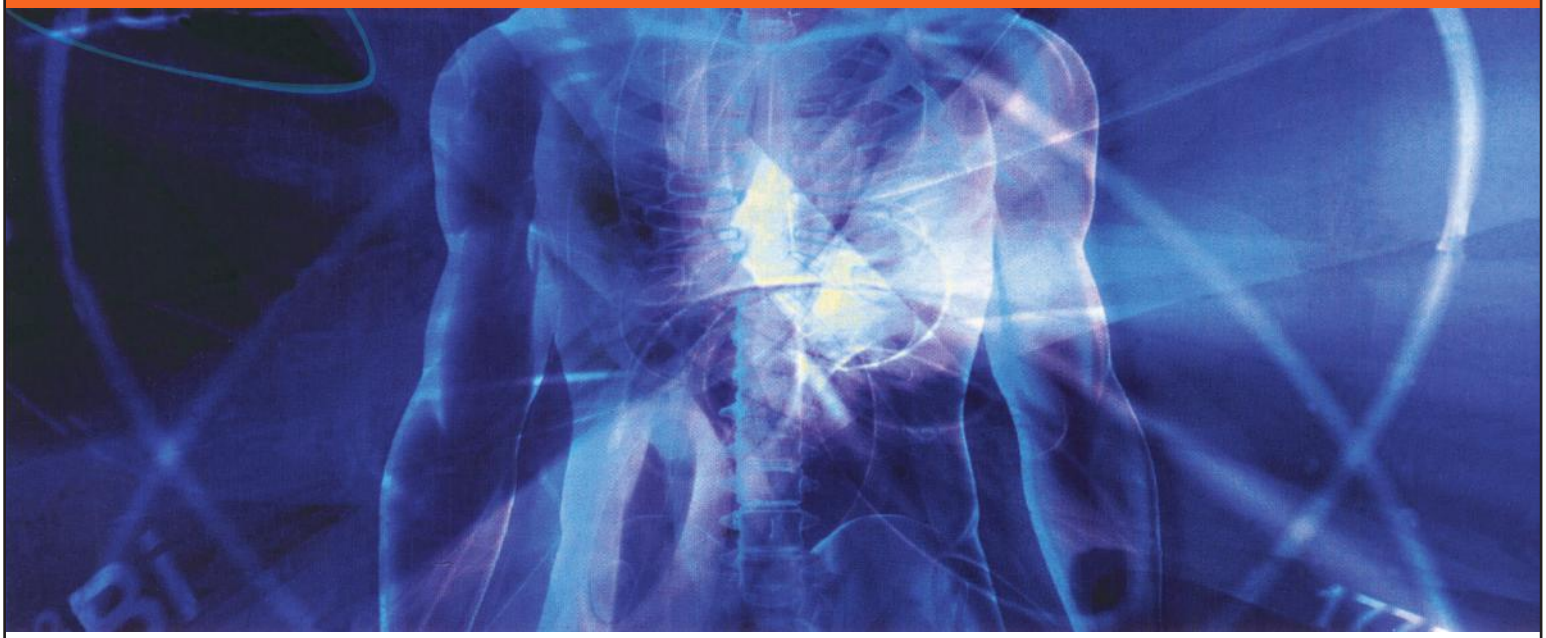
Volume-5, Issue-4, October-December, 2015

ISSN: 2220-7562

JBUMDC

Recognized by PMDC

The Journal of Bahria University Medical and Dental College



Bahria University Medical & Dental College,
Adjacent PNS Shifa, DHA Phase II, Karachi.

JBUMDC **ISSN 2220-7562**

The Journal of Bahria University Medical and Dental College Karachi, Pakistan

Peer Reviewed Multidisciplinary Quaterly Published Journal Indexed with PakMediNet

CONTENTS Volume-5, Issue-4, October-December, 2015

EDITORIAL

Towards Academic Culture in Pakistan: Role of Medical Conference and How Challenging it is to Survive with Evolving Technology Advancement 155
Nighat Huda

REVIEW ARTICLE

Assessing Breast Cancer Incidence and Risk Factors from 2005-2015 in Pakistan 157
Madeeha Nisar, Tahira Zamir

ORIGINAL ARTICLES

1. Effect of Methanol Extract of Brassica Oleracea on Body Weight and Hematological Parameters in Rabbits 162
Tahira Zamir, Ishrat Younus, Talea Hoor, Rabia Arshad
2. Seronegative Rubella IgG Status in Pregnant Women Visiting Tertiary Care Hospital 167
Atifa Afsheen Sharique, Muhammad Sharique, Asha Mahesh, Syed Wajahat Shah
3. Effect of Green Tea Consumption on HDL-Cholesterol 171
Khalid Niaz, Ejaz Fatima, Gulshan Ara Jalbani, Shah Murad
4. Effects of Ethmoid Surgery on Proptosis and Vision 174
Masood Akhtar, M Saleem Sheikh, Maroof Aziz, M Asim Shafique, M Maroof
5. Dental Students' Perception on Preclinical Operative Dentistry Course 178
Meisha Gul, Shama Asghar, Zara Sami
6. Role of Sonography in Prenatal Evaluation of Placenta Accreta 184
Rahila Usman, Sumayya Fatima, Sadia Rashid, Sehrish Mehmood, Kashif Shazlee, Kamran Hamid
7. Methotrexate in Rheumatoid Arthritis: Effect on Blood, Liver and Renal Laboratory Parameters 187
Fuad Shaikh, Rabia Arshad, Fahad Azam, Nasim Karim
8. Knowledge, Attitude and Practice Regarding Smokeless Tobacco among Adolesence of Two Private Schools of Gadap Town Karachi 191
Mahwish Bano, Asghar Ali, Muhammad Ali Leghari, Samreen Mazhar
9. Association between Obesity and Low Serum Vitamin D Concentrations in Healthy Adult Females: A Public Health Perspective 196
Khola Noreen, Nadia Khalid, Imran Shaikh, Rabia Anwar

COMMENTARY

New Aspects of β_2-Adrenergic Agonists 201
Touseef Sayyar

STUDENT CORNER

Research Day: Department of Community Health Sciences (CHS), BUMDC 203
Imran Shaikh, Nadia Khalid, Khola Noreen

CASE REPORT

Ocular Syphilis-Uncommon but not Rare 205
Qamar Ul Islam, Dilshad Ali

LETTER TO EDITOR

Antibiotic Resistance: A Neglected Aspect in Clinical Practice 208
Aamir Hussain

INSTRUCTION TO AUTHORS JBUMDC 209

REVIEWER`S LIST JBUMDC, VOLUME-5, 2015 212

AUTHOR`S INDEX, VOLUME- 5, 2015 213

EDITORIAL

Towards Academic Culture in Pakistan: Role of Medical Conference and How Challenging it is to Survive with Evolving Technology Advancement

Nighat Huda

For years, scientific medical conferences have been the pillar of academic culture development worldwide. In Pakistan as well medical conferences no doubt have become the mainstay of universities, professional institutions, professional associations, and government statutory bodies of higher learning. In the past decade we have seen a dramatic shift in how Conference is positioned within institutions. This may be attributed to the Higher Education Commission(HEC) Pakistan[1] which places strong value to conferences and supports institutions, in particular young researchers to share their results and eventually publish those studies in peer-reviewed journals.Moreover, HEC ranks universities higher on organizing conferences for Pakistani scientists as well as inviting research scholars of international repute.[2]

There is no disagreement on conference purpose; however, several concerns have been expressed on copyright issue related to abstracts, conference presentations,particularly presenters who focus on limited data presentations which become source of publicity by the media.[3]Technological advancement beyond doubt has raised copyright issues particularly when organizers or presenters post presentations on websites for free access.[3] Also with the increased use of power point, researchers have become more focused on preparing slick presentations, which at times fail to differentiate between cited work and original researcher data and conclusion.[4]Realizing the menace of technology, plagiarism software has now been used by universities and journals to check the authenticity of scientific thesis and articles.[5,6]In Pakistan, the Association for Excellence in Medical Education(AEME)[7]in its call for abstracts reinforces the criteria of institutional /ethical review board approval of local institutions that researchers' represent.[8]This is an example of how conference organizers can approach the issue of copyright. The benefits of conferences should not be overwhelmed by copyright issue. Conferences have several other benefits. For example, young researchers find conferences as a source for networking, interaction with national and international experts, while the organizers gain recognition, fame, tax free benefits and not the least additional source of income.[3]There is no harm in such benefits as long as the academic culture of scientific conferences continues to provide a platform for budding researchers.

In Pakistan,in the past decade increasing number of conferences were held on wide ranging specialized medical issues. Despite being a new field of science, in 2015 alone, two separate international conferences were held on Health Professions Education (HPE) or medical education; one was organized by AEME in Islamabad[8] and within a span of eight months second conference was hosted by the University of Health Sciences in Lahore.[9]In both conferences, the format was dominated by keynote speakers presentations and parallel sessions of presenters 'studies on different themes in education. Obviously, these conferences reflect greater interest of Pakistani educators' in recent developments with an impact on future health professions education. But then in such circumstances many educators are compelled to make choice of one conference due to high cost of conference participation expense[10] and secondly, researchers may not have any new studies for submission for the second conference due to limited studies undertaken. Then the stake is high of several papers get repeated if more than one conference are held one within a span of few months. What is suggested is more collaboration among different organizers who should consider innovative strategies that will make room for researchers to participate through online.

Despite the challenges for adopting technology in conferences, this is an exciting time for incorporating technology as it opens the doors for great innovation and overall structure of future conferences. It is evident that virtual conference and mobile applications will continue to push conference organizers to re-examine their existing conference models.[10] Ultimately what we must stay focused on is that this is about promoting academic culture and networking; it is about providing researchers venues to share and accept criticism on their studies. This will have an impact on changing mental model and helping researchers challenge existing ideas and expand their views of the disciplines and the world. The protocols for presentations and publication will support researchers and institution goals.Thus Pakistani researchers as well will benefit from change of the traditional conference model.

✉ **Nighat Huda**
Professor & Director Health Professions Education (HPE)
Liaquat National Hospital & Medical College
Karachi.
Email: huda@lnh.edu.pk
Received: 08-12-2015
Accepted: 10-12-2015

REFERENCES:

1. http://www.hec.gov.pk/Pages/HECMain.aspx. Accessed December 1st , 2015
2. http://www.hec.gov.pk/InsideHEC/Divisions/RND/ConferencesandMeetings/GOSCSW/Pages/Introduction.aspx. Accessed December 1st , 2015
3. Berner, ES. Publications in Academic Medical Centers:

Technology Facilitated Culture Clash. Acad Med 2014. 89;734-7
4. Berk, RA. Research on Power Point: From Basic Features to Multimedia. Int J Technol teach Learn.2011:7;24-35
5. Kleinert S. Checking for Plagiarism, duplicate Publication and text recycling. Lancet. 2011; 377:281-2
6. Acad Med. Editorial Policy, publication, ethics and complete instruction for authors. Revised March 2013, http for authors.aspx. Accessed December 4, 2015
7. http://www.ae-me.org/ Accessed December 4, 2015
8. http://www.ae-me.org/guidelines-abstractsubmission.php. Accessed December 4, 2015
9. http://www.fui.edu.pk/FUIC/index.php/news-items-fuic/item/1-aeme-conference- 2015. Accessed December 4, 2015
10. The scientist and the smartphone.Editorial .Nature Methods 7, 87,2010 doi:10.1038/nmeth0210-87

journals.lww.com/academic medicine/Pages/Instruction

REVIEW ARTICLE

Assessing Breast Cancer Incidence and Risk Factors from 2005-2015 in Pakistan

Madeeha Nisar[1], Tahira Zamir[2]

ABSTRACT:
Carcinoma of the breast is the commonest malignancy in females all over the world and second leading cause of death due to cancer among females. In Pakistan, it is more common at a young age contrary to the west where it is more common after 60 years. Approximately one in every nine Pakistani women is likely to suffer from breast cancer showing an incidence rate of 50/100,000.Incidence of breast cancer is growing at an alarming rate in Pakistan.The main causative element remain unknown yet primary risk factors identified are sex, age, parity, genetics, lack of child bearing, breast feeding, higher hormonal levels individual lifestyle etc. Appropriate planning, prevention and cancer control measures for determination of breast cancer incidence and risk factors must be undertaken.

Keywords: Breast cancer, Incidence, Environmental factors, Genetic factors, Pakistan.

INTRODUCTION:

Breast cancer is a tumor originating from breast tissue, most commonly from the inner lining of milk ducts or the lobules supplying ducts with milk. Breast cancer is differentiated into different types on basis of staging, genetic makeup and aggressiveness. However the exact causative agents remain unknown yet primary risk factors identified are sex, age, genetics, lack of child bearing, breast feeding, higher hormonal levels and individual lifestyle.[1]Carcinoma of the breast is the commonest malignancy in females all over the world and second leading cause of death due to cancer among females. In Pakistan, it is more common at a young age contrary to the west where it is more common after 60 years.[2]All women regardless of their racial or ethnic origin or heritage are at risk of developing breast cancer. Approximately one in every nine Pakistani women is likely to suffer from breast cancer. This is one of the highest incidence rates in Asia. Pakistani women show an incidence rate of 50/100,000 and in the neighboring country India, with similar socio-cultural background the incidence rate is 19/100,000.[3] A pattern of rapid premenopausal increase in breast cancer is also seen in Pakistan, but breast cancer risk plateaus after the age of 45 years.[4]The most pragmatic solution to early detection lies in breast cancer education of women.

✉ **Dr. Madeeha Nisar**
Lecturer
Department of Pharmacology
Bahria University Medical & Dental College
Karachi.
Email: madeehanisar@gmail.com
✉ **Dr.Tahira Zamir**
Assistant Professor
Department of Pharmacology
Bahria University Medical & Dental College
Karachi.
Received: 05-11-2015
Revised: 03-12-2015
Accepted: 05-12-2015

METHODOLOGY:

Using the keywords, breast cancer, risk factor, incidence and Pakistan on search engines google scholar and PakMedinet.com from 2005-2015, a total of 30 studies were found related to breast cancer incidence in Pakistan. Refining the search by using phrases breast cancer epidemiology and incidence of breast cancer in Pakistan curtailed the available number of articles to seven that is 2005(0),2006(2),2007(1),2008(1),2009(0),2010(0) ,2011(0),2012(0),2013(2),2014(1) and 2015(1).

LITERATURE REVIEW:

GLOBOCAN is a comprehensive cancer surveillance database managed by the International Association of Cancer Registries (IARC), whose aim is to calculate incidence and cancer mortality worldwide and prevalence from major type of cancers for 184 countries of the world.[5]According to this worldwide project GLOBOCAN 2012 study, since 2008 breast cancer incidence has increased by more than 20%, while mortality has increased by 14%. Generally, trends show that in developing countries going through rapid societal and economic changes, the shift towards lifestyles typical of industrialized countries is leading to rising burden of cancers associated with reproductive, dietary, and hormonal risk factors. Incidence has been increasing in most regions of the world, but there are huge inequalities between rich and poor countries. Incidence rates remain highest in more developed regions, but mortality is relatively much higher in less developed countries due to a lack of early detection and access to treatment facilities. For example, in Western Europe, breast cancer incidence has reached more than 90 new cases per 100 000 women annually, compared with 30 per 100 000 in eastern Africa. IARC WHO has estimated incidence, mortality and prevalence of breast cancer worldwide in the year 2012 (Table 1).

Table: 1
Breast cancer estimated incidence, mortality and prevalence worldwide in 2012 (IARC WHO) [6]

Estimated numbers (thousands)	Cases	Deaths	5-year prev.
World	1671	522	6232
More developed regions	788	198	3201
Less developed regions	883	324	3032
WHO Africa region (AFRO)	100	49	318
WHO Americas region (PAHO)	408	92	1618
WHO East Mediterranean region (EMRO)	99	42	348
WHO Europe region (EURO)	494	143	1936
WHO South-East Asia region (SEARO)	240	110	735
WHO Western Pacific region (WPRO)	330	86	1276
IARC membership (24 countries)	935	257	3591
United States of America	233	44	971
China	187	48	697
India	145	70	397
European Union (EU-28)	362	92	1444

In 2006 a study was conducted by the Department of Community Health Sciences, The Aga Khan University Karachi on Breast cancer risk factor knowledge among nurses in teaching hospitals of Karachi.[7] They used cross-sectional stratified random sampling with proportional allocation and interviewed a total of 609 registered female nurses with the help of a structured questionnaire adapted from the Stager's Comprehensive Breast Cancer Knowledge Test.[8] Whereas Knowledge of breast cancer risk factors was categorized into good, fair and poor categories by Streiner's method.[9] (Table 2)

Table: 2
Individual items and respective scores assessing knowledge of breast cancer risk factors with percentage of correct responses:

Sr #	Items	Correct Answer	Score	Correct Response %
1	Breast cancer is a communicable disease	No	1	99.2
2	The irritation of a tight bra can over time cause breast cancer	No	1	59.4
3	In some women being overweight increases the risk of developing breast cancer	Yes	1	27.6
4	A woman who bears her first child after the age of 30 years is more likely to develop breast cancer*	Yes	3	50.2
5	Use of oral contraceptives increase a woman's risk of breast cancer	Yes	1	49.6
6	A hard blow to the breast may cause breast cancer later in life	No	1	24.6
7	Most breast lumps are cancerous	No	1	73.7
8	A woman, who has a first blood relative with breast cancer, is at higher risk of developing breast cancer*	Yes	3	57.8
9	Breast feeding increases the chance of breast cancer	No	1	96.4
10	Breast cancer can be a result of a curse/evil eye*	No	2	94.9
	Total		15	

*Key items

This study was undertaken thinking that nurses are the main component for disseminating breast cancer information to the women.[10] They identified whether selected factors among nurses were associated with their knowledge of breast cancer risk factors, so that relevant measures to improve knowledge of nurses could be implemented. It was found that thirty five percent of nurses had good knowledge of risk factors. Graduates from private nursing schools, nurses who had cared for breast cancer patients, those having received a breast examination themselves or those who ever examined a patient's breast had good knowledge in comparison to others. Since only about one-third of the nurses had good knowledge about risk factors, they deducted that

there was a need to introduce breast cancer education in nursing schools apart from medical students particularly in the public sector. Thus continuing nursing education at the workplace can be of additional benefit apart from continuing medical education of doctors.[7]
In 2006, Jamal worked in detail on 141 cases of diagnosed carcinoma (1992-2001), belonging to northern Pakistan. He concluded that 5.9% of these cases had carcinomas in both genders. A male to female ratio of 1:16 was observed. The age group between 50- 60 years was at higher risk. Comparison with their previous similar data showed highly significant increase in breast carcinoma cases in both sexes.[11]
In 2008, Zeb evaluated incidence of cancer in districts of Dir. by tracing the medical records of 1,105 patients registered at the Institute of Radiotherapy and Nuclear Medicine in Peshawar. Zeb concluded that the incidence of cancer was alarmingly increasing, with a mean incidence of 15.04 per 100,000 in 2000-2004. Of the 1,105 patients, 62% were male and 38% were female with affected age range of 41-60 in females.[12]
In 2013, a mini review survey on epidemiology, major risk factors and genetic predisposition for Breast Cancer in the Pakistani population documented that the occurrence of breast cancer is related to genetic as well as cultural, environmental and life-style factors.[13] The mini review narrated that the initial data regarding breast cancer incidence was published by Karachi Cancer Registry in 2000, for population of the Karachi South district from 1995-1997. This data indicated incidence rate for all cancers in Karachi as 91.8 per 100,000 for males and 163.2 per 100,000 for females.[14]The review also mentioned the work conducted by Jamal and Zeb as previously mentioned in their years.
In 2013, another observational study was conducted from the period of 2013-2014. This study described the demographic and clinical features of females presenting with breast malignancies at the Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH & RC), Lahore, Pakistan.[15]This observational study was done through a retrospective review of the medical records of the registered patients. Information was collated on variables recorded from January 2008 to December 2012 (5-years). The clinical features regarding breast cancer included were age at disease presentation, histology, tumor grade, stage of the disease, and hormone receptor status. Grade was classified according to the ICD-O-3 classification.[16] Stage was grouped using the American Joint Committee on Cancer staging schemes.[17,18] In this study, if any other family member had breast cancer, regardless of whether it was a first degree or a second-degree relative, family history of breast cancer was taken as being positive. According to this study 4366 female breast malignancies were recorded. Nearly 80.4% of the patients belonged to Punjab. Mean age at presentation was 48.6 ±12.2 years, at menarche was 13.2 ±1.2 years, and at first childbirth was 23.7 ±4.8 years. Mean Body Mass Index (BMI) was 29.0 ±5.7 kg/m^2. In 60.1%, history of breast feeding was positive. In 55.7%, there was no history of use of any Oral Contraceptive Pills (OCP)/Hormone Replacement Therapy (HRT). Nearly 42.7% were postmenopausal, 85.2% had infiltrating ductal carcinoma, 49.6% had grade 3 tumor, 60.7% had stage II disease, and 37.3% were Estrogen Receptor (ER)/Progesterone Receptor (PR) positive, Human Epidermal Growth Factor Receptor 2 (HER2) negative. Family history of breast cancer was positive in 16.9% of the cases. This is not representative of the population of the country but this large cohort of breast cancer patients from SKMCH and RC represents one of the largest cohorts of breast cancer patients from any single institution in Pakistan. Country wise Age-Standardized Incidence Rates (ASIR) showed that in Iran, the mean age has been reported to be around 51.3 years,[19] whereas, in India, it has been stated to be about 51 years.[20] The mean presenting age in American studies has been documented to be around 54.2 years (African-Americans) and 60.4 years (Caucasians).[21] Additionally, in the United Kingdom, one study has reported the mean age for women to be around 64 years, while in Australia, it has been confirmed to be 60.7 years.[22] Thus it can be concluded that the mean presenting age in this study was found to be lower than what has been recorded in the west.
In 2014,[23] another researcher evaluated the data of breast cancer from various hospitals in Karachi such as Jinnah Hospital, KIRAN (Karachi Institute of Radiotherapy and Nuclear Medicine), and Civil hospital. The data was available for the years 2004-2011. It was found that a total of 5331 new cases of female breast cancer were registered during this period. They analyzed the data in 5-year age groups 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64,65-69, 70-74, 75$^+$. Nonparametric smoothing were used to obtained age-specific incidence curves, and then the curves were decomposed using principal components analysis to fit FTS (functional time series) model[24,25]followed by exponential smoothing stat space models to estimate the forecasts of incidence curve and construct prediction intervals. Analysis on the result showed that the breast cancer incidence rates in Karachi increased with age for all available years. The rates increased monotonically and were relatively sharp with the age from 15 years to 50 years and then they showed variability after the age of 50 years. 10-year forecasts for the female breast cancer incidence rates in Karachi showed that the future rates are expected to remain stable for the age-groups 15-50 years, but they will increase for the females of 50-years and over. Hence in future, the newly diagnosed breast cancer cases in the older women in Karachi are expected to increase.[23]
In 2015, The Pakistan Atomic Energy Commission Cancer Registry (PAECCR) program made the availability of cancer incidence database. Cancer incidence data from nuclear medicine and oncology institutes were gathered and presented for the last 30 years 1984-2014.The data analysis concerning occurrence, trends of common cancers in male and female patients, stage-wise distribution, and mortality/follow-up cases was

also incorporated for the last 10 years (2004-2014). It was found that the incidence of breast cancer was 46.7%. Overall cancer incidence of the thirty years demonstrated that head and neck and breast cancers in males and in females accounts for most of the cases in Lahore, Punjab.[26] This data from a major population of Punjab province could be helpful for implementation of appropriate planning, prevention and cancer control measures and for determination of risk factors within the country. In 2015, another study[27] aimed at finding out the association of various risk factors with breast cancer. They have documented that breast cancer is a health problem with increasing incidence and identification of the risk factors may help in chalking out the future health policies for the prevention of breast cancer. Age was considered as one of the major risk factors for breast cancer with advancing age amplifying the risk of breast cancer[28]. After every ten years the risk for breast cancer doubles until menopause when it declines[29]. Breast cancer patients in this study were comparatively young. The most affected age group at diagnosis for cancer of the breast was 36 to 45 years with median age 43 years which is in accordance with studies carried out in other Asian subgroups i.e., Iranian[30] and Indians[31]. This study data showed that the breast cancer patients and the controls did not differ in age at menarche and menopausal status. Early menarche was considered a risk factor that was not statistically significant in Asian studies.[32, 33] This type of result for Asian studies may be due to the recall bias as most women are illiterate and poor who do not remember their age at menarche. Gajalakashmi[34]and Pakseresht[35] carried out studies on Indians and found no relationship between age at menarche and breast cancer risk. A study on Pakistani females by Gilani[36] demonstrated that early age menarche and menopause at late age are protective. Women with natural menopause at age more than 50 years compared to those having menopause at less than 50 years are at increased risk of developing breast cancer. Ewertz and Duffy[37] also demonstrated an increased risk for women with late menopause. However early age at menopause has also been associated with breast cancer risk[38]. An increase in risk of breast cancer is associated with women who use oral contraceptives[28]. Pervaiz[39] also documented in another Pakistani study that oral contraceptive use is significantly associated with breast cancer.

This study is in agreement with the studies mentioned above and it shows that nulliparous women have more risk of breast cancer as compared to parous women. Earlier local studies mentioned above have established conflicting results contradictory to well-established protective effect of parity concerning breast cancer risk and parity.[36, 40] Our females have more children than do western women, and this is one of the major causes of somewhat low incidence of breast cancer in our women as compared to women in west.

CONCLUSION:

Very few studies have been documented as per available on the specified search engines from 2005-2015 regarding assessment of breast cancer incidence and its risk factors among Pakistani population. Assessment of literature from 2005-2015 showed that breast cancer incidence rates in Karachi is increasing with age for all available years but overall cancer incidence of the last thirty years demonstrated that breast cancer in females accounted for most of the cases in Lahore, Punjab. Appropriate planning, prevention and cancer control measures for determination of breast cancer incidence and risk factors must be undertaken.

It is suggested that the awareness of breast cancer among people should be spread through electronic media, health campaigns, seminars and symposiums. Females should be counseled regarding self-examination of breast, especially all females attending gynecology out-patient departments must be provided awareness regarding breast cancer. Moreover they must be given advice for urgent access to doctor in case they notice any signs of malignancy.

REFERENCES:

1. https://en.wikipedia.org/wiki/Breast_cancer Accessed on November 20, 2015
2. Mahmood S, Rana TF, Ahmad M. Common determinants of Ca Breast: a case control study in Lahore. Ann King Edward MedColl2006; 12:227-8
3. Sohail S, Alam SN. Breast cancer in Pakistan: awareness and early detection. J Coll Physicians Surg Pak 2007; 17:711-2
4. Alexander L, Malik IA, Aziz Z, Rios PD, Kwan E, Narod SA. Contribution of BRCA1 and BRCA2 mutations to breast and ovarian cancer in Pakistan.Am J Hum Genet 2002; 71:595-606
5. http://globocan.iarc.fr/Pages/population.aspx Assessed on November 22, 2015
6. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C et al. Incidence/mortality data: GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer. Available from http://globocan.iarc.fr 2013
7. Ahmed F, Mahmud S, Hatcher J, Khan SM. Breast cancer risk factor knowledge among nurses in teaching hospitals of Karachi, Pakistan: a cross-sectional study BMC Nursing 2006, 5:6 doi: 10.1186/1472-6955-5-6
8. Stager JL: The comprehensive Breast Cancer Knowledge Test: validity and reliability. J AdvNurs1993, 18(7):1133-40
9. Streiner DL, Norman GR: Devising the Items. In Health Measurement Scales New York, Oxford University Press Inc.; 2002:152-7
10. Tessaro I: The natural helping role of nurses in promoting healthy behaviors in communities. AdvPractNurs Q 1997, 2(4):73-8
11. Jamal S, Mamoon N, Mushtaq S, Luqman M. Carcinoma of the male breast: a study of 141 cases from Northern Pakistan. Asian Pac J Cancer Prev. 2006; 7: 119-21
12. Zeb A, Rasool A, Nasreen S. Cancer incidence in the districts of dir (North West Frontier Province), Pakistan: a preliminary study. J Chin Med Assoc. 2008; 71: 62-5
13. Shaukat U, Ismail M, Mehmood N. Epidemiology, Major Risk Factors and Genetic Predisposition for Breast Cancer in the Pakistani Population Asian Pac J Cancer Prev. 2013; 14 (10): 5625-9
14. Bhurgri Y, Bhurgri A, Hassan SH. Cancer incidence in

Karachi, Pakistan: First results from Karachi Cancer Registry. Int J Cancer. 2000; 85: 325-9
15. Badar F, Mahmood S, Faraz R, Yousaf A, Quader AU, Asif H et al. Epidemiology of Breast Cancer at the ShaukatKhanum Memorial Cancer Hospital and Research Center, Lahore, Pakistan, Journal of the College of Physicians and Surgeons Pakistan 2015; 25 (10): 738-42
16. Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM et al. 6th Digit Code for histologic grading and differentiation. In: Fritz A, editor. International classification of diseases for oncology. 3rd ed. WHO Geneva: Switzerland 2000
17. Greene FL, Page DL, Fleming ID, Fritz AG, Balch CM, Haller DG et al. editors. AJCC Cancer Staging Manual, American Joint Committee on Cancer, 6th ed. New York: Springer-Verlag; 2002
18. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, editors. AJCC Cancer Staging Manual, American Joint Committee on Cancer, 7th ed. New York: Springer-Verlag; 2010
19. Mousavi SM, Mohagheghi MA, Mousavi-Jerrahi A, Nahvijou A, Seddighi Z. Outcome of breast cancer in Iran: a study of Tehran Cancer Registry data. Asian Pacific J Cancer Prev 2008; 9:275-8
20. Ali R, Mathew A, Rajan B. Effects of socio-economic and demographic factors in delayed reporting and late-stage presentation among patients with breast cancer in a major cancer hospital in South India. Asian Pacific J Cancer Prev. 2008; 9:703-7
21. El-Tamer MB, Wait RB. Age at presentation of African-American and Caucasian breast cancer patients.J Am CollSurg1999; 188:237-40
22. Gukas ID, Jennings BA, Mandong BM, Manasseh AN, Harvey I, Leinster SJ. A comparison of the pattern of occurrence of breast cancer in Nigerian and British women.Breast 2006;15:90-5
23. YasmeenF, ZaheerS. Functional Time Series Models to Estimate Future Age-Specific Breast Cancer Incidence Rates for Women in Karachi, Pakistan, Journal of Health Science 2014; 2: 213-21
24. Ramsay JO, Dalzell CJ. Some tools for functional data analysis with discussions, Journal of Royal Statistical Society, Series B 53. 1991: 539-72
25. A Kneip, KJ Utikal. Inference for density families using functional principal component analysis, J. Am. Statis. Assoc. 2001; 96(454): 519-32
26. Masood K, MasoodA, ZafarJ, ShahidA, KamranM, Murad S. Trends and Analysis of Cancer Incidence for Common Male and Female Cancers in the Population of Punjab Province of Pakistan during 1984 to 2014, Asian Pac J Cancer Prev. 2015; 16 (13): 5297-304
27. Nazir N, Waheed A, Farhat K, Ismail M, Mansoor Q, Javed G.A case control study of risk factors associated with female breast cancer, Pak Armed Forces Med J 2015; 65(3):391-6
28. Stephen GD, Hoorn AD, Lopez CJ, Murray L, Ezzati M. The Comparative Risk Assessment collaborating group (Cancers). Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. Lancet 2005; 366:1784-93
29. McPherson K, Steel CM, Dixon JM. ABC of breast diseases: breast cancer epidemiology, risk factors, and genetics. BMJ 2000; 309: 1003-6
30. Ebrahimi M, Vahdaninia M, Montazeri A. Risk factors for breast cancer in Iran: a case-control study. Breast Cancer Res 2002; 4(5): R10
31. Gupta P, Sharma RG, Verma M. Review of breast cancer cases in Jaipur region. J Ind Med Assoc 2002; 100: 282-84
32. Ng EH, Gao F, Ji CY, Ho JH, Soo KC. Risk factors for breast carcinoma in Singaporean Chinese women. Cancer 1997; 80: 725-31
33. Rao DN, Ganesh B, Desai PB. Role of reproductive factors in breast cancer in a low-risk area: a case-control study, Br J Cancer 1994; 70: 129-32
34. Gajalakshmi CK, Shanta V. Risk factors for female breast cancer. A hospital-based case-control study in Madras, India.ActaOncol 1991; 30 (5): 569-74
35. Pakseresht S, Ingle GK, Bahadur AK. Risk factors with breast cancer among women in Delhi. Indian J Cancer 2009; 46 (2): 132-8
36. Gilani GM. Statistical aspects of epidemiology of breast cancer in Punjab, Pakistan, in Institute of Statistics. University of the Punjab Lahore: 2003; 231-3
37. Ewertz M, Duffy SW. Risk of breast cancer in relation to reproductive factors in Denmark. Br J Cancer 1988; 58: 99-100
38. Talamini R, Franceschi S, La Vecchia C, Negri E, Borsa L, Montella M. The role of reproductive and menstrual factors in cancer of the breast before and after menopause. Eur J Cancer: 1996; 32A:303-10
39. Parvez T, Anwar MS, Sheikh AM. Study of risk factors for carcinoma breast in adult female general population in Lahore. J Coll Physicians Surg Pak 2001; 11: 291-3
40. Mahmood S, Rana TF, Ahmad M. Common deterninants of CA breast- A case control study in Lahore. Annals of KEMU 2006; 12 (2): 227-8

ORIGINAL ARTICLE

Effect of Methanol Extract of Brassica Oleracea on Body Weight and Hematological Parameters in Rabbits

Tahira Zamir[1], Ishrat Younus [2], Talea Hoor,[3] Rabia Arshad[4]

ABSTRACT:
Objective: To evaluate the effect of methanol extract of Brassica oleracea var. capitata on body weight and hematological parameters in rabbits.
Materials and Methods: The study was conducted on 28 healthy white rabbits of either sex. All animals were equally divided into four groups. Animals of test groups were administered methanolic extract of Brassica oleracae in three different concentrations example 100, 300 and 500 mg/kg body weight respectively for 30 days. Whereas animals of normal control group received normal saline 1 ml/day equivalent to the volume of doses given to test animals. Body weights were recorded weekly on weighing machine. Hematological assay was performed twice once at 16th day and then at the end of dosing that is at 31st day.
Results: Administration of methanolic extract of Brassica oleracae for a period of 30 days resulted in dose dependent gradual decrease in mean body weight. The reduction was significant (6% P value <0.05) at the dose of 300 mg/kg body weight while highly significant (14% P value < 0.01) at the dose of 500 mg/kg body weight. Hematological assay performed at 16th day showed significant decrease in platelet count as compared to the normal control group at the doses of 300 and 500 mg/kg body weight. Whereas the decrease in platelet count was significant (P<0.05) as compared to the control group at the dose of 300 mg/kg body weight while highly significantly (P<0.01) at the dose of 500 mg/kg body weight at 31st. day on hematological examination.
Conclusion: Methanolic extract of Brassica oleracae exhibited weight reducing effect in rabbits and decreased the number of platelets in blood.
Keywords: Brassica oleracae, Body weight, Hematological assay, Rabbits.

INTRODUCTION:

Research on medicinal plants is increasing worldwide showing their vast potential in the field of pharmacology.[1] Various plants have been studied using modern scientific techniques.[2] Presently, these are reported to be used against a wide range of health problems.[3] Natural products have always played a crucial role in the discovery of new biologically active molecules and drug development. It is documented that 25% of all medicines prescribed today are developed from plant source.[4] Brassica oleracea L. var. capitata (Cruciferae) commonly called cabbage is a specie of Brassica. It is an inhabitant of Coastal Southern and Western Europe, near limestone sea cliffs and is similar to other Brassica vegetables in constituents.[5] It is available in wide range of colors like green, red and purple. The most popular types are green, red, savoy and Chinese.[6]Brassica oleracea is commonly used as a vegetable as well as in the therapy of different diseases all around the world.[7] It is stated in the literature to have anticancer, antioxidant , antiplatelet and cholesterol lowering activities.[8] Compounds involved in these actions of Brassica oleracea include isothiocyanates, glucosinolates, phenolics including flavonoids.[9] Brassica oleracea is rich in antioxidant compounds, which regulate immune system and provide protection against various diseases such as cardiac diseases and cancer. Furthermore, it contains caroteine, lutein, and zeaxanthin.[10] Increased body weight can cause many complications in the form of chronic heart disease, diabetes, and stroke.[11] Prior studies have suggested that low-fat, plant-based diets reduce body weight, improve cardiovascular risk factors, provide glycemic control, and, in combination with other lifestyle interventions reverse atherosclerosis.[12] Many plants are recommended in the literature for weight loss. Research should be conducted to find out scientific evidence of these claims on plants.[13] Fresh cabbage juice, prepared either separately or mixed with other vegetables such as carrot and celery, is often included in many commercial weight-loss diets.[14] Hematological assays can be used to determine the effect of the bioactive compounds in the extract on the blood.[15] There is a dire need to investigate these effects of Brassica oleraca, so as to ascertain its safe use. With this background, present study was specifically designed to evaluate the effect of Brassica oleracea L. var. capitata on body weight and hematological parameters in rabbits.

Dr. Tahira Zamir
Assistant Professor
Department of Pharmacology
Bahria University Medical and Dental College
Karachi
Email: drtahiraaasad@yahoo.com
Ishrat Younus
Assistant Professor
Faculty of Pharmacy
Hamdard University
Karachi
Dr. Talea Hoor
Associate Professor
Department of Pharmacology
Bahria University Medical and Dental College
Karachi
Dr. Rabia Arshad
Assistant Professor and Head
Department of Pharmacology
Altamash Institute of Dental Medicine
Karachi
Received: 04-10-2015
Revised: 18-11-2015
Accepted: 23-11-2015

MATERIALS AND METHODS:

This study was conducted in the Department of Pharmacology, Faculty of Pharmacy, University of Karachi after getting approval from Board of Advance Study and Research (BASR).

Plant material and preparation of extract: Fresh cabbages were purchased from local market in Karachi and identified at Director Centre for Plant Conservation Herbarium and Botanic Garden, University of Karachi. The voucher specimen (H.No.BO-09-12) was deposited in the Department of Pharmacognosy, University of Karachi. The crude extract was prepared through cold extraction process.[16] After thorough washing, 5 kg of Brassica oleracea leaves were chopped into small pieces and dried under shade for about a week. The dried material was ground to coarse powder. This powder was soaked in 80% methanol for 10 days with occasional shaking and stirring. The solvent was filtered through cotton and then through filter paper (What-mann No.1). After filtration, the methanol extract was evaporated under reduced pressure in a rotary evaporator at 40°C - 45°C and then followed by freeze drying at -30°C. the extract so obtained was kept at -20°C until further use. The resultant yield of extract obtained was 19.3% of dry weight.

Animals: The study was conducted on 28 healthy white rabbits of both sexes (1600g to 2200g), housed at the animal house of Department of Pharmacology, University of Karachi, under controlled condition of temperature (22 ± 2C) and humidity (50 to 60%) in an alternating 12-hour of light/dark cycle. The animals were kept in separate cages and were given standard diet and water regularly. The use of animals in this experiment was in accordance with the "National Institute of Health (NIH) Guide for the care and use of laboratory animals.[17]

Preparation of dosage of plant extract: Brassica oleracea extract was given in sterilized water in such a concentration that each 1 ml contained the required dose of the extract in three different concentrations i.e. 100, 300 and 500 mg/kg of the body weight respectively.

Dosing: All animals were uniformly divided into four groups, each, consisting of 7 animals. Three groups were treated as test animals and were given methanolic extract of Brassica oleracae extract in three different concentrations that is 100mg, 300mg, and 500mg. While one group served as normal control, and received normal saline 1ml/day equivalent to the volume of doses given to test animals. Extract and test drugs were administered continuously for 30 days through oral route once daily at the same time.

Weight measurement: Initially base line body weight (in gm) of all the animals was recorded on weighing machine. Thereafter, it was recorded weekly till the end of dosing

Sample collection: Blood samples of about 5 ml were collected twice, once at 16th day and the other at the end of dosing that is at 31st day through ear veins of animals in all groups in vaccum blood collection tubes that is Ethylene-Diamine-Tetra Acetic acid Vacuette (EDTA, K3) for hematological examination.

Hematological assay: Huma count plus ,a fully automated hematology analyzer (Human Germany) was used to analyze the hematological parameters which includes hemoglobin concentration (Hb), packed cell volume (PCV) mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH),mean corpuscular hemoglobin concentration (MCHC), red blood cell count (RBCs) ,white blood cell count (WBCs) and ,platelet count (PLT).

Statistical analysis: All values were compared with the control by taking mean and standard error to the mean. Values of $P<0.05$ were considered as significant and $P<0.01$ as highly significant following student t test. All statistical methods were performed using SPSS version 17.0.

RESULTS:

Effect on body weight: Results shown that animals received methanolic extract of Brassica Oleracae in a dose of 100 mg/kg body weight showed insignificant decrease (P value > 0.05) in mean body weight (1783±2.4)at the end of fourth week in comparison to the control animals (1957±4.92). Wheras animals received methanolic extract of Brassica Oleracae in a dose of 300 mg/kg body weight showed significant decrease in mean body weight (1799±1.2* P value <0.05) at the end of fourth week in comparison to the control animals (1957±4.92). While the administration of methanolic extract of Brassica Oleracae in a dose of 500 mg/kg body weight showed significant decrease in mean body weight (1800±6.3* P value <0.05) at the end of 3rd week and highly significant decrease in mean body weight (1733±1.02** P value <0.01) at the end of fourth week in comparison to the control animals (1957±0.1 and 1957±4.92 P value > 0.05) respectively.(Table 1)

Table: 1
Mean body weight during one month period in different groups

	Time interval (Weeks)	Control Group	Brassica oleracae extract in three different concentrations		
		NS1ml/kg body weight	100 mg/kg body weight	300 mg/kg body weight	500 mg/kg body weight
Mean Body Weight (gm)	First week	1958±3.2	1829±6.7	1900±3.2	2015±1.7
	Second week	1958±2.9	1823±3.2	1897±1.2	1983±9.2
	Third week	1957±0.1	1800±9.2	1850±2.8	1800±6.3*
	Fourth week	1957±4.92	1783±2.4	1799±1.2*	1733±1.02**

n = 7 , Average value ± S.E.M , *P < 0.05 as compared to control , **P <0.01 as compared to control

Animals at low, moderate and high doses showed 46gm, 101gm and 282 gm decrease in mean body weight respectively at the end of fourth week in comparison to the control animals (1gm).While the percent decrease in mean body weight was 3%, 6% and 14% respectively in same treated groups in comparison to the control animals (0%).(Table 2)

Table: 2
Effect of methanolic extract of Brassica oleracae on body weight of rabbits in one month

Effect on body weight	Control Group	Brassica oleracae extract in three different concentrations		
	NS1ml/kg body weight	100mg/kg body weight	300mg/kg body weight	500mg /kg body weight
Initial Mean body weight	1958±3.2	1829±6.7	1900±3.2	2015±1.7
Final Mean body weight	1957±4.92	1783±2.4	1799±1.2	1733±1.02
Difference (gm)	1gm	46gm	101gm	282gm
Difference (percentage)	0%	3%	6%	14%

n = 7, Average value ± S.E.M, *P < 0.05 as compared to control, **P <0.01 as compared to control

Table: 3
Base line values of hematological parameters in rabbits of all experimental groups

Hematological parameters	Control Group	Experimental Groups		
	NS 1ml/kg body weight	Group 1 (100mg/kg body Weight)	Group 2 (300mg/kg body weight)	Group 3 (500mg/kg body weight)
Hb g/dl	12.66±0.71	12.81±0.66	12.41±0.21	12.99±0.33
PCV (%)	36.76±2.77	36.43±2.81	38.34±3.21	37.27±3.28
MCV (fl)	63.68±2.83	63.15±1.08	63.67±2.89	62.19±1.67
MCH (Pg)	20±0.04	20±0.01	20±1.32	20±0.08
MCHC (g/dl)	32±0.04	32±0.18	32±0.20	32±0.09
RBC $\times 10^{6}$/ul	4.13±0.20	4.13 ±0.18	4.10±0.07	4.17±0.31
WBC$\times 10^{9}$/ul	4.8±0.05	4.3±0.04	4.00±0.09	4.7±0.01
PLT$\times 10^{9}$/ul	223.51±33	223±9.21	217±12.32*	199.03±3.21*

n = 7, Average value ± S.E.M, *P < 0.05 as compared to control, **P <0.01 as compared to control

Table: 4a
Effect of Brassica oleacae on hematological parameters after 15 days

Hematological parameters	Control Group	Treated Groups		
	NS 1ml/kg body weight	100mg/kg body weight	300mg/kg body weight	500mg/kg body weight
Hb g/dl	12.66±0.71	12.77±0.66	12.49±0.21	12.99±0.77
PCV (%)	36.76±2.77	36.46±2.81	38.39±3.21	37.27±3.22
MCV (fl)	63.68±2.83	63.15±1.08	63.67±2.77	62.19±1.67
MCH (Pg)	20±0.04	20±0.06	20±1.66	20±0.09
MCHC (g/dl)	32±0.04	32±0.19	32±0.00	32±0.12
RBC $\times 10^{6}$/ul	4.13±0.20	4±0.18	4.10±0.06	4.17±0.37
WBC$\times 10^{9}$/ul	4.8±0.05	4.3±0.09	4.00±0.07	4.7±0.00
PLT$\times 10^{9}$/ul	223.51±33	223±9.00	222±12.44	224.03±3.0

n = 7, Average value ± S.E.M, *P < 0.05 as compared to control, **P <0.01 as compared to control

Table: 4b
Effect of Brassica oleacae on hematological parameters after 30 days

Hematological parameters	Control Group	Treated Groups		
	NS 1ml/kg body weight	100mg/kg/ body weight	300mg/kg body weight	500mg/kg/ body weight
Hb g/dl	12.91±0.56	12.88±0.43	12.98±0.78	11.87±0.3
PCV (%)	36.93±1.2	36.88±2.81	37.31±3.21	37.19±1.00
MCV (fl)	63.15±1.52	63.29±1.00	63.67±1.32	62.93±0.02
MCH (Pg)	20±1.3	20±0.05	20±0.02	20±1.4
MCHC (g/dl)	32±1.2	32±0.19	32±0.18	32±1.3
RBC $\times 10^{6}$/ul	4.07±0.29	4.13 ± 0.19	4.08±0.32	4.19±1.2
WBC$\times 10^{9}$/ul	4.6±0.02	4.3±0.03	4.7±0.01	4.3±0.03
PLT$\times 10^{9}$/ul	221.48±31	220±11.99	193±8.82*	187.31±3.12**

n = 7, Average value ± S.E.M, *P < 0.05 as compared to control, **P <0.01 as compared to control

Effect on hematological parameters: Base line values of haematological parameters in rabbits of all experimental groups is given in Table 3. Table 4a reveals the comparison of hemoglobin concentration (Hb), packed cell volume (PCV) mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red blood cell (RBC) count ,white blood cell (WBC) count and , platelet (PLT)count in animals of control group and animals received Brassica olerace in three different concentrations i.e 100, 300 and 500 mg/kg after 15 days while a similar comparison between the same groups of animals after 30 days is shown in Table 4b. Animals received methanolic extract of Brassica oleracae in the dose of 100 mg /kg body weight for a period of 15 days did not show any change in any parameter. While the animals received methanolic extract of Brassica oleracae in the dose of 300 mg/kg body weight for a period of 15 days showed significant decrease in platelet count (217±12.32* P value < 0.05) in comparison to the control animals (223.51±33 P value > 0.05). Similarly, the effect on all the other parameters was insignificant. The animals received methanolic extract of Brassica oleracae in the dose of 500 mg /kg body weight for a period of 15 days showed significant decrease in platelet count (199.03±3.21* P value <0.05) in comparison to the control animals (223.51±33 P value > 0.05). The effect on all the other parameters was insignificant. Administration of methanolic extract of Brassica oleracae extract in the dose of 100 mg/kg for a period of 30 days did not show any change in any parameter. While the administration of methanolic extract of Brassica oleracae in the dose of 300 mg/kg body weight for a period of 30 days showed significant decrease in platelet count (193±8.82*) in comparison to the control animals (221.48± 31). The effect on all the other parameters was insignificant. Similarly,the animals received methanolic extract of Brassica oleracae in the dose of 500 mg for a period of 30 days showed highly significant decrease in platelet count (187.31±3.12**) in comparison to the control animals (221.48±31).The effect on all the other parameters was insignificant.

DISCUSSION:

Obesity is the fifth leading cause of death worldwide. At least, 2.8 million adults die each year as a result of being overweight .In addition, 44% of the diabetes burden, 23% of the Ischemic heart diseases and between 7% to 14% of some cancers occur due to obesity.[18] Increase in body weight occurs due to imbalance between calories consumed and calories stored. The increased intake of animal's meat, partially hydrogenated fats, refined carbohydrates and lower intake of fiber diet has resulted in increased incidence of obesity and degenerative diseases.[19] On the other hand, the populations that consume pre dominantly plant based diets that is high in whole plant foods, rich in fiber and protective phytochemicals are reported to have less incidence of these diseases.[20] Several studies have demonstrated the effectiveness of plant based dietary patterns in the management of obesity and cardiovascular risk factors.[21] A variety of natural products including natural extracts and isolated compounds from plants have been reported to cause weight loss.[22] Moreover, a nutritional based remedy is an inexpensive solution to weight management.[23]

Administration of methanolic extract of brassica oleracae caused dose dependent gradual decrease in mean body weight in all the treated animals. However, the reduction was significant at 300 and 500 mg/kg body weight of doses. In literature, Brassica oleracae is documented to have hypolipidemic effect in animals. It can be assumed that the weight lowering potential of brassica oleracae can be due to its hypolipidemic effect.[8]

Antioxidant compounds are able to reduce the blood levels of glucose, triglycerides and LDL levels, increase energy utilization, fat oxidation, as well as lower body weight and adiposity.[24] They are also able to inhibit enzymes involved in lipid metabolism like pancreatic lipase, lipoprotein lipase and glycerophosphate dehydrogenase.[25] It can be ascertained that the weight lowering potential of Brassica oleracae can be due to its antioxidant activity as mentioned earlier. In the present study, administration of methanolic extract of Brassica oleracae resulted in decrease in platelet count. The reduction was highly significant at 500 mg/kg body weight of dose at the end of 30 days of dosing. Flavonoids are reported to have antiplatelet activity.[26] Brassica oleracae is rich in favonoids. The antiplatelet effect of Brassica oleracae might be due to its flavanoid content as reported for other plants of Brassica family.[27] Various mechanisms have been proposed for antiplatelet ativity of flavonoids, that is, by lowering intracellular Ca levels, alteration in the metabolism of cAMP and thromboxane A2.[28] Thus it may inferred that the antiplatelet activity of Brassica oleracae might be mediated by these mechanisms. Platelet aggregation leads to pathogenesis of various thrombotic disorders. Moreover, platelets play an important role in the initiation as well as stability of atherosclerotic plaques. Antiplatelet agents are prescribed to patients at risk for myocardial ischemia, unstable angina and acute myocardial infarction.[29] The extract therefore can be useful in the management of cardiovascular diseases.

The non-significant effect of the extract on the RBC and WBCs is an indication that the balance between their production and destruction is not disturbed. MCH and MCHC are related to individual's red blood cells while Hb, RBC and PCV are correlated to the total population of red blood cells. The non significant effect of extract on all these parameters could mean that neither the incorporation of hemoglobin into red blood cells, nor the morphology and osmotic fragility of red blood cells were altered.[30]

CONCLUSION:

Methanolic extract of Brassica oleracae exhibited weight reducing effect in rabbits. Moreover, it decreased the total number of platelets in blood. Reduction in platelet

count can be helpful in the prevention of cardiovascular diseases. This study should be conducted on humans also for the development of new herbal drug for the above mentioned effect. Brassica oleracae can be a nutritive alternative for weight management. Whereas reduction in platelet count produced by brassica oleracae can be helpful in the prevention of cardiovascular diseases and in other conditions where low platelet levels are required.

REFERENCES:

1. Dahanukar S. A Kulkami R. A, Rege N N. Pharmacology of Medicinal Plants and Natural Products. Indian J. Pharm. 2000; 32:518-81
2. Auddy B, Ferreiro M, Blasina F, Lafon L, Arredondo F, Dajas F et al. Screening of Antioxidant Activity of Three Indian Medicinal Plants Traditionally used for the Management of Neurodegenerative Diseases. J. Ethnopharm. 2003; 84:131-8
3. Jimenez- Arellanes A, Meckes M, Ramireez R, Torres J, Luna - Herrera J. Activity against multidrug-resistant mycobacterium tuberculosis in Mexican plants used to treat respiratory diseases. J Phytother Res.2003;17: 90 -8
4. Raskin I, Ripoll C. Can an apple a day keep the doctor away? Curr Pharm Dec 2004; 10(27):3419-29
5. Gross D. Indole Phytoalexins from Brassica oleracea var. gongylodes. Planta Med, 1994, 59: A-618
6. Byers T, Nestle M, McTiernan A. American Cancer Society 2001 Nutrition and Physical Activity Guidelines Advisory Committee. American cancer society guidelines on nutrition and physical activity for cancer prevention: Reducing the risk of cancer with healthy food choices and physical activity. CA. Cancer. J. Clin, 2002, 52: 92-119
7. Kris-Etherton PM, Hecker KD, Bonanome A. Bioactive compounds in foods: Their role in the prevention of cardiovascular disease and cancer. Am. J. Med, 2002;113: 71S-88S
8. Waqar MA, Mahmood Y. Antiplatelet, antihypercholesterolemic and antioxidant activities of Brassica oleracea in high fat diet provided rats. World. Appl. Sci. J, 2010;8: 107-12
9. Jeffery EH, Araya M. Physiological effects of broccoli consumption. Phytochem Rev, 2009; 8: 283-98
10. Kane MP, Abu-Baker A, Busch RS. The utility of oral diabetes medications in type 2 diabetes of the young. Curr Diabetes. Rev, 2005;1: 83-92
11. Hasani-Ranjbar S, Jouyandeh Z, Abdollahi M J. A systematic review of anti-obesity medicinal plants - an update. Diabetes Metab Disord, 2013 Jun 19;12(1):28. doi: 10.1186/2251-6581-12-28
12. Nicholson AS, Sklar M, Barnard ND, Gore S, Sullivan R, Browning S. Toward improved management of NIDDM: a randomized, controlled, pilot intervention using a low fat, vegetarian diet. Prev Med. 1999; 29: 87-91
13. Dickel ML, Rates SM, Ritter Mr. Plants popularly used for loosing weight purposes in Porto Alegre, South Brazil ,J Ethno pharmacol ,2007;109(1):60-71
14. Samec D, Piljac-Zegarac J, Bogovi M. Antioxidant potency of white (Brassica oleracea L. var. capitata) and Chinese (Brassica rapa L. var. pekinensis (Lour.) cabbage: The influence of development stage, cultivar choice and seed selection. Sci Hort, 2011;128:78-83
15. Yakubu MT, Akanji MA, Oladiji AT. Alterations in serum lipid profile of male rats by oral administration of aqueous extract of Fadogia argrestis stem.Res. J.Med.Plant, 2008;2:66-73
16. Hossain MS, Ahmed M, Islam A. Hypolipidemic and hepatoprotective effects of different fractions of ethanolic extract of immature leaves of Mangifera indica (Linn.) in alloxan induced diabetic rats. IJPSR, 2010, 1: 132-8
17. National Research Council. Guide for the Care and Use of Laboratory Animals. Washington, DC: National Academy Press, 1996: 1-7
18. World Health Organization. Nutrition. Obesity, preventing and managing the global epidemic, Report of a WHO consultation (WHO technical) Report Series 894) WHO, 2000
19. Popkin BM: Global nutrition dynamics: the world is shifting rapidly toward a diet linked with noncommunicable diseases. Am J Clin Nutr 2006, 84:289-98
20. Connor WE, Duell PB, Connor SL: Benefits and hazards of dietary carbohydrate. Curr Atheroscler Rep 2005, 7:428-3
21. Gardner CD, Coulston A, Chatterjee L. The effect of a plant-based diet on plasma lipids in hypercholesterolemic adults: a randomized trial. Ann Intern Med 2005, 142:725-33
22. Han LK, KimuraY, Okuda H. Antiobesity effects of natural products. Stud. Nat. Prod,chen, 2005;30:79-110
23. Swinburn, Caterson, Seidell, James. Diet, Nutrition and the prevention of excess weight Gain and Obesity." Public Health Nutrition, 2004; 7(1a): 123-46
24. Terra X, Motagut G, Busto M, Lloplz N, Ardevol A ,Blade C et al..Grape seed procyanidins prevent low grade inflammation by modulating cytokine expression in rats fed on high fat diet. J .Nutr.Biochem.2009,20:210-18
25. Slanc P, Doljak B, Kreft S, Luda M, Janes D, Strulelj B. Screening of selected food and medicinal plant extracts for pancreatic lipase inhibition.Phytother; Res.2009; 874-7
26. Harnafi H, Amrani S. Review article. Flavonoids as potent phytochemicals in Cardiovascular Diseases Prevention. Phcog rev,2007; 1:193-202
27. Buhler D R Miranda. Antioxidant activities of flavonoids. Department of Environmental and Molecular Toxicology. Oragan state of University. Linus Pauling Institute. 2000
28. Kang WS, Chung KH, Lee JV, Park JB, Zhang YH, Yoo HS et al. Antiplatelet activity of green tea catechins is mediated by inhibition of cytoplasmic calcium increase.J.Cardiovasc.Pharmacol,2001;38:875-84
29. George JN.Platelets.Lancet.2000; 335:1531-9
30. Adebayo JO, Adesokan AA, Olatunji LA, Buoro Do, Soladoye AO. Effect of ethanolic extract of Bougainvillea Spectabilis leaves on haematological and serum lipid variables in rats.Biochem. 2005;17:45-50

ORIGINAL ARTICLE

Seronegative Rubella IgG Status in Pregnant Women Visiting Tertiary Care Hospital

Atifa Afsheen Sharique[1], Muhammad Sharique[2],Asha Mahesh[3], Syed Wajahat Shah[4]

ABSTRACT:
Objective: To determine the seronegative rubella IgG status in pregnant women visiting antenatal clinic at Jinnah Medical College Hospital.
Materials and Methods: This cross sectional study was carried out after ethical approval in Jinnah Medical College Hospital, Karachi from 1st April 2014 to 31st March 2015.Ninety three primigravidae in first trimester presenting to antenatal clinic were selected from the obstetrics and gynecology OPD. Blood samples of all women were taken and sent to laboratory for evaluation of IgG rubella antibody by ELISA technique. SPSS version 20 was used for data analysis.
Results: Out of 93 pregnant women, 11(11.8%) were negative for rubella IgG antibody in the first trimester of pregnancy. Mean ±SD of age of the study participants was 25.66(± 6.29) years. Majority of the women patients belonged to low socioeconomic group having educational status less than matriculation.
Conclusion: Rubella seronegativity is common in pregnant women visiting tertiary care hospital.
Keywords: Congenital rubella syndrome, Immunization, Seronegativity, Pregnancy

INTRODUCTION:

Rubella is a teratogenic virus.[1]Congenital rubella syndrome(CRS) is characterized by deafness, cataract and heart malformation. In addition the affected children can have microcephaly, hepatosplenomegaly and thrombocytopenia.[2]When a woman acquires rubella virus early in pregnancy, she has a 90% chance of passing the virus on to her fetus. This can cause the death of the fetus, and may cause CRS.[3]Before the introduction of rubella vaccine, the incidence of CRS varied from 0.1 to 0.2/1000 live births during endemic periods, and from 0.8 to 4/1000 live births during rubella epidemics. However, rubella vaccination during the past decades has drastically reduced or practically eliminated rubella and CRS in many developed countries and in some developing countries.[4]

Pakistan falls in moderate to high susceptibility risk zone but without documented congenital rubella syndrome.[5] In many developing countries, congenital rubella syndrome is an under-recognized Public Health Problem.[6] Inclusion of rubella vaccine in the national immunization program was found to be implemented in less than one third of developing countries as per the review conducted by WHO[7]. So, there is a need for mechanism to identify and vaccinate non-immune women[8].Therefore, the aim of this study was to identify the frequency of seronegative pregnant women so as do determine the proportion eligible for immunization against rubella and devise program to cover the population and prevent morbidity.

✉ **Dr. Atifa Afsheen Sharique**
Assistant Professor
Department of Obstetrics & Gynecology
Jinnah Medical & Dental College Hospital
Email: dratifa2000@gmail.com
✉ **Dr. Muhammad Sharique**
Consultant Anesthetist
Kohi Goth Hospital
Karachi
✉ **Dr. Asha Mahesh**
Professor & Head
Department of Obstetrics & Gynecology
Jinnah Medical & Dental College Hospital
Karachi
✉ **Mr. Syed Wajahat Shah**
Research Assistant/Biostatistician
Jinnah Medical & Dental College Hospital
Karachi
Received: 09-10-2015
Revised: 11-11-2015
Accepted: 12-11-2015

MATERIALS AND METHODS:

This consecutive cross sectional study was conducted at Jinnah Medical & Dental College Hospital Karachi, for a period of one year from April 2014 to March 2015. Sample size was calculated by using the formula in which we selected 95% confidence interval with 10% margin of error and proportion of presence of rubella is 40% seronegative patients. During this period 93 pregnant women presented in the obstetrics and gynecology OPD, all being primigravidae and of child bearing age (14-49) with first trimester of pregnancy confirmed by ultrasound, were enrolled for the study.Data was collected after taking informed consent for enrollment in the study. Blood sample was collected for detection of rubella-IgG antibodies and was analyzed by ELISA technique using ETI-RUBEK G plus kits.All sera with antibody titer equal to or less than 10.1 IU/ml were regarded as seronegative, between 9.9-10.1 IU/ml was considered as equivocal and titers greater than 10.1 IU/ml was regarded as seropositive, as indicated in kit prospectus.The data of patients was collected on constructed proforma designed for the study which contained demographic information (name and age), hospital registration number, gestational age (in weeks), educational status (i.e. illiterate, < matric, > matric, intermediate and >intermediate), and rubella IgG status (positive or negative).Confounding variables were controlled by excluding pregnant women of second and third trimester of gestation, multigravidae and those women who had history of flu-like symptoms with

maculopapular rash or exposure to rubella like rash in less than 06-months of duration. Bias was minimized by obtaining results of rubella IgG status from same laboratory. Software program SPSS 20, was utilized for all statistical analyses. Frequencies and percentages were used to summarize categorical variables like rubella IgG status and educational status. Mean ± standard deviation (SD) were computed for numerical variables like age distribution and gestational age. Stratification with regards to age, educational status and gestational age was done to control the effect modifiers. Any inferential test of significance was not applicable for this cross sectional study.

RESULTS:

The range of age of women was between 17 to 46 years. Majority of these women were between 21 to 25 years of age. Twenty one women (22.6%) were between 26 to 30 years of age. Seventeen (18.3%) were between 14 to 20 years, and five were between 31-35 and 36 to 40 years of age group respectively. Only four (4.3%) women were between 41 to 49 years of age group in this study. Mean (± SD) age was 25.66 (±6.29) years. In this study, mostly positive Rubella IgG status was encountered in women up to 30 years of age group. (Table 1) Detection of rubella IgG antibody status in majority of these primigravidae was carried out at thirteenth weeks of gestation. Twenty four (25.8%) women were attending antenatal clinic at twelfth weeks of their gestational age. The range of their gestational age was between 7th to 13th weeks in this study. Mean (± SD) gestational age was 11.91 (±1.53) weeks. As major bulk of women attended antenatal clinic at twelfth and thirteenth weeks, therefore significant proportion of positive Rubella IgG status observed at these gestational age groups. (Table 2) In this study, educational status of major proportion of pregnant women was below matric. Intermediate was 19(20.4%) and illiteracy rate was observed in 14(15.1%) women. Educational status of above intermediate was noticed in only 10(10.8%) pregnant ladies. This was attributed to belonging of these women to middle and low socioeconomic class. Hence, majority of positive Rubella IgG status was detected in these women. (Table 3) Out of 93 pregnant women, 11(11.8%) were negative for rubella IgG antibodies in the first trimester of pregnancy. Seropositivity was encountered in the rest of 82(88.2%) pregnant women.

Table: 1
Age distribution of women in relation to Rubella IgG status

AGE OF WOMEN (Years)	FREQUENCY (n= 93)	PERCENTAGE (%)	RUBELLA IgG STATUS Present n = 82	(%)	Absent n = 11	(%)
14-20	17	18.3	16	19.5	1	9.1
21-25	41	44.1	36	43.9	5	45.5
26-30	21	22.6	18	22	3	27.3
31-35	5	5.4	4	4.9	1	9.1
36-40	5	5.4	5	6.1	0	0
41-45	3	3.2	2	2.4	1	9.1
46-49	1	1.1	1	1.2	0	0

Mean age± S.D = 25.66± 6.29

Table: 2
Gestational age distribution in relation to Rubella IgG status

Gestational Age (Weeks)	Frequency (n= 93)	Percentage (%)	RUBELLA IgG STATUS Present n = 82	(%)	Absent n = 11	(%)
Seventh	3	3.2	3	3	0	0
Eighth	2	2.2	2	2	0	0
Ninth	3	3.2	2	2	1	1.1
Tenth	7	7.5	6	6	1	1.1
Eleventh	8	8.6	8	8	0	0
Twelfth	24	25.8	22	22	2	2.2
Thirteenth	46	49.5	39	39	7	7.5

Mean gestational age ± S.D = 11.91 ± 1.53

Table: 3
Educational status in relation to Rubella IgG status

Educational Status	Rubella IgG Status Present	Presentage	Absent	Presentage
	n = 82	(%)	n = 11	(%)
Illiterate	10	12.2	4	36.4
<Matric	30	36.6	6	54.5
>Matric	14	17.1	0	0
Intermediate	18	22	1	9.1
>Intermediate	10	12.2	0	0

DISCUSSION:

Rubella virus is the common agent of prenatal infection. Congenital malformation rate is very high among pregnant women who are infected with rubella primarily during the first trimester of pregnancy[9]. In this study screening of rubella IgG antibody status was carried out during first trimester of pregnancy.

Excluding pregnancy where it causes fetal morbidities, rubella infection carries little morbidity and apparently only minor complications during childhood.[10] Thus, the primary objective of rubella immunization program is prevention of congenital rubella syndrome.[11] In developing countries like Pakistan, rubella outbreaks can occur without clinical recognition. In one study that screened four hundred cases for IgG rubella antibody status using ELISA technique increase prevalence of antibody with increasing age was observed. Moreover, 81.78% pregnant women were seropositive to rubella antibody. Finally, they concluded that there is persistent horizontal transmission of virus in the environment.[12] Therefore, in developing countries, need for determination of rubella antibody status of all pregnant women and immunization of non-immune women have been emphasized by WHO.[7]

Rubella susceptibility in pregnant women from low socioeconomic class is 10 times higher.[13]than the high socioeconomic class. This is due to lack of awareness, poor literacy rates and healthcare facilities and also due to financial constraints.[14] In this study, majority of the pregnant women belonged to low socioeconomic group having literacy rate less than matriculation. The prevalence of rubella and the incidence of rubella infection in pregnancy and thus the risk of congenital rubella syndrome cannot be assessed without serological evidence. Serological studies have been undertaken in many developing countries to assess the proportion of the population susceptible to rubella by age, and thus to define the degree of risk to women of childbearing age. Results vary widely between countries and between different parts of same country.[10]In a recent study from India, the serological status of 1,329 healthy adolescent school girls, aged 12-15years, from 12 districts, has documented overall rubella seropositivity of 76.4%. The urban population had a comparatively better immune status than that of the rural population (80.2% versus 73.1%).[15]Protective levels of antirubella IgG were documented in 72% of pregnant women in sudan[16] and 53% in Nigeria[17], 93% in Cartogena(Columbia).[18]A study in Toronto examined data among 5783 consecutive women for rubella susceptibility. They encountered low rubella immunity among women immigrant from North Africa and Middle East as compared to Canadian born nationals. This is due to improper or lack of immunization program in these developing areas.[19]

A study in the Gynecology Department of Shifa International Hospital, Islamabad in the year 2002, showed seronegativity of 39% for rubella in pregnant women.[20] Contrary to this, a study from Lahore has documented that 81.78% females of child bearing age had immunity to rubella[12] which is comparable to the results of our study. Thus, a wide range of seroprevalence exist among different cites of Pakistan. This is probably because of epidemic outbreaks of rubella in our general population as previously mentioned by Iqbal and Bokhari.[21]

A study conducted at Department of Obstetrics and Gynecology, Jinnah Postgraduate Medical center, Karachi observed 94% of seropositivity and 6% of seronegativity for rubella in pregnant women[22]. Similar type of study conducted in the same Department showed 89% of pregnant women were immune to rubella[23]. The overall seropositivity for IgG in studies from Karachi among pregnant women was observed from 89 to 94%. Hence, 6% to 11% of pregnant women are susceptible. In this study, 11.8% of gravid females were shown no immunity to rubella, which is in the range of seronegative pregnant women of above mentioned studies.

The rationale of this study was to focus on those women who show no immunity against rubella, as shown by IgG levels, give them rubella vaccine after the completion of pregnancy. Furthermore, measures should be performed to cover the population at risk and prevent morbidity.

Rubella vaccine, in the form of MMR vaccine, is a live attenuated vaccine and cannot be given during pregnancy. However, the best method of personal prevention is for women to have their rubella immunity checked before trying to conceive and to get immunized if necessary. It is necessary to realize that treatment of CRS is costly whereas rubella vaccination programs are highly cost effective.[24]The introduction of rubella vaccine requires ongoing strengthening of routine immunization services and surveillance systems.[25]

CONCLUSION:

Significant number of pregnant women visiting tertiary care hospital was not immune to rubella virus. Hence, their fetuses were susceptible to congenital anomalies. Therefore, screening of pregnant women should be recommended to determine those who are eligible for immunization against rubella.

REFERENCES:

1. Rasmussen SA, Human teratogens update 2011: Can we ensure safety during pregnancy? Birth Defects Res A ClinMolTeratol 2012;94(3):123-8
2. Adam MP, Polifka JE, Friedman JM. Evolving knowledge of the teratogenicity of medications in human pregnancy. Am J Med Genet C Semin Med Genet.2011;157:175-82
3. WHO. Rubella vaccines. Position paper WklyEpidemiol Rec 2011;86(29): 301-16
4. Honarvar B, Moghadami M, Moattari A, Emami A, Oodoomi N. Seroprevalence of Anti-Rubella and Anti-Measles IgG Antibodies in pregnant women in Shiraz, Southern Iran: Outcomes of a Nationwide Measles-Rubella Mass Vaccination Compaign. PLOS ONE 2013; 8(1): e55043. Doi: 10.1371/ journal. Pone.0055043
5. Cutts FT, Robertson SE, Diaz-Ortega JL, Samuel R. Control of rubella and congenital rubella syndrome (CRS) in developing countries, Part 1: Burden of disease from CRS. Bull World Health Organ 1997; 75:55-68
6. Aksakal FN, Maral I, Cirak MY, Aygun R. Rubella seroprevalence among women of childbearing age residing in a rural region: is there a need for rubella vaccination in Turkey? Jpn J Infect Dis 2007; 60:157-60
7. Cutts FT, Vynnycky E. Modeling the incidence of congenital rubella syndrome in developing countries. Int J Epidemiol. 1999; 28:1176-84
8. Condon RJ, Bower C. Rubella vaccination and congenital rubella syndrome in Western Australia.Med J Aust. 1993; 158:379-82
9. Lee JY, Bowden DS. Rubella virus replication and links to teratogenicity. ClinMicrobiol Rev 2000; 13:571-87
10. Obican S, Scialli AR. Teratogenic exposures. Am J Med Genet C Semin Med Genet. 2012;157:150-69
11. Center for Disease Control and Prevention (CDC). Revised ACIP recommendation for avoiding pregnancy after receiving a rubella-containing vaccine. MMWR Morb Mortal Wkly Rep 2001; 50:111-7
12. Iqbal A, Bokhari SR. Status of Rubella IgG antibody in general population at Lahore. Pak J Pathol 1997; 8:37-41
13. Vargas-Leguás H, CampinsMartí M, Juste Sánchez C, Martínez Gómez X, Hermosilla Pérez E, CaberoRoura L. Rubella susceptibility of immigrant pregnant women in Catalonia. Med Clin (Barc). 2009; 132:344-7
14. Miller CL. Rubella in the developing world. Epidemiol Infect. 1991; 107:63-8
15. Sharma HJ, Padbidri VS, Kapre SV, Jadhav SS, Dhere RM, Parekh SS, et al. Seroprevalence of rubella and immunogenicity following rubella vaccination in adolescent girls in India. J Infect DevCtries. 2011; 5:74-81
16. Hamdan HZ, Abdelbagi IE, Nasser NM, Adam I. Seroprevalence of cytomegalovirus and rubella among pregnant women in western Sudan. Virol J 2011; 8: 217
17. Onakewhor JU, Chiwuzie J. Seroprevalence survey of rubella infection in pregnancy at the University of Benin Teaching Hospital, Benin City, Nigeria. Niger J ClinPract 2011. 14(2): 140-5
18. Mora-Garci´a GJ, Ramos-Clason E, Mazenett E, Go´mez-Camargo D. The seroprevalence of IgG antibodies against rubella (German measles) in 10– 49 year-old women from Cartagena, Colombia 2011; Rev SaludPublica (Bogota).13(2): 288–97
19. McElroy R, Laskin M, Jiang D, Shah R, Ray JG. Rates of rubella immunity among immigrant and non-immigrant pregnant women. J ObstetGynaecol Can 2009; 31(5):409-13
20. Adil MM, Zubair M, Alam AY, Raja KS. Identification of seronegative pregnant women eligible for immunization against Rubella. Rawal Med J 2005; 30:22-4
21. Iqbal A, Bokhari SR. Occurance of Rubella antibody IgG in General Population. Mother & Child. 1997; 35:17-22
22. Kharal SA, Khan MA. Prevalence of Rubella Seropositivity at successive stages of Pregnancy. Pak Armed Forces Med J 1997; 47:11-4
23. Kharal SA, Khan MA. Rubella antibodies in Women with Full-Term Normal Delivery and in their Neonates. Pak J ObstetGynaecol 1996; 9:29-31
24. Babigumira JB, Morgan I, Levin A: Health economics of rubella: a systematic review to assess the value of rubella vaccination. BMC Public Health 2013; 13:406-17
25. Robertson SE, Featherstone DA, Gacic-Dobo M, Hersh BS. Rubella and congenital rubella syndrome: global update. Rev Panam Salud Publica 2003; 14:306-15

ORIGINAL ARTICLE

Effect of Green Tea Consumption on HDL-Cholesterol

Khalid Niaz[1], Ejaz Fatima[2], Gulshan Ara Jalbani[3], Shah Murad[4]

ABSTRACT:
Objective: To evaluate the effect of green tea consumption on HDL-cholesterol level in hyperlipidemic patients
Materials and Methods: Forty hyperlipidemic patients were selected from Ghurki Trust Teaching Hospital Lahore and divided in two groups with 20 patients in each group.Group-I was advised to take, six hourly 180 ml green tea prepared by conventional method for two months. Group-II was labeled as control, not to take green tea for 2 months. Their HDL-cholesterol was measured at day-0 and on day-60. HDL-cholesterol was measured by separating other lipoprotein fractions using chemical precipitation with divalent ions such as Mg^{2+}, then coupling the products of a cholesterol oxidase reaction to an indicator reaction.
Results: After two months, it was observed that green tea consumption raised HDL-cholesterol by 7.5 mg/dl, while control group's HDL-cholesterol was raised 0.8 mg/dl only in this period.
Conclusion: Consumption of green tea raised HDL-cholesterol significantly and can be considered as negative risk factor for development of coronary artery disease.
Keywords: HDL level, Hyperlipidemic patients, Green tea

INTRODUCTION:

There are many reasons to develop atherogenesis in human body by using high fat diets and medicines. Atherogenesis can cause coronary artery disease leading to mortality due to heart attack and cardiac arrhythmias.Patients with coronary artery disease (CAD) commonly have low HDL cholesterol (HDL-C) and mildly elevated LDL cholesterol (LDL-C), leading to uncertainty as to whether the appropriate goal of therapy should be lowering LDL-C or raising HDL-C.[1,2,3,4,5,6,7] Many clinical studies suggest that HDL of 60 mg/dl is associated with dramatic reduction in rate of heart attack. Several studies suggest that higher levels of HDL are associated with less carotid and coronary atherosclerotic plaque. HDL particles are also protective against infections and even cancer, and are a major player in the body's fight against inflammatory patterns. In other words, HDL has clearly established itself as a blood particle that provides powerful protective functions.[8,9,10,11,12] Tea, prepared from the leaves of Camella sinensis, is the most popular beverage in the world except water. Black tea, made from the mild oxidation of green tea leaves, amounts to 80% of world tea production. Flavonoids are a group of polyphenols present in vegetables, fruits and beverages such as tea and wine[13,14,15]. Recent research studies shows that green tea lowers total cholesterol and raises HDL ("good") cholesterol in both animals and people. One population-based clinical study found that men who drink green tea are more likely to have lower total cholesterol than those who do not drink green tea. Results from one animal study suggest that polyphenols in green tea may block cholesterol from being absorbed in the intestine and also help the body get rid of cholesterol. In another small study of male smokers, researchers found that green tea significantly reduced blood levels of harmful LDL cholesterol[2,3,4]. It is thought that the antioxidants catechin and caffeine found in green tea may have a role in helping the body burn more calories-sometimes referred to as speeding up the metabolism-which can help weight loss[3,4,5,6,7]. Green tea preparations used for losing weight are extracts of green tea that contain a higher concen-tration of catechins and caffeine than the typical green tea beverage prepared from a tea bag and boiling water.[16] Eleven research studies involving 821 people found daily consumption of green and black tea (as a drink or a capsule) could help lower cholesterol and blood pressure.[17,18,19,20]

✉ **Dr. Khalid Niaz**
Assistant Professor
Department of Pharmacology
Islamabad Medical & Dental College (IM&DC)
Islamabad
Email: drkhalid.niaz@gmail.com
✉ **Dr. Ejaz Fatima**
Assistant Professor
Department of Pharmacology
Lahore Medical and Dental College (LMDC)
Lahore
✉ **Dr. Gulshan Ara Jalbani**
Associate Professor
Department of Pharmacology
Peoples Medical College (PMC)
Nawabshah
✉ **Dr. Shah Murad**
Professor
Department of Pharmacology
Islamabad Medical & Dental College (IM&DC)
Islamabad
Received: 12-10-2015
Revised: 25-11-2015
Accepted: 27-11-2015

MATERIAL & METHOD:

This research study was conducted at Ghurki trust teaching hospital (GTTH), Lahore Pakistan from June 2015 to September 2015. Forty hyperlipidemic patients were selected from GTTH for the study. Age of patients ranged from 18 to 70 years. Both gender male and female patients were enrolled. They were advised to discontinue any hypolipidemic medications and foods. Patients suffering from any metabolic disease, renal impairment, liver disease, and already victimized by cardiac problems were excluded from the research study.Forty patients were divided in two groups, twenty

individuals in each group. Group-1 was advised to take 180 ml green tea boiled in hot water every six hourly for the period of eight weeks. Group-II was considered as control group and was advised not to take green tea, black tea or coffee for eight weeks. Their baseline values of HDL-cholesterol were measured by separating other lipoprotein fractions using chemical precipitation with divalent ions such as Mg^{2+}, then coupling the products of a cholesterol oxidase reaction to an indicator reaction.

Statistical Analysis: Mean values with SD and SEM were analysed statistically by using SPSS version 22.0.0.0. Statistical significant was considered as p-value of changed parameter from day-0 to day-60. P-value of <0.001 was labeled as significant and p-value of >0.05 was considered as non-significant change.

RESULTS:

After eight weeks of trial, following changes were observed in selected parameter of HDL-cholesterol. In Group A HDL-C increased from 32.08±2.22 mg/dl to 39.54±1.96 mg/dl with a change of 7.5 mg/dl from base line day-0 to day- 60.This was found to be statistically significant. However in group B, HDL-C increased from 35.10±2.03 mg/dl to 35.92±3.14 mg/dl with a change of 0.8 mg/dl only and was statistically non significant.(Table-1)

Table: 1
HDL-C level before and after consumption of green tea

Group	Parameter	At D-0	At D-60	Change	p-value
Group-A (n=20)	HDL-C	32.08±2.22	39.54±1.96	7.5 mg/dl	<0.01
Group-B (n= 20)	HDL-C	35.10±2.03	35.92±3.14	0.8 mg/dl	>0.05

Group-A is tested group, Group-B is placebo group. 'n' in groups indicates sample size, mean values are measured as mg/dl, HDL-C stands for high density lipoprotein cholesterol, ± indicates SEM. P-value <0.01 indicates significant change and p-value >0.05 indicates non-significant change in parameter

DISCUSSION:

Green tea is alleged to boost weight loss, reduce cholesterol, combat cardiovascular disease, and prevent Cancer and Alzheimer's disease. We retested and reviewed its HDL-cholesterol raising effects in hyperlipidemic patients. By two months consumption of green tea (180 ml/six hourly) it was proved that green tea increased 7.5 mg/dl of HDL-cholesterol, which is significant raise in the parameter. These results match with results of study conducted by Zhang C [21] who proved that green tea consumption for 5 weeks raised high density cholesterol from 39 mg/dl to 45 mg/dl in 20 hyperlipidemic patients. Our results are in contrast with results of study conducted by Khan[22] who proved only 2.08 mg/dl raise in plasma HDL-cholesterol, when green tea was used by 17 hyperlipidemic patients for one month. This contrast may be due to less frequency of taking green tea by patients; ie 12 hourly. In our study control groups HDL-cholesterol was raised from 35.10±2.03 mg/dl to 35.92±3.14 mg/dl which is only 0.8 mg/dl increase in HDL-cholesterol. This change is non-significant when analysed statistically. Arab [23] described that less consumption or no consumption of green tea does not mean that hyperlipidemic patients HDL cholesterol can not increase by other healthy habits like aerobic exercise and less frequency of taking junk food which contain lesser raw fat. Khalesi [24] explained that lesser the predisposing factors for coronary artery disease, lesser the risk for developing heart attack and cardiac arrhythmias in human beings. Our results match with results of study conducted by Johson[25] in which 10 mg/dl HDL cholesterol was increased in 39 hyperlipidemic patients when they took 200 ml green tea every four hourly for the period of three months. They also mentioned hypoglycemic, and hypotensive effects of green tea consumption by primary hyperlipidemic patients suffering from metabolic syndrome. Not to smoke cigarettes, non-alcoholics and aerobic exercise can increase high density cholesterol in plasma. It is proved by cohort studies conducted by Peng[26] that old age, renal diseases, liver diseases, lesser lung function may contribute to lower high density lipoprotein cholesterol leading to development of atherogenesis, cardiac arrhythmias and cardiac arrest.

CONCLUSION:

After the research study it was concluded that green tea can raise HDL-cholesterol significantly and can be considered as negative risk factor for development of coronary artery disease.

REFERENCES:

1. Zheng XX, Xu YL, Li SH, Hui R, Wu YJ, Huang XH. Effects of green tea catechins with or without caffeine on glycemic control in adults: a meta-analysis of randomized controlled trials . Am J Clin Nutr (Meta-Analysis) 2013;97 (4): 750-62
2. Liu K, Zhou R, Wang B, Chen K, Shi LY, Zhu JD etal Effect of green tea on glucose control and insulin sensitivity: a meta-analysis of 17 randomized controlled trials . Am J Clin Nutr (Meta-Analysis) 2013;98 (2): 340-8
3. Tang J, Zheng JS, Fang L, Jin Y, Cai W, Li D.Tea consumption and mortality of all cancers, CVD and all causes: a meta-analysis of eighteen prospective cohort studies. Br J Nutr (Meta-analysis): 2015;3:1-11
4. Zheng JS, Yang J, Fu YQ, Huang T, Huang YJ, Li D. Effects of green tea, black tea, and coffee consumption on the risk of esophageal cancer: a systematic review and meta-analysis of observational studies. Nutr Cancer (Systematic Review and Meta-Analysis) 2013;65 (1): 1-16
5. Huang YQ, Lu X, Min H, Wu QQ, Shi XT, Bian KQ etal. Green tea and liver cancer risk: A meta-analysis of prospective cohort studies in Asian populations. Nutrition (Meta-Analysis).2015; S0899-9007 (15): 00237-3
6. Liu G, Mi XN, Zheng XX, Xu YL, Lu J, Huang XH. Effects of tea intake on blood pressure: a meta-analysis of randomised controlled trials". Br J Nutr (Meta-Analysis)2014; 112 (7): 1043-54
7. Larsson SC. Coffee, tea, and cocoa and risk of stroke. Stroke (Review) 2014;45 (1): 309-14
8. Serban C, Sahebkar A, Antal D, Ursoniu S, Banach M. Effects of supplementation with green tea catechins on

plasma HDL-cholesterol: A systematic review and meta-analysis of randomized controlled trials. Nutrition (Systematic review & meta-analysis) 2015;31 (9): 1061-71
9. Jurgens TM, Whelan AM, Killian L, Doucette S, Kirk S, Foy E. Green tea for weight loss and weight maintenance in overweight or obese adults. Cochrane Database Syst Rev 2012; 12: 111-3
10. Suzuki Y, Tsubono Y, Nakaya N, Suzuki Y, Koizumi Y, Tsuji I. Green tea and the risk of breast cancer: pooled analysis of two prospective studies in Japan. Br J Cancer 2004;90(7)1361-3
11. Thatte U, Bagadey S, Dahanukar S. Modulation of programmed cell death by medicinal plants. Cell Mol Biol. 2000;46(1):199-214
12. Thavanesan N. The putative effects of green tea on body fat: an evaluation of the evidence and a review of the potential mechanisms. Br J Nutr. 2011;3:1-13
13. Trudel D, Labbe DP, Bairati I, Fradet V, Bazinet L, Tetu B. Green tea for ovarian cancer prevention and treatment: a systemic review of the in vitro, in vivo and epidemiological studies. Gynecol Oncol. 2012; 126(3):491-8
14. Tsubono Y, Nishino Y, Komatsu S, et al. Green tea and the risk of gastric cancer in Japan.N Engl J Med. 2001; 344(9):632-6
15. Vinson JA, Teufel K, Wu N. Green and black teas inhibit atherosclerosis by lipid, antioxidant, and fibrinolytic mechanisms. J Agric Food Chem. 2004;52(11):3661-5
16. Wargovich MJ, Woods C, Hollis DM, Zander ME. Herbals, cancer prevention and health. J Nutr. 2001;131(11 Suppl):3034S-6S
17. Westerterp-Plantenga MS, Lejeune MP, Kovacs EM. Body weight and weight maintenance in relation to habitual caffeine intake and green tea. Obes Res 2005;13(7): 1195-1204
18. Wu AH, Butler LM. Green tea and breast cancer. Mol Nutr Food Res. 2011;55(6):921-30
19. Yuan JM. Green tea and prevention of esophageal and lung cancers. Mol Nutr Food Res. 2011;55(6):886-904
20. Lambert JD, Sang S, Yang C."Possible controversy over dietary polyphenols",Chem Res Toxicol 2007;20(4):583-5
21. Zhang C, Qin YY, Wei X, Yu FF, Zhou YH, He J. Tea consumption and raised HDL cholesterol. Eur J Epidemiology (Systematic Review and Meta-Analysis) 2015;30 (2): 103-13
22. Khan N, Mukhtar H. Tea and HDL-cholesterol: studies in humans. Current pharmaceutical design 2013; 19 (34): 6141-7
23. Arab L, Khan F, Lam H. Tea consumption and cardiovascular disease risk. Am J Clin Nutr 2013;98 (6 Suppl): 1651S-9S
24. Khalesi S, Sun J, Buys N, Jamshidi A, Nikbakht-Nasrabadi E, Khosravi-Boroujeni H. Green tea catechins and lipoprotein HDL: a systematic review and meta-analysis of randomised controlled trials. Eur J Nutr(Systematic Review and Meta-Analysis) 2014; 53 (6): 1299-131
25. Johnson R, Bryant S, Huntley AL. Green tea and green tea catechin extracts: an overview of the clinical evidence on HDL-cholesterol. Maturitas (Review) 2012;73 (4): 280-7
26. Peng X, Zhou R, Wang B, Yu X, Yang X, Liu K et al Effect of green tea consumption on blood pressure: a meta-analysis of 13 randomized controlled trials. Sci Rep 2014; 4: 6251

ORIGINAL ARTICLE

Effects of Ethmoid Surgery on Proptosis and Vision

Masood Akhtar[1],M Saleem Sheikh[2],Maroof Aziz[3],M Asim Shafique[4],M Maroof[5]

ABSTRACT:
Objective: To evaluate the role of external ethmoidectomy in improvement of proptosis and vision due to ethmoid disease.
Materials and Methods: This interventional study was conducted in the department of Otorhipolaryngology and Head and Neck Surgery Quaid-e-Azam Medical College and Bahawal Victoria Hospital BahawalPur, Pakistan, from September 2013 to February 2014. Twenty four males and females who presented in the OPD with proptosis due to polyposis and allergic fungal sinusitis were included in this study. All the patients were electively prepared for this operation. All patients had pre operative CT scan of nose, PNS, Orbit and Brain. Proptosis and vision was checked by the ophthalmologist. Informed written consent was taken from all patients. All underwent external ethmoidectomy operation via Lynch Howarth approach which provided a direct and in depth view of the ethmoids and orbit.
Results: 13 patients were males and 11 were females with mean age 22.46 ± 10.15 years (range 7-45 years). All patients had proptosis and size of proptosis improved in17 patients (70.83%). Impaired vision was seen in 17 cases and improvement was seen in 11 cases (64.70%).There were no major post operative complications and the minor complications like external scar, lacrimation and anterior nasal discharge resolved completely.
Conclusion: External ethmoidectomy has a role in improvement of proptosis and vision due to ethmoid disease. Orbital complications due to ethmoid disease should therefore be timely diagnosed and treated so as to have remarkable improvement in proptosis and vision.
Keywords: Proptosis, Vision, Ethmoid Surgery, Lynch Howarth approach, Orbital decompression, Ethmoiditis

INTRODUCTION:

Proptosis is a latin word, which means, prolapse.The contents of the orbit are present within rigid confines of the bony orbital walls. Any disease process within the orbit or adjacent region has a tendency to displace the orbital contents forwards, this displacement of the globe is known as proptosis. Though proptosis may seem to be primarily the concern of the ophthalmologist, but because of the close proximity of the orbit and the paranasal sinuses and various connecting fissures and foramina between the two, many fronto-ethmoidal lesions present with proptosis.[1]Ethmoid labyrinth is a group of small sinuses on each side that lie between upper part of nasal cavity and orbit, and separated from later by paper thin bone, lamina papyracia or orbital plate of ethmoid. This presents poor barrier to infection which may therefore spread into orbit.[2] The fronto-ethmoidal diseases causing proptosis usually present as nasal polyps and mucoceles.[3]

✉ **Dr. Masood Akhtar**
Associate Professor
Department of ENT
Quaid-e Azam Medical College
Bahawalpur
Email:entdrmasood@yahoo.com
✉ **Dr. M Saleem Sheikh**
Associate Professor
Department of ENT
Quaid-e Azam Medical College
Bahawalpur
✉ **Dr.Maroof Aziz**
Professor
Department of ENT
Quaid-e Azam Medical College
Bahawalpur
✉ **Dr. M Asim Shafique**
Senior Registrar
Department of ENT
Quaid-e Azam Medical College
Bahawalpur
✉ **Dr. M Maroof**
Medical Officer
Department of ENT
Quaid-e Azam Medical College
Bahawalpur
Received: 12-10-2015
Revised: 22-11-2015
Accepted: 25-11-2015

Nasal polypi are frequently seen in ENT practice.The word polyp is basically of Greek terminology meaning many footed (poly-pous). It was recognized in India for the first time and by 1000 BC. Curettes had been devised to remove them.[4]Nasal polypi are prolapsed lining of the edematous nasal or sinus mucosa. They block the nose to a variable degree depending on their size, and cause nasal obstruction. On clinical examination, nasal polypi appear as pale, smooth, shining, glistening, multiple bags like bunch of grapes. Allergy is an important cause of polyp formation.Both imaging and clinical techniques help the clinician to determine the axial position of the globe in relation to the orbital bony rim. An exophthalmo-meter of an accurate design is necessary for diagnosis of proptosis.[5]Surgical intervention performed to treat an underlying fronto-ethmoidal disease causes decrease in volume of the orbital contents, and hence improvement in proptosis. The external fronto-ethmoidectomy gains its widest applications in treating patients with fronto-ethmoidal lesions.[6] External ethmoidectomy is an operation designed to gain access to the ethmoid sinuses via an external incision placed between the corner of the eye and the nose. This operation is indicated for cleaning irreversible mucosal disease in the sinus, recurrent sinus disease, polyposis, chronic obstruction to the drainage of infection from the sinuses and sometimes, as an approach to the sphenoid and pituitary gland. Occasionally, this operation is also performed to remove a mucocele or a tumor of the ethmoids. It gives better visualization and access to all

the ethmoidal cells. But the disadvantage of this surgery is external scar, which may be minimal with meticulous suturing.This early surgical intervention not only improves the cosmetic look of the patient by relieving proptosis, but would also avoid consequences such as visual loss[7]and intracranial extension.[8]Present study was designed with the objective to highlight the improvement of proptosis and vision in patients who underwent Lynch Howarth procedure for an underlying fronto- ethmoidal disease.

MATERIALS AND METHODS:

This study was conducted at department of ENT & Head and Neck Surgery of Quaid-e-Azam Medical College and Bahawal Victoria Hospital BahawalPur from September 2013 to February 2014. Patients with nasal polyposis and proptosis were admitted. Proper history and examination was carried out, relevant investigations and CT scan of nose, paranasal sinuses were done in all patients.With the help of ophthalmologist, vision and proptosis was measured preoperatively. Proptosis was measured in millimeters with the help of exophthalmometer. Protrusion of the eye ball 19 mm or more was labelled as proptosis. Post operative decrease in size of proptois was labeled as improvement, and noted in millimeters. Similarly vision was checked by ophthalmologist by Snell'n chart, and labeled 6/6, 6/9, 6/12, 6/18 etc. with decreasing vision. One step improvement in vision was labeled as one line improvement. A performa was designed and filled with care. All patients under went external ethmoidectomy operation by LynchHowarth approach. Improvement in vision and proptosis was measured, 7 days and then 30 days after surgery.Patients with proptosis (19 mm and above) due to nasal polypi and allergic fungal sinusitis of any age and of any gender with or without visual impairment were included in the study. Whereas patients with proptosis due to orbital disease, patients with intracranial extension of disease, patients with proptosis due to nasal tumours/mucocele and patients with blindness were excluded from the study.

RESULTS:

A total of 24 patients with proptosis due to nasal polypi and allergic fungal sinusitis were included in the study. Out of these 13(54.16%) were male, and 11 (45.83%) were female. The mean age was 22.46 ± 10.15 years (range 7-45 years).All patients under went external ethmoidectomy approach. Proptosis and vision was measured 7 days and 30 days after surgery, but results were finalized 30 days after surgery. Improvement of proptosis was seen in 17 (70.83%) cases(Table 1). Average improvement in proptosis was 0.90 mm after seven days, and 1.95 mm after 30 days (Table 2) Impaired vision was seen in 17 cases, out of which 11 cases (64.70%) showed improvement in vision.In 6 cases no improvement of vision was seen (Table 3)Average improvement in vision was 0.82 lines after 7 days, and 1.17 lines improvement after 30 days(Table 4)

Table: 1
Improvement in Proptosis

Proptosis	No. of patients
Improvement	17 (70.83%)
No improvement	7 (29.16%)
Total	24

Table: 2
Average improvement in Proptosis

	After 7 days	After one month
Average improvement in proptosis	0.90 mm	1.95 mm

Table: 3
Improvement in Vision

Vision	No. of patients
Improvement	11(64.70%)
No improvement	6(35.29%)
Total	17

Table: 4
Average improvement in Vision

	After 7 days	After one month
Average improvement in vision	0.82 lines	1.17 lines

DISCUSSION:

The forward displacement of eye ball is called proptosis. Majority of cases of unilateral and bilateral proptosis are seen by ophthalmologist and only few are referred to ENT departments.[9] The cause of proptosis in Otorhinolaryngology is mainly the disease in the frontal and the ethmoidal sinuses.[10]The fronto-ethmoidal disease causing proptosis usually presents as nasal polypi and mucoceles.[3]Proptosis is the most common ophthalmic sign of allergic fungal sinusitis.[11] Orbital involvement must be ruled out whenever an ENT patient presents with orbital complaints like proptosis, ophthalmoplegia, neurological dysfunction of eye, chemosis or epiphora.[12] Ballooning of edematous sinus or nasal mucosa is called nasal polypi. Patients may present with simple nasal polypi or polypi with fungus. Some of the patients with nasal polypi may also have intraorbital or intracranial extension. The treatment of nasal polypi, especially to prevent recurrence, has always been a challenging task for ENT surgeons. Small polypi without introrbital or intracranial extension may respond to oral or nasal corticosteroids, but the recurrence rate is high and usually surgery is required.[13]The surgical treatment is intranasal polypectomy or ethmoidectomy. Although the chances of cure after surgical treatment are considered more, they are not free from complications like hemorrhage, infection, intraorbital or intracranial complications.

Recently a new technique of nasal polypectomy or ethmoidectomy has been developed, which is done with the help of Endoscope, called Functional Endoscopic Sinus Surgery (FESS).The Concept of Surgery was developed in 1970s, by Stammberger.[14]Whichever technique of surgery is used, there is quite a high incidence of recurrence of nasal polypi after the operation, so surgery should be followed by corticosteroid nasal spray.[15]The rate of recurrence is higher in patients with asthma, eczema and aspirin hypersensitivity.[16] Patients with proptosis due to nasal polypi and allergic fungal sinusitis (thick viscous mucin) were included in our study. Allergic fungal sinusitis is a non invasive, but vigorous, inflammatory response to mold that occurs in immunocompetent patients with chronic sinusitis and nasal polyposis. It typically occurs in patients who have a history of atopic disease. Occasionally, the patients with allergic fungal sinusitis present with ophthalmic signs and symptoms, most commonly proptosis and diplopia.[17] CT scans of these patients show hypertrophic sinusitis and often hyper attenuating allergic mucin within the sinus cavities. Extra sinus extension of disease is common. Surgical histopathology shows eosinophilic-lymphocytic mucosal inflammation and inspissated allergic mucin containing non-invasive fungal hyphae[18,19,20]

Fewer relevant data is available on the subject of treating these fronto-ethmoidal lesions with proptosis. Some surgeons do Lynch Howarth approach while others prefer endoscopic approach. Still a lot of research work is required in this regard. Endoscopic sinus surgery is now frequently used newer technique. But it is costly and not available in every centre. That is why some surgeons still prefer external ethmoidectomy approach for the treatment of nasal polypi, especially to avoid recurrence, with good results.[21] Saeed[22] showed 97% success rate and Baig[23] 100% success rate with external ethmoidectomy regarding recurrence of nasal polypi.The current study evaluated the improvement of proptosis and vision after Lynch Howarth external ethmoidectomy approach. As we don't have the facility of endoscopic sinus surgery, so we preferred this approach with good results.Qureshi[24] performed Lynch Howarth external ethmoidectomy in 10 patients with polyposis and proptosis. Two patients (20%) had change in colour vision, indicating that the eye was at risk. These two patients underwent an emergency external ethmoidectomy procedure to save the eye. The results were remarkable with improvement of proptosis in all patients (100%) which is quiet high, while our study has showed improvement of proptosis in 70.83% cases.Aziz[6]conducted similar study on 70 patients with proptosis due to frontoethmoidal disease. He noted improvement in protosis in 42 patients (60%), which is comparable with our study.Sheikh[25] also reported a single case with marked improvement in vision and dystopia after external ethmoidectomy approach. Thus external ethmoidectomy operation via Lynch Howarth approach provides a direct and in depth view of the ethmoids and orbit.Centers where endoscopic sinus surgery is not available, this approach could be practiced. It offers not only access and illumination to this area but as mentioned earlier also a good perception of depth in ethmoids and orbit, to prevent complications like, hemorrhage and blindness. Although this technique has the disadvantage of external scarring but this can be minimized with meticulous suturing techniques. The scar also fades with passage of time.

CONCLUSION:

External ethmoidectomy approach has given remarkable results in improvement of the proptosis and vision. Orbital complications due to ethmoid disease should be timely diagnosed and treated to save the eye and prevent external deformity.

REFERENCES:

1. Sinha V, Bhardwaj D, George A, Memon RA. Proptosis through eyes of ENT surgeon. Indian J Otolaryngol Head & Neck surgery. 2005; 57(3):207-9
2. Standring S, Borley NR, Collins P, Crossman AR, Gatz-oulis MA, Healy JC et al. Elsevier,Churchill Livingstone, 2008 4thed 558Grays anatomy
3. Herndon M, McMain KC, Kountakis SE. Presentation and management of extensive fronto- orbital ethmoidm-ucoceles.Am J Otolaryngol. 2007; 28(3):145-7
4. Vancil ME. A historical survey of treatment for nasal polyposis. Laryngoscope 1969;79:435-45
5. Vardizer Y, Berendschot TJM, Mourits MP. Effects of Exophthalmometer design on its accuracy. Ophthal Plas ReconstrSurg,2005; 21(6): 427-30
6. Aziz B, Ghouri SM, Rasheed A, Hameed A. Frequency of Improvement of Proptosis for an Underlying Fronto-Ethmoidal disease after Lynch procedure. Pak J Med Health Sci. 2012; 6(4): 882-4
7. Fasunla JA, Adeleye AO, Onakoya PA, Okolo CA, Nwa-orgu GO. Recurrent nasal polyp and pansinusmucopyo-cele associated with blilateral blindness: A case report. Ghana Med J. 2010;44(4):165-8
8. Viola GM, Sutton R. Allergic fungal sinusitis complicated by fungal brain mass. Int J Infect Dis. 2010; 14 Suppl 3:S299-301
9. ZaidiSH.Unilateral proptosis in ENTpractice. J of Pak Med Assoc. 1991; 41(10): 248-50
10. Khan NH, Moin M, Khan MA, Hameed A. Unilateral proptosis: a local experience.Biomedica. 2004; 20(2): 1114-6
11. Carter KD, Graham SM, Carpenter KM. Ophthalmic manifestation of allergic fungal sinusitis. Am J Ophthal-mol. 1999;127(2):189-95
12. Sikarwar V, Bisht RS, Kumar D, Shukla RK. Ophthalmic Manifestations in ENT Diseases & Surgical Procedures. J of Dental and Medical Sciences. 2013; 11(4): 87-92
13. Yoo JK, Seikaly H. Extended use of topical nasal deco-ngestents. Laryngoscope 1997;107:40-3
14. Stammberger H, Endoscopic surgery for mycotic and chronic recurring sinusitis. Ann Otol Rhinol Laryngol 1985;94:1-11
15. Lidholdt T, Runderantz H.Glococorticoid treatment for nasal polpi.Article of oto-laryngology and head and neck surgery 1997;123:595-600
16. Bolyard F, Gosset P, Lamblin C, Bergoin C, Tonnel AB, Wallaert B.Cell and cytokine profiles in nasal secretions from patients with nasal polyposis: effects of topical

steroids and surgical treatment. Allergy. 2001;56:333-8
17. Coop CA, England RW. Allergic fungal sinusitis presenting with proptosis and diplopia: a review of ophthalmologic complications and treatment. Allergy Asthma Proc.2006;27(1):72-6
18. Schubert MS. Medical treatment of allergic fungal sinusitis. Ann Allergy Asthma Immunol. 2000;85(2):90-7; quiz97-101
19. Khong JJ, Malhotra R, Wormald PJ, Selva D. Endoscopic sinus surgery for paranasal sinus mucocoele with orbital involvement. Eye. 2004;18:877–81
20. Akeem O L, Aderemi A A.Traditional open surgery for advanced benign nasal tumours: review of 38 cases. Afr J Health Sci 2007;14:44-8
21. Ameet Singh,Conner J masey,Arlem D Meyers.Acute Frontal Sinusitis Surgery Medscape 2015,15 dec; section Drugs and Diseases (Col 2)
22. Saeed M, Mian FA. Recurrent Ethmoidal Polypi: Surgical management. Professional Med J. 2005; 12(4): 466-72
23. Baig MM, Hussain T.Recurrent Ethmoidal Polypi: A Prospective Study. J Rawal Med Coll. 2008; 12(1): 33-6
24. Qureshi N. Eye in danger of ENT: Role of External Ethmoidectomy in Orbital Decompression due to Ethmoiditis. J Rawal Med Coll. 2007; 11(2): 90-3
25. Sheikh SI, Rashid A, Azeem A, Khan MA, Hameed A, Samee A. Eye Dystopia in ENT. Pak J Med Health Sci. 2012; 6(4): 905-6

ORIGINAL ARTICLE

Dental Students' Perception on Preclinical Operative Dentistry Course

Meisha Gul[1], Shama Asghar[2],Zara Sami[3]

ABSTRACT:

Objective: To determine student's perception on preclinical operative dentistry course in different dental colleges of Karachi.

Materials and Methods: This descriptive study was conducted at three different dental colleges of Karachi .Total of 130, 2nd year BDS students participated. Specially designed questionnaire including demographics was used. This research was conducted after getting permission from respective authority and verbal consent from all respondents. Analysis was done using SPSS version 17.

Results: Total 130 participants responded out of which 109 (86.3%) were female and 21 (13.7%) were male. The mean age of the respondents was 20.54 ± 1.037 years (a range of 18-25 years). More than 80% of the students reported that preclinical course helped them in understanding the subject, increased their motivation to gain knowledge and would help them in final year respectively.71.5% and 75.4% stated improved confidence and easier to work in clinic.60.8% and 33.1% found that the course was adequate and extensive respectively.54.6% of the participant perception was that every lecture should be accompanied by clinical visit. Reason to attend preclinical course included 35.4% (essential preparation for clinical dentistry), 3.8% just because of attendance. 81.5% of the students want to have structured manual of the course.

Conclusion:Students showed positive response regarding preclinical course in order to increase their interest and to become a successful clinician. However, some revisions need to be made in educational methods and contents.

Keywords: Dental education, Preclinical course, Operative dentistry, Psychomotor skills.

INTRODUCTION:

Dental education is considered as a complex, challenging and often stressful educational procedure.[1] Acquisition of psychomotor skills by undergraduate students is an important step in many health professions, particularly dentistry to become a successful professional.[2]Before performing procedures that may be invasive and/or irreversible in patients, it is essential that the dental students should spend time to learn essential psychomotor skills through various teaching strategies during their preclinical laboratory projects to meet patient needs–either aesthetic or functional.[3]These projects vary from the use of traditional bench-top typodonts mounted manikins adapted to phantom heads to highly sophisticated devices, such as the virtual reality simulators.[4,5]

Curriculum of BDS prepared by Pakistan Medical & Dental Council (PMDC) and the Higher Education Commission (HEC) include 25 lecture hours and 110 practical hours for pre-clinical instruction in second year and 20 lecture hours and 80 practical hours for pre-clinical operative dentistry in third year.[6,7]Factors affecting clinical learning include varieties of clinical cases encountered, the quality of supervision and feedback, good organization of the experiences of learners and teachers. The central concern in dental education is to prepare dental students to independently provide patient care. The learner's views of their educational experiences is important in modifying the educational process.[1] Students View point regarding quality and efficacy of dental education is very important because they are the main consumers of dental education and their opinions is considered as the major determinants of teaching effectiveness. For continuous improvement a feedback mechanism is required.The present study was conducted to assess the perceptions of dental students on preclinical operative dentistry course in three different dental colleges of Karachi.

✉ **Dr. Meisha Gul**
Lecturer
Department of Biochemistry
Bahria University Medical and Dental College
Karachi
E-mail: meishagul@gmail.com
✉ **Dr. Shama Asghar**
Assistant Professor & Head
Department of Operative Dentistry
Bahria University Medical and Dental College
Karachi
✉ **Dr. Zara Sami**
Lecturer
Department of Biochemistry.
Bahria University Medical and Dental College
Karachi
Received: 14-10-2015
Revised: 17-11-2015
Accepted: 19-11-2015

MATERIAL AND METHODS:

This descriptive study was conducted at three different dental colleges of Karachi, Bahria University Medical and Dental College (BUMDC), Karachi Medical and Dental College (KMDC) and Dow University of Health Sciences (DUHS). A specially designed self-administered questionnaire was distributed among dental students at the end of their respective lectures on the day of study. Questionnaires were answered anonymously by students and no personal information except their age and gender was obtained. The questionnaire consisted of 18 close-ended questions with different options to mark against and some were simply yes/no type questions. A total of 130 students participated in the study, out of which 109 were females and 21 were male students. Inclusion criteria include students of second year BDS. First year, third year and final year students were

excluded. This research was conducted after getting permission from respective authority and verbal consent from all respondents. All respondents participated voluntarily in this study. Confidentiality of the response of the respondents has been maintained.Data were obtained and analysed using SPSS software (version 17.0) for statistical analysis.

RESULTS:

Total 130 participants responded out of which 109 (86.3%) were female and 21 (13.7%) were male (Figure 1). The mean age of the respondents was 20.54 ± 1.037 years (a range of 18-25 years). The questionnaire was distributed among 2nd year students in three different dental colleges of Karachi, the percentage of participants from each college is shown in Figure 2. Student response regarding the academic year most suitable to teach preclinical course is shown(Figure 3).

According to 79(60.8%) students the course content was adequate, 43(33.1%) students thought it was too extensive, 6(4.6%) and 2 (1.5%) students found it too easy and inadequate respectively. Regarding question about teacher attention received by the students, 79 (60.8%) responded that they received enough attention, 33 (25.4%) chose more than enough, 15 (11.5%) were not satisfied and marked not enough. Out of total 53 (40.8%) students selected excellent and satisfactory for the ability of the teachers to clarify concepts, 17(13.1%) chose between satisfactory and not good enough. 71 (54.6 %),11 (8.5%) students suggested that each lecture should be accompanied by visits to the dental clinic to see the live procedures and separate class rooms should be available for preclinical lecture and exercises respectively. In response to question about facilities 11 (8.5%) students reported about the difficulty in getting extracted teeth, 10 (7.7 %) students mention that getting plaster model at the right time was a great problem, 10 (7.7 %) chose that there should be proper syllabus.(Table 1).

Another question regarding reasons to attend the course revealed that 46 (35.4%), 37(28.5%), 20(15.4%), 14 (10.8%), 5 (3.8%) and 6 (4.6 %) responded that it was an essential part of preparation for clinical dentistry, they would not have to go directly to patients without prior practice, made them feel like dentists for the first time,genuinely interested in having the course, just because of attendance,chose more than one reason respectively. students reported that they used more than one source of study, most reported educational resources used by the students include more than one source37 (28.5%),McCabe's Dental Materials 31 (23.8%), lecture handouts24 (18.5%),copied multimedia presentations19 (14.6%)and only 6 (4.6%) used Practical Manual of Operative Dentistry (Table 1).

Majority of the students 113 (86.9%),101 (77.7%) and 98 (75.4%) and 93 (71.5%) believed that the course had increased their motivation in gaining knowledge about techniques,would help in better patient handling and care and would be easier to work in clinics after this course and improved confidence level for further exercise respectively. According to 83 (63.8%) students the environment was conducive to learning and 32 (24.6%) replied it was not. 86 (66.2%) students felt that they would be capable of evaluating their own work after the course, 15 (11.5%) could not and 29(22.3%) don't know. 33 (25.4%) students responded that more topics should be added, 86 (66.2%) and106 (81.5%) students thought no more topics should be added and a manual specially tailored for the course should be available. 111 (85.4%) students response showed that clinical rotation to observe procedures being done after every clinical exercise will be helpful (Table 2).

Figure: 1
Gender distribution

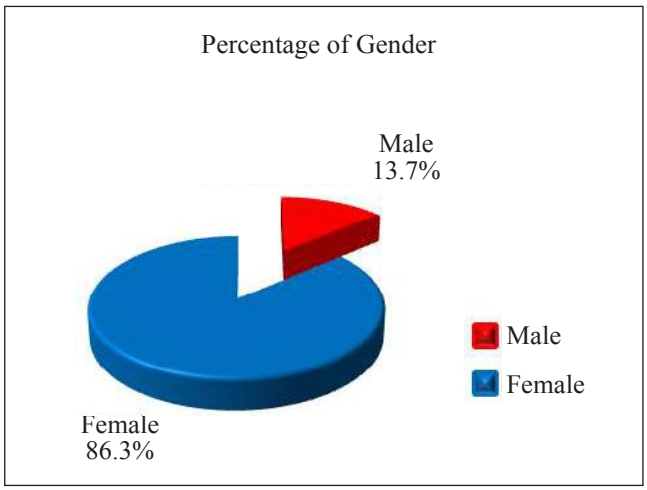


Figure: 2
Percentage of participants from each college

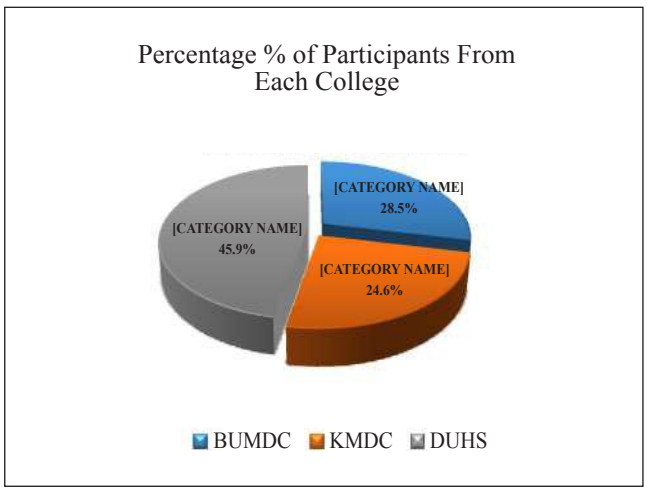


Table: 1
Frequencies and Percentage of different variables

S.#	Questions	Options	Count (n)	Percentages %
1	Course content was	Adequate	79	60.8
		Too extensive	43	33.1
		Too easy	6	4.6
		Inadequate	2	1.5
2	Do you think you receive enough attention by your teacher	Enough	79	60.8
		More than enough	15	11.5
		Not enough	33	25.4
		Did not reply	3	2.3
3	Do you think teacher are able to clarify concepts	Excellent	17	13.1
		Between excellent and satisfactory	53	40.8
		Satisfactory	35	26.9
		Between satisfactory and not good enough	17	13.1
		Not good enough	8	6.2
4	What is your perception about facilities provided to you during your preclinical courses?	Getting extracted teeth was a great Problem	11	8.5
		Problem getting plaster models at the right time	10	7.7
		Separate classroom should be available	11	8.5
		Each lecture exercise to be accompanied by visits to the clinic to see the procedure being done	71	54.6
		Syllabus would be a good idea	10	7.7
		Did not reply	13	10.0
		More than one option	4	3.1
5	Your reason to attend preclinical course	Genuinely interested in having the course	14	10.8
		Essential preparation for clinical dentistry	46	35.4
		Made them feel like dentists for the first time	20	15.4
		Would not have to go directly onto patients without prior practice	37	28.5
		Attendance	5	3.8
		More than one reason	6	4.6
		Did not reply	2	1.5
6	Which educational resource did you use for study during your preclinical course	Notes	7	5.4
		Lecture handouts	24	18.5
		Student assignments	1	.8
		McCabe's Dental Materials	31	23.8
		Copied Multimedia presentations	19	14.6
		Practical Manual of Operative Dentistry	6	4.6
		Students reporting more than one source of study	37	28.5
		Internet/senior notes	3	2.3
		Did not reply	2	1.5

Figure: 3
Students response about the academic year most suitable to teach preclinical course

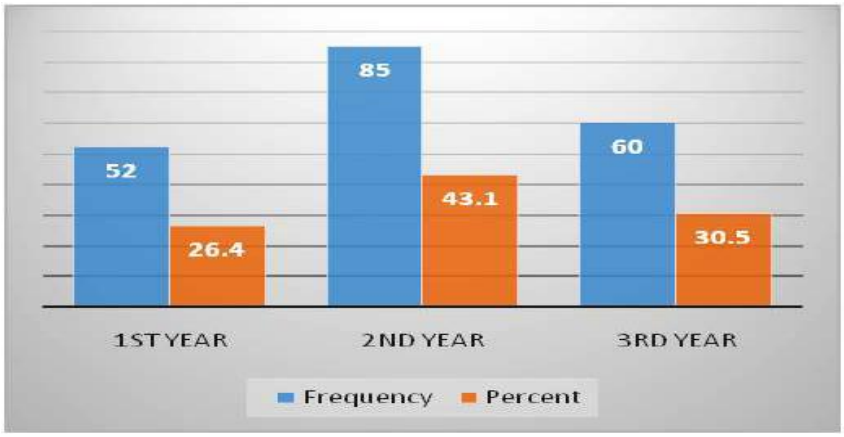


Table: 2
Frequencies and Percentage of different variables

S.#	Questions		Options		
			YES	NO	DON'TKNOW
1.	It would help you in final year	Count(n)	106	4	20
		Percentage %	81.5	3.1	15.4
2.	Course has any role in motivating to increase your knowledge about techniques	Count(n)	113	15	2
		Percentage %	86.9	11.5	1.5
3.	It would help you in better understanding of the subject	Count(n)	112	8	10
		Percentage %	86.2	6.2	7.7
4.	It would help you in better patient handling after this course	Count(n)	101	8	16
		Percentage %	77.7	6.2	12.3
5.	It would be easier to work in clinics after this course	Count(n)	98	15	17
		Percentage %	75.4	11.5	13.1
6.	It would improve confidence level for further exercise	Count(n)	93	17	20
		Percentage %	71.5	13.1	15.4
7.	Environment was conductive to learning	Count(n)	83	32	15
		Percentage %	63.8	24.6	11.5
8.	you would be capable of evaluating your own work after the course	Count(n)	86	15	29
		Percentage %	66.2	11.5	22.3
9.	Do you think more topics should be added in your course	Count(n)	33	86	11
		Percentage %	25.4	66.2	8.5
10.	There should be structured manual of the course.	Count(n)	106	8	16
		Percentage %	81.5	6.2	12.3
11.	Going to clinic to observe procedures being done after every clinical exercise is helpful	Count(n)	111	5	14
		Percentage %	85.4	3.8	10.8

DISCUSSION:

There is increasing awareness that learner's views of their educational experiences and responses are crucial in modifying the educational procedure. Therefore, quantitative data collection methods, primarily surveys, have been widely used to evaluate dental student's perspective on the effectiveness of courses in areas such as operative dentistry.[8]

Operative skills development in a preclinical setting is of importance for the training of undergraduate students.[9]This study aimed to explore dental student's views regarding the reason and advantages of attending the preclinical course, the learning environment, course content, quality of teaching, learning facilities and the educational resources used by the students. Student's suggestion was also taken into consideration. In our study 113 (86.9%) of the students perception was that the course had motivated them to increase their knowledge regarding techniques and 106 (81.5%) thought course would help them in final year. Ahmed reported in his study that 100% students responsed that pre-clinical course had increased their motivation and would help them in final year.[10] More than 80% students perception was that the course would help in better understanding of the subject. Preclinical course really help students to better correlate their theoretical knowledge with clinical application and this integration increase student interest in the subject and at the same time help in better understanding of the subject. In our study 77.7% and 75.4% students perception were that after attending the preclinical course it would be easy to handle the patient and easier to work in clinic respectively. Bianca's study results also suggested that preclinical training on the typodont and in the classroom was related with clinical performance.[11]11.5% of the students perception was that the course is not related to clinical success. Both Curtis[12]and Nunez[13] studies found that preclinical training was not an accurate interpreter of success in clinic. The literature is full with illustrations regarding self-evaluation which explains that self-evaluation skills of students are not accurate.[14,15] Expert judgement and advice is needed for accurate evaluation yet 66.2% of the second year students stated that they could evaluate their own work after attending the course.This is in direct contrast with studies evaluating the self-assessment skills of students, it showed that students were too assertive when evaluating their own self-assessment skills.[16,17]

In order to match the learning styles of all students learning resources should be different. In our study most of the students use more than one source of study. Some students preferred more difficult textbooks while others relied on notes and handouts. An ideal dental educational setting should aid students to acquire the necessary clinical,theoretical and interpersonal competences and expose them to 'clinical experiences' equivalent to the environment in which they are probably be practicing dentistry.[15]In our study 85.4% responded that clinical rotation to observe procedures on patients should be included in the curriculum. 63.8% students thought that the environment was conducive to learning, 32 (24.6%) were not in favour and 11.5% students don't know. In Betsy's survey students also felt that the learning environment contributes to their learning. The working environment has to be optimal in order to get the best out of anyone, whether a teacher or astudent. If it is pleasant, the final result is definitely going to be better than if the environment were to be stressful or not so pleasant.[18]Among dental students the experience of sever eanxiety and stress is well-recognized. Stress-related symptoms reported by the students range from mild anxiety to eating and sleep disorders, as well as poor performance, lack of ability to concentrate, aggression, sadness and other devastating effects. Commonly reported sources of stress include academic overload.[19,20,21,22,23,24,25]81.5% suggested that there should be structured manual of the course. 33.1% and 66.2% students opinion was that the course was too extensive and no more topics should be added.

In this study 35.4% students thought that it is essential part of preparation for clinical dentistry, 28.5% chose they would not have to go directly onto patients without practice, 15.4% attend this course because it make them feel like dentists for the first time and 10.8% students were genuinely interested in having the course. Ahmed's survey also supported our view that it is important preparation for future clinical practice and made them feel like real dentist and increase their interest in the subject.[10]

Students also felt that a good student-teacher relationship facilitates student's learning and leads them to achieve their learning goals.[1] 60.8% students reported that they received enough attention from teacher, 25.4% responded more than enough, 11.5% were not satisfied. Majority of the students were satisfied from the teacher's ability to clarify concept but some students were not, reasons include poor attendance, communication gap between student and teacher, problem with the basic concept.

CONCLUSION:

It is important to understand that education is much more than gaining knowledge or training. It is essential to view dental studies from a student centred perspective. In this study majority of the students were in favour of attending the preclinical course and understand its importance in building up their confidence, better understanding of the subject and better patient handling in future dental practice. Course should also be included in first year for better understanding of dental materials. Every preclinical lecture should be accompanied by clinical visits. There should be structured manual for preclinical course for guidance along with especially trained separate teaching faculty should be appointed so that the students receive enough attention and their queries can be better responded.

REFERENCES:

1. Ansary J, Ara I, Talukder H, Alam A, Amin S, Rahman S. Views of students regarding effective clinical teaching and learning in dental education. Bangladesh Journal of Medical Education 2014;2(1):1-5
2. Afify AR, Zawawi KH, Othman HI, Al-Dharrab AA. Correlation of psychomotor skills and didactic performance among dental students in Saudi Arabia. Adv Med EducPract 2013;4:223
3. Diniz IMA, Santos EM, de Souza-Rodrigues RD, Donda TR, Vieira GF. Wear of depth perception and shade matching outcome in the pre-clinical setting. Braz. Dent. Sci 2015;18(1):44-50

4. Wierinck E, Puttemans V, Swinnen S, Steenberghe D. Effect of augmented visual feedback from a virtual reality simulation system on manual dexterity training. EurJ Dent Educ2005;9(1):10-6
5. Wierinck E, Puttemans V, Van Steenberghe D. Effect of tutorial input in addition to augmented feedback on manual dexterity training and its retention. EurJ Dent Educ 2006;10(1):24-31
6. Pakistan Medical & Dental Council. Regulations for the degree of Batchelor of Dental Surgery (B.D.S). 2006. [cited 2015 july 19]
7. Higher Education Commission of Pakistan. Curriculum of BDS. 2005. [cited 2015 july19]. Available from: http: // BDS%202005.pdf
8. Long N, Zullo T, Hinkelman K. A comparison of two teaching simulations in preclinical operative dentistry. Operative dentistry 1996;22(3):133-7
9. Villarroel M, Fahl N, DSousa A, D Oliveira OB. Direct esthetic restorations based on translucency and opacity of composite resins. J Esthet Dent2011;23(2):73-87
10. Ahmed A, Hasan M, Shahnawaz A. Pre-clinical operative dentistry: students viewpoints. PODJ2011;31(2):447-52
11. Velayo BC, Stark PC, Eisen SE, Kugel G. Using dental students' preclinical performance as an indicator of clinical success. J Dent Educ2014; 78(6):823-8
12. Curtis DA, Lind SL, Brear S, Finzen FC. The correlation of student performance in preclinical and clinical prosthodontic assessments. J Dent Educ 2007;71(3):365-72
13. Nunez DW, Taleghani M, Wathen WF, Abdellatif HM. Typodont versus live patient: predicting dental students' clinical performance. J Dent Educ 2012;76(4):407-13
14. Goldie J. AMEE Education guide no. 29: Evaluating educational programmes. Med Teacher 2006;28:210-224
15. Divaris K, Barlow PJ, Chendea SA, Cheong WS, Dounis A, Dragan IF et al. The academic environment: the students' perspective. Eur J Dent Educ 2008;12Suppl 1:120-30
16. Polyzios I, McLoughlin J, Kelly A, Claffey N. Clinical teaching in restorative dentistry and the variation between students'and supervisors' perceptions of its effectiveness. Eur J Dent Educ 2010;14:92-8
17. Nance ET, Lanning SK, Gunsolley JC. Dental anatomy carving computer-assisted instruction program: an assessment of student performance and perceptions. J Dent Educ2009;73(8):972-9
18. Betsy ST, Reem RA, Mohan A,Ramnarayan K. Students' perceptions regarding educational environment in an Indian dental school. Medical Teacher 2009;31:e185-e188
19. Stewart DW, De Vries J, Singer DL, Degen GG, Wener P. Canadian dental students' perceptions of their learning environment and psychological functioning over time. J Dent Educ 2006;70:972-81
20. Muirhead V, Locker D. Canadian dental students' perceptions of stress. J Can Dent Assoc 2007;73:323
21. Morse Z, Dravo U. Stress levels of dental students at the Fiji School of Medicine. Eur J Dent Educ 2007;11:99-103
22. Pau A, Rowland ML, Naidoo S. Emotional intelligence and perceived stress in dental undergraduates: a multinational survey. J Dent Educ 2007;71:197-204
23. Polychronopoulou A, Divaris K. Perceived sources of stress among Greek dental students. J Dent Educ 2005; 69:687-92
24. Acharya S. Factors affecting stress among Indian dental students. J Dent Educ 2003;67:1140-8
25. Rajab LD. Perceived sources of stress among dental students at the University of Jordan. J Dent Educ 2001; 65:232-41

ORIGINAL ARTICLE

Role of Sonography in Prenatal Evaluation of Placenta Accreta

Rahila Usman[1], Sumayya Fatima[2], Sadia Rashid[3], Sehrish Mehmood[4], Kashif Shazlee[5], Kamran Hamid[6]

ABSTRACT:
Objective: To evaluate the diagnostic accuracy of gray scale and doppler examination in antenatal diagnosis of placenta accreta.
Materials and Methods: This is a prospective study done in a tertiary care center having large number of obstetrical cases,Ziauddin University hospital during a period of ten months from 12th August 2014 to 11th June 2015.Thirty seven pregnant high risk cases all with clinical suspicion of placenta accreta were subjected to sonographic evaluation using gray scale and color doppler imaging by senior radiologists. Presence of vascular lacunae with turbulent flow, loss of retro-placental clear space, vessels traversing the uterine serosa, thin out myometrium and interrupted retro-placental flow was evaluated sonographically. Maternal delivery records were reviewed for delivery outcomes and sonographic findings were confirmed at delivery on surgical and clinical findings.
Results: The diagnostic sensitivity of ultrasound for placenta accreta was 93.3% and specificity was 85.7%. Positive predictive value was 96.5% whereas negative predictive value of 75%.
Conclusion: Gray scale and color Doppler sonography has fairly good sensitivity for prenatal diagnosis of placenta accreta
Keywords: Placenta accreta, Sonography, Color Doppler, Sensitivity, Specificity

INTRODUCTION:

Placenta accreta is an important cause of maternal morbidity and mortality and is becoming the major reason for emergent postpartum hysterectomy. Two recent studies conducted in the United States propose a prevalence of one in 2500 deliveries, with both studies using both clinical and pathologic diagnoses.[1,2,3]The incidence of placenta accreta has increased with the growing number of cesarean deliveries. Recent estimate signifies a 25% to 50% incidence of placenta accreta in patients with placenta previa and prior cesarean delivery.[1]Morbidly adherent placenta implies an abnormal implantation of placenta into the uterine wall which could be placenta accrete vera, increta or percreta. In Placenta accrete vera placental villi adhere directly to the myometrium. In placenta increta placental villi invade into the myometrium and in placenta percreta placental villi invade through the myometrium and into the serosa. Placenta previa and previous cesarean section are the most important known risk factors for Placenta accreta. The clinical outcome of Placenta accreta is massive hemorrhage during placental separation. Hysterectomy is frequently required, serving to serious co-morbidities such as cystotomy (15.4% of cases), ureteral injury (2.1%), and pulmonary embolus (2.1%), with 26.6% of patients admitted to the intensive care unit.[4] Placenta percreta can also lead to the damage of adjacent organs, mostly leads to bladder injury. The exact pathogenesis of placenta accreta is not obvious, however, there have been several theories proposed. It is documented that abnormal vascularization due to scarring process after surgery with secondary localized hypoxia can lead to both faulty decidualization and disproportionate trophoblastic invasion.[5,6,7] Prenatal diagnosis of placenta accreta can help reducing the complication rate by enabling a surgeon to plan for the type of resources required at the time of delivery. Cesarean section is generally planned at 36 weeks gestation to minimize the risk of spontaneous labor. Surgical preparation regarding matters such as site of incision and need for uterine artery balloon occlusion can be individualized. The accuracy of sonography using gray scale and Color Doppler techniques for prenatal diagnosis of placenta accreta varies broadly in different studies. Its sensitivity has been described in range of 33% and 100%, and the specificity also varies broadly.[8,9,10,11,12,13] The aim of present study was to evaluate the accuracy of sonography in prenatal diagnosis

✉ **Dr. Rahila Usman**
Assistant Professor
Department of Radiology
Ziauddin University Hospital
Email: docrahila@yahoo.com
✉ **Dr. Sumayya Fatima**
Senior Registrar
Department of Radiology
Ziauddin University Hospital
Karachi
✉ **Dr.Sadia Rashid**
Senior registrar
Department of Radiology
Ziauddin University Hospital
Karachi
✉ **Dr.Sehrish Mehmood**
Resident
Department of Radiology
Ziauddin University Hospital
Karachi
✉ **Dr.Kashif Shazlee**
Head
Department of Radiology
Ziauddin University Hospital
Karachi
✉ **Dr. Kamran Hamid**
Assistant Professor
Department of Radiology
Ziauddin University Hospital
Karachi
Received: 21-10-2015
Revised: 29-11-2015
Accepted: 02-12-2015

of placenta accreta.

MATERIALS AND METHODS:

It is a prospective study done in Ziauddin University Hospital during a period of ten months between 12th August 2014 to 11th June 2015. It is a tertiary care institute with large number of obstetric patients. Our study population included 37 pregnant females. All cases having clinical suspicion of placenta accreta were sonographically evaluated using Gray scale and Color Doppler imaging by senior radiologists. Presence of vascular lacunae with turbulent flow, loss of retroplacental clear space, vessels traversing the uterine serosa, thin out myometrium and interrupted retroplacental flow was evaluated sonographically. Maternal delivery records were reviewed for delivery outcomes.

The placenta was considered normal if it was easily delivered during cesarean delivery without any bleeding complications. Ideally, the standard of reference for the diagnosis of abnormal adherent placenta is histological evaluation after hysterectomy has been performed. However, hysterectomy is not always clinically indicated and management should be conservative (decision to leave the placenta to involute in situ if bleeding is controlled, or pre-surgical uterine artery balloon embolization). Therefore, in these cases pathologic evaluation was unavailable therefore the diagnosis was based on clinical information provided at the time of delivery and surgery. The placenta was considered as accreta by clinical criteria including hemorrhage and adherent placenta during cesarean section or when it was evident that the placenta had reached the uterine serosa or the adjacent organs.The sensitivity, specificity, positive predictive value (PPV), and negative predictive value(NPV) were calculated for sonographic diagnosis of placenta accreta. All calculations were done using SPSS version 19.

RESULTS:

37 patients underwent sonographic evaluation for prenatal diagnosis of placenta accreta.29 patients were given the diagnosis of placenta accreta on the basis of ultrasound findings and 28 out of 29 patients were found to have placenta accreta on final diagnosis. Out of 37 patients 8 patients were given no sonographic evidence of placenta accreta. Out of these 8 patients 6 patients were clinically positive for absence of placenta accreta.The diagnostic sensitivity of ultrasound for placenta accreta was establish as 93.3% and specificity as 85.7% with positive predictive value of 96.5% and negative predictive value of 75%.Placental lacunae showing turbulent flow on color doppler were found to be the most sensitive imaging feature to predict the sonographic evidence of placenta accreta with sensitivity of 92% and specificity of 82%.Vessel traversing the uterine serosa was established as the most specific feature to diagnose placenta accrete sonographically with specificity of 95%.Presence of placenta previa and prior history of cesarean section are strongly associated with increased risk of placenta accreta. We have found that the risk of accreta increases with increased number of previous cesarean sections. Out of 37 patients all had history of previous cesarean scar and out of them only 5 (n=13) had history of single cesarean section. 86% (n = 32) of patient had low lying placenta, among these 32 patients 15 patients had grade 3 placenta previa, 5 had grade 4 placenta previa, 8 presented with grade 2 and 4 patients had grade 1 placenta previa. Increased maternal age was also found to be associated with increased risk of placenta accreta, mean age of the patients diagnosed with placenta accrete was calculated as 27 years.Most of the cases were diagnosed between 32 to 36 weeks of gestation.Out of 37 cases about half of them were confirmed of having placenta accreta on clinical and surgical criteria.

Table: 1

Sensitivity	93.3%
Specificity	85.7%
Positive predictive value	96.5%
Negative predictive value	75%

DISCUSSION:

Placenta accreta is a considerable source of maternal morbidity and mortality and is now the most common cause of peripartal hemorrhage resulting in emergent postpartum hysterectomy. Our study evaluated that ultrasound using color doppler imaging can correctly diagnose placenta accrete antenatally for proper surgical planning in order to reduce the risk of life threatening peripartal hemorrhage. The incidence of placenta previa and placenta accreta was amplified as regards to increased rate of cesarean sections, frequency of placenta accreta in the existence of placenta previa rising from 24% after one cesarean section to about 67% after four or more cesarean sections.[14]These results agree with our study which signifies the history of previous cesarean section in all patients with placenta accreta and only five had previous single cesarean scar, so we establish that the risk of placenta accreta increases with the increase in number of previous cesarean section.The study done by Dwyer[15]in 32 patients established the sensitivity of sonography for diagnosis of placenta accreta as 93% and specificity as 71%. They have mentioned in their study limitations that their study might have underestimated the sensitivity and specificity of sonography. This justifies our study results that have estimated the sensitivity of sonography for evaluation of placenta accreta as 93.3% and specificity of 85.7%. Esakoff[16]in 108 patients, have documented sensitivity of 89.5%, specificity 91%, positive predictive value(PPV) of 68%, and negative predictive value (NPV) of 98%. Shih[17]evaluated 170 patients and found sensitivity of 97%, specificity of 92%, PPV of 77% and NPV 99%.Warshak[18]in 453 patients have documented sensitivity of 77%, specificity of 96%, PPV of 65% and NPV of 98%.Wong [19]in 66 patients found sensitivity of 89%, specificity of 98%, PPV of 89% and NPV of 98%. In our study 37patients were evaluated and we found sensitivity of 93.3%, specificity of 85.7%, PPV of 96.5% and NPV of 75%. Our results are coinciding with all

these studies. Thus Sonographic imaging is the cheapest and prompt imaging technique to use for the evaluation of placenta accreta with high sensitivity and specificity.Ultrasound examination with color Doppler imaging and MRI have all been used in the diagnosis of placenta accreta with varying specificity and sensitivity. Ultrasound and color Doppler examination are the first step for the diagnosis of placenta accreta.[20,21,22,23,24]MRI should be used as a complementary tool when ultrasound evaluation is equivocal or when the placenta is hardly visualized on ultrasound examination.[25]

The limitation of our study was that not all the cases went through pathological evaluation as about half of cases were confirmed on clinical and surgical findings.

CONCLUSION:

Both gray scale ultrasound and color Doppler examination are highly accurate in predicting the radiological patterns of placenta accreta. It can save not only the time and money but life of high risk and clinically diagnosed cases of placenta accreta.

REFERENCES:

1. Miller DA, Chollet JA, Goodwin TM. Clinical risk factors for placenta previa-placenta accreta. Am JObstetGynecol 1997;177:210-14
2. ACOG Committee on Obstetric Practice. ACOGCommittee opinion no. 266, January 2002: placenta accreta. ObstetGynecol 2002;99:169-70
3. Silver RM, Landon MB, Rouse DJ. Maternal morbidity associated with multiple repeat cesarean deliveries. ObstetGynecol 2006;107:1226-32
4. Usta IM, Hobeika EM, Musa AA, Gabriel GE, Nassar AH. Placenta previa-accreta: risk factors and complications. Am J Obstet Gynecol 2005;193:1045-9
5. Wehrum MJ, Buhimschi IA, Salafia C. Accreta complicating complete placenta previa is characterized by reduced systemic levels of vascular endothelial growth factor and by epithelial-to-mesenchymal transition of the invasive trophoblast. Am J ObstetGynecol2011; 204:411.e1-411.e11
6. Tantbirojn P, Crum CP, Parast MM. Pathophysiology of placenta accreta: the role of deciduas and extravilloustrophoblast. Placenta 2008;29:639-45
7. Strickland S, Richards WG. Invasion of the trophoblast. Cell 1992;71:355-7
8. Lam G, Kuller J, McMahon M. Use of magnetic resonance imaging and ultrasound in the antenatal diagnosis of placenta accreta. J SocGynecolInvestig 2002;9:37-40
9. Finberg HJ, Williams JW. Placenta accreta: prospective diagnosis in patients with placenta previa and prior cesarean section. J Ultrasound Med 1992;11:333-43
10. Levine D, Hulka CA, Ludmir J, Li W, Edelman RR. Placenta accreta: evaluation with color Doppler US, power Doppler US, and MR imaging. Radiology 1997; 205:773-6
11. Chou MM, Tseng JJ, Ho ESC. Prenatal diagnosis of placenta previaaccreta by transabdominal color Doppler ultrasound. Ultrasound Obstet Gynecol 2000;15:28-35
12. Comstock CH, Love JJ Jr, Bronsteen RA. Sonographic detection of placenta accreta in the second and third trimesters of pregnancy. Am J Obstet Gynecol 2004;190: 1135-40
13. Wong HS, Zucollo J, Parker S, Burns K, Tait J, Pringle KC. Antenatal diagnosis of non-previa placenta increta with histological confirmation. Ultrasound Obstet Gynecol 2006;27:467-9
14. Japaraj RP, Mimin TS, Makudan K. Antenatal diagnosis of placenta previaaccreta in patients with previous cesarean scar. J Obstet Gynecol 2007;33(4):431-7
15. Dwyer BK, Belogolovkin V, Tran L. Prenatal diagnosis of placenta accreta: sonography or magnetic resonance imaging? J Ultrasound Med 2008; 27:1275-81
16. Esakoff TF, Sparks TN, Kaimal AJ. Diagnosis and morbidity of placenta accreta. Ultrasound ObstetGynecol2011; 37:324-7
17. Shih JC, Palacios Jaraquemada JM, Su YN. Role of three-dimensional power Doppler in the antenatal diagnosis of placenta accreta: comparison with gray-scale and color Doppler techniques. Ultrasound Obstet Gynecol2009; 33:193-203
18. Warshak CR, Eskander R, Hull AD. Accuracy of ultrasonography and magnetic resonance imaging in the diagnosis of placenta accreta.Obstet Gynecol 2006; 108:573-81
19. Wong HS, Cheung YK, Zuccollo J, Tait J, Pringle JC. Evaluation of sonographic diagnostic criteria for placenta accreta. J Clin Ultrasound 2008; 36:551-9
20. Chou MM, Ho ES, Lee YH. Prenatal diagnosis of placenta previa accreta by transabdominal color Doppler ultrasound. Ultrasound ObstetGynecol2000; 15:28-35
21. Lau WC, Fung HY, Rogers MS. Ten year experienceof caesarean and postpartum hysterectomy in a teaching hospital in Hong Kong. Eur J Obstet Gynecol Reprod Biol 1997;74:133-7
22. Grobman WA, Gersnoviez R, Landon MB.Pregnancy outcomes for women with placenta previain relation to the number of prior cesarean deliveries Obstet Gynecol 2007;110:1249-55
23. Levine D, Hulka CA, Ludmir J, Li W, Edelman RR.Placenta accreta: evaluation with color Doppler US,power Doppler US, and MR imaging. Radiology 1997;205:773-6
24. Japaraj RP, Mimin TS, Mukudan K. Antenatal diagnosis of placenta previa accreta in patients with previous cesarean scar. J Obstet Gynaecol Res 2007; 33:431-7
25. Comstock CH. Antenatal diagnosis of placenta accreta: a review. Ultrasound Obstet Gynecol 2005;26:89-96

ORIGINAL ARTICLE

Methotrexate in Rheumatoid Arthritis: Effect on Blood, Liver and Renal Laboratory Parameters

Fuad Shaikh[1], Rabia Arshad[2], Fahad Azam[3], Nasim Karim[4]

ABSTRACT:

Objective: To evaluate the effect of Methotrexate on blood, liver and renal laboratory parameters in patients having rheumatoid arthritis.

Materials and Methods : A 24-week, single-blind, interventional study was carried out on 155 consecutive patients, aged 29-70 years, diagnosed with rheumatoid arthritis. They received tablet Methotrexate, 10 mg (2.5 mg, 4 tablets) weekly, orally. Laboratory tests like hemoglobin level, total white cell and platelet counts, erythrocyte sedimentation rate, serum glutamic pyruvic transaminase and serum creatinine levels were recorded at the initial visit as well as at 6, 14 and 24 weeks follow-up visits.

Results: At the end of 24 weeks hemoglobin level increased to 12.43 ± 0.92 grams per deciliter (g/dl) from a baseline of 10.76 ± 1.12 g/dl, white cell count fell to 7,142.46 ± 1332.23 per cubic mm (cmm) from 8,572 ± 1445/cmm, the ESR fell to 40.14 ±15.78 mm of Hg in 1st hour from 81.03 ±17.98 mm of Hg, the platelet count fell to 2, 33,738.10 ± 59,769/ cmm from 2, 90,278 ± 68,813/cmm, the SGPT levels increased to 55.29 ± 21.97 international units per litre (IU/l) from 31.67 ± 7.37 IU/l and the serum creatinine increased to 1.11 ± 0.14 mg/dl from 0.95 ± 0.16 mg/dl, all values being highly significant statistically ($p<0.001$).

Conclusion: Methotrexate exerted significant effects on the blood, liver and renal laboratory parameters. These parameters may be utilized for monitoring the response and safety of methotrexate use in RA.

Keywords: Rheumatoid arthritis, Methotrexate, Laboratory parameters, Monitoring, Response, Drug safety

INTRODUCTION:

Rheumatoid arthritis is a progressive, autoimmune disorder of long duration which involves the entire body and is manifested by symmetric, small joint synovitis. It can be a painful condition in which joint destruction, with subsequently deformed joints and loss of function, leads to disability and worsening in a patient's health status. [1] The natural course of the disease is one of persistent symptoms with varying intensity and progressive joint damage resulting in deformities and disability.

The average annual incidence of RA is around 0.03% with a 1% worldwide prevalence rate.[2] Almost one-sixth of the world population lives in India and Pakistan with prevalence rates of 0.5% and 0.2-1% respectively.[3] A prevalence rate of 0.9 and 1.98 per thousand cases was seen in the poor and affluent districts of Karachi respectively.[4] The exact etiology is unknown. Genetic risk factors have been identified like the presence of HLA-DR4/DR1 (human leukocyte antigen) marker cluster in 90% of RA patients.[5] Similarly, research has shown a strong link between the presence of (EBV) and (HHV-6) and the probability of developing RA, as patients with the disease have shown an abnormal immune response to infection with EBV.[6,7,8,9] Classification of RA depends on the ACR criteria given by the American College of Rheumatology (Table 1).[10] Person fulfilling four of these criteria can be said to be suffering from RA. It is now established that permanent joint damage starts early on in the disease in patients with active polyarticular disease.[11] The available treatment options are DMARDs (disease-modifying, anti-rheumatic drugs), anti-inflammatory agents and analgesics.[12,13] DMARDs have been in use in patients with RA for the last several years[14] Anti-inflammatory drugs and analgesics have no effect on joint damage or rate of disease progression though they may reduce the intensity of pain and joint stiffness. Methotrexate (MTX), a DMARD approved by FDA in 1988 for use in the treatment of RA, is the most widely used DMARD today[15,16,17] The 2006 EULAR recommendations consider it as the anchor, first-line drug in the treatment of RA regardless of the severity of disease.[18]

Methotrexate has a three-fold action in RA. Its anti-inflammatory effect may involve inhibition of production of those cells which cause synovitis, inhibition of products of toxic agents seen in chronic inflammation, reduction of intracellular glutathione levels resulting in reduction of macrophage recruitment and function, release of adenosine or probably a combination of these mechanisms. It also blocks dihydrofolate reductase (DHFR), which converts dihydrofolate to tetrahydro-

✉ **Dr. Fuad Shaikh**
Assistant Professor
Department of Pharmacology & Therapeutics
Dow Medical College
Dow University of Health Sciences
Karachi
E-mail: fuad.shaikh@hotmail.com

✉ **Dr. Rabia Arshad**
Assistant Professor & Head
Department of Pharmacology
Altamash Institute of Dental Medicine
Karachi

✉ **Dr. Fahad Azam**
Assistant Professor
Department of Pharmacology & Therapeutics
Shifa College of Medicine
Islamabad

✉ **Dr. Nasim Karim**
Professor & Head
Department of Pharmacology
Bahria University Medical & Dental College
Karachi

Received: 03-11-2015
Revised: 08-12-2015
Accepted: 09-12-2015

folate, thereby preventing the production of chemicals and proteins needed for the production of cells involved in the inflammatory process. Its anti-metabolic effect is due to the inhibition of growth of rapidly proliferating cells by acting on the S-phase of the cell cycle.[19,20,21,22] Thus methotrexate acts by inhibiting amino-imidazole-carboxamide ribonucleotide (AICAR) transformylase and thymidylate synthetase. AICAR produces accumulation of adenosine monophosphate (AMP) which in turn is converted to adenosine and inhibits inflammation.[23] It has demonstrated effects on blood parameters, renal and liver function.[24]

These very effects of Methotrexate could be used to monitor response to therapy in controlling the disease process and to determine its safety of use in RA patients. With this background the present study was designed to evaluate the effect of Methotrexate on blood, liver and renal laboratory parameters in patients having rheumatoid arthritis.

MATERIALS & METHODS:

This was a 24-week, prospective, single-blind, interventional study conducted between October, 2009 to March, 2011, on patients of either sex suffering from rheumatoid arthritis who visited the out-patient department of a private teaching hospital and a private consultant's clinic in Korangi, Karachi. Approval was obtained from and granted by the Dow University of Health Sciences (DUHS) Institutional Review Board (IRB). 155 consecutive patients, fulfilling the ACR criteria, were chosen and put on 10 mg of Methotrexate (4 tablets of 2.5 mg) orally, weekly. They were given drugs and directed to return for follow up with laboratory tests (hemoglobin level, total white cell and platelet counts, erythrocyte sedimentation rate, serum glutamic pyruvic transaminase and serum creatinine levels,) at which time they were given drugs for further use. Follow ups were conducted at 6, 14 & 24 weeks. Statistical analysis was done by SPSS version 18.0 with paired t-test. The results are shown as mean along with standard deviation. The cut off P value was taken to be less than 0.05.

RESULTS:

Of the 155 recruited patients 29 were lost to follow up. Of the remaining 126 patients 89 (70.6 %) were female and 77 (61.1%) were positive for Rheumatoid factor. They had a mean age of 45.57 ± 10.32 years, ranging between 29 to 70 years.

The mean baseline hemoglobin was 10.76 ± 1.12 grams per deciliter (g/dl), mean white cell count was 8,572 ± 1445 per cubic mm (/cmm), ESR was 81.03 ±17.98 mm in 1st hour, mean platelet count was 2, 90,278 ± 68,813/cmm, mean SGPT value was 31.67 ± 7.37 international units per litre (IU/l) and mean serum creatinine was 0.95 ± 0.16 mg/dl (Table 2). At the end of the study at 24 weeks the hemoglobin increased to 12.43 ± 0.92 g/dl, white cell count fell to 7,142.46 ± 1332.23 /cmm, the ESR fell to 40.14 ± 15.78 mm of Hg, the platelet count fell to 2, 33,738.10 ± 59,769 /cmm, the SGPT levels increased to 55.29 ± 21.97 IU/l and the serum creatinine increased to 1.11 ± 0.14 mg/dl, all values being statistically significant (P<0.001, Table 3). A total of 19 patients (15.1%, 14 female & 5 male) showed elevations of SGPT which were greater than twice the upper limit of normal (Table 4).

Table: 1
The American College of Rheumatology classification criteria

S.#	Parameter	Features
1	Morning stiffness	>1 hour most mornings
2	Arthritis and soft-tissue swelling	of >3 of 14 joints/
3	Arthritis of hand joints	Inflammation of joints of the hands
4	Symmetric arthritis	Arthritis of the same joints on both sides of the body.
5	Subcutaneous nodules	Usually found over bony prominences that sustain repeated mechanical stress e.g olecranon, calcaneum
6	Rheumatoid factor	Present
7	Radiological changes	Suggestive of joint erosion

Criteria 1-4 should have been present for at least 6 weeks.
At least 4 criteria have to be met for classification as Rheumatoid arthritis

Table: 2
Laboratory parameters: baseline and follow up visits
N = 126

Parameter	Baseline Mean ± SD	6 weeks Mean ± SD	14 weeks Mean ± SD	24 weeks Mean ± SD
Hemoglobin (g/dl)	10.76 ± 1.12	11.729 ± 1.1389	11.913 ± 1.6673	12.43 ± 0.92
Total leucocyte count (per cubic mm)	8572.1 ± 1445.1	8,018.25 ± 1,334.310	7,430.95 ± 1,244.281	7,142.46 ± 1,332.23
Erythrocyte Sedimentation Rate (mm of Hg in 1st hour)	81.03 ± 17.98	65.09 ± 17.441	52.02 ± 15.838	40.14 ± 15.78
Platelet count (per cubic mm)	2,90,277.8 ± 68,813.7	260,452.38 ± 63,342.069	256,666.67 ± 131,073.048	2,33,738.10 ± 59,769.58
Serum glutamic pyruvic transaminase (SGPT, IU/l)	31.67 ± 7.37	33.01 ± 10.244	42.54 ± 14.110	55.29 ± 21.97
Serum creatinine (mg/dl)	0.95 ± 0.16	.886 ± 0 .1511	.986 ± 0.1164	1.11 ± 0.14

SD : Standard deviation, g/dl: grams per deciliter, mm of Hg: millimeters of mercury,
IU/l: international units per litre, mg/dl: milligrams per deciliter

Table: 3
Methotrexate
Baseline v/s 24 weeks
N = 126

Parameter	Mean ± SD	P value
Hemoglobin, (g/dl) Hemoglobin, (g/dl), 24 weeks	10.76 ± 1.12 12.43 ± 0.92	<0.001 ***
White cell count (per cubic mm) White cell count (per cubic mm), 24 weeks	8,572.06 ± 1445.08 7,142.46 ±1332.23	<0.001 ***
Erythrocyte sedimentation rate, (mm of Hg in 1st hour) Erythrocyte sedimentation rate, (mm of Hg in 1st hour), 24 weeks	81.03 ± 17.98 40.14 ± 15.78	<0.001 ***
Platelet count (per cubic mm) Platelet count (per cubic mm), 24 weeks	2,90,277.78 ± 68,813.68 2,33,738.10 ± 59,769.58	<0.001 *** <0.001 ***
Serum glutamic pyruvic transaminase (SGPT, IU/l) Serum glutamic pyruvic transaminase (SGPT, IU/l), 24 weeks	31.67 ± 7.37 55.29 ± 21.97	
Serum creatinine (mg/dl) Serum creatinine, (mg/dl), 24 weeks	0.95 ± 0.17 1.11 ± 0.14	<0.001 ***

*** = very highly significant, Paired T-test utilized, SD : Standard deviation, g/dl: grams per deciliter
mm of Hg: millimeters of mercury, IU/l: international units per litre, mg/dl: milligrams per deciliter

Table: 4
Methotrexate
Serum glutamic pyruvic transaminase (SGPT)
N=126

	6 weeks		14 weeks		24 weeks	
Sex	No of Patients	%	No of Patients	%	No of Patients	%
Male	0	00	0	00	5	13.5
Female	0	00	3	3.4	14	15.7
Total	0	00	3	2.4	19	15.1

No of Patients = Number of patients with > 2 x upper limit of normal (> 68 IU/L in females & > 90 IU/L in males)

DISCUSSION:

DMARDs, having the ability to slow down joint destruction, are regarded as the drugs of first choice in treating RA. Since permanent joint damage starts early in patients with active, polyarticular RA initiating therapy with a DMARD shows promising results. The current treatment options can adequately control the acute symptoms and hold the promise of a good prognosis in the long run.[25]

Folic acid deficiency, a known risk factor for Methotrexate-induced cytopenias, affects the rapid multiplication of the cells in the bone marrow and persons treated with Methotrexate show a fall in their cellular folic acid content.[26] The depressant effect of Methotrexate, especially on hemoglobin levels, is transient and the latter is seen to rise gradually about one month after starting the drug. Emery et al showed an improvement in the hemoglobin level accompanied with a fall in the leucocyte and platelet counts.[27] In our study the improvement in the hemoglobin level was statistically very highly significant when comparing end values with its baseline value; 10.76 g/dl to 12.43 g/dl ($p< 0.001$) Similarly the mean leucocyte count fell from a mean baseline value of 8,572 /cmm to 7,142 /cmm, ($p<0.001$) when comparing baseline and 24-week values. Changes in the platelet count too were statistically very highly significant ($p<0.001$). Ishaq has documented a fall of ESR from 52.5 mm of Hg to 24.3 mm of Hg ($p = 0.0001$).[28] This is coinciding with our results as ESR values in our study fell from a mean baseline level of 81.03 mm in 1st hour to 40.14 mm in 1st hour ($p<0.001$). These features indicate that our patients responded favorably to therapy, had tolerated the drugs well and the blood indices had not deteriorated to the extent that any dose alteration was needed. This may have been due to the fact that they belonged to a younger age group (mean ~ 46 years) in comparison to the studies mentioned above.

Londono studying the efficacy of Methotrexate found elevations of SGPT levels in 26% of their patients while Attar in a study seeing the adverse effects of Methotrexate found SGPT elevations in 14% of patients. [29,30] In another study Alves showed abnormal levels of liver enzymesÊin 11.5% of patients using Methotrexate.[31] In our patients changes in SGPT levels were seen in 15% of patients, a figure corresponding to that of the above authors, with the levels rising from a baseline value of 31.67 IU/l to 55.29 IU/l ($p <0.001$). Methotrexate-associated hepatic toxicity may be due to interference with homocysteine metabolism leading to increased homocysteine levels in the blood. Administration of folic acid has been seen to normalize the MTX-induced increase in plasma homocysteine.[23] Lack of folate supplementation may have contributed to the incidence of liver toxicity seen in our patients. [32] Furthermore, the difference seen in the number of patients affected is most probably due to the fact that our patients were younger and our values were obtained at the end of 24 weeks as opposed to the other studies which were of a longer duration that is 52 weeks.

Tousson, using Methotrexate, demonstrated an increase in the serum creatinine levels to 1.12 ± 0.159mg/dl from a baseline of 0.97 ± 0.089 mg/dl ($p< 0.01$) whereas the serum creatinine level in our study rose from a baseline level of 0.95 mg/dl to 1.11 mg/dl ($p< 0.001$).[33] The reason for this increment could not be ascertained in our study participants.

CONCLUSION:

Methotrexate, the drug of first choice in all types of RA patients, has exerted significant effects on various parameters of blood, liver and kidney. These parameters could be utilized for monitoring the response and safety of use of Methotrexate in patients having rheumatoid arthritis.

REFERENCES:

1. Allaire SH, Prashker MJ, Meenan RF. The costs of rheumatoid arthritis. Pharmaco Economics. 1994; 6:513–22
2. Del Puente A, Knowler WC, Pettit DJ, Bennett PH. High incidence and prevalence of rheumatoid arthritis in Pima Indians. Am J Epidemiol. 1989; 129:1170-8
3. Akhter E, Bilal S, Kiani A, Haque U. Prevalence of arthritis in India and Pakistan: a review. Rheumatol Int. 2011; 31(7):849-55
4. Hameed K, Gibson G, Kadir M. The prevalence of rheumatoid arthritis in affluent and poor urban communities of Pakistan. Br J Rheumatol. 1995; 34:252-6
5. Pisetsky DS. Laboratory testing in rheumatic diseases. Ch 278 in Cecil's Medicine, eds. Goldman L, Aesiello D. Saunders, Elsevier. 2007; 23rd ed: 1967
6. Álvarez-Lafuente R, Fernández-Gutiérrez B, Miguel S de, Jover JA, Rollin R, Loza E et al. Annals of the Rheumatic Diseases. 2005; 64:1357-9
7. Ferrell PB, Aitcheson CT, Pearson GR, Tan E.M. Sero-epidemiological study of relationships between Epstein-Barr virus and rheumatoid arthritis. J Clin Invest. 1981; 67(3): 681-7
8. Catalano MA, Carson DA, Slovin SF, Richman DD, Vaughan JH. . Proc. Natl. Acad. Sci. USA, Immunology. 1979; 76 (11):5825-8
9. Balandraud N, Roudier J. Epstein–Barr virus and rheumatoid arthritis. Autoimmunity Reviews. July 2004; 3 (5):362-7
10. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS et al. Arthritis Rheum. 1988; 31 (3): 315-24
11. Plant MJ, Saklatvala J, Borg AA, Jones PW, Dawes PT. Measurement and prediction of radiological progression in early rheumatoid arthritis. J Rheumatol. 1994; 10:1808-13
12. O'Dell J. Therapeutic strategies for rheumatoid arthritis. N Engl J Med. 2004; 350 (25): 2591-602
13. Hasler P. Biological therapies directed against cells in autoimmune disease. Springer Semin Immunopathol. 2006; 27 (4): 443-56
14. Ward MM , Fries JF. Trends in anti-rheumatic medication use among patients with rheumatoid arthritis,1981-1996. J Rheumatol. 1998; 25:408-16
15. Eustice C. The facts of Methotrexate. Updated May, 17, 2007, about.com guide
16. Kaltsonoudis E, Papagoras C, Drosos AA. Current and future role of methotrexate in the therapeutic armamentarium for rheumatoid arthritis; Int J Clin Rheumatol. 2012;7(2):179-89
17. Lopez-Olivo MA, Siddhanamatha HR, Shea B, Tugwell P, Wells GA, Suarez-Almazor ME. Methotrexate for treating rheumatoid arthritis. Cochrane Database Syst Rev. Jun 10, 2014
18. Combe B, Landewe R, Lukas C. EULAR recommendations for the management of early arthritis: report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis. 2007; 66:34-45
19. Quemeneur L, Gerland LM, Flacher M, French M, Revillard JP, Genestier L. Differential control of cell cycle, proliferation and survival of primary T lymphocytes by purine and pyrimidine nucleotides. J Immunol. 2003; 170: 4986-95
20. Nesher G, Osborn TG, Moore TL. In vitro effects of Methotrexate on polyamine levels in lymphocytes from rheumatoid arthritis patients. Clin Exp Rheumatol. 1996; 14: 395-9
21. Phillips DC, Woollard KJ, Griffiths HR. The anti-inflammatory actions of Methotrexate are critically dependent upon the production of reactive oxygen species. Br J Pharmacol. 2003; 138: 501-11
22. Sung JY, Hong JH, Kang HS, Choi I, Lim SD, Lee JK et al. Methotrexate suppresses the interleukin-6 induced generation of reactive oxygen species in the synoviocytes of rheumatoid arthritis. Immunopharmacology. 2000; 47: 35-44
23. Whittle SL, Hughes RA. Folate supplementation and Methotrexate treatment in rheumatoid arthritis: a review; Rheumatology, 2004, 43 (3): 267-71
24. Hazra SC, Choudhury AM, Khondker L, Khan MSI, Ahmed N. Hematological and Biochemical Parameter Changes Related to Methotrexate Therapy; Bangladesh Medical Journal 2011; 40(3):40-3
25. Nemazee D, Hogquist KA. Antigen receptor selection by editing or down regulation of V (D) J recombination. Curr. Opin. Immunol. 2003; 15: 182-9
26. Ortiz Z, Shea B, Suarez-Almazor ME, Moher D, Wells GA, Tugwell P. The efficacy of folic acid and folinic acid in reducing methotrexate gastrointestinal toxicity in rheumatoid arthritis. A meta-analysis of randomized controlled trials. J Rheumatol. 1998; 1:36-43
27. Emery P, Breedveld FC, Lemmel EM, JP, B et al. A comparison of the efficacy & safety of Leflunomide and Methotrexate for the treatment of rheumatoid arthritis. . 2000; 39(6)655-65
28. Ishaq M, Muhammad JS, Hameed K, Mirza AI. Leflunomide or methotrexate? Comparison of clinical efficacy and safety in low socio-economic rheumatoid arthritis patients, Mod Rheumatol 2011; 21(4): 375-80
29. Londono J, Santos AM, Santos PI, Cubidez MF, Guzman C, Valle-Oñate R. Therapeutic efficacy and safety of methotrexate + leflunomide in Colombian patients with active rheumatoid arthritis refractory to conventional treatment, Rev. Bras. Reumatol.2012; 52 (6):837-45
30. Attar SM, Adverse effects of low dose methotrexate in rheumatoid arthritis patients. A hospital-based study. 2010; 31(8):909-15
31. Alves JANR, Fialho SCS, Morato EF, de Castro GRW, Ribeiro GG, Zimmermann AF et al. Liver toxicity is rare in rheumatoid arthritis patients using combination therapy with leflunomide and methotrexate. São Paulo. Rev. Bras. Reumatol. 2011; 51(2): 141-4
32. Morgan SL, Baggott JE, Vaughn WH. Supplementation with folic acid during methotrexate therapy for rheumatoid arthritis. A double-blind, placebo-controlled trial. Ann Intern Med. 1994; 121:833-41
33. Tousson E, Zaki ZT, Abu-Shaeir W A, Hassan H. Methotrexate-induced Hepatic and Renal Toxicity: Role of L-carnitine in Treatment. Biomedicine and Biotechnology, 2014, 2(4), 85-92

ORIGINAL ARTICLE

Knowledge, Attitude and Practice Regarding Smokeless Tobacco among Adolesence of Two Private Schools of Gadap Town Karachi

Mahwish Bano[1],Asghar Ali[2], Muhammad Ali Leghari[3],Samreen Mazhar[4]

ABSTRACT

Objective: To evaluate the knowledge, attitude and practice regarding smokeless tobacco among adolescence of two private schools of Gadap Town Karachi

Materials and Methods: This descriptive cross sectional study was carried out in 300 school going children of two private schools of Gadap Town Karachi. The children were 11-19 years of age. The study was conducted for a period of six months from October 2014 to March 2015. Data was collected by self structured questionnaire related to personal information regarding the use of smokeless tobacco habits and the diseases that could be caused by the consumption of smokeless tobacco.Simple Random Sampling technique was used for data collection. Informed consent was taken from the principals of both private schools.Data was analyzed using SPSS software version 20.

Results: The study participants, 93.0% had the knowledge about smokeless tobacco while 2.7% subjects had no knowledge and 4.3% were in a category of "Idon't know" about smokeless tobacco.32% participants had the habit of chewing chalia, 10.7% individuals were placing gutka in the mouth while mawa was placed by 7.3% and mainpuri 6%. Pan chewing habit was 9% and often naswar placing was 4%.One packet of smokeless tobacco was used by 18.7% individuals per day and 22% students used two packets per day.

Conclusion: Knowledge, attitude and practice about smokeless tobacco among adolescence of two private schools of Gadap Town Karachi was unsatisfactory. High prevalence of daily use of smokeless tobacco has been identified in this peri-urban area of Karachi.

Keywords: Knowledge, Attitude, Practice, Smokeless tobacco products, School children

INTRODUCTION:

Most of the oral diseases are directly related to lifestyle, Oral disease can be considered a public health problem due to its high prevalence and significant social and psychological impact and there is an important consideration to reduce harmful oral health habits related to chewing, such a reduction can be achieved through appropriate awareness programs regarding health education.[1] Smokeless tobacco is consumed extensively throughout the world and it's a public health problem especially in Asian countries like India and Pakistan.[2] The most important preventable cause of disease burden and death all over the world is tobacco. The smokeless tobacco products have received increasing attention by the tobacco industry and public health community.[3] Cigarette manufacturers have developed new smokeless products, including moist snuff and snus brands, presented in attractive packaging and available in various flavors.[4]The use of tobacco remains responsible for being one of the largest contributors to premature death, causing every year millions of deaths worldwide. An international research study has estimated the number of betel quid users globally to be 600 million.[5,6,7] Smokeless tobacco users in India and Pakistan together have been estimated to be 100 million in number. Habitual betel quid chewing is commonly practiced by men and women in Bangladesh, India, Pakistan and Sri Lanka, while tobacco smoking is much more common among men in these countries compared to women, except for certain small geographic areas.[8]Smokeless, tobacco is associated with increased risk of chronic diseases.[9]These diseases include destructive periodontitis,oral and oropharyngeal cancers, oral potentially malignant disorders, notably leukoplakia, erythroplakia, and oral sub-mucous fibrosis and cardiovascular disorders including stroke. The other diseases associated with tobacco consumption include erectile dysfunction and problems in pregnancy, including stillbirth and low birth weight babies.[10]Smokeless tobacco is available in various forms that are either placed in the mouth or inhaled, including a finely ground or shredded tobacco known

✉ **Dr. Mahwish Bano**
Demonstrator
Department of Community Dentistry
Baqai Dental College
Baqai Medical University
Karachi
Email: drmahwishsyed@yahoo.com

✉ **Dr. Asghar Ali**
Associate Professor & Head
Department of Community Dentistry
Baqai Dental College
Baqai Medical University
Karachi

✉ **Dr. Muhammad Ali Leghari**
Senior Lecturer
Department of Community Dentistry
Baqai Dental College
Baqai Medical University
Karachi

✉ **Dr. Samreen Mazhar**
Assistant Professor
Department of Community Dentistry
Baqai Dental College
Baqai Medical University
Karachi

Received: 13-11-2015
Revised: 06-12-2015
Accepted: 08-12-2015

as snuff that may be in dry and moist forms and loose leaf forms known as chewing tobacco; and newer dissolvable compressed powdered tobacco tablets etc.[11,12] Studies related to use of tobacco have documented that deaths from tobacco will become double in 2030 comparing with 1999 due to increased tendency to use tobacco. Although, already about 50% of deaths due to tobacco are in high-income countries, but we should expect that tobacco-related mortality and morbidity will move towards developing countries because of addictive tobacco use in these countries.[13,14] Studies have identified personal, social, and environmental factors which are involved in the decision to try smokeless tobacco products and in the progression to regular use and nicotine addiction.Some studies have examined concurrent correlate use of smokeless tobacco especially in young people or longitudinal predictors of use in selected geographic regions, but prospective studies are not much reported among the area of US national sample of young people.[14,15]In Pakistan also there is scarcity of literature on smokeless tobacco use in adolescence. Present study was undertaken to evaluate the knowledge, attitude and practice regarding smokeless tobacco among adolescence of two private schools of Gadap Town Karachi.

MATERIALS AND METHODS:

This descriptive cross sectional study was carried out for a period of six months from October 2014 to March 2015 among adolescence of two private schools of Gadap Town Karachi. Data was collected by self structured questionnaire related to personal information regarding use of smokeless tobacco habits and the diseases that could be caused by the consumption of smokeless tobacco. 300 males and females study participants were evaluated.

The questionnaires for children was circulated in the class by trained teachers of the school and were collected on the same day after they have filled out the answers. The data for this study was collected by carrying out an interview among participants. The stratified simple random sampling technique was used. The questionnaire was divided into four parts. First part included questions on demographic characteristics of children that is the age, gender, educational status and father's occupation. Second part of the questionnaire included questions to test the knowledge of children regarding the family and its opinion, harmful effects and ban on purchase of smokeless tobacco products etc. Third part comprised of questions related to their attitude towards the use and duration of smokeless tobacco e.g., pan, chalia, maawa, mainpuri, naswar etc. Fourth part consist of questions related to their frequency and plan regarding the use of smokeless tobacco etc. A written consent was taken from school principal as well as children before the collection of data. Data was entered and analyzed by Statistical Package for Social Sciences (SPSS 20). Descriptive statistics of socio-demographic information and knowledge, attitude and practices of each chewing product was determined.

RESULTS:

Knowledge Regarding Smokeless Tobacco: A total of 300 enrolled subjects, 65.7% (197) were males and 34.3% (103) were females. The mean age of male and female was 1.34 with standard deviation +0.476. Out of 300 study participants 93.0% had the knowledge about smokeless tobacco while 2.7% subjects had no knowledge and 4.3% were in a category of "I don't know about smokeless tobacco". 51% study participant's family had knowledge about the use of smokeless tobacco whereas the 43.7% participant's family had no knowledge regarding the use of smokeless tobacco and 5.3% of those study participants had not known about the use of smokeless tobacco.2.3% subjects knew that smokeless tobacco is not good for human health while 87.7% subjects had no opinion of smokeless tobacco being related to health and 10% of participants said I don't Know, regarding smokeless tobacco.79.7% subjects said yes about the harmful effects of smokeless tobacco that can cause oral cancer while 4.3% study participants responded no, about the harmful effects of smokeless tobacco but 16% subjects said I don`t not know about the injurious effects of smokeless tobacco. 32.7% participants got knowledge from parents about the injurious effects of smokeless tobacco whereas the 5.3% participants knew the dangerous effects of smokeless tobacco use through self learning while the 18% participants learn the harmful effects of smokeless tobacco from books and education but dentist provide information to 4.7% participants regarding the injurious effects of smokeless tobacco, on the other hand 19% individuals knew the harmful effects of smokeless tobacco by TV. only 3.3% individuals knew the risk of smokeless tobacco through radio, although 1.7% study participants knew the dangerous effects of smokeless tobacco by newspapers.56.3% subjects wanted a ban on the purchase of smokeless tobacco products on the other hand 9.7% subjects did not want a ban on the purchase of smokeless tobacco whereas the 34% individual did not know about any ban on buying smokeless tobacco products (Table 1).

Attitude Regarding Smokeless Tobacco: 32% participants chewed chalia. 10.7% individuals placed or used gutka in the mouth; On the other hand placing mawa & mainpuri was 7.3% and 6% respectively. Chewing pan habit was found to be 9% and naswar placing was 4%. Individuals who used all of the above (chalia, gutka, mawa, mainpuri, paan, and naswar) were 2.7%.The participants not using smokeless tobacco were 29.3%. Regarding the mode use for the use of smokeless tobacco, 29.3% participants placed tobacco between upper or lower lips and gums while tobacco was chewed by 42.3% students. The duration of smokeless tobacco use was 1 year 21%, 2 year 19.3%, 3 year 20.3% and more than 3 years (others) were 11.3%. 24.3% students used smokeless tobacco when they were hungry, in contrast 30.7% individuals did not use smokeless tobacco when they were hungry.17% was in the category of "I don't know" about the status of hungry and using smokeless tobacco.The effect on appetite after using

smokeless tobacco was increased appetite 4%, decreased appetite 26%, no change in appetite 18% and Idon't know regarding appetite was 24%.The participants using smokeless tobacco under stress were 22% while not using smokeless tobacco under stress were 33.7%.The participants not knowing about use of smokeless tobacco in stress were16.3%.The students clean their teeth after smokeless tobacco use were 15% on the other hand those who did not clean were 43.7% and students who were in category of "I don't know" were 13.3%(Table 2).

Table: 1
Knowledge regarding smokeless tobacco

	Variable	Frequency	Percentage
Knowledge of ST	Yes	279	93.0
	No	8	2.7
	I don't know	13	4.3
	Total	300	100.0
Family use of ST	Yes	153	51.0
	No	131	43.7
	I don't know	16	5.3
	Total	300	100.0
Opinion of ST	Yes	7	2.3
	No	263	87.7
	I don't know	30	10.0
	Total	300	100.0
Harmful effect of ST	Oral cancer occur	239	79.7
	Oral cancer do not occur	13	4.3
	I don't know	48	16.0
	Total	300	100.0
How you know the harmful effect of ST	Parents	98	32.7
	Self learning	16	5.3
	Books/Education	54	18.0
	Dentist	14	4.7
	TV	57	19.0
	Radio	10	3.3
	Newspaper and magazines	05	1.7
Ban on purchase of ST	Yes	169	56.3
	No	29	9.7
	I don't know	102	34.0
	Total	300	100.0

Practice Regarding Smokeless Tobacco: 18.7% individuals used one packet of smokeless tobacco per day and 22% students used two packets per day. 22.3% participants used three packets of smokeless tobacco per day while 9% individuals used more than three(others) packets per day. 40.3% students spent 10 rupees per day on purchase of smokeless tobacco and 20.3% participants spent 20 rupees. 7.7% students spent 30 rupees while 3.7% spent more than 30 rupees (others).The frequency of smokeless tobacco in family of participants daily was 38.7% , weekly 4.7, monthly 2.7% and occasionally 7%.The 16.7% participant's family member never used smokeless tobacco,while 5.3% individuals did not know about family member use of smokeless tobacco. 37.7% individuals restricted the use of smokeless tobacco in family while 9.7% students were not restricting the use in family. 11.3% participants were in category of "I don't know" about restricting the use of smokeless tobacco in family. 22.3% individuals had a plan to reduce the consumption of smokeless tobacco while19% did not have any plan regarding the use of smokeless tobacco. 12.3% students had a plan to quit the use of smokeless tobacco. 17% did not know about their use of smokeless tobacco in future (Table 3).

Table: 2
Attitude regarding smokeless tobacco

Variable		Frequency	Percentage
Types of ST	Chalia	96	32.0
	Gutka	32	10.7
	Mawa	22	7.3
	Mainpuri	18	6.0
	Pan	27	9.0
	Naswar	12	4.0
	All of the above	8	2.7
	No	85	28.3
Mode of ST use	Placed tobacco b/w upper or lower lips & gums	88	29.3
	Chewing tobacco	127	42.3
Duration of ST	1 year	63	21.0
	2 year	58	19.3
	3 year	61	20.3
	Others	34	11.3
Use when Hungry	Yes	73	24.3
	No	92	30.7
	I don't know	51	17.0
Effect on appetite	Increase appetite	12	4.0
	Decrease appetite	78	26.0
	No change	54	18.0
	I don't know	72	24.0
Use tobacco in stress	Yes	66	22.0
	No	101	33.7
	I don't know	49	16.3
Cleaning of teeth after ST use	Yes	45	15.0
	No	131	43.7
	I don't know	40	13.3

Table: 3
Practice regarding smokeless tobacco

Variable		Frequency	Percentage
Packets use per day	One	56	18.7
	Two	66	22.0
	Three	67	22.3
	More	27	9.0
Rupees spend on ST	10 Rs	121	40.3
	20 Rs	61	20.3
	30 Rs	23	7.7
	Others	11	3.7
Frequency of ST in family	Daily	116	38.7
	Weekly	14	4.7
	Monthly	8	2.7
	Occasionally	21	7.0
	Never	50	16.7
	I don't know	16	5.3
Restrict the use of ST in family	Yes	113	37.7
	No	29	9.7
	I don't know	34	11.3
Plan for ST	To reduce consumption	70	23.3
	No plan	57	19.0
	To quit	37	12.3
	I don't know	51	17.0

DISCUSSION:

Awareness regarding smokeless tobacco use and its hazards is an important but often neglected topic. Probably this study is the first of its kind that was carried out among schools of Gadap Town Karachi. The socio-economic and demographic data of the study population typically represented a low socioeconomic group of Pakistan. As larger proportion of Pakistani population belongs to this less privileged section and chewing habits are more commonly practiced by this disadvantaged segment of the society, such a population readily makes an ideal choice for the study we have conducted. The smokeless tobacco using habits among the lower socioeconomic strata of Pakistan studied in our study was very high as 32% of the participants were using at least one of the items under investigation on daily basis.[16]Epidemiological studies on the tobacco chewing and smoking habits in Pakistan have been lacking. Sporadic data is available, limited to a few studies carried out in a couple of cities, has analyzed the same data used in this study, however, only smoking habits were reported and the variables were not analyzed in detail, required to initiate a cessation program.[17] Present study reports detailed analysis of smokeless tobacco habits. It has included parameters required to initiate a cessation program.

In the absence of comprehensive data on tobacco use in Pakistan, a review of the consumption and trends cannot be made. However, considering that the tobacco industry in Pakistan is expanding and there has been an increase in land used for tobacco cultivation, it is reasonable to infer that tobacco use has increased in Pakistan over the years. 48% men and 7% women use smokeless tobacco in the developing countries while 42% men and 24% women use smokeless tobacco reside in developed countries.[18] Present data shows that tobacco use is alarmingly high amongst Pakistani population. Such a high prevalence of tobacco (both smoking and smokeless) has also been seen in other developing countries like India, Bangladesh, China, Indonesia, Malaysia, Africa, South Africa, Nigeria, Israel, Estonia, Bulgaria, and Syria[19]. In Czech Republic the incidence of tobacco use is reported to be low among the males but is increasing among the females. Incidence of smoking in the North America is decreasing, at the same time the use of smokeless tobacco is on the rise.[20]

In our study 93%participants had heard about the term smokeless tobacco and their products pan, chalia, naswar, mawa, mainpuri, and gutka. The perception of the people about the products was based on correct as well as incorrect information, in contrast to studies carried out in Indian and Bangladeshi populations that have reported a perception regarding smokeless tobacco to be beneficial to the body. However others did not find any clear association or found a negative association with the level of education, household income, area of residence and tobacco use[21].

In our study about 32% individuals were using at least one item of smokeless tobacco on daily basis. Same results are documented in a study conducted among Asians in UK, reported 32% participants were chewing smokeless tobacco on regular basis.[22] Moreover, in our population overall mean frequency of use among daily chewers was higher than the individual frequency of most items, indicating that more than one substance was being used on daily basis among most daily chewers. Children and younger people are more likely to get exposed to these products, and such exposure could lead them to develop lifelong habit. Male gender and young age group were the main identified risk factors for the daily use of chewing substance. These finding are in coherence with those reported in another study from Asian subcontinent.[23]

In this study lowest naswar use per day was 4%, followed by10.7% gutka, 7.3% mawa, 6% mainpuri, 9% paan which hints towards the addictive potential of these substances. 32% chaalia was the most common substance of daily use while 29.3% participants placed tobacco between upper or lower lips and gums and 42.3% used chewing tobacco. Pakistanis do not commonly use "Pan". The reason for this limited use by the rural low economic group may be the low affordability of pan as compared to chaalia and cigarettes. The current study did not look into the type of quid used for "pan". The carcinogenic potential of the type of quid used cannot be overlooked. The level of tobacco and pan use may be under estimated for women that may be due to under reporting because of cultural prohibitions but further studies are recommended in these areas.[24]

Pakistan has to reinforce its political and public health efforts to control this preventable killer and build an

alliance between the ministries of health, education, commerce, agriculture, the Central Board of Revenue and the provincial governments to ban all forms of tobacco advertisements, sponsorship and marketing. Ban on all forms of tobacco consumption in all public places and increase in the excise taxes on all forms of tobacco should also be undertaken.[25]Thus high prevalence of daily use of smokeless tobacco products has been identified in adolescence residing in peri-urban area of Karachi, Pakistan.

CONCLUSION:

Knowledge, attitude and practice regarding smokeless tobacco among adolescence of two private schools of Gadap Town Karachi were found to below and unsatisfactory. Knowledge especially about the carcinogenicity of these items among the studied population was unsatisfactory. However, positive attitudes were also identified regarding the measures to restrain their production, marketing and use which should be used to facilitate the formulation of policies against these items.

REFERENCES:

1. Javed F, Al-Hezaimi K, Warnakulasuriya S. Areca-nut chewing habit is a significant risk factor for metabolic syndrome: a systematic review. 2012; 16:445-8
2. Heck JE, Marcotte EL, Argos M, Parvez F, Ahmed A, Islam T et al. Betel quid chewing in rural Bangladesh: prevalence, predictors and relationship to blood pressure. Int J Epidemiol 2012; 41:462-71
3. Tsai WC, Wu MT, Wang GJ, Lee KT, Lee CH, Lu YH et al. Chewing areca nut increases the risk of coronary artery disease in Taiwanese men: a case-control study. 2012; 7:162-8
4. Muttagi SS, Chaturvedi P, Gaikwad R, Singh B, Pawar P. Ind J Med and PaedOncol 2012; 33:32-5
5. Shafique K, Mirza SS, Vart P, Memon AR, Arain MI, Tareen MF, et al. Areca nut chewing and systemic inflammation: evidence of a common pathway for systemic diseases. 2012; 9:22-9
6. World Health Organization. Defining and Assessing Risks to Health [Online]. 2002 Available from: URL: http://www.who.int/whr/2002/en/
7. PSC. The snus experience: Lessons from Norway, Sweden and Canada on the public health consequences of widespread oral tobacco use. Physicians for a Smoke-Free Canada: Ottawa, 2007. Retrieved Aug 24, 2008 from, http://www.smoke-free.ca/pdf_1/Snus-comparative-experiences.pdf.
8. Wayne GF, Connolly GN. How cigarette design can affect youth initiation into smoking: Camel cigarettes 1983–93. Tob Control 2002;1:132-9
9. World Health Organization. Quantifying selected major risks to health. The World Health report 2002-Reducing risks, promoting healthy life
10. Gupta PC, Warnakulasuriya S. Global epidemiology of areca nut usage. Addict. Biol. 2002; 7: 77-83
11. International Union Against Cancer. Tobacco Control Fact Sheet 8, December. International Union Against Cancer, Tobacco and Cancer Programme, Geneva, 1996
12. World Bank Economics of Tobacco for the South Asia Region, 2003. http://www.worldbank.org/ tobacco/pdf/country%20briefs/South%20Asia%20Region.doc Accessed 6 July, 2003
13. Critchley JA,Unal B. Health effects associated with smokeless tobacco: a systematic review. Thorax. 2003;58, 435-43
14. Gupta PC, Ray CS. Smokeless tobacco and health in India and South Asia. Respirology. 2003; 8, 419-31
15. Nair U, Bartsch H, Nair J. Alert for an epidemic of oral cancer due to use of the betel quid substitutes gutkha and pan masala: a review of agents and causative mechanisms. Mutagenesis. 2004;19, 251-62
16. Mack TM. The pan-Asian paan problem. Lancet.2001; 357, 1638-9
17. Maher R, Devji S. Prevalence of smoking among Karachi Population. JPMA 2002; 52(6): 250-3
18. Merchant AT, Luby SP, Perveen G. Smoking among males in a low socioeconomic area of Karachi. JPMA 1998; 48(3):62-3
19. Alam SE. Prevalence and pattern of smoking in Pakistan. JPMA 1998;48(3) 64-6
20. Shah SH, Shah SN, Rizwanullah. Prevalence and pattern of tobacco use in rural area of Peshawar. JAMC 1993;6 (2): 5-8
21. Tobacco or Health: A Global Status Report. Country Profile 1997. wvvvv.cdc.gov/tobacco/who/Pakistan.htm down-loaded on 30.11.02
22. Maziak W. Smoking in Syria; profile of a developing Arab country. Int. J Tuberc Lung Disease 2002; 6(3): 183-91
23. Skodova Z, Cifkova R, Adamkova V, Duskova A, Ilauserova G, Hejl Z, et al. Development of smoking habits in the population of the Czech Republic from 1985 to 1997/98 (Abstract). CasLekCesk 2000; 139(5); 143-7
24. Centre for disease control and prevention. Cigarette smoking- attributable mortality and years of potential life lost-United States, 1990.MMWR 1993; 42: 645-9
25. Balabanova D, Bobak M, McKee M. Patterns of smoking in Bulgaria. Tobacco Control 1998 Winter; 7(4); 383-5

ORIGINAL ARTICLE

Association between Obesity and Low Serum Vitamin D Concentrations in Healthy Adult Females: A Public Health Perspective

Khola Noreen[1], Nadia Khalid[2], Imran Shaikh[3], Rabia Anwar[4]

ABSTRACT:
Objective: To find out the association between obesity and low serum vitamin D concentrations among females.
Materials and Methods: This cross sectional study was conducted in females aged 20-45 years reporting to dietitian and family OPD of PNS Shifa Hospital from September 2014 to January 2015. Three forty seven females underwent physical examination for anthropometric data. Weight was measured using weight scale. Height was recorded using wall mounted stadiometer in erect position without shoes. BMI was calculated by weight in kilogram (kg) divided by height in square meter (m^2). Waist was recorded by placing measuring tape at midpoint of upper border of iliac crest and lower margin of last palpable rib (WHO STEPS protocol). Serum Vitamin D level was measured by electro-chemiluminiscence immunoassay.
Results: Mean serum vitamin D level was significantly lower among over weight (≥18.5-24.9 kg/m^2) and obese females(≥30 kg/m^2) as compared to normal weight (≥18.5-24.9kg/m^2) and underweight category (≤ 18.49 kg/m^2). Univariate regression analysis for BMI and age showed every 1 kg/m^2 increase in BMI associated with 0.61 nmol/l decrease in serum vitamin D levels. It also showed that every one year increase in age decreased 0.22 nmol/l of serum vitamin D level. Multivariate regression analysis was performed to control the effect of age and demonstrated only significant association with BMI. Pearson correlation showed that serum vitamin D level was inversely related to both BMI and waist circumference
Conclusion: Vitamin D level was low among overweight and obese females and showed an inverse association with BMI and waist circumference.
Keywords: Association, Females, Obesity, BMI, Waist circumference, Low serum vitamin D

INTRODUCTION:

Obesity is an emerging public health issue; there is continuous increase in burden of obesity all over the world. According to Global Burden of Disease Study 2013, worldwide 3.9%of years of life lost, 3.4 million deaths and 3.8% of disability-adjusted life-years(DALYs)are attributable to obesity.[1]InWHO International classification, obesity is measured by simple mathematical calculation using BMI.[2]Obesity is significantly contributing towards double burden of disease in developing country like Pakistan. It is adding to existing burden of under nutrition and infectious diseases which are already prevalent in developing and low income countries and there is rapid surge in obesity related health issues.[3]

According to data of National Health survey of Pakistan prevalence of obesity is reported to be higher in females, 14 % in rural area as compared to 37 % in urban area while in males it is 9 % versus 22% in rural and urban area respectively.[4]

In past few years several evidences have supported a possible association between obesity with low vitamin D levels.[5]Obesity is associated with increased risk for vitamin D deficiency.[6]Despite significant association between obesity and vitamin D[7] levels there is dearth of literature in this regard in our part of world. Several studies conducted in Western population[8, 9] and Pakistani immigrants[10] residing there have showed inverse relationship between obesity and low vitamin D levels. However, limited data is available in this regard in indigenous Pakistani population. Moreover owing to ethnic differences in nutritional status and vitamin D metabolism these results cannot be generalized to indigenous Pakistani population. Present study aims to find out the association between obesity and low vitamin D levels in healthy females.

✉ **Dr. Khola Noreen**
Lecturer
Department of Community Health Sciences
Bahria University Medical & Dental College
Karachi
Email: dr_khaula@yahoo.com
✉ **Dr. Nadia Khalid**
Lecturer
Department of Community Health Sciences
Bahria University
Medical & Dental College
Karachi
✉ **Dr. Imran Shaikh**
Professor & HOD
Department of Community Health Sciences
Bahria University Medical & Dental College
Karachi
✉ **Ms. Rabia Anwar**
Clinical Nutritionist
PNS-SHIFA Hospital
Bahria University Medical & Dental College
Karachi
Received: 15-11-2015
Revised: 29-11-2015
Accepted: 03-12-2015

MATERIALS AND METHODS:

This cross sectional study was conducted on females of age 20-45 years reporting to dietitian and family OPD of PNS Shifa Hospital. Study duration was from September 2014 to January 2015. Inclusion criteria for study participants included disease free healthy females with no underlying co-morbid condition or inherited chronic disease that could affect vitamin D metabolism. Exclusion criteria included females with syndromal

obesity, pharmacotherapy for obesity, taking vitamin D or other supplements. A sample size of 368 was calculated, using 5% level of significance,margin of error as 5% and expected prevalence of 60%. Total three sixty eight females fulfilled the eligibility criteria and out of these twenty one females were not willing to participate and were therefore excluded while rest of three forty seven females were subjected to physical examination in order to obtain anthropometric data. Weight was measured using weight scale. Height was recorded using wall mounted stadiometer in erect position without shoes. BMI was calculated by equation taking weight in kilogram(kg) divided by height in square meter (m^2). Under weight is graded as BMI ≤18.49kg/m^2, BMI ≥ 18.5 – 24.9 kg/m^2 is considered as normal weight, Overweightis categorized as BMI 25 –29.9kg/m^2 and BMI ≥ 30 kg/m^2 is taken for obese. Waist circumference as per Asian cut off for females <80cm and hip circumference < 90 cm is taken as normal Waist was recorded by placing measuring tape at midpoint of upper border of iliac crest and lower margin of last palpable rib as per standardized WHO STEPS protocol.Serum Vitamin D levels were measured by using electro-chemilumniscence immunoassay methodology. Vitamin D level is considered as sufficient if it was >75 nmol/l, between 50 -75 nmol/l is taken as desirable and < 50 nmol/l is graded as deficient.[11]

Statistical analysis: Data was analyzed using statistical package for social sciences (SPSS) version 20.0.Descriptive statistics were used to calculate mean and standard deviation for weight, height, BMI, waist and hip circumference. ANOVA was applied to find mean difference of vitamin D level across different BMI categories.Pearson correlation was used to find the correlation of anthropometric variables with vitamin D levels. Univariate regression analysis was done taking vitamin D level as dependent variable. Multivariate regression analysis was performed to control for confounding effect of age. P value less than 0.05 was taken as significant.

RESULTS:

Socio demographic characteristics of study participants are shown (Table 1). Mean age of study participants was 45.31 ± 6.43.Mean BMI level of study participants were 27.14 ± 4.16. Comparison of mean serum Vitamin D level across four BMI categories showed that mean serum vitamin D level was significantly lower among overweight(≥ 18.5-24.9 kg/m^2) and obese females(> 25 kg/m^2) than the normal weight (18.5-24.9 kg/m^2) and underweight category(≤ 18 kg/m^2) (Table 2). Univariate regression analysis for BMI and age showed that every 1 kg/m^2 increase in BMI was associated with 0.61 nmol/l decrease in serum vitamin D level. This also showed that every one year increase in age decreased serum 0.22 nmol/l vitamin D level (Table 3a). Multivariate regression analysis was performed to control the effect of age which demonstrated only significant association with BMI and age showed no significant association in this model (Table 3b).Pearson correlation was calculated and it was found that serum vitamin D level was inversely related to both BMI and waist circumference however association was stronger with waist circumference as compared to BMI(Table 4, Figure 1)

Table: 1
Baseline characteristics of the study population
N=347

Variable	Mean	Standard deviation
Age (years)	45.31	6.43
Height (cm)	159.13	5.45
Weight (kg)	69.76	6.75
BMI (kg/m^2)	27.14	4.16
Vitamin D level (nmol /l)	41.34	7.13

Table: 2
Mean vitamin D levels in BMI categories (Normal)
N=347

BMI(kg/m^2)	Mean ± SD Vitamin D levels	95% CI	ANOVA p value
≤18.49	32.5 ± 8.6	24.8-38.2	13.4
18.5-24.9	56.3 ± 7.5	29.3-45.5	0.001
25-29.9	29.2± 5.5	15.6-26.3	
≥30	12.6 ± 4.3	10.1-16.3	

Table: 3a
Univariate regression analysis of vitamin D level (as dependent variable) with BMI and age
N=347

Variable	B coefficient	Standard error	95% CI	P-value
BMI	-0.61	0.08	-0.76-0.55	0.001
Age	-0.22	0.06	0.02-0.21	0.04

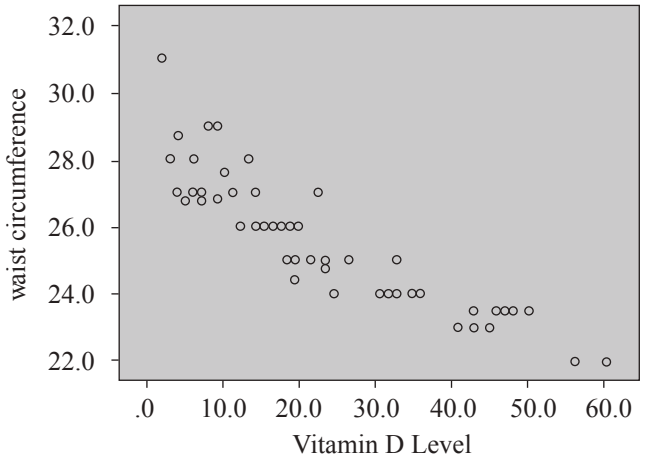
Table: 3b
Multivariate regression analysis of vitamin D level (as dependent variable) with BMI and age
N=347

Anthropometric levels	Vitamin D Levels	
	Pearson coefficient(r)	P value
BMI	-0.113	0.03
Waist circumference	-0.892	0.001

Table: 4
Correlation between anthropometric measures and vitamin D levels
N= 347

Variable	B coefficient	Standard error	95% CI	P-value
BMI	-0.63	0.06	-0.43-0.21	0.001
Age	-0.09	0.07	0.01-0.19	0.09

Figure: 1
Negative correlation between vitamin D levels and waist circumference



DISCUSSION:

Globally many regions are in the phase of rapid nutritional and epidemiological transition which accounts for increase burden of obesity related diseases.This nutritional transition is characterized by change in trends of traditional staple diet to higher calorie energy dense food which is predisposing towards increase in prevalence of obesity.[10]

According to report of World Health Organization (WHO) on Global burden of obesity, overall obesity prevalence is almost doubled up between 1980 and 2013, however prevalence in male has increased from 28.8 to 36.9%, while in females increase from 29.8% to 38% is observed.[11]However, it is predicted that by 2025 number of deaths can be reduced to 20% by targeting underlying major risk factors[12,13].This situation definitely warrants the in depth research to indentify all underlying modifiable risk factors to halt this global epidemic and to make effective strategies for future prevention find out modifiable.

We examine the relationship between vitamin D levels and obesity. Vitamin D deficiency is a critical public health issue and considered as unrecognized epidemic all over the world.[14,15,16]National Nutrition Survey of Pakistan reported prevalence of vitamin D deficiency around 46% among the urban dwellers.[17]

Results of our study have demonstrated low vitamin D concentration in overweight and obese individuals as compared to normal weight healthy disease free individuals. Several epidemiological studies have demonstrated negative association of obesity and vitamin D levels.[18,19]Report of recent meta- analysis on association between anthropometric state with vitamin D deficiency has reported that prevalence of vitamin D deficiency was more among overweight and obese individuals as compared to normal weight individuals.[20] The precise mechanism of vitamin D deficiency in obese individual is not known.However,it is hypothesized that vitamin D is sequestered in higher concentration in fat cells of obese individual resulting in decrease bioavailability of vitamin D and increase oxidative reactions within adipose tissues.[21]High fat content is responsiblefor sequestration of vitamin D in fat cells which act as reservoir for fat soluble vitamin resulting in decrease release of vitamin D from fat.[22]

On finding the correlation between obesity indices and vitamin D level it was found that waist hip ratio showed more strong inverse relationship as compare to BMI .Possible explanation can be that BMI assess obesity in term of body weight and height of an individual. It is an index for calculation of excessive body weight but it fails to demonstrate that whether this excessive weight is due to increase muscle mass or increased body fat. It does not provide accurate measurement of body fat.[22, 23]On the contrary waist circumference provide direct estimation of obesity in comparison to BMI.Results of recent randomized control trial conducted in Saudi females showed that effect of vitamin D supplementation on vitamin D deficient obese women had greater reduction in waist circumference as compared to other anthropometric variables.[24]

Similar results are supported by randomized trial on Chinese females which studied the effect of vitamin D supplementation on different anthropometric indices and have demonstrated that vitamin D supplementation in obese females had greater reduction in waist circumferenceas compared to BMI .[25]

Our results also demonstrated negative association between age and vitamin D level on univariate analysis .This is in accordance with results of previous studies.[26,27,28]In order to control the confounding effect of age on BMI, multivariate analysis was performed which showed no significant association and only vitamin D level is found to be significantly associated with BMI.

There are few limitations of our study.Although our study results demonstrated that vitamin D levels were low among overweight and obese individuals as compared to normal individual, however, it is not possible to conclude that vitamin D deficiency causes obesity because reverse causation bias is possible as vitamin D is fat soluble vitamin and can be sequestered in adipose tissue.[29]

Longitudinal studies or randomized control trial should be conducted to find out more accurate association and to overcome possible effect of reverse causation bias as well as evaluation of effect of vitamin D supplementation in obesity. Asymptomatic vitamin D deficiency can be prevented by education of the population on change in dietary habits, educating parents to expose their children regularly to sunshine, prophylaxis through periodic dosing, vitamin D fortification of foods especially milk, butter, oil and attention of government towards food fortification policies is the need of the day to combat hidden hunger and lessen the double burden of disease in Pakistan.

Limited number of anthropometric parameters was assessed due to cost and logistic constrains. Future research with measurement of anthropometric variables other than BMI and waist circumference should be conducted to find out association of these variables with

obesity. High body fat content, increased incidence abdominal obesity and increase risk of cardio metabolic risk factors at lower BMI cut offs and in Asian population should not be overlooked.

CONCLUSION:

Significant vitamin D deficiency was seen in overweight and obese females. It was found that vitamin D deficiency is associated with obesity, but its causal role has not been established. Future prospective studies should be conducted to further elaborate this association. This will provide an opportunity to health care providers to screen out the high risk individuals and need for vitamin D supplementation. This can be an effective strategy for early diagnosis and prevention. These measures can effectively reduce the burden on healthcare system

REFERENCES:

1. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013.The Lancet. 2014 Aug 30;384(9945):766-81. doi: 10.1016/S0140-6736(14)60460-8. Epub 2014 May 29
2. WHO Physical status: the use and interpretation of anthropometry. Report of WHO Expert Committee. WHO Technical Report Series 854. Geneva: World Health Organization, 2000
3. Zafar M, Malik A. Emerging Challenges and Health System Capacity: The Case of Non-Communicable Diseases in Pakistan; a Review. J Infect Dis Ther2014 ;2:127
4. Nishtar S. Health Indicators of Pakistan – Gateway Paper II. Islamabad, Pakistan: Heartfile; 2007
5. Earthman CP, Beckman LM, Masodkar K, Sibley SD.The link between obesity and low circulating 25-hydroxyvitamin D concentrations: considerations and implications. Int J Obes2012; 36: 387-96
6. Vimales W, Karani S. Causal Relationship between Obesity and Vitamin D Status: Bi-Directional Mendelian Randomization Analysis of Multiple Cohorts. Ed. Cosetta Minelli. PLoS Medicine 10.2 (2013): e1001383.
7. Liu S, Song Y, Ford ES, Manson JE, Buring JE, Ridker PM. Dietary calcium, vitamin D, and the prevalence of metabolic syndrome in middle-aged and older U.S. women. Diabetes Care 2005;28(29):26-32
8. Forouhi NG, Luan J, Cooper A, Boucher BJ, Wareham NJ. Baseline serum 25-hydroxy vitamin D is predictive of future glycemic status and insulin resistance: The medical research council Ely prospective study 1990-2000. Diabetes 2008;57(26):19-25
9. Bodnar LM, Simhan HN, Powers RW, Frank MP, Cooperstein E, Roberts JM. High prevalence of vitamin D deficiency in black and white pregnant women residing in the northern United States and their neonates. J Nutr 2007;137(2):447-52
10. Margolis KL, Ray RM, Van Horn L, Manson JE, Allison MA, Black HR, et al. Effect of calcium and vitamin D supplementation on blood pressure: The women's health initiative randomized trial. Hypertension 2008;52:847-55
11. World Health Organization. WHO STEP wise approach to chronic disease risk factor surveillance- Instrument v2.0. Department of Chronic Diseases and Health Promotion. World Health Organization. 20 Avenue Appia, 1211 Geneva 27, Switzerland.
12. Popkin BM, Adair LS, Ng SW. Now and then: the global nutrition transition: the pandemic of obesity in developingcountries. Nutr Rev. 2012;70:3-21
13. Nanan DJ.The Obesity pandemic- implications for Pakistan. J Pak Med Assoc 2002;52(8):342-6
14. WHO. Non communicable diseases country profiles. Geneva, Switzerland: WHO press; 2011 URL:http://www.who.int/nmh/publications/ncd_profiles_report.pdf.
15. Jafar TH, Haaland BA, Rahman A, Razzak JA, Bilger M, Naghavi M, et al. Non-communicable diseases and injuries in Pakistan: strategic priorities. Lancet 2013;381(22):81-90
16. Review High prevalence of vitamin D inadequacy and implications for health. Holick MFMayo Clin Proc. 2006; 81(3):353-7
17. Govt of Pakistan. Planning and Coordination Division, Planning Commission. National Nutrition Survey; 2011
18. Pereira-Santos, M. Obesity and vitamin D deficiency: a systematic review and meta-analysis. Obesity Reviews 16.4 (2015): 341-9
19. Wortsman J, Matsuoka L, Chen T, Lu Z, Holick M. Decreased bioavailability of vitamin D in obesity. Am J ClinNutr. 2000;72(3):690-3
20. Codoñer-Franch P, Tavárez-Alonso S, Simó-Jordá R, Laporta-Martín P, Carratalá-Calvo A, Alonso-Iglesias E. Vitamin D status is linked to biomarkers of oxidative stress, inflammation, and endothelial activation in obese children. J Pediatr. 2012;161(5):848-54
21. Lagunova, Z, Porojnicu AC, Lindberg F, Hexeberg S, Moan, J. The dependency of vitamin D status on body mass index, gender, age and season. Anticancer research. 2009; 29(9), 3713-20
22. Seidell JC, Kahn HS, Williamson DF, Lissner L, Valdez R. Report from a center for disease control and prevention workshop on use of adult anthropometry for public health and primary healthcase. Am J ClinNutr 2001; 73:123-6
23. Micozzi M S, Albanes D. Three limitations of the body mass index.The American journal of clinical nutrition 46.2 (1987): 376-7
24. Al-Mulhim NS, Eldin TG, Latif R, Al-Asoom LI, Al-Sunni A. Effects of vitamin D supplementation on anthropometric indices in vitamin D-deficient obese Saudi females; a randomized controlled trial. Saudi J Health Sci 2015;4:83- 7
25. Zhu W, Cai D, Wang Y, Lin N, Hu Q, Qi Y, et al. Calcium plus vitamin D3 supplementation facilitated Fat loss in overweight and obese college students with very-low calcium consumption: A randomized controlled trial. Nutr J 2013: 12(8) doi: 10.1186/1415-2891-12-8
26. Moan J, Lagunova Z, Lindberg FA, Porojnicu AC. Seasonal variation of 1,25-dihydroxyvitamin D and its association with body mass index and age. J Steroid BiochemMol Biol. 2009;113:217–21. doi: 10.1016/j.jsbmb.2009.01.001
27. Bolland MJ, Grey AB, Ames RW, Mason BH, Horne AM, Gamble GD. et al. Determinants of vitamin D status in older men living in a subtropical climate. Osteoporosis Int. 2006;17:1742–8. doi: 10.1007/s00198-006-0190-2
28. Bischof MG, Heinze G, Vierhapper H. Vitamin D status and its relation to age and body mass index. Horm Res. 2006;66:211-5. doi: 10.1159/000094932
29. Gilbert-Diamond D, Baylin A, Mora-Plazas M, Marin

C, Arsenault JE, Hughes MD,Villamor E. Vitamin D deficiency and anthropometric indicators of adiposity in school-age children: a prospective study.The American Journal of Clinical Nutrition. 2010; 92(6), 1446-51

COMMENTARY

New Aspects of β_2-Adrenergic Agonists

Touseef Sayyar

ABSTRACT:
β_2-adrenergic receptor agonists is a class of medications that act on the β_2-adrenergic receptors. They are mostly used to treat asthma and other respiratory problems at present. However, the newer research have highlighted that they can be utilized in numerous other disorders like Congenital Myasthenic Syndrome, Down syndrome, Amyotrophic lateral sclerosis, Idiopathic Stuttering Priapism & Dyslipidemia etc.
Keywords: β_2-adrenergic receptors, β_2-adrenergic receptor agonists, Indications, New aspects

INTRODUCTION:

β_2-adrenergic agonists are medications that act on β_2-adrenergic receptors. These receptors are present on smooth muscles of uterus, gastrointestinal tract, detrusor muscle of urinary bladder, seminal tract, bronchi, blood vessels and pancreas. They cause relaxation of bronchial smooth muscles, vasodilation in muscle and liver, relaxation of uterine muscle release of insulin etc. These drugs are classified into various types based on their duration of action.

- Short acting drugs like Salbutamol, Levosalbutamol, Terbutaline,Pirbuterol,Procaterol,Clenbuterol, Meta-proterenol, Fenoterol, Bitolterol mesylate, Ritodrine etc.
- Long-acting drugs like Salmeterol,Formoterol, Bambuterol,Clenbuterol,Olodaterol,Vilanterol etc.
- Ultra long acting drugs like Isoprenaline[1].

β_2-adrenergi cagonists as mentioned earlier are , familiar for the treatment of pulmonary disorders[2] but have created a new identity in medicine by the ongoing advance researches.With this background, a five year literature searching was done on Google scholar and Pakmedinet.com from 2011 to 2015 by using the key words β_2-adrenergic receptors, β_2-adrenergic agonists and new aspect of β_2-adrenergic agonists. A total of 22 studies were found related to β_2-adrenergic agonists. Refining the search by using the phrase new aspect of β_2-adrenergic agonists, curtailed the available number of articles to 5 that is 2011(0), 2012(0),2013(1),2014(2), 2015(2).This piece of information is enough for provision of insight into this particular class of drugs. A beneficial use of β_2-adrenergic agonist is found to be in congenital myasthenic syndrome.This is a rare disorder resulting from mutations in genes encoding for presynaptic, synaptic, and postsynaptic proteins that are involved in the signal transmission of the neuromuscular junction. The disease is characterized by fatigable weakness of the skeletal muscles with symptom onset from birth to early childhood[3].A study conducted on children 13 to 16 years of age were given salbutamol.

Touseef Sayyar
Pharmacist
Department of Pharmacology
Bahria University Medical &Dental College
Karachi
Email:touseef_sayyar@yahoo.com
Received: 07-10-2015
Revised: 28-10-2015
Accepted: 01-11-2015

They have documented that oral salbutamol treatment essentially improves symptoms in inherent myasthenic disorder in children[4].

Van danga in 2014 found that formoterol which is a long acting β_2-adrenergic agonist caused significant improvement in cognitive function in mice by improving dendritic complexity. Considering its widespread use in humans and positive effects on cognition in mice, formoterol or similar β_2 adrenergic receptor agonists with ability to cross the blood brain barrier might be attractive candidate for clinical trials to improve cognitive function in individuals with down syndrome[5].Down syndrome is characterized by decrease in intellectual capacity due to degeneration of locus coeruleus, a noteworthy player in logical learning. Sean in 2014 have found that formoterol might instigate mitochondrial biogenesis, restore the expression and capacity of mitochondrial proteins and expand the duplicate number of numerous qualities included in the mitochondrial electron transport chain, apparently through actuation of down-stream interpretation pathways[6].

It is also documented that β_2-adrenoceptor agonistsslow down the progression of ALS (Amyotrophic lateral sclerosis) by effectively treating its symptoms. Amyotrophic lateral sclerosis (ALS; also known as Lou Gehrig's disease) is a neuromuscular disorder in which there occursa gradual loss of function and eventual death of motor neurons in the spinal cord and brain, as well as significant atrophy of the muscles[7].Clinically, it is characterized by stiff and/or twitching muscles and significant muscle weakness due to gradual muscle wasting, resulting in difficulty in ambulating, speaking, swallowing, and eventually breathing. Bartusa et al have found in 2015 that orally-dynamic β_2-agonists might give a novel and helpful intends to diminish the side effects of ALS and potentially postpone illness movement[8].

β_2-adrenergic agonists can also be used in idiopathic stuttering priapism. According to the findings of newer case report study which showed that Idiopathic stuttering priapism can be treated with salbutamol orally. Recurrent ischaemic priapism also known as stuttering priapism is an uncommon form of ischaemic priapism, and its treatment is not yet clearly defined. If left untreated, it may evolve into classic form of acute ischaemic priapism and lead to erectile dysfunction due to fibrosis of corpora cavernosa. Hormonal therapy such as cyproterone acetate, oestrogen, bicalutamide or Lh-Rh agonist are often effective but can cause side effects such as hypogonadal state and infertility. Other medical options are 5-alpha-

reductase and phosphodiesterase-5 inhibitors, ketoconazole, baclofen, digoxin, gabapentin and ß2-adrenergic agonist terbutaline.This study reported the first case of stuttering priapism treated with ß2-adrenergic agonist salbutamol.This study proved that beta-2-agonist salbutamol is effective for the treatment of stuttering priapism[9].

Another advance role of ß2-agonist drugs has been found in Dyslipidemia.Makiin 1996[10] found that albuterol administration was associated with favorable changes in the serum lipid profile with significant lowering of LDL-c and increases in HDL-c in a small human trial without marked impairment of glucose tolerance or its physiologic determinants. His finding have been encoded by Yanrui in 2015.[11] He has documented that selective β_2-agonist, bambuterol also significantly lowered LDL-c in a relatively small healthy volunteer population.It is due to the fact that β_2-adrenergic agonism stimulates intracellular cAMP, which regulates a number of pathways involved in lipid and glucose metabolism. Sterol regulatory element-binding proteins (SREBPs) are major transcription factors regulating the biosynthesis of cholesterol, fatty acids and triglycerides[12].SREBP is controlled by cAMP, which may explain why β_2-agonism may affect LDL-c, HDL-c and triglycerides[13].

Thus working on newer aspects of older or conventional drugs is an open venture for future years. Already available or older drugs enjoy the confidence of experience and safety with their pharmacokinetics, pharmacodynamics and chemical properties discernible at present to all along with endorsement and approval by the standard regulatory authorities. Their by they provide good opportunity to begin with utilization of less resources than a totally new start altogether for discovery of a new drug.

REFERENCES:

1. Cherezov V, Rosenbaum DM, Hanson MA, Rasmussen SG, Thian FS, KobilkaTS .High-resolution crystal structure of an engineered human 2-adrenergic G protein-coupled receptor.Science 2007; 318 (3): 1266-73
2. Birrel MA, Bonvini SJ, Michael A , James B.The role of adenylyl cyclase isoform 6 in ß-adrenoceptor signalling in murine airways. BJP.2014;173(2): 253-412
3. Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH et al .Congenital Myasthenic Syndromes. AJHG .2012; 91(1) :193-201
4. Burke G, Hiscock A, Klein A, NiksEH. Salbutamol benefits children with congenital myasthenic syndrome due to DOK7 mutations in Neuromuscular Disorders . Elsevier 2013 ;23(2): 170-5
5. Dang v, Medina B, Das D, Moghadam S, Martin KJ.Formoterol Improves Cognitive Function and Promotes Dendritic Complexity in a Mouse Model of Down Syndrome Biological Psychiatry .Elsevier.2014 ;75(3):179-88
6. Jesinkey SR, Funk JA, Stallons LJ, Wills LP .Formoterolrestores mitochondrial and renal function after ischemia-reperfusion injury.JASN. 2013;21(3):160-76
7. Cozzolinoa M, CarrìaMT. Mitochondrial dysfunction in ALS Progress in Neurobiology.Elsevier .2012; 97 (2): 54-66
8. Bartus RT, Bétourné A, Basile A, Peterson BL. β_2-Adrenoceptor agonists as novel, safe and potentially effective therapies for Amyotrophic lateral sclerosis (ALS) in Neurobiology of Disease.Elsevier;2015; 85 (1):11–24
9. Migliorini F, Porcaro AB, BaldassarreR ,ArtibaniW. Idiopathic stuttering priapism treated with salbutamol orally.Androgolia. 2015;1439(1):13-22
10. Maki KC, Skorodin MS, Jessen JH, Laghi F. Effects of oral albuterol on serum lipids and carbohydrate metabolism in healthy men .Elsevier.1996; 45(6) :712-7
11. Yanrui Ye, Hang Xu, Quan L, Zhu L, Zeng J, Zhou T, et al. The Lipid-lowering Effects of R-bambuterol in Healthy Chinese Volunteers .Elsevier .2015; 2(4):356-64
12. Zhou HC, Sun YY, Cai W, He XT, Yi F, Li BM.Activation of β_2-adrenoceptor enhances synaptic potentiation and behavioral memory via cAMP-PKA signaling in the medial prefrontal cortex of rats Cold Spring Harbor Laboratory Press.2013; 3(2):54-65
13. Davidson MH. ß2-Agonism: A potential therapeutic target for dyslipidemia.Elsevier.2015; 2(4):356-64

STUDENTS CORNER

Research Day
Department of Community Health Sciences (CHS)
BUMDC

Imran Shaikh[1], Nadia Khalid[2], Khola Noreen[3]

In order to achieve Bahria University Medical & Dental College stated mission, the emphasis of the undergraduate medical curriculum is on community-oriented education (COME), an integrated curriculum and problem based learning strategy with emphasis on active research, the CHS curriculum is designed to "Produce Research Oriented Graduates Skilled to Manage Effectively and Efficiently the Health Problems of Individuals and Families in Community Setting".

To achieve the objectives the Department of CHS plans and discusses quantitati ve subjects of Biostatistics, Epidemiology, Survey and Research methodology. They are imparted to develop skills for analyzing health of the population. To achieve the above mentioned objectives, students are asked to conduct research in groups. In the initial step students have to submit a synopsis of the research they want to conduct. Then they are asked to collect data from the field and enter it in SPSS for analysis. The research is monitored by the nominated supervisors from CHS faculty.After analysis they have to submit the research and a presentation by the group leader.

Research Day was organized for fourth year on Oct 13, 2015, which was attended by a large group of students and faculty. Director General and Principal BUMDC were the chief guests. The jury comprises of three senior Professors from Basic and Clinical Sciences. Senior faculty from Ziauddin Medical College was also among the guests. There were eighteen groups of year four who presented their research. The jury, after the presentations gave their decision about the first three research presentations. Awards to first three groups were distributed by Director General BUMDC. 1st position was taken by Group-16. Marvi Mahesar, the group leader presented on "Frequency of Thalasemia in Children of Parents with Consanguineous Marriage"Abdullah, Ahmed Shamim, Hira Suleman, Mashael Hussain, Sarah Zafar, Umaima Dhamrah were the members of this group 2nd position was hunted by Group 13. The group comprised of Uzma Khan, Tehseen Arshad, Yusra, Rana Mubashir and Saud. The group leader Uzma Khan presented "KAP Survey About Risk Factors of Coronary Heart Disease (CHD) Among General Public in Urban Population of Karachi"3rd position was earned by Group 8. Khusboo Soomro, the leader of the group presented "Study on Effect of Interactive Session and Problem Based Learning Session with Regard to Students` Learning in BUMDC. The members of this group were Ramsha, M.Abid, Ainul Akbar, Adil Dawach, and Sohail Moosa.

✉ **Dr. Imran Shaikh**
Professor & HOD
Department of Community Health Sciences
Bahria University Medical & Dental College
Karachi
Email: dr_is2009@yahoo.com
✉ **Dr. Nadia Khalid**
Lecturer
Department of Community Health Sciences
Bahria University Medical & Dental College
Karachi
✉ **Dr. Khola Noreen**
Lecturer
Department of Community Health Sciences
Bahria University Medical & Dental College
Karachi
Received: 06-12-2015
Revised: 07-12-2015
Accepted: 08-12-2015

Welcome Address by Prof. Dr. Imran Sheikh

Group Leaders in Question Answer Session

Group Awarded 1st Position Receiving Shield from DG

Group Awarded 2nd Position Receiving Shield from DG

Group Awarded 3rdPosition Receiving Shield from DG

DG-BUMDC Receiving Souvenir from Prof. Dr. Asadullah Khan, HOD Surgery

Judges Evaluating the Presenters

Audience at the Occasion

CASE REPORT

Ocular Syphilis – Uncommon but not Rare

Qamar Ul Islam[1], Dilshad Ali[2]

ABSTRACT:
Syphilis is a multisystem bacterial infection caused by the spirochete TreponemaPallidum, which has regained attention as a new epidemic due to worldwide increase in the cases of this disease. Ocular syphilis is an unusual manifestation of disease, mostly occurring in the secondary or tertiary stage of disease. Ocular involvement may be the presenting manifestation of syphilis and it is often associated with delayed diagnosis and treatment, which may result in irreversible structural and functional ocular damage. Although, ocular syphilis can affect any part of eye, uveitis is the most common ocular manifestation of the disease. A high index of suspicion is mandatory as ocular syphilis can mimic variety of other ocular inflammations. We report two cases of syphilitic panuveitis where high index of suspicion resulted in the correct diagnosis and management.
Keywords: Ocular Syphilis, Uveitis, Panuveitis, Neurosyphilis.

INTRODUCTION:

Due to its highly variable ocular manifestations, syphilis is known as "the great masquerader" resulting from infection by the spirochete Treponema Pallidum. During the last two decades, there is resurgence of the disease with a WHO estimate of about 11 million new cases of syphilis worldwide every year, over 90% of which occur in developing countries.[1] The infection has also re-emerged in developed countries in homosexual population with high number of cases co-infected with HIV.[2,3] Ocular syphilis is an uncommon presentation of syphilis that can occur in any stage of the disease and involve any ocular tissue, but typically occurs in secondary and tertiary stage.[1,4] Common ocular manifestations of syphilis include interstitial keratitis, anterior, intermediate and posterior uveitis, vitritis, chorioretinitis, retinitis, retinal vasculitis, secondary glaucoma, cataract, and cranial nerve and optic neuropathy.[5,6,7]

Uveitis is the most common ocular manifestation of syphilis and poses a diagnostic and therapeutic challenge as it is resistant to the conventional treatment of uveitis. Diagnosis can be confirmed on serological analysis that includes non treponemal tests [Venereal Disease Research Laboratory (VDRL) and Rapid Plasma Reagin (RPR) tests] and treponemal tests [Fluorescent treponemal antibody absorption (FTA-ABS) and Treponema Pallidum Haemagglutination assay (TPHA) test]. We report two cases of syphilitic uveitis where high index of suspicion resulted in the correct diagnosis and timely management with favorable outcome.

✉ **Dr. Qamar Ul Islam**
Assistant Professor
Department of Opthalmology
PNS-SHIFA Hospital
Bahria University Medical & Dental College
Karachi.
Email: qamarulislam71@gmail.com
✉ **Dr. Dilshad Ali**
Registrar
Department of Ophthalmology
CMH
Peshawar
Received: 15-10-2015
Revised: 27-10-2015
Accepted: 01-11-2015

CASE REPORT:

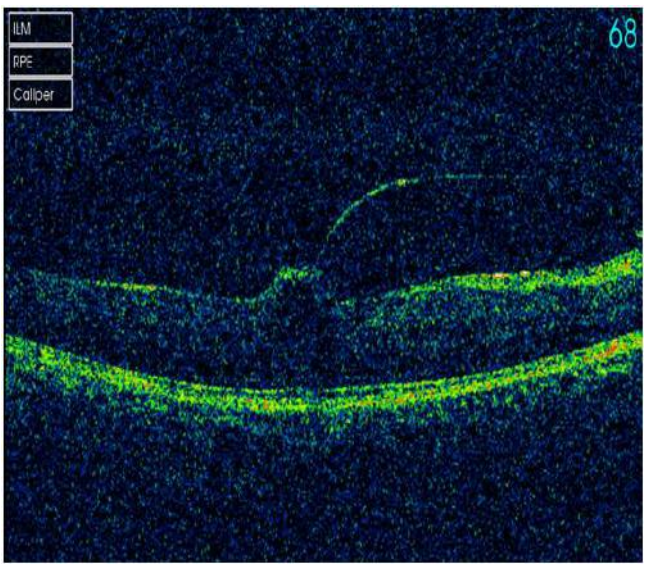
Case 1: A 42-year-old male presented with bilateral progressive painless visual deterioration and floaters for the last two years. Available medical record revealed that he has been treated with topical steroids for recurrent uveitis by various ophthalmologists. Systemic inquiry revealed history of frequent extra marital sexual contacts and penile ulceration 3 years ago. General physical and systemic examination did not reveal any abnormality. On ocular examination, his best corrected visual acuity (BCVA) was 6/18 in both eyes. Anterior segment examination showed cells (++) in both eyes with intraocular pressures (IOP) of 19 and 16 mm Hg. Posterior segment examination revealed bilateral vitreous haze and snow ball opacities in inferior vitreous along with dull foveal reflex. Serological studies revealed positive TPHA test (1/320 titer) and Hepatitis Anti HCV antibody, while VDRL test and HIV test were negative. CSF examination revealed elevated protein levels of 100 mg/dl while CSF VDRL and TPHA were negative. Once the diagnosis of ocular syphilis was established, he was given intravenous injection Penicillin 1 Million units 6 hourly for two weeks followed by 3 weekly doses of intramuscular injection Benzatheine Penicillin (2.4 M units) under supervision of consultant dermatologist. Concomitant treatment with topical 1% Prednisolone acetate eye drops, Nepafenac eye drops and 1% Cyclopentolate eye drops was continued for ocular inflammation. At 6 months follow up visit patient was asymptomatic with BCVA of 6/6 in right eye and 6/7.5 in left eye with negative VDRL and TPHA reports.

Case 2:A 40-year-old male reported in eye OPD with a history of pain, redness and decrease vision in both eyes for the last 3 months. Detailed systemic history revealed appearance of skin rashes about 3 months ago but he denied any extra marital sexual exposure. General physical examination showed fading papulo squamous rashes on palms and soles (Figure 1a). At presentation, his BCVA was counting fingers at 1 meter in right eye and 6/18 in left eye. Anterior segment examination showed cells (+++), posterior synechiae and pigment deposit on lens in both eyes with IOP of 10 mm Hgin each eye. Posterior segment examination of right eye showed vitreous haze and opacities along with macular odema, whereas left eye revealed vascular sheathing

along with vitreous cells and opacities. Serological studies revealed positive TPHA test (1/320 titer) and VDRL test (1/8 titer). However, CSF examination did not reveal any abnormality. Other investigations including HIV test were negative. Initially he was managed with topical and posterior sub-tenon steroid injections by eye specialist. Subsequently, on confirmation of ocular syphilis on serology, consultant dermatologist started him on intravenous injection Penicillin for 14 days followed by 3 weekly doses of injection Benzathene Penicillin 2.4 Million units intramuscularly. At 3 month follow up, he had BCVA of 1/60 in right eye and 6/9 in left eye. Posterior segment examination of right eye showed a few vitreous opacities along with vitreomacular traction and thin cystic retina, whereas left eye showed scattered vitreous opacities and few patches of chorioretinal atrophy and cellophane maculopathy (Figure 1b).

Figure: 1a
Syphilitic palmer Rash

Figure: 1b
Vitreo macular Traction on OCT



DISCUSSION:

Although uncommon, ocular syphilis posses diagnostic challenge for the ophthalmologists because of its protean features and lack of any pathognomonic manifestations. Syphilitic uveitis is an uncommon cause of uveitis accounting for 1.6 -4.5% of cases and it may be granulomatous or non-granulomatous, unilateral or bilateral and can involve anterior, intermediate or posterior segment of eye.[4]Birnbaum in a retrospective analysis of etiology of chronic anterior uveitis over a period of 35 years found ocular syphilis as a cause of anterior uveitis in 2.7% of cases.[8]Both of our cases had bilateral panuveitis. Variable presentation of ocular manifestations associated with ocular syphilis has been reported in worldwide literature. Anshu[9] in a series of 22 consecutive patients in Singapore, reported non granulomatous anterior uveitis (81.8%) as the most frequent finding in ocular syphilis, followed by vitritis (65.4%), papillitis (27.5%), scleritis/episcleritis (22.7%), interstitial keratitis (22.7%), granulomatous uveitis (13.7%), vasculitis (13.7%) and chorioretinitis (13.7%).In British ocular syphilis study (BOSS), [2] panuveitis was the commonest diagnosis affecting 41.3% of eyes followed by optic neuritis (22%), posterior uveitis (12.7%) and pure anterior uveitis (9.5%). Amaratunge[10] in his review article reported posterior uveitis as the commonest presentation of ocular syphilis followed by pan uveitis. Hong[6] found pan uveitis in 78.6%, anterior uveitis in 14.3% and posterior uveitis in 7.1% of eyes of patients with ocular syphilis.Awais[11] reported a case of syphilitic pan uveitis in a young Pakistani male who was managed with intravenous Penicillin G and systemic and periocular steroids. One of our patients had papulo-squamous rashes on palms and soles. Mathew[2] in their prospective study found systemic signs of early syphilis in 29.3% of patients with ocular syphilis which include generalized rash, mucosal lesions and lymphadenopathy, whereas, Francesco[1]et al reported history of papulo-macular rash on the trunk and palms in 26.3% of patients of ocular syphilis. It is recommended that all patients with ocular syphilis should undergo CSF examination and managed for neurosyphilis by giving intravenous Penicillin G (18-24 million units daily) for 10-14 days as per United States center for disease control (CDC) sexually transmitted disease treatment guidelines. Favorable visual and anatomical outcome in cases of ocular syphilis depends on early diagnosis and intervention. Three out of four (75%) eyes in our study achieved final BCVA of 6/12 or better. Mathew[2] reported BCVA of 6/12 or better in 92.1% of eyes after treatment, whereas, Francesco[1]et al found improved BCVA shortly after therapy in 93.3% of cases.

CONCLUSION:

Diagnosis of ocular syphilis may remain elusive due to extreme variation in presentation and mimicking other ocular inflammations. Awareness of the re-emergence of syphilis and keeping a high index of clinical suspicion in cases of uveitis can allow ophthalmologists to diagnose and treat the disease early, with favorable outcome and

reduced ocular morbidity.

REFERENCES:

1. Pichi F, Ciardella AP, Cunningham ET. Jr , Morara M, Veronese C, Jumper JMet al. Spectral domain optical coherence tomography findings in patients with acute syphilitic posterior placoid chorioretinopathy. Retina 2014; 34 (2):373-84
2. Mathew RG, Goh BT, Westcott MC. British Ocular Syphilis Study(BOSS): 2-year national surveillancestudy of intraocular inflammation secondaryto ocular syphilis. Invest Ophthalmol Vis Sci 2014; 55:(5)394-400
3. Wahab AA, Rahman MM, Mohammad M, Hussin S. Case series of syphilis and HIV co-infections. Pak J Med Sci 2013; 29(3):856-8
4. Benson CE, Soliman MK, Knezevic A, Xu DD, Nguyen QD, Do DV. Bilateral papillitis and unilateral focalchoroiretinitis as the presenting features of syphilis.J Ophthalmic Inflamm Infect 2015; 5:16 doi: 10.1186/s12348-015-0045-0
5. Lutchman C, WeisbrodDJ, Schwartz CE. Diagnosis and management of syphilis after unique ocular presentation. Can Fam Physician 2011; 57:896-9
6. Hong MC, Sheu SJ, Wu TT, Chuang CT. Ocular uveitis as the initial presentation of syphilis. J Chin Med Assoc 2007; 70(7):274-80
7. Pan SW, Yusof NS, Hitam WHW, Noor RAM, Embong Z. Syphiliticuveitis: report of 3 cases. Int J Ophthalmol 2010; 3(4):361-4
8. Birnbaum AD, Little DM, Tessler HH,Goldstein DA. Etiologies of chronic anterior uveitis at a tertiary referral center over 35 Years. OculImmunolInflamm 2011; 19(1):19-25
9. Anshu A, Cheng CL, Chee SP: Syphilitic uveitis: an Asian perspective. Br J Ophthalmol 2008; 92:594-7
10. Amaratunge BC, Camuglia JE, Hall AJ. Syphilitic uveitis: a review ofclinical manifestations and treatment outcomes of syphilitic uveitis inhuman immunodeficiency virus-positive and negative patients. ClinExpOphthalmol 2010 38(1):68-74
11. Awais M, Zafar O. Syphilitic Uveitis: A Therapeutic Challenge. Pak Armed Forces Med J 2012; 62(3): 464-6

LETTER TO EDITOR

Antibiotic Resistance: A Neglected Aspect in Clinical Practice

Aamir Hussain

To,
The editor,

Drug resistance is an inevitable biological process, however even though as physicians, we are augmenting it. After discovery, Nobel Prize winner Alexander Fleming said, "The thoughtless person playing with penicillin treatment is morally responsible for the death of a man who succumbs to infection with a penicillin-resistant organism." Most people didn't die of cancer or chronic lifestyle diseases, because they didn't live sufficient to develop them. Unfortunately, they died of infections yet again because of a fact named antibiotic resistance.[1]Penicillin was strewn in 1943, as over the counter drug, thus became resistantonly after two years. Likewise, recently, Daptomycin, became resistant after only one year in 2004. Bacteria develop resistance so quickly that pharmaceutical companies have decided making antibiotics is not in their best interest, so there are infections moving across the world for which, out of more than100 antibiotics available on the market, two drugs might work with side effects, or one drug, or none.[2]In 2008, the Center for Disease Control and Prevention (CDC) identified, doctors in Sweden diagnosed a man from India with a different infection resistant to all but one drug that time. The gene that creates that resistance, known as NDM, has now spread from India into China, Asia, Africa, Europe and Canada, and the United States. In United States and Europe, 50,000 people a year die of infections which no drug can help. In the United States, 50 percent of the antibiotics given in hospitals are unnecessary. In the United States, possibly 80 percent of the antibiotics sold every year go to farm animals, not to humans, creating resistant bacteria that move off the farm in water, in dust and in the meat of the animals. Aquaculture depends on antibiotics too, particularly in Asia, and fruit growing relies on antibiotics to protect apples, pears, and citrus, against disease. And because bacteria can pass their DNA to each other like a traveler handing off a suitcase at an airport, once we have encouraged that resistance into existence, there is no knowing where it will spread.[3] To combat this, first “World Antibiotic Awareness Week”,celebrated from 16 to 22 November, this year, in effort to increase awareness of large-scale antibiotic resistance and to encourage best practices among the patients, physicians, paramedics and other stakeholders, to avoid further surfacing and stretch of antibiotic resistance. Furthermore, it’s our own responsibility as the vigilant member of the clinical society to prevail ethical practice regarding tackling antibiotic resistance.[4]We could relinquish prescribing antibiotics if we aren’t certain it's the accurate one. We could discontinue insisting on a drug/medicine for our children throat illness before we're convinced what the bug is causing it. We potentially undertake each other never again to purchase chick or shrimp or fruit raised with everyday antibiotic utilization, and if we did those things, we would halter the arrival of the post-antibiotic era. But we’ve to do it as early as possible.[5]

REFERENCES:

1. Marsden BD, Knapp S. Doing more than just the structure-structural genomics in kinase drug discovery. Curr Opin Chem Biol. 2008 ; 12(1):40-5
2. WHO (2015). Drug resistance available from: http://www.who.int/drugresistance/documents/baselinesurveynov 2015/en/
3. The Center for Disease Control and Prevention .2012. Available from: http://www.cdc.gov/drugresistance/
4. Chu SH, Small D. Mechanisms of resistance to FLT3 inhibitors. Drug Resist Updat.2009 ;12(1-2):8-16
5. WHO.2015. Antibiotic drug resistance factsheet available from: http://www.who.int/drugresistance/en/

Dr. Aamir Hussain
Senior Lecturer (LIII)
Department of Community Medicine
Liaquat National Hospital and Medical College
Karachi.
Email: dr.aamirhussain786@gmail.com

Received: 05-12-2015
Accepted: 08-12-2015

INSTRUCTION TO AUTHORS JBUMDC

The Journal of Bahria University Medical and Dental College abbreviated as JBUMDC is a peer reviewed biannual multidisciplinary biomedical journal of basic and clinical health sciences.It accepts manuscripts prepared in accordance with the "Uniform Requirements for Submission of Manuscripts for Biomedical Journals, updated October 2008", adopted by International Committee of Medical Journal Editors (ICMJE) www.icmje.org. & PMDC guidelines for medical & Dental journals www.pmdc.gov.pk.The Journal will encompass manuscripts from all fields of biomedical sciences in the form of Editorial (Invited),Original Article, Review Article,Short Communication, (Commentary),Case report and Letter to editor.

Peer Review Policy:

Every paper will be read by the editor. Selected papers will be sent to two reviewers .If statistical analysis is included examination by the staff statistician will be carried out.

Plagiarism:

JBUMDC follows the ICMJE, PMDC and HEC guidelines for plagiarism.

Preparation of Manuscript:

Type the manuscript on ISO A4 (212 × 297 mm), with margins of at least 25 mm (1 inch). Type or print on only one side of the paper. Use double spacing throughout the manuscript. Start each section on new page.Number pages consecutively, beginning with the title page. Put the page number in the lower right-hand corner of each page.

Contents of Manuscript for submission:

Submission items include a Covering letter, Letter of undertaking duly signed by all authors,Title page and the Manuscript [Abstract,Key words,Introduction, Materials & Methods, Results, discussion, conclusion, acknowledgement, Authorship, Conflict of interest, References, Tables , Figures].Title page should have complete title of the manuscript, the names of all authors with qualifications, their department ,affiliation, telephone number,e-mail, corresponding author ,address for correspondence, short running title,source of funding(grant/equipment/drugs), number of figures and tables, total word count, total number of pages.

1. Abstract

It should have no more than 150 words for unstructured abstracts or 250 words for structured abstracts. The abstract should state the purpose of the study(objective), basic procedures (materials & methods with study design, subjects/animals, place & duration of study, drug/chemical/ equipment, procedure or protocol), main findings (results) and conclusion. It should emphasize new and important aspects of the study.Below the abstract provide, 3-10 key words that will assist indexers in cross-indexing the article and may be published with the abstract.

2. Introduction

State the purpose of the article and summarize the rationale for the study. Give only strictly pertinent references and do not include data or conclusions from the work being reported.

3. Materials &Methods

Describe your selection of the observational or experimental subjects (patients or laboratory animals, including controls) clearly. Identify the age, sex, and other important characteristics of the subjects. Identify the methods, apparatus (give the manufacturer's name and address in parentheses), and procedures in sufficient detail to allow other workers to reproduce the results.. Identify precisely all drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration.For randomized clinical trials provide information on all major study elements, including the protocol (study population, interventions or exposures, outcomes, and the rationale for statistical analysis), assignment of interventions (methods of randomization, concealment of allocation to treatment groups), and the method of masking (blinding). Authors submitting review manuscripts should include a section describing the methods used for locating, selecting, extracting, and synthesizing data. These methods should also be summarized in the abstract.All studies must be approved by the relevant Ethics Committee/InstitutionReview Board of the respective institutions.

4. Results

Present your results in logical sequence in the text, tables, and illustrations. Do not repeat in the text all the data in the tables or illustrations; emphasize or summarize only important observations. Describe appropriate indicators of measurement error or uncertaintysuch as confidence intervals, P values. Report complications of treatment & dropouts from a clinical trial. Specify any general-use computer programs employed for analysis.

5. Discussion& Conclusion

Emphasize the new and important aspects of the study and the conclusions that follow from them. Do not repeat in detail data or other material given in the Introduction or the Results section. Include in the Discussion section the implications of the findings and their limitations, including implications for future research. Relate the observations to other relevant studies. Link the conclusions with the goals of the study

6. Acknowledgment

List all contributors who do not meet the criteria for authorship, such as a person who provided purely technical help, writing assistance, or a department chair who provided only general support. Financial and material support should also be acknowledged.

7. Authorship

Authorship credit is based only on 1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) drafting the article or revising it critically for important intellectual content; and 3) final approval of the version to be published. Conditions 1, 2, and 3 must all be met.Authors should provide a description of what each contributed.

8. Conflict of interest

All authors have to disclose and submit any financial /personnel relationship that might bias and inappropriately influence their work.

9. References

Majority of the references must be from last five years. Local references must also be included. Vancouver style should be followed. Examples are:

a) Standard journal article

List the first six authors followed by et al.

I)Less than 6 authors:

Vega KJ, Pina I, Krevsky B. Heart transplantation is associated with an increased risk for pancreato-biliary disease. Ann Intern Med 1996 Jun 1;124 (11):980-3.

II) More than six authors:

Parkin DM, Clayton D, Black RJ, Masuyer E, Friedl HP, Ivanov E, et al. Childhood leukaemia in Europe after Chernobyl: 5 year follow-up. Br J Cancer 1996;73:1006- 12.

b) Organization as author

The Cardiac Society of Australia and New Zealand. Clinical exercise stress testing. Safety and performance guidelines. Med J Aust 1996; 164: 282-4.

c) No author given

Cancer in South Africa [editorial]. S Afr Med J 1994;84:15.

d) Chapter in a book

Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension: pathophysiology, diagnosis, and management. 2nd ed. New York: Raven Press; 1995. p. 465-78.

e) Newspaper

HasanMansoor. Excessive use of drugs creating resistance to antibiotics. The Dawn 2013, 24 June; sect. Metropolitan (col.1-4)

10. Tables

Type or print out each table with double spacing on a separate sheet of paper. Number tables consecutively in the order of their first citation in the text and supply a brief title for each. Give each column a short or abbreviated heading. Place explanatory matter in footnotes. Explain in footnotes all nonstandard abbreviations that are used in each table. Identify statistical measures of variations, such as standard deviation and standard error of the mean.Do not use internal horizontal and vertical rules.

11. Illustrations (Figures)

Figures should be professionally drawn and photographed. Photographic prints 127 × 173 mm (5 × 7 inches). Photomicrographs should have internal scale markers. Symbols, arrows, or letters used in photomicrographs should contrast with the background.If photographs of people are used, either the subjects must not be identifiable or their pictures must be accompanied by written permission to use the photograph Figures should be numbered consecutively according to the order in which they have been first cited in the text. If a figure has been published, acknowledge the original source and submit written permission from the copyright holder to reproduce the material.

Legends for Illustrations

Type or print out legends for illustrations using double spacing, starting on a separate page, with Arabic numerals corresponding to the illustrations. When symbols, arrows, numbers, or letters are used to identify parts of the illustrations, identify and explain each one clearly in the legend. Explain the internal scale and identify the method of staining in photomicrographs.

Units of Measurement

Measurements of length, height, weight, and volume should be reported in metric units. Temperatures in degrees Celsius, Blood pressure in millimeters of mercury & all hematologic and clinical chemistry measurements in the metric system in terms of the International System of Units (SI).

Abbreviations and Symbols

Use only standard abbreviations. Avoid abbreviations in the title and abstract. The full term for which an abbreviation stands should precede its first use in the text unless it is a standard unit of measurement.

Sending the Manuscript to the Journal

Submit manuscript by e-mail: editor.bumdc@bahria.edu.pk or by post on CD with two hard copies to: Editor, JBUMDC, Bahria University Medical & Dental College, DHA Phase-II, Adjacent PNS Shifa, Karachi. All correspondence regarding submitted manuscripts will be via e-mail.

S #	Type of Article	Abstract type & word count	Key words	Total word count	References	Tables (Max)	Figures (Max)
1	Editorial	-	-	1000-1500	10-12	-	-
2	Review Article	Unstructured (150)	3-6	3000-3500	40-60	4	2
3	Original Article	Structured (250)	3-10	2500-3000	25-35	4	3
4	Medical Education	1. Original Structured (250)	3-10	2500-3000	25-35	4	3
		2. Review Unstructured (150)	3-6	3000-3500	40-60	4	2
		3. Reproducible work (guidelines, questionnaire)	Mention Source, Accessed on, Retrieval date				
5	Short Communication /Commentary/ Opinions/ Perspective	Unstructured (150)	3-6	1200-1500	15-20	2	1
6	Student Corner	1. Original article Structured (250)	3-10	2500-3000	25-35	4	3
		2. Views' Perspectives, Opinions Unstructured (150)	3-6	1200-1500	8-10	1	1
7	Case Report	Unstructured (150)	3-5	1200-1300	10-12	1	2
8	Letter to Editor	-	-	400-500	5	-	-
9	Instruction to Author	Please See the Text Detail					

Reviewers List
JBUMDC, VOLUME-5
2015

The editor JBUMDC extends gratitude to the following colleagues for reviewing the manuscripts of JBUMDC from January 2015-December 2015.

- Afshan Siddique
- Aiesha Ishaque
- Asadullah Khan
- Atiya Fasih
- Dawood Mirza
- Farhan Akhtar
- Fuad Shaikh
- Hasan Ali
- Imran Shaikh
- Iqbal Udaipurwala
- Khalida Nasreen
- Kulsoom Rizvi
- Mehreen Latif
- Mohiuddin Alamgir
- Munawar Alam
- Nadeem Shaikh
- Nasim Karim
- Nighat Huda
- Nisar Ahmed
- Razia Korejo
- Rozina Mustafa
- Saba Sohail
- Sajid Abbas
- Saman Hakim
- Samia Pervaiz
- Syed Sanowar Ali
- Shahida Rasheed
- Shakeel Ahmed
- Shama Asghar
- Syed Saud Hasan
- Tabassum
- Tahir Khadim
- Talea Hoor
- Zahida Memon
- Zia-Ul-Islam

AUTHOR'S INDEX VOLUME-5, 2015

A

ABBAS S
Walking: Step Towards Healthy Life(letter to editor) JBUMDC 2015; 5(1): 45

AKHTAR M
Effects of Ethmoid Surgery on Proptosis and Vision (original article) JBUMDC 2015; 5(4): 174-177
SHEIKH M S See AKHTAR M
AZIZ M See AKHTAR M
SHAFIQUE M A See AKHTAR M
MAROOF M See AKHTAR M

ALI S S
Disaster Management (editorial) JBUMDC 2015; 5(3): 102-104

ARSHAD R
Vasculo-Protective Cover: A Novel Action of Metformin (review article) JBUMDC 2015; 5(3): 105-108
KARIM N See ARSHAD R

ASAD M
Frequency of Medical Conditions in Patients of Low Socioeconomic Status Seeking Dental Treatment (original article)JBUMDC 2015; 5(3): 139-142
IKRAM K See ASAD M
MIRZA A J See ASAD M
BERKATHULLAH M See ASAD M

ASGHAR S
Frequency of Dental Caries on Individual Tooth Surfaces of First Permanent Molars Between 6-13 Years Old Children (original article) JBUMDC 2015; 5(1): 16-19
BUTT R A See ASGHAR S
JAFARI S I A See ASGHAR S
NASIR A See ASGHAR S
ADEEL S See ASGHAR S

AZHAR M A
Diagnostic Utility of Ultrasound in Acute Appendicitis in Correlation with Total Leukocyte Count (original article)JBUMDC 2015; 5(2): 81-85
LATIF A See AZHAR M A
AHMAD M See AZHAR M A
MAHMOOD F See AZHAR M A

B

BANO M
Knowledge Attitude and Practice Regarding Smokeless Tobacco among Adolesence of Two Private Schools of Gadap Town Karachi (original article) JBUMDC 2015; 5(4): 191-195
ALI A See BANO M
LEGHARI M A See BANO M
MAZHAR S See BANO M

F

FASIH A
Obstetric Restless Legs Syndrome in Industrialized Area of Pakistan (original article)JBUMDC 2015; 5(2): 69-72
ABDULLAH K N See FASIH A
IQBAL S See FASIH A

FATIMA H
Analysis of BMD and Serum Calcium Level in Patients with or without Bony Metastatic Breast Cancer. (original article)JBUMDC 2015; 5(3): 127-130
TAGAR H R See FATIMA H
CHODHRY A See FATIMA H
QAMAR S See FATIMA H

G

GUL M
Dental Students' Perception on Preclinical Operative Dentistry Course (original article) JBUMDC 2015; 5(4): 178-183
ASGHAR S See GUL M
SAMI Z See GUL M

H

HUDA N
Towards Academic Culture in Pakistan: Role of Medical Conference and How Challenging to Survive with Evolving Technology Advancement (editorial) JBUMDC 2015; 5(4): 155-156

HUSSAIN A
Alarming Scarcity of Blood Donations (letter to editor) JBUMDC 2015; 5(2): 98

HUSSAIN A
Antibiotic Resistance: A Neglected Aspect in Clinical Practice (letter to editor) JBUMDC 2015; 5(4): 20

HYDRI A S
A Large Extra-Osseous, Solitary Neurofibroma of the Hard Palate (case report) JBUMDC 2015; 5(3): 148-150
HUSSAIN S S See HYDRI A S
UDAIPURWALA I H See HYDRI A S
SIDDIQUI F See HYDRI A S

I

ISHAQ S M
Evaluation of Retinoblastoma according to Histological Grading, TNM Staging and Age at Presentation. (original article) JBUMDC 2015; 5(3): 113-115
KEHAR S I See ISHAQ S M
RAHAT N See ISHAQ S M
JAN A SEE ISHAQ S M

QAMARULISLAM
Ocular Syphilis–Uncommon but not Rare (case report) JBUMDC 2015; 5(4): 205-207
ALI D See QAMARULISLAM

J

JAFFRY S A
Heat Stroke: Deadly but Preventable (editorial) JBUMDC 2015; 5(2): 49-50

JAFFRI S A
Dengue: Beat Dengue Bite by Prevention (letter to editor)JBUMDC 2015; 5(3): 151

K

KARIM N
Vitamin D - not Just a Simple Vitamin. (commentary)JBUMDC 2015; 5(3): 143-145
HOOR T See KARIM N

KHADIM M T
Pulmonary Alveolar Microlithiasis with Klippel-Feil Syndrome:
The Eye Does Not See What The Mind Does Not Know (case report) JBUMDC 2015; 5(2): 95-97
AHMED N See KHADIM M T
ASGHAR A See KHADIM M T
RAO R See KHADIM M T
NAUMAN K See KHADIM M T
JAFFAR S R See KHADIM M T

KHAN A
Knowledge, Attitude and Practice Regarding Pulmonary Tuberculosis Awareness among Non-Medical Students of Karachi
Student Corner (original article) JBUMDC 2015; 5(1): 37-40
ALI H See KHAN A
SHAH M A See KHAN A
ZUNAIR S See KHAN A
MEHMOOD E See KHAN A
RABAIL N See KHAN A
ZIA S See KHAN A
KUMAR C See KHAN A
AHMED S See KHAN A
KHALID N See KHAN A

KHAN Y
Surgical Treatment of Chronic Subdural Hematoma-Single Burr Hole: Clinical Characteristics and Outcome (original article) JBUMDC 2015; 5(1): 8-11
ASHRAF A T See KHAN Y
SHAKIL N See KHAN Y
FAROOQUI H See KHAN Y
SIBTAIN S M See KHAN Y

M

MAHESAR M
Trauma Management: Should it be a part of Medical Curriculum? Student Corner (commentary) JBUMDC 2015; 5(2): 92-94
SALMAN H See MAHESAR M
KHATRI N See MAHESAR M
ZAFAR S See MAHESAR M
DHAMRAH U See MAHESAR M
HYDRI A S See MAHESAR M

MALIK F R
Are we Caring those who Deserve Special Care? Frequency of Depression among Older Population Residing in a Nursing Home at Karachi (original article) JBUMDC 2015; 5(3): 116-120
QURESHI M S H See MALIK F R
MAHFOOZ A See MALIK F R
QURESHI B W See MALIK F R

MEMON A B
Pattern of Missing Teeth among Patients Visiting Hamdard University Dental Hospital Karachi.(original article) JBUMDC 2015; 5(3): 131-134
KHATRI D R See MEMON A B
BHANGHAR F See MEMON A B
MIRZA D See MEMON A B
KUMAR S See MEMON A B
SOOMRO Z H See MEMON A B

MIRZA I A
Naegleria Fowleri – Simple Facts about Brain Eating Amoeba(editorial)
JBUMDC 2015; 5(1): 1-2

MIRZA S
Impact of Maternal Education on Children's Health in Slum Area of Karachi (original article) JBUMDC 2015; 5(1): 29-31
ALI S S See MIRZA S
KARIM N See MIRZA S

MOHYUDDIN M
Clinical Profile of Acute Myocardial Infarction Patients at PNS -SHIFA Hospital Karachi (original article) JBUMDC 2015; 5(1): 12-15
KHAN I A See MOHYUDDIN M
LODHI W See MOHYUDDIN M

MUNIR M
Pharmacology Students Competition 2015. Post Competition Report (student corner)JBUMDC 2015; 5(3): 146-147
AHMED A See MUNIR M

MUSTAFA R
Immediate Post-Placental Insertion versus Interval Insertion of Intrauterine Devices for Contraception (original article)JBUMDC 2015; 5(2): 77-80
QAMAR H See MUSTAFA R
NASREEN K See MUSTAFA R

N

NAJEEB T
Clincal Presentation of Malignant Tumours of Tonsil and its Association with Unilateral Enlarged Tonsil in Different Age Groups (original article)JBUMDC 2015; 5(2): 60-64
SHOAIB R M See NAJEEB T
AYUB N See NAJEEB T

NASREEN K
Heterotopic Pregnancy Following Ovulation Induction By Clomiphene Citrate And A Normally Growing Intrauterine Pregnancy: A Case Report (case report) JBUMDC 2015; 5(1): 43-44
IQBAL S See NASREEN K
FASIH A See NASREEN K

NAVAID F
Family Medicine: Necessity but Still a Neglected Medical Specialty in Pakistan(review article)JBUMDC 2015; 5(1): 3-7
ZAMIR T See NAVAID F

NIAZ K
Effect of Green Tea Consumption on HDL-Cholesterol (original article) JBUMDC 2015; 5(4): 171-173
FATIMA E See NIAZ K
JALBANI G A See NIAZ K
MURAD S See NIAZ K

NISAR M
Assessing Breast Cancer Incidence and Risk Factors from 2005-2015 in Pakistan (review article) JBUMDC 2015; 5(4): 157-161
ZAMIR T See NISAR M

NOREEN K
Association between Obesity and Low Serum Vitamin D Concentrations in HealthyAdult Females: A public Health perspective (original article) JBUMDC 2015; 5(4): 196-200
KHALID N See NOREEN K
SHAIKH I See NOREEN K
ANWAR R See NOREEN K

Q

QAMAR A
Toxic Effects of Corn Oil on Liver Histology in Albino Rats (original article) JBUMDC 2015; 5(1): 25-28
WAQAR H See QAMAR A
SIDDIQUI A See QAMAR A
KUMAR H See QAMAR A
SAEEDUDDIN M S See QAMAR A

QURESHI S I A
Awareness among the Patients of Chronic Suppurative Otitis Media about the Disease and its Complications (original article)JBUMDC 2015; 5(2): 73-76
CHOHAN M A See QURESHI S I A
HASSAN H See QURESHI S I A
CHOHAN S A See QURESHI S I A

S

SALAT M Y
Comparative Study of Verapamil and Amytriptyline in Acute Opioid Abstinence Syndrome (original article) JBUMDC 2015; 5(1): 32-36
BALOCH N See SALAT M Y
SULTANA M See SALAT M Y
HASAN S S See SALAT M Y
AHMED S N See SALAT M Y

SAMI A
Health Promoting Schools: A Powerful Means of Improving Community Oral Health for Future Generations of Pakistan(commentary) JBUMDC 2015; 5(2): 90-91
RIZVI K F See SAMI A

SANA F
Comparison of Neutrophil Gelatinase Associated Lipocalin with Serum Creatinine for Early Detection of Decrease in Estimated Glomerular Filtration Rate (original article)JBUMDC 2015; 5(2): 56-59
JAFFAR S R See SANA F
KHAN D A See SANA F
NAJAMUDDIN See SANA F
MAGSI M A See SANA F
KHADIM M T See SANA F
MIRZA I A See SANA F
AKHTAR F See SANA F

SAYYAR T
New Aspects of β_2-Adrenergic Agonists (commentary) JBUMDC 2015; 5(4): 201-202

SHAHEEN A
A Modified and Cost-Effective HPLC Method for Determination of Plasma Concentrations of Rifampicin in Pulmonary TB Patients (original article)JBUMDC 2015; 5(3): 121-126
RAJPUT T A See SHAHEEN A
AZAM F See SHAHEEN A

SHAHEEN S
Relationship of Body Mass Index, Bone Turnover Marker and Bone Mineral Density in Postmenopausal Women (original article)JBUMDC 2015; 5(3): 135-138
NOOR S S See SHAHEEN S
MEMON Z See SHAHEEN S

SHAIKH F
Methotrexate in Rheumatoid Arthritis: Effect on Blood, Liver and Renal Laboratory Parameters (original article) JBUMDC 2015; 5(4): 187-190
ARSHAD R See SHAIKH F
AZAM F See SHAIKH F
KARIM N See SHAIKH F

SHAIKH I
Research Day: Department of Community Health Sciences (CHS), BUMDC
(student corner) JBUMDC 2015; 5(4): 203-204
KHALID N See SHAIKH I
NOREEN K See SHAIKH I

SHAKIL S
Misconceptions: How to Diagnose and Clarify Them in Undergraduate Medical Students (commentary) JBUMDC 2015; 5(1): 41-42

SHARIQUE A A
Seronegative Rubella IGG Status in Pregnant Women Visiting Tertiary Care Hospital (original article) JBUMDC 2015; 5(4): 167-170
SHARIQUE M See SHARIQUEA A
MAHESH A See SHARIQUE A A
SHAH S W See SHARIQUE A A

SHEIKH F
Safety Profile of Methotrexate and Leflunomide in Rheumatoid Arthritis (original article) JBUMDC 2015; 5(1): 20-24
ARSHAD R See SHEIKH F
KARIM N See SHEIKH F

SIBTAIN S
Maternal and Fetal Outcomes in Pregnancies Conceived with in Vitro Fertilization (original article)JBUMDC 2015; 5(2): 65-68
GHANI R See SIBTAIN S
CHUI D See SIBTAIN S
ZAIDI J See SIBTAIN S

T

TAGAR H M R
Total Sialic Acid (TSA) Level as a Tumor Marker in the Diagnosis of Oral Cancer (original article)JBUMDC 2015; 5(3): 109-112
ZUBERI N A See TAGAR H M R
FATIMA H See TAGAR H M R
KEHAR S I See TAGAR H M R
TUNIO S A See TAGAR H M R

TIRMIZI S Z A
Mortality Associated with Neck Compression Deaths – An Autopsy Based Study (original article)JBUMDC 2015; 5(2): 86-89
NADIR K See TIRMIZI S Z A
ALI S S See TIRMIZI S Z A
ALI S M See TIRMIZI S Z A

U

USMAN R
Role of Sonography in Prenatal Evaluation of Placenta Accreta (original article) JBUMDC 2015; 5(4): 184-186
FATIMA S See USMAN R
RASHID SSee USMAN R
MEHMOOD S See USMAN R
SHAZLEE K See USMAN R
HAMID K See USMAN R

USMANI A
Role of Micro RNA in Breast Cancer(review article)JBUMDC 2015; 5(2): 51-55
SHORO A A See USMANI A

Z

ZAMIR T
Effect of Methanol Extract of Brassica Oleracea on Body Weight and Hematological Parameters in Rabbits (original article) JBUMDC 2015; 5(4): 162-166
YOUNUS I See ZAMIR T
HOOR T See ZAMIR T
ARSHAD R See ZAMIR T

Bahria University Medical and Dental College, Karachi

Published by: Bahria University Medical & Dental College
Adjacent PNS Shifa DHA Phase II Karachi, Pakistan.
Ph: +92-21-35319491-9
Website: http://jbumdc.bahria.edu.pk
JBUMDC Web Mail: editor.bumdc@bahria.edu.pk