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

Components of manuscript should be in the following sequence:

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

- The title of the article. Authors should include all information in the title that will make electronic retrieval of the article both sensitive and specific. The title should be clear and concise. The title length should not exceed more than 14 words. Do not capitalize the first letter of each word in the title unless it is a proper noun. Do not use abbreviations in the title.

- Name of authors with highest academic degrees of each, their postal addresses, fax, phone number and mobile numbers.

- The name of the department(s) and institution(s) to which the work should be attributed.

- Disclaimers, if any.

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

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

MANUSCRIPT FORMAT:

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

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

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

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

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

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HEALTH POLICY ADVANCEMENT AND POPULATION HEALTH: PAKISTAN IN PERSPECTIVE

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ABSTRACT

Health policy development in an appropriate cultural context under social justice with full community awareness and participation is the key to achieving a successful population health outcome. This non empirical conceptual study reviewed Pakistan's health policy, social determinants of the population health, the role of inequality and inequity in the country's life expectancy and the need for developing an acceptable culturally- appropriate health policy to improve the population health.

With a population below poverty line at 70%; unemployment rate at 23.9%; household income or consumption by percentage share at 1.8% lowest and literacy level for males and females at 69.2% and 49.7% respectively; it identified poor income, gender discrimination and illiteracy as social determinants of health.

It also found that inequality and inequity are inextricably linked to the 53.02years poor life expectancy at birth and that being aware of the culture of a community and taking that into cognizance, helps to channel one's energy appropriately in getting better health results. This makes it possible for you to fashion your health intervention programs for better outcome.

Efforts being made by Pakistan for better population health outcome includes; the health system strengthening through focus on primary health care and improved health insurance coverage; as well as economic empowerment of citizens through the national economic empowerment development strategy.
It concluded that a successful culturally- appropriate policy development involves community support and community engagement.

Health policy is broadly defined as 'goals and means, policy environments and instruments, processes and styles of decision-making, implementation and assessment. It deals with institutions, political power and influence, people and professionals, at different levels from local to global' (Lee et al.,2008). Major thrusts of Pakistan's health policy revised in 2002 includes; national health system and management, national health care resources, national health interventions, national health information system, partnership for health development, health research and national health care laws. The overall objective of this policy was to strengthen the national health system so that it will be able to provide quality, efficient, effective, accessible and affordable health services to improve the population health of Pakistan

Population health begets the health of individuals and individual health brings about the health of the cell and body and not the other way round.

Population health is now the focus of public health experts around the world. The concerns are to find out why a patient is not well and not what disease the patient has. In asking this, experts holistically put to mind all the factors that affect health and well being of the society. How healthy a population is can be evaluated from how many in the population that receive a living wage or from their average disposable income, level of unemployment and underemployment. Population health can be measured from various parameters such as the literacy level of the society. How many have good housing and safe, and constant water supply. What about the energy needs of the population, how clean is their environment? Is there a quality, affordable and accessible healthcare? All these should be the indices and basis of political, economic and social justice and by extension guarantee the health of the population. Health inequality means the difference in the health status or in the distribution of health determinants

between population groups (WHO2, 2015). An example is the difference in the mortality rates among populations with different social classes. "A child in Glasgow suburban has a life of 28years shorter than that of another child a few kilometers away". "A girl in Lesotho is likely to live 42 years less than another in Japan" (WHO, 2008). Inequality thus can be natural or genetic and as such, is inevitable. But when it is unnatural and avoidable, it becomes inequity. Inequity is unacceptable social injustice that affects life expectancy of any population. It is the consequence of huge inequality in the society due to mal-distribution of wealth. It is influenced by population-focused health determinants which includes; income, education and social determinants of health(Herbes-Sommers& Smith, 2008).

Government intervention in Pakistan to reducing health inequity is centered on two key areas; health system reforms and economic empowerment (WHO,2005). The health system focuses on the revised national health policy with all its major thrusts paying special attention to primary health care. The health sector reform with the national health bill in the national assembly "ensures among others, that the three tiers of Government have their roles clearly defined, consumers awareness are enhanced, and that governments seek partnerships with the private sector, development partners, donors and NGOs" (WHO, 2005). Another effort is in the area of health insurance cover. The establishment of national economic empowerment and development strategy (NEEDS) is to fight poverty by creating entrepreneurial spirit in the citizens. This is to close the unemployment gaps by creating jobs and enabling environments for local investors to thrive. National directorate of employment and national poverty eradication programs were also established to compliment and empower citizens to be self -dependent and self –sufficient (WHO,2005).

Health Policy Advancement
Key Features of The Policy
1. The new policy has the following key features
- Health sector investments are viewed as part of Government's poverty Alleviation Plan;
- Priority attention is accorded to primary and secondary sectors of health to replace the earlier concentration on Tertiary Care;
- Good governance is seen as the basis of health sector reform to achieve quality health care.

Overall Vision.
2. The overall national vision for health sector is based on "Health-For-All" approach. The new Health Policy aims to implement the strategy of protecting people against hazardous diseases; of promoting public health; and of upgrading curative care facilities.
3. A series of measures, programmes and projects have been identified as the means for enhancing equity, efficiency and effectiveness in the health sector through focused interventions.
4. The present policy document is a blueprint of planned improvements in the overall national health scenario. It will require commensurate investments and interventions by Provincial Governments for improving health infrastructure and healthcare services. The Federal Government will continue to play a supportive and coordinative role in key areas like communicable disease control programmes.

Concretising the Vision: 10 Specific Areas of Reforms
5. In order to concretize the above vision, 10 specific areas have been identified. These are:
- Reducing widespread prevalence of communicable diseases;
- Addressing inadequacies in primary/secondary health care services;
- Removing professional/managerial deficiencies in the District Health System;
- Promoting greater gender equity;
- Bridging basic nutrition gaps in the target-population;
- Correcting urban bias in health sector;
- Introducing required regulation in private medical sector;
- Creating Mass Awareness in Public Health matters;
- Effecting Improvements in the Drug Sector;
- Capacity-building for Health Policy Monitoring.
6. In each of these areas, strategic objectives have been identified and implementation modalities determined. The new health policy has developed a clear view of what is required to be done in key areas and the measure to be taken to achieve the envisioned goals. The succeeding paragraphs will spell out both the strategy and the implementation modalities in tandem. The policy also incorporates essential aspects like an appropriate time frame for implementation and indications of target wherever possible.
7. The National Health Policy, 2001 will act as a collective frame-work and provide guidelines to the Provinces while implementing plans in

the health sector in accordance with their requirements and priorities.

Key Area No. 1: To reduce the Widespread Prevalence of communicable Diseases (i.e. EPI cluster of childhood diseases, TB, Malaria, Hepatitis-B and HIV-Aids.

Implementation Modalities

- The protective and promotive health programmes will be implemented as National Programmes with clear cut Federal/Provincial spheres of responsibility. The Federal Government authorities will assist in planning, monitoring, evaluation, training and research activities while the Provincial Governments will undertake service delivery.

- The national Programme on EPI will be expanded through introduction of Hepatitis-B vaccine with effect from July, 2001.

- Routine EPI facilities in the Provinces, especially cold-chain equipment will be strengthened through GAVI's grant assistance over the next 5 years.

- National Immunization Days against Poliomyelitis will continue to be observed annually to ensure WHO Certification by 2005.

- A National Programme for immunizing mothers against Neonatal Tetanus will be implemented in 57 selected High-Risk Districts of the country over 3 years.

- A new national programme will be introduced against Tuberculosis based on DOTS (Directly Observed Treatment Short Course) mode of implementation. The main feature of this are – training of federal, provincial and district level managers; case detection through sputum smear technology; observed treatment of patients; standardizing drug regime; and operational research.

- A new national malaria control programme will be implemented, focusing on malaria microscopy through upgraded basic health facilities; and early diagnosis with prompt treatment. Mass spraying will be replaced by selective sprays only.

- The current PC-1 on HIV-AIDS will be enlarged to incorporate the following components – prevention of HIV transmission through health education; surveillance system, early detection of Sexually Transmitted Infections Transfusion. A uniform law will be enacted to set up Blood Control Authorities in the Provinces.

Targets and Time Frame:

- Immunization coverage will be increased to 80% by 2005 and full coverage reached by 2010.

- Polio cases will be reduced to less than 100 by end 2001 with WHO Certification achieved by 2005.

- Hepatitis-B Coverage will be available in 70% of districts by 2002 and 100% by 2003 providing 17.3 million doses annually over next 5 years.

- Full DOTs coverage of TB will be achieved in all districts of the country by 2005. The detection rate will be 70% and cure rate 85% by then. It will reduce TB prevalence by 50% by 2010.

- Malaria cases also will be reduced by 50% by 2010. Plasmodium Falciparum cases will be kept at less than 40% of all malaria infections.

Key Area No.2: To address inadequacies in primary/secondary health care services

8. The main inadequacies are identified as the deficient state of equipment and medical personnel at BHU/RHC level. Absenteeism is common. At the district/tehsil level hospitals there are major shortcomings in emergency care, surgical services, anesthesia and laboratory facilities. There is no referral system in operation.

Implementation Modalities:

- Trained Lady Health Workers will be utilized to cover the un-served population at the primary level. This would ensure family planning and the primary health care services at the doorstep of the population through an integrated community-based approach.

- 58,000 Lady Health Workers under Ministry of Health and 13,000 Village-based Family Planning Workers under Ministry of Population Welfare will be integrated from 1st July 2001 to create a cadre of 71.000 Family Health Workers under the National Programme for Family Planning and Primary Health Care. This cadre will be increased to 100,000 by the year 2005.

- Provinces will undertake improvement of District/Tehsil Hospitals under a phased plan. A minimum of 6 specialties (Medicine, Surgery, Paediatrics, Gynae, ENT and Ophthalmology) will be made available at these facilities.

- District and Tehsil Hospitals will be upgraded to the desired standard through Provincial Master Plans. The Provincial Governments

have prepared the following hospital up gradation plan over 5 years:

Punjab: 25 District Hospitals and 44 Tehsil Hospitals at a cost of Rs.1665 million.

Sindh: 11 District Hospitals and 44 Tehsil Hospitals at a cost of Rs.330 million.

NWFP: 19 District Hospitals and 11 Tehsil Hospitals at a cost of Rs.989 million.

Balochistan: 3 District Hospitals and 30 Tehsil Hospitals at a cost of Rs.540 million.

- The performance of RHCs/BHUs will be specially reviewed and only those facilities will be upgraded which can actually serve the population. Adequately functioning facilities will be strengthened by filling up of staff positions and allocation of financial resources based on performance/utilization. Poorly functioning facilities will be contracted out to the private sector or other alternative uses explored.
- Foreign assistance for the primary/secondary sectors as per above priorities will be sought by all concerned authorities including Economic Affairs Division and Planning and Development Division.
- A model referral system in selected districts of each Province will be developed by 2002 to be replicated countrywide by 2005.
- Appointments against vacant posts of staff in rural facilities will be facility specific on contractual basis.

Targets and Time Frame:
- 100,000 Family Health Workers will be recruited and trained by 2005 to cover the entire target population.
- Rationalization study of RHCs/BHUs will be completed by 2002.
- 58 District and 137 Tehsil Hospitals will be upgraded over a period of 5 years.

Key Area No.3: To Remove Professional and managerial deficiencies in district health system

9. The main deficiencies have been identified as the ineffectiveness of the district health office to supervise health services in a district. DHOs generally lack in essential qualifications and management skills.
10. A large number of posts of male and female doctors and paramedics at the primary and secondary health facilities are vacant, as well as specialist positions in Districts and Tehsil Hospitals. Mega-Hospitals are managed in an adhoc manner.

Implementation Modalities:
- Adequate financial and administrative powers will be given to the district health office under the Devolution plan to effectively manage priority programmes at district level.
- DHOs will be appointed on merit base criteria, with a Masters in public health or equivalent as minimum qualification. District health managers will undergo compulsory in-service training courses at health academies.
- A package to improve the working/living conditions of doctors, nurses, and paramedics in rural areas will be developed. A proposal embracing rural area compensatory Allowance, non-practicing Allowance, Anesthesia Allowance and nursing Allowance has been submitted to the pay and Pension Committee for consideration. Improvement in living conditions may also be funded through poverty Alleviation Programme.
- Posting Policy will insure presence of doctors at primary and secondary levels in a District. Medical graduates after completing their House Jobs will have to be posted on vacant posts in primary and secondary facilities for a minimum period of one year. Medical graduates will be selected for such appointments in an order of priority involving inter-alia, place of domicile (village, tehsil and district) and quote availed for entry to medical college. Such medical graduates will receive only provisional registration from PMDC and will be eligible for permanent registration only after completing the mandatory period of rural medical service.
- In-service officers belonging to MOs cadre will be required to serve for a minimum period of two years in primary and secondary health facilities by way of compulsory rural medical service to become eligible for promotion from BPS-17 to BPS-18.
- Specialists in non-teaching hospitals will serve for a minimum period of 2 years in rural medical service before being considered for promotion from BPS-18 to BPS-19.
- As an incentive, preference will be given to those Medical Officers and Medical Graduates to enter postgraduate programmes who have completed 2 years rural medical service.
- Medical Officers and health workers working in district and tehsil hospitals will be given hands-on training in anesthesia and obstetric to

address the acute shortage to trained staff in these priority areas. This measure will improve the availability and quantity of emergency services in hospitals.

- Mega-hospitals under autonomy arrangements will be institutionalized. Their Chief Executives will be appointed on prescribed criteria through a transparent selection process. Administrative and financial powers will be properly notified. Autonomy will be linked to revenue generation through rational user-charges and quality service delivery criteria. A system of monitoring the performance of autonomy-based mega-hospitals will be established.
- Private practice specialists will be replaced by the system of Institutional Practice in mega-hospitals. Rules will be framed for this purpose by the respective governments.

Key Area No.4: To promote greater gender equity in the health sector

Implementation Modalities:

- Focused reproductive health services to child-bearing women through a life cycle approach will be provided at their doorsteps. This will ensure provision of Safe Motherhood facilities to the majority of mothers, thereby enhancing child survival rated.
- Access to primary health services will be provided to the majority of women by expanding the Lady Health Workers Programme at the grassroots level. A cadre of 100,000 community-based trained lady health workers will provide basic services to the family at the household level.
- Emergency Obstetric Care facilities will be provided through the establishment of "Women-Friendly-Hospitals" in 20 Districts of Pakistan under Women Health Project.
- A referral system between the village level and the Health Care facilities up to District Hospital level will be established under the Women Health Project.
- More jobs opportunities will be provided to women as LHWs under the above programme. Additional enrolment of Midwifery Schools and Public Health Schools.
- All vacancies in Government Sector of WMOs, Nurses, LHVs and Women cadres will be filled up on priority basis.

Targets and Time Frame

- By 2005, 100,000 Family Health Workers will be duly trained as community workers and deployed in the field.
- The number of nurses will increase from 23,000 to 35,000 by 2005 and 55,000 by 2010.

Key Area No. 5: To bridge the Basis Nutrition Gaps in the target-population i.e. children, women and vulnerable population groups.

Implementation Modalities

- Vitamin-A Supplementation will be provided annually to all under-5 children (about 30 million) along with OPV on National Immunization Days through EPI network.
- Provision of iodized salt will be ensured along with introduction of fortified flour and vegetable oil by addition of micronutrients like Iron and Vitamin-A.
- Nutrition Project through PSDP will ensure a food fortification programme in coordination with local food industry.
- Provision of Health Nutrition Package through 100,000 Family Health Workers which includes Vitamin-B Complex Syrup. Ferrous Fumerate and Folic Acid to deserving person, especially childbearing women and sick family members.
- Mass awareness/health education programmes will be run through multi-media.

Targets/Time Frame

1. Reduce Low Birth Weight babies from 25% to 15% by 2010.
2. Vitamin-A Supplementation to approximately 30 million children a year.

Key Area No.6: To correct urban bias in the health sector

Implementation Modalities:

- Every Medical College both in public and private sector will be required to adopt at least one district/tehsil hospital or primary health facility in addition to the Teaching Hospital affiliated to it. This will entail mandatory visits on rotation basis by faculty/medical students to spend more time in rural settings while helping to provide selective specialist cover to the beneficiary population. Detailed schemes on these lines will be chalked out by the Provincial Governments/Boards of management of medical colleges.
- The compulsory rural service of new medical graduates selected to fill up available vacancies in Government health institutes in rural areas will further contribute in promoting rural orientation.

Key Area No. 7: To introduce required

regulation in the private medical sector with a view to ensuring proper standards of equipment and services in hospitals, clinics and laboratories as well as private medical colleges and Tibb/ Homeopathic teaching institutions.

Implementation Modalities:

- Draft laws/regulations on accreditation of private hospitals, clinics and laboratories have been circulated to all Provincial Governments and stakeholders. These will be finalized and submitted to the Federal Cabinet.
- A law to ensure that private medical colleges adhere to PMDC approved standards before they start admitting students have been circulated as above. This will be submitted to the Federal Cabinet after processing.
- The existing law on Tibbs and Homeopathy will be amended to recognize degree and postgraduate level courses in Traditional Medicine thus removing the existence lacuna on this account. The amendments will be submitted to the Federal Cabinet.
- Each Provincial Government will develop an appropriate framework for encouraging private-public co-operation in the health sector, especially for operationalizing un-utilized or under-utilized health facilities through NGOs, individual entrepreneurs or doctors group.

Key Area.8: To create mass awareness in public health matters.

Implementation Strategy:

- Optimal use will be made of multimedia to disseminate health and nutrition education.
- TV/Radio Authorities will be asked to air programmes dedicated to health and nutrition, in close coordination with health and education Ministries, and institutions like National Institute of Health. Health Services Academy and National Programme Authorities of Anti-TB, Malaria and HIV-AIDS Control Projects.
- A Nutrition Cell will be established in the Ministry of Health through the Nutrition Project with required nutrition experts and mass communication specialists.
- Appropriate interpersonal skills training will be imparted to Family Health Workers as well under the Family Planning and Primary Health Care training programme.
- Greater participation of NGOs and civil society in Mass Awareness programmes.

Key Area No.9: To effect improvements in the Drug Sector with a view to ensuring the availability, affordability and quality of drugs in the country.

Implementation Modalities:

- Local manufacture of required drugs, both by multinational and national companies will be encouraged to engender maximum market competition.
- Imported drugs found to be in chronic short supply will be prioritized for local manufacturing.
- Balanced and fair pricing policies will be pursued to encourage investment in the pharmaceutical sector.
- The Drug Control Organization's capacity for market surveillance and quality control will be strengthened by posting additional staff and upgrading laboratories at Karachi and NIII Islamabad.
- While the availability of life-saving drugs will be specially monitored in the market, the provision of free life-saving drugs in the public sector hospitals will be limited to areas like emergency/casualty. The mustahikeen will however be eligible to free treatment including drugs through the Zakat system. The Family Health Workers' Health Package will also be available to the target population free of charge.

Key Area No.10: Capacity Building for Health Policy Monitoring in the Ministry of Health

Implementation:

- A Policy Analysis and Research Unit is proposed to be set up in the Ministry of Health. The Unit will also be responsible for monitoring the progress of Health Policy implementation in the key areas for submission to the Chief Executive/Federal Cabinet periodically. The unit will also provide technical facilities to Provincial Governments on need basis.

Conclusion

This study has looked at health policy issue as vital element that impacts on the determinants of population health. It explored the socio-economic and health status indices in Pakistan and identified poverty, illiteracy and unemployment as social determinants of health of the population. It also found that inequality and inequity are inextricably linked to poor life expectancy at birth. It finally emphasized on the importance of health literacy and culturally appropriate policy development that involves full community mobilization and participation as key to achieving successful population health outcome.

References

Center for disease control. CDC(2015). Learn about health literacy. Retrieved from http:// www.cdc.gov/ healthliteracy/learn/index.html.

Fortier, J. (2008).Tohono O'odham Community Action (TOCA)—Cultural renewal to improve health. Retrieved from http://www.unnaturalcauses.org/video_clips_detail.php?res_id=46

Herbes-Sommers, C. & Smith, L.M. (2008).Health in America. Laureate Education. Retrieved from www.unnaturalcauses.org

Lee, K., Buse, K. &Fustukian, S. (Eds.). (2002). Health policy in a globalising world. Cambridge, United

World Health Organization.(2015). Social determinants of Health. Retrieved from www.who. int/ social_determinants/en/

World Health Organization.(2015). Glossary of terms used. Retrieved from www.who.int/ hia/about/ glos/en.

PATIENT PERCEPTION REGARDING THE SATISFACTION OF HEALTH CARE SERVICES PROVIDED AT BASIC HEALTH UNITS OF DISTRICT ATTOCK, PUNJAB, PAKISTAN

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Abstract

The perception level of the community regarding provided health care services must be assessed to enhance the effectiveness of the participation of basic health units in health system.

Objectives: To assess patient perception regarding the satisfaction of health care services provided at basic health units.

Method: A cross sectional study was conducted at the basic health units of Kot Fateh Khan, Qutbal, Kunyal, Dhurnal, District Attock, Punjab, with a sample size of 368 adults. Study duration was 4 months from May 2017 to August 2017. Data was collected with pre- tested questionnaire and analyzed by SPSS 20. Percentages for variables were collected and result was calculated by WHO provided Overall Care Index.

Results: The study revealed that 87.58% of the patients were satisfied with the general experience and the behavior of the health-care provider and 85.9% were satisfied with the treatment and care provided, only 50.5% were satisfied with the physical environment of the facility. However, the percentage of patients who would recommend the facility to their friends and other family members was overwhelming (98.6%).

Conclusions: The results show that primary health-care facilities are still the first choice for any form of medical care. However, there is definitely a gap between the increasing expectations of the patients for more information, better patient–provider interaction, more control over the treatment process and better amenities even at the primary care level, which needs to be fulfilled to facilitate better utilization of primary health-care services in the community and reduce pressure on tertiary care services in order to ensure effective health coverage. This study also showed that there is a need to improve the physical environment of the basic health facilities covering better accommodation, wards, waiting area and accessibility from the main road.

Key words: basic health units, primary health care, patient perceptions

Health care system is one of the most important systems operating in the country. Worldwide, the health care system consists of primary, secondary and tertiary health care systems. According to WHO "primary health care is the essential health care made universally accessible to individuals and families in the community by means accessible to them through their full participation and at a cost that the community and country can afford"[1]. The primary health system covers two types of facilities consisting of outreach health services and facility based curative health care. Outreach health services include various immunization and disease control programs. The facility based primary health system consist of basic health units, rural health centers, mother and child health centers and rural dispensaries.[2] Each union council has one basic health unit which covers a population of 5000-10000 persons and an area of 24-40km radius.[3] Total number of basic health units in Punjab is 2461.[4] A basic health unit consists of outreach staff that includes communicable disease control supervisor, sanitary inspector, EPI vacci-nator and lady health worker, and the stationed staff that includes 1 medical officer, 1 dispenser, trained birth assistants, male and female health technician, peon and sweeper. A lady health worker covers about 200-250 houses and provides the antenatal care at the door step, sanitary inspector works for the inspection of vendors and shops in his area, EPI vaccinator provides vaccination according to the EPI schedule and communicable disease control super-visor takes cares of the fogging and spraying of

insecticide and clearing of the stagnant pools. Building of the basic health unit consists of one room each for medical officer, lady health visitor, sanitary inspector, dispensary, antenatal examination, storage and a 2-bed ward. The principal of operation of basic health units is health promotion through education on nutrition, sanitation and maternal health, prevention though immunization and chemo-prophylaxis schedules, treatment of various ailments, minor surgical procedures, obstetric care and referral.

Patient satisfaction is a key marker for the quality of health care delivery at the basic heath units and an important indicator for evaluation and improvement of health care services.[5] Studies of patient satisfaction in health care evaluation first originated in the USA during the 1950s. The earliest studies attempted to identify characteristics such as age, gender, and race of the patient to predict satisfaction levels.[6] Another study analyzed health-care attributes such as nursing care, physician care, etc. to identify factors that influence the overall patient satisfaction.[7] The importance of including the perspective of the patient in the evaluation of health care programs is now widely recognized.[8] Patient-based assessments of medical care are being used to measure the quality of health care.[9] Patient satisfaction with the health care system is an important dimension of evaluation that is examined only rarely specially in developing countries.[10]

The importance of our study is to find out all the short comings regarding the delivery of health care services to all the patients visiting health care centers. After identification of these lapses in the primary health care delivery system, it may be informed to higher authorities so that these problems should be addressed as soon as possible for the reduction in morbidity and mortality due to various common conditions that remain untreated due to ineffective communication and utility of resources and to strengthen the belief of common people on the primary health care system provided at their door step.

Objectives

To assess patient perception regarding the satisfaction of health care services provided at basic health units of District Attock, Punjab, Pakistan.

Operational Definitions

Health: According to WHO, health is a state of complete physical, mental and social well being and not mere an absence of disease or infirmity.
Health Education: It is a type of teaching process of society to promote the understanding of how to maintain personal health.
Health Care System: It is the organization of people, institutions and resources that deliver health care services to meet the health needs of target population. It consists of primary, secondary and tertiary components in the form of basic health units, rural health centers, tehsil headquarters, district headquarters and teaching hospitals.
Basic Health Units: It is a component of primary health care system that delivers health education, promotion, prophylaxis and treatment facilities at the door step of the common people by means accessible and cost effective to them.
Patient Satisfaction: is a measure of the extent to which a patient is content with the health care which they received from their health care provider. In evaluations of health care quality, patient satisfaction is a performance indicator measured in a self-report study and a specific type of customer satisfaction metric.

Methods

A Cross-Sectional Study was carried out over a period of 4 months from 1st May 2017 to 31st August 2017 at all the basic health units in areas of the union councils of Kunyal, Qutbal, Kot Fateh Khan, Dhurnal, District Attock, Punjab. About368 samples were collected using Simple Random technique.
Inclusion Criteria: All adult male and female patients visiting basic health unit of the mentioned areas.
Exclusion Criteria: Patients other than adulthood age, all patients from other than nominated areas and non-cooperative patients were excluded.

Data Collection Procedure

Data was collected by researchers with the help of pretested questionnaire (data collection tool)after informed consent has been taken. We tested our questionnaire on 20 patients to correct our question and answer language. When it was found perfect to collect the data then we used this questionnaire for collection of our data. Questionnaire included questions regarding biodata of the patient, patient perception of the environment of the facility, behavior of staff, time to wait for meeting the doctor, accessibility of the facility, health counselling including various preventive methods, proper information of the ailment, discussion of various treatment options, consideration of the patient choice of treatment, availability of medicine and vaccines, family planning methods and referral system. The questionnaires were handed over to the

health technician at the facility. He guided every patient visiting the facility to fill the performa based upon their own satisfaction and perception level while he helped in understanding the questions.

Data Analysis

Four options were given to the patient including excellent, very good, good and poor. Percentages of different variables were calculated for the different answers. Weighted score based on WHO provided Overall Care index was calculated for the total score of 100. Data was analyzed using SPSS 20 software. Percentages of the patients answering various questions were calculated. WHO provided overall care index was calculated. Descriptive statistical analysis of the data was done.

Results

Statistical Analysis:

Out of 368 questionnaires handed over, 350 were returned filled, with a response rate of 95%. Most of the respondents were in the age group 30-45 (83%). About 10%were in the age group of 50-60. Most of the patients (86%)were females who visited the facility and responded.

All the patients visiting the facility of age group 30-40 were either elementary or matric pass. Whereas younger patients were more educated, demanded more counseling and information regarding their treatment and were less satisfied than the elderly patients. However, these educated patients had more knowledge of their symptoms, described their condition more explicitly than elderly. Male patients were easier to guide regarding their ailment and treatment.

A majority of the patients rated the interpersonal skills of the doctor, including respect, courtesy, and empathy shown to the patients as excellent (54%) and 35% gave it a grading of very good. Most of the patients (98%) told that they didn't have to wait to meet the doctor. They were entertained as soon as they reached the facility. More male patients (60.71%) were inclined to give a rating of excellent to the aspect of time given by the doctor, while a lesser number of the female patients (59.09%) rated the time given by the doctor as excellent. A number of patients gave a rating of very good to this part of health care, giving a score of 91.36% by female patients, 90.36% by male patients with a combined score of 90.86% to this aspect of health-care services.

About 48%complained that the center is located far from the main locality of the residential area with difficult approach via public transport.

Majority of the patients (46%) came to the clinic on foot, with 18% and 17% coming by two-wheeler and auto-rickshaw, respectively. A large group of patients (60%) were dissatisfied with the sitting area as it was not properly aerated. All the patients were satisfied with availability of drinking water and sanitation at the center. About 70%told that they became to know about the facilities available at the center by the guidance of the lady health workers.

Specific Information:

All of the visiting patients already knew about the availability of TB prophylaxis medication, family planning medication, delivery facilities and referral services provided at the center. This information was mostly (98%) provided to them by the lady health workers. About 84.5% of the patients were satisfied with the treatment provided at the basic health center. Most of these patients were females i.e.71%. Regarding proper counselling and guidance about the disease and its different modes of treatments, 93%of the patients have reported to be properly provided with the required information. However, modes of treatment available, were limited at the level of basic health unit but about 48% patients reported that they were also referred to secondary and tertiary care centers for further workup. A large number of patients 80.4% responded that they were given a time of 8-10 minutes for the checkup. Due to lack of knowledge, most of the patients did not know about their disease and accepted the mode of treatment chosen by their physician for them. About 97% patient responded that they were provided all the prescribed medicine from the center. About 89%of patients were happy with the dealing of their physician.

Regarding improvements at the basic health level, 60% patients reported that the load of number of patients per doctor is the main factor behind the slight lack in doctor patient association. All of the patients were satisfied with the timings of the center. About 75%of the patients were satisfied with the behavior of staff. About 60%of patients actively asked questions regarding their illness and treatment. All of the patients coming at the facility further recommend their family and friends to visit the center for minor illnesses, counselling and guidance regarding referral and further workup. Total score calculated with WHO provided overall care index is 77.58.

Overall Care Index:

Weightage of all the values are given in percentage

Total Weighted Score: 100

Calculated Score: 77.582
Graphical Representation:

Discussion:

Our study showed that the overall satisfaction level of the patients with the working of the basic health units is 93% as compared to overall 72% determined in the study in India.[11] Reports from various researches have shown low quality of care at the primary health level.[12]

In our study about 89% and 75% patients are satisfied with the behavior of doctor and staff respectively compared to a majority of studies where a greater percentage of patients were dissatisfied. In a survey in Burkina Faso on perception of quality of Antenatal care the mean reception score was 14.7 (73.5% equivalent) (maximum achievable score =20).[13] In Calabar, Nigeria, it was found out that poor attitude of health staff was a major cause of dissatisfaction of the patients.[14] In this study 114 patients (81.4%) reported poor attitude of health staff as major area of dissatisfaction.

The primary health care system based on basic health units in Pakistan, has improved a big deal over past with the result that most of the visiting patients were completely satisfied with the treatment, medication and referral for workup provided at the facilities, as compared to other studies where doctor-patient relationships are a major factor for lack in effective working of centers. In a study, patients felt that more personal care will result in better communication and more patient involvement, patient satisfaction, hence better quality of care.[15] In the domain of communication, a study carried out in Ilorin revealed that 47.3% of outpatients were given adequate information on their ailments.[16] In the domain of respect for patients' opinion, a study in Mexico on patient satisfaction showed that the mean score of patients in allowing patients to give an opinion was 3.09+1.2 (maximum allowable score=5).[17] It was reported from a study in Scotland, that one of the major determinants of patient satisfaction was respect for patients' preferences.[18] Up to 80% of the patients complaint that the disciplinary bodies are a reason behind the breakdown of communication between patients and doctors. The main reason for the establishment of health institutions is the clients. Their experiences with the health system will determine their attitude toward health institutions, frequency of follow up, compliance with treatment and achievement of better treatment success.[19]

In our study most of the patients belong to the age group 30-40 and were not very educated. Whereas younger patients with relatively higher level of education, demanding more counseling and information, were less satisfied than the elderly patients as they were more knowledgeable of their symptoms. In a study in Zambia on examining patients' perception of care, it was revealed that older patients tended to be more satisfied than younger patients.[20] In a related study on patient satisfaction with primary health care services in the United Arab

GENERAL PATIENT EXPERIENCE 15%	TREATMENT AND RELATED INFORMATION 40%	RESPONSE OF PARAMEDICAL STAFF 15%	PHYSICAL ENVIRONMENT 15%	OVERALL EXPERIENCE 15%
Treated with respect and skill 90.8%	Explanation of treatment and medication 93%	Behavior and dealing of staff 75%	Waiting area 40%	Overall response 93%
Waiting time 98%	Explanation for need of tests 70%		Drinking water 90%	
Accessibility 83%	Asked questions 60%		Ease of Transportation 52%	
Availability of doctor 95%				
91%	74.33%	75%	60%	93%

Weighted scores of all parameters

CRITERIA	GENERAL EXPERIENCE	TREATMENT AND INFORMATION	PHSICAL ENVIRONMENT	RESPONSE OF STAFF	OVERALL EXPERIENCE
Score %	91%	74.33%	60%	75%	93%
Weighted score	13.65	29.732	9	11.25	13.95

Emirates age was statistically significant for the domains of comprehensiveness. Older people felt that the clinic service was more comprehensive than younger people.[21] A positive association was found
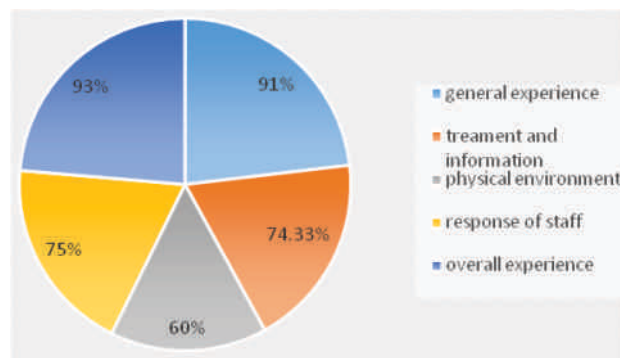
between age and satisfaction so that individuals aged > 70years were more likely to be satisfied with the health system than individuals' 18-29years.[22] In the same study educational status was statistically significant for the domain of effectiveness. People with higher levels of education felt that the clinic service was less effective than those who were less educated.

However, there is still need to improve the physical environment of the centers as 60% of patients have dissatisfaction regarding it as compared to other countries mentioned in the study where patients are well satisfied with the physical environment. Total score calculated with WHO provided overall care index is 77.58.

This study has certain limitation including, use of standardized questionnaires for evaluation of patient satisfaction may limit the patient's opportunity to express concerns about different aspects of care. Patients may have a complex set of important beliefs that cannot be expressed in terms of simple satisfaction. Another limitation was introduced by the fact that the survey was carried out by the health-care provider, leading to bias on the part of the patients. It is important, therefore, that any patient satisfaction surveys to be carried out must be by an obviously uninvolved, uninterested third party to yield a more accurate picture of patient expectations, experiences and levels of satisfaction with the health-care facility. Studies performed in primary care settings are not able to ensure precise randomization of the patient sample, as visits to the physician did not follow principles that could be planned or predicted. For this reason, all patients coming to the practice were requested to take a survey questionnaire, accepting their choice to come for a visit and take the survey as part of the selection procedure. There are no standardized treatment protocols for

general use for most diseases and symptom complexes, leading to improper and inaccurate assessment of competence of the providers.

Since primary health care centers (basic health units) are usually the first point of contact for a vast majority of people, further studies need to be carried out to understand the lacunae and drawbacks in the quality and what needs to be done to ensure universal and equitable health care.

Conclusion

The results show that primary health-care facilities are still the first choice for any form of medical care. However, there is definitely a gap between the increasing expectations of the patients for more information, better patient–provider interaction, more control over the treatment process and better amenities even at the primary care level, which needs to be fulfilled to facilitate better utilization of primary health care services in the community and reduce pressure on tertiary care services in order to ensure effective health coverage. This study also showed that there is a need to improve the physical environment of the basic health facilities covering better accommodation, wards, waiting area and accessibility from the main road.

Implications: The survey reflects the patients' opinions and not the actual performance of the physician. It gives us vital information regarding the acceptability and appropriateness of the health care services being provided at the health care center. Further patient behavior, such as compliance with the prescribed treatment, follow-up visits, etc. depend on the patients' perceptions and experiences at the clinic and therefore, from the perspective of future results, their opinions and satisfaction levels with the health-care providers are an important indicator of the final outcome.

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NIL
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NIL

References

1. Declaration of Alma Ata. International Conference on Primary Health Care, Alma Ata, USSR. 1978
2. Afzal S. Concepts in Community Medicine. 1st Edition. Lahore: Zubair Book Depot; 2014:18-20
3. Alam NM. Community Medicine. 6th Edition. Faisalabad: Study Aid foundation; 2012:180
4. Available from: www.pshealth.punjab.gov.pk
5. Patro BK, Kumar R, Goswami A, Nongkynrih B, Pandav CS UG Study Group. Community perception and client satisfaction about the primary health care services in an urban resettlement colony of New

Delhi. Indian J Community Med. 2008; 33:250–4. [PMC free article] [PubMed]

6. Bertakis KD, Roter D, Putnam SM. The relationship of physician medical interview style to patient satisfaction. J Fam Pract. 1991 Feb;32:81-2. [PubMed]

7. Bertakis KD, Roter D, Putnam SM. The relationship of physician medical interview style to patient satisfaction. J Fam Pract. 1991 Feb; 32:175–81. [PubMed]

8. Hekkink, C., Sixma HJ et all. An instrument for assessing quality of hiv care from the patients' perspective. Quality Safety Health Care Journal.2003; 12:188-193.

9. Ajayi I, Olumide E, Oyediran O. Patient satisfaction with the services provided at a general outpatient department clinic, university college hospital Ibadan. Africa Journal of Medical Science.2009; 34: 133-140.

10. Ariba A, ThanniL, Adebayo O. Patient perception of quality emergency care in a nigerian teaching hospital: The influence of patient-provider interactions. Nigeria Postgraduate Medical Journal.2007; 14(4): 296-301.

11. Ardey R, Ardey R. Patient Perceptions and Expectations from Primary Health-care Providers in India. Journal of Family Medicine and Primary Care. 2015;4(1):53-63.

12. Coulter A, Cleary P. Continuity of care: Patient experience with hospital care in countries. Health Affairs.2000; 20: 204-252.

13. Kameli Y, Nikiema L, Capon G, Sondo B et al. Quality of antenatal care and obstetric coverage in rural burkina faso. J Health Popul Nutr.2010; 28(1): 67-75.

14. Oyo-ita A, Etuk SJ, I. BM. Patients' perception of obstetric practice in Calabar, Nigeria. Nigeria Journal of Clinical Practice.2010; 10(3): 224-228.

15. Yuchi T, Guannming C. Patient satisfaction with and recommendation of a primary care provider: Association of perceived quality and patient education. International Journal for Quality in Health Care. 2009;21(3): 206-213.

16. Akande, T., 2002. Patients' perception on communication between patients and doctors in a teaching hospital. Sahel Medical Journal, 5(4): 178-181.

17. Doubova, S., Peres-Cuevas R, Zepeda-Arias M and F.-H. S., 2009. Satisfaction of patient suffering from type 2 diabetes and/or hypertensive with care offered in family medicine clinics in Mexico. Salud Publica Mex, 51(3).

18. Jenkinson et al. Patient's experience and satisfaction with health care. Journal of Asian Scientific Research. 2013; 3(7):775-785

19. Olumide A. Quality of management in healthcare: Fundamentals of health service management for doctors and senior health workers in Africa. Kemta Publishers.1997; 94: 94-100.

20. Faxelid, E., B. Ahlber, M. Maimbolwa and K. I., 1997. Quality of sexually transmitted diseases' care in an urban Zambian setting: The providers' perspective. Intl Journal of Nursing Studies, 34(5): 353-357.

21. Margolis S, Almarzouqi S, R. T. Patient satisfaction with primary care services in the United Arab Emirates. International Journal for Quality in Health care.2003;15(3): 241-249

22. Bluementhal D. The origins of the quality-of-care debate. New England Journal of Medicine.1996; 335(15): 1146-1149.

ASSOCIATION OF RAISED MATERNAL SERUM COPEPTIN LEVELS WITH INTRAUTERINE GROWTH RESTRICTION

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Abstract

Background: In obstetrical world, intrauterine growth restriction (IUGR) occupies second slot as a cause of small for gestation neonates, first being premature birth, both of which result in potential neonatal morbidities and mortalities. IUGR is defined as an estimated fetal weight at one point in time at or below 10th percentile for gestational age. Annually about thirty million babies suffer from IUGR and out of these about 75% are Asians. IUGR has been found to be associated with increased levels of Copeptin. As copeptin is a marker of endogenous stress, so increased copeptin levels can indicate fetal and maternal stress in IUGR.

Objectives: The objectives of this study were to compare maternal serum copeptin levels in pregnancies with IUGR and pregnancies with adequate for gestational age fetuses and to establish association between copeptin and IUGR.

Method: This was a cross-sectional comparative study in which maternal serum copeptin levels were measured and compared in 60 patients divided in two groups, pregnancies with IUGR and normal pregnancies with adequate for gestation age fetuses between 28-35 weeks of gestation.

Results: Maternal serum copeptin levels were raised in pregnant women with IUGR as compared to that in pregnant women with adequate for gestational age fetuses. Mean ± SD maternal serum copeptin levels were 97.5 ± 6 pg/ml in pregnant women with AGA fetuses and 121 ± 7.8 pg/ml in pregnant women with IUGR.

Conclusion: Raised maternal serum copeptin levels are associated with IUGR.

Key words: copeptin, intrauterine growth restriction

In human life cycle, intrauterine period of growth is most important period which has direct influence on birth weight.[1] Ironically it was misunderstood that the only reason of low birth weight was preterm birth, ignoring the concept of intrauterine growth restriction (IUGR). On the basis of data of epidemiological studies, World Health Organization (WHO) in 1961 cleared the misconception that "low birth weight (LBW) is synonym for preterm". Later the gap was filled by the introduction of a more self explanatory term "intrauterine growth restriction".[2] About 23.8% of the newborns suffer from IUGR. Annually approximately thirty million babies get affected by IUGR and out of them about 75% are Asians. Unfortunately in Pakistan there is 10-25% incidence of IUGR which is not a healthy sign.[3] According to American guidelines "An estimated fetal weight (EFW) at one point in time at or below 10th percentile for gestational age is labeled as IUGR." It is a pathological variant of SGA.[4] In clinical setting, estimated fetal weight at or below 10th percentile is used as a cutoff point to label intrauterine growth restriction but if date of last menstrual period is uncertain then follow up is recommended.[5] American college of gynecology

(ACOG) and Royal college of obstetrics and gynecology (RCOG) has approved the limit of 10th percentile as cutoff value to mark IUGR but certain other parameters are not yet cleared e.g. the role of amniotic fluid in IUGR is still debatable between these two societies. According to the society of obstetricians and gynecologists of Canada, EFW of less than 10th percentile (according to the gestational age) is diagnostic figure for declaring IUGR. In a study it was pointed out that about 30 % of fetus with EFW less than 10 percentile are IUGR while other falls in category of constitutionally small fetus. Hence umbilical artery Doppler scan helps in establishing an exact and accurate diagnosis of IUGR by differentiating intrauterine growth restriction from constitutionally small fetus and normal pregnancy.[6] The ultrasound biometry is 86.44% sensitive,82.92% specific with a diagnostic accuracy of 85%. The umbilical artery Doppler scan systolic velocity / diastolic velocity ratio has a diagnostic accuracy of 75%.[7]

Holwerda was the first scientist who described copeptin in 1972.[8] Copeptin (CT-AVP) is also known as COOH–terminal pro arginine vaso-pressin,[9] carboxy terminal glycoprotein of provas-sopressin

and arginine associated glycoprotein. Copeptin is regarded as a neuroendocrine hormone of hypothalamic hypophysial axis.[10] Arginine vasopressin and copeptin are co synthesized in equimolar quantities in hypothalamic supraoptic and paraventicular nuclei and then released in blood from neurohypophysis.[11] It is encoded by the same gene that encodes arginine vasopressin. It is located on 20th chromosome position 13 in tandem fashion and reverse order with oxytocin gene. It is synthesized as preprohormone (168 amino acids) which is broken down by a series of reactions mediated by endopeptideases, mononoxygenases and lyases respectively into prohormone.[12] Copeptin is referred as surrogate marker for AVP. Despite of being secreted in equimolar quantities and same response to fluctuations in plasma osmolarity, it is cumbersome to measure AVP as compared to copeptin.[13]

The exact physiological function of copeptin is not yet defined.[14,15] Unlike cortisol copeptin levels stay higher even in cases of prolonged chronic stress. Copeptin is considered to be preferable marker for detection for stress as it is independent from hypothalamic-pituitary-adrenal axis. Further circadian rhythm does not influence copeptin in contrast to cortisol.[16]

Stressful conditions in body stimulate various hormonal, autonomic and behavioral responses which are helpful in short term and long term adaptation to stress. In this regard hormones of HPA axis especially AVP and CRH are of vital importance.[17] The potential mechanism of association between IUGR and copeptin is still debatable. However importance of copeptin as a potential biomarker of stress is established. Copeptin is considered to be associated with stressful conditions like placental ischemia and cardiovascular stress.[18] Elevated cord copeptin levels depict fetal stress like asphyxia and decreased perfusion of placenta. IUGR has been found to be associated with increased levels of copeptin in a recently published study. Activation of HPA axis by psychological stress has been suggested as one of the potential cause of association between copeptin and IUGR.[19] It is observed that in conditions of perinatal stress e.g. IUGR the vasopressincopeptin system of neonates as well as mother gets stimulated. In a recent research study it was pointed out that uterine artery indices and maternal copeptin are inversely proportional to each other depicting effect of copeptin on function of endothelial cells.[16] One possible mechanism of association of copeptin and IUGR is that in IUGR already placental vessels are compromised because of chronic hypoxia complicated with placental insufficiency.[20] In humans, perinatal asphyxia and stress promotes secretion of AVP.[21] AVP causes vasoconstriction of placental vessels decreasing the ability of uterine arteries to keep up with the increasing demand of blood as well as nutrients for the developing fetus. AVP plays a significant role in immune dysfunction, endothelial dysfunction, angiogenesis and oxidative stress. AVP promotes expression of vascular endothelial growth factor (VEGF) on smooth muscles of blood vessels. AVP and VEGF tends to increase resistance of blood vessels and leads to fetal asphyxia, a significant cause of IUGR.[22] This chronic hypoxia results in failure of fetus to grow up to his genetically determined growth potential. Hence resulting in intrauterine growth restriction.[21] Raised copeptin levels are associated with low birth weight, decreased head circumference, low APGAR score, less gestational age and decreased fetal growth. This inverse relation supports the association between copeptin and IUGR.[23]

Method

It was an observational cross sectional, comparative study conducted in the Department of Physiology, Shaikh Zayed Postgraduate Medical Institute, Lahore and Obstetrics and Gynecology department, Shaikh Zayed hospital, Lahore after taking permission from the respective head of departments. The study duration was one year.

A study population of 60 pregnant women was selected according to inclusion and exclusion criteria, and was categorized into 2 groups, as follows:

Group A: 30 Pregnant women (between 28-35 weeks of gestation) with adequate for age uncomplicated normal pregnancy

Group B: 30 pregnant women (between 28-35 weeks of gestation) with intrauterine growth restricted pregnancy

Convenient (non probability) sampling was done.

The subjects selected were:

- Pregnant females between the ages of 20-40 years, with the evidence of intrauterine growth restricted fetus by ultrasound scan between 28-35 weeks of gestation.
- Pregnant females between the ages of 20-40 years, with the evidence of adequate for gestational age fetus by ultrasound scan between 28-35 weeks of gestation.

The pregnant women with following conditions

were excluded:

- Twin pregnancies or multifetal gestation
- Oligo/polyhydroamnios
- Chronic Hypertension
- Diabetes Mellitus

Pregnant women were selected from the outpatient department and obstetric ward of Shaikh

Table 1: *Showing comparison of Copeptin pg/dl level between both groups*

	Copeptin pg/dl			
	Mean ± SD	Minimum	Maximum	p- value
Group A	97.5 ± 6.0	87.9	110.2	< 0.001
Group B	121.4 ± 7.8	104.6	134.8	

Zayed medical complex fulfilling the inclusion criteria. After getting written informed consent, the demographic data of all the subjects was collected and every individual was assessed by taking history and using specially designed questionnaire. Blood sample was taken. Copeptin levels were estimated by using ELISA technique in Pathology Laboratory of Shaikh Zayed Medical Complex.

The data was entered into and analyzed by SPSS (Statistical Package for Social Sciences) version 17.0. Mann-Whitney U test were used to observe differences of medians in both groups. p value less than 0.05 was considered as statistically significant.
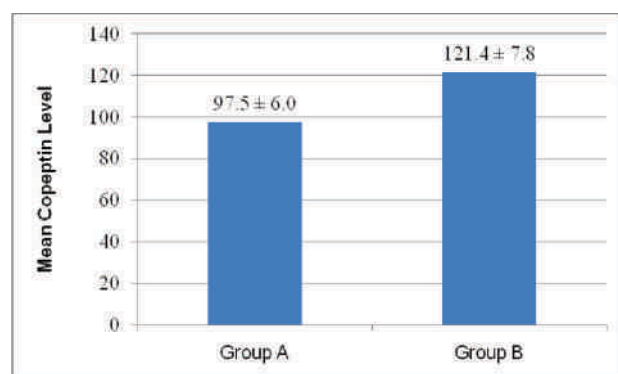
Results
Following results were obtained:
Figure 2: *Showing comparison of Copeptin (pg/dl) level between both groups*

Discussion
In this study, maternal serum copeptin levels were measured to be 97.5 ± 6 pg/ml in pregnant women with AGA fetuses and 121 ± 7.8 pg/ml in pregnant women with IUGR.

In a recent study Foda and Aal I pointed out that maternal serum copeptin levels were significantly raised in pregnant women with IUGR as compared to pregnant women with AGA fetuses, (115.76± 20.32 pg/ml vs. 98.6±10.19 pg/ml) (p<0.01)and raised maternal serum copeptin levels can be indicative of stress in intrauterine growth restriction. This study also reported significant raised maternal serum copeptin levels in group with IUGR as compared to group with constitutionally small fetuses (115.76±20.32 pg/ml vs.104.7±9.132 pg/ml) (p<0.05), hence predicting the importance of copeptin to differentiate IUGR from constitutionally small fetuses. However the difference between maternal serum copeptin levels in group with AGA fetuses and that with constitutionally small fetuses was not significant (98.64±10.19 pg/ml vs. 104.7±9.132 pg/ml) (p>0.904).[23]

In a research Burkhadrt et al. found out at mean gestational age of 34.3 weeks, significantly raised umbilical cord copeptin levels in pregnancies effected by IUGR as compared to normal pregnancies (6.7 – 449 pmol/L vs. 2.5 – 53 pmol/L) (p<0.01).[16]

In another study Bulbul et al. also suggested an increased maternal serum copeptin levels in pregnant women with IUGR as compared with pregnant women with AGA fetuses (0.36±0.18 ng/ml vs.0.26±0.17 ng/ml) (p=0.042).So our study supports the previous studies that maternal serum copeptin levels are raised in pregnant women with IUGR as compared to pregnant women with adequate for gestational age fetuses which can be helpful in detection of IUGR.[24]

However another study denies this increase in levels of maternal serum copeptin in IUGR. According to Hansen A, Sandager P, Uldbjerg N and Hvas A it was pointed out that copeptin levels does not show any differences in normal pregnancies with AGA fetuses and pregnancies with IUGR during 12-19 weeks of gestation. It was observed that in pregnant women with AGA fetuses, copeptin levels didn't show any significant change from 12-19 weeks of gestation (p=0.61).However in pregnant women with IUGR, Copeptin levels are observed to decline from first to second trimester (p=0.02). In pregnant women with AGA fetuses, at 12 weeks of gestation copeptin levels were 1.24 – 5.51 pmol/L with geometric mean of 2.62 pmol/L and at 19 weeks of gestation copeptin levels were 1.3 – 5.09 pmol/L with a geometric mean of 2.57 pmol/L (p=0.61). In pregnant women with IUGR, at 12 weeks of gestation geometric mean of copeptin levels was 2.95 pmol/L and at 19 weeks of gestation geometric mean of copeptin levels was 2.61 pmol/L.[18]

This difference can be justified by differences in gestational age of the intrauterine growth

restricted pregnancies. In this study the gestational age of group with IUGR was 12 weeks and 19 weeks as compared to 28-35 weeks in our study. Our study however showed an increase in maternal serum copeptin in pregnancies with IUGR. So our study supported the association of maternal serum copeptin with IUGR.

Conclusion

As very less studies are available on the topic of IUGR and copeptin in South Asian population, this study will be helpful to identify possible association between IUGR and copeptin in Asian population and also raised maternal serum copeptin levels in pregnant women with IUGR can represent as a possible clinical biomarker for identification of intrauterine growth restriction.

References

1. Melve K and Skjaerven R .Birth weight and perinatal mortality: paradoxes, social class and sibling dependencies. Int J Epidemiol.2003; 32:625-32

2. Wilcox AJ. On the importance and the unimportance of birth weight. Int J Epidemiol.2001; 30:1233-41

3. Muhammad T, Khattak A, Rehman S, Khan M, Khan A and Khan M. Maternal factors associated with intrauterine growth restriction. J Ayub Med Coll.2010;22:64-9

4. Smith-Bindman R, Chu PW, Ecker JL, Feldstein VA, Filly RA and Bacchetti P.US evaluation of fetal growth: Prediction of neonatal outcomes. RSNA. 2002; 223:101-8

5. Malhotra N, Puri R, Malhotra J, Malhotra N and Rao J. Maternal fetal workup and management in intrauterine growth restriction. DSJUOG. 2010;4: 427-32

6. Suhag A and Berghella V. Intrauterine growth restriction: etiology and diagnosis. Current gynecology and obstetrical reports, Springer journal. 2013;2:102-11

7. Majid A, Mehmood S and Akbar A. Role of ultrasonography in detection of intrauterine growth retardation. Biomedica.2014; 30:280-3

8. Gandhi PU and Januzzi JL. Can Copeptin emerge from the growing shadow of the troponins. Eur Heart J.2015; 36:333-6

9. Riphagen IJ, Boertien WE, Alkhalaf A, Kleefstra N, Gansevoort RT, Groenier KH, van Hateren KJ, Struck J, Navis G, Bilo HJ and Bakker SJ. Copeptin a surrogate marker for Arginine vasopressin is associated with cardiovascular and all cause mortality in patients with type 2 diabetes mellitus. Diabetes Care journal.2013; 36:3201-7

10. Kattan M, Muller B and Christ-Crain M. Copeptin a new and promising diagnostic and prognostic marker.Crit Care.2008; 12:117-23

11. Christ-Crain M and Fenske W. Copeptin in the diagnosis of vasopressin dependant disorders of fluid homeostasis .Nat Rev Endocrinol. 2016; 12:168-76

12. Elshafei A, Abdalla G, El-Motaal O and Salman T. Copeptin: A neuroendocrine biomarker in acute myocardial infarction. Annu Res Rev Biol.2013; 34:1040-54

13. Christ-Crain M, Morgenthaler NG, Struck J, Bergmann A and Mueller B. Copeptin a precursor of vasopressin in critically ill patients-an observational study. Endocrine abstracts.2006; 61:201-7

14. Dammann O, Leviton A, Gappa M and Dammann CE. Lung and brain damage in preterm newborns and their association with gestational age, prematurity subgroup, infection/inflammation and long term outcome. Beilstein J Org Chem.2005; 112:4-9

15. Burd I, Srinivas S ,Pare E, Dharan V and Wang E.Is sonographic assessment of weight influenced by formula selection. J Ultrasound Med, 2009;8:1019-24

16. Barkhardt T, Schwabe S, Morgenthaler N, Ntalucci G, Zimmermann R and Wellman S. Copeptin: a marker for stress reactions in fetuses with Intrauterine growth restriction. AJOG.2012:207; 497-502

17. Bolignano D, Cabassi A, Fiaccadori E, Ghigo E, Pasquali R, Peracino A, Peri A, Plebani M, Santoro A, Settanni F and Zoccali C. Coppetin (CT proAVP) a new tool for understanding the role of vasopressin in pathophysiology. ClinChem Lab Med. 2014; 52:1447-56

18. Hansen A, Sandager P, Uldbjerg N and Hvas A. Copeptin is not a useful biomarker for small for gestational age: a case control study. Scand J Clin Lab Invest.2014; 74:687-92

19. Wellmann S, Benzing J, Cippa G, Admaty D, Creutzfeldt R, Mieth R, Beinder E, Lapaire O, Morgenthelar NG, Haagen U, Szinnai G, Buhrer C and Bucher H.High copeptin concentration in umbilical cord after vaginal delivery and birth acidosis.J ClinEncrinol Metab.2010;11:5091-6

20. Hutter D, Kingdom J and Jaeggi E. Causes and mechanism of intrauterine hypoxia and its importance in fetal cardiovascular system: A review. Int J pediatr.2010

21. Santillan M, Santillan D, Scroggins J, Min J, Sandgren J, Pearson N, Leslie K, Hunter S, Zamba G, Corley K and Grobe J. Vassopressin in preeclampsia.Hypertension.2014;64:852-9

22. Akinlade K, Adediji I, Rahamon S, Fawole A and Tongo O. Serum copeptin and pregnancy outcome in preeclampsia. Niger Med J.2015; 56:362-8

23. Foda A and Aal I. Maternal serum copeptin as a marker for fetal growth restriction. Middle East FertilSoc J.2013; 18:159-64

24. Bulbul G, Kumru S, Erol O, Isenlik B, Ozdemir O, Caglar M, Yilmaz M, Kalayci M and Aydin S. Maternal and umbilical cord copeptin levels in pregnancies complicated by fetal growth restriction. J Matern Fetal Neonatal Med.2014; 39:121-12

BRONCHIAL BRUSHING: AN EFFECTIVE TOOL TO SUB CLASSIFY NON-SMALL CELL LUNG CARCINOMA INTO SQUAMOUS CELL CARCINOMA AND ADENOCARCINOMA

Sohail SK, Rizvi SF, Sameen S

Abstract

Lung cancer is the commonest cause of organ malignancy and leading cause of cancer deaths among Pakistani men. Due to nonspecific complaints patients usually present in late stages and diagnosis for these non resectable tumors mainly depends upon endoscopic biopsy and cytological specimen. Recently a lot of advancements have been made in identifying molecular differences of different types of lung carcinoma. Development of targeted therapies for Non-small cell lung carcinoma (NSCLC) has necessitated the need to accurately differentiate Squamous cell carcinoma (SQCC) from Adenocarcinoma (ADC). This Descriptive Cross-sectional survey was designed to find out the accuracy of bronchial brushing in diagnosing SQCC and ADC. Bronchial brushing has long been used as adjunct to bronchial biopsy for diagnosing malignant and non-malignant lesions of lung however the efficiency for subtyping NSCLC on these cytological specimens needs to be found. The study was conducted in pathology department of Allama Iqbal medical college, Lahore over a period of one year. 60 cases of NSCLC were included. Bronchial brushing and corresponding bronchial biopsies were collected, processed and microscopically examined to determine the subtype of carcinoma. Cases were diagnosed as Squamous cell carcinoma and Adenocarcinoma according to morphological features. Those cases with no well defined histological type were labelled as NSCLC-not otherwise specified. Bronchial brushings had a diagnostic accuracy of 86.67% for diagnosis of SQCC and 90.0% for that of ADC. Thus bronchial brushing is an effective tool for subtyping NSCLC and can provide an accurate, timely diagnosis, by relatively less invasive technique, to treating oncologist.

Lung cancer is the commonest cause of organ malignancy and its incidence and mortality has been ranked highest among all cancers in either gender worldwide.[1] According to a published report by World Health Organization (WHO), it is the most common malignancy and the leading cause of cancer deaths among Pakistani men.[2] More than 60% cases of Lung carcinoma present in late stages thus the diagnosis mainly depends upon cytological specimens and small biopsies obtained from these non resectable tumors.[3,4] Lung carcinoma is broadly divided into small cell lung carcinoma (SCLC) and non-small cell lung carcinoma (NSCLC). NSCLC accounts for more than 85% of all lung cancer cases[2,5] and includes Adenocarcinoma (ADC), Large-cell carcinoma, Sarcomatoid carcinoma and Squamous cell carcinoma (SQCC). Till lately differentiation of SCLC and NSCLC was considered adequate for categorizing patients for treatment purposes. But Several studies reported relapse in most patients who underwent surgery for NSCLC without further categorization into its subcategories.[3] In 2011, Travis et al proposed multi-disciplinary classification of Adenocarcinoma lung with special emphasis on need to further classify NSCLC into Adenocarcinoma and Squamous cell carcinoma with help of histochemical and/or immu-

nohistochemical stains.[6]

Considering the molecular differences and differential response to emerging targeted therapies it has now become necessary to accurately subtype NSCLC into ADC and SQCC.[5,6,7,8,9] This diagnosis needs to be provided on small biopsies and cytological specimens as they are mostly the only available specimens, disease being widespread at time of presentation.[3,6] The bronchial brushing along with bronchial biopsy has long being used for diagnosis of malignant and non-malignant lesions of lung. Bronchial brushing is an effective, quick, economical and less invasive diagnostic procedure as compared to biopsy.[10] The accuracy of bronchial brushing for diagnosing malignant cases is found to be 78.4% in a recent study.[11] However the value of bronchial brushing in subtyping NSCLC needs to be studied. This study was designed to find out the accuracy, sensitivity and specificity of bronchial brushing in diagnosing ADC and SQCC. Simultaneously taken bronchial biopsy was considered as gold standard for comparison. A timely and accurate diagnosis provided by bronchial brushing can prove to be very useful for our treating oncologists for decision making, stratifying the patients and improving treatment outcome.

Methods

This Descriptive Cross-sectional survey was conducted in Department of Pathology, Allama Iqbal Medical College Lahore in collaboration with Pulmonology department of Jinnah Hospital Lahore over a period of one year. After prior consent, clinical and radiological evaluation, 60 cases of NSCLC diagnosed on either bronchial biopsy or bronchial brushing, between ages 35 to 80 years were included in this study. Inadequate, Negative for malignancy and malignant cases other than Non-small cell lung carcinoma were excluded. The sample collected by bronchial brush was smeared on glass slides & fixed immediately in 95% propanolol and later stained with Papanicolaou stain. Bronchial biopsy specimens were collected by the flexible bronchoscope. The specimens were fixed with 10% formalin and processed in automated tissue processor. Slides were prepared and stained with haematoxylin & eosin stain. Bronchial brushing smears and bronchial biopsy were separately examined microscopically. Non-small cell lung carcinomas included in this study were sub classified on the basis of cytological or histological features into Squamous cell carcinoma (SQCC) (Fig 1)and Adenocarcinoma (ADC) (Fig 2). Tumors having no definite morphology were designated as Non-small cell lung carcinoma- not otherwise specified (NSCLC- NOS).

Results

Age of the patients in the present study ranged from 35 to 80 years. The mean age was 56.5 years ± 12.04SD. In this study population 50 (83.3%) were males and 10 (16.7%) were females with a male to female ratio of 5:1. In this study 39 (65.0%) cases were found to be smokers and 21 (35.0%) were non-smokers. In bronchial brushing diagnosis of SQCC, ADC and NSCLC-NOS was rendered in 37(61.7%), 19(31.6%) and 04(6.7%) cases respectively. In bronchial biopsies diagnosis of SQCC, ADC and NSCLC-NOS was rendered in 39 (65.0%), 13 (21.7%) and 08(13.3%) cases respectively.The numbers of observed agreements between bronchial biopsy and conventional bronchial brushing diagnosis were seen in 47 out of 60 cases amounting to 78.33%(Table 1). Thus SQCC was more frequent than ADC in this study.

In the present study the bronchial brushings had a sensitivity of 87.18%, specificity of 85.71% and diagnostic accuracy of 86.67% for diagnosis of SQCC (Table 2) and had a sensitivity of 100%, specificity of 87.29% and diagnostic accuracy of 90.0% for that of ADC (Table 3).

Photomicrographs

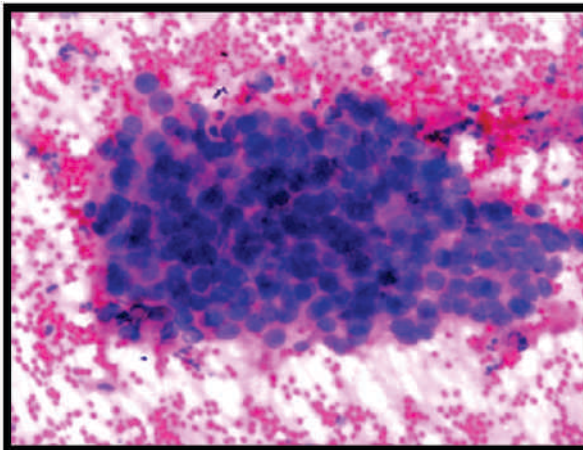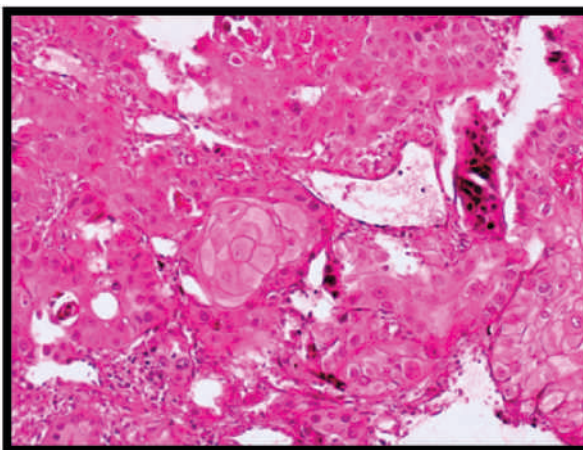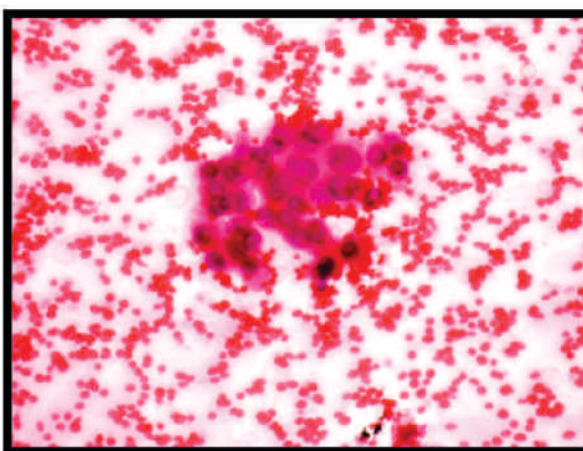**Fig 1:** *Squamous cell carcinoma on bronchial brushing and bronchial biopsy*

Fig 2: *Adenocarcinoma on bronchial brushing and bronchial biopsy*Squamous cell carcinoma –bronchial brushing (40x)

Adenocarcinoma –bronchial brushing (40x)
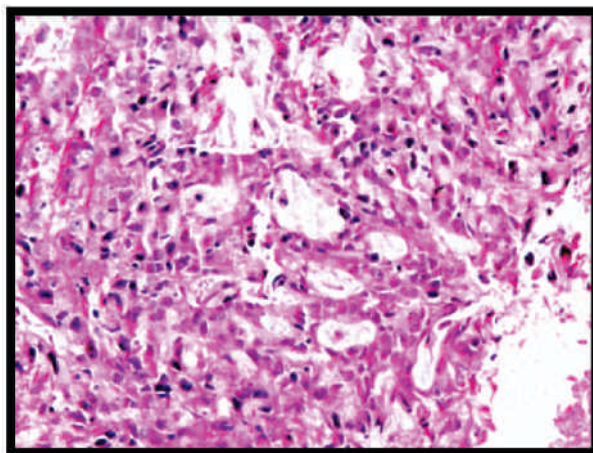
Moderately differentiated Adenocarcinoma – bronchial biopsy (20x)

Table 1: Sub Type of Nsclc Diagnosed By Bronchial Brushing And Bronchial Biopsy- Cross Tabulation

		Diagnosis on Bronchial brushing			Total
		SQCC	ADC	NOS	
Diagnosis on bronchial biopsy	SQCC	34	01	04	39
	ADC	00	13	00	13
	NOS	03	05	00	08
Total		37	19	04	**60**

Table 2: Squamous Cell Carcinoma Diagnosed By Bronchial Brushing And Bronchial Biopsy- Cross Tabulation

		DIAGNOSIS ON BRONCHIAL BIOPSY		
		SQCC	NON-SQCC	
DIAGNOSIS ON BRONCHIAL BRUSHING	SQCC	34	3	37
	NON-SQCC	5	18	23
		39	21	60

Sensitivity	87.18%	
Specificity	85.71%	
Positive predictive value	91.89%	95% CI 78.699 to 97.203%
Negative predictive value	78.26%	95% CI 58.096 to 90.336%
Accuracy	86.67%	

Well Differentiated Squamous cell carcinoma – bronchial biopsy (20x)

Discussion

Lung carcinoma is typically a disease of older individuals and rarely occurs below the age of 40 years. Age range of the patients in the present study was 35 to 80 years with a mean age of 56.5 ± 12.04 years which tallies with the range reported by most of the studies from Asian and European countries including those of Mahmood et al3 and Pancharia et al.[12]

In this study a predominance of lung carcinoma in male was seen. Out of 60cases, 50(83.3%) were male and 10 (16.7%) were females with the male to female ratio being 5:1. The result is in accordance with the gender ratio reported by Naseem et al.[2]

Cigarette smoking is a known etiological and risk factor for lung carcinoma. Smoking increases lung cancer by several folds. In this study 39 (65.0%) cases were found to be smokers and 21 (35.0%) were non-smokers. Out of all smokers 2 (5.1%) were females and 37 (94.8%) were males. Studies conducted by Naseem et al[2] and Hussain et al[13] on cohort of lung cancer patients presented in Gulab Devi hospital over a period of time reveal similar

Table 3: Adenocarcinoma Diagnosed By Bronchial Brushing And Bronchial Biopsy- Cross Tabulation

		DIAGNOSIS ON BRONCHIAL BIOPSY		
		ADC	NON-ADC	
DIAGNOSIS ON BRONCHIAL BRUSHING	ADC	13	06	19
	NON-ADC	00	41	41
		13	47	60

Sensitivity	100.0%	
Specificity	**87.29%**	
Positive predictive value	68.42%	95% CI 46.010 to 84.635%
Negative predictive value	100.0%	95% CI 91.433 to 100.00%
Accuracy	90.00%	

incidence of smoking.

Although in western population ADC has surpassed SQCC, it is still the most frequent histologic type of NSCLC encountered in our population. In our study SQCC was more frequent accounting for 39(65.0%) cases while ADC was diagnosed in 13(21.7%) cases. This finding is in concordance with the results of study conducted by Naseemet al.[2] Similarly studies conducted in a tertiary care

hospital of Nepal showed that SQCC was the most frequent histologic type of lung carcinoma.[10]

Sixty cases of non-small cell lung carcinoma included in this study were sub classified on the basis of cytological or histological diagnosis into Squamous cell carcinoma (SQCC) and Adenocarcinoma (ADC). On cytological examination of bronchial brushing SQCC and ADC accounted for 37(61.7%) and 19(31.6%) cases respectively. The cases without features for any specific histological type were classified as NSCLC-NOS that accounted for 04 (6.7%) of cases. On histological examination of bronchial biopsySQCC was diagnosed in 39(65.0%) cases while ADC was diagnosed in 13(21.7%) cases. NSCLC-NOS accounted for 08 (13.33%) cases.

Bronchial brushing and bronchial biopsies are usually simultaneously taken during the endoscopic procedure. A better detection rate of bronchial brushing is reported in studies done by Piyaet al[10] and Sigel et al.[14] This was attributed to larger area sampled by bronchial brushing and several technical difficulties during bronchial biopsy for example stenosis, bleeding and peripheral location of the tumor.[10] However studies done by Vyasiet al[11] and Gaber et al[15] have showed better detection rate for bronchial biopsy than brushing. Combination of both modalities gives highest detection rate and is recommended as adjunct to each other.[10,11,14]

In the concise review by IASLC/ATS/ERS, Travis et al stated that poorly differentiated tumors are diagnosed as NSCLC-NOS in 10 to 30% of small biopsies and/or cytology specimens.[6] Ou et al in their study reported NSCLC-NOS in more than 30% of histological and close to 40% of cytological specimens.[16] Our study the diagnosis of NSCLC-NOS was rendered in 13.33% of histological diagnosis and 6.67% of Cytological diagnosis. In addition to lack of characteristic morphologic features other factors like crush artifact, necrosis, and less than optimal tissue fixation also play a part in making distinction of PD-NSCLC very difficult.

The numbers of observed agreements between bronchial biopsy and conventional bronchial brushing diagnosis were seen in 47 out of 60 cases amounting to 78.33%.This result is in accordance with the moderate degree of agreement found in sub type of lung carcinoma by bronchial brushing and bronchial biopsy in studies done by Pancharia et al.[12] Similarly Kim et al. accurately sub typed NSCLC based on morphologic features of routine H&E smears in 78% of the cases.[17] In the present study the bronchial brushings had a sensitivity of 87.18% and specificity of 85.71% and diagnostic accuracy of 86.67% for SQCC and a sensitivity of 100% specificity of 87.29% and diagnostic accuracy of 90.0% for ADC. A recent study in India show that bronchial brushings has a sensitivity of 78%, specificity of 100% and diagnostic accuracy of 78.43% for malignant cases.[11] In another study conducted in Nepal the Sensitivity of the bronchial brushing was 94.6% for lung carcinoma.[10] Thus bronchial brushing proves to be an effective tool for subtyping NSCLC into SQCC and ADC.

Conclusion

This study shows a high sensitivity and specificity of bronchial brushing in subtyping non-small cell lung carcinoma. Thus bronchial brushing can provide an accurate, dependable and timely diagnosis to oncologist for stratifying the patients for proper treatment.

The diagnosis can later be refined by use of histochemical and immunohistochemical stains on either cytological specimens or biopsy samples.

References

1. American Cancer Society. Cancer Facts & Figures 2013. Available at: http://www.cancer.org/acs/groups/content/ @ epidemiologysurveilance/documents/document/acspc-036845.pdfLast cited: 24-08-2014.

2. NaseemN, Reyaz N, Nagi AH, Ashraf M, Sami W. Immunohistochemical Expression of Cytokeratin-19 in Non Small Cell Lung Carcinomas - An Experience from a Tertiary Care Hospital in Lahore. Int J Pathol 2010; 8(2):54 – 58.

3. Mahmood SR, Alam JM, Hussain A, Alam SM. Determination of Neuron Specific Enolase (NSE) in Small Cell Lung Carcinoma (SCLC) and Non-Small Cell Lung Carcinoma (NSCLC) patients. Pak J Pharma 2011; 28:23 – 32.

4. Rekhtman N, Brandt SM, Sigel CS, Friedlander MA, Riely GJ, Travis WD et al. Suitability of thoracic cytology for new therapeutic paradigms in non-small cell lung carcinoma: high accuracy of tumor subtyping and feasibility of EGFR and KRAS molecular testing.JThoracOncol. 2011;6:451–458.

5. Ettinger DS, Akerley W, Borghaei H, Chang AC, Cheney RT, Chirieac LR, et al. Non−Small Cell Lung Cancer. J NatlComprCancNetw 2012; 10(10): 1236 – 1271.

6. Travis WD, Brambilla E, Noguchi M, Nicholson AG, Geisinger KR, Yatabe Y et al.International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society International Multidisciplinary Classification of Lung Adenocarcinoma. J ThoracOncol 2011; 6(2): 244 – 285.

7. Ocque R, Tochigi N, Ohori NP, Dacic S. Usefulness of Immunohistochemical and Histochemical

Studies in the Classification of Lung Adenocarcinoma and Squamous Cell Carcinoma in Cytologic Specimens. Am J ClinPathol 2011; 136: 81 – 87.

8. Azzoli CG, Baker S,Temin S, Pao W. American Society of Clinical Oncology Clinical Practice Guideline Update on Chemotherapy for Stage IV Non–Small-Cell Lung Cancer. JCO 2009; 27:6251 – 6266.

9. Travis WD, Brambilla E, Noguchi M, Nicholson AG, Geisinger KR, Yatabe Y et al. Diagnosis of lung cancer in small biopsies and cytology: implications of the 2011 International Association for the Study of Lung Cancer/American Thoracic Society/ European Respiratory Society classification. Arch Pathol Lab Med. 2013; 137 : 668 – 684.

10. Piya E, Sayami G, Srivastava B. Correlation of bronchial brushing cytology with bronchial biopsy in diagnosis of lung cancer. Medical Journal of Shree Birendra Hospital 2011; 10: 4 – 7

11. Vyasi SP, Dhaka JP, Choudhary M, Sharma SP, Verma R. A Correlational Study of Bronchial Brushing With Bronchoscopic Biopsy in Diagnosis of Malignant Lung Neoplasms. IJSRM2017; 5: 5186 – 519.

12. Pancharia A, Yadav V, Taneja C, Chauhan S, Chauhan R, Gauttam V. A Study Of Correlation Of Bronchial Brushing Cytology With Bronchial Biopsy In Diagnosis Of Lung Cancer. J Pharm Biomed Sci 2014; 04: 492 – 496.

13. Hussain MR, Khan SA, Bukhari MH. Role of Smoking in Primary Pulmonary Malignancies in Central Punjab. ANNALS 2011; 17(1): 18 – 21.

14. Sigel CS, Moreira AL, Travis WD, Zakowski MF; Thornton RH, Riely GJ et al. Subtyping of non-small cell lung carcinoma: a comparison of small biopsy and cytology specimens. J ThoracOncol. 2011; 6:1849–1856.

15. Gaber KA, Goldman JM, Farrell J. Cytologic examination of whole endobronchial brush in bronchoscopic diagnosis of lung cancer. Respiratory Medicine 2002; 96: 259 – 261.

16. Ou, Sai-Hong Ignatius, and Jason A. Zell. Carcinoma NOS is a common histologic diagnosis and is increasing in proportion among non-small cell lung cancer histologies.J ThoracOncol. 2009: 4; 1202 – 1211.

17. Kim GY, Lim SJ, Kim WS, Lee GK. A Minimal Immunohistochemical Panel for Subtyping Poorly Differentiated Non-Small Cell Lung Carcinoma. A Tissue Microarray Study Simulating Small Biopsy Conditions. J Lung Cancer 2012; 11:21 – 32.

COMPARISON OF TREATMENT SUCCESS RATE BETWEEN BROMOCRIPTINE AND BROMOCRIPTINE PLUS CLOMIPHENE CITRATE IN CASES OF HYPERPROLACTINEMIC INFERTILITY PATIENTS

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Abstract

Objectives: To compare the treatment success rate between bromocriptine and bromocriptine plus clomiphene citrate in cases of hyperprolactinemic infertility patients.

Materials & Methods: Total 180 cases of hyperprolactinaemic infertility having age range from 20-40 years were selected from the Department of Obstetrics & Gynaecology, DHQ Hospital Sahiwal from January 2016 to December 2016. All the selected were randomly divided into two groups A and B. patients of group A were treated with bromocriptine and patients of group B were treated with bromocriptine plus clomiphene citrate. Final outcome was measured in terms that patient had reported back in OPD at monthly basis and pregnancy was confirmed by measuring serum β-HCG (≥5 mIU/ml of β-HCG was taken as occurrence of pregnancy and level <5 mIU/ml was taken as absent pregnancy) every month for total duration of one year after start of therapy

Results: Mean age of the patients was 29.68 ± 5.45 years, mean age of group A and B was 28.47 ± 3.22 years and 27.58 ± 4.52 years respectively. Comparison of treatment success rate between both groups was done. In study group A treatment success was noted in 56 (62.22%) patients. In study group B, treatment success was noted in 73 (81.11) patients. Statistically significant higher treatment success rate was noted in patients of study group B as compared to study group A with p value 0.0078.

Conclusion: Results of this study showed that bromocriptine plus clomiphene citrate is more effective than bromocriptine alone in the treatment of hyperprolactinaemic infertility. So, we recommend that these particular patients should be treated with bromocriptine plus clomiphene citrate instead of bromocriptine alone in order to achieve maximum number of pregnancies in hyperprolactinemic infertile women.

Keywords: pregnancy, prolactin, female infertility, bromocriptine, clomiphene citrate.

Introduction:

Prolactin (PRL) is one of several hormones that are produced by the pituitary gland. PRLhas many different roles throughout the body. Prolactin is a 198-amino acid protein (23-KD) produced in the lactotroph cells of the anterior pituitary gland. In individuals with pathological hyperprolactinaemia, glucose and fat homeostasis have been reported to be negatively influenced.1 Hyperprolactinemia causes infertility in up to one-third of women with reproductive disorders.2

Approximately 75% of patients presenting with g a l a c t o r r h e a a n d a m e n o r r h e a h a v e hyperprolactinaemia.3Prolactinomas are the most common type of functional pituitary tumours, with predictable incidence of 6–10 cases per million population per year and a prevalence of around 60–100 cases per million.1-2 According to previous reports, it accounts for 40–45% of pituitary

tumours.3,4 Its occurrence varies with age and gender, developing more commonly in females of age between 20–50 years with the female-to-male ratio of around 10:1.5

In woman hyperprolactinemia can be defined as the presence of abnormally high level of prolactin in the blood. Normal levels are typically 10–35 ng/ml and 1 ng is equivalent to 21.2 mU/ml.6

Majority of patients with prolactinomas, both micro- and macroprolactinomas, can be successfully treated with dopamine D2 receptor agonists as first-line treatment, with normalization of prolactin secretion and gonadal function.7The most commonly used dopamine agonists are bromocriptine, pergolide, quinagolide and cabergoline. When comparing the plasma half-life, efficacy and tolerability of these drugs are different, there is also important to evaluate the risk/ benefits profile of each product. Nowadays, clomiphene citrate is also used with the

bromocriptine in the treatment of hyperprolactinemic infertile women with menstrual irregularities and anovulatory cycles in order to achieve earliear pregnancies.8

This study was conducted to compare the treatment success rate between bromocriptine and bromocriptine plus clomiphene citrate in cases of hyperprolactinemic infertility patients so that some practical recommendations could be made to achieve maximum number of pregnancies in hyperprolactinemic infertile women with more efficacious treatment regime.

Material and Methods:

After approval from local ethical committee of this randomized controlled trial, total 180 cases of hyperprolactinaemic infertility having age range

Table 1: *Comparison of treatment success rate between the two groups*

| Study Group | Success Rate | | Total | P. Value |
	Yes (%)	No (%)		
A (bromocriptine group)	56 (62.22)	34 (37.78)	90	
B (bromocriptine plus clomiphene citrate group)	73 (81.11)	17 (18.89)	90	0.0078

from 20-40 years were selected from the Department

Table 2: *Comparison between Efficacy of both groups according to age.*

| Group | Treatment Success | | Total |
	Yes (%)	No (%)	
20-30 years (P=0.2263)			
A	40 (75.47%)	13 (24.53%)	53
B	48 (85.71%)	08 (14.29%)	56
31-40 years (P=0.0157)			
A	16 (43.24%)	21 (56.76%)	37
B	25 (73.53%)	9 (26.470%)	34

of Obstetrics & Gynaecology, DHQ Hospital Sahiwal fromJanuary 2016 to December 2016.Patients with other causes of infertility i.e. tubal factors, male factor and unexplained infertility, polycystic ovarian disease, macroadenoma of

Table 3: *Comparison between Efficacy of both groups according to duration of Infertility.*

| Group | Treatment Success | | Total |
	Yes (%)	No (%)	
1-5 years (P=0.0405)			
A	45 (77.59%)	13 (22.41%)	58
B	56 (91.8%)	05 (8.12%)	61
6-10 years (P=0.0746)			
A	11 (34.38%)	21 (56.76%)	32
B	17 (58.62%)	12 (41.38%)	29

pituitary gland, hyperthyroidism and h/o drugs like dopamine depleting, dopamine receptor blocking, H-2 blocker and verapamil intake were excluded. Written informed consent was taken from every patient.

Selected patients were randomly divided into two groups A & B.

A dose of 1.25 mg of bromocriptine was prescribed to patients of group A at bedtime with a snack and gradually increased to 2.5 mg two times a day with food over 3-4 weeks and this treatment was continued for 6 months. Occurrence of pregnancy was awaited for one year after start of therapy. While in Group B, all patients were treated with bromocrriptine with same dosage and methodology as was mentioned in group A. With the onset of menses, at day 2-6 of menstrual cycle, clomiphene citrate was started at initial daily dose of 50 mg two times a day for first two cycles, then 50 mg three times a day for third and fourth cycles and 100 mg two times a day for fifth and sixth cycles. Clomiphene citrate was stopped when ovulation was achieved which was confirmed by follicular tracking on trans-vaginal sonography at day 12 of each menstrual cycle. Occurrence of pregnancy was awaited for one year after start of therapy.

Final outcome was measured in terms that patient had reported back in OPD at monthly basis and pregnancy was confirmed by measuring serum β-HCG (≥ 5 mIU/ml of β-HCG was taken as occurrence of pregnancy and level <5 mIU/ml was taken as absent pregnancy) every month for total duration of one year after start of therapy. All the collected data alongwith demographic profile of the patients were entered in predesigned proforma.

All the data was entered and analyzed by using SPSS version 18. Mean and SD was calculated for age and duration of infertility. Efficacy of the treatment regimens in both groups was presented by frequency

and percentages. Efficacy of both treatment regimens was compared in two groups by chi square test. P value ≤0.05 was considered as statistically significant.

Results:

Total 180 patients of hyperprolactinaemic infertility having age range from 20-40 years were selected for this study. Mean age of the patients was 29.68 ± 5.45 years, mean age of group A and B was 28.47 ± 3.22 years and 27.58 ± 4.52 years respectively.

Patients of study group A were treated with bromocriptine alone and patients of study group B were treated with bromocriptine plus clomiphene citrate. Comparison of treatment success rate between both groups was done. In study group A treatment success was noted in 56 (62.22%) patients. In study group B, treatment success was noted in 73 (81.11) patients. Statistically significant higher treatment success rate was noted in patients of study group B as compared to study group A with p value 0.0078. (Table 1)

Patients of both groups were divided into two age groups i.e. age group 20-30 years and age group 31-40 years. In study group A, out of 90 patients of group A, 53 patients belonged to age group 20-30 years and 37 patients belonged to age group 31-40 years. In study group B, out of 90 patients 56 patients belonged to age group 20-30 years and 34 patients belonged to age group 31-40 years. In age group 20-30 years, treatment success was noted in 40 (75.47%) patients and 48 (85.71%) patients respectively in study group A and B. Difference of treatment success rate was statistically insignificant with p value 0.2263. In age group 31-40 years, treatment success was noted in 16 (43.24%) patients of group A and 25 (73.53%) patients of group B and the difference was statistically significant with p value 0.0157. (Table 2)

In this study, minimum duration of infertility was 1 year and maximum duration of infertility was 10 years. patients were divided into two groups according to duration of infertility i.e. 1-5 years and 6-10 years. Total 58 patients of study group A and 61 patients of study group B belonged to 1-5 years of infertility group. Treatment success rate was noted in 45 (77.59%) patients and 56 (91.8%) patients respectively group A and B. Difference of treatment rate between the both groups was statistically significant with p value 0.0405. In 6-10 years duration of infertility group, total 32 patients belonged to study group A 29 patients belonged to study group B. Treatment success was noted in 11 (34.38%) patients of group A and 17 (58.62%)

patients of group B. Difference of treatment success rate between both groups was statistically insignificant with p value 0.0746. (Table 3)

Discussion:

The purpose of this study was to compare the treatment success rate between bromocriptine and bromocriptine plus clomiphene citrate in cases of hyperprolactinemic infertility patients.

Mean age of the patients was 29.68 ± 5.45 years, mean age of group A and B was 28.47 ± 3.22 years and 27.58 ± 4.52 years respectively.

In one study by Motazedian S et al[9] mean age of the patients of hyperprolactinemic infertility was 28 years which is comparable with our study. Similar mean age (29 years) of patients with hyperprolactinemic infertility was reported by Al-Husaynei AJ et al[10] in their study.

In present study, mean duration of infertility was 5.69 ± 3.47 years which is higher than some previous studies.[11-12] The reason for this late presentation may be due to hakeem culture and lack of awareness in our society.

Patients of study group A were treated with bromocriptine alone and patients of study group B were treated with bromocriptine plus clomiphene citrate. Comparison of treatment success rate between both groups was done. In study group A treatment success was noted in 56 (62.22%) patients. In study group B, treatment success was noted in 73 (81.11) patients. Statistically significant higher treatment success rate was noted in patients of study group B as compared to study group A with p value 0.0078.

Mahmood S et al[13] in their randomized study has compared the two regime i.e. bromocriptine alone versus bromocriptine plus clomiphene citrate in treating hyperprolactinemic infertility and found the bromocriptine combined with clomiphene citrate superior as compared to bromocriptine alone. He has found the efficacy of bromocriptine as 65% and bromocriptine plus clomiphene citrate as 75% in occurrence of pregnancy in hyperprolactinemic infertile women. These results are very much comparable to our results. Tripathy et al[14] reported also reported treatment success of clomiphene with bromocriptine as 75.8% which is also comparable with our results.

In another study done by Anate M et al[15] also showed better efficacy of bromocriptine plus clomiphene citrate in achieving pregnancy compared to bromocriptine alone. On the whole it is concluded that bromocriptine is effective in the

treatment of hyperprilactinemic infertility. But bromocriptine plus clomiphene citrate has the advantage over bromocriptine alone in terms of both efficacy (achieving pregnancy) and tolerability.The efficacy of bromocriptine found in this study was 62.22% which is very much comparable with the studies of Sabuncu T et al16 and Webster J et17 al who had noted this as 59% and 58% respectively. But Motazedian S et al9 and Mahmood IH et al18 had found bromocriptine efficacy as 56% in their studies which is a little lower than our study.

Conclusion:

Results of this study showed that bromocriptine plus clomiphene citrate is more effective than bromocriptine alone in the treatment of hyperprolactinaemic infertility. So, we recommend that these particular patients should be treated with bromocriptine plus clomiphene citrate instead of bromocriptine alone in order to achieve maximum number of pregnancies in hyperprolactinemic infertile women.

References:

1. Nilsson LA, Roepstorff C, Kiens B. Prolactin suppresses malonyl-CoA concentration in human adipose tissue. Horm Metab Res. 2009;41:747-51.
2. Biller BM, Luciano A, Crosignani PG, Molitch M, Olive D,Rebar R, et al. Guidelines for the diagnosis and treatment of hyperprolactinemia. J Reprod Med. 1999;44:1075-84.
3. Melmed S, Casanueva FF, Hoffman AR. Diagnosis and treatment of hyperprolactinaemia: an endocrine society clinical practice guidline. J Clin Endocrinol Metab. 2011;96:273-88.
4. GGillam MP, Molitch ME, Lombardi G, Colao A. Advances in the treatment of prolactinaemia. Endocrine Rev. 2006;27:485-534.
5. Malik S, Hussain SZ, Basit R, Idress N, Habib A, Zaman M, et al. Demographic characteristics, presentations and treatment outcome of patients with prolactinoma. Journal of Ayub Medical College Abbottabad. 2014;26(3):269–274.
6. Crosignani PG. Management of hyperprolactinemic infertility. Middle East Fertility Society Journal. 2012 Jun 1;17(2):63–9.
7. Wang AT, Mullan RJ, Lane MA, Hazem A, Prasad C, Gathaiya NW, et al. Treatment of hyperprolactinemia: a systematic review and meta-analysis. Syst Rev. 2012 Jul 24;1:33.
8. Kaiser UB. Hyperprolactinemia and infertility: new insights. J Clin Invest. 2012 Oct 1;122(10):3467–8.
9. Motazedian S, Babakhani L, Fereshtehnejad SM, Mojtahedi K. A comparison of bromocrptine and cabergoline on fertility outcome of hyperprolactinemic infertile women undergoing intrauterine insemination. Ind J Med Res. 2010;131:670-4.
10. Al-Husaynei AJ, Mahmood IH, Al-Jubori ZS. Comparison of the effects of cabergoline and bromocriptine in women with hyperprolactinemic amenorrhea. Middle East Fer Soc J. 2008;13(1):33-8.
11. Ladipo OA. Experience with clomiphene and bromocryptine in the treatment of infertility. J Nat Med Assoc. 1980;72(4):339-42.
12. AbdElghani SEA, Elmugadam AA, Elsanousi MM. Hyperprolactinemia as a cause of female primary infertility and its prevalence in Gezira State, Central Sudan. Egypt Acad J Biol Sci. 2013;5(1):31-6.
13. Mahmood S. Hyperprolactinaemic infertility. Professional Med J. 2002;9:201-6.
14. Tripathy S, Mohapatra S, M M, Chandrasekhar A. Induction of Ovulation with Clomiphene Citrate Versus Clomiphene with Bromocriptine in PCOS Patients with Normal Prolactin: A Comparative Study. J Clin Diagn Res. 2013 Nov;7(11):2541–3.
15. Anate M, Olatinwo AW. Anovulatory infertility: a report of four cases and literature review. Niger J Med. 2001;10(2):85-90.
16. Sabuncu T, Arikan E, Tasan E, Hatemi H. Comparison of the effects of cabergoline and bromcriptine on prolactine levels in hyperprolactinemic patients. Intern Med. 2001;40:857-61.
17. Webster J, Piscitelli G, Polli A, Ferrari CI, Ismail I, Scanlon MF. A comparison of cabergoline and bromocriptine in the treatment of hyperprolactine-micamenorrhea. New Eng J Med. 1994;331:904-9.
18. Mahmood IH, Al-Husaynei AJ,Mohamad SH. Comparative effects of bromocriptine and cabergoline on serum prolactin levels, liver and kidney function tests inhyperprolactinemic women. Pak J Med Sci. 2010;26(2):255-60.

EVALUATION OF EFFECTS OF DRUGS ON PLASMA INSULIN LEVELS IN CHEMICALLY INDUCED DIABETES MELLITUS IN RATS

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Abstract

Objectives: This study is designed to analyze the effects of drug on beta cell function through their ability to change insulin secretion of pancreatic beta cells.

Study design: This Randomized control trial (RCT) was carried out for 6 weeks.

Materials & Methods: Forty Wistarrats were randomly allocated into four groups A,B,C & D. Group A rats were taken as control whereas type 2 diabetes mellitus (T2DM) was produced in group B, C and D rats by giving intraperitoneal injection of STZ i.e. 47mg/kg dose. After 48 hours of induction, the rats exhibiting FBS >200mg/dl were taken as diabetics. Group B rats were taken as negative control, group C diabetic rats were treated withGlibenclamide and group D rats withdiazoxide. This treatment protocol was given for six weeks.Functional capacity of the pancreatic beta cells was quantitatively measured by Enzyme Linked Immunosorbent Assay (ELISA). Fasting plasma insulin (FPI) levelswere measured on day 0, 14, 28 and 42 of the study.

Statistical Analysis: Mean+-S.D was used. ANOVA at different times was applied. P value of ≤ 0.05 was considered statistically significant.

Results: There was statistically insignificant difference found at day 0 & 14 of the study between four groups with P-value 0.558 & 0.079 respectively. Fasting plasma Insulin (FPI) levels in STZ-induced diabetic rats of group B and C were significantly low at day 28 and 42 of the study with p-value 0.007, 0.038 respectively as compared to that of control group A rats but there was insignificant difference found in FPI between group A & D with P-value 1.000.

Conclusion: There is a gradual reduction in FPI in group B rats over the course of 28 days which is of practical importance in showing that STZ-induced diabetic rats undergo progressive pancreatic beta cell failure as it occurs during the normal course of development of T2DM.Diazoxide has a protective effect on beta cell function.

Keywords: streprozotocin (STZ); fasting plasma insulin (FPI), type 2 diabetes mellitus (T2DM)

Introduction:

Diabetes mellitus is a syndrome of impaired carbohydrate, fat and protein metabolism caused by either relative or absolute deficiency of insulin secretion or decreased sensitivity of tissue to insulin. This chronic metabolic disorder is characterized by a high blood glucose concentration __ hyperglycemia (fasting blood glucose >7.0mmol/l, or plasma glucose >11.1mmol/l 2hrs after a meal) and glycosuria1. The Animal model of diabetes mellitus are used to understand the pathophysiology of diabetes and to evaluate the effect of drugs in these models to introduce new drug therapy to fight against this haunting disease. There are two main categories i.e. type 1 Diabetes mellitus and type 2 diabetes mellitus. Type 1 diabetes mellitus usually affects younger age group. It is characterized by absolute lack of insulin due to>90%autoimmune destruction of beta cells and it is achieved in rat and mice models by chemical destruction of beta cells e.g. with intraperitoneal or intravenous injection of streptozotocin and allaxon, by pancreatectomy and now genetically and virally induced models has also been introduced.

T2DM accounts for 90-95% cases of diabetes mellitus. It is characterized by hyperglycemia resulting from insulin resistance and progressive beta cell failure. T2DM is modelled in both obese and non-obese animal models with varying degrees of insulin resistance and beta cell failure e.g monogenic obese models as as a result of leptin receptor mutation Lepob/ob mice, Zucker fatty rats and Zucker diabetic fatty ratsi.e. ZDF Rats etc and Obese models (polygenic) NZO mice & High fat feeding (mice or rats). Non-obese models include GK rat & AKITA mice. These models are expensive and not freely available although represent major features of T2DM like obesity, insulin resistance,

beta cell failure2.

In the current research streptozotocin (STZ) is used to produce diabetes model in wistar rats. STZ Streptozotocin (Streptozocin, STZ, CAS No. 18883-66-4) is a monofunctionalnitrosourea derivative isolated from Streptomyces achromogenes. It has broad spectrum antibiotic activity and antineoplastic properties. It is often used to induce diabetes mellitus in experimental animals through its toxic effects on pancreatic β cells. STZ is a potent alkylating agent known to directly methylate DNA and is highly genotoxic, producing DNA strand breaks, alkali-labile sites, unscheduled DNA synthesis, DNA adducts, chromosomal aberrations, micronuclei, sister chromatid exchanges, and cell deat3. STZ is also a source of free radicals that can also contribute to DNA damage and subsequent cell death. It is used clinically to counter hypoglycemia in infants due to insulinomas. .After induction of diabetes, plasma insulin levels were checked in normal and STZ-induced diabetic rats to quantify beta cell failure3. Drugs which alter insulin secretion at beta cell level i.e. Glibenclamide&diazoxide, were also employed to demonstrate their effects on plasma insulin levels in STZ-induced diabetic rats4,5.

Material & Method

In this randomized control trial forty wistar rat were allocated into four groups A, B, C and D. Group A rats were taken as control whereas type 2 diabetes mellitus (T2DM) was produced in group B, C and D rats by giving intraperitoneal injection of STZ i.e. 47mg/kg dose6. After 48 hours of induction, the rats exhibiting FBS >200mg/dl were taken as diabetics. Group B rats were taken as negative control, group C diabetic rats were treated with Glibenclamide and group D rats with diazoxide. This treatment protocol was given for six weeks. Functional capacity of the pancreatic beta cells was quantitatively measured by Enzyme Linked Immunosorbent Assay (ELISA)7 Fasting plasma insulin (FPI) levels were measured on day 0, 14, 28 and 42 of the study. Rat blood samples were taken by cardiac puncture after putting rats for few seconds in the drop jar containing Ether. After centrifugation serum samples were stored in eppondrof tubes at -20 degree centigrade. At the end of the study all samples were brought to room temperature and 90 samples were on 90 well ELISA microplate kit. It took 3 hours for complete assay to

be done according to standard procedure prescribed

Table 1: *: Comparison of FPI in ng/dl among groups at day 0,14, 28,42 of the study by using ANOVA*

		Sum of Squares	Df	Mean Square	F	....
Pl ng/dl 0	Between Groups	11.750	4	2.937	.762	0.558
	Within Groups	115.681	30	3.856		
	Total	127.431	34			
Pl ng/dl 14	Between Groups	26.863	4	6.716	2.332	0.079
	Within Groups	86.400	30	2.880		
	Total	113.264	34			
Pl ng/dl 28	Between Groups	34.096	4	8.524	4.784	0.004
	Within Groups	53.449	30	1.782		
	Total	87.545	34			
Pl ng/dl 42	Between Groups	41.886	4	10.471	6.503	0.001
	Within Groups	48.304	30	1.610		
	Total	90.190	34			

Table 2: : : *Comparison of FPI in ng/dl at day 28,42 among various groups by using Bonferroni method*

(I) Group-A	(J) Group-A	Mean Difference (I-J)	Std. Error	P - value	95% Confudence Interval	
Positive Control	Negative Control	2.683729(*)	0.71	0.007	0.52206	4.84540
	Diabetic With Glibenclamide	2.237214(*)	0.71	0.038	0.07554	4.39889
	Diabetic With diazoxide	1.031300	0.71	1.000	1.13037	3.19297
Negative Control	Diabetic With Glibenclamide	-.446514	0.71	1.000	2.60819	1.71516
	Diabetic With diazoxide	-1.652429	0.71	0.276	3.81410	0.50924
Diabetic with Drug 1	Diabetic with Drug 2	-1.205914	0.71	1.000	3.36759	0.95576

by the kit manufacturer.

Statistical Analysis:
The data was entered and analyzed by using SPSS version. 15.0. Mean+-S.D was used. ANOVA at different times was applied. Post Hoc Bonferroni test was also used. P value of ≤ 0.05 was considered statistically significant.

Results

Discussion:
T2DM has constituted a global public health and economic burden due to its late stage macro and microvascular complications e.g. nephropathy, retinopathy neuropathy and cardiovascular events. Rat diabetes models are designed to elucidate the pathophysiology and to design pharmacotherapy.

In the current research STZ treated rats of group B, C , & D showed statistically insignificant difference of plasma insulin levels from at day 14 of the study with p-value 0.079as compared to that of control group A rats but this difference became statistically significant between group A and group B & C at day 28 with P-value value 0.007.It showed that following I.P. injection of STZ, beta cell function reduced gradually over a period of 28 days of the study. Although STZ is a DNA alkylating agent which is cytotoxic to beta but it didn't cause immediate, massive destruction in our study.

STZ has produced hyperglycemia after 48 hours of induction but plasma insulin levels reduce significantly over 28 days of the study7'8. It therefore favors that dose of STZ 47mg/kg which we

used for induction has produced beta cell failure gradually which resembles with the finding of UKPDS finding that suggested a progressive beta cell damage in the course of development of T2DM in humans.According to United Kingdom prospective Diabetes study (UKPDS) group, it has been found that by the time T2DM is diagnosed and clinically manifest, beta cell function declines upto 50% and beta cell mass reduces by 60% as shown by necropsy. This progressive decline continues to occur even in the presence of conventional therapies e.g. carbohydrate low diet, exercise, insulin secretagouge i.e. sulfonylurea & D-phenyl derivatives, insulin sensitizers i.ebiguanides& Thiazolidinediones9.

Group C rats were also treated with glibenclamide, an insulin secretagouge that enhance insulin secretion by the closure ATP-sensitive –K+ channel of beta cells. Initially there was insignificant difference of PFI level between group A and C at day 14 but it became statistically significant at day 24 of the study which may be due destruction of beta cell by STZ and also as result beta cell failure due to their overstimulation by glibenclamide.Excessive frequent food intake and prolonged use of insulin seretagouge may exhaust beta cells and put stress on endoplasmic reticulum and resultant rise in cytosolic Ca++ are read as apoptotic signal for beta cells and finally these cells reduce in function and mass10,11.

Group D exhibited insignificant difference ofFPI from group A with P-value 1.000.Diazoxide has shown protective effect on beta cells as FPI insulin didn't reduce significantly below that of normal rats. Diazoxide is a potassium channel opener which

inhibits insulin secretion and give rest to beta cell12,13.

Conclusion:

Streptozotocin produceddiabetes in wistar rats characterized by hyperglycemia and gradually reduce plasma insulin levels. This progressive decline in beta cell function is an important indication of T2DM model. Diazoxide has slows down beta cell failure in this model.

REFERENCES

1. A.C. Guyton, J.E. Hall. Insulin, Glucagon and Diabetes Mellitus. 13 Editions. ISBN Number: 9781455770052, 2016.
2. Aljendaro D Bolzan, Martha S Bianchi. Genotoxicity of Streptozotocin Elsevier 2002 Volume 512 (2-3):121–134
3. Bjorklund A, Bondo Hansen J, Falkmer S et.al. Openers of ATP-dependent K+-channels protect against a signal-transduction-linked and not freely reversible defect of insulin secretion in a rat islet transplantation model of type 2 diabetes. Diabetologia2004;(47):885–91.
4. Matsuda M, Kawasaki F, MikamiY,Takeuchi Y, Saito M, Eto M et.al. Rescue of ß exhaustion by diazoxide after the development of diabetes mellitus in rats with streptozotocin-induced diabetes. Eur J Pharmacol .2002;(453):14 1–8.
5. Low Dose Streptozotocin Induction Protocol. AMDCC(Animal Model Of Diabetic Complications Consorium) The Michigan MedicalCente, Frank Brosius.;(1): 1-4
6. PhikelelanSiphosethuNgubane, SilindileInnocentiaHadebe, Metse Regina Serumula et al .The effects of transdermal insulin treatment of streptozotocin-induced diabetic rats on kidney function and renal expression of glucose transporters. Informa Healthcare USA.2015;37(1): 151–159.
7. Sai Varsha MKN, Thiagarajan R, Manikandan et al Vitamin K1 alleviates streptozotocin-inducedtype 1 diabetes by mitigating free radical stress, as well asinhibiting NF-kB activation and iNOS expression in ratpancreas. Nutrition. 2015; 31: 214–222.
8. Effect of Streptozotocin on Plasma Insulin Levels of Rats and Mice: A Meta-analysis Study DOI: http://dx.doi.org/10.3889/oamjms.2015.093
9. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet. 1998; (352):837–53.
10. Tehseen Abaid, Najiba Qamar, Sajida Malik et al. Evaluation of pancreatic Islet beta cell loss in hyperglycemic rats after glibenclamide treatment. JAIMC 2014; (12):45-8
11. Maedler K, Carr RD, Bosco D. Sulfonylurea induced β-cell apoptosis in cultured human islets. J. Clin. Endocrinol. Metab. 2005;90(1):501–06
12. Quin Huang, Shizhong BU, Linhui Yang, Yongwei Yu, ZhiyongGuo, GautmanGhantnekar, et.al. Diazoxide prevents diabetes through inhibiting pancreatic B-cells from apoptosis via Bcl-2/Bax rate andP38- Mitogen activated protein kinase. The Endocrine Society 2007; 148: 181-91.
13. . Tehseen Abaid, Najiba Qamar, Rukhsana Sher et al. Role of diazoxide in the prevention of progressive B-cell failure in experimentally induced Type 2 diabetes mellitus in rats. JAIMC 2013; (2) 29-32

EXPERIENCE OF CONDUCTING GYNECOLOGICAL CAMPS IN OUT REACH NORTHERN AREAS OF PAKISTAN

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Abstract

In northern areas of Pakistan, health care provision is mainly by public sector but overall there is serious shortage of health care facilities and trained medical and paramedical staff in entire area. So in collaboration with an NGO, Jinnah hospital, Lahore started to provide medical and surgical services in this area i.e Skardu. Jinnah hospital has now been declared as sister organization.

The first gynecological camp was started in 2006 and services are being offered till now. Patients are seen not only on OPD basis but all types of major and minor gynecological surgeries are performed. However more complicated patients requiring intensive unit care postoperatively are referred to JHL. In addition to this diagnostic services are also offered like ultrasonography.

So far 11 gynecological camps have been conducted. Through this service almost 5212 patients are seen in OPD, treated and sent home. The most common health problems noted were uterovaginal prolapse, PID, infertility, genital tuberculosis and grand multiparity. Moreover 678 patients have undergone major and minor procedures. There have been no intra or post-operative complications in any patient. The patients referred to JHL were 710 in number.

Conclusion; It is desired that such services should be offered to other outreach areas to serve those who can not reach us and who remain subserved.

Key Words; gynae camps, out reach northern areas, Gilgit/ Baltistan Pakistan

S kardu is one of the five districts of Gilgit / Baltistan Province which is fifth province of Pakistan. It has a total population of 281, 899, while female population is 79,362.

Overall there is serious shortage of proper health care facilities in entire area. The health care provision is mainly by public sector health department of northern areas providing preventive, primitive, curative and rehabilitative work. Even mother and child care centers established under the world bank loan, mostly remain non-functional. The big issue is that due to gross shortage of skilled medical and paramedical personnel and due to financial constraints, majority of these areas are underutilized. The public health situation in skardu Baltistan is as follow ;

Total health care facilities – 353

- DHQs – 3 (1 in skardu)
- Civil Hospitals – 22 (4 in skardu)
- Rural health centers – 8 (1 in skardu)
- Basic health units – 16 (4 in skardu)
- MCH centers – 55 (30 in skardu)
- Dispensaries – 103 (40 in skardu)
- First Aid posts – 146 (26 in skardu)

The loopholes in existing system include Non availability of female gynecologist. So the female population has suffered the most. They are suffered otherwise also due to early marriages and hard domestic work. They have the grueling task of bringing fire, wood and water from far away, either up or down the mountain slopes. There would be no let up in their responsibilities in even advanced stages of pregnancy and illness. So the female population is in need of health care facilities in this

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area. Due to Financial constraints there is non availability of required equipments, Drugs, supplies, Vaccines and FP services. So is the absence of credible and quality diagnostic facilities. Health situation in skardu is comparatively worse due to varied topography and inaccessible location.

The situation of available female Gynae Medical staff is revealed by the table.

So the pathetic situation is quite clear that despite infrastructure, human resource availability is quite suboptimal. Despite an acute dearth of health facilities in Gilgit/ Baltistan, the government has not been able to bring any significant changes in this sector for a long period of time. So the investment by civil society organizations/ Donors tries to fill the gap. There are about 15 small local NGOs, engaged in the delivery of MCH services in the selected areas only.

Before medical camps, a large number of gynae patients from Baltistan visited Lahore for their treatment in our ward. Many patients are very poor and deserving, who can not afford the cost of travel and treatment outside skardu. Considering all this situation our mission was to provide updated health care facilities at the door step of this sub-served community. For achievement of this mission, Jinnah hospital Lahore has been declared as a sister organization.

Why camps are needed in remote areas

Provision of outreach services is more expensive and requires additional investment on the part of providers and health care system when compared to hospital based care. Time and cost to access health facilities often constitute a major obstacle to seek

Hospital	No of Gynecologists	No of Lady Doctors
DHQ- Skardu	2	3
DHQ- Khaplu	Nil	1
Civil Hospital Shiger	Nil	1
Civil Hospital Kharmang	Nil	Nil
Civil Hospital Rondu	Nil	Nil
Civil Hospital Gul Tari	Nil	Nil

care. So camps tackle with this issue. Patients can have access to care without spending time and money on a long journey to the health facility. Medical camps are, though temporary but effective means to meet some urgent health care demands of this area

How we established OBST/ GYN services at camps?

Keeping in view all these facts, we decided to establish gynecology camp in Baltistan. These camps have contributed tremendously in delivery of health care services for skardu population. Despite the lack of proper facilities, the camps are the success. These are conducted under supervision of senior consultants and with help of volunteer doctors and paramedical staff.

The First gynecology Camps started in 2006 and the services are being offered till date.

Usual time of camps is between June to August every year, rarely in May and September.

The camp is conducted for a period of 10-12 days. On arrival day, only OPD is conducted for whole day and the patients are screened for the need and complexity of surgery and anaesthesia fitness. The selected patients undergo surgeries on daily basis. The unfit and complicated patients are referred to tertiary care centers of Lahore and Islamabad.

Achievements

All major and minor surgeries were performed for which facilities were not available in Baltistan.

Common Diseases of Patients observed in OPD

Many chronic diseases were observed, which could be treated at initial stages thus improving the patients' health.
- Utero-vaginal prolapse
- Infertility
- Genital tuberculosis
- Menstrual disturbances
- Pelvic inflammatory Disease
- Acid peptic Disease
- Worm infestation
- Malnutrition

All above mentions health issues are addressed effectively and treated adequately in the camps. More complicated cases are referred to tertiary care facilities at Lahore and Islamabad.

Suggestions / Recommendations to enhance health services in Skardu
- Provide proper training to LHVs and Nurses and other paramedics.
- Updated training of Lady Doctors working in Skardu.
- Arrangement of lectures to Ladies for awareness of health issues.
- Community health education.

Future Health Plans;

A 500 bedded multidisciplinary Hospital is under construction nowadays by a Kuwait based NGO and planned to be completed by year 2018. It

will provide state of the art health care facilities to Skardu population.

Conclusion

The outreach programs and camps, not only improve access to health care, but can be a key in

Camp Work	Number
Gynae camps since 2006	11
Gynae surgeries done in medical camps	678
OPD patients in medical camps	5212
Patients referred to and treated at Jinnah Hospital, Lahore	710

Major Surgical Procedures

Procedure	Number
Abdominal Hysterectomy with and without BSO	60
Vaginal Hysterectomy	134
Laparotomy	23
Cesarean Section	9

Minor Surgical Procedures

Procedure	Number
BTL	402
Anterior-posterior vaginal repair	31
D&C/ E&C and other minor gynecological procedures	58

decreasing the sense of isolation felt by the population of this region.

Camp OPD

In wards

In operation theatre

Gynae Team

OPD in shiger valley

FETOMATERNAL OUTCOME FOLLOWING DIAGNOSIS OF OLIGOHYDRAMNIOS AT TERM

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Abstract

Objective: To correlate low aminotic fluid index with pregnancy outcome in terms of mode of delivery and perinatal morbidity and mortality.
Setting: Department of Obstetrics and Gynecology AIMCS Lahore.
Results: Three hundred women were examined in AIMCS after fulfilling the inclusion criteria. Induction of labour was done in 46.3% and emergency c/s was done in 61%. Low birthweight was found in 22% and 21% had low APGAR score (<7) at 5 min after delivery. Early neonatal death was seen in 12.3%.
Conclusion: There is increased rate of emergency cesarean section and poor perinatal outcome in patients having oligohydramnios at term.
Key words:- Oligohydramnios, amniotic flid index, APGAR score

Amniotic fluid provides the fetus a protective, low resistance environment suitable for growth and development.[1] The ultra sonographic assessment of decreased amniotic fluid volume has been recognized as a predictor of adverse perinatal outcome.[2] The incidence of isolated oligohydramnios has been reported as 24%. The presence of oligohydramnios (which is defined as an amniotic fluid index $\leq$ 5cm) has been associated with increased labour induction, emergency cesarean section,[3] admission to the neonatal intensive care nursery and neonatal death,[4] low APGAR score i.e. <7 at 5 min[5] and low birth weight at risk (i.e. <2.5kg). Labour induction increases the risk of cesarean delivery, particularly for the primiparous woman with an unripe cervix.[6]

Methods

This descriptive study was carried out in the department of Obstetrics and Gynaecology AIMCS Lahore. Three hundred women were admitted after fulfilling the inclusion criteria after taking written informed consent. Demographic data, age and gestational age was obtained. These women had been scanned and diagnosed as having oligo-hydramnios at term and were followed for maternal outcome i.e. induction of labour, emergency cesarean section and fetal outcome i.e. low APGAR score, low birth weight and early neonatal death.

Results

Total three hundred patients were included in the study and were evaluated for the impact of oligohydromnios on the maternal and perinatal outcomes. Most important parameter was booking status of the patients. Results showed that 74% unbooked when diagnosed and only 26% booked developed oligohydromnios at term. Induction of labour was done in 46.3% and emergency cesarean section was done in 61%.

Neonatal birth weight were found to be significantly less in 66 infants (22%) while 63 babies (21%) had low APGAR score (<7) at five minutes after delivery. Early neonatal deaths were found in 37 babies (12.3%)

Discussion

Oligohydramnios (AFI <5cm) has been found to be associated with poor perinatal outcome. Different studies both national and international have confirmed the adverse relationship of reduced AFV with poor fetal outcome. Concluding results of studies reveal poor fetal outcome associated with reduced amniotic fluid volume and to overcome them subsequent increased rates of induction of labour, with all its associated complications. The

adverse outcome of pregnancies complicated by oligohydromnios not only extend to the perinatal period but goes beyond as well. Zwerdling had observed that there is an increased risk of infant loss upto 2 years in the babies to the olighohydramnios.[13,14] In this study it was observed that those outcome between the mode of on set of labour, mode of delivery and neonatal outcomes was better in booked patients as compared to unbooked patients. Roberts showed odd's ratio 34.4 for induction comparable to 39% in this study.[7] 61% of the patients in this study underwent cesarean section. Similar high rates were found by Casey et al,[4] where C/S rate

Booking Status of Patients			
No complic-ations	72 (24%)	56 (18.6%)	128 (42.6%)

Table 1:

Booking status	No. Of patients	Percentage
Booked	78	26.0
Unbooked	222	74.0

Table 2: *Maternal outcome in relation to booking status*

Booking status	No. Of patients	
	Induced Labour	**Emergency Cesarean Section**
Booked	47(15.6%)	31(10.3%)
Unbooked	70(23.3%)	152 (50.6%)
Total	117 (39%)	183 (61%)

Table 3: *Fetal outcome in relation to booking status*

	Booked	Unbooked	Total
Low apgar score	16 (5.3%)	47 (15.6%)	63 (21%)
Low birth weight	16 (5.3%)	56 (18.6%)	72 (24%)
Early neonatal death	11 (3.6%)	26 (8.6%	37 (12.3%)
No complications	72 (24%)	56 (18.6%)	128 (42.6%)

was 51%. Sriya et al[8] had 43.05% rate of cesarean section. Chandra et al[9] had even higher rate of 76.92% cesarean section. It was observed that low APGAR score was related to the amount of liquor, lesser liquor volume associate with low APGAR score as compared to amniotic fluid index more than 5cm (21%) of the patient with low APGAR score in this study. These results are in accordance with studies of Casey et al4, has described APGAR Score <7 at 5 minutes in 23%. Casey et al4, Chandra Pet al9 and Sriya et al[8] have reported 35%, 61.53% and

58.38% low birth weight rates in their studies respectively, where as in our study low birth weight were 24%. The study results of Aneela Umber demonstrated that oligohydromnios was associated with increased chances of induction of labour (41%), cesarean delivery (32%), APGAR score <7 at 5 minutes (6%) and neonatal ICU admission (7%). Our study results are comparable to these results 12. In view of the poor fetal outcome in pregnancy complicated by oligohydraminios, the number of early neonatal death was (12.3%) and as compared to (5%) in other studies.

Conclusion

In this study there is increased rate of emergency Cesarean section and poor perinatal outcome in unbooked patients compared to booked one in patients having oligohydramnios at term

References

1. Taylor MJO, Fisk NM. Hydramnios and oligo-hydramnios. In: James DK, Weiner Cp, Steer Pj, Gonik B, editor. High risk pregnancy: management options. Philadephia: W.B. Saunders; 2006. 272-90.
2. Voxman EG, Trans S, Wing DA. Low amniotic fluid index as a predictor of adverse perinatal outcome. J Perinatol. 2002; 22:282-5.
3. Elsandabesee D, Majumdar S, Sinha S. Obstetricians' attitudes towards 'isolated' oligo-hydramnios at term. J Obstet Gynaecol. 2007; 27: 574-6.
4. Casey BM, Mclntire DD, Bloom SL, Lucas MJ, Santos R, Twickler DM, et al. Pregnancy outcomes after antepartum diagnosis of oligohydramnios at or beyond 34 weeks' gestation. Am J Obstet Gynecol. 2000; 182: 909-12.
5. Locatelli A, Vergani P, Toso L, Verderio M, Pezzullo JC, Ghidini A. Perinatal outcome associated with oligohydramnios in uncomplicated term pregnancies. Arch gynecol obstet. 2004; 269: 130-3.
6. Cunningham FG, editor. The morphological and functional development of the fetus. William's obstetrics. Stamford: Appleton and Lang; 1997. 151-97.
7. Roberts D, Nwosu EC, Walkinshaw SA. The fetal outcome in pregnancies with isolated reduced amniotic fluid volume in the third trimester. J Perinat Med 1998; 26: 390-5.
8. Sirya R, Singhai S. Perinatal outcome in patients with amniostic fluid index < 5cm. J Obstet Gynaecol India 2001; 51: 98-100.
9. Chandra P, Kaur SP, Hans DK, Kapila AK. The Impact of amniotic fluid volume assessed intrapar-tum on perinatal outcome. Obstet Gynae Today 2000; 5: 478-81.
10. Manning FA. Antipartum foetal survelliance current opinion: review paper. Obstet Gynaecol. 1995; 7:

146-9.

11. Rutherford SE, Jeffrey P, Phelan J, Smith CV, Jacobs N. The four quadrani assessment of amniotic fluid volume. An adjunct to antepartum fetal heart rate testing. Obstet Gynecol. 1987; 70: 353-5.

12. Umber A. Perinatal outcome in pregnancies compli-cated by isolated oligohydramnios at term. Annuals 2009; 15: 35-7.

13. Zweldling M. Factors pertaining to prolonged pregnancy and its outcome. Paediat 1967; 40: 202-9.

14. Hilder L, Casteloe K, Thilaganathan B. Prolonged pregnancy. Br J Obstet Gynaecol 1998; 105: 169-73.

FREQUENCY OF MRSA NASAL CARRIAGE IN HCWS OF A BURN CENTRE AND MINIMUM INHIBITORY CONCENTRATION VALUE OF VANCOMYCIN FOR THE ISOLATES

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Abstract

Objectives: To determine the nasal carriage rate of S. aureus and MRSA among Health Care Workers (HCWs) of a burn center and to see the minimum inhibitory concentration values of Vancomycin for the isolated MRSA.

Methods: A cross sectional study was conducted on 236 HCWs. Nasal swabs were collected during February - April 2017, and cultured on mannitol salt agar. The isolates were identified as S. aureus based on colony morphology, mannitol fermentation, Gram stain, catalase test and coagulase test. The resistance to methicillin was determined using Cefoxitin disk (30 µg) according to CLSI guidelines. The MICs value of Vancomycin for MRSA were detected using E-test strips as per manufacturer's instructions and interpreted according to CLSI guidelines.

Results: Out of the 236 healthcare workers, 53 (22.4%) carried S. aureus, of which 15 (28.3%) were MRSA. Therefore, 6% of all HCWs were identified as MRSA carriers. MRSA carriage rate was highest among doctors (15%), followed by janitorial staff (6%) whereas the carriage rate among nurses and paramedic staff was (3%) in each group. The MICs for vancomycin lie between 0.1 microgram to 1.5 microgram which all fall in the sensitive zone according to CLSI criteria.

Conclusion: The rate of nasal carriage of MRSA among healthcare workers of burn centre in this study is low. All the isolated MRSA are sensitive to vancomycin.

Keywords: MRSA, healthcare workers, nasal carriage, vancomycin MICs, E-test .

Burn patients are often more susceptible to infection due to the loss of skin, which is the basic protective barrier, and decreased cellular and humoral immunity[1]. Burn infection remains a major complication in burn patients after initial period of shock and the chance of infection persist until complete wound healing[2,3,4]. It is estimated that infection in burn patients is responsible for more than 70% of the mortality [5,6].

Methicillin-resistant Staphylococcus aureus continues to be an important nosocomial pathogen in burn units. The burns unit is a particularly fertile environment for MRSA because of open wounds, frequent dressing changes requiring handling by multiple health care workers (HCW), use of intra-luminal devices, and the inherent immuno-compro-mised state of burn patients[7]. Infections are often difficult to manage due to its resistance to multiple antibiotics[8]. Vancomycin has been the cornerstone of therapy for serious infections caused by this pathogen[9]. The reported resistance against vanco-mycin, one of the last resort drugs, is quite alarming [10,11].

Healthcare workers, colonized with MRSA, are important source of its nosocomial transmission[12,13]. Knowledge of prevalence of MRSA in the HCWs and its antimicrobial profile including vancomycin should be known for any institution. Screening for and eradication of MRSA from colonized HCWs have been recognized and recommended as an important part of a comprehensive infection control policy for this organism[14].

Methods

The present study was conducted on the health care workers from Jinnah Burn and Reconstructive Surgery Centre, Lahore after taking informed consent. The working category of the health care workers participating in the study was categorized as doctor, nurse, paramedic staff (operation theatre assistant, anesthesia assistant, dressor, ward boy, physiotherapist and dispenser) and janitorial staff (sweeper and aya). Nasal swabs were collected from the anterior nares of the HCWs using a moistened cotton swab and immediately transported to microbiology laboratory.

The specimens were inoculated on Mannitol

salt agar plates along with the positive and negative controls. All cultured plates were incubated at 35° C for 24 hours. Mannitol fermenting, yellow colored colonies were subjected to Gram staining. After finding Gram positive cocci in clusters, further biochemical tests like Catalase and Coagulase were performed for the confirmation of Staphylococcus aureus. The resistance to Methicillin was determined by disk diffusion method using 30 μg Cefoxitin disk (Oxoid Ltd) on Mueller Hinton agar plates. For each strain, a bacterial suspension adjusted to 0.5 McFarland turbidity standards was used. The plates were incubated for 24 hours at 35°C. Interpretation was done according to CLSI criteria. MRSA ATCC 33591 was used as positive control and MSSA ATCC 25923 was used as negative control.

All MRSA isolates were tested for minimum inhibitory concentration of vancomycin. MIC testing was performed using the E-test method, following manufacturer's guidelines. For each strain, a bacterial suspension adjusted to 0.5 McFarland turbidity standards was used. The plates were incubated for 16-18 hours at 37°C. The antibiotic E-test strips (Oxoid Ltd) were applied to the agar surface using an E-test applicator and were not moved following application. MIC values were read where the respective inhibition ellipses intersected the strip according to CLSI 2016. MRSA ATCC 33591 andMSSA ATCC 25923 were used as positive and negative control respectively. MIC testing of the organisms was performed over a period of 4 weeks in a single laboratory. All MICs were read by a single observer.

Results

Nasal samples were taken from 236 healthcare workers. Out of these, 53 (22.4%) carried S. aureus, of which 15 (28.3%) were identified as MRSA. Therefore, 6% of all HCWs were MRSA carriers. MRSA carriage rate was highest among doctors (15%), followed by janitorial staff (6%) whereas the carriage rate among nurses and paramedic staff was 3% in each group. Distribution of Staphylococcus aureus and MRSA in various working categories of HCWs is given in Table 1. Overall there was no significant difference in MRSA nasal carriage among male and female HCWs as shown in figure 1.

The MIC values of vancomycin for MRSA isolates lie between 0.1 microgram to 1.5 microgram which all fall in the sensitive zone as shown in figure2.
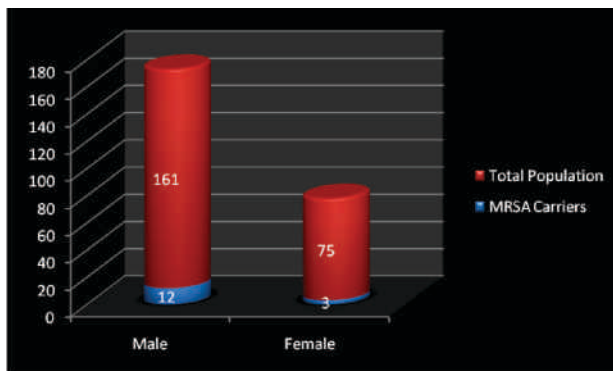
Figure 1: *MRSA distribution among male and female HCWs*
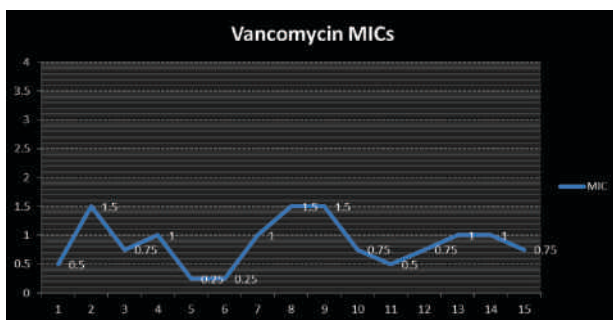
Figure 2: *Vancomycin MIC values for MRSA isolates*

Discussion

Detection of MRSA nasal carriage among HCWs in any hospital is necessary particularly for those working in the critical care areas and burn centres. These individuals can act as a potential

Table 1: *Distribution of S. aureus and MRSA carriage among different healthcare professionals*

Health workers	No. of samples	Staphylococcus aureus (%)	MRSA (%)
Doctors	53	19 (36)	8 (15)
Nurses	63	10 (16)	2 (3)
Paramedics	104	22 (21)	4 (3)
Janitorial staff	16	2 (13)	1 (6)

(P value > 0.05)

source of infection to their immunocompromised patients, resulting in increased morbidity and mortality and their extended stay in the hospital[15]. The survey for MRSA carriage among HCWs has mostly been conducted to investigate outbreaks or endemics but not in non-outbreak situations[16]. To our knowledge, it is the first study to be conducted to estimate the nasal carriage rate of MRSA in HCWs of a burn centre, in a non outbreak situation, in

Pakistan.

The nasal carriage rate of MRSA in our burn unit is quite low (6%) as compared to a study conducted at a burn unit of India by Aravind et al[7], which showed the carriage rate to be 50%.

Taking into consideration the general health-care facilities, the estimated prevalence of MRSA in our study was comparable to reported studies conducted in Nepal (3.4%)[17], Iran (5.3 %) [18], and Bangalore (8%) [19].

Differences in the prevalence of nasal carriage of MRSA strains between countries and hospitals may be explained in part by differences in the size of samples, the use of different microbiological methods (from sampling technique to culture media) and different interpretation guidelines. Moreover, different levels of commitment to infection control measures may contribute to these differences.

Vancomycin has been the main therapeutic agent for the treatment of MRSA infections but the high rate of use and exposure pressure of vanco-mycin have resulted in increasing levels of resis-tance strains i.e. heteroresistant vancomycin inter-mediate Staphylococcus aureus (hVISA), vancomy-cin intermediate Staphylococcus aureus (VISA) and vancomycin resistant Staphylococcus aureus (VRSA)[20]. If HCWs become colonized with such MRSA strains, and spread it, then the subsequent infection caused by such strain will be catastrophic for the patient. We checked the vancomycin MIC values for the MRSA isolated from HCWs in a burn unit to screen for any resistance to Vancomycin. All the isolates were sensitive to vancomycin with MICs ranging from 0.5 to 1.5 micrograms.

To our knowledge, it is the first study in Pakistan to estimate the MIC values of vancomycin for the nasally carried MRSA isolates.

References

1   Wong TH, Tan BJ, Ling ML, Song C. Multi-resistant Acinetobacterbaumannii on a burns unit – clinical riskfactors and prognosis. Burns. 2002; 28(4): 349-357.

2   Pallua N, Fuchs PC, Hafemann B, VolpelU, Noah M, Lutticken R. A new technique for quantitative bacterial assessment on burn wounds by modified dermabrasion. J Hosp Infect. 1999;42: 329-337.

3   Gang RK, Bang RL, Sanyal SC, MokaddasE, Lari AR. Pseudomonas aeruginosa septicaemia in burns. Burns. 1999; 25: 611-616.

4   Kaushik R, Kumar S, Sharma R, Lal P. Bacteriology of burn wounds, thefirst three years in a new burn unit at Medical College Chandigarh. Burns. 2003; 27(6): 595-597.

5   Singh NP, Goyal R, Manchanda V, Das .,Kaur I, Talwar V. Changing trends in bacteriology of burns in theburns unit, Delhi, India. Burns, 2003;29(2): 129-132.

6   Nasser S, Mabrouk A, Maher A. Colonization of burn wounds in AinShams University Burn Unit. Burns. 2003;29(3): 229-233.

7   Aravind P, Krishnan PU., Srinivasa H, Joseph, V. Screening of burns unit staff of a tertiary care hospital for methicillin-resistant Staphylococcus aureus colonisation. McGill Journal of Medicine. 2000; 5(2): 80-84.

8   Khanal R, Sah P, Lamichhane P, Lamsal A, Upadhaya S, Pahwa V K. Nasal carriage of methicillin resistant Staphylococcus aureus among health care workers at a tertiary care hospital in Western Nepal. Antimicrobial resistance and infec-tion control. 2015;4(1): 39.

9   Robert C,Moellering J.Vancomycin: A 50 Year Reassessment. Clin.Infect.Dis.2005; 42(1):S3-4.

10 Sakoulas G, GoldH S, Venkataraman L, DeGirolami PC, Eliopoulos GM Qian Q. Methicillin-resistant Staphylococcus aureus: comparison of suscepti-bility testing methods and analysis of mecA-positive susceptible strains. Journal of clinical microbiology. 2001; 39(11): 3946-3951.

11 Stevens DL. The role of vancomycin in the treatment paradigm. Clinical infectious diseases. 2003; 42(Supplement 1): S51-S57.

12 Shibabaw A, Abebe T, Mihret A. Nasal carriage rate of methicillin resistant Staphylococcus aureus among Dessie Referral Hospital health care workers; Dessie, Northeast Ethiopia. Antimicrobial resistance and infection control.2013; 2: 25.

13 Salgado CD, Farr BM, Calfee DP. Community-acquired methicillin-resistant Staphylococcus aureus: a meta-analysis of prevalence and risk factors. Clinical Infectious Diseases. 2003; 36(2): 131-139.

14 El Aila NA, Al Laham N A, Ayesh, B M. Nasal carriage of methicillin resistant Staphylococcus aureus among health care workers at Al Shifa hospital in Gaza Strip. BMC Infectious Diseases. 2017;17(1), 28.

15 Malini J, Shruti AH, Padmavathy M, Umapathy BL, Navaneeth BV, KeerthiMannan J, Girish MS. Methicillin-resistant Staphylococcus aureus-carriage among the health care workers in a tertiary care hospital. JCDR. 2012;6(5):791–3.

16 lbrich WC, Harbarth S. Health-care workers: source, vector, or victim of MRSA? Lancet Infect Dis. 2008;8:289–301.

17 Khanal R, Sah P, Lamichhane P, Lamsal A, Upadhaya S, Pahwa VK. Nasal carriage of methicillin resistant Staphylococcus aureus among health care workers at a tertiary care hospital in Western Nepal. Antimicrob Resist Infect Control. 2015;4:39.

18 Askarian M, Zeinalzadeh A, Japoni A, Alborzi A, Memish ZA. Prevalence of nasal carriage of

methicillin-resistant Staphylococcus aureus and its antibiotic susceptibility pattern in healthcare workers at Namazi Hospital, Shiraz, Iran. Int J Infect Dis. 2009;13:e241–247.

19 Malini J, Shruti AH, Padmavathy M, Umapathy BL, Navaneeth BV, KeerthiMannan J, Girish MS. Methicillin - resistant Staphylococcus aureus carriage among the health care workers in a tertiary care hospital. JCDR. 2012;6(5):791–3

20 Sharma P, Vishwanath G. Study of Vancomycin Susceptibility in methicillin resistant Staphylococcus aureus isolated from clinical specimens. Ann Trop Med Public Health. 2012; 5 (3): 178-180.

MAJOR RISK FOR CARDIOVASCULAR DISEASES - HYPERTENSION

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Abstract

Introduction:- Hypertension is major risk factor for cardiovascular diseases, being more common than cigarette smoking, dyslipidemia, and diabetes, the other major risk factors.

Purpose of study:- Assessment of the cardiovascular risks of hypertension.

Material and methods:- This prospective study was carried out in outdoor of AIMCS Lahore during the period from January 2015 to December 2015. A total of 100 individuals were included in the study who was attending outdoor of the hospital.

Results:- Current risk status of the 100 subjects who developed cardiovascular disease (myocardial infarction, angina, coronary bypass surgery, angioplasty, or stroke) during the study period was compared with healthy subjects, there were few differences. However, the results were different when the original risk status was used. Those patients who remained healthy had had significantly lower blood pressure (121/79 versus 134/83 mmHg) and plasma cholesterol levels (211 versus 226 mg/dL [5.45 versus 5.84 mmol/L]) 25 years before.

Conclusion:- Antihypertensive drugs should be instituted if, after several different blood pressure measurements, the average blood pressure is above 140/90.

Key words:- cardiovascular disease, dyslipidemia, antihypertensive drugs.

Hypertension is quantitatively the major risk factor for premature cardiovascular disease, being more common than cigarette smoking, dyslipidemia, and diabetes, the other major risk factors[1]. In the worldwide inter heart study of patients from 52 countries, hypertension accounted for 18 percent of the population attributable risk of a first MI[2].

Hypertension leads to left ventricular hypertrophy, and it increases the risk for a variety of cardiovascular diseases. These include stroke, coronary artery disease, heart failure, and peripheral vascular disease. Increased mortality is also observed with elevations in blood pressure. Coronary disease in men and stroke in women are the principal first cardiovascular events noted after hypertension onset, as observed from data from the Framingham Heart Study[3].

The risk for both coronary disease and stroke increases progressively with every increment in blood pressure above 110/75 mmHg. This has been demonstrated in epidemiologic studies in the general population[4,5,6,7,8] and in patients with known coronary disease[9]. However, these observations do not prove a causal relationship, since increasing blood pressure could be a marker for other risk factors such as increasing body weight, which is associated with dyslipidemia, glucose intolerance, and the metabolic syndrome. The best evidence for a causal role of increasing blood pressure in cardiovascular complications is an improvement in outcome with antihypertensive therapy.

The increase in cardiovascular risk has primarily been described in terms of systolic and diastolic hypertension. There is also evidence that the pulse pressure, which is the difference between the systolic and diastolic blood pressures and is determined primarily by large artery stiffness, is a predictor of risk.

Purpose Of Study
To assess the cardiovascular risks of hypertension.

Methods

This prospective study was carried out in outdoor of AIMCS Lahore during the period from January 2015 to December 2015. A total of 100 individuals were included in the study who was attending outdoor of the hospital.

Results

Current risk status of the 100 subjects who developed cardiovascular disease (myocardial infarction, angina, coronary bypass surgery, angioplasty, or stroke) during the study period was compared with healthy subjects, there were few differences. However, the results were different when the original risk status was used. Those patients who remained healthy had had significantly lower blood pressure (121/79 versus 134/83 mmHg) and plasma cholesterol levels (211 versus 226 mg/dL [5.45 versus 5.84 mmol/L]) 25 years before.

Discussion

A group from New Zealand has taken these risk factors into account in determining the overall risk status of individual patients, along with their level of blood pressure, age and gender[10]. They then examined the evidence of benefits of antihypertensive therapy from the clinical trials and considered the costs of such therapy, concluding that antihypertensive therapy can be justified only if the risk for a major cardiovascular event over the next 10 years was 20 percent or greater or if the level of blood pressure was so high as to mandate therapy regardless of overall risk status (170/100 mmHg). This approach requires that age, gender, and a number of cardiovascular risk factors be taken into account when considering when hypertension should be treated; the risk is lowest in younger patients, women, and those with no other risk factors[11].

Most physicians in the United States are probably unwilling to be as conservative as the New Zealand monogram recommends. They would almost certainly begin antihypertensive therapy in most patients with an overall 10-year risk of 10 percent or greater.

In addition to the specific patient population[12], another problem with the use of such data is that the risk status that is currently assessed may not reflect what was present previously. This is an important issue because it is the prior risk status that is more likely to be responsible for the current health of the individual. As an example, although blood pressure at the time of risk assessment (current blood pressure) is typically used in most prediction algorithms, this does not accurately reflect an individual's past blood pressure experience; the use of long-term average blood pressure is more accurate. This is supported by data from the Framingham Heart Study, which found that recent and remote antecedent blood pressure (systolic, diastolic, and pulse pressure) predicted cardiovascular risk incrementally over current blood pressure[13] This effect was seen in men and women, younger and older subjects, and lower and higher blood pressure groups. These data suggest that effective prevention of cardiovascular disease requires adequate blood pressure throughout life.

The potential magnitude of this problem has been documented in a follow-up of 1604 men whose risk status was first assessed when they were aged 45 to 64 and free of clinically obvious cardiovascular disease and then reassessed 25 years later when they were aged 70 to 90. Most patients changed their risk status over this time period, moving forward or backward.

Since midlife values are more likely to represent lifelong exposure values that, in turn, make the main contribution to the development of atherosclerosis, investigators and clinicians may need to be cautious in using risk factor values measured late in life as the only means of assessing risk for subsequent disease.

Conclusion

Antihypertensive drugs should be instituted if, after several different blood pressure measurements, the average blood pressure is above 140/90.

References

1. Wilson PW. Established risk factors and coronary artery disease: The Framingham Study. Am J Hypertens 1994; 7: 7S.
2. Yusuf S, Hawken S, Ounpuu S. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries - case-control study. Lancet 2004; 364: 937.
3. Lloyd-Jones DM, Leip EP, Larson MG. Novel approach to examining first cardiovascular events after hypertension onset. Hypertension 2005; 45: 39.
4. Lewington S, Clarke R, Qizilbash N. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002; 360: 1903.
5. Pastor-Barriuso R, Banegas JR, Damian J, Appel LJ. Systolic blood pressure, diastolic blood pressure, and pulse pressure: An evaluation of their joint effect on mortality. Ann Intern Med 2003; 139: 731.
6. Kannel WB. Blood pressure as a cardiovascular risk factor. JAMA 1996; 275: 1571.
7. MacMahon S, Peto R, Cutler J. Blood pressure,

stroke, and coronary heart disease. Part 1, Prolonged differences in blood pressure: Prospective observational studies corrected for the regression dilution bias. Lancet 1990; 335: 765.

8. Lloyd-Jones DM, Evans JC, Levy D. Hypertension in adults across the age spectrum: current outcomes and control in the community. JAMA 2005; 294: 466.

9. Sipahi I, Tuzcu EM, Schoenhagen P. Effects of normal, pre-hypertensive, and hypertensive blood pressure levels on progression of coronary atherosclerosis. J Am Coll Cardiol 2006; 48: 833.

10. Jackson R, Barham P, Bills J. Management of raised blood pressure in New Zealand: A discussion document. Br Med J 1993; 307: 107.

11. Jackson R, Lawes CM, Bennett DA. Treatment with drugs to lower blood pressure and blood cholesterol based on an individual's absolute cardiovascular risk. Lancet 2005; 365: 434.

12. Bastuji-Garin S, Deverly A, Moyse D, Castaigne A. The Framingham prediction rule is not valid in a European population of treated hypertensive patients. J Hypertens 2002; 20: 1973.

13. Vasan RS, Massaro JM, Wilson PW. Antecedent blood pressure and risk of cardiovascular disease: the Framingham heart study. Circulation 2002; 105: 48.

FREQUENCY OF GROUP B STREPTOCOCCUS CARRIAGE IN 500 PREGNANT WOMEN

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ABSTRACT

Objective: To find out vaginal colonization rate of group B streptococcus (GBS) in antenatal population of Lahore area.

Study design: Analytical cross sectional study.

Place and duration of study: This study was conducted at the Microbiology Department, University of Health Sciences, Lahore from Sep. 2007 to Sep. 2008.

Methodology: Lower vaginal swabs from 500 pregnant women at 35-37 weeks of gestational age were collected from 5 hospitals of Lahore. Detailed gynecological and obstetrical history were recorded. Amies transport swabs were inoculated on to the surface of Islam's agar and Blood agar plates and were incubated aerobically as well as anaerobically at 35°C for 72 hours. GBS was identified   by standard morphological, cultural, biochemical and serological techniques.

Results: Thirty one (6.2%) women were found to be positive for GBS. Statistical analyses showed no significant relationship between demographics, reproductive histories and obstetric characteristics of cases with the test results.

Conclusion: Maternal GBS colonization rate of 6.2 % in pregnant cases justifies for routine screening and treatment of theGBScarrying women.

Key words: GBS, lower vaginal swabs, Islam's agar.

Group B streptococcus (GBS) or Streptococcus agalactiae is normally found in vaginal and fecal flora of 10-30% of healthy adult women.[1-3] GBS infections occur as early onset disease of the neonate (day 0-7)or late onset disease (day 7-90).[4-6] It is estimated that 4 million deaths occur annually in developing world in neonatal period attributable mostly to infections, asphyxia and premature birth.[7] Asymptomatic colonization of the genital tract of pregnant women has most important role in transmission of GBS and several risk factors are connected to neonatal infections.[8]

Infants become colonized on the skin or mucous surfaces by vertical transmission from mother either in utero or during passage through the birth canal.[9,10] GBS can cause several disease states including pneumonia, sepsis and meningitis in infants.[6] Identification of GB Scolonized women is critical for prevention of neonatal GBS infection.

The prevalence of GBS in pregnant women varies from place to place, as reported by several researchers world over. Intra country differences occur and isolated studies fromIndia and Pakistan have reported GBS to be an important cause of Early onset group B streptococcal disease.[11,12]

In the last few years the importance of GBS as the cause of serious neonatal sepsis has become more evident. In western world, implementation of Center of Disease Control (CDC) guidelines reduced maternal carriage rate of GBS and thus minimized chances of neonatal infections but in developing countries the problem has not been adequately studied.[13,14] Currently GBS screening is not covered in our hospitals. The aim of our study is to determine vaginal colonization rate of GBS pregnant women between 35-37 weeks and provide baseline information of maternal GBS carriage rate in population of Lahore area.

Methodology

This Analytical cross sectional study was conducted at the Microbiology Department, University of Health Sciences, Lahorefrom Sep. 2007 to Sep. 2008 over a period of one year. Samples were collected from 4 tertiary care (Jinnah Hospital, Services Hospital, Lahore General Hospital and Fatima Memorial Hospital) and one private hospital (Family Health Hospital) of Lahore.

Pregnant women of 18-40 years at 35-37 weeks of gestation were included. Women with systemic illness like diabetes mellitus, asthma, hypertension, and obstetrical problems like placenta previa and polyhydroamnios were excluded from the study. Complete gynecological and obstetrical history was also recorded. A total of 500 lower vaginal swabs (Copan venture transystem swabs, Italy) were taken according to CDC guidelines. This was done by inserting the swab 2-3 cm into the vagina and

rotating it in a circular motion, leaving it into there for approximately 5 seconds. (Without a speculum)

The swabs were placed in Amies agar gel medium (non nutritive transport medium). Transport medium maintains the viability of group B streptococci for up to 04 days at room or refrigerator temperature. The swabs were inoculated on to the surface of Islam's agar (GBS agar) and Blood agar plates. The plates were incubated both aerobically and anaerobically at 35° C for 72 hours. GBS was identified by standard morphological, cultural and biochemical profile (API-20 Strep, bio Merieux, France). Serological identification was performed by using Streptex (Remel, UK). The plates negative for GBS growth were re-incubated anerobically on Islam's agar for an additional period of 72 hours to rule out any slow growing GBS before discarding. The data was analyzed using computer software, Statistical Package for Social Sciences (SPSS 15.0). Pearson chi square and Fishers Exact test were applied to observe associations between qualitative variables. A p- value of < 0.05 was considered statistically significant.

Results

Among 500 pregnant women, 31(6.2%) were positive for GBS. Eight (25.8 %) of these GBS positive were primigravida and the rest (23) were multigravida.

No significant association was observed between maternal GBS carriage rate and gravidity.

Twenty cases (64.51%) attended the antenatal clinics and remaining did not. Only three (9.6%) cases have had history of preterm delivery. Previous abortions occurred in 12 (38.70 %) cases while the remaining 19 (61.2%) cases had no such history. Statistical analyses showed no significant relationship between demographics, reproductive histories and obstetric characteristics of cases with the test results.

Statistical analysis of demographics, reproductive histories and obstetric characteristics related to GBS carriage are shown in the table 2.

Discussion

Group B streptococcus has been a continuing focus of debate in the pediatric and obstetric world-ssince early 1970s.[15] In developed countries these organism are amongst the leading causes of neonatal sepsis, however in developing countries the problem has not been studied adequately.[16] Rates of GBS colonization varies throughout the world. Until recently little had been published on maternal GBS carriage rate in Pakistan. This study aimed to find out

the prevalence of GBS in pregnant women from different areas of Lahore.

Table 1: *Number of primigravidas and multigravidas coming to different hospitals.*

			Gravida		Total
			Primary Gravida	Multgravida	
GBS	Present	Count	8	23	31
		% of Total	1.6%	4.6%	6.2%
	Absent	Count	158	311	469
		% of Total	31.6%	62.2%	93.8 %
Total		Count	166	334	500
		% of Total	33.2%	66.8%	100.0 %
Pearson Chi - Square = 0.815, p value < 0.367					

No significant association was observed between maternal GBS carriage rate and gravidity, p value < 0.367 showing that from a total of 500 ladies, 166 (33.2 %) were primi gravida and 334 (66.8 %) were multigravida.

Table 2: *Demographics and Obstetrical history of GBS positive pregnant women*

HISTORY		GBS +ve (n=31)	GBS + ve% (n=31)	GBS+ve % (n=500)	P values
Gravida					<0.367
	Primigravida	8	25.80%	1.60%	
	Multigravida	23	74.20%	4.60%	
Antenatal visits					<0.302
	Yes	20	64.51%	4.00%	
	No	11	35.49%	2.20%	
H/O Preterm Deliveries					<0.863
	Yes	3	9.67%	0.60%	
	No	28	90.33	5.60%	
H/O Previous Abortions					<0.108
	Yes	12	38.70%	2.40%	
	No	19	61.30%	4.80%	
Occupation					<0.546
	Housewives	28	90.33%	5.60%	
	Working ladies	3	9.67%	0.60%	
Educational status					<0.886
	Educated	17	54.83%	3.40%	
	Illiterate	14	45.17%	2.80%	

p value less than <0.05 is significant, GBS: Group B streptococcus, n: number

Out of 500 cases included in the study, 6.2% were found to be positive for vaginal carriage of GBS. No statistical relationship could be established

between age, educational level, occupation and GBS carriage. In addition none of the factors that might contribute to colonization like history of abortion and preterm delivery were found to be significantly associated with GBS colonization status. This demonstrates that we cannot correlate demographics or obstetrical history with GBS colonization in pregnant women.

In contrast to our results, a group of researchers at Combined Military Hospital Lahore, observed GBS maternal colonization rate to be 4.5%[11].It is possible that inadequate culture techniques and microbiological methods might be responsible for this lower rate. In addition, we took lower vaginal swabs in comparison to high vaginal swab, number of women is greater in our study(500) as compared to previous study(200), moreover we used Islam's agar which is designed to exploit the ability of most group B streptococci to produce orange/ red pigmented colonies.

Out of 31 GBS isolated, 21 (67.75%) gave orange pigmentation on third day of incubation while the rest 10 (32.25%) produced pigmentation only after re incubation for another 72 hours. The significance of re incubation of plates, initially negative for GBS growth, is thus justified.

The results of our study are in accordance with other studies conducted in India and Peru where this percentage was found to be around 5-6%.[12,17] In contrast, in Thailand, West Indies, Kuwait and Turkey this percentage was observed to be quite higher i.e. 8.7% to 32.9% of the total cases included. [16,18-20]

In developed countries like USA, Canada and Australia this percentage varies between 10.5% to 34 %. [21][22], In 1996, CDC recommended screening and culturing all pregnant women at 35-37 weeks gestational age for GBS colonization.[16] These guidelines were revised in 2002 and are currently being applied in developed world.[23] After provision of simple antibiotics to GBS carrier pregnant women and to high risk infants, the incidence of neonatal disease in Canada and USA dramatically decreased from 2-3/1000 to 0.5/1000.[24]

In developing areas like Pakistan more extensive data on the prevalence of GBS neonatal disease, preventive measures, and out come of infected infants are greatly needed.

In conclusion, our results indicate that the relatively high maternal GBS colonization rate in pregnant women warrants a routine screening and prophylactic treatment of GBS carrying women in our society.

References
1. Regan JA, Klebanoff MA, Nugent RP. The epidemiology of group B streptococcal colonization in pregnancy. Vaginal infections and prematurity study group. Obstet Gynecol 1991;77:604-10.
2. Hansen SM, Uldbjerg N, Kilian M, Sorensen UB. Dynamics of Streptococcus agalctiae colonization in women during and after pregnancy and in their infants. J ClinMicrobiol2004;42:83-9.
3. Isaacs D, Barfield CP, Grimwood K, McPhee AJ, Minutillo C, Tudehope DI. Systemic bacterial and fungal infections in infants in Australian neonatal units. Med J Aust 1995;162:198-201.
4. Ali Z. Neonatal bacterial septicemia at the Mount-Hope women's hospital, Trinidad. Ann Trop Paediatr 2004;24:41-4.
5. Movahedian AH, Moniri R, Mosayebi Z. Bacterial culture of neonatal sepsis. Iranian J Publ Health 2006;35:84-9.
6. Gilbert R. Prenatal screening for group B streptococcal infection: gaps in the evidence. International J of Epidemiol 2003;33:2-8.
7. Osrin D, Vergnano S, Costello A. Serious bacterial infections in newborn infants in developing countries. CurrOpin Infect Dis 2004;17:217-24.
8. Shet A, Ferrieri P. Neonatal and maternal group B streptococcal infections: A comprehensive review. Indian J Med Res 2004;120:141-50.
9. M de Cueto , MJ Sanchez, A Sampedro , JA Miranda, AJ Herruzo, M Rosa-Fraile.Timing of intra partum ampicillin and prevention of vertical transmission of group B streptococcus. Obstet Gynecol 1998;91:112-4.
10. Connellan M, Wallace EM. Prevention of perinatal group B streptococcal disease: screening practice in public hospitals in Victoria. Med J Aust 2000;172:317-20.
11. Normal vaginal flora in pregnant women. J Pakistan Ins Med 1997;7:437-40.
12. Kulkarni AA, Pawar SG, DharmadhikariCA, Kulkarni RD. Colonization of pregnant women and their newborn infants with group B streptococci. Indian J Med Micrbiol2001;19:1-4.
13. Schrag SJ, Zell ER, Lynfield R, Roome A, Arnold KE, Craig AS, Harrison LH, Reingold A, Stefonek K, Smith G, Gamble M, Schuchat A;Active Bacterial Core Surveillance Team. A population based comparison of strategies to prevent early onset group B streptococcal disease in neonates. N Engl J Med 2002;347:233-9.
14. ACOG Committee Opinion: number 279,2002. Prevention of early onset group B streptococcal disease in the newborns. Obstetgynecol 2002;100:1405-12.
15. Brozanski BS, Jones JG, Krohn MA, Sweet RL. Effect of a screening based prevention policy on prevalence of early onset group B streptococcal sepsis. ObstetGynecol 2000;95:496-501.
16. Tor-Udom S, Tor-Udom P, Hiriote W. The prevalenc

of streptoccusagalactiae colonization in pregnant women at Thammasat hospital. J Med Assoc Thai 2006;89:411-4.

17. Collins TS, Calderon M, Gilman RH, Vivar A, Charache P. Group B Streptococcal colonization in a developing country: its association with sexually transmitted disease and socioeconomic factors. Am J Tro Med Hyg 1998;59:633-6.

18. Orrett A F. Colonization with group B streptococci in pregnancy and outcome of infected neonates in Trinidad. Pediatrics International 2003 ;45:319-23.

19. Al-Sweih N, Maiyegun S, Diejomaoh M, Rotimi V, Khodakhast F, Hassan N, George S, Baig S. Streptococcus agalactiae (Group B Streptococci) Carriage in Late Pregnancy in Kuwait. Med PrincPract 2004;13:10-14

20. Ayata A, Guvenc H, Felek S, Aygun AD, Kocabay K, Bektas S. Maternal carriage and neonatal coloni-

zation of group B streptococci in labour are uncommon in Turkey. Pediatr   Perinatal epidemiol 1994; 8:188-92.

21. Sunna E, el- Dehar N, Bustami K, Nawas T. A study of group B streptococcal carrier state during late pregnancy. Trop Geogr Med 1991;43:161-4.

22. Daley AJ, Isaacs D; Australasian Study Group for Neonatal   Infections. Ten year study on the effect of intrapartum antibiotic prophylaxis on early onset group B streptococcal and Escherichia coli neonatal sepsis in Australia. Pediatr InfectDis J 2004;23:630-4.

23. Gibbs RS, Schrag S, Schuchat A. Perinatal infections due to group B streptococci. Obstet-Gynecol 2004;104:1062-76.

24. Money D M, Dobson S. The prevention of early onset neonatal group B streptococcal disease. J ObstetGynecol Can 2004;26:826-32.

SMOKING KNOWLEDGE, ATTITUDE AND PRACTICE AMONG MEDICAL AND NON-MEDICAL STUDENTS OF BAHAWALPUR

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Abstract

Objective: To compare the knowledge, attitude and practice of smoking between medical and non-medical students of Bahawalpur.

Study design: Descriptive cross-sectional comparative study

Methods: The study was conducted through a survey using comprehensive questionnaire. The study involved 200 medical students (100 males and 100 females) of Quaid-e-Azam Medical College, Bahawalpur and 200 non-medical students (100 males and 100 females)of the Islamia University of Bahawalpur. The survey was conducted during the time period of January,2017 to March,2017. Students were asked about their knowledge, attitude and practice of smoking.

Results: Prevalence of smoking among medical students (13%) was greater than the prevalence of smoking among non-medical students (9.5%).

Conclusion: Despite of more knowledge and awareness regarding smoking and its related health risks, prevalence of smoking among medical students was greater than non-medical students. Government should promote anti-tobacco campaigns in colleges and universities.

Smoking can be defined as a practice of burning a substance and inhaling the smoke. This is done with the aim to taste the smoke and absorb the substance into blood stream for desired effects. A number of substances are being smoked, but the most common one, used for this practice is tobacco[1]. The deleterious effects of tobacco smoking on general health are well documented and on average, cigarette smokers die ten years earlier than non-smokers[2]. Several disorders originate in humans due to this malpractice including coronary artery disease, lung cancer, bladder cancer, pulmonary emphysema, peripheral vascular disease and neonatal mortality[3]. The first definitive knowledge of tobacco smoking and malignancy (lung x) interaction was presented as early as 1950s from the British physicians[4].

As reported by World Health Organization (WHO) in 2015, fatality rate in case of tobacco (smoking) addiction is more than 15%. It has been estimated that more than 6 million people die either as a result of direct cost of tobacco smoking or other less common addiction methods. And amongst these, more than 3/4th deaths are associated with direct smoking, while the rest are attributed to passive smoking. Nearly 80% of smokers are reported to be the residents of low or middle income class of less developed or developing countries[5]. The fatal incidents are more common in developing countries like Pakistan, which has the highest prevalence of male smokers (about 45%) in South Asia. Interestingly enough, smokingof cigarettes

decreases with education, with only 18% of men with higher education being the smokers[6].

There is an increasingly prevalence of smoking among young people, especially students at all levels (15-21year age) and it is more in uneducated people than educated ones. Male students are found to be more involved in smoking as compared to female students. The addiction seems to be related to alleviation of stress, life problems, peer pressure, social acceptance, family history of smoking, lower educational level of parents and the desire to attain high personality profile[7]. In contrast, religion, negative health effects, bad taste / smell, adverse physiological responses and issues related to family are considerably significant reasons for not smo-king[7,8]. Moreover, there are many factors which contribute in cessation of smoking like religious beliefs and parent's smoking behaviors, as smoking behaviors are less prevalent among students with high religious beliefs and whose parents are non-smokers[9].

Physicians and working environments also play important role in the establishment of healthy environment for patients. As doctors are considered a role model for the patients to live a healthy life and he or she should not be a smoker, because it may have a positive impact on the mindset of the patient, who is a smoker already. The previous researches, however, has shown that prevalence of smoking is increasing day by day among medical students.

The purpose of study is to establish the preva-

lence of knowledge, attitude and practice of smoking among medical and non-medical students in Bahawalpur. The students were asked about their knowledge of harmful consequences of smoking and whether smokers should have opportunities to attend smoking cessation programs by the health professionals at public and private sectors.

Methods

Study design:

Descriptive cross-sectional comparative study.

Setting:

Study was conducted between medical and non-medical students of Bahawalpur.

Duration:

Study was conducted during the time period of January,2017 to March,2017.

Sample:

In the study total 400 students participated; 200 (100 males and 100 females) were themedic al studentsof Quaid-e-Azam Medical College, Bahawalpur and 200 (100 males and 100 females) were the non-medical students of the Islamia University of Bahawalpur.

Method:

Study was conducted through a well defined questionnaire. Students were asked about their knowledge regarding smoking, its effect on health, their attitude towards smoking, practice of smoking and proposed methods to reduce smoking. They were also asked about the age at which they started smoking and with whom they were, when they started. Followings are some operational definitions in present study:

Smoker: is one who (regularly or occasionally) smokes.

Non-smoker: is one who doesn't smokes.

Results

The results of study are described in the following captions.

Knowledge of smoking and its hazards:

The data given in table No.1 showed that about 92% medical and 90% non-medical students believed that smoking is harmful for health. Almost all the medical (98.5%) and non-medical (98%) students believed that both active and passive smoking are injurious to health. When questioned on the ensuring risks related to smoking, most of the medical (96%) and non-medical (95%) students recognized lung cancer, 91.5% medical and 90% non-medical students believed that smoking might cause oral or laryngeal cancers, while 90% medical and 89% non-medical students believed that

smoking might be the cause of cardiovascular disorders. Few medical (17.5%) and non-medical (24%) students only knew the legal age of smoking in Pakistan. It was noticed that 56% medical and 75% non-medical students believed that physicians are responsible for educating people to stop smoking. However, 55% medical and 60% non-medical students were of the opinion that their knowledge is sufficient to counsel the person, who wants to quit smoking.

Attitude towards smoking:

The data given in table No.2 illustrated that majority of medical (88.5%) and non-medical (86%) students believed that people are influenced by the family members / friends who are smokers. Few of the medical (11.5%) and some non-medical (33%) students thought that government is taking proper measures to reduce smoking. Smoking can affect relations with others as believed by 69.5% of medical and 88% of non-medical students, while 87.5% medical and 89% non-medical students agreed upon that negative message conveyed to public if a medical student / doctor smokes. Regarding role of education, 71.5% medical and 80% non-medical students believed that education helps to reduce smoking trend. Among all, more than half medical (59.5%) and non-medical (62%) students thought that if a smoker wants to stop smoking, health might be the main reason.

Beliefs about smoking control:

It is depicted from the data given in table No.3 that 93% medical and 95% non-medical students agreed to ban the smoking at work place. The same strength(93%) of medical and non-medical students suggested the ban of smoking in their institutions. Almost half of the medical (54.5%) and non-medical (53%) students were of the opinion that separate smoking areas should be available, while 89% of all medical and non-medical students recommended a strict ban on smoking advertisements. However, 77% medical and 83% non-medical students were of the opinion that smoking can be minimized through increasing the price of cigarettes.

Practice of smoking:

Of the respondents, 13% medical students (24% males and 2% females) while only 9.5% non-medical students (18% males and 1% females) in Bahawalpur are smokers.

Discussion

Smoking is increasing day by day specially in developing countries. It was noted that medical students had more knowledge and awareness of

smoking and its related health risks, but unfortunately prevalence of smoking is more among medical students as compared to non-medical students, which is in contradiction to previous studies[12]. It could be related to high study stress. Only 17.5% medical students and 24% non-medical students knew the legal age of smoking in Pakistan (which is 18 years). Almost all students thought that smoking (either active or passive) is injurious to health. Most of the students in our study thought that people are influenced by the parental smoking habits. Their beliefs are in line with other studies showing a statistically significant positive correlation between parental smoking and the risk of smoking among students[11].Current study showed that friends are the main reason for initiation of smoking. Moreover, majority of the students were of the opinion that smoking of medical students or doctors decreased the credibility of antismoking message to the public.

Conclusion

Survey revealed that medical students had more knowledge and awareness of smoking and its related health risks, but unfortunately prevalence of smoking is more among medical students as compared to non-medical students. Government should promote anti-tobacco campaign in the colleges /universities and smoking should be banned in colleges, universities, hospitals and public places.

Table 1: *Knowledge of smoking and its hazards*

Items	Medical students agreed (n=200)	Nonmedical students agreed (n=200)
Students who knew the legal age of smoking in Pakistan	35(17.5%)	48(24%)
Smoking is harmful	184(92%)	180(90%)
Both active and passive smoking are injurious to health	197(98.5%)	196(98%)
Smoking may cause lung cancer	192(96%)	190(95%)
Smoking may cause oral or laryngeal cancer	183(91.5%)	180(90%)
Smoking may become the cause of cardiovascular disease	180(90%)	178(89%)
Physicians are responsible for educating people to stop smoking	112(56%)	150(75%)
My own knowledge is sufficient to counsel person who wants to quit	110(55%)	120(60%)

Table 2: *Attitude of students towards smoking*

Items	Medical students agreed (n=200)	Nonmedical students agreed (n=200)
People are influenced by family members/friends who are smokers	177(88.5%)	160(80%)
Government is taking measures to reduce smoking	23(11.5%)	66(33%)
Smoking can affect relations with others	139(69.5%)	176(88%)
It conveys negative message to public, if a medical student/doctor smokes	175(87.5)	178(89%)
Education helps to reduce smoking trends	143(71.5%)	160(80%)
If smoker wants to stop smoking then health may be the reason	119(59.5%)	124(62%)

Table 3: *Beliefs about smoking control*

Items	Medical students agreed (n=200)	Nonmedical students agreed (n=200)
Smoking should be banned at workplace	186(93%)	190(95%)
Smoking should be banned in this institution	186(93%)	186(93%)
Separate smoking areas should be available	109(54.5%)	106(53%)
Cigarettes advertisements should be banned	178(89%)	178(89%)
Prices of cigarettes should be increased	154(77%)	166(83%)

Table 4: *Practice of smoking*

Smoking status	Medical students	Nonmedical students
Smokers		
Males (n=100)	24(24%)	18(18%)
Females(n=100)	2(2%)	1(1%)
Total (n=200)	26(13%)	19(9.5%)

References

1. Gately I. 2001. Tobacco: A cultural history of ho an exotic plant seduced civilization. Simon & Schuster Ltd, UK. :3-7.
2. [1]Doll R, Peto R, Boreham J, Sutherland I. 2004. Mortality in relation to smoking: 50 years' observations on male British doctors. BMJ. 26:1519-1533. [2]Mothers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. Plos Med e2006;3(11):e442. DOI: 10.1371/journal.pmed.0030442 .
3. [1]Dhala A, Pinsker K, Prezant DJ. Respiratory health

consequences of environmental tobacco smoke. Medical clinics of North America, 2004, 88:1535–5./ [2] Doll R et al. Mortality in relation to smoking: 50 years' observations on male British doctors. British medical journal, 2004, 328:1519. / [3]Doll R et al. Mortality from cancer in relation to smoking: 50 years observations on British doctors. British journal of cancer, 2005, 92(3):426–9.

4. Doll R, Peto R, Boreham J. Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. BMJ 2004;328(7455):1519

5. World Health Organization (WHO). Tobacco, factsheet No.339 2015. (Accessed 01.10.2015)

6. National Institute of Population Studies [Pakistan] and ICF International. National Institute of Population Studies [Pakistan] and ICF International. Calverton, Maryland, USA: National Institute of Statistics and ICF International; [Jul,2016]. 2013. Pakistan Demographic and Health Survey 2012-13. Key Findings.

7. Maziak W et al. Characteristics of cigarette smoking and quitting among university students in Syria. Preventive medicine, 2004, 39(2):330–6.

8. Felimban F, Jarallah J. Smoking habits of secondary school boys in Riyadh, Saudi Arabia. Saudi medical journal, 1994, 15:438–42

9. Bassiony M. Smoking in Saudia Arabia. Review articles. Saudi Med J 2009:vol.30 (9)

10. Rosser WW. The role of the family physicians in smoking cessation. Canadian Family Physician 1984;30:160-162

11. Rozi S et al. Prevalence and factors associated with current smoking among high school adolescents in Karachi, Pakistan. Southeast Asian journal of tropical medicine and public health, 2005, 36(2): 498-504

12. Mansour, M.A.M, H.Ahmad, M.Yousaf, N.Ahmad, A.A.Mawaydeh, R.A.Ibrahim, R.A.Ayasreh. 2015.Awareness, Attitude and Practice of Smoking among Medical Sciences& Non-Medical Sciences Students at TaifUniversity.Int.J.Sci&Res. 4(1):255-264

VITAMIN D DEFICIENCY IN PATIENTS PRESENTED IN A PRIVATE CLINIC

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Abstract

Objective:- To determine the incidence of vitamin-D deficiency in patients presented to us with complaits of aches and pain in body.

Methods:- This prospective study was carried out in Zafar Clinic Yateem Khana Lahore from January 2016 to May 2016. A total of 120 patients were included in the study.

Result:- Out of 120 patients, 80 (66.7%) were female and 40 (33.3%) male. 56 (70%) out of 80 female patients had vitamin-D deficiency (<20 ng/mL) and 14 (17.5%) out of 80 patients had vitamin-D insufficiency (21-29 ng/mL). 25 (62.5%) out of 40 male patients had vitamin-D deficiency (<20 ng/mL) and 8 (20%) out of 40 male patients had vitamin-D insufficiency (21-29 ng/mL). So, out of 120 patients 81 (67.5%) had vitamin-D deficiency (<20 ng/mL) and 22 (18.3%) patients had vitamin-D insufficiency (21-29 ng/mL). Total 103 (85.8%) out of 120 patients were suffering from vitamin-D deficiency/insufficiency (<30 ng/mL). 17 (14.13%) out of 120 patients had sufficient levels of vitamin D (>30 ng/mL).

Conclusion:- Prevalence of Vitamin D deficiency is alarmingly high in patients presenting with fatigue, even more than that seen in other parts of the world..

Keywords:- body aches and pains, vitamin D deficiency, OPD patients.

Complaint of easy fatigability is more common these days than ever before. One can talk to any patient or seemingly healthy person and will find complaints of lethargy and poor stamina. This phenomenon is on the rise. Important diseases that can cause fatigue include endocrine illnesses like thyroid dysfunction, diabetes mellitus, and chronic diseases such as chronic obstructive airway disease, chronic infections (e.g. chronic hepatitis, infective endocarditis), congestive cardiac failure, anemia autoimmune disorders and neoplasia. Alcoholism and certain drugs like sedatives and Beta-blockers can also cause similar clinical picture. Lastly, psychological conditions such as fibromyalgia, depression and sleep disorders etc. can also cause lethargy and body aches[1,2,3]. Fatigue of unknown cause or related to psychological illness exceeds that secondary to physical ailment and drugs[4]. In recent times, hazards of vitamin D deficiency are in the limelight in clinical research. Vitamin D deficiency is not only associated with metabolic bone disease such as Osteomalacia and rickets but it can present with easy fatigability without evidence of osteopenia. It works at mitochondrial level in myositis, impairing cellular respiration thereby causing fatigue[5,6]. Many cases labeled as fibromyalgia were actually found to have vitamin D deficiency, so it remains a diagnosis of exclusion[7,8]. Vitamin D, also called "Sun vitamin", is a hormone produced in our skin following exposure to sunlight in its primitive form called as Provitamin D (7 deoxy cholesterol) which under goes hydroxylation first in the liver and then in the kidneys to produce active form of vitamin D (1, 25 dihydroxy cholicalciferol). This is the most important source of vitamin D for humans[9]. Other sources of vitamin D include mushrooms and oily fish. Excessive cooking spoils vitamin D content in these sources[10,11]. More than 85% of the people in our region are reported to be suffering from vitamin-D deficiency/ insufficiency (<30ng/mL)[12,13].

Objective

To determine the prevalence of vitamin-D deficiency in patients presented to us with/ body aches and pains.

Methods

This prospective study was carried out in Zafar Clinic Yateem Khana Lahore from January 2016 to May 2016. A total of 120 patients were included in the study

Results

Out of 120 patients, 80 (66.7%) were female and 40 (33.3%) male patients. 56 (70%) out of 80 female patients had vitamin-D deficiency (<20 ng/mL) and 14 (17.5%) out of 80 patients had vitamin D insufficiency (21-29 ng/mL). 25 (62.5%) out of 40 male patients had vitamin-D deficiency (<20 ng/mL) and 8(20%) out of 40 male patients had vitamin-D insufficiency (21-29 ng/mL). So, out of total 120 patients 81 (67.5%) had vitamin-D deficiency (<20 ng/mL) and 22 (18.3%) patients had vitamin-D insufficiency (21-29 ng/mL). Total 103 (85.8%) out of 120 patients were suffering from vitamin-D deficiency/insufficiency (<30 ng/mL). 17 (14.3%) out of 120 patients had sufficient levels of vitamin-D ($\geq$30 ng/dL).

DISCUSSION

The study revealed that majority of patients with fatigue had low vitamin D levels. This favors international and national literature on the subject. A study showed frequency of vitamin D deficiency to be 45% in patients at a primary care clinic.[14] Another study in multi ethnic general practice reported vitamin D deficiency in 58% of patients. In these, 1/3rd of ethnic Norwegians and 83% of patients from Middle East, Africa and South Asia had low vitamin D levels. Baig A et al[15], in patients visiting Abbasi Shaheed Hospital Karachi, showed frequency of vitamin D deficiency to be 92%[16]. This is the same figure as present study revealed. A similar percentage (92.85%) was recorded by Aslam M et al in their study from Faisalabad conducted in an antenatal clinic.[17] Another study on adult patients from visiting medical outpatient department showed low vitamin D levels in 89.3% patients with vitamin D deficiency in 73.2% and insufficiency in 16.1%. D[29]ata from neighboring countries of Pakistan in South Asia showed similar figures regarding vitamin D deficiency. Habit of chewing betel nut has been incriminated for this by modulating the activity of enzymes which regulate circulating levels of 1,25 OH D. Asia[18] with pigmented skin despite having immense sun exposure, have much less vitamin D levels as compared to European and American population. This ca[19,20]n be explained by the fact that high degree of pollution prevents ultra violet rays from penetrating the human skin., 821 (67.5%) out of 120 patients in our study had vitamin-D deficiency (<20ng/mL). A study showed that 69% patients were suffering from vitamin-D deficiency which is slightly higher16 but near to our study. This difference can be due patients were presented with body aches and pains in medical OPD and were diagnosed as fibromyalgia. With the slight difference, these results can be compared, also slightly less than the study done in 40 female patients presented in medical OPD with fibromyalgia with the results of 80% and 20% of the patients suffering from vitamin-D deficiency and insufficiency respectively[17]. This slight difference may be due to smaller size of the study. In our study the results of vitamin-D deficiency in female 56 (70%) out of 80 patients were also comparable with the study done by Ali et al in which vitamin-D deficiency was present in 53 (74%) out of 75 women having tibial tenderness[18] and generalized aches and pains in pre-menopausal age presented at tertiary care center in Lahore, Pakistan.

Conclusion

Prevalence of Vitamin D deficiency is alarmingly high in patients presenting with fatigue, even more than that seen in other parts of the world.

References

1. Hakeem R, Fawwad A, Diabetes in Pakistan.. J Diabetology 2010; 3: 4.
2. Coen G. Vitamin D. J Nepnrol 2008; 21: 313-23
3. Papadakis MA, McPhee SJ. Current medical treatment and diagnosis. 52nd edition. McGraw Hill company.2013; 38-40.
4. Aasheim ET, Hofso D, Hjelmesaeth J, Birkeland KI, Bolmer T. Vitamin D status in morbidly obese patients. Am J Clin Nutr 2008; 87: 362-9.
5. Ecemis GC, Atmaca A. Quality of life is impaired not only in vitamin D deficient but also in vitamin insufficient premenopausal women. J Endocrinol Invest 2013; 36(8): 622-7.
6. Hollick MF. Sunlight and vitamin-D for bone health and prevention of autoimmune diseases, cancers and cardiovascular disease. Am J Clin Nutr 2004; 80(6): 1678S–88S.
7. Holick MF. Vitamin-D status. Ann Epidemiol 2009; 19(2): 73-8.
8. Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson HB. Global vitamin-D status and determinants of hypovitaminosis D. Osteoporos Int 2009; 20: 1807–20.
9. Ali JMM. Vitamin-D deficiency in outpatient department: Eastern Province of KSA experience. Rawal Med J 2010; 35: 221–3.
10. Lips P. Worldwide status of vitamin D nutrition. J Steroid Biochem Mol Biol 2010; 121: 297–300.
11. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA. Evaluation, treatment, and

prevention of vitamin d deficiency. J Clin Endocrinol Metab 2011; 96: 1911–30.

12. Arya V, Bhambri R, Godbole MM. Vitamin-D status and its relationship with bone mineral density in healthy Asian Indians. Osteoporos Int 2004; 15: 56–61.

13. Harinarayan CV. Prevalence of vitamin-D insufficiency in postmenopausal south Indian women. Osteoporos Int 2005; 16: 397–402.

14. Merlo C, Ross C, Trummler M, Zeller A. Prevalence and symptoms of vitamin D deficiency in general practice. Praxis 2012; 101(22): 1417-22.

15. Knutsen KV, Brekke M, Gjelstad S, Lagerlov. Vitamin D status in patients with musculoskeletal pain, fatigue and headache. Scand J Prim Healthcare.2010; 28(3):166-71.

16. Baig A, Parwez A, Khan MK, Islam N, Rahman A. Patterns of serum vitamin D in OPD patients. Pak J Surg 2007, 23(2): 145-9.

17. Aslam M, Sattar A, Masood Z, Qudsia M. Vitamin D deficiency; prevalence in pregnant women. Prof 2012; 19(2): 208-13.

18. Mufti MA, Malhi UR, Zubair A, Badar I, Mufti M. vitamin D level in adults in Northern Pakistan. Rawal Med J 2012: 37: 2-5.

19. Ogunkolade WB, Boucher BJ, Bustin SA, Burrin JM, Noorian K, Mannan N et al. Vitamin D metabolism in peripheral blood mononuclear cells is influenced by chewing "betel nut" (Areca catechu) in vitamin D status. J Clin Endocr Metab 2006, 91(7): 2612-7.

20. Hollick MF. The vitamin D solution. 1st edition. Newyork. Penguin Group 2010; 45

21. Mahmood K, Akhtar ST, Taib A, Haider I. Vitamin D status in a population of healthy adults in Pakistan. Pak J Med Sci 2009: 25(4) : 545-50.

FREQUENCY AND DETERMINANTS OF ASTHMA

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Abstract

Background:

Asthma is a major cause of disability, health resource utilization and poor quality of life world-wide. We set out to generate estimates of the frequency of asthma in medical students of a public medical college and also to identify the factors implicated in its causation, exacerbation and remission so that effective measures can be taken for its optimum control.

Objective: To determine the frequency of asthma and to identify the factors associated with it in medical students of Allama Iqbal Medical College Lahore. To test whether the association between family history of asthma and frequency of asthma in medical students is significant or not.

Methodology: It is a cross sectional analytical study. The study was conducted in Allama Iqbal medical college; Lahore which is a government institution affiliated with Jinnah hospital. 300 medical students of Allama Iqbal Medical College, Lahore (1st year-5th year) were included in the study.

Results: Of the 300 participants the age on average was 20.9 years of which 58.67% were females and 41.33% were males, 11.3% of the total students were asthmatics and 44% of these asthmatics had a positive family history for asthma.

Conclusions: Asthmatic medical students have a good awareness about asthma and they undergo periodic medical checkups due to good available health facilities however they do not take medications regularly.

Keywords: ssthma, wheezing, chest tightness, nocturnal chest tightness, family history of asthma, obesity, smoking

Asthma is a chronic inflammatory disease characterized by reversible airway obstruction, increased sensitivity of the airway to allergens, smooth muscle hypertrophy and hyperplasia of the mucosal glands of the airway[12] .Common symptoms include wheezing, coughing, chest tightness, and shortness of breath[16].

The prevalence of asthma is increasing worldwide .About 300 million subjects are currently having asthma. It affects both sexes and almost all ages. The male to female ratio is about 1.5 in children, 1.0 in late adolescence and less than 1.0 in adults, when more females have symptoms.[23]

According to the world health survey conducted by WHO , the global prevalence rates of doctor diagnosed asthma, clinical/treated asthma and wheezing in adults were 4.3%, 4.5%, and 8.6% respectively, and varied by as much as 21-fold amongst the 70 countries. Australia reported the highest rate of doctor diagnosed, clinical/treated asthma, and wheezing (21.0%, 21.5%, and 27.4%).Amongst those with clinical/treated asthma, almost 24% were current smokers, half reported wheezing, and 20% had never been treated for asthma [17].

According to a study conducted by students of Army medical college Rawalpindi, male prevalence came out to be 6.29% , female 12.02% and overall 9.2 % .[3]

The diagnosis is made clinically by physicians [12]. However, the lack of a clinical definition of asthma coupled with the absence of optimum standardized tools have made it difficult to conduct epidemiological studies in an effective manner and consequently have resulted in its under diagnosis [3].

Asthma is caused by a complex interaction between genetic and environmental factors.[14] Asthma can be triggered by dust, allergens, anxiety, cigarette smoking and infections by different microbial organisms.[6].The famous hygiene hypothesis attributes the development of asthma in children to the reduced exposure to bacterial and viral pathogens early in life.[3]

Disturbed sleep accompanied by nocturnal awakening is a common symptom amongst asthmatic patients. This is associated with increased absence from work and as a result the patient resorts to using reliever medications more frequently to prevent the symptoms from exacerbating. [8]

A positive correlation exists between cigarette smoking and asthma as smoking has induced asthma in previously non atopic individuals. [2, 4]

METHODOLOGY

This cross sectional analytical study was conducted in Allama Iqbal medical college Lahore which is a government institution affiliated with Jinnah hospital. 300 medical students of Allama Iqbal Medical College, Lahore (1st year-5th year) were included. The study last for one month. Non probability / purposive sampling was used.

DATA COLLECTION PROCEDURE:

Data was collected using self-administered anonymous questionnaires. The questionnaire was designed keeping in consideration the questions asked in the EUROPEAN COMMUNITY RESPIRATORY HEALTH SURVEY II. . The questions were close ended in nature in order to invoke a definitive reply from the students.

DATA ANALYSIS PROCEDURE:

SPSS 17 was used for this purpose. Demographic and asthmatic status data was summarized using descriptive statistics. Categorical variables were reported using frequencies, while continuous data was analyzed using means and standard deviation. In addition we also used pie charts and bar charts to show the extent to which different risk factors are associated with asthma amongst the student population. We also performed the Chi square test to test whether the association between family history of asthma and frequency of asthma in medical students is significant or not.

RESULTS AND MAIN FINDINGS:

Table 1: *Diagnosed by a doctor for asthma* n=300

Asthma status	Frequency	Percent
No	266	88.7
Yes	34	11.3
Total	300	100.0

Table 2: *: Symptoms of asthmatics* n=34

Symptoms	Responses	
	N	Percent
Chest tightness at night in last 12 months	26	76.5
Shortness of breath in last 12 months	31	91.2
wheezing or whistling in chest at anytime in last 12 months	29	85.3
Shortness of breath following strenuous exercise in last 12 months	26	76.5

Table 3: *Risk factor frequencies of asthmatics* n=34

Risk Factor	Responses	
	N	Percent
Family history	15	44.1
Nasal allergy	22	64.7
Smoking	1	2.9
Trees, grass or flowers	25	73.5
Stressed	27	79.4
Outdoor pollution	24	70.6
Carpets, rugs or mats	17	50
Near animals	16	47.06

FAMILY HISTORY OF ASTHMA	STUDENT HAS ASTHMA	STUDENT DOES NOT HAVE ASTHMA	TOTAL
Parents Or Siblings Have Asthma	15	8	23
Parents Or Siblings Do Not Have Asthma	19	258	277
TOTAL	34	266	300

Consultation to physician for asthma in last 12 months
- once
- twice
- thrice
- more than 3 times
- Did not consult for Asthma

2.94% 1 Did not consult for Asthma
17.65% 6 more than 3 times
11.76% 4 thrice
50.00% 17 once
17.65% 6 twice
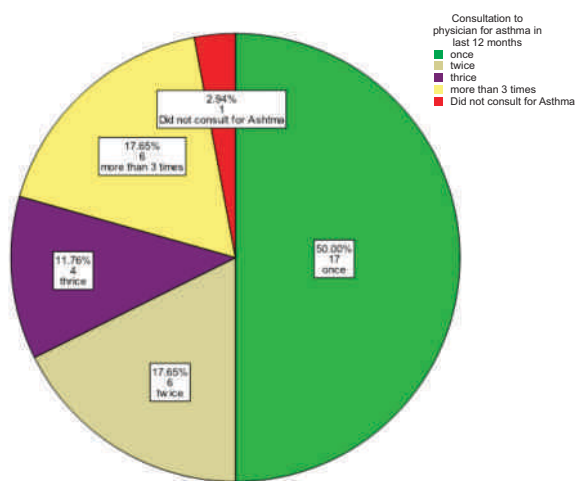
NULL HYPOTHESIS=
There is no significant association between asthma in medical students and a positive family history of asthma (asthma in parents or siblings)
ALTERNATIVE HYPOTHESIS=
There is a significant association between asthma in medical students and a positive family history of asthma (asthma in parents or siblings)

CHI SQUARE CALCULATED VALUE $=\sum$ (O-E) 2/E

$$= 71.98$$

Since the calculated value of chi square which is 71.98 is greater than the table value of 3.84 at d.f=1 and p<0.05(value of p is 0.00) thus the null hypothesis is rejected and there is a statistically significant association between doctor diagnosed cases of asthma and a positive family history of asthma.

RESULTS:

A total of 340 questionnaires were randomly distributed amongst students of AIMC out of which 300 were returned, response rate being 88.23% .Of the 300 participants, the average age was 20.9067 years, the standard deviation was 1.447 years and 67 % of the students belonged to the 20-22 year age group. Out of these 300 students, 58.67% were female and 41.33% were male. Of the 300 students, 44.33% were day scholar whereas 55.67% were boarder. 34 students (11.3%) were found to have doctor diagnosed asthma. However, we also asked questions regarding wheezing, chest tightness and nocturnal awakening from students. Since many patients have asthmatic symptoms however they do not have doctor diagnosed asthma as they don't consult physicians, the primary reason being that people fear lifelong treatment of asthma. 11.7% reported an attack of chest tightness that led to nocturnal awakening.14.3% of the students reported an attack of wheezing in the last 12 months.15% reported shortness of breath at rest. In addition 16.7% of the students reported shortness of breath following strenuous exercise in the last 12 months. Now after determining that there were 34 doctor diagnosed asthmatics, we then analyzed the factors which were associated with asthma in these patients. The frequency of asthma turned out to be higher in female students as almost 62% of the asthmatic students were females. The frequency of asthma in boarders turned out to be almost 65% which is slightly higher considering the fact that 55.67% of the students were boarders, the rest being day scholars.Family history plays a key role in the pathogenesis of asthma as almost 44% of asthmatics reported that their parents or siblings have asthma.

Chest tightness leading to nocturnal awakening which is an important pathognomonic sign of asthma was reported by an overwhelming 77% of asthmatics, however shortness of breath turned out to be the most common symptom as it was reported by 91% of the students. Wheezing was reported by nearly 85% of the students, making it the second most common symptom. Asthma is usually accompanied by concomitant nasal allergy and nearly 65% of the students had a positive history of nasal allergy, however the exact allergen causing the allergy was not investigated since it requires specialized radioallergosorbent tests. The highest frequency of asthma attacks (44%) were reported in the months of March/April followed by January/February and November/December. July/August and September/October reported the least number of attacks.

Outdoor pollution in the form of dust and smoke is known to trigger asthma attacks and nearly 71% of the asthmatics reported that they suffer from increased severity of asthma when they keep their windows open. Stress reduction is an important agent in the prevention and subsequent decrease in severity of asthma. Almost 80% of the students believed that stress is a major factor in their poor asthma control. It was encouraging to see that only 20 percent of the diagnosed asthmatics were overweight and none was obese. Nearly 40% of the students said that they did not take any asthmatic treatment in the form of inhalers, steroids or oral tablets. 97 percent of the patients consulted their physicians for asthma in the last 12 months. Emergency hospital visits were reported to be 44%. Smoking increases severity of asthmatic symptoms since it is associated with chronic bronchitis and emphysema which like asthma are obstructive pathologies of the lung, however a mere 3% of the students who were asthmatics said that they were smokers.

DISCUSSION:

The purpose of this study was to evaluate the frequency of asthma amongst medical students of Allama Iqbal Medical College Lahore and then to determine the extent to which different factors are associated with it. 34 students (11.3%) were found to have doctor diagnosed asthma. However we also asked questions regarding wheezing, chest tightness and nocturnal awakening from students since many patients have asthmatic symptoms however they do not have doctor diagnosed asthma because they do not consult physicians, the primary reason being that people fear lifelong treatment of asthma 11.7% reported an attack of chest tightness that led to nocturnal awakening.14.3% of the students reported an attack of wheezing in the last 12 months. 15% reported shortness of breath. Since the variation between doctors diagnosed asthma and other

asthmatic symptoms is less this means that students have access to good health facilities and are aware of the consequences of not getting their asthma treated .The improved diagnosis is a reflection of easy access to Jinnah hospital which is located nearby. These results are similar to a study conducted by students of Army medical college Rawalpindi in which wheezing turned out to be 17.8%, 13.2% subjects documented tightness of chest and 10.74% shortness of breath respectively. [3] The frequency of asthma turned out to be higher in female students as almost 62% of the asthmatic students are females. This is understandable since 59% of college students are females. In addition globally asthma is more prevalent in the female gender. A similar study conducted amongst university students of Khartoum, Sudan revealed 57% of asthmatics to be women and just like our study women constituted a greater proportion of the student population. [23]

The greatest numbers of asthma attacks (44%) were reported in the months of March/April followed by January/February and November/December.The increased frequency in March/April correlates with the generalized increase in the pollen content of the atmosphere. Cold temperature has long been considered an important agent in the exacerbation of pathologies of the respiratory tract and possibly accounted for the increased frequency in the winter months. July/August and September/October reported the least number of attacks.

Smoking although increases severity of asthmatic symptoms since it is associated with chronic bronchitis and emphysema which like asthma are obstructive pathologies of the lung however a mere 3% of the students who were asthmatics said that they were smokers. This result of our study is highly inconsistent with the world health survey conducted by WHO which reported that 23.5% of asthmatics are smokers. [17]This could be either due to increased awareness of medical students about the adverse effects of smoking and hence lesser consumption of cigarettes or it is also possible that they do not want to disclose it.

It was encouraging to see that only 20 percent of the diagnosed asthmatics were overweight and none was obese reflecting the fact that students are conscious of their weight as obesity is associated with poor asthma control and possible future complications of the cardiovascular system. Our results when compared with a study conducted in South Carolina are highly inconsistent because nearly 50 percent of the diagnosed asthmatics were obese. This variation could be due to international differences in food

consumption and exercise patterns and could also be because of the fact that the study in Carolina was conducted on nearly 12000 people which is a significantly larger sample size as compared to our sample of only 300 students. [24] Family history plays a key role in the pathogenesis of asthma. In our study 44% of asthmatics reported that their parents or siblings have asthma. A study conducted at Isra University Hospital between September 2005 to August 2006 also showed that almost 70 percent of asthmatic children had a positive family history of asthma.Yahya et al.showed 47% of asthmatic children to have a positive family history of asthma.[14]. In another study from Hyderabad by Sheikh et al. 50% asthmatic children had a positive family history.[16] .In order to further check the significance of the association between family history of asthma and frequency of asthma in medical students we performed the chi square test. The p value was set at 0.05. Since the calculated value of chi square which is 71.98 is greater than the table value of 3.84 at d.f=1 and p<0.05, thus the null hypothesis is rejected and there is a statistically significant association between doctor diagnosed cases of asthma and a positive family history of asthma.

Presence of carpets and rugs have also been implicated in the pathogenesis of asthma since they have a tendency to trap dust mites. Almost 62% of the asthmatics reported that their symptoms were aggravated in the presence of carpets. This association is much higher than a similar study conducted at Isra university hospital in which 24% reported association of exposure to rugs and carpets with asthma. [14]. The marked difference might be explained on the basis of the fact that since majority of students live in hostels and almost all the rooms are carpeted so there is an increased association between the two.

Stress reduction is an important agent in the prevention and subsequent reduction of asthma severity .Since medical students live under constant stress because of their rigid and tough coursework so they are more likely to experience increased asthmatic attacks. Almost 80% of the students believed that stress contributes to increased asthma severity. A review article about the role of psychological stress in asthma showed that 15-30% of patients responded with increased bronchoconstriction in stressful situations. The difference in the findings could be because stress is a subjective variable and individuals differ in their ability to react to stressful conditions. [25]

Almost 47 percent of the asthmatics reported worsening of asthma on exposure to pets this relationship is higher as compared to a similar study conducted on school children of Islamabad in which almost half (23%) of asthmatic children reported having pets at home.[7] The difference between the results could be due to the fact that we took a smaller sample of 300 students which might not be fully representative of the student population.

Allergic diseases also appear to play an important role in prevalence of asthma. In our research almost 65% of asthmatics reported having allergies. This association is much higher than a similar study conducted at Allergy Centre National Institute of Health which showed that 20% of asthmatics have allergies.[5] The difference may be due to greater air pollution in Lahore.

Nearly 40% of the students said that they did not take any asthmatic treatment in the form of inhalers, steroids or oral tablets, however it is not clear that whether this is due to improved asthma control or carelessness on part of the students, But since 97 percent of the patients consulted their physicians for asthma in the last 12 months so it is likely that it could be due to lack of seriousness regarding appropriate control of asthma. This might in itself have led to increased emergency hospital visits which were reported to be 44% further signifying poor control of asthma.

Our results are based on a survey in a major medical school in Lahore and are not necessarily representative either of the of the student population or of the entire country. The asthmatic status of subjects was assessed only by means of self- report, potentially rendering our results less reliable. This study may not be necessarily representative of young adults of the general population or students of other non medical colleges since medical students have greater awareness about asthma as it is an integral part of their curriculum, being taught as a part of both basic and clinical sciences and students also have easier access to quality health care facilities as they visit the attached teaching hospitals regularly.

CONCLUSION:

The conclusion of our study is:

The frequency of asthma(11.3%) corresponds with the global frequency.The number of students who have asthma and smoke is much lower than those found in other studies.Obesity does not seem to be an important associated factor since none of the asthmatics is obese.Although medical students have a good awareness about asthma however control of asthma is poor.Family history is an important determinant of asthma frequency in medical students.

REFERENCES:

1. Basagana X, Sunyer J, Zock J, Kogevinas M, Urrutia I, Maldonado JA, et al. Incidence of Asthma and its Determinants among Adults in Spain. Am J Respir Crit Care Med. 2001;164:1133-7.
2. Jindal SK, Gupta D. The Relationship between Tobacco Smoke & Bronchial Asthma. Indian J Med Res. 2004 Nov;120:443-53.
3. Khan HD, Amir M, Khan MN, Khan U. Frequency of Asthma among students of Army Medical College. Ann. Pak. Inst. Med. Sci. 2011;7(3):142-5
4. Thomson NC, Chaudhuri R, Livingston E. Asthma and Cigarette Smoking. Eur Respir J. 2004;24:822-33.
5. Ahmad F, Yousaf F, Asif S. Prevalence of Allergic Diseases and related Allergens in Pakistan in 2007. JPMI. 2011;25(01):14-23.
6. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F, et al. International study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. Eurp Respir J. 1995;8:483-91.
7. Waqar MA, Khan M, Hasnain SM, Saleem A, Shaukat S, Sarwar F, et al. Prevalence of Allergy and Asthma in School Children of Islamabad. World Applied Sciences Journal. 2009;6(3):426-32.
8. Mustafa G, Khan PA, Iqbal I. Nocturnal Asthma in School Children of South Punjab, Pakistan. J Ayub Med Coll Abbottabad. 2008;20(3):36-9.
9. Farrokhi S, Gheybi MK, Movahhed A, Dehdari R, Gooya M, Keshvari S, et al. Prevalence and Risk Factors of Asthma and allergic diseases in Primary school children living in Bushehr, Iran: Phase I, III ISAAC Protocol. Iran J Allergy Asthma Immunol . 2014 Oct;13(5):348-55.
10. Delgado J, Barranco P, Quirce S. Obesity and Asthma. J Investig Allergol Clin Immunol. 2008;18(6):420-5.
11. Takkouche B, Barcala FJG, Etminan M, FitzGerald M. Exposure to furry pets and the risk of Asthma and Allergic Rhinitis: a meta-analysis. Allergy. 2008;63:857-64.
12. Demiralay R. Asthma Knowledge of the Medical Students. Turkish Respiratory Journal. 2002 Aug;3(2):53-8.
13. Van Lieshout RJ , MacQueen G. Psychological Factors in Asthma. Allergy, Asthma And Clinical Immunology. 2008; 4(1):12-28.
14. Majeed R, Rajar UDM, Shaikh N, Majeed F,Arain AA. Risk Factors Associated with Childhood Asthma . Journal Of College Of Physicians And Surgeons Pakistan. 2008;18(5):299-302.
15. Bloomberg GR, Chen E. The relationship of Psychologic Stress with Childhood Asthma. Immunol Allergy Clin N Am. 2005;25:83-105.

16. Rais H, Arif F, Santosh S. Asthmatic Children; Knowledge and practices in the parents. The Professional Medical Journal. 2014;21(4):739-44.

17. To T, Stanojevic S, Moores G, Gershon AS, Bateman ED, Cruz AA, et al. Global Asthma prevalence in Adults: findings from the cross sectional world health survey. BMC Public Health. 2012;12:1-8.

18. Pawanker R. Allergic diseases and Asthma: a global public health concern and a call to action. World Allergy Organization journal. 2014;7:1-3.

19. Pal R, Dahal S, Pal S. Prevalence of Bronchial Asthma in Indian Children. Indian Journal Community Medicine. 2009 Oct;34(4):310-16.

20. Beasley R, Crane J, Lai CK.W, Pearce N. Prevalence and etiology of Asthma. J Allergy Clin Immunol. 2000 Feb;105(2):466-72.

21. Liebhart J, Malolepszy J, Wojtyniak B, Pisiewicz K, Plusa T, Gladysz U, et al. Prevalence and risk factors for Asthma in Poland: Results from the PMSEAD Study. J Investig Allergol Clin Immunol. 2007;17(6):367-74.

22. Black PN, Sharpe S. Dietary Fat and Asthma: is there a connection? Eur Respir J. 1997;10:6-12.

23. Alawad AO, A.KH.H K, Merghani TH. Prevalence of Asthma among University Students and Workers in Khartoum State, Sudan. Al-Neelain Medical Journal. 2011 Jan;1(3):32-7.

24. Liu Y, Pleasants RA, Croft JB, Lugogo N, Ohar J, Heidari K, et al. Body mass index, respiratory conditions, Asthma, and chronic obstructive pulmonary disease. Respiratory Medicine.2015,doi:10.1016/j.rmed.2015.05.006:1-31.

25. Wright RJ, Rodriguez M, Cohen S. Review of psychosocial Stress and Asthma: an integrated biopsychosocial approach. Thorax. 1998;53:1066-74.

PRIMARY CARDIAC OSTEOSARCOMA IN A PREGNANT A WOMAN----- A CASE REPORT AND REVIEW OF LITERATURE.

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Abstract

 Primary malignant cardiac tumors are extremely rare; accounting upto 0.002 to 0.28 % of   all the primary cardiac tumors. Patients usually present with non specific symptoms; making early diagnosis a real challenge. These tumors have poor prognosis because of aggressive behavior. This report describes a 23-year-old pregnant female patient who presented to medical emergency of Jinnah Hospital Lahore with low grade fever, productive cough, difficulty in speaking and altered behavior. She also had   neck and shoulder pain. The patient underwent resective surgery and tumor was diagnosed on histopathology as cardiac osteosarcoma.

Keywords: cardiac tumor, pulmonary hypertension, cardiac osteosarcoma, resective surgery.

Primary malignant cardiac sarcomas are extremely rare; accounting upto 0.002 to 0.28 % of all the primary cardiac malignancies[1,2]. Primary osteosarcoma is a rare clinical and pathological entity accounting for less than 10% of primary cardiac tumors. Most of the cardiac tumors are metastatic and are more common than the primary cardiac osteosarcomas. Metastatic osteosarcomas most commonly occur in the right atrium while primary cardiac osteosarcomas most commonly occur in the left atrium[3]. We encountered a 23-year-old pregnant female with primary cardiac osteosarcoma arising in the left atrium with an attachment to interatrial septum. It was causing mitral valve obstruction and severe pulmonary hypertension. This case is being described in this report.

Case Presentation

A 23- year-old pregnant female patient presented to medical emergency of Jinnah Hospital Lahore with low grade fever, productive cough and difficulty in speaking . She also had altered behaviour associated with neck and shoulder pain. These symptoms started two months back and got worse in last 08 days before her presentation into the emergency. On physical examination her blood pressure was 120/90 mmHg, pulse was regular with a rate of 110/min and Oxygen saturation was 96%. Examination of the chest showed normal thoracoabdominal breathing pattern with bilateral basal fine crackles and loud S2 and P2. Neurological examination revealed that the patient was unable to speak and follow commands. However, her reflexes and muscle tone were normal.

Chest radiograph showed a borderline increase in the cardiac size. Lung fields were clear and cardiopulmonary angles were sharp. Echocardio-graphy showed a left atrial tumor measuring 54 mm x 42 mm in size. The tumor was heterogenous in consistency; with cystic spots and some calcified areas. In addition there was severe pulmonary hypertension ; estimated PAP 65 mm Hg (Normal range is 8-20 mm Hg) . Mitral valve showed normal morphology and mobility (Figure 1). USG abdomen showed a single viable intrauterine pregnancy of 15^{+4} week. CT scan of brain done to find out the cause of aphasia and altered behavior was normal. So a provisional diagnosis of atrial myxoma was considered. The patient underwent surgery and the tumor was resected. Specimen was submitted to Department of Pathology, Allama Iqbal Medical College, Lahore. On macroscopic examination   the tumor was a single fibromyxoid mass measuring 5.5×4.4× 3.0cm in size and weighing 80 grams. Serial sectioning revealed tan white homogenous cut surface. No necrotic areas were identified (Figure 2).
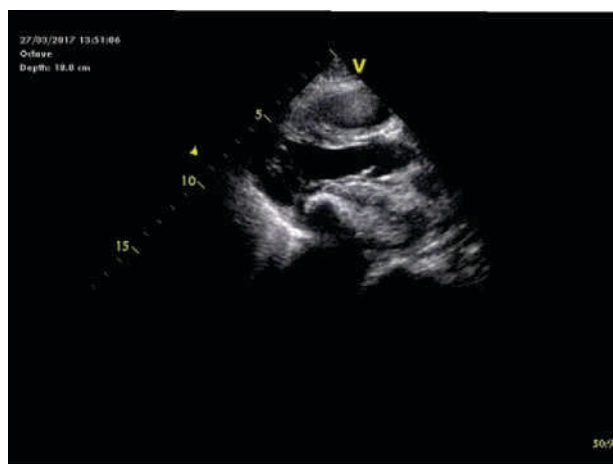

Figure 1. *Echocardiogram showing a mass in the left atrium with its attachment to interatrial septum.*
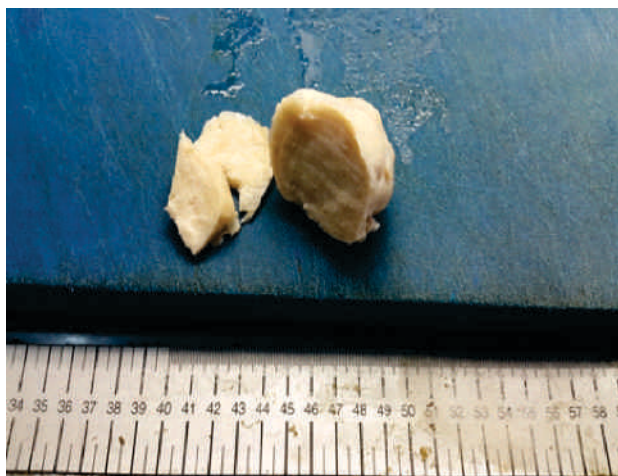
Figure 2. *Photograph showing gross appearance of tumor mass.*

Microscopic examination of the tumor mass revealed a malignant neoplasm comprised of spindle to polygonal shaped cells. These cells had pleomorphic hyperchromatic nuclei. Osteoid production by the tumor cells was seen at various places. Areas of chondroid differentiation were also present. Foci of necrosis, atypical mitosis and occasional multinucleated giant cells were also present. Features were suggestive of Cardiac Osteosarcoma (Figure: 3 & 4).
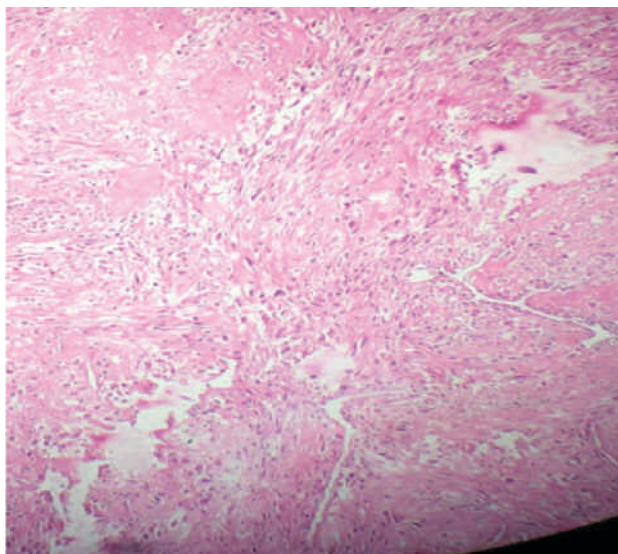

Figure 3. *Hitopathological appearance of the tumor showing atypical spindle to polygonal shaped cells*

Patient was discharged from hospital on 7th post-operative day on conservative treatment. Later on her condition improved and she began to speak and recognize those around her. Symptoms attributable to pulmonary hypertension like productive
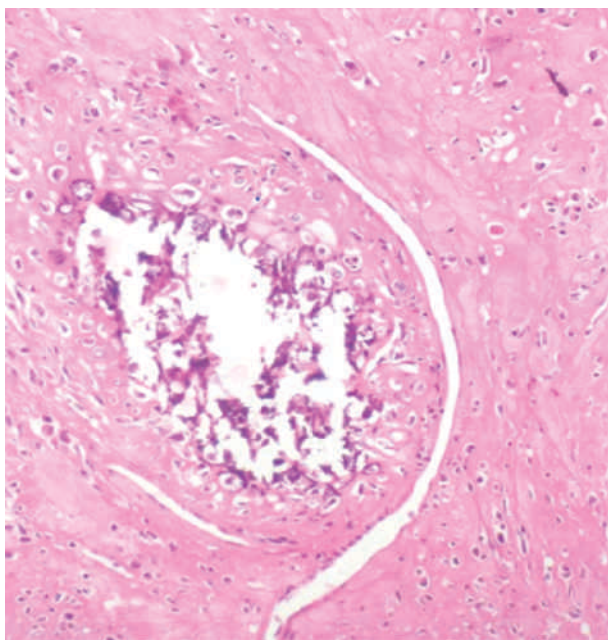
cough and low grade fever also improved.

Figure 4. *Photomicrograph showing osteoid formation by the tumor cells.*

Discussion

Cardiac tumors are rare entities. Almost 75 % are benign tumors[1,4]. Among the benign tumors, myxomas are most common at 33% [1,7,8] and others are lipoma and papillary fibroelastoma. Malignant tumors make almost 25% of the total cardiac tumors and these include angiosarcomas, leiomyosarcomas, mesotheliomas, fibrosarcomas and malignant lymphomas [1,3,8,9]. Most of the malignant cardiac tumor are metastatic with primary usually arising from malignant melanomas, breast carcinoma and lung carcinoma. They are 20 to 40 times more common than primary malignant cardiac tumors[1]. However; primary malignant cardiac sarcomas are very rare accounting upto 0.002 to 0.03% of all the malignant cardiac tumors [1,2].

Primary osteosarcoma don't have any gender and age specification predilection. As compared with extracardiac osteosarcomas, the prognosis of cardiac osteosarcoma is very poor[1,4]. Clinical presentation of the cardiac tumors depends upon the anatomical location, obstruction, embolization and invasion of specific intracardiac strutures. There is wide range of clinical presentations e.g left sided tumors can present with pulmonary hypertension, pleural effusion, cough, hemoptysis, edema and cardiac failure. Invasive tumors can present with valve dysfunction and arrhythmias. Embolization of the tumor can cause neurological deficit, syncope

and altered liver enzymes in serum[3,4]. In our patient; the mass was arising from interatrial septum and projecting into left atrium. It was causing mild to moderate element of mitral valve obstruction and causing low grade fever, productive cough and difficulty in speaking. She also had altered behaviour associated with neck and shoulder pain; representing the signs of possible metastasis. After initial workup it was difficult to decide whether the cardiac tumor is a benign tumor like myxoma, a primary cardiac malignancy or a metastatic tumor. Most of the metastatic cardiac osteosarcomas are located in right atrium and primary osteosarcomas are usually located in left atrium and frequently confused with atrial myxoma[3,10]. Our case was also initially thought to be an atrial myxoma.

Primary osteosarcomas are very aggressive tumors with high rates of local recurrence and distant metastasis. Most of the tumors have metastatised to other sites by the time of presentation[3]. In our case there was no detectable metastasis. Most common sites of metastasis are skin, brain, thyroid, lung, stomach, liver, kidney, muscle, intestine, peritoneum, and bone[3,11]. Osteosarcomas are very rare tumors and unfortunately imaging studies don't clearly distinguishing them from benign tumors such as myxoma. Therefore only surgical resection followed by histopathological reporting is confirmatory. CT scan, MRI and bone scan help in diagnosing distant metastasis. Pathological confirmation is still the gold standard to confirm the diagnosis. So excision of the tumor is the most important part of treatment of cardiac osteosarcoma.

Value of adjuvant treatments after surgery remains to be defined. Llombart-cussac et al in their retrospective review of 15 patients undergoing adjuvant chemotherapy after surgery found that this approach failed to modify the natural course and prognosis of the disease [6]. Similarly; Isayama et al reported a case treated with chemotherapy under percutaneous trasluminal coronary injection, but this did not improve the prognosis of the patient[12]. Hence; complete surgical resection is the preferred mode of treatment for cardiac osteosarcomas.

In our case, the mass was arising from interatrial septum and projecting into left atrium. It was causing a mild to moderate degree of mitral valve obstruction. Patient underwent cardiac surgery and tumor was resected. Histopathological reporting revealed it as cardiac osteosarcoma. After surgical resection; patient's symptoms improved dramatically and follow up of the patient was advised. She was given chemotherapy and later on she delivered a healthy baby boy on 26th August, 2017 through SVD. Patient is alive and well at the time of writing this report after surgery.

References

1. Takeuchi I, Kawaguchi T, Kimura Y, Kojima J, Shimamura H, Shimizu N, et al. Primary cardiac osteosarcoma in a young man with severe congestive heart failure. J Int Med 2007; DOI:46.6267.
2. Simpson L, Kumar SK, Okuno SH, Schaff HV, Porrara LF, Buckner JC, et al. Malignant primary cardiac tumors: review of a single institution experience. Cancer 2008; 112:2440-6.
3. Song E, Kwon S, Youn H, kim S, Shin J and Oh J. Imaging findings of a primary cardiac osteosarcoma arising from the left atrium and mitral posterior leaflet with multiple metastases in a 58 year old women. Iran J Radiol. Inpress 2016:e31757.
4. Ozen D, Ozturk M, Selcukbiricik F, Esatoglu S, Turna Z, Beyaz P, et al. Primary osteosarcoma of the heart : experience of an unusual case. Case Rep Oncol 2013;6:224-228.
5. Mich RJ, Gillam LD, Weyman AE. Osteogenic sarcoma mimicking left atrial myxoma: clinical and two-dimensional echocardiographic features. J Am Coll Cardio 1985; 6:1422-7.
6. Llombart-Cussac A, Pivot X, Contesso G. Adjuvant chemotherapy for primary cardiac sarcomas: the IGR experience. Br J Cancer 1998;78:1624-1628.
7. Vander Salm TJ. Unusual primary tumor of the heart. Smin Thorac Cardiovasc Surg 2000;12:89-100.
8. McCallister HA, Fenoglio JJ. Tumors of the cardiovascular system. Atlas of tumor pathology, series 2. Armed Forces Institute of pathology, Washington DC 1978: 72-96.
9. Putnam JB, Sweeney MS, Colon R, Lanaza A, Frazier OH, Cooley DA. Primary cardiac sarcoma . Ann Thorac Surg 1991; 51: 906-910.
10. Araoz PA, Eklund HE, Welch TJ, Breen JF. CT and MRI imaging of primary cardiac malignancies. Radiographics 1999;19.6 1421-34.
11. Aguilar CA, Donet JA, Galarreta CI. A primary cardiac osteosarcoma: case report and review of the literature. J Cardiol case 2013;729-33.
12. Isayama H, Takeuchi H, Kasao M. A case of primary cardiac osteosarcoma treated with percutaneous transluminal coronary chemotherapy. Shinzo 1995;27: 843-848.