood of having a malnourished child is significantly reduced. Secondary education had noteworthy effect on child nutritional status while primary education of mothers. Child level factors including sex and birth weight are independently and strongly associated with stunning. While the association between birth weight and nutritional status has been well documented and understood, few studies have documented gender difference with regard to malnutrition in young children. It has been argued that such differences occur in low socio-economic status settings. Despite the strong significance of these child level factors in influences child stunning, our study includes that do not substantially alter the effect of education on child stunning. In addition to child level factors, maternal level factors including marital status, parity, ethnicity and mothers' health knowledge and health related behavior including pregnancy intentions used as a proxy for family planning, and place of

delivery used as a health seeking behavior were significantly related to child stunning. The relationship between maternal level factors and child nutritional status has also been documented in several other studies. The factors however only minimally attenuate the effect of mother's education on stunning.

Socioeconomic status is the primary pathway explaining the effect of maternal education on child nutritional status. Watching television was found to be an important source of public health campaigning and awareness. Maternal education transforms behavior from traditional view of health care to the acceptance and utilization of modern heath care service. Mothers having proper education took care of themselves properly; this was also beneficial to children.

CONCLUSION:

In conclusion, there were higher levels of under nutrition in children aged 2-5 years from households with low earnings, low parental education or households in rural areas. The result also indicated that by improving nutrition, children's growth and development is increased and maternal education status plays pivotal role in increasing children's growth and prevent complications due to malnutrition through continuous training of parents. The training must be strong, scientific and based on reason that meats nutritional problem caused by cultural, social, superstitious and other interventions. In order to achieve this matter, a comprehensive cooperation of media, cultural groups, ministry of Health and government policies are required.

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RELATIONSHIP BETWEEN HYPERTENSION AND BODY MASS INDEX IN MALE AND FEMALE PATIENTS VISITING OUTDOOR PATIENT DEPARTMENT OF VARIOUS PUBLIC SECTOR HOSPITALS OF LAHORE

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ABSTRACT

Background and objectives: Hypertension is strongly correlated with body mass index (BMI). Obesity was noted to be a single best predictor of hypertension incidence. The incidence of obesity and hypertension is increasing in our society. Present study was conducted to investigate the relation of hypertension with body mass index. The objective of this study was to find the relationship between body mass index and hypertension. As well as to find out the prevalence of hypertension and obesity in male and female Patient Outdoor Department of various public sector hospitals of Lahore, Pakistan.

Material and Methods: This is Cross sectional type of study conducted at outdoor departments of various public sector Teaching hospitals of Lahore including "Mayo Hospital, Services Hospital, Jinnah Hospital and Lahore General Hospital" during April – June, 2015 (03 months) with sample size of 300 patients. Consecutive non-probability sampling technique was used to recruit the patients.

Data Collection and analysis: 300 subject those fulfilling the inclusion criteria were recruited for study visiting outdoor departments of various public sector Teaching hospitals of Lahore including "Mayo Hospital, Services Hospital, Jinnah Hospital and Lahore General Hospital". After approval from ethical committee and informed consent from subjects detail demographic information collected. All the information entered in a structured questionnaire. Weight, height, body mass index and blood pressure were taken. Data analyzed in SPSS Version: 17.0.

Result: The results showed a strong association of hypertension with body mass index. The incidence of hypertension increases with increasing BMI in both males and females. . The relation of BMI normal with hypertension is 31.7% and overweight is 64.8% while that of obese is 73.9% indicating a significant relationship of hypertension with BMI.

Conclusions: The results showed a higher trend of hypertension with increasing BMI. In females the prevalence of hypertension in general is high in all age groups.

Key words: Hypertension, Body Mass Index, Obesity, Blood Pressure.

Hypertension is estimated to cause 7.1 million deaths worldwide. Overweight and obesity increases the risk of high blood pressure. The developing countries are increasingly faced with the burden of hypertension and other cardiovascular diseases. Body mass index is positively and independently associated with morbidity and mortality from hypertension[1]. The relationship between body mass index and blood pressure has long been the subject of epidemiological research.

Body mass index is calculated by dividing the weight in kilograms by the square of height in meters (kg/m²). The World Health Organization has devised a classification wherein persons with body mass index below 18.5–24.9 are considered underweight; those with body mass index's above this range are considered overweight or "at risk," and those with body mass index's greater than or equal to 30 are considered obese[14]. Obesity is an independent risk factor for cardiovascular diseases. There is a direct

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association of obesity with hypertension and heart diseases.[5]

Over a body mass index range from 16 to 31 kg/m², the relationship between body mass index and systolic and diastolic blood pressure is linear. Over the body mass index range of 25-31 kg/m² each body mass index unit is related with a difference of 1.0 mm Hg in diastolic blood pressure.6 Over the body mass index range 16-25 kg/m² each body mass index unit is related with a difference of 0.89 mmHg in diastolic blood pressure. The relative risks of developing hypertension for men with a body mass index of 22.4 to 23.6 is 1.20, with body mass index of 23.7 to 24.7 is 1.31, with body mass index of 24.8 to 26.4 is 1.56 and for > 26.4 kg/m² is 1.85. Hence there is a strong gradient between higher body mass index and increased risk of hypertension even among men within "normal" and mildly "overweight" body mass index range. Therefore, overweight and obesity can be prevented to reduce the risk of developing hypertension.[9]

There is also a strong association between obesity and blood pressure in Children. An increase in the body mass index is conclusively associated with elevated systolic blood pressure and diastolic blood pressure in children also. An increase of 1 body mass index unit was associated with, on average, an increase of 0.56 mm Hg and 0.54 mm Hg in systolic and diastolic blood pressure respectively, for obese children. In non obese children, the increase in systolic blood pressure and diastolic blood pressure was 1.22 mm Hg and 1.20 mm Hg, respectively.[3]

OBJECTIVES:

The objective of this study was to

- To find the relationship between body mass index and hypertension.
- To find out the prevalence of hypertension and obesity in male and female population.

OPERATIONAL DEFINITION:

- Hypertension meant the blood pressure measurement greater than or equal to 140/90mmHg.
- Normal weight: A person having body mass index value between 18.5 and 24.9.
- Overweight: A person having body mass index value between 25 and 30.
- Obese: A person with the body mass index value above 30.

Material and Methods:

This is Cross sectional type of study conducted at outdoor departments of various public sector Teaching hospitals of Lahore including "Mayo Hospital, Services Hospital, Jinnah Hospital and Lahore General Hospital" during April – June, 2015 (03 months) with sample size of 300 patients. Consecutive non-probability sampling technique was used to recruit the patients.

DATA COLLECTION PROCEDURE:

300 subject those fulfilling the inclusion criteria were recruited for study visiting outdoor departments of various public sector Teaching hospitals of Lahore including "Mayo Hospital, Services Hospital, Jinnah Hospital and Lahore General Hospital". Body mass index which is most commonly used indicator of obesity in population studies was determined from height and weight. All the participants were screened through a medical history questionnaire, physical examination and lifestyle. Weight was taken in kilograms and height was being measured in centimeters.

Measurements of blood pressure were taken with a mercury sphygmomanometer which is a reliable apparatus. In order to record the blood pressure, subjects were seated quietly for at least 5 minutes in a chair (rather than on an exam table) with their backs supported and their arms bared and supported at heart level. For hypertension WHO classification was used according to which subjects having a blood pressure of 140/90 mmHg or greater was labeled as hypertensive.

DATA ANALYSIS PROCEDURE:

All the data collected was entered and analyzed in SPSS Version: 17.0. Frequencies and percentages were calculated variables like age, body mass index and blood pressure. Results were recorded as bar charts, crosstabs and pie charts. Pearson chi-squared test was also done.

Body Mass Index Distribution
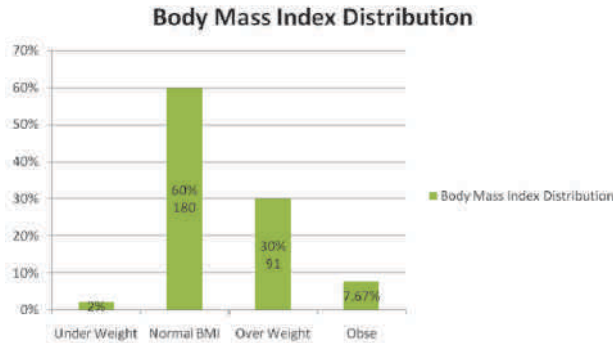
RESULTS AND MAIN FINDINGS:

Table: Age-BMI Cross tabulation

			Body Mass Index				Total
			Under-weight	Normal BMI	Overweight	Obese	
Age	20-39	Count	0	51	29	3	83
		% within Body Mass Index	.0%	28.3%	31.9%	13.0%	27.7%
	40-59	Count	6	102	49	17	174
		% within Body Mass Index	100.0%	56.7%	53.8%	73.9%	58.0%
	60 and above	Count	0	27	13	3	43
		% within Body Mass Index	.0%	15.0%	14.3%	13.0%	14.3%
Total		Count	6	180	91	23	300
		% within Body Mass Index	100.0%	100.0%	100.0%	100.0%	100.0%

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	8.145[a]	6	.228

Table: Gender-Body Mass Index Cross tabulation

			Body Mass Index				Total
			Under-weight	Normal BMI	Overweight	Obese	
Gender	Male	Count	3	99	44	12	158
		% within Body Mass Index	50.0%	55.0%	48.4%	52.2%	52.7%
	Female	Count	3	81	47	11	142
		% within Body Mass Index	50.0%	45.0%	51.6%	47.8%	47.3%
Total		Count	6	180	91	23	300
		% within Body Mass Index	100.0%	100.0%	100.0%	100.0%	100.0%

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	1.092[a]	3	.779

Table: Age-Hypertension Cross tabulation

		Hypertension		Total
		Yes	No	
Age	20-39	30	53	83
	40-59	81	93	174
	60 and above	22	21	43
Total		133	167	300

Table: Hypertension- Body Mass Index Cross tabulation

			Body Mass Index				Total
			Under-weight	Normal BMI	Over-weight	Obese	
Hypertension	Yes	Count	0	57	59	17	133
		% within Body Mass Index	.0%	31.7%	64.8%	73.9%	44.3%
	No	Count	6	123	32	6	167
		% within Body Mass Index	100.0%	68.3%	35.2%	26.1%	55.7%
Total		Count	6	180	91	23	300
		% within Body Mass Index	100.0%	100.0%	100.0%	100.0%	100.0%

Table: Gender- Hypertension Cross tabulation

		Hypertension		Total
		Yes	No	
Gender	Male	65	93	158
	Female	68	74	142
Total		133	167	300

Table: *Gender-Hypertenstion-Body Mass Index Cross tabulation*

Body Mass Index			Hypertension Yes	Hypertension No	Total
Underweight	Gender	Male		3	3
		Female		3	3
	Total			6	6
Normal BMI	Gender	Male	30	69	99
		Female	27	54	81
	Total		57	123	180
Overweight	Gender	Male	26	18	44
		Female	33	14	47
	Total		59	32	91
Obese	Gender	Male	9	3	12
		Female	8	3	11
	Total		17	6	23

Table: *Body Mass Index- Hypertension- Age Cross tabulation*

Age			Hypertension Yes	Hypertension No	Total
20-39	Body Mass Index	Normal BMI	12	39	51
		Overweight	15	14	29
		Obese	3	0	3
	Total		30	53	83
40-59	Body Mass Index	Underweight	0	6	6
		Normal BMI	33	69	102
		Overweight	34	15	49
		Obese	14	3	17
	Total		81	93	174
60 and above	Body Mass Index	Normal BMI	12	15	27
		Overweight	10	3	13
		Obese	0	3	3
	Total		22	21	43

RESULTS:

Out of 300 people interviewed, 158(56.7%) were males and 142(47.3%) were females. 83(27.7%) people were in age Group I i.e. 20–39 yrs, 174(58%) people were in age Group II i.e. 40–59 yrs and 43(14.3%) people were in age Group III (≥60

years). 6(2%) subjects were underweight, 180(60%) subjects had normal BMI, 91(33.3%) subjects were overweight and 23(7.7%) were obese.

Out of 300 subjects, 133 were hypertensive and 167 were non-hypertensive. In the age Group I, 30(36.1%) out 83 adults were hypertensive in which most of them were overweight females while in Group II, 81(46.5%) subjects out of 174 subjects and in Group III, 22(51.1%) out of 43 subjects were hypertensive. Out of 158 males, 65 (41.1%) were hypertensive and out of 142 females, 68(47.8%) were hypertensive. The relation of BMI normal with hypertension is 31.7% and overweight is 64.8% while that of obese is 73.9% indicating a strong relationship of hypertension with BMI.

No subject in the underweight category was found to be hypertensive. In normal BMI category, 30.3% males and 33.3% females were hypertensive. 59.1% males and 70.2% females in overweight category was found to be hypertensive while in obese category, 75% of males and 72.7% of females had hypertension[11]. In age Group I (20–39 yrs), the prevalence of hypertension in normal BMI, overweight and obese population is 23.5%, 51.7%, and 100% respectively while in Group II, the prevalence was 32.9%, 69.3% and 82.3% respectively. In Group III, the prevalence of hypertension in normal BMI and overweight population was 44.4% and 76.9% respectively while no obese person was found to be hypertensive in this age group.[4]

DISCUSSION:

The results indicate that there was a strong association of hypertension to body mass index. The increased prevalence of hypertension with advancing age was also evident from the results. The prevalence of hypertension in males was less as compared to females.

This result is not consistent with the results of Brown et al1 and Hu et al[3]. According to the findings of Brown et al, the prevalence of hypertension is equal in both males and females and it was greater in males as documented by Hu et al.[3]

In obese BMI category, the prevalence of hypertension in males was higher than females while in rest of BMI categories, the prevalence was higher in females. These results are similar to that documented by Brown et al[1]. The higher incidence of hypertension in obese BMI class in males may be closely related to diet and socioeconomic conditions. The diet factor was mainly attributed to the involvement in social activities such as wedding parties, where the diet is mostly rich in calories and

high in fat. Other factors include overwork, lack of physical activities and low energy expenditure. There was much higher prevalence of hypertension in females in overweight BMI category as compared to the results documented by other research papers.

In age Group I (20–39 yrs), there was 100% prevalence rate of hypertension in obese BMI group, much higher than that documented by Brown et al. This very high rate of hypertension in this age group may be due to the increasing trend of western diet and lack of exercise. Surprisingly, no obese person was found to be hypertensive in age Group III which is contrary to the results of Brown et al.

Overall, the percentage of hypertensive subjects was 44.3%, which is much greater as compared to the results of other researchers. It may be due to the increasing trend of western diet in our society especially in young people. The lack of exercise and increased usage of saturated fats is increasing the incidence of hypertension and obesity especially in females. Being overweight is associated with a higher risk of disease, particularly if body fat is concentrated around the abdomen. Moreover increased workload is causing physical and mental stress which contributes to hypertension.

CONCLUSION:
- ✓ Hypertension is directly related with BMI, with the increase in the BMI, the trend of hypertension rises in both females and males.
- ✓ In females the prevalence of hypertension in general is high in all age groups.
- ✓ Hypertension is also related to age, the increase in age is associated with increased incidence of hypertension.

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POST-SURGICAL COMPLICATIONS OF ABDOMINAL CLOSURE TECHNIQUES: A COMPARISON BETWEEN OUTCOMES OF TENSION RELIEVING SUTURES AND LAYERED CLOSURE OF FASCIA

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ABSTRACT

Study objective: To demonstrate the surgical outcomes of abdominal closure techniques: a comparison between tension relieving sutures and closure of fascia.

MATERIALS AND METHODS: This retrospective cohort study was carried out at Jinnah Hospital, which is a tertiary care teaching hospital attached to Allama Iqbal Medical College Lahore Pakistan. The data pertain to the period from August 2001 to August 2012. Cases of blunt abdominal trauma presenting in the surgical Emergency Room with haemoperitoneum and solid visceral injury were included in this study. The sample size was five hundred (500).The cases were chosen through convenience sampling whose records were complete and those that were fulfiling the inclusion criteria. The cases were divided into two equal groups on the basis of the method used for the abdominal closure. In half (250/500) of the cases continuous closure of Linea alba with Prolene No. 1, 40 mm needle (group A) was the method used for abdominal closure. In the other half (250/500) tension relieving sutures with Prolene No. 1, 90mm needle as mass closure (Group B) were applied. The skin was left open in all the cases. Solid visceral injury included injury to liver and spleen.

Descriptive statistics were used to analyze the data via IBM SPSS version 24. Chi-square test of significance for qualitative variables was applied to detect whether or not there was any statistically significant difference between the two groups with regards to the post-surgical complications.

RESULTS: Data showed that in Group A, 18 (7.2%) patients had wound dehiscence and sutures had to be reapplied. In Group B in 01 (0.4%) case only, sutures were reapplied due to cutting through of the initial sutures. Twenty five (25) (10%) cases of infection were reported in group A while two(02) (0.8%) incidents of wound infection occurred in group B.In Group B sutures were removed on day 21 without the need for skin closure while in Group A, the sutures were left in vivo with delayed primary closure. The infected cases of Group A were healed by secondary closure. All procedures were done under General Anesthesia.

Statistically analyzed, the data showed that there was a highly significant difference between the two groups as regards to post-surgical wound dehiscence and infection. Group A has higher incidence rate for both wound dehiscence and infection than group B (P<.0005) with chi-square values of 15.8 and 20.7 respectively.

CONCLUSION: Tension relieving sutures have preference over continuous closure of Linea alba as the former has far less rate of wound infection and wound dehiscence.

Key words: Tension relieving sutures, Solid visceral injury, Haemoperitoneum

The outcomes of wound closure depend upon the closure technique, type of suture material used and co morbid conditions of the patients. Although a vast range of advanced suture materials and techniques of surgery are available, the technique of closure of abdominal incisions largely depends largely on personal preference of the operating surgeon.[1] Whatever technique or materials are employed, the procedure of closure of abdominal fascia should be easy, time efficient, cost effective

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and free of wound related complications. [2,3]

The two most commonly employed techniques are closure in layers/continuous closure of linea alba and mass closure using tension relieving sutures. The layered closure technique is claimed to be associated with better wound strength, decrease incidence of dehiscence, intraperitoneal adhesion and leakage of peritoneal contents.[4,5] On the other hand, the mass closure technique is claimed to have reduced incidence of wound dehiscence. Mass closure technique was first described by Smead in 1900 followed by Jones in 1941, thus known as "Smead-Jones technique". In 1970, Dudley showed that when steel wire was used as suture material, results of mass closure were better than those of layered closure.[6] In a study by Golligher, rate of wound dehiscence was found to be11 % in layered closure as compared to 1% in mass closure.[7] In another study of 1129 abdominal surgeries by Bucknall et al., the rate of wound dehiscence was significantly more in layered closure than with mass closure (3.81% vs. 0.76%).[8] This has also been confirmed in recent meta-analyses that shows significantly reduced rate of wound dehiscence and incisional hernias in mass closure technique.[9]

MATERIALS AND METHODS

The data for this retrospectivecohort study was collected at Jinnah Hospital Lahore which pertains to the period from August 2001 to August 2012. The objective of this study was to compare the two procedures of abdominal closure as mentioned above. The data of patients presenting with blunt abdominal trauma and solid visceral injury in ER were extracted from records. The cases were divided into 2 groups-A & B, on the basis of the method used for abdominal closure. In each group 250 patients were selected. Patients between ages 35 to 50 years of both genders with no concomitant disease were included in the study. No female patient was reported positive for the Beta-HCG in urine.

Cases with bacterial and chemical peritonitis were excluded from the study. A standardized data entry form was designed to collect the information i.e. patient age, gender, setting of surgery, mechanism of injury, surgical technique used and post-surgical outcomes.

RESULTS

Data of 500 cases were extracted on data collection forms. The gender distribution was 350 males and 150 females (2.6:1) with a mean age of 42.5 years (Table 1).

In Group A, data of 250 patients who were treated with single continuous suturing of linea alba with prolene 1 were included. In Group B, data of 250 caseswho were treated with tension relieving sutures were included. Skin was left open in both groups.

The technique of continuous repair of linea alba was to start at one end of linea alba 1.5cm from the edge of the wound to the other end. The technique of tension relieving sutures was to apply sutures 1 inch from the edge of the wound and through and through all abdominal layers including skin. In Group A, 18 (7.2%) patients had wound dehiscence that had to be re-sutured. From Group B, 01 (0.4%) patient had to undergo reapplication of tension relieving sutures due to cut through suture.

Twenty five 25 (10%) patients got wound infection in group A while surgical wound was infected in 02 (0.8%) of the patients in group B (Table 2).

In Group B sutures were removed on day 21 without the need for skin closure while in Group A, the sutures were left in vivo with delayed primary closure. The infected cases of Group A were healed by secondary closure. All procedures were done

Table 1: *Gender Distribution*

Males	Females	Total
350	150	500

under General Anesthesia.

$x^2 = 15.8$

$df = 1$

$p < 0.001$

There is a highly statistically significant difference in group A and group B regarding wound dehiscence and therefore the need for suturing post-operatively.

In group A, the incidence of wound dehiscence and the need for reaplication of sutures post-operatively is significantly high than in group B.

$x^2 = 20.7$

$df = 1$

$p < 0.0001$

There is a highly statistically significant difference between group A and group B as regard to post-surgical wound infection. The incidence of post-surgical wound infection in group A is significantly high than in group B.

DISCUSSION

Table 2: *Frequency of Post-Surgical Complications in Two Surgical Methods of Abdominal Closure.*

Post-surgical complications	Group A	Group B	Total
Wound infection	25	02	27
Wound dehiscence	18	01	19
Total	43	03	46

The technique of closure of laparotomy wound is quite debatable. Smead introduced the technique of mass closure which was adopted by many surgeons. The continous closure technique has the advantage of uniformly distributed tension on suture line, cost effectiveness due to consumption of less suture material and time efficient as it takes half as much time.[12] Also the bursting strength of a wound increases significantly in continuous closure

Table 3: *Cross tabulation between the surgical methods used and wound dehiscence*

Groups	Yes	No	Row Total
A	18(a))	232 (b)	250 (e)
B	01(c)	249(d)	250(f)
Column total	19(g)	481(h)	500(N)

technique.[12] The mass closure technique is associated with as less wound dehiscence rate as 1% after abdominal wound closure. Also the rate of wound infection is less in mass closure technique.[7] As wound infection is associated with high rates of incisional hernia, mass closure technique is ssociated with lesser rate of hernia formation.[10,11] Use of tension relieving suture is proposed by many surgeons . Bender et al. used retention sutures to close abdominal wound in 17 patients of abdminaal trauma. Koniaris et al. employed dynamic-retention suture closure technique to close the abdomen.[13] Our

Table 4: *Cross tabulation between the surgical methods used and the occurrence of post-surgical wound infection*

Groups	Yes	No	Row Total
A	25 (a)	225 (b)	250 (e)
B	02 (c)	248 (d)	250 (f)
Column total	27 (g)	473 (h)	500 (N)

study clearly indicates that method of tension relieving sutures has far less incidence of wound dehiscence and infections compared to continuous closure of linea alba.

CONCLUSION

The method of closure of abdomen following trauma with tension relieving sutures has preference over closure of lineaalba because of less incidence rate of wound infection, and wound dehiscence.

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STATISTICAL ANALYSIS OF ACUTE BURN PATIENTS –A RETROSPECTIVE STUDY FROM CHILDREN RECONSTRUCTIVE SURGERY DEPARTMENT SHALAMAR HOSPITAL, LAHORE PAKISTAN

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ABSTRACT

Objective: To statistically evaluate gender difference and age classification in burn patients and to find the most common causes of burns in all age groups.

Methodology: This quantitative study design was conducted with the help of old patients' files from Shalamar hospital, CRSRC department. The sample consisted of a total of 362 acute burn patients treated from July 2016 to December 2016. The data was entered in excel sheets and results were drawn in the form of percentage charts, pie charts, columns and bar charts.

Results: The results showed that out of the total sample 55% were female burn patients and 45% male. The most common burn injuries were reported in children under the age of 4 years (59%).followed by ages 4 to 10 years (15%), ages 20 to 40 years (12%), ages 10 to 20 years (9%) and the least affected population is of adults above the age of 10 years, gender difference is vast. Among the leading causes of burn, scalds or hot liquid burns (76%) seem to be the most common cause of burn, followed by hot objects (6%), open fire (10%) and others. Floor stoves, open flames, hot boiling water, hot tea are the most common causes for burn injuries.

Conclusion: Burn injuries are most common in children under the age of four years and the most common cause of burn injuries among children is scalds or burn by hot liquids. This is majorly due to careless behavior of parents, floor stoves, lack of proper life necessities such as hot water, gas etc in the lower socioeconomic class of Pakistan. Although the overall gender difference is not very far off, females are still more affected as compared to men and this gender difference is much more evident after the age of 10 years when the gender roles are properly defined.

According to World Health Organization, burns are the 11th leading cause of death worldwide, especially in children between the ages of one and nine (Medina, 1992). WHO has reported Pakistan to have the highest incidence of burns i.e. 1388/100,000 per annum in comparison to global incidence of 110/100,000 annually (Othman & Kendrick, 2010). A burn is a type of wound or injury to the skin or flesh cause by hot liquids, chemicals, heat, electricity, radiation and much more (Herndon). When the flesh comes in contact with any matter (solid, liquid or gas) with a temperature above 44°C or 111°F, the proteins start losing their original form and begin breaking down (John, 2010). The breaking down of proteins results in cell and tissue damage which causes disruption in skin's

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sensation, prevention of water loss and ability to regulate body temperature (Tintinalli, 2010).

Burns can be of various types such as superficial or most commonly known as first degree burns. Others include superficial partial thickness burn or deep partial thickness (second degree), full thickness (third degree) and fourth degree. The first degree or superficial burns usually involve the epidermis and are slightly painful (Granger, 2009). Second degree burns extend to the superficial dermis and is very painful. It causes redness with blisters and takes less than 2-3 weeks to heal (Herdon). Deep partial thickness of the second degree burn extends deep into the reticular dermis and appears to be yellow or white (Judith, 2010). Next is the full thickness of burn or more commonly known as the third degree burn. This degree extends and burns through the entire dermis and is painless due to loss of sensation because of nerve damage. The fourth and final category of burn is the fourth degree. This extends through the skin and inside the fat, muscles and bones with a black charred appearance. This type of burn is also painless due to nerve damage and usually involves amputation, functional impairment and, sometimes, even death (Tintinalli, 2010).

An average of 265,000 deaths occurs every year due to burns and the vast majority occurs in low or middle class families (WHO, 2014). In 2004, 11 million burn injuries, worldwide, required medical assistance and resulted in 300,000 deaths (Peck, 2011). They are said to be the 4th leading cause of accidents and injuries after vehicle accidents, falls and violence.

According to a study by Peck in 2011, about 90% burn accidents and injuries occur in the developing countries. Almost nearly 60% of fetal burn injuries occur in the Southern Asia region (Herndon). Burns are also among the leading causes of disabilities in lower or middle socio-economic countries. In Bangladesh, Colombia, Egypt and Pakistan, 17% of children with burns have a temporary disability and 18% have a permanent disability (WHO, 2014).

A survey conducted by Global Burden of Disease (2004) stated that the majority of burns occurred to children under the age of 20. According to Global Burden of Disease, infants and toddlers, below age one, have the highest rate of burns and children from age one to four have the second highest rate. The study also suggests that children belonging to the lower or middle socio-economic class and countries have a higher rate of burn injuries as compared to children belonging to high socio-economic countries. The low and middle socio-economic countries belong to Africa, South-East Asia and the Eastern Mediterranean (WHO, 2004). According to Herdon's research, Prevention of Burn Injuries, children in the developing countries have ten times more risk of burn injuries then children in developed countries.

In the 2011 study conducted by Peck, "Epidemiology of burns throughout the world. Part I: Distribution and risk factors", the researcher stated that burns are more common in developing countries in comparison to developed countries. These findings are homogeneous with the previously mentioned research by Word Health Organization (2004) stating that countries with low income level have a higher rate of burn cases. Peck's (2011) study also documents that in developed countries, males have a higher rate of burns as compared to females due their highly risky occupations and risk-involving activities. On the contrary, Peck highlights the fact that women are at twice the risk of burn injuries then men in developing countries. This is mainly due accidents in kitchen while cooking or as a result of domestic violence (Peck, 2011). A longitudinal study conducted by Bain et al. (2001-2010) in Central India concluded that out of a total 2499 patients, 66.8% were females and 38.2% were males, supporting the fact that gender difference is very much evident in burn accidents and that women are more prone to such risks as compared to men. According to the study, most burn injuries occur in homes (96%) with most common causes such as flames from stoves, kerosene lamp, hot liquids etc.

Another study conducted by Muqim et al. (2007) in Peshawar reported that out of the total burn patients, 52.2% were females and majority patients were children under the age of 10 making 31.66% of the total lot. This study also suggested that scalds were most common in children.

Age factor is one of the most important aspects in burn accidents and burn injuries. According to a study by Shah (2013), children under the age of five are at a higher risk of burn injuries and scalds. This, he stated, was due to the development age of children leading to reaching out and curiosity behaviors. Another study conducted by Flavin and his colleagues (2006), reported that among infants (0-11 months), burns were the highest cause of injuries in comparison to collision, fall etc and the risk decreased with increased age. Flavin (2006) also suggested most percentage of injuries occur inside the homes. The National Fire Protection Association (NFPA) in US conducted a survey in 2007. This survey highlighted the risk of burns in fires at home. According to NFPA, home fires cause an average of 400 civilian deaths and 5,080 burn injuries. Cooking and cooking related equipment is said to be the leading cause of home burn and fire injuries (Ahrens, 2013). Unattended cooking is by far the most contributing factor to fire burns and deaths. NFPA also stated that children under the age of five are more at risk of getting non-fire burns associated with cookware such as hot pots and pans, hot food or beverage etc (Ahrens, 2013).

Burns are caused by various types of mediums. Most common causes of burns are an open flame or fire, hot liquid, hot objects and other substances such as chemicals, electrical current, hot steam etc. Hot liquids usually include hot tea, hot boiling water, hot soup, and hot oil. According to a statistical survey by Massachusetts Burn Injury Reporting System (2013), scalds from hot liquids cause 83% off burns in children under the age of five. Hot objects can be classified into any article that causes burn or skin damage. Hot objects include a plugged in pressing iron, hair rods and straighteners, hot cylinders etc.

Burns caused by electricity passing through the body and causing instant damage are known as burn injuries. Roughly 1,000 deaths are reported every year in United States caused by electric injuries (Cushing, 2011). These types of burns are usually caused by touching electrical objects, short-circuiting, placing fingers into electrical sockets and coming in contact with electrified water (Figgiano et al., 1998).

When an individual gets burns, either by scald or by dry heat, the extent of their injuries are usually assessed with the help of the Total Burn Surface Area (TBSA). The Wallace rule of nines is most commonly used to determent the total burn area of the victim (Wedro, 20140). Children and infants' burn injuries are assessed with the Lund and Bowder Chart. More than 50% TBSA is said to have a 100% mortality rate.

METHODOLOGY

This quantitative study design was conducted with the help of old patients' files from Shalamar Hospital. The purposive sampling was done by obtaining information of acute burn cases from the CRSRC department of Shalamar Hospital. The sample consisted of a total of 362 acute burn patients treated from July 2014 to December 2014. There were a total of 199 females and 162 males of all age groups. The patients were divided into two groups. Group 1 consisted of all the 362 patients containing details such as their age, gender and cause of burn.

Group 2 consisted of 264 patients from Group 1. The remaining patients 98 patients were not included in Group 2 due to the lack of detailed information such as the percentage of burn area, the depth of burn and the area of burn. The data was assembled in Microsoft Excel sheets and results were drawn in form of percentage charts, bar charts, pie charts and columns. The results included gender differences, age differences, burn percentage and depth of burn and causes of burns

1.1: GENDER CLASSIFICATION

Out of total 362 patients, 199 were females and

162 were males. The overall group 1 gender difference stated 45% male and 55% female burn patients.

Comparing the gender age difference in group 1 and group 2, the above figures depict minimum difference in the male to female ratio.

1.2: GENDER CLASSIFICATION IN ACCORDANCE WITH AGE:

To carry on with further classifications of gender, Group 1 was divided into 10 groups according to age range. These 10 groups contained patients with the following age range:

Figure 1.1: Over all Gender Classification (Group 1)
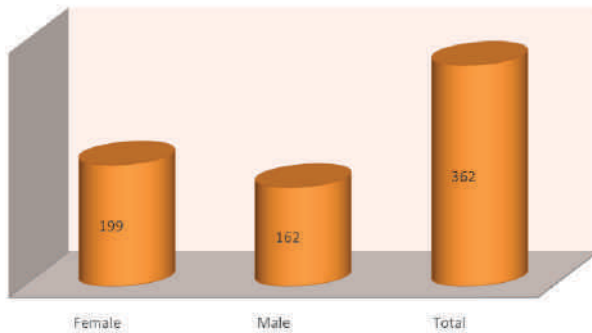
Figure 1.2: Percentage Gender Classification (Group 1)
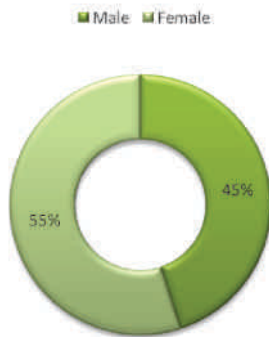
Figure 1.3: Gender Classification of Both Groups

1) Birth to 1 year
2) 1+ to 2 years
3) 2+ to 4 years
4) 4+ to 6 years
5) 6+ to 10 years
6) 10+ to 15 years
7) 15+ to 20 years
8) 20+ to 30 years
9) 30+ to 40 years
10) 40+ years

According to the displayed results (Fig. 2) the most burn accidents have been recorded in patients of the 2nd age group, which is 1+ to 2 years. In this age group, males are in majority as compared to the female burn patients. In the complete list of patients from the 2nd age group, 46% out of the total are male. The second highest recording of burn accidents can be seen in the 3rd age group which includes patients from the ages 2+ to 4 years. In this age group, females have majority of burn cases over

Figure 2: Gender Classification According to Age (Group 1)
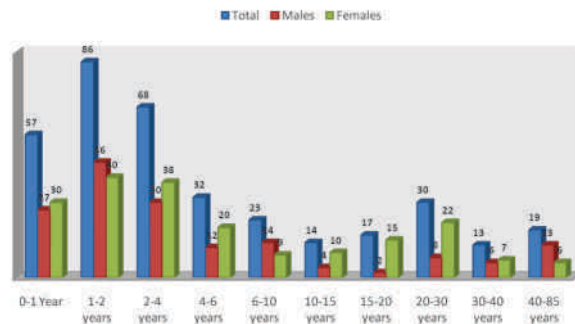
male patients i.e. 38%.

1.3 PERCENTAGE CLASSIFICATION IN ACCORDANCE WITH AGE:

The results of the burn percentage according to age were driven by dividing the age groups in two ways. First the percentage classification of the burn victims were done with the same 10 age groups as mentioned in section 1.2. These were the small age groups with less age gaps. The analysis of the smaller age groups revealed (Fig 3.1) that the children from ages 1 to 2 years are at the highest risk

of burn accidents and they make an entire of 24% of the total lot of patients of different age groups. The next age group with the 2nd highest recorded burn accidents is the age 2 to 4 years making 19% of the total patients.

The 10 age groups of burn patients were classified according to percentages and outcome can be clearly seen in table below.

The most burn cases were recorded in age groups 1,2 and 3 i.e mostly in children under age of 5 years

As the first 6 groups in this classification contained smaller age gaps and the gaps increased with age (group 7-10), the 2nd percentage classification was done by making a lesser number

Figure 3.1: Percentage Classification of Burns (Group 1) (with small age groups)
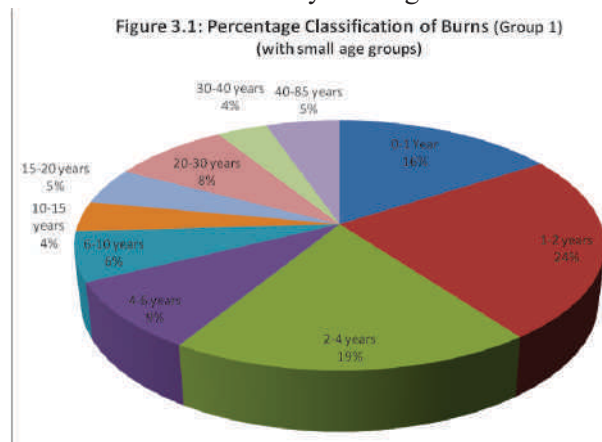
of groups with larger age gaps (Fig 3.2).

For the second classification, the patients were divided into five large age groups. These were as follows:

Table :

Age group	Percentage
0-1years	16%
1-2 years	24%
2-4 years	19%
4-6 years	9%
6-10 years	6%
10-15 years	4%
15-20 years	5%
20-30 years	8%
30-40 years	4%
40-85 years	5%

The results (Fig 3.2) clearly state that the children from birth to 4 years have the highest percentage of burn injuries and make 59% of the total. The next group with the second highest numbers of burn accidents contains children from age 4+ to 10 years. The age group least affected are adults who are 40 years and above. These results

Figure 3.2: Percentage Classification of Burns (Group 1) (with large age groups)
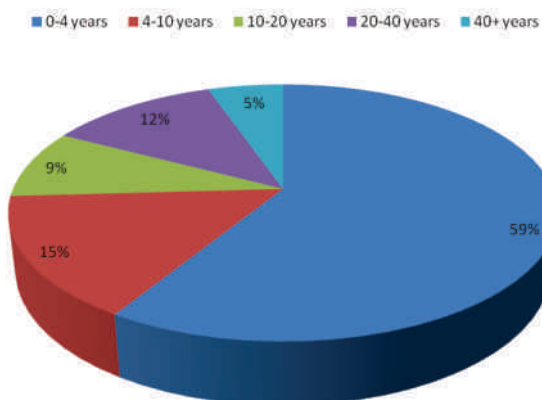
Figure 3.2: Percentage Classification of Burns (Group 1) (with large age groups)
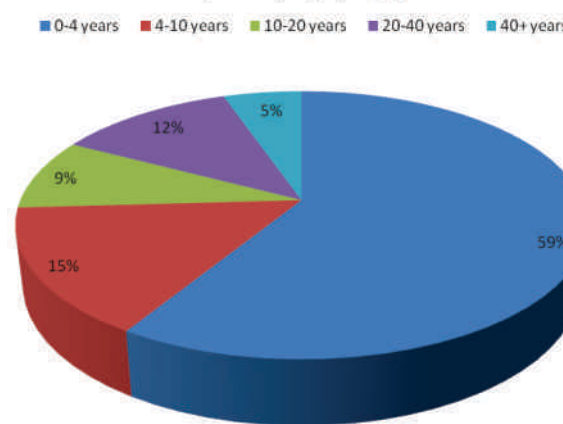
suggest that children under 10 are recorded to have the most burn injuries as compared to any other age group.

Table 2:

Age group	Percentage
0-4 years	59%
4-10 years	15%
10-20 years	9%
20-40 years	12%
40+ years	5%

1.4: BURN CAUSE CLASSIFICATION:

After the detailed analysis of the study, the results highlighted a number of causes for burn injuries which include hot liquids (hot tea, water, milk, oil etc). Other causes included hot objects, flame burns, chemical burns, steam burns and electric burns.

After categorizing the causes of burns, the obtained data was divided into age wise classification and as the results can be seen. Hot liquids (including hot tea and hot water) make up almost 65% of cause of burns in children from birth up to a year making it the largest cause of burn in this age group. In the total causes of burns in children of age 1+ year through 4 years of age, hot liquids make up a total of 68% and 75%. After the age of four, the burns caused by hot liquids start decreasing in percentage at almost 51% in the age group 4+ years to age 6, but still is the largest cause of burns as compared to any other category. After scalds, open fire burns have been reported as leading cause of burn especially in age group of 4-15 years.

After classifying the burn causes according to age, the study did an overall analysis of the cause of burn injuries and the results depicted (Fig. 5) that hot liquids (including hot water, hot tea, hot milk and other liquids) are the most leading cause of burn injuries (inclusive of all age groups) making 76% of the total burn cause. 6% burn injuries are due to hot objects, 10% due to open fire/flame and 8% include all the other causes of burns such as car accidents, candles, electric burns, steam burns etc.

Figure 4: Burn Casue Classification According to Age (Group 1)
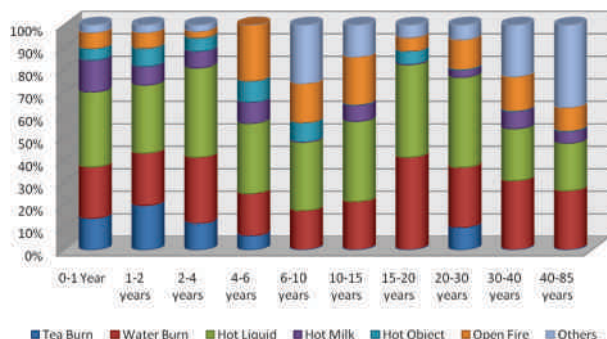
1.5: CLASSIFICATION OF TOTAL BURN SURFACE AREA:

The study also derived results for the most commonly occurring Total Burn Surface Area (TBSA) in patients of all age groups.3-4% TBSA was most common, followed by 5-6% TBSA, 1-2%TBSA and so on.

Statistical analysis revealed that most

Figure 5: Overall Burn Casue Classification (Group 1)
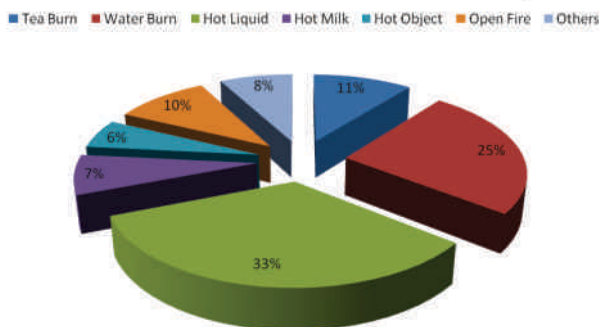
commonly patients reported with acute burn injury had superficial burns.

Figure 6: Classification of Burn % (Group 2)
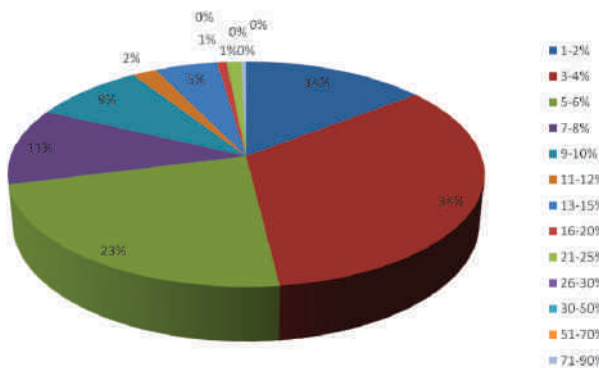
LITERATURE REVIEW

With reference to our above mentioned study, we can study burn with help of different variables like age difference, gender difference, TBSA involved and causative factors involved in burn.

Gender Classification:

The analysis of the results revealed that females are more prone to burn accidents as compared to males. Most cases of female burns were due to either

Figure 7: Depth of Burns (Group 2)
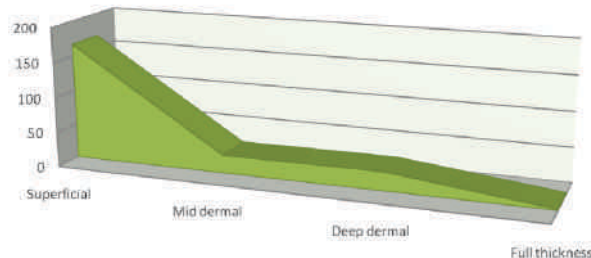
scalds from hot liquids or flame burns. In developing countries like Pakistan, India etc, females are expected to begin doing household chores at an earlier age making them more exposed to hot liquids ad fire in kitchen. According to a study by Dr Harish (2013), almost 79% of women get burnt during kitchen accidents.

Another leading cause of burns in women is fire burn. But again the male to female ratio is not very far apart. Males also receive burns almost as much as females but the majority males are children under age of 6 years.

Gender Classification According To Age:

According to above done study, the most burn victims were of age group 13 months-2 years. In this age group, males are in majority as compared to female patients but this difference is not vast. 54% among total patients in second age group were male. The second highest incidence of burn accidents occur in 3rd age group including children from 2+ to 4 years. Females had majority of burn cases in this age group as compared to males but difference is not vast. Therefore we can say on basis of aforementioned explanation that there is not enough evidence to support the claim that either of the gender is more prone to burn accidents in age group 1-4 years.

The next group more prone to burn accidents is first age group which is from birth to 1 year. Again female burn patients were greater as compared to males in this age group. Burns in this age group were reported mostly due to negligence of parents towards children.

The overall results of the age wise gender classification shows that burn accident risk increase from birth to year 1 and 2 and then start declining as individuals grow older. Flavin et al (2006) also verified the result of current study stating that risk of burn injuries decrease with increasing age.

Both male and female children under the age of 10 years are at equal risk of burn accidents. But the major difference between the genders can be evidently seen after the age of 10 where female to male ratio increases till age of 40 years. The most common burn injuries in females between age of 10-30 years occur during household chores (96%). After this age the risk of burn decreases both in females and males (Barin et al., 2001-2010).

Percentage classification according to age:

During study, whole sample was divided into different age groups in two ways. First percentage classification of burn victims was done with 10 age groups. These were small age groups with less age gaps. The analysis of smaller age groups revealed that children from age 1-2 years are at highest risk of burn accidents (24%). Next age group with 2nd highest peak of burn accidents is age 2-4 years (19%). These findings were also verified with a study by Muqim et al. (2007).

2nd percentage classification was done by making a lesser number of groups with larger age gaps. The result of study clearly stated that children from birth to 4 years have the highest percentage of burn injuries (59%). Next age group with second highest number of burn accidents contains children from age 4+ to 10+ years. These findings were similar to studies of Flavin (2006) and Shah (2013).

Burn cause classification:

After categorizing the causes of burns, a detailed analysis of burn cause in correspondence to age was done. Hot liquids came out to be the highest cause of burn injury in children from birth to 1 year (65%). In children of age +1 and 4 years, hot liquids make up a total of 68% and 75% respectively. According to a statistical survey by Massachusetts Burn Injury Report System (2013), scalds from liquids cause 83% of burn injuries in children under 5 years. Shah (2013) also verified the results in his study. The burns caused by hot liquids start decreasing in age 4-6 years (51%).

Among age group of 6-10 years, the percentage of burns caused by hot liquids to all other causes of burns is 42% to 58% respectively.

Hot liquids are the leading cause of burn in age group 15-20years making 78% of total burn causes. Hot liquids are the leading cause of burn injuries in

next age group i.e. 20-30 years.

After classifying causes of burn according to age groups, study described overall analysis of most common causative agents of burns. It showed that hot liquids are the most leading cause of burn injuries making 76% of the total burn causes. 6% burn injuries are due to hot objects, 10% are due to open fire and 8% include all other cause of burns.

The American Burn Association (ABA) (2007) reported a total of 500,000 burns each year in US. According to ABA, the leading cause of burns in US is due to open fire burn (46%), followed by scalding (32%), thermal burns (8%), electric burns (4%) and 7% of the other causes. But according to a study done by Aslam et al. (2012) in Peshawar, the leading cause of burns in all cases were scalds, making 65.4% of total sample. The remaining causes included open fire (25.7%), electric burns (1.7%), steam (1.6%), contact burn (0.5%) and friction (0.1%). The main reasons for this evident difference are socioeconomic and household differences between US and Pakistan.

Total Burn Surface Area:

The results of this study depicted that TBSA has no relationship with age or gender of patient. But TBSA does determine the outcome and mortality rate. TBSA>50% is associated with a high mortality rate. According to a study by Subramaniam (1991) all the patients with TBSA>60% resulted in deaths. Below 14% TBSA, the mortality rate was 12.5%.

In current study most pts in sample had <18% TBSA involved and were mostly curable.

Depth of Burns:

As per results, most common cases reported had second degree or superficial burns.

CONCLUSION:

Burn injuries are most common in children under age of 4 years (59%) and the most common cause of burn injuries is by hot liquids. Although the overall gender difference is not very far off, females (55%) are still more affected as compared to men (45%) and this gender difference is much more evident after 10 years of age. The most common cases are second degree burns.

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BREAST CANCER IN YOUNG WOMEN (35 YEARS OR LESS): 5 YEARS EXPERIENCE AT A TEACHING HOSPTIAL IN PAKISTAN

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ABSTRACT

Fewer than 5% of all breast cancers are diagnosed in women under the age of 40 in US. Despite young age, the tumors tend to be advanced by stage and triple negative by molecular phenotype conferring poor prognosis. In this study, we have presented the histopathological features of 71 breast cancers in young women reported at the Department of Pathology, Fatima Memorial Hospital (Lahore) during the period of last 5 years. Materials & Methods: Routine H&E staining and immunohistochemistry (IHC, wherever applicable) were performed on every breast cancer case. The results were interpreted by the histopathologists and reported. The histopathology reports from January 2011 to August 2015 were retrieved and the data was analyzed. Results: Out of total 548 diagnosed breast cancer cases during the five-year study period, 71 (12.9%) of the breast cancers were in women aged 35 or less. Around 60% of the cases were in the age group of 31-35 years. The cancer involved left breast in 40 (56.3%) cases, right breast in 20 (28.2%) cases and both breasts in 2 (2.8%) cases. The side of specimen was not specified in 9 cases. The diagnosis of invasive ductal carcinoma (IDC) was rendered in 65 (91.5%) cases, invasive lobular carcinoma in 1 (1.5%) case and invasive mammary carcinoma (IHC recommended) in 5 (7.0%) cases. Regarding histologic grade, 32 (45.1%) were grade 2 and 39 (54.9%) were grade 3. The tumors range in size from 22mm to 80mm. Among 9 cases with available T staging data, pT2, pT3 and pT4 cases were 5, 3 and 1 respectively. Pathological N staging was available in 6 cases which showed 2, 1 and 3 cases of pN0, pN1a and pN2a respectively. Receptor studies for molecular subtyping were available in 27 cases which showed 18.6% luminal A (ER+, HER2-), 33.3% luminal B (ER+, HER+), 37.0% triple negative (ER-, HER2-), and 11.1% HER2 only (ER-, HER2+) subtypes. Conclusions: Breast cancer in young women is more prevalent in our population than the West. Left sided cancer is the most frequent side and IDC is the most frequent type in these cancers. The tumors have high histological grade and advanced pathological stage. Triple negative/basal-like is the most common molecular subtype. Our findings are in accordance with the available literature.

KEYWORDS: Young women, breast cancer, case series

Breast cancer is the most common cancer in women worldwide, with nearly 1.7 million new cases diagnosed each year. This represents 25% of all cancers occurring in women.[1] There is an increase in incidence of breast cancer with increasing age, from an average incidence per million of 1.30 in 15 to 19-year-old, to 12.10 in 20 to 24 years old to 81.10 in 25 to 29 years old.[2,3]

The breast cancer is hormone related and factors that modify the risk of this cancer when diagnosed premenopausal and when diagnosed post-menopausal are not the same.[4] Breast cancers in very young women are typically aggressive, in part owing to the high histological grade, triple-negative tumors, but young age is an independent negative predictor of cancer-specific survival.[4,5] Diagnosing breast cancer earlier in women under age 35 years old is more difficult because of increased density of breast tissue in younger women.[5]

Breast cancer in young women tends to be aggressive and less likely to respond to treatment. Women who are diagnosed at a younger age also are most likely to have a mutated BRCA I or BRCA 2 gene. There are more chances of these women getting a highly aggressive malignancy at a very young age[6]. The objective of this study was to

document the increased occurrence of early onset breast cancer in our population and to assess various predictive and prognostic factors affecting survival (hormone receptor status, and lymph node status) in our patients.

MATERIAL & METHODS

Record of 548 female patients diagnosed as breast carcinoma during the last four years (Jan 2011– Aug 2015) at Histopathology department, Fatima Memorial Medical and Dental College was retrieved using the FMH department archived data. From this record, all cases of breast carcinoma, 71 in number diagnosed in young females, 35 years of age or less were selected. Patients were divided into two groups as group-1 < 30 years and group-2 31-35 years. The cases were then analyzed for various predictive and prognostic factors such as age, site, size, type and grade of tumor, lymph node status, stage of disease according TNM staging system and estrogen/progesterone receptor status. Then routine H&E staining and immunohistochemistry (IHC, wherever applicable) were performed on every breast cancer case. The results were interpreted by the histopathologists and reported.

RESULTS

Out of total 548 diagnosed breast cancer cases during the five-year study period, 71 (12.9%) (Table.1) of the breast cancers were in women aged 35 or less. Around 60% of the cases were in the age group of 31-35 years (Table.2). The cancer involved left breast in 40 (56.3%) cases, right breast in 20 (28.2%) cases and both breast in 2 (2.8%) cases. The side of specimen was not specified in 9 cases (Table.3). The diagnosis of invasive ductal carcinoma (IDC) was rendered in 65 (91.5%) cases, invasive lobular carcinoma in 1 (1.5%) case and invasive mammary carcinoma (IHC recommended) in 5 (7.0%) cases (Table.4). Regarding histologic grade, 32 (45.1%) were grade 2 and 39 (54.9%) were grade 3 (Table.5). The tumors range in size from 22mm to 80mm. Among 9 cases with available T

staging data, pT2, pT3 and pT4 cases were 5, 3 and I respectively (Table.6). Pathological N staging was available in 6 cases which showed 2, 1 and 3 cases of pN0, pN1a and pN2a respectively (Table.7). Receptor studies for molecular subtyping were available in 27 cases which showed 18.6% luminal A (ER+, HER2-), 33.3% luminal B (ER+, HER+), 37.0% triple negative (ER-, PR-, HER2-), and 11.1% HER2 only (ER-, HER2+) subtypes (Table.7).

Table 1: *Frequency of Breast Cancer in Young Patients.*

Total Number of Patients	No. of Young Patients (aged 35 or less)	Percentage
548	71	12.9%

Table 2: *Age wise Distribution of the Patients. (n=71)*

Age (years)	No. of Cases	Percentage
30 and below	28	40.00%
31 -35	43	60.00%
Range	20-35 years	
Mean	29 years	

Table 3: *Side of the Specimens. (n=71)*

Side	No. of Cases	Percentage
Right	20	28.17%
Left	40	56.33%
Bilateral	2	2.80%
Not Specified	9	12.67%

Table 4: *Type of Tumor. (n=71)*

Procedure	No. of Cases	Percentage
IDC	65	91.50%
ILC	01	1.50%
Mammary Carcinoma	05	7.0%

Table 5: *Histologic Grade of Tumor. (n=71)*

Procedure	No. of Cases	Percentage
Grade-3	39	54.09%
Grade-2	32	45.10%

Table 6: *T-Staging. (n=9)*

TNM Stage	No. of Cases	Percentage
pT2	5	55.55%
pT3	3	33.33%
pT4	1	11.11%

Table 7: *N-Staging. (n=6)*

TNM Stage	No. of Cases	Percentage
pN0	2	33.33%
pN1a	1	16.66%
pN2a	3	50.0%

Table 8: *Molecular subtypes. (n=27)*

Molecular subtypes.	No. of Cases	Percentage
Luminal A (ER+, HER2-)	5	18.60%
Luminal B (ER+, HER2+)	9	33.30%
Triple negative/Basal-like (ER-, HER2-)	10	37.00%
HER2 only (ER-, HER2+)	3	11.10%

DISCUSSION

Age is a strong negative predictor in breast carcinoma. The definition of a young woman varies greatly in breast oncology and fluctuates between 30 to 40 years[7]. In our study, we took reference age below 35 years. Out of total 548 diagnosed breast cancer cases during the five-year study period, 71 (12.9%) of the breast cancers were in women aged 35 or less. Around 60% of the cases were in the age group of 31-35 years (Table.1). According to a study[7] 7% patients were younger than 40 years. Another study conducted in 1976 showed 10 % cases in younger women within the same age range. According to an American study conducted in 1998, BRCA positive women tend to have breast carcinoma in young age. The results of various studies conducted at AFIP showed 10.2% cases in young women[8]. Few other Pakistani studies have reported similar results such as Siddiqui et al[25], Malik et al[27], Amna Khurshid et al[9], and Rasheed et al[20].

Histological subtype is a valuable predictor of survival in breast carcinoma. Invasive ductal type is most commonly seen histological subtype seen in young women cancer cases. In studies by Saleh and Abdeen and Okugawa et al invasive ductal carcinoma constituted 93% an 83.1% of invasive ductal carcinomas respectively. In our study, the diagnosis of invasive ductal carcinoma (IDC) was rendered in 65 (91.5%) cases, invasive lobular carcinoma in 1 (1.5%) case and invasive mammary carcinoma (IHC recommended) in 5 (7.0%) cases. Another study conducted at AFIP by Mamoon et al showed 88.7% cases were of ductal type and only 5.4 % cases were of invasive lobular carcinoma8.

Another important variable for breast carcinoma is histological grading. Breast cancer grading is actually representative of aggressive potential of the tumor. Most commonly employed grading system is Nottingham grading system. In our study, regarding histologic grade, 32 (45.1%) were grade 2 and 39 (54.9%) were grade 3. In study of Kroma et al combined percentage of Grade 2 and 3 tumors was 63%. Kothari's study revealed a percentage of 63 for Grade 3 tumors. In study by Jimor et al[15] 81% and 19% of tumors were Grade 3 and 2 respectively. Likewise, Okugawa[23] reported percentages of Grade 1, 2 and tumors respectively as 24%, 53% and 23% and Saleh et al study reported these percentages as 10.2%, 50.6% and 23%.[28]

Pathological T staging is also a valuable predictor of survival in breast cancer patients. . In our study, among 9 cases with available T staging data, pT2, pT3 and pT4 cases were 5, 3 and I respectively. According to a study conducted at Italy 47.6% cancer cases presented with TNM stage pT1 (colleoni et al)[30].

Pathological N staging is a significant prognostic factor. Pathological N staging was available in 6 cases which showed 2, 1 and 3 cases of pN0, pN1a and pN2a respectively. According to a study conducted at Chicago, 72% cases were node positive. In study conducted by Okugawa23 54% patients had pN0, 21% had pN1a and 25% had pN2a pathological N stage. More the number of lymph nodes with metastasis, lesser is the survival.

Molecular subtyping has gained much interest in recent years. In our study, receptor studies for molecular subtyping were available in 27 cases which showed 18.6% luminal A (ER+, HER2-), 33.3% luminal B (ER+, HER+), 37.0% ripple negative (ER-, HER2-), and 11.1% HER2 only (ER-, HER2+) subtypes. In study conducted at Taiwan, (Cheng et al)31 less than 67% cases were luminal A and only 9% had basal like subtype. The study conducted at Chicago (Dezheng et al) 27% was basal like, 27% luminal A, 2% luminal B and 15% Her2 positive. In the study conducted by Collins et al 33% were luminal A, 35% were luminal B, 11% Her2 positive and 22% were triple negative. In a study conducted by Carney et al in 2006, basal like phenotype was the most prevalent phenotype among premenopausal African American women.

CONCLUSION

Breast cancer in young women is more prevalent in our population than the west. Left sided cancer is more frequent side and IDC is the most frequent type in these cancers. The tumors have high histological grade and advanced pathological stage. Triple negative/basal-like is the most common

molecular subtype. Our findings are in accordance with the available literature.

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CLINICO-PATHOLOGICAL PROFILE OF NEW SMEAR POSITIVE PULMONARY TUBERCULOSIS CASES REGISTERED IN DOTS IMPLEMENTED TERTIARY CARE SETTING

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ABSTRACT

The key to control TB is to cure infectious patients at an early stage. However, the diagnosis is often delayed or missed due to incorrect diagnosis by the health care providers rather than the patients delay in seeking medical advice.The clinical manifestations of pulmonary TB are protean and non-specific. Doctor`s awareness of the clinical spectrum of pulmonary tuberculosis is therefore essential for rapid diagnosis. With this in mind this study was conducted and we documented the clinico-pathological presentation of new smear positive pulmonary tuberculosis patients who were treated in our department.

Setting and study design: This descriptive study was carried out in chest clinic of Sir Ganga Ram Hospital Lahore.

Study duration: One year from January 2011 to December 2011.

Patients and method: 229 patient of smear positive pulmonary tuberculosis aged 15 years and above of either sex were selected for the study. Purposive non-probability sampling technique was used. Cases with previous history of tuberculosis and patients currently receiving anti-tuberculosis treatment were excluded from the study.A detailed history and clinical examination of all selected patients was under taken by investigator. Demographic data, current symptoms, and relevant co-morbid conditions were retrieved by means of a questionnaire. A set of other necessary investigations were also done in all the selected patients. HIV screening was not performed.

Results: A total number of 229 diagnosed cases of new smear positive pulmonary tuberculosis of either sex belonging to age fifteen and above were included in the study. (80.34) patients had age range 15-54 year and (19.65%)patients were above 55 years of age.(49.78%) were male and (50.21%) were female

The most common presenting symptoms were cough(100%),malaise(93.44%),weight loss(83.84%), fever (80.78%),sputum production(76.41%),breathlessness(72.48%),chest pain(68.12%).Other presenting complaints were night sweats(63.75%), appetite loss(62.44%),haemoptysis(18.34%). (27.07%) patients had minimal radiological lesions, (18.77%) had moderately advanced radiological lesions while (54.14%) had far advanced radiological lesions. (9.67%) patients had ESR in the range of <20 mm after first hour while (90.32%) had ESR in the range of >20. Regarding hemoglobin levels of 229 study population, (80.34%) had hemoglobin (Hb) in the range of <11mg/dl and (19.65%) had Hb in the range of >11 mg/dl.

Conclusion: This study showed that the clinical presentations vary in smear positive pulmonary tuberculosis. The x-ray presentations of new smear positive pulmonary tuberculosis are heterogeneous.High index of suspicion for tuberculosis among doctors is necessary, so that diagnosis is not missed.

Key Words: Tuberculosis (TB), Pulmonary Tuberculosis (PTB,Haemoglobin (Hb), Erythrocyte Sedimentation Rate (ESR)

The World Health Organization (WHO) estimates that till 2020 the global burden of tuberculosis infection will reach to more than one billion[1]. Pakistan currently ranks fifth amongst countries with highest burden of tuberculosis. In an estimated population of around 180 million with annual incidence of TB being 231/100,000, Pakistan reports about 420,000 new cases annually[2].

The key to control TB is to cure infectious patients at an early stage. However, the diagnosis is

often delayed or missed due to incorrect diagnosis by the health care providers rather than the patients delay in seeking medical advice[3]. The clinical manifestations of pulmonary TB are protean and non-specific. Doctor`s awareness of the clinical spectrum of pulmonary tuberculosis is therefore is essential for rapid diagnosis. With this in mind this study was conducted and we documented the clinico-pathological presentation of new smear positive pulmonary tuberculosis patients who were treated in our department.

PATIENTS AND METHODS:

A descriptive observational study was conducted at Sir Ganga Ram Hospital Lahore and Fatima Jinnah Medical College, Lahore from January 2011 to December 2011.

229 patient of smear positive pulmonary tuberculosis aged 15 years and above of either sex were selected for the study. Purposive non-probability sampling technique was used. Cases with previous history of tuberculosis and patients currently receiving anti-tuberculosis treatment were excluded from the study.

Informed written consent from subjects was taken before enrolment in the study. A detailed history and clinical examination of all selected patients was under taken by investigator. Demographic data, current symptoms, and relevant co-morbid conditions were retrieved by means of a questionnaire. A set of other necessary investigations were also done in all the selected patients. HIV screening was not performed. Ethical approval was obtained from the Ethical Review Committee of the institution.

RESULTS

A total number of 229 diagnosed cases of new smear positive pulmonary tuberculosis of either sex belonging to age fifteen and above were included in the study. Among the 229 patients with smear positive pulmonary tuberculosis, 114(49.78%) were male and 115(50.21%) were female. 184(80.34)

patients had age range 15-54 year and 45(19.65%) patients were above 55 years of age.

In the 229 studied population, 30(96.77%) patients had history of cough while 1(3.22%) had no history of cough. 175(76.41%) patients had history of sputum production while 54(23.58%) had no history of sputum production. 166(72.48%) patients had history of breathlessness while 63(27.51%) had no history of breathlessness. 42(18.34%) patients hadhistory of haemoptysis while 187(81.65%) had no history of haemoptysis. 156(68.12%) patients had history of chest pain while 73(31.87%) had no history of chest pain. (Table -2).

Table 1 shows non-respiratory symptoms of 229 smear positive study population. 185(80.78%) patients had history of fever while 44(19.21%) had no history of fever. 146(63.75%) patients had history of night sweats while 83(36.24%) had no history of night sweats. 143(62.44%) patients had history of appetite loss while 86(37.55%) had no history of appetite loss. 192(83.84%) patients had history of weight loss while 37(16.15%) had no history of weight loss. 214(93.44%) patients had history of malaise while one (6.55%) patient had no history of malaise.

Regarding extent of lesion on x-ray chest of 229 smear positive patients, 62 (27.07%) patients had minimal radiological lesions, 43(18.77%) had moderately advanced radiological lesions while 124(54.14%) had far advanced radiological lesions

Table 1: *Symptoms of Smear- positive pulmonary tuberculosis Cases n-229.*

Patients with Symptoms	Smear Positive Cases
Cough	229(100%)
Sputum production	175(76.41%)
Breathlessness	166(72.48%)
Haemoptysis	42(18.34%)
Chest pain	156(68.12%)
Fever	185(80.78%)
Night sweats	146(63.75%)
Loss of appetite	143(62.44%)
Weight loss	192(83.84%)
Malaise	214(93.44%)

(Table -2).

Out of 229 smear positive patients, 22(9.67%) patients had ESR in the range of <20 mm after first hour while 209(90.32%) had ESR in the range of >20. Regarding hemoglobin levels of 229 study population, 184(80.34%) had hemoglobin (Hb) in the range of <11mg/dl and 45(19.65%) had Hb in the range of >11 mg/dl.

Table 2: *X-ray lesion of Smear- positive pulmonary tuberculosis Cases n-229*

X-ray lesion	Smear Positive Cases
Minimal lesion	62 (27.07%)
Moderately advanced lesion	43(18.77%)
Far advanced lesion	124(54.14%)

Table 3: *Hemoglobin and ESR Estimation in Smear- positive pulmonary tuberculosis Cases n-229*

Category	Results
Hb (mg/dl)	
<11	184(80.34 %)
>11	45(19.65 %)
Mean Hemoglobin ± 2SD Value (normal range12-14mg/dl)	10.42 ± 1.1
ESR (mm after first hour)	
<20	22 (9.67 %)
>20	207(90.32 %)
Mean ESR ± 2 SD Value (normal range 0-13mm/hour)	55 ± 22.8

DISCUSSION:

Tuberculosis (TB) remains a major global health problem and is the most frequent cause of death from a single infectious agent. The clinical manifestations of pulmonary tuberculosis are protean and non-specific. Classic symptoms of prolonged cough and fever are not present in every case of pulmonary tuberculosis.

It is obvious from the present study that majority of patients (68- 100%) suffered from cough, sputum production, breathlessness and chest pain(table -1). Some of the symptoms like haemoptysis (18.34%) and chest pain (68.12%) appears to be more alarming (Table -1) as these compelled the patients to seek immediate medical treatment, while among non-respiratory symptoms,

fever, loss of appetite, weight loss and malaise appeared to be more obvious, ranging from 62-93%. These findings are in accordance with the study conducted by Khushman et al (2006)1,who reported cough (79%), weight loss (74%), fatigue (69%), fever (69%), night sweating (55%), chest pain (41%) and dyspnoea (39%) as most common presenting symptoms of pulmonary tuberculosis. English et al (2006)2 reported that the common symptoms in smear positive patients were cough (100%), breathless (70%), sputum production (63%), weight loss (50%), and night sweating (50%). EL-Sony et al (2003)[3] stated that among smear positive patients, the majority complained of cough (94.3%), breathlessness (74.8%), chest pain (57.7%), haemoptysis (19.8%), fever (78.2%), night sweats (62.8%). Arslan S (2010)4 reported 93.4% patients presented with common symptoms of tuberculosis. Rathman G et al (2003)5reported cough (100%), weight loss (97%) and malaise (70%) as the most common symptoms in their study. The findings of all these studies are in accordance with our study. Symptoms of tuberculosis (except haemoptysis) reported by Rizwan et al (2002)[6] corresponds with the present study. Miller et al (2000)[7] reported only 22.4% of patients had classic symptoms of pulmonary tuberculosis. This finding is similar to that reported by Ismail Y (2003)8 in his study.

It has been established from the literature that x-ray lesion in smear positive patients varies from minimal to far advance lesions.Present study showed that 54.14% of smear positive patients had far advanced lesion, as a study conducted in New Zealand where 31% patients had far advanced lesion9. The findings of this study is not in consistent with study of Rathman et al (2003)10 which showed 97% smear positive cases had far advanced lesion Smear positive patients may have minimal disease on x-ray chest examination with low bacilliary count rather than far advanced disease[11]. This finding is also supported in the present study as 27.07% cases had minimal lesion on x-ray chest. The study conducted in Lahore by Iffat et al (2007)[12] also supports the present study.

Erythrocyte sedimentation rate (ESR) is a non-specific marker of inflammation and is elevated in a number of infectious and non-infectious conditions including tuberculosis. Studies from the developing countries reported high ESR values in cases of active tuberculosis[13]. This high ESR values can be used to start anti-tuberculosis treatment in the presence of relevant clinical symptoms[14]. In the present study, higher value of ESR (55+22.8 with normal range 0-13 mm/h) was seen in patients with active

pulmonary TB. This finding is supported by the studies, conducted by Hassan et al (1996)[15] and by Bushra et al (2008)[16] which reported high ESR 90+31 and 44+31 respectively.

All chronic infections including tuberculosis produce anaemia from different mechanisms[17]. Decreased level of haemoglobin in pulmonary tuberculosis is usually due to suppression of erythropoiesis by inflammatory mediators[18], along with nutritional deficiency19. Decreased level of Hb was also reported by Singh et al (2001)[20] (9.58+1.55) and Lee et al (2006)[21] (<10 g/dl) in 31.9% patients. The present study also showed increased incidence of anaemia (Hb 10.42+1.1) in patients with smear positive pulmonary TB.

In this study, we have reported the clinico-pathological profile of 229 smear-positive pulmonary tuberculosis patients. This study showed that the clinical presentations vary in smear positive pulmonary tuberculosis. The x-ray presentations of new smear positive pulmonary tuberculosis are heterogeneous. High index of suspicion for tuberculosis among doctors is necessary, so that diagnosis is not missed.

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COMPARISON OF DIABETES MELLITUS IN PATIENTS HAVING SCHIZOPHRENIA WITH AND WITHOUT ANTIPSYCHOTIC MEDICATIONS

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ABSTRACT

Aim: To compare the frequency of impaired glucose tolerance and Diabetes Mellitus in drug naive and drug taking patients having Schizophrenia.

Design and duration of study: Cross-Sectional research design was used. The study was conducted over a time period of six months (Sept 2007 to March 2008).

Method: Total 60 patients having schizophrenia were taken and assigned in two different groups. Group I consisted of drug naive patients of schizophrenia where as Group II consisted of drug taking patients with schizophrenia. Patients in group II were further divided according to their sub categories of drugs (olanzapine, quetiapine and resperidone). All these patients were then undergone fasting blood sugar testing and those with abnormal levels more than 126mg/dl were subjected to Oral Glucose Tolerance Test.

Results: In group I, out of 30 patients there were 2 (6.7%) patients who had Diabetes Mellitus and in group II, out of 30 patients there were 4 in olanzapiane sub category (13.3%) patients who had Diabetes Mellitus, (p>0.05.) None of the patients had impaired glucose tolerance test.

Conclusions: Although there were no significant difference between both of the groups, Diabetes Mellitus is seen more frequently in patients with antipsychotic drug (especially olanzapine).

Key words: Diabetes Miletus, Impaired glucose tolerance, Antipsychotic medication

Schizophrenia is a medical illness which is characterized by disintegration of thinking, behavior, movement and feeling[1]. It is associated with excessive rate of medical morbidity and mortality[2]. Research concluded that patients with schizophrenia have two to three times high mortality rate in comparison with general population which is mostly caused by cardiovascular diseases[3]. Moreover, patients having schizophrenia have increased rate of insulin resistance, impaired glucose tolerance and type 2 diabetes mellitus than those reported for the general population[4]. Patients with schizophrenia have suffered from diabetes mellitus on almost at double rate[5].

Diabetes mellitus is a group of metabolic diseases which is characterized by excessive amount of glucose in blood stream caused by deficit in either insulin secretion or insulin action. The chronic condition of diabetes would lead of dysfunction, damage or failure of various organs, especially kidneys, blood vessels, heart and eyes. Type II diabetes mellitus which makes up about 90% of diabetes cases is caused by inadequate insulin secretion response and body resistance to insulin action. Whereas other 10% are related to type 1 diabetes which is caused by deficiency of insulin secretion and gestational diabetes which is characterized by high blood sugar level during pregnancy[6]. In Pakistan recent research suggest that the prevalence of diabetes mellitus type 1diabetttis mellitus was 0.21 while type 2 was observed at a prevalence rate of 0.72[7]. Shera, Jawad & Maqsood

(2007) found that the prevalence of overall glucose intolerance was found to be 22% in urban and 17% in rural areas [8].

As compared to general population research shows that patients having schizophrenia are more susceptible of developing impaired glucose tolerance and diabetes mellitus[9]. Mukerjee et al. (1996) concluded 15.8 % prevalence of diabetes mellitus among patients having schizophrenia in Italy which is higher as compared to general population[10]. Similarly, Dixon et al. (2000) found that in patients with schizophrenia, rate of diagnosed diabetes (14.9%) exceeds general population even before the widespread use of atypical antipsychotic drugs [11].

Atypical and typical antipsychotics have been related with elevated risk of diabetes mellitus in patients having schizophrenia. Typical antipsychotic i.e phenothiazine leads to glucoregulatory abnormality[12] which include either aggravation of existing diabetes[13] or onset of type 2 diabetes [14,15]. Similarly atypical antipsychotic medications especially clozapine and olanzapine were observed to contribute to significantly elevated hyperglycemia, diabetic ketoacidosis, increase in existing level of diabetes and new onset of type 2 diabetes [16,17,18] Recent evidence suggests that the mechanism of action of atypical drugs is to bind and block glucose transporter protein [19].

Few studies have assessed diabetes mellitus in schizophrenia in Pakistan and none has been studied this phenomena in Lahore, so we planned a study with the aim to evaluate the frequency of impaired glucose tolerance and diabetes mellitus in patients with schizophrenia using antipsychotics in comparison with drug naive group of patients having schizophrenia. Both groups were matched on the basis of age, gender and socioeconomic status.

MATERIAL AND METHOD

The cross sectional study was carried out at indoor and outpatient department of Psychiatry, Jinnah hospital, Lahore over a period of six months, from Sept 2007 to March 2008 after taking permission from the institutional review board of the relevant department. Purposive sampling was used to include only those patients that fulfilled the diagnostic criteria of schizophrenia according of ICD-10 and their age ranged from 20 to 60 years. Total 60 patients were included in the study and they were divided in two groups. Patients in group 1 included drug naive patients who were referred by primary physicians whereas patients in group 2 included those patients who were taking antipsychotic medications. It was insured that patients of both groups had duration of at least six months. Patients in group 2 were further divided into three main categories according to the drug they used (olanzapine, resperidone, quetiapine). Patients with severe co-morbid illnesses contributing towards impaired glycemic control, or those patients who were diagnosed with diabetes mellitus prior to onset of schizophrenia or patients with type 1 diabetes mellitus requiring insulin therapy were excluded from both groups. Informed consent was obtained from patient before assigning them to any group according to their illness presentation.

SUBJECTS

From a total of 60 participants, 32(53.3%) were males and 28(46.7 %) were females. The mean age of the patients in group I was 28 years (16 males, 14 females). In group II, the mean age of the patients was 37 years (16 males, 14 females). All these patients were then undergone fasting blood sugar testing and those with abnormal levels more than 126mg/dl were subjected to Oral Glucose Tolerance Test by checking their serum glucose at fasting and then at half hour, one hour and two hour post-glucose intervals in hospital laboratory. Results of impaired glucose tolerance were interpreted according to guide lines given by American Diabetic Association. Data analysis was done using SPSS version 10.0. Descriptive statistics is summarized as frequency and percentage. Chi- Square test is used to determine the significant difference in presence of impaired glucose tolerance and diabetes mellitus among patients of group I and group II.

RESULTS

The research participants consisted of two groups. Group I included drug naive schizophrenia subjects while group II included drug taking patients having schizophrenia. Group II was further sub-

divided into three groups according to their nature of drug. Each subgroup consisting of ten patients who were taking olanzapine, risperidone, quetiapine respectively. The important socio demographic variables are given in Table 1. Results of chi square for presence of diabetes mellitus in group I and group II are given in table 2. In both groups, there were no patients who had impaired glucose tolerance test positive therefore the two groups could not be computed for test of significance.

Table 1 identified that in group I majority of the patients fall in the age range of 41-50 years where as in group II equal numbers of patients fall in age range of 31-40 and 41-50 years of age. Male outnumbered females in both groups. Majority of the patients belonged to lower class socioeconomic status. More than half of the patients in group I and half of the patients in group II have eight months or above duration of illness.

Table 2 shows that in group I the two patients fulfilling the criteria of diabetes mellitus fall in age range of 51-60 years while in group II, three diabetic patients fall in age range of 20-30 years where as one patient all in age range of 31-40 years.

Table 3 revealed that there is no statistically significant difference in presence of diabetes mellitus among group I and group II patients. Among the sub-groups in group II, four patients out of ten (who were on olanzapine) were positive for Diabetes Mellitus. None of patient on risperidone and quetiapine showed positive result for Diabetes Mellitus.

DISCUSSION

In this research we tried to compute the significant difference between the frequency of impaired glucose tolerance and diabetes mellitus in patients having schizophrenia with and without antipsychotic medications. To the best of our knowledge no such research exists in literature from this city (Lahore) before.

Our research finding suggests that diabetic patients in drug naive group fall in age group of 51-60 years. This finding is in line with result of Subramaniam, Chong & Pek (2003) which present that majority of patient with schizophrenia suffered from diabetes mellitus type 2 fall in age range of 50 - 59 years[20]. In our research, patients in drug taking

Table 1: *Frequencies and Percentages of demographic characteristics of research participants*

	Group I		Group II	
	f	%	f	%
Age in years				
20-30	21	70	9	30
31-40	6	20	10	33.3
41-50	3	10	10	33.3
51-60	0	0	1	3.4
Gender				
Male	16	53.3	16	53.3
Female	14	46.7	14	46.7
Socioeconomic Status				
Low	27	90	19	63.3
Middle	3	10	11	36.7
Duration of Illness				
< 8 Months	18	60	15	50
9-12 Months	12	40	11	36.7
> 12 Months	0	0	4	13.3

Note: N=60, f=frequency, %=percentage

group have highest frequency of diabetes mellitus in age range of 21-30 followed by 31-40 years of age. The study of Michael & Frank (2003) support our finding that in patients having schizophrenia taking atypical antipsychotic drugs, under 40 years of age group shows an increase vulnerability of developing type 2 diabetes[21].

Patients in both groups did not get positive test when tested for impaired glucose tolerance test. This

Table 2: *Age Specific frequency of diabetes mellitus among research participants*

	Group I		Group II	
	f	%	f	%
Age in years				
20-30	_	-	3	75
31-40	_	-	1	25
41-50	_	-	-	-
51-60	2	100	-	-

Note: N=6, f=frequency, %=percentage

absence of impaired glucose tolerance in the present study could be due to low mean of the illness duration 8 months for group I and 10 months for group II of the patients.

Our results indicate that patients having

Table 3: *Results of Chi-square test and descriptive statistics of presence of Diabetes Mellitus for drug naive (group I) and drug taking (group II) patients*

	Group I	Group II
Diabetes Mellitus		
Yes	2 (6.7)	4 (13.3)
No	28 (93.3)	26 (86.7)

Note. $\chi^2 = 1.69$, df = 1, p > .05, numbers in parentheses indicate column percentages.

schizophrenia in both groups did not show any significant difference in the presence of diabetes mellitus when compared to each other. Although the result of chi square was not statistically significant in terms of presence of diabetes mellitus in the two groups. However the findings of the study suggested that there was increased frequency of diabetes mellitus (13.3%) in patients on antipsychotic drugs (olanzapine subgroup) as compared to drug naive group (6.7%). This finding is supported by research of Suvisaari et al(2008) who observed that in patients having schizophrenia users of all types of antipsychotic medication had increased prevalence of type 2 Diabetes Mellitus[22]. Similarly Gupta, et al. (2003) reported the prevalence rate of 17% for diabetes in patients having psychotic disorders who were receiving antipsychotic drugs[23] which is in accordance with our research findings. (13% vs 17%).

Our research observation of elevated plasma glucose elevation in olanzapine taking patient group can be explained by research finding of Wirshing, et al. (1998) which proposed serotonergic model regarding olanzapine induced diabetes which shows that 5-HT1A antagonism reduces responsiveness of pancreatic β-cell which leads to reduction of insulin secretion and elevation of serum glucose levels[24]. Shernayk et al. (2002) concluded that the prevalence of diabetes mellitus was significantly elevated for patients with schizophrenia who received olanzapine as compared to resperidone which second our research findings [25].

Olanzapine is currently used as a first line therapy for schizophrenia as it offer better efficacy than other antipsychotic drugs and lesser extra pyramidal symptoms[26,27]. However with the increase in evidences of hyperglycemic effects a caution is required to assess each drug efficacy and its potential to cause metabolic side effects[28]. As schizophrenia is a chronic disease that requires continuous medication, an antipsychotic drug with less dibetogenic potential can be used to prevent relapse with least effects on glucose deregulation.

CONCLUSION

Although, results of the study were not significant in terms of presence of Diabetes Mellitus in patients with Schizophrenia, the frequency of Diabetes Mellitus was more in patients with Schizophrenia on antipsychotic drugs as compared to drug naive group. However, large, multicentre clinical trials are required to identify antipsychotic drugs as a cause of Diabetes Mellitus.

Limitations and Recommendations

- Our research is conducted in only one government run hospital and thus represents a specific section of population.
- As it was a cross sectional study so longitudinal course of illness could not be followed.
- Routine screening, family history of type 2 diabetes mellitus and the development of pragmatic pathways for Diabetes Mellitus risk management in all patients with Schizophrenia are recommended and we should advise them about diet and exercise.
- Perhaps the most important area of intervention is that of raising awareness of psychiatrists, primary care physicians and mental health professionals about the vulnerability of diabetes mellitus in patients using atypical antipsychotics especially olanzapine.
- If there is an elevation in plasma glucose level of patient on antipsychotic is observed, it is recommended to switch to low risk drug and patient should be monitored for further glucose deregulation.

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PERCEPTION AND AWARENESS REGARDING VITAMIN D DEFICIENCY AND ITS COMPLICATIONS AMONG THE MEDICAL STUDENTS OF ALLAMA IQBAL MEDICAL COLLEGE, LAHORE

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ABSTRACT

Objective: To assess the level of perception and awareness regarding Vitamin D deficiency and its complications among the medical students of Allama Iqbal Medical College, Lahore

Methodology: In this cross sectional study, a total of 250 medical students of all five years were interviewed at Allama Iqbal Medical College, Lahore (affiliated with Jinnah Hospital, a 1200 bedded tertiary care hospital). The study was conducted between 21st April, 2016 and 6th June, 2016. Students were selected through non-probability/purposive sampling. The selected students were asked to fill a paper based standardized questionnaire after consent. Results were analyzed using SPSS 21.

Results: Out of the 250 respondents, majority were female (56.63%) and the remaining were male (43.37%). Majority (65.2%) of the respondents answered correctly and were in the good awareness category whereas the remaining (34.8%) had poor/average awareness. The mean average score of awareness progressed with each class, starting from 2.54 (1st year) to 2.94 (5th year).

Conclusion: Majority of the students were well aware and had sound perception regarding Vitamin D deficiency and its complications, meaning that they have good basic knowledge about the vitamin.

Key Words: Vitamin D, Deficiency

The D vitamins are a group of lipid soluble sterols that have a hormone-like function[1]. This group consists of vitamin D_3 (active form 1, 25-dihydroxycholecalciferol [1,25-diOH-D3]) and vitamin D_2 [2]. The major function of vitamin D is calcium homeostasis, thus assuming importance in lifelong skeletal development[2]. Additionally, it helps in cell regulation, renin inhibition[2], insulin secretion[3], immunomodulation, and treatment of disorders like psoriasis[5]. Sunlight constitutes the most important source of vitamin D[2]; additional sources include fortified milk, eggs, and fish[4]. According to a study conducted by Michael F. Holick and his colleagues, exposure of the skin to a duration of sunlight amounting to one minimal erythemal dose (MED: that causing slight redness of skin) equates to 10,000 – 25,000 IU of oral vitamin D[6]. Vitamin D deficiency is defined as serum 25OHD levels lower than 20 ng/ml[10]. Additionally, insufficiency may be defined as serum levels between 20 ng/ml-30 ng/ml[10]. The most important

causes of vitamin D deficiency are lack of exposure to sunlight and reduced intake of fortified foods[2]. Recent studies indicate that Pakistan is a microcosm of a global pandemic of vitamin D deficiency[7,9], partially due to the darker skins and culture (that is, covered clothing) of the populace[7], with Junaid Kashaf reporting deficiencies in 90% of pre-menopausal women in Lahore in 2012[8]; Aysha Habib Khan and her colleague from Aga Khan University at Karachi observed an even more distressing trend, with deficiencies seen in 97% of volunteer subjects in 2010[12]. Vitamin D deficiency leads to several complications. Classically, these are hypocalcemia and rickets/osteomalacia[10], but also an increased risk of osteoporosis[4], fractures[4], several cancers[11], infections[11], multiple sclerosis[20], hypertension[2], chronic pain and depression[16,18], among others. Misconceptions about vitamin D continue to rise, despite recent publications attempting to correct these[13]. For example, according to a recent study conducted in Sharjah, the

mean score on a test regarding awareness of vitamin D deficiency was 39%, highlighting a very low level of awareness[17]. Expert consensus advises a dietary intake of 800-1000 IU vitamin D/day at all ages in the absence of adequate sun exposure[4]. Up to 2000 IU/day are considered safe[4]. The fortification of foods with Vitamin D coordinated with public health strategies is required to combat extant high deficiency in widespread population[14,15]. Whilst overdose is unlikely with vitamin D supplements, concomitant calcium supplementation increases the risk of renal stones, and monitoring of serum calcium levels is recommended [11].

METHODOLOGY

This cross-sectional study was conducted in Allama Iqbal Medical College, a public sector medical college affiliated with University of Health Sciences (UHS), Lahore. The college is attached to Jinnah Hospital (a 1200 bedded tertiary care hospital). The study was conducted by the Department of Community Medicine, Allama Iqbal Medical College, Lahore during a period of two months (April 2016 - May 2016). A total of 250 students (both male and female) out of a total of 1649 students of MBBS in Allama Iqbal Medical College, Lahore were surveyed.

Sampling Technique:

The sample was chosen using non probability / purposive sampling.

Data Collection:

A paper based standardized questionnaire was provided to the MBBS students of Allama Iqbal Medical College, after taking the consent, to be duly filled by them.

Data Analysis:

Data was entered and analyzed using SPSS version 21. Frequency and percentages were calculated for nominal variable. Cross tabulation was done between dependent and independent variable.

RESULTS

A total of 250 students of Allama Iqbal Medical College, comprising specifically of 50 students per year (from 1st Year to 5th Year) enrolled in the MBBS degree program, were interviewed for the collection of data regarding perception and awareness of Vitamin D deficiency and its

complications. The data were collected through the provision of an approved questionnaire, which was duly consented to and collected upon completion. Out of the 250 students surveyed, 108 were male (43.37%), 141 were female (56.63%), and one (0.4%) chose not to answer this query. No doctors from Allama Iqbal Medical

College or Jinnah Hospital were approached for data collection. Overall, considering the question-naire as a whole, as Table 1 shows, the 1st Year students achieved a scaled score of 2.54, the 2nd Year students achieved a scaled score of 2.6, the 3rd Year students achieved a scaled score of 2.54, the 4th Year students achieved a scaled score of 2.76, and the 5th Year students achieved a scaled score of 2.94, signifying a general increase in knowledge with each advancing class. The mean scaled score of the college as a whole was 2.676.

	Score Category				
	1. Poor (0-4)	2. Average (5-9)	3. Good (10-14)	4. Excellent (15-20)	Scaled Score (from 1-4)
1st Year	1 *(2%)*	21 *(42%)*	28 *(56%)*	0 *(0%)*	2.54
2nd Year	2 *(4%)*	20 *(40%)*	24 *(48%)*	4 *(8%)*	2.6
3rd Year	0 *(0%)*	23 *(46%)*	27 *(54%)*	0 *(0%)*	2.54
4th Year	1 *(2%)*	12 *(24%)*	35 *(70%)*	2 *(4%)*	2.76
5th Year	3 *(6%)*	4 *(8%)*	36 *(72%)*	7 *(14%)*	2.94
Total	7 **(2.8%)**	80 **(32%)**	150 **(60%)**	13 **(5.2%)**	2.676

Table 1: Division of score categories by class of respondents. Italicized percentages indicate percent of response within the specific category per year, whereas the bolded percentages at the end indicate the percent of response within the specific category across all five years. Scaled score has been calculated using percentage of responses within each category, with each category assigned a value (poor=1, average = 2, good = 3, excellent = 4), multiplied by the category value, with all categories summated per class and for all five classes to provide an average score for the college. Categories were determined according to number of questions, out of 20 total, correctly answered (poor being 0-4, average 5-9, good 10-14, excellent 15-20).

Crucially, the query regarding awareness of the very nature of Vitamin D was correctly answered by

77.2% of respondents. This level of awareness was almost mirrored in the query regarding the optimum period of the day for maximum Vitamin D production from sunlight, with 64.8% of respondents aware of the potency of sunlight in this regard from 10am to 4pm (Figure 1).
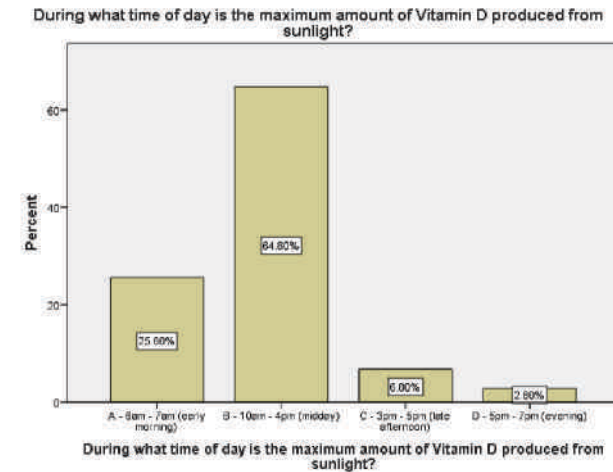
Figure 1: Knowledge among respondents regarding optimum period of sunlight exposure to maximize Vitamin D production.

However, the majority of students were not aware of the effect of melanin on Vitamin D production, with only 19.68% of respondents knowing that melanin decreases production of Vitamin D (Figure 3), an essential consideration, especially in the tan-skinned South Asian populace.
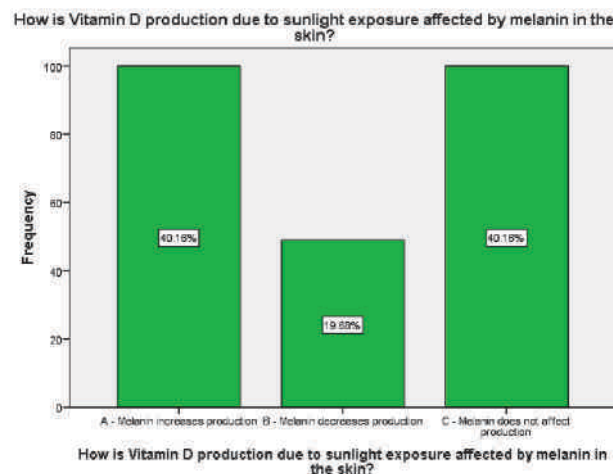
Figure 2: Awareness among respondents regarding effect of melanin on Vitamin D production

Additionally, only a similar level (19.2%) of those interviewed were correct in displaying

recognition of the multiple roles of Vitamin D in the body (Figure 3).
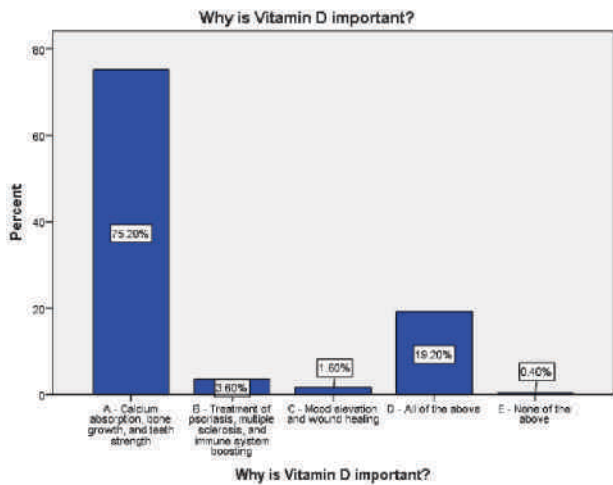
Figure 3: Perception of respondents regarding importance of Vitamin D

Furthermore, whilst 89.6% of respondents were aware that tube/bulb light would not be useful in Vitamin D production (Table 2), less than half (44.8%) were correctly aware that sunlight passing through a normal glass window would not result in Vitamin D production.

The relationships of class and the knowledge of the most important source of Vitamin D; of class and importance of Vitamin D; and of class and knowledge regarding necessity of Vitamin D in nutrient absorption are all statistically insignificant. The relationship between class and knowledge of the most important complication of Vitamin D deficiency is statistically significant ($p<0.05$; Chi-square value = 27.396; df = 12). The relationship between class and knowledge of time of day of maximum Vitamin D production is statistically significant ($p<0.05$; Chi-square value = 26.950; df = 12). The relationship between class and knowledge of the effect of melanin on Vitamin D production is statistically significant ($p<0.05$; Chi-square value = 28.535; df = 8).

DISCUSSION:

In the past few years, Vitamin D and its deficiency has become the subject of much research, a trend which consequently has produced novel

Is bulb/tube light useful in making Vitamin D		Is Vitamin D produced when sunlight passes through a normal glass window	
Yes	No	Yes	No
9.6%	89.6%	54%	44.8%

Table 2: *Awareness regarding possibility of extraneous methods of Vitamin D production*

discoveries about the role of Vitamin D in medicine. We set out to evaluate the general perception and awareness about vitamin D deficiency/ complications amongst the medical students enrolled in the MBBS program at Allama Iqbal Medical College, Lahore, and then compared the results of each class, from first year to fifth year.

Our research showed that 60% of the students have good general awareness regarding Vitamin D, 32% have an average level of awareness, a rare 5.2% have excellent awareness, and a low 2.8% have a poor level of awareness. This is in contrast to a 39% awareness on vitamin D deficiency, as per a study conducted in Sharjah(17); this may be attributed to the fact that our research was conducted on medical students. As per our expectations, the results of our research improved with each progressive class, except for a small dip due to 3rd year results (average scaled scores: 1st year [2.54], 2nd year [2.6], 3rd year [2.54], 4th year [2.76], 5th year [2.94]). A possible reason for this may be a low level of concentration amongst the 3rd year students due to their upcoming Pharmacology test the same day. An impressive 76% were well aware of sunlight as the major source of vitamin D, whilst 17% students perceived milk and dairy products as the most important sources. However, it is pertinent to mention here that an alarming 54% of the students wrongly assumed that Vitamin D is still produced when passed through a normal glass window. Moreover, only 44% believed that direct contact with sunlight is required for its production. As expected, most (75%) of the students think Vitamin D is important only for calcium absorption, bone growth and teeth strength, whilst only an inadequate 19% were correctly aware that Vitamin D is important not only for the aforementioned reason,

but also for its role in boosting immunity, in the treatment of psoriasis and multiple sclerosis, mood elevation, and wound healing. This may be due to the fact that vitamin D has always been associated with calcium, bones, and teeth in the textbooks in medical school. Conversely, 64% of the students were well aware that sunlight during 10am to 4am was used in making Vitamin D, but a considerable (25%) number of students thought that early morning sunlight (6am to 7am) is the best for Vitamin D production. Regarding awareness about the role of skin pigment i.e. melanin in Vitamin D production, a majority of the students (80%) were wrong. Only 19% were correctly aware that melanin decreases Vitamin D production in the body. From this, we infer that tan skinned people (who have higher melanin content) require more time in the sun for ample Vitamin D production. It may be highlighted here that Pakistan is a microcosm of a global pandemic of vitamin D deficiency[7,9]. As far as awareness of the biochemical and metabolic importance of Vitamin D is concerned, about 78% of the respondents were well equipped with the knowledge that Vitamin D is necessary for calcium absorption, but a significant 14% incorrectly thought it was important for absorption of calcium, iron and folic acid. Finally, 85% of the people considered checking their Vitamin D levels as important, depicting their level of consciousness, as against the 15% who don't consider it important, possibly because of its high cost in the private labs.

Due to this fact and a general lack of awareness about the full extent of the roles of Vitamin D in medicine, doctors could overlook the importance of this vitamin and patients may thus be misdiagnosed. Corrective efforts, such as food fortification, more exposure to the sun, less sunblock usage, etc. must be initiated. [15].

CONCLUSION:

The result of our study concluded that the medical students enrolled in the MBBS program at Allama Iqbal Medical College, Lahore were well versed with the general concept of Vitamin D. However, they lacked awareness regarding the novel importance of this Vitamin and its deficiency, which is understandable since this information is hardly referred to in medical school textbooks, if at all, and to our knowledge, it is likely that medical students

seldom read research articles online. However, it was heartening to learn that a good percentage of students are curious about its importance and consider estimating their own Vitamin D levels once a year, a necessity. There was a general rising trend of awareness with each progressive class, as per our expectations.

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HYPERHOMOCYSTEINEMIA IS A SIGNIFICANT RISK FACTOR FOR WHITE MATTER LESION IN NON INSULIN DEPENDENT DIABETIC STROKE PATIENTS

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ABSTRACT

BACKGROUND: The incidence of diabetes mellitus, especially, type 2 is rapidly increasing (90%globally). In patients with type 2 diabetes mellitus, the risk of cardiovascular ailments is two to four folds more than in the non-diabetic population. Therefore, the presence of diabetes is linked with 10–15years reduced life expectancy.1Atherosclerosis, in diabetes is complex and includes a novel factor homocysteine, in addition to diabetes-related and traditional factors.

AIMS AND OBJECTIVES: The presence of white matter lesion is correlated with homocysteine levels in type 2 diabetic stroke patients.

METHODS: We included 26 diabetic type 2 stroke patients who were diagnosed to be suffering from clinical stroke on the basis of history and physical examination of the patient. The diagnosis was further confirmed by CT (Computerized Tomography) scan of brain. These patients were recruited from neurology and emergency wards of two community hospitals of Lahore. Blood samples were collected from the same stroke patients.

STUDY DESIGN: It is a cross-sectional analytical study.

SETTING: Neurology and emergency wards of Sheikh Zayed Medical and Dental Complex and Jinnah Hospital Lahore.

DURATION OF STUDY: August 2010 till September 2011.

SAMPLE SIZE: Twenty six non-insulin dependent diabetic stroke patients participated in the study.

SAMPLING TECHNIQUE: Convenient sampling

DATA ANALYSIS: All analysis of data was entered and analyzed by using SPSS software version 20. The data was compiled as the means ± SD. Differences between the two groups were inspected for continuous variables by means of the Student's t-test and for categorical variables with the chi square test. Logistic regression analysis was integrated to evaluate the impact of expounding variables on WML.

RESULTS: Multivariate logistic regression revealed that the presence of WML is significantly connected with total homocysteine in type 2 diabetic stroke patients. In step 1, the risk of white matter lesion was found to be associated with total homocysteine, OR .695, 95% CI= .495 -.978 P .0037. Similarly in the next three steps we have found a strong association between WML and tHcy with OR .722, 95% CI= .556 -.936 and a p value of .014 in the last step.

CONCLUSION: In our study total homocysteine has been found to be an independent and significant hazardous issue for the existence of white matter lesion in adult onset type 2 diabetic stroke patients.

KEY WORDS: White matter lesion, CT brain, homocysteine, adult onset diabetes mellitus

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The existence of white matter lesion (WML) has been recognized as an essential predictive issue for the development of cerebral stroke.[2,3] Plasma total homocysteine (tHcy) which rises with diabetes has been identified to be a new aspect for the occurrence of cerebrovascular events.[4]

WML owes its occurrence due to a chronic course of action created by continuing blockage of small piercing vessels resulting in decreased blood supply to white matter.[5,6,7] Age and hypertension are the main causes of WML. Vascular risk factors such as smoking, diabetes, and vascular diseases enhance the process. WML is considerably linked with a threat of stroke both in common population and in high risk population who have already suffered from stroke.[3]

Like hypertension,[8,9,10] diabetes[11] is associated with a greater burden of WML. There is an increasing curiosity in recognizing potentially modifiable risk factors. Elevated homocysteine (Hcy) has been acknowledged as a causative factor for atherosclerosis that has been implicated in the increased incidence of cardio and cerebrovascular disease.

Homocysteine is a non-protein forming 4-carbon sulphur containing amino acid.[12,13] It is an essential amino acid derived from methionine. It is an intermediate product formed by the conversion of methionine into cysteine.

To date, numerous studies have associated WML to elevated tHcy.[14,15,16,17,18] Similarly insulin resistance has been allied to established risk factors for atherosclerosis such as hypertension, hyperlipidemia and obesity. All these risk elements enhance the process of atherosclerosis.

Hypothesis

In this study we hypothesized that the existence of WML is related to tHcy in stroke patients with type 2 diabetes.

MATERIALS AND METHODS

OPERATIONAL DEFINITIONS:

Homocysteine has been recognized as a risk factor for atherosclerosis. It is an essential amino acid derived from mithionine. It is a biomarker for heart disease, stroke, peripheral vascular disease and venous thromboembolism.

White Matter Lesion is caused by gradual occlusion of small penetrating vessels leading to hypoperfusion of white matter. It predicts the risk of stroke, dementia, mortality and a host of other poor outcomes.

Inclusion criteria

The non-insulin dependent diabetic stroke patients who had CT scan that confirmed the diagnosis of ischemic or hemorrhagic stroke were included in the study. Moreover, they reported within 12 hours of the onset of stroke symptoms.

Exclusion criteria

The patients of secondary hypertension, renal insufficiency, atherothrombotic disease or any other chronic disease were not included. Those who were treated with insulin in the past and the postmenopausal women on hormone replacement therapy were also excluded.

Study population

We selected 26 stroke patients with type 2 diabetes during the period of August 2010 till September 2011. The stroke patients admitted in Neurology and Emergency wards of Sheikh Zayed Medical Complex and Jinnah Hospital Lahore were recruited in our study. Demographic data was collected by a proforma.

The experiments were undertaken with the understanding and written consent of the subject himself or his near relative. Endorsement of our study was obtained from the research ethical committee, Institution Review Board (IRB), Sheikh Zayed Medical Complex.

Laboratory Methods

Fasting blood samples were taken from antecubital vein. Blood tests included serum cholesterol and fasting plasma glucose. The

commercially available ELISA kit (Axis-Shield Homocysteine ELISA kit, UK) was used to estimate total Hcy level.

Evaluation of WML on CT brain

All the patients underwent CT scan brain. WML was interpreted on the same criteria as Wahlund scale.19 CT was read by the same radiologist to confirm the presence and intensity of WML. He was not aware of the clinical picture of the patients.

Statistical Analysis

To test our hypothesis we divided the stroke patients with type 2 diabetes into two groups: with WML and those without WML. We compared CT brain, metabolic profile and tHcy in the two groups. We also evaluated the independent predictors of WML in these patients.

All analysis of data was entered and analyzed by using SPSS software version 20.

1. The data was compiled as the means ± SD. Differences between the two groups were inspected for continuous variables by means of the Student's t-test and for categorical variables with the chi square test. Logistic regression analysis was incorporated to evaluate the impact of expounding variables on WML.

2. Univariate logistic regression analysis with WML as the dependent variable in adult onset diabetes mellitus.

3. Multivariate logistic regression analysis with WML as the dependent variable in adult onset diabetes mellitus.

RESULTS

This was a cross-sectional analytical study endorsed on 26 NID diabetic stroke patients. The data for gender, hypertension, heart disease, smoking and WML were described by using frequency and percentages. The quantitative variables, age, BMI, total cholesterol, fasting plasma glucose (FPG) and Hcy were expressed in terms of mean ±SD. Differences between the groups of

continuous variables were tested by using Student's t test. The tHcy was found to be highly significantly connected with the occurrence of WML in type 2 diabetic stroke patients $p = 0.0001$(Table 2).

There were 16 (61.5%) males, and 10 (38.5%) females. 19 (73.1%) were hypertensive, 6 (38%) had known heart disease. In addition, there were 3 (11%) smokers. The WML was found in 14 (53.8%) patients.

There was no association of the presence of WML with gender, hypertension, heart disease and smoking when tested by using Pearson Chi-square likelihood ratio test.

Logistic regression analysis was applied to appraise the impact of expounding variables on WML in which age, BMI, total cholesterol, FPG and Hcy were included. A logistical regression was chosen with a cutoff level of 0.05 for significance.

Stepwise multiple backwards regressions were enforced to figure out the association between the incidence of WML and other factors. Differences were recognized statistically significant at $p < 0.05$.

Model of Logistic Regression

$Log(WML) = -1.721 - 0.326 \ (Homocystein) + 0.338(BMI)$

In step 1, the risk of WML was found to be linked with tHcy, OR .695, 95% CI= .495 -.978 P .0037. Similarly in the next three steps we have found a strong association between WML and tHcy with OR .722, 95% CI= .556 -.936 and a p value of .014 in the last step (Table 3)

In our study tHcy has been found to be an independent and significant risk element for the

Table 1: *Testing of Normality of Data*

Variable (n=26)	P Value*
Age	0.200
Body Mass Index	0.200
Total Cholestrol	0.049*
Fasting Plasma Glucose	0.190
Homocysteine	0.047*

*P-value obtained by applying Kolmogrov Simrnov Test

**P-value<0.05 considered statistically significant

presence of WML.

Table 2: *Table. 2 Clinical characteristics of type 2 diabetic patients showing tHcy significantly associated with WML*

	WML	N	Mean	Standard Deviation	Student's t test
Age of Subjects	1	14	58.4286	8.37316	0.591
	2	12	60.6667	12.47786	
Body Mass Index	1	14	22.8264	4.21520	0.207
	2	12	24.9050	3.94753	
Total Cholesterol	1	14	2.3214	69.62632	0.923
	2	12	2.3000	32.48776	
Fasting Plasma Glucose	1	14	2.0207	85.86346	0.165
	2	12	1.6002	58.49391	
Homocysteine	1	14	30.8036	10.21832	<0.0001*
	2	12	12.7867	6.17450	

n= number of patients, 1=WML present, 2= WML absent
P value < 0.001highly significant difference

Table 3: *Univariate and multivariate Logistic Regression analysis with WML as a dependent variable in type 2 diabetic patients.*

		B	Sig.	Odds Ratio	95.0% CI for EXP(B)	
					Lower	Upper
Step 1[a]	Age	.048	.514	1.049	.908	1.212
	BMI	.417	.113	1.517	.906	2.540
	Total cholesterol	-.002	.934	.998	.948	1.050
	FPG	.006	.739	1.006	.971	1.042
	Hcy	-.363	.037**	.695	.495	.978
	Constant	-6.504	.533	.001		
Step 2[a]	Age	.049	.503	1.050	.910	1.211
	BMI	.417	.113	1.517	.906	2.540
	FPG	.005	.721	1.005	.978	1.033
	Hcy	-.357	.020**	.700	.519	.945
	Constant	-6.984	.425	.001		
Step 3[a]	Age	.044	.537	1.045	.908	1.203
	BMI	.405	.118	1.499	.903	2.490
	Hcy	-.343	.021**	.710	.531	.949
	Constant	-5.794	.462	.003		
Step 4[a]	BMI	.338	.106	1.402	.930	2.113
	Hcy	-.326	.014**	.722	.556	.936
	Constant	-1.721	.661	.179		

DISCUSSION

In this study, we have found that tHcy is elevated in with-WML group than in without-WML group. Hyperhomocysteinemia (HHcy) is an independent hazard for the incidence of WML in type 2 diabetic stroke patients as demonstrated by multivariate logistic analysis.

Vermeer et al[14] were the first research group to study the relation between white matter lesions and plasma homocysteine levels (Rotterdam Study). They conducted their study in a sizable elderly sample, and found total homocysteine levels to be associated with WML (and silent brain infarcts) independent of other cardiovascular risk factors. In one of the Japanese study, Shimumara et al 4, found that plasma tHcy increases with diabetes which is responsible for WML in the brain. They concluded that body mass index, insulin resistance, triglycerides and uric acid were marked up in diabetic patients which show WML on their CT scans. In a set of psychiatric patients, both high tHcy and low folate levels were found to be significantly allied with WML.[20] In a cross sectional study, Northern Manhattan Study, provided further verification that higher than normal tHcy was a risk aspect for WML.[10] The Cardiovascular Determinants of Dementia (CASCADE) Study, claimed the predominance of WML dimensions in the diabetic group than in the non-diabetic group.[11] Another Japanese study found a parallel association in Japanese women with rheumatoid arthritis.[21] Currently, Rost et al found high tHcy levels to be independently coupled with widespread WML in patients with stroke.[22]

In spite of all this data, in 2008, de Lau et al., in a genetic study, did not find an association of Hcy-related enzyme polymorphisms and WML in participants aged 60–90 years.[23] A prospective study by Dufouil et al, assessed the alliance between tHcy and recession of cognition in 1241 subjects aged 61–73 years; they were of the opinion that WML is not linked with Hcy in healthy elderly people.[24]

Some former studies have also shown dearth of association between plasma tHcy levels and WML.[25,26]

The alliance between HHcy and WML could be linked to the atherogenic affects of Hcy. The Hcy causes atherothrombosis through numerous mechanisms such as oxidative stress, smooth muscle production, impairment of endothelial dependent vasodilatation etc.[27, 16] Other detrimental affects produced by HHcy include decreased synthesis of apo-lipoprotein A-1 leading to a fall in HDL.[28] It also induces calcium as a second messenger in smooth muscle cells120, endothelial cell apoptosis[29,30] and release of endothelin is enhanced.[31,32] In one of the studies it has been pointed that high plasma level of tHcy interacts with hyper-cholestrolemia that hastens plaque formation, thereby impairing endothelial function and promoting thrombosis.[33] Barbato et al, reported a novel mechanism in which Hcy reacts with metallothionein forming a disulfide intracellular conjugate that accelerates vascular disease.[34]

In type 2 NIDD a rise in Hcy plasma level is ascribed to insulin resistance. The proposed mechanisms are multiple: Insulin resistance interferes with the activity of enzymes involved in Hcy metabolism thereby raising plasma Hcy level. Jacob et al, experimented on rats and found an increase in Hcy due to diminished action of CBS (cystathionine beta-synthase) enzyme in diabetic rats in the absence of insulin.[35] Similarly, Fonseca and associates found that hyper-insulinemia in rats with insulin resistance depress CBS activity with a compensatory elevation in the activity of MTHFR, (5,10 metyl tetrahydrofolate reductase) which consequently led to the development of HHcy.[36] Furthermore, glucose toxicity, irregularities in cerebral insulin homeostasis and micro-vascular anomalies have been held accountable for the presence of WML.[4]

Stienberg et al, reported that diabetes and obesity which are insulin resistant states were affiliated with decline in endothelium dependent vasodilatation[37] and arterial compliance may be partially secondary to the decreased release of nitrous oxide.[38] In vitro, insulin has been revealed to reduce vascular smooth muscle production and migration.[39] In view of these prepositions and evidences it may be concluded that connections among the existence of WML, high tHcy levels and insulin resistance support one another through mechanisms related to decline in endothelial dependent vasodilatation.

Hassan and his associates proclaimed that endothelial malfunction seemed to be the anticipated underlying mechanism for small vessel disease of brain.[40]

The age of diabetic stroke patient is insignificantly associated with the occurrence of WML in our present study. Our patients were in the age that ranged from 45 to 65 with the mean age of 58 years. The previous studies were on patients older than 65 years. Age, hypertension and HHcy > 13.65µm/L are the key risk factors in a very latest study.[41]

LIMITATIONS TO THE STUDY

When these patients were enrolled for the study, they were already suffering from essential hypertension. They were being treated with one or more antihypertensives like calcium antagonists, ACE inhibitors or angiotensin II receptor blockers. All these three drugs are known to decrease insulin resistance. So this medication may have inclined the results. We did not investigate the dietary status of these patients, that is, serum folate and vitamin B12 levels. These vitamins are involved in Hcy metabolism as co-factors or substrates and their deficiency leads to a rise in tHcy. Supplementation with folic acid decreased the tHcy plasma level in healthy young males.42 However, it is not assured if it would affect the incidence of WML in type 2 diabetic patients.

CONCLUSION

The findings of our study propose that, metabolite tHcy is an independent and significant

risk factor for the existence of WML in adult onset diabetic stroke patients. Multivariate logistic regression revealed that the presence of WML is significantly connected with tHcy in type 2 diabetic stroke patients. In step 1, the risk of white matter lesion was found to be associated with tHcy, OR .695, 95% CI= .495 -.978 P .0037. Similarly in the next three steps we have found a strong association between WML and tHcy with OR .722, 95% CI= .556 -.936 and a p value of .014 in the last step.

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IMPROVEMENT OF GLYCEMIC AND LIPID PROFILE STATUS WITH ALOE VERA IN ALLOXAN INDUCED DIABETIC RABBITS

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ABSTRACT

Objectives: The study was designed to investigate the effect of aloe vera leaf gel extract on Blood glucose levels and lipid profile parameters in alloxan induced diabetic rabbits.

Materials and methods: The rabbits were made diabetic by injecting alloxan monohydrate and divided in two groups of eight each. Group A was treated with distilled water and Group B was treated with ethanolic extract of aloe vera leaf gel for 28 days. The pre-treatment and post-treatment level of blood sugar and lipid profile parameters were recorded and compared. Statistical analysis was done with help of independent t-test. The effects in two experimental groups were analyzed with help of paired t-test.

Results: After 28 days of treatment the mean cholesterol level reduced to 80.9 from 97.1, the mean triglycerides reduced to 149.9 from182.6 and mean LDL reduced to 30.8 from 35.6 mg/dl in the aloe vera group. The mean HDL levels increased to 28.2 from 24.5 mg/dl. The mean BSR reduced from 288.3 to 215.1 mg/dl.

Conclusions: There was significant lowering of lipid profile parameters and BSR with aloe vera leaf gel extract in alloxan induced diabetic rabbits.

Keywords: aloe vera, diabetes mellitus, lipid profile, rabbits.

The world wide prevalence of diabetes is on a continuous rise. In 2010, 285 million people suffered from the disease whereas the number increased to 382 millions in 2013. The estimated number will be doubled in 2030[1]. Type-2 diabetes has long been known as a risk factor for coronary heart disease. A conservative estimation is that it may increase the risk of fatal event by two folds. The risk is associated with increased serum levels of total cholesterol, triglycerides and low density lipoproteins[2].

Multiple anti- hyperglycemic and anti-hyperlipidemic drugs with different mechanisms of action are often required for effective treatment hyper-lipidemia in type-2 diabetics[3]. Conventional pharmacological agents used for such condition do exhibit adverse effects on long term use. Therefore, search for a harmless and clinically useful indigenous preparation which should decrease the LDL-cholesterol is warranted[4].

Currently, there is a renewed interest in the plant based medicinal treatment and functional foods modulating physiological effects in the prevention and cure of type-2 diabetes and related complications. About 200 plants have been considered for their possible efficacy in the management of this condition[5].

Aloe vera, with botanical nomenclature as aloe Barbadensis Miller, belongs to liliaceae family. A number of studies have been carried out internationally to explore the pharmacological properties of aloe vera.The plant was shown to have wound healing, anti-inflamatory, anti-diabetes, antibacterial and anti-cancer properties[6]. Furthermore, aloe vera gel reduced total cholesterol, triglycerides and LDL levels in streptozotocin induced diabetic rats[7]. The present study was carried out to explore the effect of aloe vera leaf gel extract on lipid profile of alloxan induced diabetic rabbits.

MATERIALS AND METHOD:

The study was carried out in the department of pharmacology, SIMS/PGMI Lahore in 2010. Healthy male rabbits weighing 1000 to 1700 gm were purchased from the market. The animals were acclimatized to the animal house of PGMI Lahore for 7 days prior to induction of diabetes. Green fodder, grains, plentiful of water and cereals were fed to them. All the rabbits were then made diabetic by injecting alloxan monohydrate into their ear

veins[7]. The dose of alloxan was calculated according to Puri et al 8. Eight day after induction of diabetes, 16 rabbits, of BSR levels > 250 mg/dl were taken in the study and divided in two groups (n=8). Group-A, the control group, was treated with distilled water whereas, Group-B, the test group, was treated with ethanolic extract of aloe vera leaf gel. The ethanolic extract of aloe vera leaf gel was prepared in Herbal Heritage centre Department of Plant Pathology Punjab University Lahore. The mucilaginous pulp of aloe vera leaves was homogenized and filtered. The filtrate was freeze dried and the end product was obtained in the form of grayish white powder. The powder was collected in colored bottles and stored at room temperature. A baseline recording of lipid profile parameters including total cholesterol, triglycerides, LDL, HDL and BSR was done in both groups. After overnight fasting, 2 ml blood was collected from marginal ear veins of rabbits[9]. The serum was separated from the samples. BSR and various lipid profile parameters were estimated in biochemistry department of PGMI Lahore.

The diabetic rabbits were then treated with their respective protocols for twenty eight days. Group-A was treated with 10 ml of distilled water daily and Group-B was treated with aloe vera leaf gel extract in a dose of 300 mg/kg dissolved in 10 ml of distilled water. The drugs were administered through an 8 Fr nasogastric tube as a single daily dose[10]. A second recording of biochemical parameters was done after 28 days of treatment. Pre-treatment and post-treatment values were compared in both groups. Statistical analysis was done with help of student-t test and effects in both experimental groups were analyzed with help of paired-t test.

RESULTS:

Table-1 shows the pre-treatment and post-treatment levels of serum cholesterol, triglycerides, LDL HDL and BSR in control group of alloxan induced diabetic rabbits treated with distilled water. In control group, there were no stastically significant changes in these parameters after 28 days. Table-2 and figure-2 show the effect of aloe vera leaf gel extract on lipid profile parameters and BSR of alloxan induced diabetic rabbits after 28 days of treatment. The mean levels of total cholesterol reduced from 97.1 mg/dl to 91.0 mg/dl and the change was significant. Similarly, mean triglycerides and LDL levels reduced from 182.6 mg/dl and

35.6 mg/dl to 149.9 mg/dl and 30.8 mg/dl respectively. The mean BSR levels reduced from 288.3 to 215.1 mg/dl. All these changes were statistically significant. The mean HDL levels increased from 24.5 mg/dl to 28.2 mg/dl which is also stastically significant beneficial change.

Table 1: *Lipid profile parameters in diabetic rabbits treated with distilled water*

Parameter	Pre-Tm Mean ± SD	Post-Tm Mean ± SD	p-value
Cholesterol	93.1±7.5	91.04±7.6	0.411
Triglycerides	181.2±7.5	178.5±9.7	0.522
LDL	31.1±13.1	31.7±13.5	0.575
HDL	26.2±2.9	25.9±2.4	0.188
BSR	291.7±21.9	291.8±23.5	0.587

Table 2: *Lipid profile parameters in diabetic rabbits treated with aloe vera gel extract*

Parameter	Pre-Tm Mean ± SD	Post-Tm Mean ± SD	p-value
Cholesterol	97.1±7.2	80.9±6.0	0.003
Triglycerides	182.6±11.2	149.9±20.1	0.002
LDL	35.6±3.2	30.8±2.8	0.003
HDL	24.5±2.9	28.2±2.4	0.003
BSR	288.3±19.4	215.1±11.0	0.002
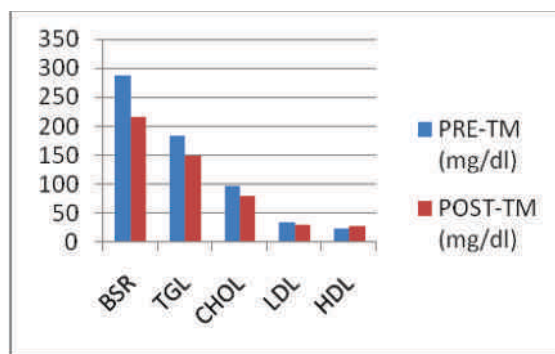
Figute-1 *Aloe vera shows a significant decrease in BSR, total cholesterol, triglycerides and LDL after 28 days. There is a beneficial increase in HDL levels.*

DISCUSSION:

Diabetes mellitus is perhaps the fastest growing metabolic disorder in the world. As the condition exhibit a multi-factorial and heterogeneous nature, the need for search of more challenging and appropriate therapies is increasing. Traditional plant remedies have been used throughout the world for

the range of diabetes complications[11]. Plant extract are considered to be less toxic than synthetic agents. In previous studies, aloe vera extracts have shown a hypoglycemic effect in experimental diabetic animals. Lipid profile was also shown to be altered in these experimental animals as a result of induced diabetes[12]. In the present study, aloe vera extract treatment significantly decreased total cholesterol, triglycerides and LDL levels whereas the HDL levels increased, exhibiting beneficial effects. All these results suggest that aloe vera could improve lipid metabolism disorders in type-2 diabetes mellitus.

Significant lowering of total cholesterol, triglycerides and LDL and an increase in HDL levels is very much desirable biochemical state for prevention of atherosclerosis and ischemic conditions. Various studies of medicinal plants have reported a similar lipid lowering activity. Few studies about the effects of aloe vera on lipid profile metabolism are cited in literature[13]. Furthermore, the bioactives and mechanisms involved in lipid lowering actions of aloe vera were not investigated. Few studies have been conducted on the isolation of bioactive compounds mediating the anti-hyperglycemic actions of aloe vera gel extracts. Trace elements and five phytosterols isolated from the gel were responsible for anti-hyperglycemic actions of aloe vera in STZ induced type-2 diabetic rat models[14].

The bioactives and mechanisms underlying the lipid lowering effects of aloe vera gel have not been studied so far. Considering the results of the present study, further and larger clinical trials concerning the efficacy and safety of aloe vera gel extract in the treatment of patients with type-2 diabetes and associated hyperlipidemia as well as studies addressing the bioactives and mechanisms involved in anti-hyperlipidemic actions seem necessary.

CONCLUSIONS:

Administration of aloe vera leaf gel extract in a dose of 300 mg/kg to alloxan induced diabetic rabbits significantly reduced BSR, Triglycerides, Cholesterol and LDL. There was an increase in HDL levels. There is scope for further studies in humans to establish the possible role of aloe vera in preventing complications of type 2 diabetes.

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RESULTS OF ANTERIOR STABILIZATION OF SACROILIAC DISRUPTION WITH TWO RECONSTRUCTION PLATES

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ABSTRACT

Pelvic fractures diagnosis and management depend upon on the patient characteristics, mechanism of injury and hemodynamic status at the time of presentation in emergency department. Definitive fixation and stabilization of pelvic ring disruption is a challenge to orthopedic surgeon. Anatomical reduction and stabilization is important to minimize pain and long term disability especially in Tile's C fractures.

Objectives of current study is to assess the efficacy of open reduction and internal fixation of Tiles type C pelvic fractures with reconstruction plate in terms of pain, work, sitting, sexual intercourse, standing ,gaits and walking distance.

This prospective study was conducted at orthopedic unit 2, Jinnah Hospital, Lahore in 2 years (2010-2012). All patients with Tile's Type C pelvic injuries were admitted through emergency. Twenty five patients were included in this study. These fractures were operated, reduced and fixed with reconstruction plates. The follow up for functional outcome of these cases was assessed by applying Majeed score

Data was analyzed by using SPSS software. All patients were followed up clinically and radio logically for period of one year. 20 patients had excellent results, 3 patients had good to fair results and remaining 2 patients had poor results as they were already having L4 nerve injury. Our study showed that open reduction and internal fixation with reconstruction plates is an effective mode of fixation in Tile`s type C pelvic fractures regarding the pain, mobility, stability, fracture union and walking abilities.

KEY WORDS: reconstruction plate, pelvic fractures, tiles type C.

Pelvic fractures resulting from high energy trauma are big challenge to orthopedic surgeon. Regarding age most of the patients having fracture pelvis, they are of young age. The common cause of death are motor vehicle accidents[6,18,19], fall from height and pedestrians. The history dates back to Charles Hewitt Moore's seminal publication from 1851.[1]

Pelvic fractures are 3% - 8% of all orthopedic injuries[4,5] while in multiple injured patients almost 20% patient had pelvic injuries. No single treatment modality[8,9,10] is available for fixation of these fractures. Early mortality is because of hemorrhage, hemodynamic instability, abdominal injuries including genitourinary organ damage and associated brain and spine injuries.[16] Mortality rate associated with pelvic fractures ranges from as low as 5-10 % and as high as 50-60% in orthopedic emergency. While open fractures in which there was

communication with the skin, rectum or vagina include 2-4 % of all pelvic fractures6. Late mortality is because of sepsis and multisystem organ failure.

Even following ATLS protocols, aggressive fracture management and advanced critical care, mortality rate for open fractures is as high as 25-50%.

Bony and ligamentous anatomy is straight forward. This anatomical region is unique because of its contents which are protected by pelvic bones and sacrum with fine ligamentous balancing and muscular support. Moreover it is the channel for load transmission from axial skeleton to the lower extremities for walking, standing and sitting. Basin like bony pelvis supported by muscles, ligaments and tendons as pelvic floor which is pierced by urethra, vagina and anus.[2,3,4]

As a result of pelvic trauma, huge amount of blood is extravasated into retroperitoneal space[6].

Pelvis is at the border of axial skeleton and lower extremity. It is the region where blood supply, innervations and multidisciplinary approaches have their own significance.

Definitive fixation of these fractures remains a challenge to orthopedics surgeon. However anatomical reduction and stabilization is important to minimize long term disability[16]. Long term implication of pelvic fractures was chronic pain, pelvic obliquity, gait problems, limb length discrepancy, urological and sexual dysfunctions, psycho-socio economic problems and long term unemployment.

MATERIALS AND METHODS:

This prospective study was conducted at department of orthopedic surgery Jinnah hospital Lahore. It included 25 patients with Tile`s type C fractures. All patients were admitted through emergency of this hospital. All 25 patients with type C fractures were fixed with Reconstruction plate. These fractures were protected with AO pelvic fixator in group A. All patients were in age group ranging from 16-65 years. On an average each patient was operated after 5 days (5-7 days) of injury. Patient under 16 years and above 65 years, patients with Rheumatoid Arthritis and other inflammatory disorders were excluded from the study. All patients were resuscitated according to ATLS protocols.

These fractures were classified after x ray pelvis AP views, inlet and outlet views. Further evaluation was done with 3-D CT scan. Visceral injuries were assessed by Ultrasonography.

I/V analgesia, I/V antibiotics & DVT prophylaxis were given and skeletal traction was applied for all vertically unstable fractures. All fractures were displaced more than 3cm (on an average) vertically in preoperative AP view radiographs.

Each patient was advised antibiotic coverage post operatively for 7 to 10 days.

FOLLOW UP

All patients were followed up clinically and radiologically up to one year.

A standard physical and radiological examination was conducted based on Performa documenting about the pain, work, standing, sitting, sexual intercourse, walking ability with or without assistive device use, hip motion, pelvic strength and deformity was assessed by using Majeed's Pelvic score.

In all patients the initial assessment was made after 2 weeks. The subsequent assessments were made periodically after every month for three months and after every three months for 1 year.

All patients started walking with assistive device (crutches) at 8th week and without assistive device at 3rd month and all patients started walking independently at 4th month.

In this study 20 patients had excellent results regarding pain, standing, sitting, work, ambulation, fracture union and return to their original job. Three patients had good to fair result while 2 patients had
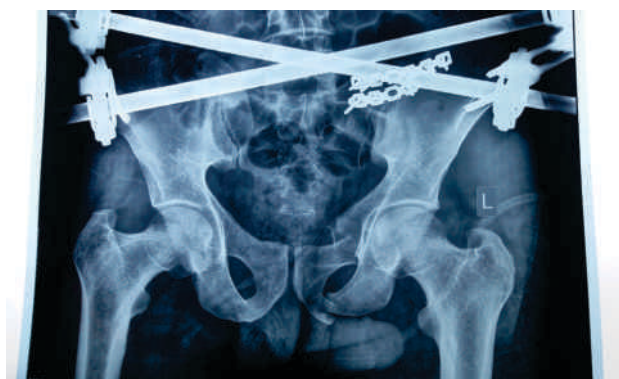
poor result as they had to change their job. In both these 2 patients there was already L4 nerve injury

Majeed Score

Pain   20 points
Work   30 points
Standing   36 points
Sitting   10 points
Sexual intercourse 4 points
Total   100 points

A= walking aids   12 points
B= gait unaided   12 points
C=walking distance   12 points

Clinical course was based upon score of 100 points for working.

>85 excellent, 70-84 good, 55-69 fair & <55 poor.

Data Analysis

Treatment outcomes were assessed by using Majeed's pelvic score i.e. pain, work, sitting, sexual intercourse, standing, walking aids, gaits and walking distance. Moreover performance at work before and after trauma was also assessed. Maximum score was 100.

All data was analyzed with the help of Proforma using SPSS software (version 11.5) & chi square

No. of patients	Results of study	Percentage (Score acc. To Majeed Pelvic Score)
20	Excellent	90%
2	Good	80%
1	Fair	66%
2	Poor	52%

test.

No. of patients	Mechanism of Injury	Percentage
18	Motor bike vs. Car	72%
5	Fall from height	20%
2	Car vs. electric pole	8%

Results of Study

Mechanism of Injury

DISCUSSION

Pelvic ring play an important role in the axial skeleton. It contains intra-pelvic organs and transmits the body weight to the lower extremities. It is therefore essential for the pelvis to be stabilized. The work of those such as Pennal et al[2], Tiles, Denis et al[3] and Young & Burgess[4] has formed our current understanding of patho-anatomy of pelvic fractures in adults. Such fractures are commonly encountered in young persons with incidence reported to range between 3-8% of all orthopedic injuries[5]. Sacroiliac fracture dislocations and fractures of iliac bone occur most commonly as a result of motor vehicle accidents[6].

In our study, in 72% of patients mechanism of injury was motor car vs. bike accidents. In a similar study by Dalal et al (58%) 19 motor car accidents were the major reason for pelvic injuries. Study of Cryer et al (57%) 20 has also mentioned road traffic accidents as a major reason for pelvic injuries.

In this study, we operated 25 patients for vertical (Type C) fractures of pelvis with reconstruction plate. In all these patients we applied 2 reconstruction plates for vertical fractures (Type C) of pelvis, which were further protected with pelvic external fixator. An external fixator alone is insufficient for this sort of injury. Lindah et al found that external fixator as a definitive device, has got limited value in fixation of Tile's type C fractures.[18] Numerous techniques with variable success rates have been devised to overcome this problem.[15,16,17] These include anterior plate stabilization, posterior iliosacral screw fixation, percutaneous reconstruction plate application and percutaneous iliosacral screw fixations.[7,8,9]

Among 25 patients, 20 patients had excellent results regarding the pain, mobility, deformity, fracture union and neurological complications. 3 patients had good to fair results while 2 patients had poor results. These 2 patients had L4 nerve injury preoperatively that did not return post operatively with conservative measures.

In one year, there was no displacement of hemi pelvis and all fractures healed un eventfully.

Lot of studies show the results comparable to our study. In a similar study conducted by Kabaks et al[7] in which open reduction and internal fixation was carried out in 40 cases of unstable pelvic ring fractures (Type C). This study reveals that internal fixation in vertical unstable fractures (Type C) resulted in satisfactory clinical and radiological outcomes.

Study of Ward EF, Tomasin J, Vander Griend RA et al1O also revealed that open reduction and internal fixation with sacroiliac screw fixation is a safe and effective procedure for vertical shear fractures.

A study conducted by Mohammed M. Elmanawy et al also shows the good results with anterior fixation of sacroiliac joint disruption[11] while similar results have been shown by Simpson LA al.[13]

In our study there were two female patients who were in child bearing age, also had vertical (Type C) pelvic fractures. In both these patients close reduction and internal fixation was done. Both these patients did not have any complications and they delivered normally. Although studies show that pelvic and acetabular fractures in pregnancy are associated with high fetal and maternal morbidity and mortality rate.[12]

In a study conducted by Leggon RE, Wood GC, Indeck MC et al[12] on pelvic fractures in pregnancy show that pelvic and acetabular fractures have high fetal and maternal mortality rate.

Regarding the timing for fixation of these fractures we fixed the pelvic fractures on fifth post injury day on an average when the patient physiological and psychological status is conducive to the surgery. In his study Katsoulis E, Giannoudis PV et al[14] reviewed the 37 pelvic and acetabular injuries. They performed the definitive fixation for pelvic fractures on the 4th post injury day when the hemodynamic, physiological and psychological status of the patient is conducive for the surgery. However in poly trauma patients the damage control orthopedic principle should be applied for hemodyna-mic and skeletal stabilization.

In this study patient was kept in bed for 6 weeks. He was allowed to assume upright position at 4th – 6th week and at 8th week all patients were allowed to walk with crutches. These patients were allowed to walk independently without assistive devices. In their study Tile and Heara suggested at least 3 - 6 weeks complete bed rest is mandatory for the pelvic injury patients.[21]

CONCLUSION

It is concluded from our study that surgical anterior stabilization for Tile's type C injuries with two reconstruction plates provide excellent outcomes. It has got minor complications. Stabilization of sacroiliac disruption reduces the risk of post operative arthritis if these injuries are stabilized timely.

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AN OPEN NON-COMPARATIVE STUDY OF EFFICACY & SAFETY OF DOXAZOSIN IN THE TREATMENT OF MILD TO MODERATE ESSENTIAL HYPERTENSION

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ABSTRACT

We carried out a study on efficacy and safety of doxazosin in mild to moderate hypertension. In all 40 patients were enrolled and out of these 38 (95 %) completed the study. There was an average drop of 21 mmHg in DBP and 21 mmHg in SBP. Almost all of the patients required 2-8mg of doxazosin for control of their BP. The drug was well tolerated, only 5% having adverse effects. We conclude that the drug is an effective alternate for the control of mild to moderate hypertension.

KEY WORDS: Hypertension - Doxazosin Cardiovascular - Safety

Systemic Hypertension is one of the commonest diseases and one of the three risk factors responsible for the development of coronary artery disease (CAD).[1] The other two risk factors are smoking[2] and elevated serum cholesterol.[3] The risk of cardiovascular morbidity and mortality is directly related to the severity and duration of hypertension.

Most deaths resulting from hypertension, an estimated 800,000 per year in U.S.A., are due to CAD. As such, the primary aim of hypertension management should be to prevent CAD. However data from the major hypertension intervention trials of the past 20 years have failed to show a satisfactory reduction in the incidence of CAD. The reduction in the CAD events observed in the trials was only 60% of that expected from prospective data, suggesting that the management of hypertensive patients in these trials was less than optimal.[1] However control of High blood pressure in patients with mild to moderate essential hypertension has reduced the incidence of Left Ventricular Hypertrophy (LVH) and Left Ventricular Failure (LVF).[4] It is possible that anti-hypertensive drugs although beneficially modifying one of the established coronary risk factors namely high blood pressure may completely neutralizes this benefit by adversely affecting other risk factors.[4] In this respect neither of the two most commonly prescribed classes of antihypertensive agents, thiazide diuretics and B blockers, is superior to the others. In the last few decades the pharmacological spectrum of anti-hypertension agents has broadened tremendously. Most commonly used groups namely, Beta Blockers (BB), Calcium Channel Blockers (CCB), Angiotensin Converting Enzyme Inhibitors (ACEI), Angiotensin II blockers (ATIIB), act mostly through a peripheral mechanism of action. "Primary Hypertension" is multifactorial disease in which catecholamine may play an important role by increasing the cardiac output and peripheral vascular resistance. Therefore the drugs that block catecholamine release by a central mechanism can play an important therapeutic role.

Daxazosin is a novel quinazoline derivative that is clinically related to prazosin and terazosin. These drugs block post synaptic - α_1 receptors and reduces blood pressure by lowering peripheral resistance while causing little reflex tachycardia.[3] They have the additional advantage of producing favorable changes in lipid profile.[5] Clinical and pharmacological studies have established that Doxazosin is potent α_1 antagonist with a more gradual onset of action and longer elimination half life than prazosin.[6] Stroke volume and cardiac output are maintained at rest as well as during exercise. Doxazosin has been found to be effective in maintaining blood pressure control when given once daily.[7] Well controlled clini-cal studies indicated that Doxazosin appears to have added advantages as a first line therapy with its beneficial effect on lipid profile.[8,11,12] The efficacy of Doxazosin is well established in the treatment of all grades of hypertension, as either monotherapy or in addition to other antihypertension agents, such as a thiazide

diuretics, a BB, CCB, or ACEI. Doxazosin is now recommended as first line therapy in the guidelines issued by a number of organizations including the WHO, International Society of Hypertension, Joint National Committee on detection, evaluation and treatment of high blood pressure and the British Hypertension Society.[8] Doxazosin is also indicated for the treatment of the urinary out flow obstruction and symptoms with benign prostatic hyperplasia. Doxazosin may be used in Benign Prostatic Hypertrophy (BPH) patients who are either hypertensive or normotensive. The blood pressure changes in normotensive patients with BPH are clinically insignificant. However, in patients with hypertension and BPH the drug has a dual advantage and can be used as a monotherapy.[13,14]

Most of the clinical data has been so far obtained on Western population. Its efficacy in our environmental conditions has not been studied. Thus a clinical trial was planned to assess the safety and efficacy of doxazosin in mild to moderate essential hypertension in clinical practice in Pakistan.

PATIENTS AND METHODS

A total of 45 patients with mild to moderate hypertension from both sexes were screened. Out of which 40 patients with following inclusion criteria were enrolled in the study after taking an informed consent.

i) Adults over 21 years of age with mild to moderate hypertension as defined by JNCH IV.
ii) New, previously untreated, or treated hypertensives, who have discontinued their antihypertensive therapy.

EXCLUSION CRITERIA

Patients with following were excluded from the study.

1. Malignant or secondary hypertension, including estrogen dependent hypertension.
2. Current pregnancy or lactation in female.
3. A documented or clinically suspected serious drug reaction or idiosyncrasy to alpha-adrenergic blocking drugs.
4. Orthostatic hypotension
5. Patients with medical conditions that might interfere with the completion of the study.
6. Unstable angina pectoris.
7. Congestive heart failure.

8. Clinically significant hepatic, gastro-intestinal or haematologic disease.
9. Renal insufficiency (serum creatinine exceeding 200 mmol/1).
10. A previous prostatectomy.
11. Treatment with tricyclic anti-depressants or other drugs affecting blood pressure or vasoactive medication.
12. Intention to donate blood during and for one month after the study.

After an optional washout or run in period of two weeks the patients were put on an initial dose of 1mg of Doxazosin. Blood pressure recordings in sitting position were made at every two weeks intervals, following the standard recommendations, for a total period of 10 weeks.

Patients were evaluated between 2 and 12 hours post dosing. At each review visit blood pressure and Heart Rate (HR) were determined by the same arm and at each visit blood pressure was determined after patients had been sitting quietly for five minutes. Each blood pressure determination was the average of two consecutive measurements and no more than ±2mmHg approximate at any determination. HR was determined immediately before the blood pressure measurements were taken in the sitting position. Laboratory test, lipid measurements including triglyceride; total cholesterol was done at base line and at the end of the study. After 2 weeks phase I base line period, the patient entered the titration/maintenance phase of 10 weeks. The initial daily dose of Doxazosin was lmg. Dosage was increased at intervals of 2 weeks (Table 1) until one of the following objectives were achieved.

i) The DBP was <90 mmHg.
ii) A maximum daily dose of 16mg Doxazosin was administered.
iii) Significant adverse effects precluding further increase in dosage was noted.

At the end of the study following data was analyzed:

i) Dose dependent changes in systolic blood pressure (SBP) and Diastolic Blood Pressure (DBP).
ii) Dose dependent changes in HR.
iii) Dose depended tolerance and side effects.

RESULTS

In all 45 patients were screened. Outs of these 40 were enrolled and 38 or 95% completed the study. There were 26 (65%) males and 14 (35%) females. Their age ranged from, among the males 21-60 years (mean 44. l) and for females 31-60 years (mean 47.3) (Table 2). History of previous treatment was present in 13 (32.5%) patients where as 27 (67.5%) were newly diagnosed hypertensives (Table 4). Enrolled group had mean blood pressure of 153 mmHg systolic and 104 mmHg of diastolic. The mean reduction in blood pressure from base line to end of the study is given in figure 1. Among the completed group one patient remained on 1mg whereas the dose was increased to 2, 4, 8mg in 15, 14 and 8 patients respectively (Table 6) there was an average drop of 21 mmHg in DBP and 21 mmHg drop in SBP. Mean reduction in blood pressure from base line to the end of the study is shown in figure I. This drop in blood pressure observed during the course of trial was statistically significant (P<0.05) and was not associated with any significant change in Heart Rate (Figure 2).

In only two patients the drug has to be discontinued due to adverse events and were withdrawn from the study at 4 and 8 weeks. No abnormalities in different biochemical parameters were observed in any of the patient. There was no significant change in the mean weight of the patients (Table 3).

There was slight insignificant (P>0.05) decrease in total cholesterol and LDL. It fell from 220 mg/dl and 150 mg/dl to 212 mg/dl and 142 mg/dl respectively, while HDL and triglycerides remained unaltered. (Table 5)

Fig. 1: Mean reduction of the BP (systolic & diastolic) from baseline to the end of the study.

Fig. 2: Changes in Heart Rate from baseline to the end of the study.

DISCUSSION

Selective blockage of α_1 adrenergic receptor, has been of value in treating patients with mild to moderate hypertension. Doxazosin is new selective antagonist of α_1 adrenergic receptor. The affinity of

daxazosin for α_1 receptor is 400 times greater than its affinity for α_1, receptor. It lowers the blood pressure by reducing the peripheral resistance without causing reflex tachycardia. Stroke volume and cardiac out put are maintained at rest as well as during exercise.[8,15]

The efficacy of doxazosin is well established in the treatment of mild to moderate hypertension as either monotherapy or in addition to other anti-hypertension agents. The drug is well tolerated in the dose of l-8mg. The maximum drop in blood pressure is usually within first 4 weeks, and persists at subsequent follow up to six months or beyond. The drug has no adverse effects on various biochemical

Table 1: MAINTENANCE DOSE DISTRIBUTION

Weeks	1-2	3-4	5-6	7-8	9-10
Doxazosin	1mg	2mg	4mg	8mg	16mg

Table 2: Age and Distribution of the patients evaluated in the study N = 40

Age in Years	Male	Female
21-30 Years	1	_
31 -40 Years	7	1
41-50 Years	12	8
51 -60 Years	4	5
More than 60 Years	2	-
TOTAL	26	14

Mean age in males:44.1Years
Mean age in females: 47.3 Years
Mean age in both:45.3Years

Table 3: Mean weight of the patients evaluated in the study N = 40

	At Baseline	At the end of the study
Male	72.6 kgs	71.7 kgs
Female	64.2 kgs	63.8 kgs

Table 4: Most recent antihypertensive therapy N=40

Therapy	No. of Patients
Captopril	2
Methyldopa	1
Tanatril	1
Atenolol	5
Monoxidine	1
Blokium	1
Amlodipine	2
No drug in	27

Table 5: *Effect of Doxazosin on the lipid profile from baseline to the end of the study N=38*

Visits	Baseline	End week 10	P Value
Total Cholesterol	220.0 mg/dl	212.0 mg/dl	V .05
HDL	37.0 mg/dl	37.0 mg/dl	V ,05
LDL	150.0 mg/dl	142.0 mg/dl	V .05
Triglycerides	167.0 mg/dl	167.0 mg/dl	V .05

Table 6: *Drug Dosage Administration N=40*

Visits	IMG	2MG	4MG	8MG	16MG
Week-2	40	-	-	-	-
Week-4*	1	38	-	-	-
Week-6	1	18	20	-	-
Week-8**	1	15	15	7	-
Week-10	1	15	14	8	-

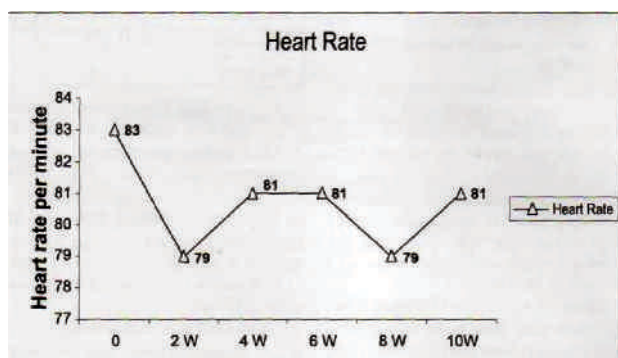*   1patientdiscontinued treatment permanently due to advese events and was withdraw from the study at Week=4.

** 1 patient discontinued treatment permanently due to advese events and was withdraw from the study at Week=8.

parameters seen .with ACEI, BB and diuretics.[15]

In small scale trial published by Castrignano
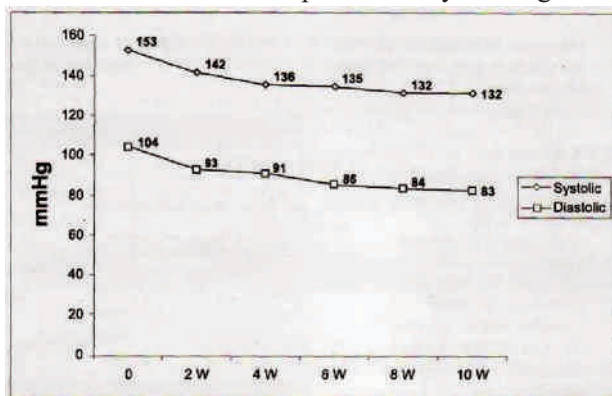
and co-workers (1998),[9] a reduction in sitting BP of

26/17 mmHg was observed by final visit. Statistically significant (P<0.05) reductions from

mean baseline blood pressures (systolic and diastolic) were observed throughout the study period. All patients showed improvement in the severity of their hypertension at the final visit and all hypertensive patients had their blood pressure normalized. In this study[9] 21 patients accumulated 69 patients months exposure to doxazosin; five patients experienced a single side effect, none of which was severe. No patients required dose reduction or discontinuation of therapy because of those side effects. In this study[9] total of 1995 individual laboratory parameters were analyzed among all patients and no patient was excluded from laboratory analysis. In most cases laboratory safety data remained unchanged after treatment.

In our study 95% of the patients responded well to a daily dose of 2-8mg of doxazosin. The mean reduction in blood pressure was from baseline 153/104 mmHg to 132/83 at end of the study with mean reduction of 21/21 mmHg and all the patients had their BP normalized. The maximum drop in blood pressure was observed with dose of 2-4 mg at 2-4 weeks. This drop in blood pressure is comparable with the above study. In our study no significant postural drop of blood pressure was noted. Only two out of 40 (5%) experienced adverse events. One presented with tachycardia and other experienced right sided hemiplegia with gradual improvement in the next three months. In both patients the medication was permanently discontinued and they were withdrawn from the study. In our study no abnormalities in different biochemial parameters were observed in any of the patients.

In another trial published by Cubeddu and associates (1998),[8] the incidence of side effects was small and comparable to the placebo group. Postural dizziness was the most common side effect of doxazosin. Postural hypotension is an expected side effect in patient treated with α_1 ; antagonist because of concomitant effect of drugs on pre-load and after-load. The vasodilatory action of the drug is the most likely cause of the orthostatic hypotension. Clinical

studies have demonstrated that doxazosin has beneficial effect on serum lipid profile of hypertensive patients. Doxazosin lowers the level of total cholesterol, LDL cholesterol and triglycerides and increases the level of the HDL and the ratio of HDL cholesterol to total cholesterol.[8,10] However in our study there was a statistically insignificant (P>0.05) fall in LDL and in total cholesterol. There was no effect on HDL cholesterol and triglycerides.

CONCLUSION

Doxazosin is a new centrally acting post synaptic α_1 blocker. We found it to be very effective anti-hypertensive and well tolerated drug. It can be used as monotherapy or in combination with other anti-hypertensive drugs. Since it has no effect on various biochemical parameters, it can be safely used in patients suffering from metabolic disorders, like diabetes mellitus, hyperuricemia and chronic renal failure or hepatic insufficiency and dyslipidemia. It also has a special place among those hypertensive patients who suffer concurrently from BPH.

ACKNOWLEDGMENTS

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LATERAL INTERNAL SPHINCTEROTOMY VERSUS ANAL DILATATION (LORD'S OPERATION)FOR CHRONIC ANAL FISSURE: A PROSPECTIVE RANDOMIZED STUDy at DHQ HOSPITAL MUZAFFARGARH

Muhammad Khalid Ijaz, Ghulam Akbar Khan, Hannan Zafar

ABSTRACT

BACKGROUND: There are several surgical methods for the treatment of chronic anal fissure. The most popular are anal dilatation (AD) aka Lord's operation, and lateral internalsphincterotomy (LIS). The objective of the current study was to prospectively evaluate the results of these two procedures in terms of recurrence rate, complications and patient satisfaction.

METHODS: The study enrolled all patients who required operation for chronic anal fissure in District Head Quarter Hospital Muzaffargarh between the March 2013&March 2016. Exclusion criteria were acute anal fissure or inflammatory bowel disease.

RESULTS: A total of 128 patients participated in the study, ranging from 31 years and 56 years with an average age of 43.5 years (SD=12.5). The patients were randomly assigned to two groups; one for AD (61 patients, 47.66%) and one for LIS (67 patients, 52.34%). There was a protocol of questionnaire and a physical examination performed at 1, 2, 3, 6 and 12 months after operation. The questionnaire contained questions about features of pain, bloody stool, feces consistency, incontinence for gas, and soiling. The patients were also asked about their contentment on an equivalent scale from 1 to 10. The average follow-up was 10.8 months (SD=3.8). Minor incontinence occurred in 7 patients of AD group and in 3 patients of LIS group (p<0.005). Recurrence occurred in 6 cases of the AD group and in 2 cases of the LIS group (p<0.003). Satisfaction score was insignificantly higher in the LIS group (9.0+/-0.8 in the LIS group and 7.2+/-1.8 in the AD group).

CONCLUSIONS: These results suggest thatlateral internal sphincterotomyis the preferred method for the treatment for chronic anal fissure.

KEY WORDS: anal dilatation (AD), lateral internal sphincterotomy (LIS), anal fissure, fecal incontinence, pain

A tear in anoderm distal to the dentate line is defined as anal fissure. One of the most common benign anorectal conditions is anal fissure which may result from high anal pressure. Anal fissures may be acute or chronic. Acute fissures may result from local trauma or may be secondary to an underlying condition either medical or surgical. Anal fissures patients present with severe pain, fresh blood during defecation, and constipation[1].

Anal fissure has idiopathic etiology. It usually arises with local trauma which is generally caused by burdensome defecation due to hard stools and hypertonia of internal anal sphincter, perseverance of this condition which in turn reduces the blood flow to posterior wall resulting higher posterior anal canal pressure, even at rest[2].

An acute anal fissure generally has the six weeks of life and heals with conservative local treatment, while a chronic anal fissure fails conservative management and requires a more dynamic, hostile, surgical approach. Anal fissure may be primary or secondary depending upon the etiology. Primary anal fissures are due to local trauma mostly while secondary have an underlying cause like inflammatory bowel disease, malignancy etc. [3]

MATERIAL AND METHOD:

This study was conducted in DHQ Hospital

Muzaffargarh in a period of three years from March 2013 to March 2016. Patients were selected from surgical OPD after designing an inclusion and exclusion criteria. All the patients were evaluated by consultant, and were adequately investigated. Patients who had acute anal fissure (less than six weeks), immunocompromised, suffering from chronic underlying disease e.g. tuberculosis and inflammatory bowel disease were excluded from the study. Patients who had recurrent anal fissure, who have tried medical therapy (topical nitroglycerin or calcium channel blockers (e.g. diltiazem), or injection of botulinum toxin into the anal sphincter) for at least one to three months and have not healed were included in the study after taking informed consent.

Patients were advised baseline investigations. All the operations were carried out in spinal anesthesia (saddle bloc). With the patient anesthetized, the intersphincteric groove was palpated at the anal verge. In the open method 1- to 2-cm circumferential incision was made at the anal verge over the free edge of internal anal sphincter. Blunt scissor dissection opened the plane inside and outside the internal sphincter to free it. The free lower end of internal sphincter was then grasped, drawn into the wound and its distal portion divided. In the closed methoda pointed no. 11 blade was introduced between the internal sphincter and the anoderm parallel to the anal skin. It was then rotated to face outward and gently pressed against the distal portion of internal sphincter, which was held taut with the bivalve retractor. The scalpel was withdrawn and on digital palpation the tight band of distal internal sphincter was released. The residual band 'gave way' on gentle digital pressure on the anoderm over the area of release. This is safer than reintroducing the scalpel. The wounds were left open.

DISCUSSION:

An anal fissure is a tear in the anoderm distal to the dentate line[1]. Anal fissure is one of the most common benign anorectal conditions that may result from high anal pressure[2]. Anal fissures may be acute or chronic. Acute fissures may result from local trauma or may be secondary to an underlying medical/surgical condition[2]. By definition, an acute anal fissure typically heals within six weeks with conservative local management, while a chronic anal fissure fails conservative management and requires a more aggressive, surgical approach[2].

The etiology of the fissure determines if it is primary (e.g. local trauma) or secondary (e.g. inflammatory bowel disease, malignancy)[1].

Anal fissure is due to the stretching of the anal mucosa above its normal capacity. After the tear has occurred, it begins a cycle leading to repeated injury[3]. Internal sphincter muscle beneath the tear goes into spasm which is exposed due to injury. Beside severe pain, the spasm pulls the edges of the fissure apart, which impedes wound healing. The spasm also leads to further tearing of the mucosa with the passage of further bowel movements. This cycle leads to the development of a chronic anal fissure in approximately 40 percent of patients[3].

It has been proposed that ischemia may contribute to the development of an anal fissure. Most common site of anal fissure is posterior midline and blood flow to anoderm at this position is less than one-half than in other quadrants in the anal canal[4]. Moreover, the perfusion rate is inversely related to anal pressure. In one study, for example, patients with chronic anal fissure had higher anal pressures than those with other colorectal disorders likefecal incontinence, hemorrhoids etc. The demonstration of reduced blood flow provided the rationale for the use of topical nitroglycerin in the treatment of this disorder[10].

The elevated anal pressure in patients with chronic anal fissure is due to increased tone of the internal anal sphincter, which can be measured by manometry. Manometry was performed in 10 patients with chronic anal fissure and in 10 controls in one study. The mean average resting pressure of the internal sphincter was significantly higher in patients with a chronic anal fissure (120 versus 83 mmHg)[11].

Most anal fissures are caused by stretching of the anal mucosa beyond its capability[6]. Anal fissures which are superficial and shallow look much like a paper cut, and hard to detect upon visual inspection most of the time, they will generally heal by themselves within a couple of weeks[5]. However, some anal fissures become chronic and are deep enough to self-heal. The most common cause of non-healing of deep anal fissures is spasm of the internal anal sphincter muscle which causes reduced blood supply to the anal mucosa which results in a non-healing ulcer, infected by fecal bacteria most of the time[3]. In adults, fissures may be caused by constipation, the passing of large, hard stools, or by prolonged diarrhea[6]. One of the causes of anal fissure in older adults is decreased blood flow to the area. Anal fissures which are present on lateral sides are because of tuberculosis, occult abscesses, leukemic infiltrates, carcinoma, and acquired immunodeficiency syndrome (AIDS) or inflamma-tory bowel disease mostly[2]. Some sexually transmitted infections can break the protective mucosal layer resulting in a fissure. Examples of sexually transmitted infections that may affect the anorectal area are syphilis, herpes, chlamydia and human papilloma virus [3].

Other common causes of anal fissures include:

Childbirth trauma in women [2]

Sexual Activities[2]

Crohn's disease [2]

Ulcerative colitis [2]

Poor toileting in young children[3]

For adults, the following may help prevent anal fissures:

Avoid straining during defecation. This includes treating and preventing constipation by eating food rich in dietary fiber, drinking enough water, occasional use of a stool softener, and avoiding constipating agents[14]. Similarly, prompt treatment of diarrhea may reduce anal strain[7].

Careful anal hygiene after defecation, including using soft toilet paper and cleaning with water, plus the use of sanitary wipes[7].

If there is a suspected or pre-existing anal fissure, use a lubricating ointment. An important point to remember here is that hemorrhoid ointment is contraindicated because it constricts small blood vessels, which causes a decrease in blood flow, resulting in slow process of healing[7].

In infants, frequent diaper change can prevent anal fissure. One reported cause is constipation, so make sure that infant is drinking plenty of fluids (breastmilk, proper ratios when mixing formulas etc.). In infants, after the anal fissure has occurred, finding and managing the underlying causes is usually enough to ensure healing occurs[6].

Lateral internal sphincterotomy (LIS) is an operation performed on the internal anal sphincter muscle for the treatment of chronic anal fissure. The internal anal sphincter is one of two muscles that comprise the anal sphincter which controls the passage of feces. The procedure helps by lowering the resting pressure of the internal anal sphincter, which improves blood supply to the fissure and allows faster healing [8].

LIS is a minor operation which can be carried out under either local or general anesthesia; a report in 1981 showed that general anesthesia is preferable due to high rates of fissure recurrence in patients treated under local anesthesia .This operation is generally carried out as a day case procedure. It can be performed with either "open" or "closed" techniques [8].

In open technique we make an incision across the intersphincteric groove which separates the internal sphincter from the anal mucosa by blunt dissection, and then divide the internal sphincter using scissors [8].

The closed or subcutaneous technique involves making a small incision at the intersphincteric groove, inserting a scalpel with the blade parallel to the internal sphincter and advancing it along the intersphincteric groove, and then rotating the scalpel towards the internal sphincter and dividing it [8].

In both techniques the lower one third to one half of the internal sphincter is divided, to lessen the pressure of internal sphincter at rest without destroying its effect. In closed technique there is a smaller wound, but both techniques are equally effective [8].

Anal dilation, or stretching of the anal canal (Lord's operation), has fallen out of favor in recent years, mostly due to very high incidence of fecal incontinence[12]. In addition, anal stretching can increase the rate of flatus incontinence [12].

In the early 1990s, however, a repeatable method of anal dilation proved to be very effective and showed a very low incidence of side effects[13]. Since then, at least one other controlled, randomized study has shown there to be little difference in healing rates and complications between controlled anal dilation and LIS[13]. While another has again shown high success rates with anal dilation coupled with low incidence of side effects [15].

A total of 128 patients participated in current study, ranging from 31 years and 56 years both male

and female with an average age of 43.5 years (SD=12.5). Patients were randomly assigned surgical procedures, lateral internal sphincterotomy and anal dilatation, followed after the procedure at 1,2, 3, 6 and 12 months with an average follow up of 10.8 months (SD=3.8). Complaints of patients regarding pain, anal incontinence and soiling were scaled in accordance with the questionnaire. All questions were scaled from 1 to 10 with 10 being the highest. Recurrence rate in our study was significantly lower in patients undergoing Lateral internal sphincterotomy as compared to anal dilatation. Patient satisfaction was also high among the LIS group when compared to AD in accordance with the questionnaire.

CONCLUSION:

We concluded from our study that lateral internal sphincterotomy (LIS) is preferred method to treat chronic anal fissures than anal dilatation aka Lord's operation in terms of recurrence rate, anal incontinence, pain and soiling. Anal incontinence can include inability to control gas, mild fecal soiling, or loss of solid stool.

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EFFICACY OF FAT GRAFT TECHNIQUE MYRINGOPLASTY IN SMALL CENTRAL PERFORATIONS.

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ABSTRACT

OBJECTIVE: To highlight the efficacy of fat graft myringoplasty regarding closure of perforation.

PLACE & DURATION OF STUDY: This study was conducted at the department of ENT, Maida Hospital, Abbottabad from June 2007 to August 2014.

STUDY TYPE: Descriptive study.

SUBJECTS & METHODS: 30 (Thirty) cases of tubo — tympanic type of CSOM with dry central perforations for the last two months were included in the study. Patients of either sex with age between 10-50 years were included.

RESULTS: A Total number of 30 cases were included in this study among which 20 were males and 10 were female patients. (Ratio 2:1). The mean age was 18 years. The fat graft taken from the ipsilateral lobule was used in all cases. The result showed that the graft uptake was successful in 24 patients (80%) out of 30 patients and failure was encountered in 6 patients (20%).

CONCLUSION: Myringoplasty aims to have a new reconstructed healed tympanic membrane with restoration of hearing as much as possible. In our study there was no significant difference in result by using fat graft method of Myringoplasty.

Key words: CSOM, myringoplasty, fat graft, lobule.

The tympanic membrane perforation has got a historic significance. It is as old as human species.[1] The main cause of tympanic membrane perforation is either acute or chronic suppurative otitis media (ASOM or CSOM), trauma either accidental or iatrogenic. About 70 % of small perforations heal normally while nearly 30% require an intervention.[2] perforation can be temporary or persistent. 3 % of the grommets insertion may result in iatrogenic perforations.[3] Infection is the principal cause of tympanic membrane perforation (TM?). Traumatic perforation occur from blow to the ear, sever atmospheric pressure, excessive water pressure or during wax removing. An increased incidence is noted during child hood and in young adults due to higher incidence of CSOM in this group of population.[4] Perforation without infection or cholesteatomaarepainless. In dry central perforations, myringoplasty operation is usually performed. The classical techniques have been described as underlay and onlay procedures. Underlay techniques requires the placement of graft medial to the tympanic membrane remnant and malleus.[5] Onlay Myringoplasty is more challenging and is used for total or anterior perforations. The rate of success in either technique is very much debatable, as there are studies of both procedures with variable results. Ours study is a descriptive study to assess the rate of success of myringoplasty by fat graft method which is a relatively simple method.

SUBJECTS & METHOD:

This study was conducted at the department of ENT. Maida Hospital Abbottabad from June 2007 to August 2014. 30 cases were included in this study. Fat graft taken from the ipsilateral ear lobule was uniformly applied to all the cases. Detailed history and thorough clinical examination was conducted in all cases Hearing loss of more than 40 dB were excluded from the study. Both the genders were included in study with male to female ratio of 2:1 Patient with active ear disease, mastoiditis, age below 10 years and above 50 years, Eustachian tube insufficiency, metabolic disorders, hypertension or diabetes were excluded from the study. Only two patients being children, required general anaesthesia. All others were done under local anaesthesia.

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Operating microscope was used in all cases.

RESULTS:

A total number of 30 patients were included in this study out of which 20 were males and 10 were females with male to female ratio of 2:1. The age group distribution showing majority of patients were between the ages of 15-20 years. The mean age was found to be 18 years. In our study 10 patients i.e. about 33% had small perforations occupying up to th of ear drum while rest of the patient had very small sized perforations occupying about '/2 the size of above mentioned small perforations. Large perforations and perforations more than 1/2 the size of tympanic membrane were not included in the study. Majority of patients in our study i.e.; 20 (67%) of the patients had antero- inferior perforations.8 patients i.e; about 24% had antero-superior perforations. Only 2 patients had postereo-inferior perforations i.e. only (7%). In our study partial graft was taken in 6 patient's i.e. about 19% complete closure of TM perforations was seen in about 24 patients i.e. nearly 80%.

DISCUSSION :

Myringoplasty is the closure of the perforation in pars tensa of tympanic membrane. When it is combined with ossicular reconstruction, it is called tympanoplasty. Quite often the hole in the tympanic membrane heals itself. Many patients live their lives without even knowing that they have tympanic membrane perforation usually because they are entirely asymptomatic. Patients approach ENT consultants because of some associated problems, usually a discharge or pain. There may be recurrent infections with the discharge from the ear. The benefits of closing a perforation include prevention of water entering the middle ear, which could cause recurrent infections. It may results improved hearing, but repairing the ear drum alone seldom leads to great improvement in hearing. The objective of myringoplasty needs to be properly explained to the patient prior to surgery. Councelling needs to clarify that our prime objective to close the perforation is to avoid further complications including hearing deterioration any further. Problem is often intense with bilateral perforated ear drum.

Discharging ears are usually treated conservatively to acquire a dry perforation, as the yield of grafting is much better in dry ears.

Mastoid explorations may be considered for refractory discharging ears not responding to the conservative management. If the tympanic membranes are perforated bilaterally then the worse ear should be selected first for surgery. This is done to save the better ear from iatrogenic complications. If the tympanic membrane perforation is present in a patient's single hearing ear, then only incipient life threatening complications justify repair attempts.[4, 5] medical therapy for perforations is for controlling otorrhoea.[6] Ear drops may develop ototoxicity leading to several types of ossicular defects.

Treatment of tympanic membrane perforation falls into three categories. If the hearing loss is minimal and there is no discharge or pain then no treatment is usually required. In these cases the patients are advised to avoid water entering the middle ear, hence avoid diving in water. Furthermore, they should use ear plugs or cotton soaked in olive oil to prevent water entery into the ear canal. The second option involves those ears where perforation is small and involves neither the umbo nor the annulus. Several methods in history had been applied to achieve a healed perforation. These include, cauterization of the edge of tympanic membrane with trichloroacetic acid (10%) solution and then apply a patch of cigarette paper. Single hearing ear deserves special care. It should not be operated upon unless life threatening complications justify. [9,10,11,] Regarding medical therapy, the use of ear drops must be assessed to avoid any reaction.[12] The use of cartilage as a graft material has been used successfully. [13,14,15.] Autologous temporalis fascia as a graft is mostly used under general anesthesia.[16] Success rate in different myringoplasty procedures range from 70% in marginal perforation to90% in central perforation.[17] Hearing deficit as a result of surgery is reported in nearly 1-2 percent. [18]

A fat plug myringoplasty is the valued procedure in expert hands with equally good

results.[7,8] recently reported forms of office treatment use of fibrin glue or a patch composed of a hyaluronic acid ester and a dressing component has also been used with good results. The use of basic fibroblast growth factor with a patch that consist of a silicone layer and atelo-collogen has been tried in small number of patients again with good results. The third option is to perform tympanoplasty with patient under local or general anaesthesia.

Diversity of procedure infact speaks the efficacy of none up to 100%. We prefer a fat plug graft method in small dry perforations as this procedure is simple in comparison to other procedures yet having the success rate of similar percentage. The complication like further hearing defect is very rare, one series showed approximately 1 per 500 operations while another study shows 2% of increase hearing loss. Taste disturbance, tinnitus, dizziness, facial paralysis and reaction to ear dressings have been encountered very rarely.

CONCLUSION:

The objective of myringoplasty is to have a newly reconstructed ear drum with functions close to normal. In our study this objective is achieved by fat-plug myringoplasty. The success of the procedure is close proximity to the contemporary in vogue methods of tympanic membrane repair. The experienced hand along with the facility need not mention to further enhance the result rate. Post operative follow up is mandatory for better progress especially the functioning eustachian tubes and avoidance of infection in the nose and nasopharynx.

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NASAL SEPTAL PERFORATION- AN AVOIDABLE COMPLICATION

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ABSTRACT

Nasal septal perforation is one of the commonest complications encountered in nasal septa! surgeries by the ENT surgeons. Non surgical causes of septa] perforation often render it a medical entity. Surgeons often take due care to prevent the occurrence of perforation. This is a descriptive study including 30 patients who had septoplasty operation from april 2014 to august 2014 in the department of ENT, at DHQ hospital, Abbottabad. After removing flaps, an inclined incision was given in all cases to get access to the other side of septum and hence avoiding trauma to the elevated flaps. None of them had perforation till the end of this study.

Key word: nasal septum; perforation; septa! flap.

Septal perforation is considered as a common complication after septal surgeries. The cause of septal perforation may be known and unknown —idiopathic cases of septal perforation do not have an apparent cause —local trauma due to trauma caused by nose picking or iatrogenic is only one aspect. Septal haematoma or abscess formation and granulomatosis conditions, e.g. we gener's granulomatosis or syphilis may also result in septal perforation. The symptoms depend upon the size and location of perforation small perforation result in whistling noise on respiration. Nasal septa! crusts with subsequent epistaxis may result in large perforation. For the ENT surgeries, the point to be considered seriously is how to avoid or at least reduce to the minimum the perforation which has iatrogenic causes.

The aim of this paper in to describe how surgeon can avoid septal perforation by a minor modification of the existing techniques of removal of deviated septum while minimizing morbidity.

MATERIAL AND METHODS

30 patients undergoing septoplasty procedure from april 2014 to august 2014 in the department of ENT, at DHQ hospital, Abbottabad have been studied. All the cases were given the same incision for removing the cartilage and deviated bony septum. 20 male and 10 female between the ages of 20 years to 50 years were included in the study. The objective of the study was to ascertain any septa! perforation post operatively. After inclined incision in the cartilaginous septum along the plane of floor it was observed that none of them had any perforation till the end of the study.

DISCUSSION :

Septal surgery dates back to the beginning of the last century. Killian and Freer in the year 1904 and 1902 respectively evolved the methods which are in vogue till date. Different techniques for reshaping bent sections of cartilage include morsel ization or incising cartilage in various ways. Scarring and contraction leads to an unpredictable out come if a single technique is strictly observed. Septoplasty is poorly taught and should not be considered as a simple procedure in which one operation fits all. A surgeon should have a range of techniques at their disposal to get the best results. Previously a single technique was taught which resulted in complications.

Septal perforation has been occurring with such a frequency that the need to evolve a modified

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technique to remove septal cartilage and bony septum has been considered with out damaging the overlying flaps. It has been observed that septal perforation often occur due to either at the time of elevation flaps or when removing the septal cartilage.

CONCLUSION:

In our study we have seen that by giving an inclined incision horizontally along the septum will result in an easy way to get access to the other side of septum without damaging the flap on contralateral side. In all of our cases of 30 patients none had any septal perforation post operatively.

This study highlights a common cause of septal perforation and the way how to avoid it. By adopting this technique the morbidity associated with septal perforation can be avoided.

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EVALUATION OF EFFECT OF CARICA PAPAYA (PAPAYA) LEAVES ON BLOOD CELL COUNTS IN DRUG INDUCED MYELOSUPPRESSION IN MICE

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ABSTRACT

AIMS & OBJECTIVES: The current study was undertaken to evaluate the effect of aqueous extract of Carica papaya leaves on Platelet, WBC and RBC counts in the mouse model of carboplatin induced myelosuppression.

STUDY DESIGN: Sixty healthy adult male Swiss albino mice were randomly divided into 3 groups. Group A served as positive control, group B as preventive, and group C as treatment group. On day 0, two mice from each group (total six) were sacrificed to get the baseline values of blood cells. The myelosuppression was induced in all the remaining animals by a single intraperitoneal injection of carboplatin on day 0. Aqueous extract of Carica papaya leaves was given orally by feeding tube from 0 to 18th day to group B to see preventive effect and from 6th to 18th day to group C for treatment effect. On 6th, 12th and 18th day, six mice from each group were sacrificed and blood samples were taken for evaluation of Platelet, WBC and RBC counts.

STATISTICAL ANALYSIS: Data was expressed as Mean ± SD. ANOVA was applied. P value of ≤ 0.05 was considered statistically significant.

RESULTS: Results showed that C. papaya leaf extract both in preventive and treatment groups significantly prevented the fall in platelet count as compared to positive control group throughout the study period. C. papaya leaf extract significantly prevented the decline in total WBC count on day 12 and 18 in preventive group, whereas significant elevation in WBC count was seen in treatment group on day 18 as compared to the positive control. Treatment with C. papaya leaf extract also significantly increased RBC count in both preventive and treatment groups on day 18 as compared to positive control.

CONCLUSION: Our data suggested that C. papaya leaf aqueous extract possesses significant preventive and curative properties against carboplatin induced myelosuppression, which was characterized by restoring the Platelet, WBC, and RBC counts in blood.

Key words: carica papaya leaves, myelosuppression, mice

The process by which blood cells are produced and matured in the bone marrow is called hematopoiesis. The pluripotent stem cells are responsible for normal hematopoiesis. The stem cells are capable of proliferation, differentiation and replication. The stem cell of lymphoid lineage segregates into a pre-B or pre-T stem cell, whereas myeloid lineage stem cell further singles out into erythrocyte, megakaryocyte, monocyte, eosinophil or basophil cell lines. When these cells differentiate or mature, they become the cells that we can recognize in the blood stream[1].

Myelosuppression also known as bone marrow suppression or myelotoxicity, is a disorder in which bone marrow activity is diminished. Bone marrow acts as the manufacturing center of blood cells. So, its suppression leads to deficiency of blood cells with subsequent reduced number of RBCs, WBCs, and platelets in circulation. Most immunosuppressive agents damage bone marrow cells. This condition may rapidly lead to life-threatening infections, due to decreased production of WBC. It

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may also lead to anemia due to fall in red blood cells and spontaneous hemorrhage resulting from decreased platelet count which is a documented side effect of many chemotherapy drugs. Given that many blood cells have a very short life in the body, patients start to suffer medical complications almost immediately after chemotherapy[2]. Nevertheless, reducing inevitable adverse effects resulting from conventional chemotherapy or irradiation is a serious challenge for cancer patients and doctors, so as to improve the quality of life and survival gains[3]. Autologous bone marrow or peripheral blood stem cell transplantation, transfusions and recombinant hematopoietic growth factor injections are the treatment modalities used to reduce the myelosuppression due to high dose chemotherapy but they have other implications like high cost and toxicities which limit their general use[4]. Considering these aspects, there is a growing need for a safer, economical and effective drug for the treatment of myelosuppression.

Since the beginning of human civilization, herbs have been an essential part of society and are respected for their culinary and medicinal properties[5]. The influence of natural products in seeking remedies for various diseases has been enormous; natural products extracted from microorganism, plant and animal sources have been the single most prolific foundation of clues for the development of drugs[6]. Various experimental studies have documented the role of Chinese herbal medicines in prevention and treatment of chemotherapy induced myelosuppression[7,8].

Carica papaya L. belongs to the plant family Caricaceae[9] and is an effective medicinal herb that is used as a folk remedy for the cure of various diseases all over the world[9,10]. C. papaya leaves have been revealed to contain various phytochemicals like alkaloids, cardiac glycosides, flavonoids, reducing sugars, saponins, tannins, anthraquinones, steroids, phenolics and cardenolides [11]. C. papaya shows a variety of pharmacological effects comprising, antiseptic, antibacterial, antiparasitic, anti-inflamma-tory, lipid lowering, antihypertensive, diuretic, hypoglycemic, contraceptive[12] and nephroprotective effects[13]. Various studies were conducted on C. papaya extract to prove its safety for human ingestion[14,15].

Recently, papaya leaf decoction has been effectively used in traditional medicine in Malaysia for the cure of dengue hemorrhagic fever. In an animal study, effect of palm oil suspension of C. papaya leaves on platelet count was studied[16], which showed increase in platelet count within hours. C. papaya was shown to be not only protective against lead acetate induced oxidative damage in the bone marrow but also had a curative effect on hematopoiesis in rat model[17]. The present study was designed to investigate the effect of Carica papaya leaves extract on blood cell counts in the mouse model of carboplatin induced myelosuppression.

MATERIALS & METHODS:

The study was carried out in the department of Pharmacology and Resource Laboratory, University of Health Sciences Lahore. Experimental research laboratory was used for animal care and procedures. Sixty male Swiss albino mice, weighing 25-35 gram were included in the study. Animals were kept at controlled room temperature (22-24ºC) and humidity (45-65%) in animal house. Natural dark and light cycle of 12hrs each was maintained along with standard feed and water ad libitum. Animals were acclimatized for one week before the start of experiment.

Fresh leaves of papaya tree were washed with water and shade-dried at room temperature. The dried leaves were then powdered with the help of an electric grinder, weighed and stored in a glass jar at room temperature. Fifty grams of crude powder of Carica papaya leaves were mixed in 1000 ml of water (ratio 1:20). After that it was heated and stirred on hot plate at 60–70∘C for 3 hours to convert into a concentrated solution. After being cooled on room temperature, it was filtered. Aqueous extract was then lyophilized to produce powdered form of

the extract[18]. Mice were randomly divided by lottery method into three groups having 20 mice in each group.

On day 0, before the induction of myelosupp-ression by carboplatin, 2 mice from each group were euthanized by chloroform[19] and blood samples were collected to get the baseline values of blood counts. It was considered as normal control group (6 animals, 2 from each group). After that, myelosupp-ression was induced in all the remaining animals by a single carboplatin injection (125 mg/kg) intraperito-neally[20,21] on day 0. Mice in Group-A (Positive Control) received 0.4 ml distilled water, given orally via the feeding tube as a single morning dose from day 0-18. Group-B (Preventive Group) mice received 0.4ml aqueous extract of Papaya leaf (15 mg/kg)16 given orally by feeding tube as a single morning dose from day 0-18. Group-C (Treatment Group) mice received 0.4ml aqueous extract of Papaya leaf (15mg/kg) given orally by feeding tube as a single morning dose from day 6 to day18. Six mice were euthanized from each group to collect blood samples by intracardiac puncture on day 6, 12 and 18 in EDTA (ethylene diamine tetra acetate) tubes for cell counts. Platelets, white blood cells and red blood cells were counted by specialized automated hemocytometer (Sysmax XT-1800i)[22].

STATISTICALANALYSIS:

Data was expressed as Mean ± SD using SPSS (Statistical Package for Social Sciences) version 20 and Graph-Pad Prism version 5. One-way analysis of variance (ANOVA) was performed followed by post hoc Tuckey test to arbitrate the significant difference among groups and value of $P \leq 0.05$ was considered as significant.

RESULTS:

Our findings indicated a significant decrease in all the three cell counts of positive control group as compared to control baseline values with P value < 0.001, which means carboplatin caused severe myelosuppression in positive control group. Table-1

and figure-1 shows Mean (103/µl) ± SD values of Platelet Count on Day 6, 12 and 18 in all Groups. Platelet count of preventive group (Group-B) was significantly raised in comparison to positive control group (Group-A) throughout the study period. Similarly, treatment group (Group-C) also indicated a significant increase in platelet count comparing to positive control group on 12thand 18thday of study with P value < 0.05 and < 0.001 respectively. Notably, treatment with C. papaya was initiated in this group on 6th day of experiment.

Table 1: *Mean (10^3/µl) ± SD values of Platelet Count on Day 6, 12 and 18 in all Groups (n=6)*

Groups	Day 6	Day 12	Day 18
Positive control	341.8 ± 44.17[a]	266.0 ± 101.3[a]	333.0 ± 146.1[a]
Preventive group	496.5 ± 94.50[b]	1045 ± 172.5[b]	1040 ± 136.8[b]
Treatment group	437.5 ± 107.2	501.3 ± 105.4[b]	766 ± 100.0[b]

Baseline control values 1032 ± 97.48
[a] shows a significant difference in comparison with control group.
[b] shows a significant difference in comparison with positive control group.
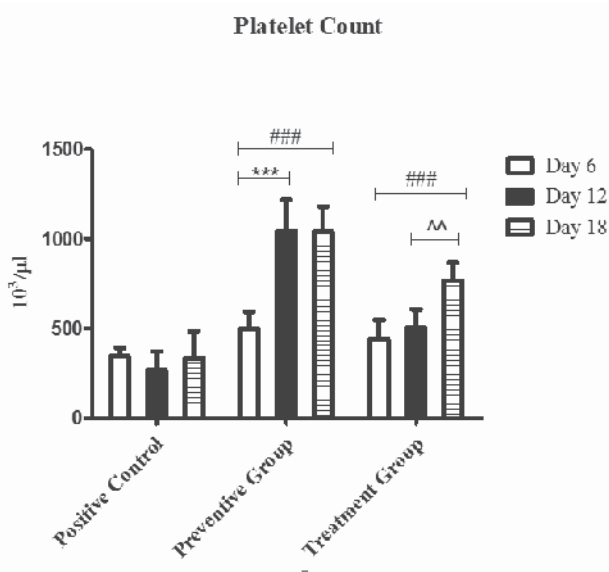
Figure # 1: *Shows Mean ± SD values of platelet count on day 6, 12 and 18 in all Groups (n=6).*
*** represents P value < 0.001 indicative of significant difference between 6th and 12th day,
shows P value < 0.001 indicative of significant difference between 6th and 18th day,
^^ represents P value < 0.01 indicative of significant

difference between 12th and 18th day

Table-2 and figure-2 shows Mean $(103/\mu l) \pm$ SD values of White Blood Cell Count on Day 6, 12 and 18 in all Groups. Preventive group (Group-B) showed a significantly increased white blood cell count as compared to positive control group (Group-A) on 12th and 18th day of study with P value < 0.01 and < 0.001 respectively. On the other hand, treatment group (Group-C) showed an insignificant increase in white blood cell count on 12th day but significant rise on 18th day in comparison to positive control group (Group-A) with P value < 0.01.
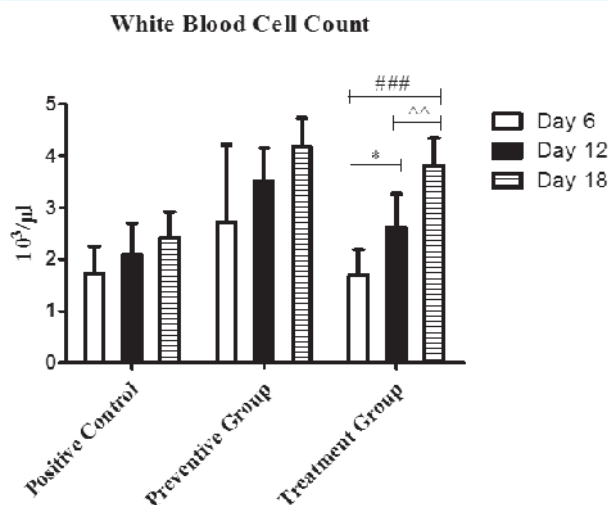
Table 2: *Mean $(10^3/\mu l) \pm$ SD values of White Blood Cell Count on Day 6, 12 and 18 in all Groups (n=6).*

Groups	Day 6	Day 12	Day 18
Positive control	1.71 ± 0.52^a	2.08 ± 0.6^a	2.41 ± 0.49^a
Preventive group	2.70 ± 1.49	3.51 ± 0.63^b	4.16 ± 0.55^b
Treatment group	1.68 ± 0.48	2.60 ± 0.65	3.81 ± 0.52^b

Baseline control values 5.16 ± 0.74
[a] shows a significant difference in comparison with control group.
[b] shows a significant difference in comparison with positive control group.

White Blood Cell Count

Figure # 2: *Shows Mean ± SD values of white blood cell count on day 6, 12 and 18 in all Groups (n=6).*

* represents P value < 0.05 indicative of significant difference between 6th and 12th day

shows P value < 0.001 indicative of significant difference between 6th and 18th day

^^ represents P value < 0.01 indicative of significant difference between 12th and 18th day

Table-3 and figure-3 shows Mean $(103/\mu l) \pm$ SD values of Red Blood Cell Count on Day 6, 12 and 18 in all Groups. No significant difference was found in red blood cell count of preventive and treatment groups as compared to positive control group on 6th and 12th day of study. Whereas, both groups showed a significant rise in red blood cell count as compared to positive control group on 18th day with P value < 0.01.

Table 3: *Mean $(10^6/\mu l) \pm$ SD values of Red Blood Cell Count on Day 6, 12 and 18 in all Groups (n=6).*

Groups	Day 6	Day 12	Day 18
Positive control	2.91 ± 0.80^a	3.11 ± 0.74	3.16 ± 0.77^a
Preventive group	2.55 ± 0.91	4.35 ± 1.08	5.78 ± 1.33^b
Treatment group	2.27 ± 0.77	3.55 ± 1.12	5.74 ± 1.25^b

Baseline control values 7.72 ± 1.45
[a] shows a significant difference in comparison with control group.
[b] shows a significant difference in comparison with positive control group.

Red Blood Cell Count
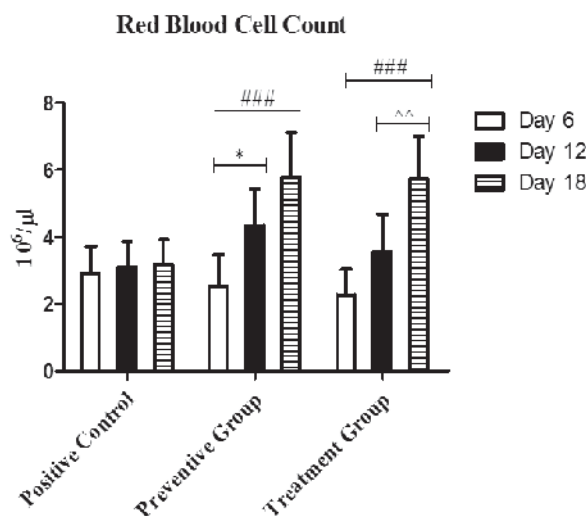
Figure # 3: *Shows Mean ± SD values of Red blood cell count on day 6, 12 and 18 in all Groups (n=6).*

* represents P value < 0.05 indicative of significant difference between 6th and 12th day

shows P value < 0.001 indicative of significant difference between 6th and 18th day

^^ represents P value < 0.01 indicative of significant difference between 12th and 18th day

DISCUSSION:

The process of blood cell production and maturation in the bone marrow is called hematopoiesis. The pluripotent stem cells are responsible for normal hematopoiesis. Myelosuppression is a condition in which bone marrow activity is diminished including thrombocytopenia, leukopenia and anemia. It is one of the common side effects of anticancer drugs[23]. Various plants having hematopoietic activities have been reported in previous studies. These medicinal plants have been evaluated for their therapeutic role in animal model of myelosuppression and are found to be beneficial with minimum adverse effects[24]. Current study investigated the hematopoietic effects of Carica papaya leaf aqueous extract in mouse model of drug induced myelosuppression.

We used a single intraperitoneal injection of carboplatin to induce myelosuppression. Carboplatin is a second-generation platinum anticancer drug used in malignant tumors mainly ovarian, testicular and small cell carcinoma of lung. The dose limiting toxicity of carboplatin is myelosuppression in 25% patients[20,21]. Our findings revealed that after administration of carboplatin injection, all three blood cell counts were significantly reduced by day 6 in positive control group in comparison to the control group, and remained significantly reduced throughout the study period of 18 days, which is in line with the results of previous studies[25,26].

Treatment with C. papaya leaf extract in preventive group significantly prevented the fall in platelet counts as compared with positive control group throughout the study. Platelet count of the mice of treatment group also started to improve with use of C. papaya leaf extract and subsequently were found significantly elevated as compared with positive control group at day 12 and 18. This is in accordance to previous study in which Carica papaya leaf aqueous extract was found to increase the platelet count significantly in cyclophosphamide induced rat model[27]. Another study demonstrated that oral use of MLC (mature leaf concentrate) of C. papaya leaf for consecutive three days cause significant increase in platelet count of normal albino wister rats[28] which is again supporting our study. Oral use of C. papaya leaf extract significantly prevented the fall in total WBC count in preventive group as compared to the positive control group on day 12 and 18. While WBC count of treatment group was significantly elevated on day 18 as compared to the positive control. Our data showed that treatment with C. papaya leaf extract significantly increased RBC count on day18 in both preventive and treatment groups as compared to positive control. These finding are in accordance to the previous study[29] in which oral use of mature leaf concentrate of Carica papaya showed a significant percentage increase in WBC and RBC counts in hydroxyurea induced thrombocytopenic murine model.

CONCLUSION:

Our findings indicated that C. papaya leaf aqueous extract possesses significant preventive and curative properties against carboplatin induced myelosuppression, which is characterized by restoring the platelets, WBC, and RBC counts in blood. The results describe the need for further studies to identify the active constituents/principles in C. papaya leaf which are responsible for this protective effect against myelosuppression to supplement the findings of the present study. Detailed toxicity studies of C. papaya leaves are also warranted to identify dose concentration and effect/toxicity relationship.

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EVALUATION OF OXIDATIVE STRESS IN PATIENTS OF RENAL CELL CARCINOMA

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ABSTRACT

INRTODUCTION: Renal cell carcinoma (RCC) is the most common kidney cancer that arises from the renal tubule (Hanak , Slaby et al., 2009). It is the third most common and the most lethal of all genitourinary malignancies. The most common subtype of RCC is Clear Cell Carcinoma, which comprises about 75% of RCC. Clear Cell Carcinoma belongs to the type of renal tumors in which significant changes occur in cellular redox balance (Pelicano, Carney et al., 2004). Oxidative stress plays an important role in carcinogenesis because of induction of DNA damage and its effects on intracellular signal transduction pathways. The degree of oxidative DNA damage in RCC can be used as a prognostic predictor for patients who undergo radical nephrectomy (Frederiks, Bosch et al., 2010).

METHODOLOGY: We had taken serum samples of 30 diagnosed cases of RCC from JINNAH HOSPITAL LAHORE and 10 normal subjects and evaluated the level of antioxidants in serum of patients with renal cell carcinoma by performing different assays such as Superoxide Dismutase (SOD), Ascorbate peroxidase(APOX), glutathione (GSH) and catalase .

RESULTS: SOD was lower in disease group (57.4± 1.07) and higher in normal group (91.0± 0.41). GSH estimated was higher in normal than disease group (7.53± 0.25). CATALASE (5.89 ± 0.49) and APOX percentages (11.4 ± 0.41) were also lower in diseased group respectively.

KEYWORDS: RCC, SOD, APOX, GSH

Renal cell carcinoma (RCC) is the most common kidney cancer that arises from the cells of renal tubule (Hanak, Slaby et al., 2009). Despite the fact renal cell carcinoma is relatively rare as compared to other cancer types, its incidence is still increasing (MILA-Kierzenkowska, Wozniak et al., 2013). Renal cell carcinoma is the third most common and most lethal of all genitourinary malignancies. RCC is a frequent form of urological tumor, associated with an alteration of multiple signaling pathways (Grange, Collino et al., 2014) .

The most common subtype of renal cell Carcinoma is Clear Cell Carcinoma, which comprises about 75% of RCC in surgical series. Although this subtype is usually definitely recognized histologically ,its molecular profile is quite variable (Sverko, Dobocanec et al., 2011). Papillary RCC, about 15% of surgical series but less in metastatic series, has been divided histologically into type I (basophilic) and II (Eosinophilic) with different biologic behaviors (Delahunt, Eble et al., 2001).

During tumor growth important changes appear in cellular redox homeostasis. RCC of clear cell type belongs to type of tumors in which significant changes occur in cellular redox balance(Pelicano, Carney et al., 2004). Therapeutic selectivity and drug resistance are the two major issues in cancer chemotherapy (LUSINI, Tripodi et al., 2001).

Oxidative stress is known as the disturbance of equilibrium among the production of reactive oxygen species (ROS) and the inherent capacity of a biological system to acquisitively detoxify the reactive intermediates (Fridovich 1978). ROS comprise of hydrogen peroxide (H_2O_2), peroxynitrite (ONOO), superoxide (O^{2-}) and hydroxyl radical (OH-). Most of the above mentioned species have been identified in RCC (Block, Gorin et. al. 2007, Block, Gorin et. al. 2010.

Oxidative stress and the associated antioxidant

defense might play an important role in RCC growth and progression (Sverko, Sobocanec et al., 2011). Oxidative stress plays an important role in carcinogenesis because of induction of DNA damage and its effects on intracellular signal transduction pathways (Frederiks, Bosch et al., 2010). The degree of oxidative DNA damage in RCC can be used as useful prognostic predictor for patients who undergo radical nephrectomy (Frederik, Bosch et al., 2010).

Glutathione is a cysteine containing peptide found in most forms of aerobic life (Meister and Anderson 1983). Glutathione has antioxidant properties since the thiol group in its moiety is a reducing agent and can be reversibly oxidized and reduced. Due to its high concentration and its central role in maintaining the cellular redox state, glutathione is one of the most important cellular antioxidants (Meister and Anderson 1983). Antioxidants have been used to prevent and treat RCC (Lee, Mannisto et al 2009.) Antioxidant depletion in the circulation may be due to scavenging of lipid peroxides as well as due to appropriation by tumor cells (Sharma, Rajappa et al., 2007). SOD and catalase are also the major antioxidant defense mechanisms. SOD catalyse the conversion of superoxide to hydrogen peroxide in mitochondria while catalase which is found in peroxisomes detoxifies hydrogen peroxide (Lu, Zhen et al., 2010).

METHODOLOGY

We had selected 30 diagnosed patients of RCC from Oncology Department of Jinnah Hospital Lahore and their blood samples were collected for biochemical analysis.10 healthy subjects were taken as control group. 5ml blood was drawn from antecubital vein of each individual in disposable syringe to estimate the biochemical levels of SOD, APOX, GSH and Catalase.

Superoxide dismutase (SOD)

SOD assay was performed with slight modifications in Beauchamp and Fridovich (1971) and Israr et al., (2006).

ASCORBATE PEROXIDASE (APOX)

Apox assay was performed with slight modifications in Israr et al and Nakano and Asada (Israr, Sahi et al., 2006).

Glutathione (GSH)

GSH assay was performed with slight modification in Israr et al (Israr , Sahi et al., 2006) and Rao et al., (Rao, Paliyath et al., 1996).

Catalase Assay

CAT assay was performed by taking two buffer solutions (Buffer1 and Buffer 2). Buffer solution 1 had 5Mm KH_2PO_4 (pH 7.0) and buffer 2 contained 12.5mM H_2O_2 in 50ml KH_2PO_4 (pH7.0). Enzyme extract of 100ul were added in two cuvettes. 900 ml buffer in first plate, while 900ml conc. of buffer 2 in other plate. In this assay both plates were placed in dark .Enzyme extract was added after that absorbance was taken at 240 nm after 45s and 60s (Yang, Song et al., 2008).
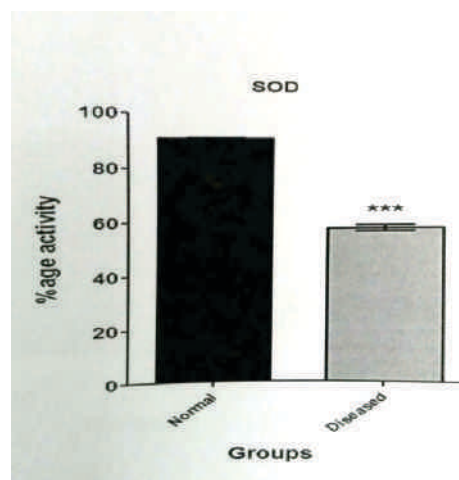
RESULTS

SUPER OXIDE DISMUTASE (SOD)

Percentage of superoxide dismutase was checked in blood serums that were obtained from normal and disease groups. SOD percentage was compared in both groups. SOD percentage was lower in disease group (57.4 ± 1.07) and higher in normal group (91.0± 0.41) as shown in the figure.

GLUTATHIONE (GSH)

Percentage of glutathione reductase was

checked in blood serums that were obtained from normal and disease groups. GSH percentage was compared in both groups. Glutathione percentage was lower in disease group (7.53 ± 0.25) and higher in normal group (28.5± 1.07) as shown in the figure.

CATALASE (CAT)

Percentage of Catalase was checked in blood
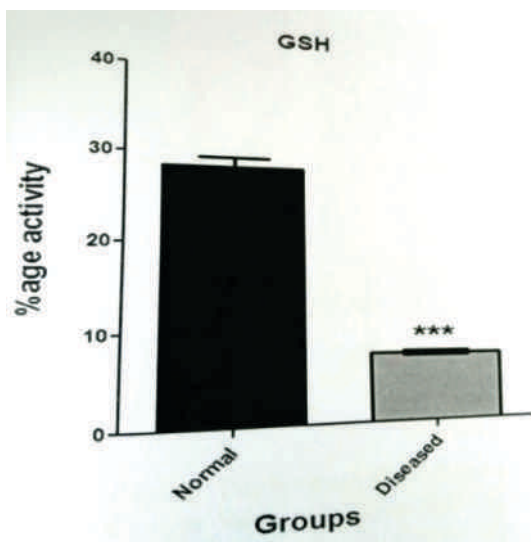
serum that were obtained from normal and disease group . Catalase percentage was compared in both groups. Catalase percentage was lower in disease group (5.89 ± 0.49) and higher in normal group (18.0± 0.07) as shown in the figure.

Ascorbate Peroxidase (APOX)

For the estimation of levels of APOX, serums of
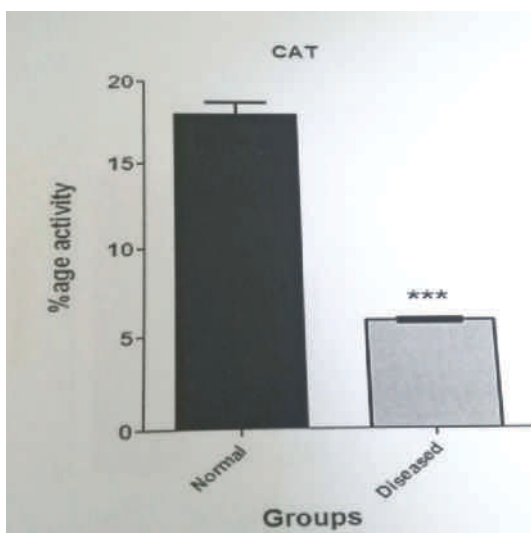
RCC group and normal subjects were obtained. APOX percentage was decreased in diseases group (11.4 ± 0.41) and increased in normal group (17.8± 0.94) as shown in the figure.

DISCUSSION
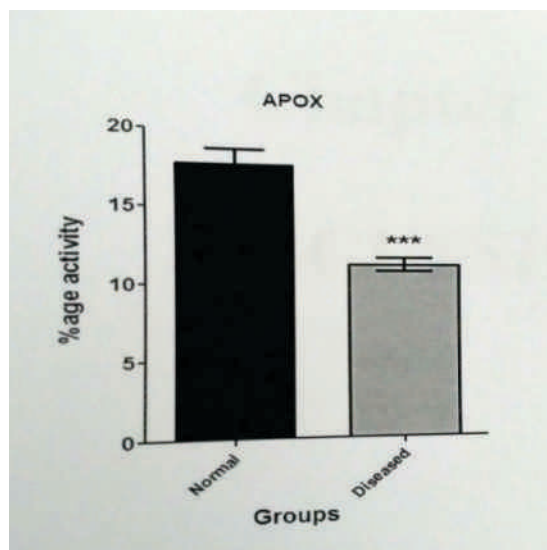
Serum Antioxidant Levels	Control Group	RCC Patients
Super Oxide Dismutase (sod)	91.0± 0.41	57.4 ± 1.07
Glutathione (gsh)	28.5± 1.07	7.53 ± 0.25
Catalase (cat)	18.0± 0.07	5.89 ± 0.49
Ascorbate Peroxidase (apox)	17.8± 0.94	11.4 ± 0.41

The study was conducted to ascertain the levels of different antioxidants in patients suffering from RCC. Excessive production of reactive oxygen species such as hydrogen peroxide and hydroxyl radical, peroxynitrite and superoxide is detected in RCC which are considered as basic free radicals involved in the development of RCC (Block, Gorin et al., 2010). For the treatment and prevention of RCC antioxidants are used (Lee,Mannistoet al 2009, Samarghandian, Afshari et al., 2011).

Samples of serum were taken from 30 subjects of RCC and from 10 normal subjects and then the level of antioxidants enzymes SOD, APOX, GSH and Catalase were evaluated in them. The most important antioxidants involved in defense mechanism are catalase and superoxide dismutase.

Our results reveal decrease levels of catalase in RCC subjects than the normal one which is in agreement with the research conducted by PIjesa et al., which stated that the level of catalase was down regulated in serum of RCC group (Pijesa – Ercegovac ,mimic –Oka et al., 2008). Pirincci et al., stated that the level of antioxidants enzyme such as SOD decreased in serum of renal cancer patient which can also be correlated with the current research which reveals that the level of SOD decreases in serum of RCC group than that of the normal . Pirincci et al., also described that the glutathione level lowered in renal cancer patient (Pirincci , Kaba et al., 2013) . Similarly our results indicate that increased oxidative stress along with decreased antioxidant GSH level in renal cancer.

Ascorbate peroxidase also has anticancer property and ability to kill cancer cells. Like other antioxidant enzymes APOX level also decrease in serum of RCC patients compared to control group.

Thus, the present study reveals that the levels of various antioxidants decrease in RCC which in turn pose oxidative stress on the body. If it is left untreated, oxidative stress can eventually progress to oxidative DNA damage and affects intracellular signal transduction pathways (Frederiks, Bosch et al., 2010). It causes the renal function disturbance and finally stress leading to organ failure and ultimately death. Thus this study will aid in understanding the role of antioxidants enzymes in renal cell carcinoma patients and also ascertain their importance in alleviating the progression of disease.

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ASSOCIATION OF BMI AND MUSCLE MASS AMONG DIABETIC PATIENTS IN DIABETIC CENTRE JINNAH HOSPITAL LAHORE

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ABSTRACT

INTRODUCTION: Diabetes is defined as a disease in which the body's ability to produce a response to the hormone insulin is impaired resulting in abnormal metabolism of carbohydrates and elevated levels of glucose in the blood. Diabetes leads to decrease in muscle mass called sarcopenia and increase in obesity. BMI disturbance and decrease in muscle mass have a positive correlation. Former Studies reflect that Obesity and Sarcopenia in the elderly diabetics may potentiate each other maximizing their effects on disability, morbidity and mortality.

OBJECTIVE: To determine the association of the muscle mass and BMI of diabetic patients.

METHODOLOGY: This study was conducted in the diabetes center of Jinnah Hospital Lahore, over a period of 2 weeks. Total of 150 diabetic patients were included in the study, through Non probability purposive sampling, and their demographic and anthropometric data was collected.

RESULTS: About 34.7% patients were obese having a BMI greater than 30 kg/m2. About 5.33% patients were sarcopenic of which 2.0% were males and 3.33 % were females. BMI and muscle mass showed a positive correlation in diabetic patients.

CONCLUSION: Sarcopenia and obesity are co-existing illnesses that lead to metabolic and functional disabilities. BMI and muscle mass have a positive correlation with each other.

KEY WORDS: obesity, BMI, muscle mass, sarcopenia.

In the world, due to an increasingly sedentary way of life, metabolic disorders like diabetes are now rampant. Diabetes is defined as a disease in which the body's ability to produce a response to the hormone insulin is impaired resulting in abnormal metabolism of carbohydrates and elevated levels of glucose in the blood[1]. Sarcopeniais a combination of inadequate muscle mass accumulation in young ones and reduced muscle mass in the elderly. Sarcopenia along with obesity has an additive effect on insulin resistance[2]. Body Mass Index is a person's weight in kilograms divided by his or her height in meters squared. Overweight are those that have a BMI of 27.3 or more for women and 27.8 or more for men. Obesity is a BMI of 30 or more for either sex. Increased BMI is deemed to be central to a rising incidence of diabetes in an early age[9].

According to International Diabetic Federation (IDF) 215.2 million males and 199.5 million females from 20-79 years were diabetics in the year 20153.

60% of diabetics live in Asia .11.6 % adults have diabetes in China. According to IDF there were 6.9 million cases of diabetes in Pakistan in 2014 and prevalence of diabetes in adults of 20-79 years of age was 6.8%.

Diabetes is linked with an increased loss of body mass and appendicular lean mass. It also causes generalized fat loss in men4. With loss of muscle mass, the loss of function and strength of muscle is also accompanied which has been positively linked to increased probability of falls which for the elderly might mean higher injury and death rates[5].

Age has a negative association with lean body mass and appendicular skeletal muscle mass has a positive association with arm and calf circumference.[6] Sarcopenia has been linked to insulin resistance, diabetes and obesity with the latter most being a causative factor to the development of insulin resistance and thus diabetes and vice versa, insulin resistance has been thought to cause

Sarcopenia[7].

There is a positive association between muscle mass and body mass index in elderly diabetic patients. There is a prevalence of obesity that is 76.8% in females and 26.8% in males [3].

Early identification of the signs of Sarcopenia and help in the nutritional and exercise categories might lead to healthier aging and thus lesser money spent on morbidity due to Sarcopenia in the longer run[8].

Due to such a high prevalence of diabetes and known associated morbidities with Sarcopenia we intend to investigate the link between the two. For this purpose we prefer anthropometry, as it is an easy and inexpensive method. Anthropometry involves the systematic measurement of physical properties of the human body, primarily dimensional descriptors of body size and shape.

METHODOLOGY:

The study was conducted in Jinnah Hospital Lahore which is a tertiary care, 5000 bed government hospital located on AllamaShabbir Ahmed Usmani road Faisal town, Lahore.

The study lasted for 4 weeks from 20th April to 20th May 2017. Sample size taken was 150 and sampling technique was Non probability purposive sampling. Inclusion criteria was of 150 compliant patients in Jinnah Hospital Lahore presented during the time period of 20th April to 20th May 2017. Exclusion criteria included non-diabetic and non-compliant patients.

DATA ANALYSIS:

Data was entered in SPSS 21 and frequency

Table 1: *The frequency distribution and percentage of BMI in diabetic patients.*

Categories of BMI	BMI ranges	Frequency	Percentage%
underweight	<18.5	6	4.0
normal	18.5-25	33	22.0
overweight	25.1-30	59	39.3
obese	>30	52	34.7
Total		150	100.0

distribution of BMI and muscle mass was calculated. Later on its correlation was found.

Table 2: *The frequency and percentage of muscle mass in diabetics.*

Muscle mass	Frequency	Percentage%
normal	11	7.33
abnormal	139	92.66
Total	150	100

Table 3: *showing correlation of BMI and Muscle mass in diabetics.*

Correlations

		in kg / meter sq.	muscle mass
in kg /meter sq.	Pearson Correlation	1	.238**
	Sig. (2-tailed)		.003
	N	150	150
muscle mass	Pearson Correlation	.238**	1
	Sig. (2-tailed)	.003	
	N	150	150

** Correlation is significant at the 0.01 level (2-tailed).

RESULTS:

Demographic and anthropometric data of one hundred and fifty diabetic patients presenting in Diabetic centre of Jinnah hospital Lahore was collected. About 60 (40%) were male and 90(60%) were female. Of all the patients 93(62%) patients had a family history of diabetes. The frequency distribution of duration of diabetes showed that most of the patients (42.8%) 65 were diabetics for less than 5 years. The diabetic patients presenting in JHL had 3 ways of managing their diabetes; 57(38%) took insulin, 62 (41.3 %) took medication while 19(12.7%) adopted both methods. But some people 12(8%) used lifestyle modification as a tool to control their diabetes. There were some perceptions regarding weight change in patients which included weight gain or loss after the development of diabetes. The data showed that 100 (66.7%) patients believed that they experienced a weight loss after diabetes while 18(12%) relayed to have gained weight after it. Some patients 32 (21.3%) had no weight change complains. The patients were

recorded for their food intake as well which showed that 15(10%) had high food intake, 34(22.7%) had low food intake and 101 (67%) had normal food intake even after the development of diabetes. About34.7% patients were obese having a BMI greater than 30 kg/m2. About 5.33% patients were sarcopenic of which 2.0% were males and 3.33 % were females. BMI and muscle mass showed a positive correlation in diabetic patients as it is 0.003 greater than 0.001.

DISCUSSION:

We studied the relationship of BMI and muscle mass in diabetic patients within the age ranges of 18-80 visiting JHL. In other researches it was found that an average association exists between obesity and Sarcopenia in diabetics[3].

We used the following formula6 to calculate the muscle mass of patients which comprises of age, weight and height;

Male: Lean mass = -15.605-(0.032x age) + (0.192x height) + (0.502x weight)

Female: Lean mass =-13.034-(0.018x age) + (0.165x height) + (0.409x weight)

We calculated the BMI by using the formula which comprises of weight and height;

BMI=weight (in kg)/height (meterssquare)

In people with diabetes Sarcopenia, the cause of insulin resistance can be increased lipolytic activity of centrally located adipocytes leading to an increase in fatty acids in the portal venous circulation resulting in decreased total hepatic insulin output causing synthesis/formation of Apo lipoprotein B and lipoproteins. So obesity and Sarcopenia can be the cause of hyperinsulinemia[5].

Present study indicated that 92.6% diabetic patients had abnormal muscle mass and only 7.34% showed normal muscle mass.in case of BMI, 22% of patients were in the normal range while 34.7% were obese.

Moreover a previous study on the collective effects of obesity and lower muscle mass in older adults showed that those patients with sarcopenic obesity have twice the risk of functional disability in daily life activities than those without sarcopenic obesity[11].

Anthropometric measurements have prognostic and therapeutic importance in approximating muscle mass. This can serve as a screening method to become a low cost diagnostic tool for evaluation of Sarcopenia initially in health care centers. After the screening, a confirmatory DEXA-scan helps to support early treatment of Dm[12].

One drawback in the evaluation of muscle mass by anthropometry could be in cases of protein energy malnutrition. The increase of water content with muscle tissues hides the loss of functional muscle proteins[2].

Our study provides baseline data of muscle mass of the diabetic patients visiting JHL. The accuracy of our findings is limited due to personal errors in anthropometric measurements. The individual variability may exist in the measurements, so the measurements should be taken more than once.

CONCLUSION:

- BMI and muscle mass have a significantly linear relationship (p<0.003)
- The direction of the relationship is positive i.e. BMI and muscle mass are positively correlated.

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NEUROLOGICAL COMPLICATIONS OF DENGUE

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ABSTRACT

Introduction: Dengue is a mosquito-transmitted acute viral infection with endemicity in tropical and subtropical areas world over. In the recent past , neurological complications of dengue have been frequently observed. In our this retrospective descriptive analytical study, we report various neurological complications in patients of dengue fever over a duration of last one year.

Materials and Methods: In our study , only confirmed dengue cases with neurological complication; having positive serology (IgM antibody) for dengue , were considered. Patients were recruited from Department of Medicine Jinnah hospital , Lahore ,and a detailed clinical and laboratory assessment including blood count, hematocrit, coagulation profile, biochemical assay, serology for dengue fever and ELISA for HIV and other relevant investigations was done.

Results: Seventeen patients with neurological complications, in association with confirmed dengue infection were observed over the last one year. Twelve of these were male patients and the rest five were female. Five patients were suffering from brachial neuritis, four had encephalopathy, three patients were diagnosed of Guillain Barre syndrome, two patients were having hypokalemic paralysis associated with dengue fever and one had acute viral myositis. Opsoclonus-myoclonus syndrome was also diagnosed in one patient, acute myelitis and acute disseminated encephalo-myelitis in one patient each.

Conclusion: Dengue is associated with neurological complications more commonly than previously considered. Brachial neuritis and Guillain Barre syndrome were also observed in association with dengue fever in this study.

Keywords: Brachial neuritis, dengue fever, myositis, Guillain Barre syndrome, neurological complications

Dengue fever is an acute arboviral infection, transmitted by Aedes aegypti mosquito. It is endemic in tropical and subtropical areas of the world with an approximate 2.5 billion population at risk of infection.[1] Dengue infection is caused by four antigenic serotypes ;DEN-1, DEN-2, DEN-3, DEN-4, belonging to the genus flavi virus.[2] Clinical presentation of the dengue viral infection varies from mild febrile ailment to severe life-threatening situation , like dengue hemorrhagic fever or dengue shock syndrome ,with widespread neurological and systemic complications. The pathogenic mechanisms being proposed are: (1)Neurotropism ; giving rise to encephalitis, meningitis, myositis and myelitis.(2) Systemic complications leading to encephalopathy and hypokalemic paralysis. (3) immune-mediated post-infectious Guillain- Barre syndrome and acute disseminated encephalo-myelitis .

In our this retrospective study, we describe dengue associated various neurological complications observed over the last one year and a comparison with previous literature has also been made.

Materials and Methods:

In our retrospective analytical study, all confirmed dengue cases having neurological manifestations were included. It includes patients admitted in Department of Medicine Jinnah hospital, Lahore from June 2015 to March 2016. The diagnosis of dengue viral infection was established on the basis of positive serum IgM antibody to dengue fever. The qualitative analysis was done by the enzyme-linked immunosorbent assay (ELISA) method using an IgM ELISA Kit, titers were not measured. In order to reconfirm the diagnosis, serum IgM ELISA testing was performed twice in the acute phase with a duration of about one week.

The demographic profile of all the patients was noted, a comprehensive history, clinical evaluation and an extensive neurological examination was performed. Muscle power was noted according to medical research council grading. Patients were examined for systemic complications like hepatosplenomegaly, lymphadenopathy, cardiac, respiratory, gastrointestinal and hematological manifestations. The laboratory investigations hemoglobin level, complete blood count, prothrombin time, activated partial thromboplastin time, serum electrolytes and creatine kinase were carried out. Chest radiography and Electrocardiogram were done in all the patients. Also, In all the patients ELISA for Dengue IgM was performed. In some selected cases, electromyography, electroencephalography, and neuroimaging studies including magnetic resonance imaging of the cranium and spine was performed. In patients of myositis, Muscle biopsy was performed. In patients with encephalopathy/encephalitis, the cerebrospinal fluid analysis was carried out to test IgM antibody for dengue infection and also polymerase chain reaction study for herpes simplex virus and Mycobacterium tuberculosis in the cerebrospinal fluid was performed. The ELISA for human immunodeficiency virus (HIV) was performed in all the patients and in patients with brachial neuritis, serum viral studies were carried out for Ebstein Barre virus and varicella zoster virus. For the exclusion of autoimmune disease, antinuclear antibody, rheumatoid factor and antiphospholipid antibodies were also carried out. At the end of three months, outcome was defined as death, partial recovery; when there was dependence for daily activities , and complete recovery when patient was able to perform activities, independently, for daily living.

RESULTS:

We observed seventeen patients of dengue fever with neurological manifestations which were admitted to Jinnah hospital, Lahore, in last one year.[figure 1]

The age of the patient ranged from 12 to 60

Frequency of different neurological complications in study group
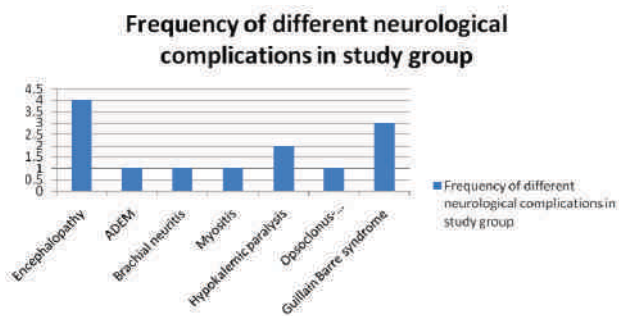
years, with a mean age of 33.05 years. Twelve patients were male and five were female. The demographic and clinical profile of the patients is described as follows

M=Male ,F = Female, DF =Dengue fever, DHF=

Age	Sex	Prior fever	Clinical dengue syndrome	Platlet count/ul	Syndromic diagnosis	Outcome
24	M	Yes	DSS	30,000	Encephalopathy	Death
40	M	Yes	DSS	45,000	Encephalopathy	Improved
37	F	Yes	DF	180,000	Encephalopathy	Improved
43	M	Yes	DF	240,000	Encephalopathy	Improved
12	M	Yes	DF	300,000	ADEM	Improved
17	F	Yes	DF	380,000	Brachial neuritis	Improved
30	M	Yes	DHF	60,800	Brachial neuritis	Improved
25	M	Yes	DF	300,000	Brachial neuritis	Improved
60	M	Yes	DF	380,000	Brachial neuritis	Partial recovery
28	M	Yes	DF	240,000	Brachial neuritis	Partial recovery
30	F	Yes	DF	320,000	Myositis	Improved
29	M	Yes	DF	280,000	Myelitis	Partial recovery
52	M	No	DF	210,000	Hypokalemic paralysis	Improved
24	M	Yes	DHF	50,000	Hypokalemic paralysis	Improved
34	F	Yes	DF	370,000	Opsoclonus-myoclonus syndrome	Improved
21	F	No	DF	320,000	Guillain- Barre syndrome	Improved
24	M	Yes	DF	240,000	Guillain- Barre syndrome	Improved
32	M	Yes	DF	300,000	Guillain- Barre syndrome	Improved

Dengue Hemorrhagic fever, DSS= Dengue shock syndrome.

In our study , a wide spectrum of neurological manifestations was observed involving almost all parts of nervous system. We classified our observation into three groups, based on the possible pathogenic mechanisms: (1) Neurotropism ; giving rise to encephalitis, meningitis, myositis and myelitis.(2) Systemic complications leading to encephalopathy and hypokalemic paralysis . (3) immune-mediated post-infectious Guillain- Barre syndrome and acute disseminated encephalomyelitis

Regarding general complications, two patients had dengue hemorrhagic fever, two were suffering from dengue shock syndrome and all the rest had dengue fever. Two patients had petechial rash (11.7%). Thrombocytopenia was observed in three patients (17.6%). Hepatosplenomegaly was observed in one patient and renal failure with high blood urea and serum creatinine in two patients. In neurotropic complications, we had four patients of encephalitis, one patient had myelitis and one patient was observed to be having myositis. Among systemic complications, we managed two patients of hypokalemic paralysis and, as far in immune-mediated complications, five patients had brachial neuritis, one patient had Acute disseminated encephalomyelitis, three patients were observed to be having Gulliain barre syndrome and one patient was diagnosed to be having opsoclonus myoclonus syndrome.

We had four patients with dengue encephalitis; among them almost all had fever, headache and myalgia for the initial 3–5 days followed by the development of seizures and altered mental status. Two patients were observed having dengue shock syndrome and severe thrombocytopenia. CSF analysis showed normal findings in two and pleocytosis (30–40 cells, all lymphocytes) in the remaining two patients. All the four patients were tested to be positive for serum IgM antibody for dengue infection but only two tested positive for the CSF IgM antibody.

One patient presented with manifestations of acute myelitis. He presented with a 5-day history of severe acute quadriparesis with bowel and bladder involvement. MRI of the cervicothoracic spine demonstrated hyperintense signals on T2-weighted images extending from the lower cervical spinal segments till the midthoracic segments of spinal cord.

One patient manifested acute myositis. He presented with severe myalgia and progressive both upper and lower limbs muscle weakness, predominantly in symmetrical, proximal manner. He had

elevated temperature and on palpation calves were tender. Serum creatine phoshpokinase was markedly elevated. EMG(Electromyography) demonstrated a myopathic pattern. Muscle biopsy illustrated inflammatory cells on the histopathological examination.

Three patients (17.6%) patients were diagnosed to be having a Guillain barre syndrome. One of them had markrd respiratory involvement and required prolonged ventilatory support. Neurophysiological studies demonstrated acute sensory motor axonal neuropathy (ASMAN) in two patients and demyelinating changes were observed in the remaining one patient.

One patient manifested features suggestive of acute disseminated encephalomyelitis. He had high grade fever, severe generalized headache and vomiting from the last 6 days followed by the onset of progressive deterioration of the mental status with an episode of seizure. On examination, he was vitally stable and was stuporous. There was spasticity present in all four limbs with brisk deep tendon reflexes and upgoing plantars. MRI of the cranium and cervical spine depicted mutifocal lesions on T2-weighted images which were predominantly involving white matter.

There were five patients in the study who presented with acute onset of proximal weakness of the upper limb. There was a history of mild to moderate pain in the shoulder region. In these five patients, the diagnosis of brachial neuritis was established. There was a history of febrile illness and in all patients, dengue serology was positive. Age ranged from 17 to 60 years (mean age, 32 years). Of them, four patients were male. The average duration between subsiding of dengue infection and onset of clinical features of brachial neuritis in the form of neuralgic pain, weakness of proximal musculature and atrophy in the upper limbs was 12.65 days. Four out of five patients had right upper limb involvement. Neurophysiological evaluation revealed axonal changes in three patients and demyelinating abnormality in the remaining two

patients.

Hypokalemic paralysis associated with dengue fever was observed in two patients. Both patients were male and had presented with an acute onset of quadriparesis with 0–1/5 power (Medical Research Council grade) over a span of 3-4 days. Both had a severe degree of hypokalemia with serum potassium ranges from 1.0 to 2.1 meq/L. Electrocardiogram demonstrated features suggestive of severe hypo-kalemia as manifested by the presence of U-wave.

Figure: *ECG of the patient demonstrating U-waves*
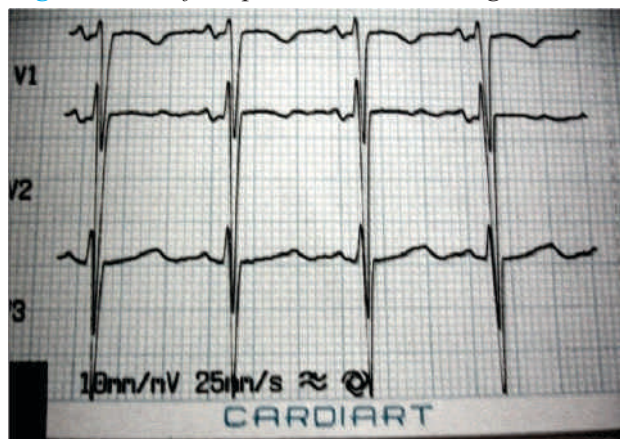
suggestive of hypokalemia

Opsoclonus myoclonus syndrome was confirmed in one patients associated with dengue fever. It was a female patient who presented with gait ataxia with bilateral conjugate multivectoral eye movements suggestive of opsoclonus. Cerebrospinal fluid analysis and MRI of the cranium were normal.

Treatment and outcome:

All the patients were given primarily a symptomatic treatment with maintenance of fluid and electrolyte imbalance. Patients of myelitis, ADEM, brachial neuritis and myositis were given intra-venous methylprednisolone and oral prednisolone. Patients of hypokalemic paralysis were given potassium supplementation in the standard regimen. Intravenous Ig in standard dose of 0.4 gm/kg/day for a duration of 5 days for Guillain barre syndrome patients and clonazepam was given to patients having opsoclonus myoclonus. Antiepileptics and other supportive management was done for the patients having seizures and encephalopathy.

Of four encephalopathy/encephalitis patients, one could not be saved. All patients of ADEM, myositis, hypokalemic paralysis, Guillain barre syndrome and opsoclonus myoclonus had complete recovery. Partial recovery with residual disability was present in one patient having myelitis and in two patients of brachial neuritis.

Figure: *Outcome of patients having neurological*

Neurological Complications(no. of patients)	Outcome		
	Improved	Partial recovery	Expired
Encephalitis/Encephalopathy(4)	3	-	1
ADEM (1)	1	-	-
Brachial neuritis (5)	3	2	-
Myositis (1)	1	-	-
Myelitis (1)	-	1	-
Hypokalemic paralysis (2)	2	-	-
Opsoclonus-Myoclonus syndrome (1)	1	-	-
Guillain-Barre syndrome(3)	3	-	-

complication in dengue fever

Discussion:

In our current study, an entire spectra of neurological manifestations in relevance to dengue fever, were observed. Patients belonged to all age with a male predominance as per the demographic profile was concerned. Among the previous studies, age ranges mentioned were 18-35 years (mean 27 years) and 5-65 years with a male predominance in relation to dengue associated neurological complications.[3,4] There is no obvious illustration of the incidence of neurological complications in association with dengue fever. All previous related studies are mainly hospital-based and more light has been thrown to the neurological manifestations in recent years. In a retrospective study, Wasay et al, reported six patients with neurological manifestations in relation to dengue fever; five were suffering from encephalitis and one from encephalomyelitis.[4] In a hospital-based study, fourty-one cases of neurological complications in relation to dengue infection , depicting both Central nervous system and Peripheral nervous system manifestations, were observed.[5] In a prospective hospital-based study, Misra et al reported seventeen patients with neurological

manifestations.[6]

In the recent past, numerous neurological complications related to dengue fever have been reported which occur in about 0.5–6% of the cases , leading to significant morbidity and mortality.[7] In dengue infection, both neurotropic and immuno-logical mechanisms are responsible for neurological manifestations. In some patients of dengue encepha-litis, dengue antigen has been detected in the brain.[9] Dengue encephalopathy could be caused by cerebral edema, cerebral hemorrhage, hypoxia, hepatic or renal insult. Immune-mediated disorders including Guillain barre syndrome and acute disseminated encephalomyelitis are explained on the basis of autoimmunity and molecular mimicry leading to destruction of the myelin sheath/self-antigens.[3,10]

In our study, we reported four patients of dengue encephalitis. Misra et al. gave the explaina-tion of 11 patients of encephalopathy in relevance with dengue infection.[6] Solomon et al. reported nine patients of dengue encephalitis. The diagnosis was confirmed on the basis of positive antibody to dengue infection in serum along with the clinical manifestation of focal neurological deficits, seizures and cerebrospinal fluid pleocytosis.[8]

We got one patient of opsoclonus myoclonus syndrome associated with dengue fever. Opsoclonus is basically a saccadic stability disorder comprising of involuntary multidirectional high-amplitude arry-thmic conjugate saccades. It is frequently accom-panied by diffuse or local myoclonus and truncal ataxia along with other cerebellar signs. In our patient, opsoclonus myoclonus syndrome ; a rare neurological condition of unknown cause, could be explained on the basis of postinfectious immune-mediated disorder. [11]

In the past few years, in relation to dengue fever a few case reports of acute disseminated encephalomyelitis have been reported. Patient had hemorrhagic demyelinating lesions and in literature it is being explained on the basis of thrombo-cytopenia.[12]

Acute myelitis as a result of dengue fever has been published through some case reports. There was a case report of acute myelitis where the dengue antigen from the central nervous system was isolated. It was a male patient who presented with fever, thrombocytopenia followed by paraperesis acutely. This report suggests that dengue virus has a propensity to direct invasion of the spinal cord, causing myelitis.[13] There has been an infrequent observation related to Guillain barre syndrome in association with dengue fever. There were three patients of Guillain barre syndrome included in our study, acute sensory motor axonal neuropathy in two patients and acute inflammatory demyelinating polyneuropathy in one patient. In a study about seven cases of Guillain barre syndrome associated with dengue-positive IgM antibody in serum, with minimal clinical symptomatology were reported. In the light of this observation, dengue infection should be routinely looked for in Guillain barre syndrome cases in an endemic zone.[14]

We had one patient of dengue myositis with a complete clinical recovery within a duration of 3 weeks. Some studies mentioned involvement of the proximal musculature leading to weakness associa-ted with dengue fever. A similar study reported six patients of motor quadriparesis in association with dengue fever. All of the patients had normal findings on nerve conduction studies, EMG demonstrated a myopathic pattern with raised serum creatine phosphokinase suggestive of acute viral myositis. All of the patients showed improvement on therapy.[6]

In this study, we observed five cases of brachial neuritis in association with dengue fever ,which is a neurological disorder characterized by severe neuropathic pain, weakness and atrophy of the proximal musculature, predominantly involving the upper limbs, due to involvement of the brachial plexus. The various causative factors considered are viral infections, immunization and autoimmune disorders.[14] Thus, post-dengue infection an autoimmune response against myelin sheath or other self-antigens causing brachial neuritis due to patchy

demyelination of brachial plexus was hypothesized.

Hypokalemic paralysis has also been recently reported in association with dengue fever. We had two patients who developed acute pure motor quadriplegia with positive serology against dengue fever. All had significant low serum potassium values and improved dramatically with potassium supplementation. Various mechanisms described in the literature leading to hypokalemia are: (b) transient renal tubular abnormalities leading to increased urinary potassium wasting (a) redistribution of potassium into the cells and (c) increased catecholamine levels secondary to infections, secondary insulin resistance leading to intracellular shift of potassium.[15]

Thus in order to evaluation and investigations for dengue virus infection it may involve detection of the virus, viral nucleic acid, antigens or antibodies (serology). In the initial 4–5 days, virus detection by culture, viral nucleic acid or antigen detection (NS 1) can be used to confirm dengue infection. However, after early acute phase, serology is preferred.

Hence, dengue infection should be considered in patients presenting with various neurological disorders without obvious etiology and should be investigated, especially if preceded by a febrile illness compatible with dengue fever.

Conclusion:

Dengue fever is an emerging disease and has significant public health problem worldover. Neurological complications of dengue infection are widespread and may involve almost all parts of the nervous system through various pathogenetic mechanisms. In this study, we had described a wide spectra of neurological complications of dengue fever: Opsoclonus myoclonus syndrome, brachial neuritis, encephalitis, meningitis, myositis, myelitis, encephalopathy and hypokalemic paralysis, Guillain- Barre syndrome and acute disseminated encephalomyelitis , thus, depicting involvement of almost all parts of nervous system.

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INSOMNIA AND CO-MORBIDITYAMONG MEDICAL STUDENTS.

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Abstract

Objective: To determine the frequency of physical and psychiatric co morbidity among insomniac medical students.

Design: Cross sectional research design.

Setting: Department of Psychiatry and Behavioral Sciences, JPMC and Jinnah Sindh Medical University, Karachi

Methodology: This study was carried out on 109 purposively selected insomniac medical students of 18-25 years old, enrolled in first to final year MBBS. Diagnosis of Insomnia has been made according to ICD 10 criteria checklist. Athens insomnia scale was used to assess severity of insomnia. Only those participants who have scored >6 were included in the study. Data analysis was done through SPSS version 20. Mean was calculated for continuous variables whereas frequency with percentage was calculated for categorical variables. Cross tabulation analysis was used to evaluate the association of severity of insomnia with study years of participants and co morbid disorders.

Results: The age of participants ranged from 18-25 years with mean age of 20.93 years. Mean insomnia score was 12.60 ranging from 06 to 17 on the Athens insomnia scale (6 to 24 maximum). Majority of insomniacs were females (87.12%). Mild insomniac students were 75.2% (n=82), moderate & severe insomniac were 21.1% (n=23) & 3.7% (n=4) respectively. Most common co morbid conditions were substance abuse, asthma, worm infestation, depression and hypertension. Other less common were hyperthyroidism and schizophrenia.

Conclusion: Physical and psychiatric co morbidities are very common among insomniac medical students. Pharmacological, behavioral therapy of insomniacs in addition to modification in study settings of the medical students are required.

Key words: psychiatric co morbidity, insomnia, medical students.

Every living being including humans on this planet spend almost one third of their life span in sleeping. Many theories describe this physiological phenomenon of lying inactive and unaware of surrounding as very crucial and utmost important for our survival and physiological and mental health.[1] Regular absence of restful sleep is called insomnia. The affected person has trouble falling asleep, staying asleep or waking up too early. It is the most commonly reported sleep disorder. About 30% of adults have symptoms of insomnia in the world. Epidemiological studies performed in Western Europe, USA and Japan has reported a prevalence of insomnia related symptoms ranging from 10% to 48%. As many as 95% of Americans have reported an episode of insomnia at some point during their

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lives.[2,3]

Psychosocial, medical or psychiatric conditions may precipitate insomnia, which suggests that those individuals have an inherent susceptibility to develop insomnia in the context of a stressful event. These factors are likely to be genetic and neurobiological in nature.[4] Insomnia appears to be predictive of a number of disorders, including depression, anxiety, alcohol dependence, drug dependence, and suicide.[5] Schizophrenia and the manic phase of bipolar illness are frequently associated with insomnia. [6]

Insomnia can affect all age groups. It can lead to obesity, poor immune system function, reduced reaction time, poor performance at work or school and an increased risk and severity of long-term illness.[7] Prevalence of all psychiatric disorders is higher in individuals affected by insomnia.[8,9] A recent study conducted in Virginia, USA reported that insomnia in college student is highly prevalent. Over 60% of the college students in the study were having a poor sleep as analyzed by Pittsburgh Sleep Quality Assessment (PSQI), only 29.4% of students reported getting 8 or more hours of total sleep time per night. Twelve percent of poor quality sleepers reported missing class three times or more in the last month because of illness, compared to less than 4% of borderline or good-quality sleepers.[10]

Medical students all over the world face a great deal of stress due to long schedules of concentrated study. This toughness of daily life makes them susceptible to insomnia, which further may cause other psychiatric disorders like depression. Association of insomnia with medical studies has been very rarely studied. This, if superimposed by a medical or psychological co morbid condition, may lead to synergistically severing of situation.[11] Insomnia may have a deep social impact both in terms of direct and indirect costs among medical students. Direct costs involve diagnosis and treatment, whereas indirect costs include loss of their studies, concentration and bad patient care in practical life.[12]

The adult and elderly patients have been found to suffer from insomnia because of coexisting medical conditions like cardiovascular disease, cancers, neurologic disease, breathing problems, but studies on medical students regarding association of medical disorders and insomnia have not been found in Pakistan. Insomnia assessment may be a good tool for the identification of suspected cases of mental disorders in medical students for further diagnostic confirmation and prevention, because early treatment might halt progression to full manifestation of mental disorder.[13] Thus there is a need to study in this matter that whether insomnia is due to studies only or any other psychiatric co morbid condition is also associated with these.

Methodology

Considering the prevalence of insomnia in medical student at the rate of 33.5% as reported at the Department of Psychiatry JPMC, the margin of error set @ 5% with 95% confidence level, the sample size calculated was 106 ~110. Ethical committee approval was obtained from JPMC. Initially the participants were approached and written consent was taken from those who were willing to participate. Demographic form consisted of age, gender and data regarding co morbidity of disorders. Diagnosis of insomnia was made according to ICD-10 criteria checklist. Athens Insomnia Scale was used to measure the severity of insomnia. Score on each item of "Athens Insomnia scale" was added to get one summary measure (possible score 0 to 24). Only those having score 6 or more were included for further analysis. Mild Insomnia score ranged from 6-10, moderate insomnia score ranged from 11-15 whereas severe insomnia score ranged from 15-24. Total 109 participants had fulfilled this inclusion criteria. Age of participants varies from 18-25 years of age, enrolled in first year to final year MBBS.

Data analysis was done through SPSS version 20. Mean were calculated for continuous variables. Frequency was calculated for categorical variables.

Cross tabulation analysis was used to evaluate the association of severity of insomnia with study years of participants and co morbid disorders.

Results

Table 1 show that respondents of age 18-19 years were 28 (25.7%), 20-22 years were 56 (51.4%) & 23-25 years were 25 (22.9%). Their age of participants ranged from 18-25 years with mean age of 20.93 years.

Table 2 shows that almost 90 percent of insomniac students were found to have on or other co morbid conditions. Most common of these were substance abuse, depression, asthma, worm infestation and hypertension. Less common were hyperthyroidism and one case of schizophrenia.

Table 3 shows that maximum participants of forth year (n=19) fall in mild category of severity, whereas maximum participants of final year falls in moderate (n=8) and severe (n=2) category of severity.

Table 4 depicts that substance use, asthma, hypertension, hyperthyroidism, worm infestation and depression seems to be related more with mild severity of insomnia whereas substance use, asthma, hyperthyroidism and depression seems to be less associated with severe intensity of insomnia.

Table 1: Age wise Frequency and Percentage distribution of participants

Age Categories	f	%
18-19	28	25.7
20-22	56	51.4
23-25	25	22.9
Total	109	100

Note: f= Frequency, %= Percentage

Figure 1: *Severity of insomnia among medical students*

Figure 2: Gender wise distribution of insomnia medical students.

Table 2: Frequency and percentage of co morbidity of disorders among participants

Co morbidity	f	%
Substance Abuse	30	27.52
Depression	17	15.60
Asthma	16	14.68
Worm infestation	16	14.68
Hypertension	12	11.01
Hyperthyroidism	8	7.34
Schizophrenia	1	0.92

Note: f= Frequency, %= Percentage

Discussion

Insomnia frequently co-occurs with psychiatric and/ or physical disorders and vice versa. This combination of insomnia with physical co morbid contributes much to poor health-related quality of life, impaired social life and limitation of functional
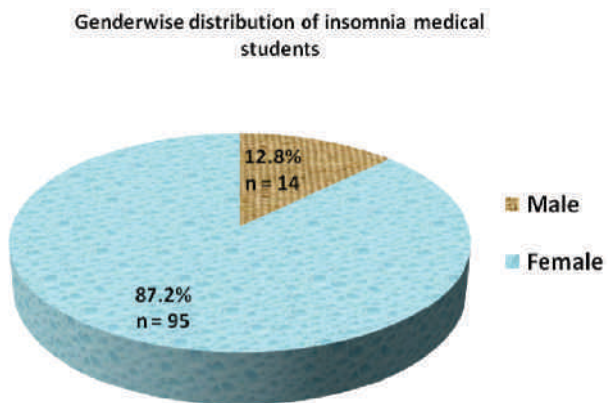
Table 3: Severity wise frequency and percentage distribution of participants as per professional study year

Year of study	Insomnia Severity			Total
	Mild	Moderate	Severe	
First Year	14 77.8%	3 16.7%	1 5.6%	18 100.0%
Second Year	18 85.7%	3 14.3%	0 0.0%	21 100.0%
Third Year	14 73.7%	4 21.1%	1 5.3%	19 100.0%
Fourth Year	19 79.2%	5 20.8%	0 0.0%	24 100.0%
Final Year	17 63.0%	8 29.6%	2 7.4%	27 100.0%
Total	82 75.2%	23 21.1%	4 3.7%	109 100.0%

activity.[7,14] Insomnia has been associated with a variety of medical conditions, including asthma, hypertension cardiac disease, thyroid problems, migraine, musculo skeletal conditions and prostate problems. Insomnia is also strongly associated with psychiatric disorders, particularly mood disorder,

Table 4: *Severity wise frequency and percentage distribution of participants as per co morbid conditions*

Co morbid	Insomnia Severity			Total
	Mild	Moderate	Severe	
Substance Abuse	23 67.76%	6 20%	1 3.33%	30 100%
Asthma	11 68.75	4 25%	1 6.25%	16 100%
Hypertension	8 66.67%	4 33.33%	0 0%	12 100%
Hyperthyroidism	5 62.5%	2 25%	1 12.5%	8 100%
Worm infestation	14 87.50%	2 12.50%	0 0%	16 100%
Depression	14 82.35%	2 11.76%	1 5.88%	17 100%
Schizophrenia	0 0%	1 100%	0 0%	1 100.0%

substance use, anxiety and depression.[8,15]

Different studies have documented that in general populations, as much as 50% of insomniac adults have high incidence of physical health & psychiatric disorders.[8,15, 16,17] A study in Pakistan on general population found that 46.3% of insomniacs had some form of physical co morbid (p value <0.001) while 57.8% had psychological distress

Severity of insomnia among medical students

factors (p value <0.001).[18]

Besides the general population, a group that appears to be at increased risk for sleep deprivation and associated co morbid is the medical students. A previous study conducted at JPMC Karachi reported

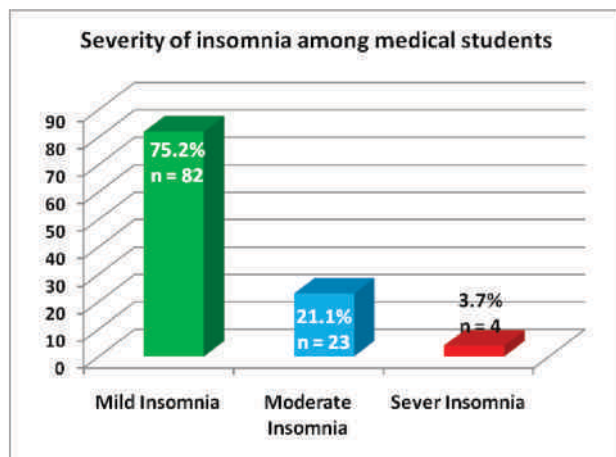Genderwise distribution of insomnia medical students

that prevalence of insomnia among medical students was 33.5%.[18] The current study evaluated insomniac medical students to explore the prevalence and association of physical and psychiatric co morbid conditions.

It was found in this study that a vast majority i-e; every three of four insomniac medical students have one or other co morbid disease. Most of these were physical co morbid like substance abuse, asthma, hypertension, hyperthyroidism, and worm infestation. Psychiatric co morbid included depression. Loayza et al. in a study found that 28.15% of sampled medical students were insomniac while prevalence of psychiatric disorder was 22.19% (overall 78.82%) among insomniac medical students.[12] Other studies like Sajwani (2009) and Bin (2012) are in match with the current study.[19,20] Whereas; Ellet (2006) found that as much as 30.6% insomniac medical student had symptoms of depression and among them 34.9% were females and 16.5% were males[21]. The current study also found that female gender had more prevalence of insomnia (P value = 0.0001). A study by Hidalgo MP, et al.[22] reported that insomniac medical students were 2.45 times more prone to have a psychiatric disorder than normosomnic medical students. Thus; overall we can comment that medical students are very much prone to insomnia and subsequent psychiatric disorders.

There is little evidence from Pakistan regarding insomnia in medical students. A local study conducted in Karachi in Agha Khan University revealed that academic performance of >90%

students were severely affected by sleep disturbances resulting in stress & ill health.[23] However the actual burden of the physical or psychiatric co morbid was not given.

Abdallah (2014) reported that in first year medical students depression was significantly associated with the physical co morbid like frequent drinking of coffee and tea (p value = 0.007) and presence of insomnia (P value < 0.001).[23] In another two studies on medical students in two different universities taking account of insomnia it was found by the researchers that a large number of students reported an increase in caffeine intake after joining their current universities.[24,25] These characteristic substance use was found common among insomniac students in the current study. It was found that insomnia was relatively more common among students of forth and final year. Most of these were using tea/coffee excessively, had asthma and depression as comorbid.

Sometimes insomnia and physical/ psychiatric disorders may give rise to confusion as which started first. Thus, there should be thorough evaluation of both.[26] We found that in most of insomniac students, physical/ psychiatric disorders had been undertreated which may be due to the prejudice concerning mental disorders especially the social circle attitude/ taboos. Also, there may be difficulties in identifying symptoms or in realizing that fact these illness can severely affect students' performance.

Sleep disturbances are strongly associated with psychiatric disorders in students of medical schools. These results are quick glance over the prevailing situation. Detailed work up followed by adequate and suitable intervention should be implemented at the earliest. Currently, the benzodiazepine receptor blockers and sedative antidepressants are the most common treatment for insomnia. Cognitive behavioral therapy for insomnia (CBT) has also been proved to be much effective over last two decades for treating insomnia symptoms[27,28] as well as also useful in alleviating the comorbid psychiatric and physical illnesses.[29]

It is a point of consideration that there is a positive relationship between adequate sleep and physical, social and general health and life satisfaction of medical student especially. The medical students are future doctors and have to deal with the lives of their patients. They need not be in the good health during their education & learning period. If they suffer from sleep deprivation, they may run a major risk of creating serious medical errors.

The current study sample consisted of students of a public sector medical college of a metropolitan city and may considerable differ from those students of private medical colleges or other smaller cities. Further geographic area may also affect the results as well. The strength of study is that standardized questionnaire and diagnostic tools have been used to remove bias. Though the study cannot determine directionality yet it highlights the incidence and importance of the relationships between insomnia and physical/ psychiatric comorbid in medical students.

Conclusion

To the best of our knowledge, the current study is from the preliminary studies of its kind. It was found that physical and psychiatric co morbidities are very common among insomniac medical students. Although direction of association could not be analyzed from this study, yet it highlights the importance of physical and mental health of future healers. It also raises the need of pharmacological as well as behavioral therapy of insomniacs and bringing changes in study settings and attitude of the medical students.

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COMPARISON OF TREATMENT SUCCESS RATE OF MAGNESIUM SULPHATE WITH NIFEDIPINE FOR TOCOLYSIS OF PRETERM LABOUR

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ABSTRACT

Objective: To compare the treatment success rate of magnesium sulphate with nifedipine for tocolysis of preterm labour.

Materials & Methods: This randomized controlled trial was conducted at Department Obstetrics and Gynaecology Sahiwal Medical College Sahiwal from July 2016 to January 2017.A total of 150 patients of preterm labour, 16 to 35 years of age with singleton pregnancy of gestational age between 28 to 36 weeks (assessed on LMP) were included in the study. Treatment success rate of magnesium sulphate with nifedipine was compared.

Results: Mean age of the patients was 25.24 ± 5.27 years. The mean age of women in group A was 25.44 ± 5.35 and in group B was 24.77 ± 5.05 years. Treatment success rate was compared between the group A & B. Out of 75 patients of group A, treatment was found successful in 68 (90.67%) patients and in group B treatment was found successful in 56 (81.11%) patients. Statistically significant difference of success rate between both groups was noted with p value 0.0165.

Conclusion: In present study magnesium sulfate found with higher treatment success rate as compared to oral nifedipine for acute tocolysis of preterm labor. Moreover, magnesium sulfate has also shown better efficacy for younger primigravida females. Magnesium sulfate should be used as a first line tocolytic agent in cessation of preterm labor.

Keywords: Tocolytic agents, preterm birth, Uterine contractions, preterm labor

Preterm labor is a very serious complication of pregnancy. Unfortunately, many women do not understand the signs of preterm labor. Early detection can help to prevent premature birth and possibly enable to carry pregnancy to term or to give baby a better chance of survival.[1]

Preterm birth accounts for 5–10% of all deliveries in developed countries. In the UK about 8% of live born babies are born preterm (less than 37 weeks of gestation). Whereas most of these are born after 28 weeks, about 0.6% are born extremely preterm (22–28 weeks). It is also noteworthy that nearly 53% of the live born multiple births are born preterm (less than 37 weeks).[2]

Preterm labour with intact membrane is responsible for approximately one-third of preterm births, which account for about 70-80% of all neonatal deaths among normally formed neonates.[3] Prematurity often results in significant immediate and long-term morbidity and is related to sepsis, intraventricular hemorrhage, respiratory distress syndrome, bronchopulmonary dysplasia, necrotizing enterocolitis and retinopathy of prematurity.[4]

For the management of preterm labour, many agents like beta-agonists, calcium channel blockers, prostaglandin synthetase inhibitors, nitric oxide donors, and oxytocin receptor antagonists are used.[5]

The primary aims of tocolytic therapy are to delay delivery to allow the administration of a complete course of antepartum glucocorticosteroids

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in order to primarily reduce the incidence and severity of idiopathic respiratory distress syndrome and to arrange in utero transfer to a center with neonatal intensive care unit facilities.[6-7] The secondary aim of tocolytic therapy is to delay delivery to reduce the perinatal mortality and morbidity associated with severe prematurity. [7]

The use of magnesium sulfate as a tocolytic agent was first described by Steer and Petrie in a randomized study of 71 women with preterm labor. Magnesium readily crosses the placenta, achieving fetal steady-state levels within one hour of the start of treatment.[8]

To date, the majority of clinical investigations evaluating the use of calcium channel blockers for the treatment of preterm labor have utilized nifedipine. Ulmsten et al[9] first reported the use of nifedipine for the treatment of preterm labor in a study involving 10 patients, with resultant cessation of uterine activity for 3 days in all patients undergoing treatment.

Nifedipine can be administered orally or in sublingual form. It is rapidly absorbed by the gastrointestinal tract, with detectable blood levels attained within 5 minutes of sublingual administration.[10]

As preterm birth is associated with high perinatal mortality and morbidity, so we have conducted a study to see which drug is more effective and rapid as acute tocolytic agent for at least 48 hours or more in preterm labour in local population. Then based on these results, some practical recommendations could be made in our routine practice for preterm labour management and some benefit could be gained from prolongation of pregnancy by enabling corticosteroid administration to accelerate fetal lung maturation which would help us to reduce perinatal mortality and morbidity of both mother and fetus.

MATERIAL AND METHODS:

This randomized controlled trial was conducted at Department Obstetrics and Gynaecology Sahiwal Medical College Sahiwal from July 2016 to January 2017. Total 150 patients with Preterm Labor having age range from 16-35 years, gestational age 28-36 weeks, Single normal fetus with cephalic presentation and patients with Regular painful uterine contractions about 3 in 10 minutes and cervical dilatation < 4cm with intact membranes were selected for this study.

Patients with systemic disease, patients who have severe intra-uterine growth retardation (IUGR), fetal distress and antepartum hemorrhage, cervix > 4cm dilated, rupture of membranes, congenital fetal malformations, chorioamnionitis and multiple pregnancy and patients with contraindication to nifedipine (allergy to nifedipine, maternal cardiac disease, hypotension <90/50 mmHg), and contraindications to Salbutamol (cardiac disease, hypertension were excluded from the study.

After a patient had given informed consent for participation in the study, all the selected patient were randomly divided into two groups A and B.

In the Group A, magnesium sulfate was given intravenously in a loading dose of 4 grams over 15 minutes, then a maintenance dose of 2-3 grams/hr IV infusion until uterine contractions were inhibited or side effects were became intolerable. While in Group B patients, nifedipine was given as 30 mg tabletstat if uterine contractions were not stopped within 20 minutes, then 30 mg tablet was repeated. If there was no response then after 30 minutes, another 30 mg was given. After this, nifedipine was continued 30 mg twice a day for further 5 days.

Efficacy was measured in terms of cessation of uterine contractions in preterm labor. If uterine contraction were ceased till 48 hours after the start of treatment, it was regarded successful otherwise labeled as unsuccessful. Findings were recorded in predesigned proforma along with demographic profile of the patients.

All the collected data was entered in SPSS version 16 and analyzed. Mean and SD was calculated for age and gestational age. Efficacy rate of treatment was presented as frequency and percentage. Comparation of efficacy rate between

both groups was analyzed by using chi-square test and p value ≤ 0.05 was considered as significant. Effect modifiers were controlled by stratification of data in terms of age, gestational age and parity. Post-stratification chi-square was applied to see the effect of these on outcome variables and p-value ≤0.05 was taken as significant.

RESULTS:

Total 150 patients with Preterm Labor having age range from 16-35 years were selected for this study. Mean age of the patients was 25.24 ± 5.27 years. The mean age of women in group A was 25.44 ± 5.35 and in group B was 24.77 ± 5.05 years. Treatment success rate was compared between the group A & B. out of 75 patients of group A, treatment was found successful in 68 (90.67%) patients and in group B treatment was found successful in 56 (81.11%) patients. Statistically significant difference of success rate between both groups was noted with p value 0.0165. (Table 1)

Patients were divided into two age groups i.e. age group 16-25 years and age group 26-35 years. Out of 50 patients of age group 16-25 years, treatment success was noted in 45 (90%) patients of

Table 1: *Comparison of treatment success rate between the two groups*

| Study Group | Success rate | | Total | P. Value |
	Yes (%)	No (%)		
A (magnesium sulfate)	68 (90.67)	7(9.33)	75	0.0165
B (nifedipine)	56 (81.11)	19(18.89)	75	

group A and out 48 patients of group B treatment success was noted in 35 (72.92%) patients. Difference of success rate between group A and B was statistically significant with p value 0.0375.

Total 25 patients of group A 27 patients of group B was belonged to age group 26-35 years. Treatment success was noted in 23 (92%) of group A and 21 (77.78%) patients of group B. The difference

of success rate between the group A and B was statistically significant with p value 0.2517. (Table 2)

Total 41 patients of group A and 32 patients of group B were primary paras. Treatment was found successful in 39 (95.12%) patients of group A and in 30 (93.75%) patients of group B. Difference of

Table 2: *Comparison between treatment success of both groups according to age.*

| Group | Treatment success | | Total |
	Yes (%)	No (%)	
16-25 years (P= 0.0375)			
A	45 (90%)	5 (10%)	50
B	35 (72.92%)	13 (27.08%)	48
26-35 years (P = 0.2517)			
A	23 (92%)	2 (8%)	25
B	21 (77.78%)	6 (22.22%)	27

success rate between both groups was statistically insignificant with p value 1.00.

Total 34 patients of group A and 43 patients of group B were multiparas. Treatment was found successful in 29 (85.29%) patients of group A and in 26 (60.47%) patients of group B. Difference of success rate between the both group was statistically significant with p value 0.022. (Table 3)

Gestational age was from 28 to 36 weeks with mean gestational age of 31.68 ± 4.24 weeks. The mean gestational age in group A was 32.49 ± 3.75 weeks and in group B was 33.7 6± 3.67 weeks.

Table 3: *Comparison between treatment success of both groups according to parity.*

| Group | Treatment success | | Total |
	Yes (%)	No (%)	
Primary Para (P= 1.00)			
A	39 (95.12%)	2 (4.88%)	41
B	30 (93.75%)	2 (6.25%)	32
Multipara (P = 0.022)			
A	29 (85.29%)	5 (14.71%)	34
B	26 (60.47%)	17 (39.53%)	43

Patients were divided into two groups according to

their gestational age i.e. 28-32 weeks gestation and 33-36 weeks gestation. In 28-32 weeks gestation group, out of 53 patients of group A treatment was found successful in 50 (94.34%) patients. Out of 41 patients of group B, treatment success was noted in 33 (80.49%) patients. Statistically significant (P= 0.0530) difference of treatment success was noted. In 33-36 weeks gestation group, there were 22 patients in group A and 34 patients in group B. success of treatment was noted in 18 (81.82%) patients and 22 (64.71%) respectively in group A and B. But the difference was statistically insignificant with p value 0.230. (Table 4)

DISCUSSION:

Despite the introduction of new diagnostic and therapeutic technologies, there has been little

Table 4: Comparison between treatment success of both groups according to gestational age.

| Group | Treatment success | | Total |
	Yes (%)	No (%)	
28-32 weeks (P= 0.0530)			
A	50 (94.34%)	3 (5.66%)	53
B	33 (80.49%)	8 (19.51%)	41
33-36 weeks (P = 0.230)			
A	18 (81.82%)	4 (18.18%)	22
B	22 (64.71%)	12 (35.29%)	34

reduction in the incidence of preterm birth over the past 30 years. While no treatment has proven highly effective in preventing preterm delivery in women who experience preterm labor, diagnosis at an early stage allows the use of interventions that may delay delivery for 48 hours or more.[11] Tocolytics are drugs given to inhibit uterine contractions. Acute tocolysis is used to decrease or stop uterine contractions and slow or halt cervical change in women during preterm labor. Maintenance tocolysis refers to medication administered after acute tocolysis, in women with arrested preterm labor, to prevent a recurrence of preterm labor.[12]

In this study, we have compared the magnesium sulfate with oral nifedipine in acute tocolysis for at least 48 hours or more in preterm labor patients. The mean age of women in group A was 25.44 ± 5.35 and in group B was 24.77 ± 5.05 years. These results were very much comparable with Taherian AA et al[13] study who had a mean age of 26 years for both groups. In our study, majority of patients were primigravida i.e. Taherian AA et al[13] has also shown 50.05% primigravida in their study. So, the results of our study had shown the increase risk of preterm labor in younger primigravida females. Study conducted by Lyell DJ et al[14] and Glock JL et al[15] have also shown that preterm labor usually develops in younger females & this may be associated with primiparity. The mean gestational age in group A was 32.49 ± 3.75 weeks and in group B was 33.7 6± 3.67 weeks, in this study while Taherian AA et al13had found mean gestational age for magnesium sulfate group as 32.06 weeks and for oral nifedipine group as 32.23 weeks.

Preterm birth is a major contributor to perinatal mortality and morbidity and affects approximately 6-7 percent of birth in developed countries.16-17 No progress had been made over the last two decades in reducing the incidence of preterm birth in the developed countries but some benefits have been identified from prolongation of pregnancy by enabling corticosteroid administration to accelerate fetal lung maturation, and the ability to transfer the pregnant woman to a center with neonatal intensive care unit facilities.[16]

In this study, there was cessation of uterine contractions in 90.67% after magnesium sulfate therapy while oral nifedipine has shown this in 81.11% patients. In a study by NazS et al[18] showed that the efficacy of oral nifedipine as a tocolytic agents in stopping uterine contractions at 48 hours was 74.1% while Kawagoe Y et al.[19] showed that after magnesium sulfate infusion, 90% patients prolonged their pregnancy for >48 hours. Lyell DJ et al[14] in their randomized trial has shown opposite results as compared to this study i.e. 38.6.8% patients in nifedipine group and 49.2% patients in

magnesium sulfate group delivered before discharge in the first 48 hours (primary tocolytic effect). Forty eight percent patients in the nifedipine group and 38% patients in the magnesium sulfate group postponed delivery for more than 48 hours (secondary tocolytic effect). Glock JL et al[20] in their comparative trial had found that both these drugs were equally effective in arresting labor and delaying delivery > 48 hours, 92% versus 93%.

So, this study concluded that magnesium sulfate was associated with higher efficacy for acute tocolysis of preterm labor as compared to oral nifedipine and gives some benefit from prolongation of pregnancy by enabling corticosteroid administration to accelerate fetal lung maturation which would help to reduce perinatal mortality and morbidity of both mother and fetus.

CONCLUSION:

In present study magnesium sulfate found with higher treatment success rate as compared to oral nifedipine for acute tocolysis of preterm labor. Moreover, magnesium sulfate has also shown better efficacy for younger primigravida females. Magnesium sulfate should be used as a first line tocolytic agent in cessation of preterm labor.

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GIANT CELL RICH OSTEOSARCOMA….A RARE VARIENT

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ABSTRACT

Osteosarcoma is common osteogenic bone tumorfrequently involving the appendicular skeleton. Giant cell rich osteosarcoma is a rare variant of conventional osteosarcoma which has worse prognosis than conventional osteosarcoma[1,2]. Clinically and histologically giant cell tumor of bone has virtually comparable picture as giant cell rich osteosarcoma and it is very challenging to reach the accurate diagnosis. It is of utmost importance to distinguish between these two entities because of different protocols of treatment followed for both[2].

KEY WORDS: giant cell rich osteosarcoma, giant cell tumor of bone, worse prognosis.

Osteosarcoma is common osteogenic bone tumor. Its incidence is 4-5 per million population[3]. Osteosarcoma does not show any association with ethnic group or race[3]. It has bimodal age distribution. First peak is seen in between 10 and 25 years of age. Another peak age incidence occurs after 40[4]. Most of the time second peak is seen in association with radiation exposure or paget disease of bone[5]. There is a slight male predominance. Ratio of effected male over female is 3:23. Most preferred location for osteosarcoma is metaphyseal area of long bone. A few cases in diaphysis and rarely in epiphyses has been reported. Less commonly osteosarcoma of flat bone has been seen[5]. Giant cell rich osteosarcoma is a rare variant of conventional osteosarcoma and comprising 3% of it[2]. Giant cell rich osteosarcoma shows aggressive behavior and worse prognosis as compared to conventional osteosarcoma[1,2].

CASE PRESENTATION:

CLINICAL HISTORY:

A 50 years male patient presented with swelling on left forearm for last 12 years. Swelling was initially small in size and non-tender for which he had consulted some general practitioner but no investigation or intervention was done at that time. Since the last 8 months swelling had increased in size and was painful.

His x-ray displayed a tumor mass involving distal ulna and MRI was reported as giant cell tumor with sarcomatous change. (figure 1)


Fig. 1:

An incisional biopsy was done. Biopsy shows pleomorphic spindle shaped cells with osteoclast type giant cells and a small focus of malignant osteoid. Biopsy was reported as giant cell rich osteosarcoma. Below elbow amputation of left forearm was done.

We received specimen of left forearm measuring 20cm in length and 34.5cm in circumference. Hand measured 19cm in length 13.5cm in width. There was a tumor in the lower aspect of the forearm measuring 17x10x8cm. Skin over tumor was ulcerated. Tumor was firm in consistency. Serial sectioning of tumor showed grey white necrotic cut surface with areas of hemorrhage. In the tumor bone and muscle weredevastated. Grossly tumor necrosis comprised 70% of tumor mass. (Figure 2)

Figure 2
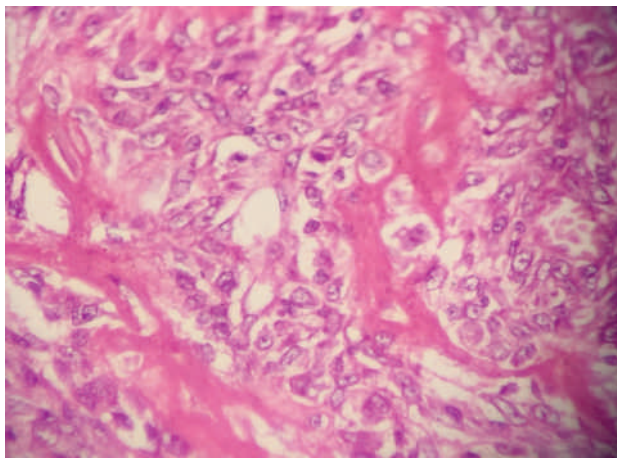
Figure 3
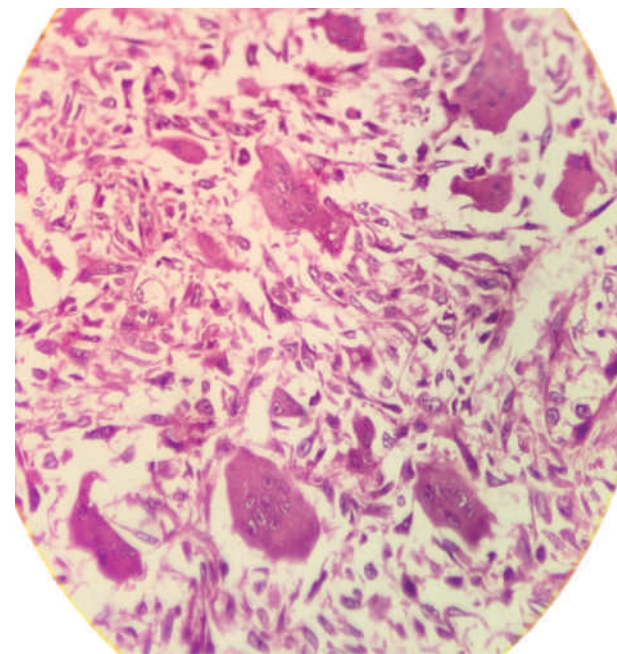
Figure 4

Histologically tumor revealed diffuse sheaths of ovoid to spindle cells with pleomorphic hyperchromatic nuclei. Mitotic count was 13/10HPF. Atypical mitotic figures were also appreciated. Osteoclast type giant cells were irregularly distributed. Necrosis was seen. Multiple areas of malignant osteoid formation were illustrated. Diagnosis was giant cell rich osteosarcoma with involved soft tissue margin. (figure 3 and 4)

DISCUSSION:

Giant cell rich osteosarcoma is a high grade tumor with very aggressive behavior. Osteosarcoma has a bimodal age distribution with a male preponderance. First peak is seen between 10 and 25 years of age. Second peak is seen after 40 years which was most of the time associated with radiation exposure or Paget disease of bone.

Our patient was 40-year-old male and fall in second peak of presentation that is 40 years and above. Osteosarcoma typically presents as painful, progressively enlarging mass. Our Patient had primarily a painless small lesion which became enlarge and was painful from last 8 months. Patients who had presented in the second peak were frequently had a predisposing condition (radiation exposure, Paget disease of bone) that leads to osteosarcoma5. Few case reports are accessible regarding the late malignant transformation of giant cell tumor of bone to osteosarcoma6. Our patient had no preceding history of radiation exposure. Patient had a history of some bone swelling since 12 years which was non-tender. In case of Paget disease most of the time patient stayed asymptomatic or had some localized abnormal structure of bone that cause no problem. If the patient is symptomatic than most frequent symptom is bone pain[7,8]. In our case there was probability that osteosarcoma may developed in preexisting Paget disease which had presented as abnormal structure of bone that had not caused any problem. But serum alkaline phosphate levels and radiological investigation had not done at the time of initial presentation. Radiologically osteosarcoma

displayed a lytic sclerotic mass with elevation of periosteum and prominent periosteal reaction (codman triangle)[4]. In our patient x-ray exhibited a tumor mass of distal ulna while on MRI giant cell tumor with sarcomatous change was appreciated. In our case MRIresults were superior to x-ray. Microscopically giant cell rich osteosarcoma revealed malignant mononuclear cells, unevenly distributed giant cells and malignant osteoid. These microscopic findings are particular for conventional osteosarcoma- giant cell rich variant. In our case microscopy of tumor exhibited sheats of ovoid to spindle cells with pleomorphic hyperchromatic nuclei. Many mitotic figures with atypical ones were appreciated. Many osteoclast type giant cells were erratically distributed. Areas of necrosis were also appreciated. Multiple areas of malignant osteoid production were present.

Giant cell rich osteosarcoma must be distinguished from giant cell tumor of bone. Giant cell tumor of bone occurs in an advanced age with histological picture showing spindle shaped cells and evenly distributed osteoclast type giant cells[9]. Treatment is intralesional curettage with or without adjuvant therapy[4]. These tumors have increased chances of recurrence with rare metastasis. Giant cell rich osteosarcoma expresses pleomorphic spindle shaped cells, irregularly dispersed osteoclast type giant cells and malignant osteoid. It necessitate multimodal treatment comprising of neoadjuvant chemotherapy with resection of tumor. It has increased likelihood of metastasis with poor prognosis. Some other giant cell rich tumor also include in the differential diagnosis such as malignant fibrous histiocytoma displaying storiform pattern with malignant component of reactive histyiocytes[9]. It is difficult to differentiate giant cell rich osteosarcoma from other giant cell rich tumor particularly giant cell tumor of boneespecially on small biopsies. Careful histological examination is essential to discriminate giant cell rich osteosarcoma from other giant cell rich tumor for targeted better management.

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