

Recognized by PMDC

CONTENTS

Recognized by HEC

Editorial

1. **Dangue Disaster 2011 in Punjab** _____ 1-6
Dr. Azhar Masud Bhatti

Original Articles

2. **Ovarian Tumors under 20 Years of Age** _____ 7-11
1. Shahida Shaikh 2. Shazia Shaikh 3. Saleem Akhter Shaikh
3. **X-Ray Induced Changes In The Epidermis Of Guinea Pigs, A Morphometric Study** _____ 12-15
1. Furrukh Mustafa 2. Ghulam Mujtaba Kolachi 3. Naheed Khan 4. Shahid Mustafa Memon
4. **Infant Mortality and its Causes in Three Different Districts of Punjab, Pakistan** _____ 16-19
1. Muhammad Saleem Rana 2. Asma Abdul Latif 3. Noreen Zafar 4. Muhammad Abdulla Zafar
5. **Outcome of Early Appendicectomy In Appendicular Mass Versus Conservative Approach** _____ 20-23
1. Muhammad Qasim Mallah, 2. Ubedullah Shaikh 3. Sikander-e-Azam 4. Qambar Ali Laghari
6. **Comparison of Fisurectomy vs. Lateral internal Sphincterotomy in Chronic Anal Fissure Surgery** _____ 24-27
*1. Khush Muhammad Sohu 2. Roshan Ali Solangi 3. A. Malik Sangri 4. G. Hyder Rind
5. S. Qarib Abbas 6. Faiza Abro*
7. **Diurnal variations in the levels of Progesterone during late pregnancy** _____ 28-30
1. Shahnaz Nadir 2. Zafarullah Khan 3. Shahid Jamil 4. Mir Hassan Khan
8. **Frequency and Type of Stroke in Hypertensive Patients** _____ 31-34
1. Rafique Ahmed Memon 2. Amir Hamzo Dahri 3. Shahzad Memon
9. **Complications of Pre-Term Infants In The Neonatal Unit** _____ 35-38
1. Aneela Shaheen 2. Saima Batool 3. M. Arshad Mahmood 4. Muhammad Naeem 5. Abdul Raheem
10. **Alfagin: A herbal product beneficial in Hypercholesterolemia** _____ 39-42
1. Fareeda Islam 2. M. Iqbal Ahsun 3. S. M. Shamim
11. **Desarda Repair - A new method of tension free repair for Inguinal Hernia - Experience of 77 cases at DHQ Hospital Abbottabad** _____ 43-45
1. Asif Saeed 2. Muhammad Nawaz 3. Samson Griffin 4. Saleem Akhtar
12. **Patterns of Refractive Errors at Independent Medical College, Teaching Hospital, Faisalabad** _____ 46-49
*1. Muhammad Ahmed 2. Sohail Rasheed 3. Faheem Ahmed Chaudhry 4. M. Sultan Mahmood
5. Mushtaq Ahmed Cheema*
13. **A hospital based study of frequency, intensity and impact of premenstrual syndrome symptoms on female patients** _____ 50-54
1. Irum Sohail 2. Arifa Bari
14. **Association Between Hypomagnesaemia and Foot Ulcers in Type II Diabetes Mellitus** _____ 55-58
1. Ashok Kumar 2. M. Saleem Faiz Bhatti 3. Anwer Jamli 4. Ubedullah Shaikh
15. **CNS Stimulant Activity of Qurs Saffron (A Herbal Medicine) in Experimental Animal Models** _____ 59-61
1. Naveed Ullah 2. Mir Azam Khan 3. Huma Waqas 4. Afraseyab Ali Shah 5. Ghayour Ahmed 6. Nouman Altaf
16. **Etiology of Hepatomegaly in Balochistan** _____ 62-65
1. Esaa Khan Tareen 2. Haroon, Atif 3. Wasim Baig

Editorial**Dengue Disaster 2011 in Punjab****Dr. Azhar Masud Bhatti**

Addl. Director Health Services, EPI Punjab, Lahore

&
Editor in Chief

The global prevalence of Dengue fever has grown dramatically in recent decades. Dengue fever is now endemic to more than 100 countries. During the past decade Dengue Hemorrhagic Fever Epidemic (DHF) have occurred in China, Sri Lanka, India, Maldives, Bangladesh and Pakistan.

In Pakistan, an outbreak of Dengue fever was first reported in Karachi in 1994. The recent outbreak of Dengue fever in Pakistan confirmed the presence of all four types of Dengue viral infections. Two of these were reported in previous outbreaks in Karachi city while third has been reported in the Lahore outbreak of 2008. In 2011, all four types of Dengue Serotypes have been confirmed in Punjab. In this year, early and heavy monsoon rains in Punjab has provided ideal conditions for Dengue carrying mosquitoes to thrive in stagnant waters. In the last year, the spread of this virus in Pakistan was on the rise during October 10 till November 10, but this year the trend was witnessed earlier.

Dengue is not such a fatal disease as being described and we need to make a collective effort for prevention against it. Dengue was a self limited illness caused by a virus called "Dengue Virus" which was transmitted by a bite of a female mosquito to called 'Aedes Egypti'. More than 1.5 billion people all over the world were at risk of this virus.

According to details obtained through independent sources from different hospitals of Lahore from January 2011 to 24th October 2011, there are 30060 positive Dengue fever cases in Lahore alone. According to Health Department's report, the total number of Dengue patients reported in Punjab from January 2011 to-date has reached 18950 out of which over 16094 were diagnosed in Lahore alone and about 300 deaths occurred due to Dengue fever.

The Health Department said that vector surveillance activities were in progress in Lahore during which 1533 places around houses were examined and 94.4% of them were found vector free. During indoor

surveillance 5902 places were checked out of which 97% places were declared vector free.

To curtail this outbreak, the involvement of the community is as important as the effort being done by the government. There were two aspects of prevention from this disease. First is to focus on the habitat of the mosquitoes that is to eliminate breeding sites to limit the growth of mosquitoes. Second is to prevent mosquito bites with the use of mosquito repellents and use of spray inside the homes in particular. Moreover, it is stressed to wear clothes that can cover our body parts well. Apart from this, one should take effective measures for not allowing stagnant water to be witnessed inside our homes during the monsoon season in particular.

The intensity of Dengue fever started decreasing in 3-4 days and the patient started recovering. The mortalities during the Dengue fever can be a result of some other complications prevailing in the patient being victim of Dengue fever.

You can save a lot of lives by timely referral of DHF patients, if you know and aware of critical signs and symptoms. Complications of Dengue fever can give rise to a more severe form called Dengue hemorrhagic fever (DHF) which is characterized by hemorrhaging blood vessels, pulse pressure less than 25 mm of Hg and may be bleeding from the nose, mouth and internal tissues. The untreated DHF may result in blood vessel collapse, causing usually fatal condition known Dengue Shock Syndrome (DSS).

In the laboratory investigations for Dengue fever, in the complete blood examination (CBC), Hemoglobin, RBCs, TLC and platelets may reduce, ESR and LFTs may rise. In serological profile, for Dengue positive, IgM will be positive in primary infection after three to four days of fever. IgG will be positive on the secondary infection. Dengue virus hampers and sometimes destroys the body's capacity to produce new platelets. The normal body's platelets is 1,50,000 to 2,50,000. A Dengue patients platelets count may have a

steep fall and become lower than 1,00,000 is alarming because it can impede clotting, cause hemorrhages and result in internal and external bleeding.

There has been a dearth of blood donations in the city which was utterly unprepared for an epidemic of this scale. A blood donation is not very easy to obtain. The fear of blood transfusion is baseless. Hospitals even governments once are very particular and strict about hygiene, blood screening for hepatitis, HIV, Syphilis and malaria and they work hard towards safe syringe disposal too.

According to the WHO report of 2009, some 2.5 billion people or two-fifths of the world's population was then (in March 2009) at a risk from Dengue, a figure which might very well have increased during the last two and a half years since the publication of this document though.

The Geneva based WHO, a specialized agency of the United Nations that is acting as a coordinating authority on international public health since 7th April 1948, had further estimated in March 2009 that there might be 50 million Dengue infections worldwide every year of which 2.5% actually die.

The afore-cited WHO report had stated: before 1970 only 9 countries had experienced Dengue hemorrhagic fever (DHF) epidemics, a number that had increased more than fourfold by 1995. The geographical spread of both the mosquito vectors and the viruses has led to the global resurgence of epidemic Dengue fever and emergence of Dengue hemorrhagic fever in the past 25 years. The DHF was first recognized in the 1950s during the Dengue epidemics in the Philippines and Thailand. This is how the encyclopedia Britannica, the oldest and the most scholarly of all encyclopedias in print today, describes Dengue: Dengue, also called breaking bone fever or dandy fever is an acute, infectious, mosquito born fever that is temporarily incapacitating but rarely fatal. Besides fever, the disease is characterized by extreme pain and stiffness of the joints. On Dengue's history the encyclopedia Britannica says the earliest account of Dengue like disease comes from the Jin dynasty (265-420AD) in China. There is also evidence that epidemics of illnesses resembling Dengue occurred in the 17th century.

However three epidemics that took place in the late 18th century mark the arrival of the disease that is today

recognized as Dengue fever. Two of these outbreaks involve an illness decidedly similar in symptoms and progression to Dengue and both occurred 1779-one in Cairo and other in Batavia (now Jakarta) in the Dutch East Indies (now Indonesia) which was reported by Dutch physician David Blyden. The third epidemic happened in 1780 in Philadelphia. American statesman and physician Benjamin Rush, who treated afflicted patients during the Philadelphia epidemic, provided the first clinical description of Dengue in his account of the Bilious, Remitting fever, which was published in 1789. Encyclopedia Britannica published in English language since 1770 at least, further states: because all three 18th century epidemics involved very similar diseases and occurred in port cities, it is believed that Dengue virus was spread from one continent to another via ships. In the early 1900s Australian naturalist Thomas Bancroft identified "Aedes Aegypti" as the carrier of Dengue fever and deduced that Dengue was caused by an organism other than a bacterium or parasite. During World War II, Dengue emerged in South East Asia and rapidly spread to other parts of the world, inciting a pandemic. In the 1950s hemorrhagic Dengue appeared in South East Asia, where it became a common cause of death among children in the 1970s. The Encyclopedia Britannica still has a bit more to say about Dengue: the serotypes continued to spread on a pandemic level, eventually reaching areas of South and Central America, Cuba and Puerto Rico where in 1977 an epidemic lasting from July to December some 355,000 people. In the following decades the increasing incidence of Dengue particularly DHF persisted.

Tiny mosquitoes have claimed the lives of some of the most formidable human of all times sending a few to their graves and rendering others bed ridden, a casual scroll through history reveals. Nimrod, the mighty King of Babylon during the times of Prophet Hazrat Ibrahim or Abraham (A.S), had perished after a mosquito had entered his nostril and ultimately the membrane of his brain on Divine orders.

The "Qisas Al-Anbiya" (Tales or the stories of the prophets adapted from the Holy Quran and other Islamic literature) which was authored by Imam Imad-din Abdul Fida Ismail Ibn Kathir, states; As reported from Ibn-e-Abbas, He said that Allah has sent a mosquito to Nimrod that stung his lip, and when he tried to catch it, it flew and entered his nose. Nimrod

tried to get rid of it, but all in vain as the mosquito finally found way into his brain. God tortured him for 40 nights and then finally destroyed him.

Abdullah Ibn-e-Abbas was a paternal cousin of Hazrat Muhammad (PBUH). He is well regarded by Muslims for his expertise in the Islamic Sunnah and Tafseer-ul-Quran or the Holy Book's exegesis. It is noteworthy that Umm al-Fadl Lubaba, the mother of Ibn-e-Abbas, was the second woman who had converted to Islam. The famous Greek conqueror Alexander the Great (356 BC-323 BC) may have died after being bitten by a mosquito. About Alexander's death, the National Geographic website states "Alexander the Great likely died of it,

At least three American Presidents-Messrs George Washington (1732-99), Abraham Lincoln (1809-65) and Ulysses Grant (1822-85) had also suffered from the same ailment during their life times. George Washington suffered from Malaria, as did Abraham Lincoln and Ulysses Grant. In the late 1800s, Malaria was so bad in Washington DC that one prominent physician lobbied-unsuccessfully to erect a gigantic wire screen around the city. A million Union Army casualties in the US Civil War are attributed to Malaria and in the pacific theatre of World War II casualties from the disease exceeded those from combat. Some scientists believe that one out of every two people who have ever lived have died of Malaria.

The World Malaria Report 2010 of WHO that there are more than 225 million cases of this disease per year-killing around 781000 or 2.23% of the total worldwide deaths. The Sydney Morning Herald (September 26, 2010) reads "Malaria is contracted by more than 250 million people a year and kills nearly 1 million".

Experts from different universities joined the Punjab University's Dengue Research Group formed to carry out research and curb Dengue virus. Vice Chancellor, University of the Punjab, Prof. Dr. Mujahid Kamran presided over third meeting of the group, which was attended by experts from University of Health Sciences (UHS), University of Veterinary and Animal Sciences (UVAS), Mayo Hospital, Fatima Memorial System and FC College University.

The experts said wrong information regarding Dengue fever has been conveyed to people. Prof. Dr. Aslam Khan of UHS said female Dengue mosquito bit humans from morning to evening and 2pm was its peak

time. After sucking blood, the female mosquito needs to lay eggs. He said crevices in trees and other such locations were ideal places for this. He said the Dengue mosquito did not rest inside homes. He said the Dengue virus was reported in the region before 1947 but after 1947, migrants used empty bottles and such other things which stopped its breeding. An American Dr. David Allan imported this virus from East Pakistan. In Southeast Asia, this virus came through the import of tyres.

The experts from Government College University Zoology Department have recommended for biological control of Dengue, observing that fumigation can be used as emergency measures but they are not the permanent solution.

"Mosquitoes after sometime develop resistance against the chemicals used in fumigation and sprays," said Zoology Department Chairperson Prof. Dr. Nusrat Jahan while addressing the university's faculty members on "prevention and control of Dengue fever". The GCU Chief Zoologist said that biological control of "biocontrol" was the use of natural enemies to manage mosquito population with a minimum risk to humans, wildlife and the environment. The use of biological agents includes predatory insects and other invertebrates, such as copepods, parasitic nematodes, larvivorous fish and microbial entomopathogens including *Bacillus thuringiensis*. GCU Chief Zoologist further said after the first outbreak, a research was started in the varsity using many biological control agents and results were evaluated on the basis of lethal concentration, larval mortalities and pupae / adult emergence both in laboratory and field bioassays.

Chief Minister Punjab Muhammad Shahbaz Sharif has directed that establishment of an environmental police force in the province should also be considered so that the plan chalked out to permanently eliminate Dengue virus can be implemented effectively.

He was presiding over a meeting of the special committee against Dengue virus. Elected representatives, chief Secretary, administrative secretaries of various departments and experts attended the meeting. The Chief Minister appreciated the experts from Sri Lanka and Indonesia and appreciated efficiency of the health secretary. The chief minister said that efforts of health department and public awareness campaign had greatly helped in apprising the

people of preventive measures against Dengue virus. He said that the campaign for the eradication of the larvae of Dengue mosquito at virus places in the light of the report of surveillance committee was also yielding positive results.

He directed the chairman of the town emergency committees to also visit trust hospitals regularly besides the government hospitals and submit a daily report regarding medical facilities available in the hospitals. He directed that cleanliness arrangements in hospitals should further be improved.

The Chief Minister also praised the measures taken by the chairman of the surveillance committee, agriculture secretary, regarding detection of Dengue larvae at different places and said that it helped in eliminating virus.

He said that chairman of the surveillance committee should also visit different hospitals to ensure complete eradication of the larvae from hospitals. He directed that documentary film regarding detection of Dengue larva and its eradication should also be produced to create awareness in the people.

He said the assembly members should also undertake checking of tube wells in their respective areas and make arrangement to drain out stagnant water and immediate repair of water leakage, If found anywhere and submit a report to him.

He said that it had also been decided to enforce regulation to check spread of viral diseases under which it would be binding on all citizens to take all such measures as were necessary to control the growth of Dengue mosquito and the outbreak of the epidemic. In response to a proposal submitted in the meeting he directed the authorities concerned to consider establishment of an environmental police.

The chief minister said that activation of primary healthcare system was of vital importance as it would not only result in availability of quality health facilities to the people at their doorstep but would also reduce the rush of patients from big hospitals. He directed the additional chief secretary to submit a plan within a few days to activate primary healthcare system. He said that Ulema should also inform the people in the Friday sermons about preventive measures against Dengue virus and stressed upon them to play an active role in the ongoing campaign for Dengue eradication.

He also issued instructions to the authorities concerned for benefiting from the latest technology for effective monitoring of the measures for controlling Dengue virus.

He said a research cell for eradication of Dengue virus and other diseases. He said the special research cell, besides taking steps for eradication of Dengue virus should also pay attention to developing an anti Dengue vaccine. He said no anti Dengue vaccine had been developed in the world so far and hoped that with the blessing of Allah Almighty and hard work of experts, Pakistan might become the first country to develop such a vaccine."

The Gallop Pakistan conducted a survey among a sample of 2689 men and women in rural and urban areas of all four provinces in the country from September to October. A huge majority of 86% Pakistanis have expressed satisfaction over Punjab Chief Minister Shahbaz Sharif's efforts in fighting against the Dengue epidemic.

Punjab Government issued Punjab Prevention and Control of Dengue (Temporary) Regulations, 2011 on the instructions of Chief Minister Punjab with immediate effect. The prevention and control of Dengue is the mutual responsibility of Government and its citizens. Government of Punjab has enforced "Punjab Prevention and Control of Dengue (Temporary) Regulations 2011" which will remain effective till November 30, 2011. Under this law, citizens are bound to carry out specific measures at their houses, shops, workshops, factory etc, to overcome the outbreak of Dengue Epidemic. Important highlights of this act are the following.

1. Immediately remove any useless and waste material such as empty bottles, lids, tyres, shopping bags, vehicles spare parts, plant pots etc.
2. Remove any obstacle in the water drainage, gutters etc and keep them clean. Do not let water stagnate anywhere. Fill the pits and low lying areas with sand or any such substance.
3. Take special care of home appliances like room cooler, air conditions and refrigerators. Do not let water accumulate to impede mosquito breeding.
4. Remove, uproot or trim water plants and any other plant, bush or shrub which may promote the breeding of mosquito.

5. Drain the water in swimming pool, ponds or any artificial collection of water at least twice a week.

6. Keep the drinking pot and utensils of animals and bird clean.

7. Administration of educational institutes should carry out insecticidal fogging or spray in the premises. They should educate students regarding measures to prevent Dengue and safety measures such as full sleeves, socks and insect repellants.

8. Administration of hospitals and laboratories should segregate the Dengue patients from other patients and use safety measures for them. They should immediately report to Government or Health Inspector in case if any patient is found to be suffering from Dengue fever.

9. Health Inspectors have been appointed to oversee the proper cutting of plants, removal of waste material, oversee cleanliness and to penalize all violators of this law. Cooperating with Health Inspectors and officials is also part of this law.

10. Legal prosecution can be carried out against individuals who violate the law, do not comply or cause any obstruction in its implementation or effectiveness. Health experts had inspected a number of tyre shops in different markets of the City and found a huge quantity of Dengue mosquito larva inside the shops. Later, they asked the CDGL officials to immediately evolve a strategy to eliminate the larva breeding site present in shops.

Presently there are around 2,567 tyre shops and godowns in all the nine towns of the city. Out of which 254 tyre shops are in Aziz Bhatti Town, 472 in Data Ganj Bakhsh Tow, 199 in Gulberg Town, 120 in Iqbal Town, 236 in Nishtar Town, 363 in Ravi Town, 220 in Samanabad, 505 in Shalimar Town and 198 shops in Wahga Town.

Every tyre shop and godown owner must have to get licence for his shop after paying fee to the CDGL within next seven days. The tyre shops and godowns will be sealed by the district government which will not have the valid licence and registration number from the CDGL. Strict action will be taken against the tyre shops owners on violation.

As unlikely as it may sound, the *Aedes Egypti* mosquito has done several things for Pakistanis and Lahoris in particular for which we may one day be actually grateful.

It has laid bare the sorry state of our health apparatus. A few thousand cases have completely paralyzed the health system, because all of them went directly to tertiary care hospitals. First and second level care facilities where the major burden of the epidemic should have been managed were absent or ineffective. Every individual would be accountable and accessible to the citizens are carrying out essential civic functions such as solid waste disposal, water drainage, cleanliness, management etc.

The mosquito killing effect is transitory, variable in its efficiency as the aerosol may not penetrate indoors to micro-habitats where adult mosquitoes are sequestered and the procedure is costly and operationally difficult. Regular monitoring of the vectors' vulnerability to insecticides is essential to switch to a more suitable alternative when required. Hence, active monitoring and surveillance of the natural mosquito population should escort control efforts to establish effectiveness. Small mosquito-eating fish have also been used to reduce mosquitoes.

There is need of an integrated vector control strategy. The mosquito sprays are not sufficient as we need a multiple approach for mosquito eradication such as biological control, larvicide, mass awareness, quaranting for patients and travel advisory. Guppy fishes are the best agent for the biological control of Dengue mosquito.

There is also a need for larger clinical studies in Pakistan and other south Asian to better understand the range of infections, endemic patterns and genetic susceptibility of different populations to Dengue virus.

The Government must involve all relevant institutions to launch a concreted research programme on the basis of this year's Dengue epidemic data of patients and deaths and areas to devise a comprehensive strategy to combat the disease during the next season. Preventive and control measures against the Dengue virus must start in January next year to avert the crises in the season ahead, different strain of the virus could potentially play havoc with the live of the people, as a large majority of the people were already affected with a strain of the virus this season.

The Government may establish filter clinics at primary and secondary care level to lesson the load of patients on tertiary care hospitals to provide quality diagnostic and treatment facilities to patients efficiently.

Dengue was a medical as well as big social problem and whole society should play its effective role in checking it. Dengue was not an infectious disease but curable. Sri Lankan experts had a vast experience of fluid management of Dengue patients and local experts had an opportunity; to improve their expertise in the field due to which better patient management was being carried out in the Government hospitals and to avoid the Dengue epidemic next year. Every citizen and institution would have to work hard in an efficient way. The Health Department must decide to enhance the capacity building of private practitioners and family physicians regarding Dengue and a training programme should be launched in all medical colleges of the Punjab. The main objective for holding the training programme for the GPs and family physicians to enhance their professional capability and capacity building for the treatment of Dengue patients at local level and patients with symptoms of hemorrhagic fever must immediately be referred to any secondary and tertiary care hospital so that the precious human lives could be saved by providing timely medical care.

Under the Dengue Control Regulations 2011, it should be mandatory for every doctor to get training about Dengue and after this Health Department would issue a certificate to all the doctors participating in the programme.

The research was in progress on development of Dengue virus vaccine and it might be available till year 2014.

Original Article**Ovarian Tumors under 20 Years of Age****1. Shahida Shaikh 2. Shazia Shaikh 3. Saleem Akhter Shaikh**1. Asstt. Prof., OBS Gynae Unit-I 2. Asstt. Prof., OBS Gynae Unit-II 3. Asstt. Prof. of Pathology,
Chandka Medical College, Larkana**ABSTRACT****Purpose:** To analyze the cases of Ovarian Tumors in less than 20 years of age and to know its outcome in same patients.**Study Design:** A Case Series Descriptive Study.**Place and Duration of Study:** This study was conducted at Sheikh Zaid Women Hospital, Gynaecology Unit II, Chandka medical college Larkana over the of period of two years from December 2007 to December 2009.**Patients and Methods:** Over the period of 2 years, a total of 30 patients with ovarian tumors of less than 20 years age were studied. Patients with more than 20 years of age were excluded.

All the patients received as out patient department except 4 cases, were admitted through emergency. Detailed history taken to know their presentation and all the patients were investigated for complete blood picture, ESR, Random Blood Sugar, Urine detailed report, Urea, Creatinine, Serum Electrolyte, LFTs, Ultrasound and X.Ray Chest. In some patients IVP, CT scan and Serological markers e.g. CA-125 were done. Management done in all patients noted and statistically analyzed.

Results: In two years period 30 patients under 20 years of age reported. Mean age of presentation was 15 ± 2 years. Out of 30 patients 25 (83.33%) had benign ovarian tumors while 5 patients only (16.66%) had malignant tumors.

Of the benign ovarian tumors mature teratoma were 10(40%), serous cyst adenoma were 5(20%), mucinous cyst adenoma were 3 (12%), endometriotic cysts were 3 (12%), corpus luteal cysts were 3 (12%), para-ovarian cyst was 1 (4%). Of the malignant variants immature teratoma was 3 (60%), dysgerminoma was 1 (20%) and endodermal sinus tumor was 1 (20%).

Most of patients had benign ovarian tumors e-g germ cell tumors . Almost in all of the patient's diagnosis was confirmed by laparotomy and histopathology. No complication was encountered peroperatively and post operatively.

Conclusion: Patients, less then 20 years of age, had mainly benign ovarian tumors, and were germ cell tumors. For benign tumors adhesion prevention strategies should be used. Surgical intervention should as much as possible be directed towards preservation of ovarian tissue.**Key Words:** Ovarian Tumors, Ovarian tissues, Germ cell tumor.**INTRODUCTION**

Female genital tract represents ovarian tumors as the most frequent tumors of it through the first twenty years of female life.¹ The ovarian tumors report just about one (1%) of all tumors of this tender age children and adolescents. It has been noted in literature that 30% of all ovarian neoplasm occurring during childhood and adolescence are malignant and although malignant variants of pelvic tumors are uncommon but less than 5% of ovarian malignancies occur in this age group². Types of ovarian tumor particular to child and adolescence patients includes germ cell and granulose cell tumor³. Benign neoplasm are the most common ovarian masses under 20 years of age^{3,4,5}. Commonest benign ovarian tumors are mature cystic teratoma (dermoid cystic) and followed by cystadenoma^{5,6}. Among the malignant ovarian tumors, dysgerminoma and endodermal sinus tumor are more common in this age group^{6,7,8,9}. Exact incidence in Pakistan is not known but it is the 4th common cancer among female of

Pakistan (if including all age groups)¹⁰. About 15% of the patients with malignant ovarian tumors are asymptomatic at the time of diagnosis¹¹. Tumors markers are extremely useful in the differential diagnosis, and to follow the patient's response to therapy and monitor for recurrence of diseases^{6,7,8,9}. Knowledge of features of the disease which relate accurately to prognosis and survival could be helpful in manage .As ovarian tumors manifest a wide spectrum of morphological and histological types of primary ovarian tumor this study was under taken to study the types of ovarian tumors and outcome of those in women less than 20 years of age.

PATIENTS AND METHODS

This study was carried out in the department of Gynae Unit-2 Sheikh Zaid Women Hospital, Chandka Medical College Larkana from December 2007 to December 2009. 30 patients under 20 years of age of ovarian tumor either benign or malignant included in this study after informed consent. Each patient was evaluated with

detailed history and thorough physical, systemic and local examination. Investigation included blood complete picture, Random Blood Sugar, liver function test, blood urea and creatinine were done. Serological markers e-g CA-125, was done in 5 patients, it was not significantly high. Ultrasound was used to detect the ovarian tumors in almost all the cases to see the site and size of tumor. Diagnostic laparoscopy was not done in any of these patients. X-Ray Chest was done in every case for preoperative anaesthesia fitness.(No abnormality was detected either). IVP was done in 4 patients in whom pre-surgical suspicious of malignant ovarian tumors was made on clinical and U/S basis and was found normal. Planning of management was made on fertility of patients and stage of tumor. The management options were surgery and chemotherapy. Type of surgery was decided pre as well as postoperatively. In suspected benign tumors where adjacent structures were not involved or no vascularization or adhesion, in those cases conservative surgery was done. In malignant tumors ascitic fluid sent for cytology and debulking surgery was done. Findings were noted on check list. Figo classification was used to stage the tumor. In cases of malignant tumors patients were sent for chemotherapy post operatively. Patients were counseled about follow up visits till one year postoperatively

RESULTS

Thirty patients were analyzed from December 2007 to December 2009.

In our study mean age of presentation with ovarian tumor was 16 ± 2 years. In this study only three patients were married and they were nulliparous, 85% patients presented usually with pain in abdomen, distention of abdomen due to mass, and menstrual disturbances. Retention of urine and acute abdomen made the emergency in just 15% patients.

Table-No.1: Types of Tumor in less than 20 years of age.(n=30)

S. No	Types of Tumor	No. of Cases	%
1	Benign	25	83.33%
2	Borderline	0	--
3	Malignant	5	16.66%

Of these 30 cases, benign ovarian tumors were commonest than malignant as shown in table No. I. Of the benign ovarian tumors, mature teratoma were seen in 10(40%) patients followed by, serous cyst adenoma, mucinous cyst adenoma, endometriotic cysts and others as in table No.2. Again among malignant tumors immature teratoma overthrown seen in 3 patients compared to dysgerminoma and endodermal sinus

tumor confirmed in one each patient also tabulated in table II with the percentage.

Table No.2: Histopathological typing of ovarian tumors

S. No	Types of Tumor	No. of Cases	%
Benign			
1	Mature Teratoma	10	40%
2	Serous cyst adenoma	5	20%
3	Mucinous cyst adenoma	3	12%
4	Endometriotic cyst	3	12%
5	Corpus luteal cyst	3	12%
6	Para ovarian cyst	1	4%
Malignant			
7	Immature Teratoma	3	60%
8	Dysgerminoma	1	20%
9	Endodermal Sinus Tumors	1	20%

Table No.3: Operative procedures performed.

S. No	Types of Surgery	No. of Cases	%
1	Cystectomy	4	16%
2	Cystectomy+Oophorectomy	6	24%
3	Salpingo-Oophorectomy	10	40%
4	Bilateral cystectomy	2	8%
5	Drainage of Endometriotic Cyst + Reconstruction of ovaries.	1	4%
6	Therapeutic ultrasound guided drainage of cyst	1	4%
7	Salpingo – Oophorectomy with wedge resection of other ovary.	1	4%
8	Debulking Surgery TAH with BSO + Omentectomy + Appendectomy.	3	60%
9	TAH with BSO	2	40%

Almost in all of the patient's diagnosis was confirmed by laparotomy and histopathology. Therapeutic ultrasound guided aspiration of cyst was done in one patient who was a diagnosed case of simple ovarian cyst on the basis of ultrasound. Otherwise laparotomy was done in all the cases. Most of the patients had benign ovarian tumor as evaluated intraoperatively and treated by conservative surgery. Unilateral cystectomy was done in 4 (16%) and bilateral cystectomy was done in 2 (8%) patients. Reconstruction of residual ovary done in above cases. Unilateral oophorectomy and cystectomy was done in 6 (24%) patients. Drainage of endometriotic cyst and reconstruction of ovaries was done in 1 (4%) patient. Unilateral salpingo/oophorectomy with wedge resection of other ovary was done in 1 (4%) patient. Total abdominal

hysterectomy was done in 2 (40%) patients as primary procedure in one woman of 18 years with bilateral ovarian involvement, ruptured capsule and moderate ascites. Debulking surgery (TAH with BSO + Omentectomy + Appendectomy) was done in 3 (60%) cases further detail in Table No. 3. Operative findings were noted on tick list. Frozen section facility is not yet available in our hospital. So surgery was decided at the time of laparotomy and then further management was decided on histopathological report. All of the patients with benign ovarian tumor were advised for 12 months follow-up and only 20 patients came for regular follow-up and further evaluation. Patients with malignant ovarian tumors sent for chemotherapy. 2 patients died due to recurrence of malignancy of endodermal sinus tumor and Dysgerminoma. 2 patients were in good condition after receiving 3 pulses of chemotherapy and 1 patient lost follow up. Mortality rate was difficult to assess because of non co-operation of the patients for follow-up. Patients are mostly irregular due to lack of knowledge and poverty.

Second look operation could not be done in any of the patients with malignant disease. Two of the patients who had regular follow up did not show any residual disease on ultrasound.

None of the patients showed complications related with surgery.

DISCUSSION

Ovarian lesion are unusual in young age group.¹ Presenting with mass abdomen or vague pain in young girls is definitely worrying sign for parents and partners. As malignant granulosa cell tumor of ovary can also present as precocious puberty which is socially unacceptable. For girls and young women another issue arises regarding their ability to conceive and carry a pregnancy in the future once they are treated.

Presentation of ovarian tumor has been found different in various studies and make the diagnosis difficult as Pomeranz et al¹² reported that 38% of such patients of ovarian lesions had preliminary diagnosis of appendicitis and appendectomy was also carried in our 3 cases along with debulking due to associated pathology of appendices.

In our series almost 85% patients presented with pain in abdomen, pelvic pain, distension of abdomen due to mass and menstrual disturbances except four patients who came through emergency with acute abdominal pain and retention of urine and this has also been reported in study done at Lahore¹³ While Lind fort's case series pain was the main presenting complaint followed by abdominal distension and torsion¹⁴

Preoperative evaluation of all cases is usually done best with ultrasound as benign and malignant tumors have

specific features. Computed tomography facility is not available at our setup so only tumor markers were sent in suspected malignant cases. Transvaginal ultrasonography has been recommended by the national Institute of Health as a preferred mean of diagnosis¹⁵ but in current study all scans were transabdominal. Doppler U/S has also been found to be helpful in suspicious of malignancy¹⁵

Tumours of ovary are classified in into epithelial tumours, germ cell tumours, sex cord-stromal cell tumours, and metastatic tumour according to the cell of origin.¹⁶

In our study we found (83.33%) ovarian tumors were benign and (16.66%) were malignant and this shows a relationship with the data from European countries where benign ovarian tumors were in the range of 75-80%.¹⁷ and also another study done in India by Pilli et al¹⁸ had in same range data where they showed that 75.2% ovarian tumors were benign. Our figures are almost same to study conducted at Nepal.¹⁹ Lind forte presented review of 81 cases of ovarian tumors where he found 35% of cases as malignant. Huffman²⁰ study reported malignancy in 30% of all of (999) his studied cases while Breen and Maxson also had seen malignant cases up to 27% tumors in children and adolescents were malignant after concluding their finding in 1309 cases.^{21, 22} In another series from Nepal malignancy rates have varied from just 10%.¹⁹ In the study conducted at our setup among 30 studied patients 16.66% of cases were malignant may be because of small sample size.

As far as histological features are concerned like international data germ cell tumors and sex cord stromal tumors were preponderate in adolescents.^{21,23} Identical results are seen in our study, where we also found prevailing group as germ cell tumor about 44% and second variety seen as serous cystadenoma. However this figure was 59.2% in study carried in Pakistan by Ahmad et al.²⁴ Another study also uncovered the germ cell tumor as commonest tumors in young age group followed by serous cystadenoma.¹⁹ Among malignant tumors again immature teratoma and dysgerminoma represented main diagnosed pathology also found same results in various studies.^{24,25} Of the various treatment modalities available for ovarian tumor, primary surgery with complete removal of tumor burden can be considered as potentially curative. Gentle tissue handling is necessary and scrupulous hemostasis and adhesion prevention approaches are definitely required for fertility preservation.

Initial careful surgical staging is important for selection of appropriate subsequent therapy. Intraoperative decision making is crucial in preserving reproductive function in girls and young women with malignant ovarian tumors. While such tumors are rare,

gynecologists should be familiar with the natural history and current management. The judicious use of surgery followed by chemotherapy remained the mainstay of treatment in majority of our patients.. Outcome of our patients was also comparable with international studies.^{19,24,25} The evolutionary development and fine-tuning of combination chemotherapy have resulted in the cure of a high percentage of patients with chemosensitive tumors, such as malignant ovarian germ-cell tumors. Post operative morbidity and mortality remained quite insignificant after surgery in our study.

CONCLUSION

In women less than 20 years of age benign germ cell tumors are common, which are easily managed by surgical measures usually without complication. Malignant germ cell tumors are common in this age group but mostly diagnosed at advanced stage. Early diagnosis is key factor to improve the prognosis and need a proper screening program in this age group even with yearly ultrasound. Ovarian tumors under 20 years of age were mainly found in un-married and nulliparous women's. So that conservative surgery to retain the uterus and contralateral ovary should be preferred. It is desirable to embark upon a second look surgery if final pathology reveals a malignancy rather than proceed with radical surgery.

REFERENCES

- Marchetti M, Padovan P, Frances M. Conservative Surgery and quality of life. *EUR-J Gynaecol* 1999;20(2):124-6.
- Breen JL, Maxson WS. Ovarian tumors in children and adolescents. *Clin Obstet Gynecol* 1977;20:607-23.
- Ind T, Shepherd J. Pelvic tumors in adolescence. *Best Pract Res Clin Obstet Gynaecol* 2003; 17: 149-68.
- Imai A, Furui T, Tamaya T. Gynecologic tumors and symptoms in childhood and adolescence; 10-years' experience. *Int J Gynaecol Obstet* 1994; 45:227-34.
- Piippo S, Mustaniemi L, Lenko H, Aine R, Maenpaa J. Surgery for ovarian masses during childhood and adolescence: a report of 79 cases. *J Pediatr Adolesc Gynecol* 1999; 12: 223-7.
- Peeyananjassri K, Chichareon S, Wootipoom V, Buhachat R, Tochareonvanich S. Ovarian tumors in children and adolescents in Songklanakarind hospital: A 12-year review. *Songkla Med J* 2002; 20: 271-5.
- McCall ML, Keaty EC, Thompson JD. Conservation of ovarian tissue in the treatment of carcinoma of the cervix with radical surgery. *Am J Obstet Gynecol* 1958;75:590- 600.
- Anderson B, La Polla J, Turner D, et al. Ovarian transposition in cervical cancer. *Gynecol Oncol* 1993; 49:206-14.
- Lovvorn HN, III, Tucci LA, Stafford PW. Ovarian masses in the pediatric patient. *Aorn J* 1998; 67: 568-76.
- Parveen S, Ilyas N, Asghar S. Pattern of care for ovarian cancer. *J Med Sci April- June 1999; 15(2): 9-15.*
- Rashid S, Sarwar G, Ali A. A clinico Pathological study of ovarian cancer. *Mother And Child* 1998;36: 117.
- Pomeranz AJ, Sabnis S. Misdiagnoses of ovarian masses in children and adolescents. *Pediatr. Emerg. Care*.2004; 20(3):172-74.
- Sohail R, Tariq S. Study of ovarian tumor in young girls. *Professional Med J Mar 2011;18(1):41-45.*
- Pfeifer SM, Gosman GG. Evaluation of adnexal masses in adolescents. *Pediatr Clin North Am* 1999;46:573-92.
- Sasaki H, et al. Follow up of women with simple ovarian cysts detected by transvaginal sonography in Tokyo metropolitan area. *Br J Obs Gyn* 1999;415-20.
- Kwok KKM, Loke TKL, Hui JPK, Lai MHY, Chan JCS. Malignant Mixed Germ Cell Tumour of the Ovary in a 10-year-old Girl .Case Report *J HK Coll Radiol*. 2008;11:92-95
- Goldstein DP, Laufer MR. Benign and malignant ovarian masses. In: Emails SJ, Laufer MR, Goldstein DP, editors. *Pediatric and adolescent gynecology*. Philadelphia: Lippincott-Raven; 1998.p.221-23
- Pilli GS, Suneeta KP, Dhaded AV, Yenni VV. Ovarian tumors: a study of 282 cases. *J Indian Med Assoc* 2002;100: 420,423-4, 447.
- Kayastha S. Study of ovarian tumours in Nepal Medical College Teaching Hospital. *Nepal Med Coll J* 2009;11(3):200-202.
- Huffman JW. *The Gynaecolgy of children andadolescents*, 3rd ed. Philadelphia: Sanders; 1968.p.173-175
- Warner BW, Kuhn JC, Barr LL. Conservative management of large ovarian cysts in children: the value of serial pelvic ultrasonography. *Surgery* 1992;112:749-55.
- Schultz KA, Sencer SF, Messinger Y, Neglia JP, Steiner ME. Pediatric ovarian tumors: A review of 67 cases. *Pediatr Blood Cancer* 2005;44:167-71.
- Cass DL, Hawkins E, Brandt ML, Chintagumpala M, Bloss RS, Milewicz AL, et al Surgery for ovarian masses in infants, children, and adolescents: 102 consecutive patients treated in a 15- year period. *J Pediatr Surg* 2001;36:693-9.

24. Choudry A, Bangash N, Malik A, Choudry H. adolescent ovarian tumors: a clinicopathological review of 15 cases. J Ayub Med Coll Abbottabad 2008;20(4)18-21
25. Hanprasertpong J, Chandeying V. Gynecologic Tumors during Childhood and Adolescence. J Med Assoc Thai 2006;89 Suppl. 4

Address for Corresponding Author:

Shahida Shaikh
Assistant Professor,
Banglow No:9 Type III New Staff Colony
Chandka Medical College Larkana
Mobile: 0333-7543377

Original Article

X-Ray Induced Changes in the Epidermis of Guinea Pigs - A Morphometric Study

**1. Furrukh Mustafa Memon 2. Ghulam Mujtaba Kolachi 3. Naheed Khan
4. Shahid Mustafa Memon**

1, 2 & 3. Assistant Professors of Anatomy, DMC (DUHS), Karachi 4. Asstt. Prof. of Pathology, LCM&D, Karachi.

ABSTRACT

Objective: Measurement of changes in the thickness of epidermis of different locations in guinea pigs after single dose X-ray irradiation.

Study Design: A prospective experimental study.

Place and Duration of Study: Department of Anatomy, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre Karachi from 2008 to 2009.

Materials and Methods: Thirty animals were taken and divided into two groups which were subdivided into three subgroups containing five animals each, according to the time of sacrifice i.e. 48 hours, 15th day and 45th day respectively. A single whole body x-radiation in a dose of 5 Gy. Animals were sacrificed under ether anaesthesia after completion of their respective period. Tissues were processed and 4 to 5 micron thick paraffin embedded sections were cut, and stained with H&E.

Results: Desquamation and decrease in thickness of epidermis was present after 48 hours which shows highly significant result when compared to control ($P < 0.001$). After wards progressively increase in hyperkeratinization was noted after 15 days which is nonsignificant ($P > 0.05$) when compared to control. After 45th day proliferation of basal cells occurred which increased the thickness of epidermis near to control.

Conclusion: The study concludes that x-radiation produces deterministic epidermal changes in all three sites i.e. face, abdomen and back of guinea pigs.

Key Words: X-ray radiation, Gy, Epidermis, hyperkeratization.

INTRODUCTION

Since the discovery of x-rays at the end of 19th century and till now their effects attract much attention. This interest is largely explained by the fact that humans (first of all skin) are exposed to this radiation during medical examination^{1,2,3}.

X- Irradiation (XRI) can affect both normal and neoplastic cells especially, rapidly growing one such as epidermal cells⁴.

X-rays are widely used for imaging and for therapeutic purposes and our knowledge about their possible injurious effects on skin is incomplete. Clinically x-rays can produce erythema, as well as dry and moist desquamation. Morphologically x-rays can produce epidermal loss, crystalolysis, cytoplasmic vacuolization, appearance of euchromatic nuclei and alter microvasculature, causes hyperkeratization, redistribution of biometals as well as basal and squamous cell carcinoma. The type and extent of these changes depends on dose, duration and frequency of x-rays⁵.

Skin injury is the deterministic effect of radiation, once the threshold dose has been exceeded the severity of radiation at any point on the skin increases with dose; threshold will vary some what among individuals⁶.

Radiation will continue to increase in importance in the diagnosis and the treatment of diseases, for this reason considerable emphasis is placed on biological basis for the use of radiation in treatment of person with malignant tumor and on the consequence to the host of radioisotopes administered therapeutically or diagnostically⁷.

Radiation induced injury is recognized for past decade as potential complication of fluoroscopically guided intervention⁸.

MATERIALS AND METHODS

This study was conducted in the department of anatomy, BMSI JPMC Karachi. Thirty adult male guinea pigs weighing 400 to 450 grams were taken from animal house of BMSI JPMC. Animals were kept under observation for one week before study to asses their behavior, and activities and were maintained on laboratory diet. Animals were divided into two groups A & B each group containing 15 animals. Group 'A' served as control. Animals were sacrificed after 48 hours, 15th and 45th day after receiving single whole body x-radiation in a dose of 5 GY at Karachi institute of radiotherapy and nuclear medicine, Pakistan atomic energy KIRAN Hospital.

All the guinea pigs were sacrifice at their respective time of treatment under ether anaesthesia. The skin of the guinea pigs was shaved and skin fragments (size of 1 cm square) from face, back and abdomen at 48 hours, 15th and 45th day were collected. Skin fragment was fixed in 10% formalin for 12-18 hours. Tissues were processed in ascending strength of alcohol and cleared in xylene and infiltrated and embedded in paraffin. 5 micron thick vertical sections were cut at rotatory microtome and floated in hot water bath and placed on glass slide. Sections were fixed in 10% formalin. Stained with H&E for morphology of skin. Statistical analysis was done on computer soft ware SPSS, student 't' test was applied and the value $P < 0.05$ was considered significant.

RESULTS

The observation and their results on the gross and light microscopic examination were recorded. The histological observations were based on the study of 4-5 micron thick paraffin embedded sections, stained with Haematoxylin and eosin.

Table No.1: Mean Thickness of Epidermal of Face of Guinea Pigs

Groups	Subgroups	Thickness of epidermis of face in micron at the sacrificial time		
A (Control)	(n=15)	48 hours	15th day	45th day
		--	--	40.32±0.32
		--	--	
B (Treated)	B1(n=5)	21.36±0.32		
	B2(n=5)	--	39.92±0.26	
	B3(n=5)	--	--	40.28±0.47

Control group A:

In gross examination, face, abdomen and back was observed in all the animals. Skin was covered by white brown and gray hair but at the back was comparatively thick. Skin fragment were collected at 45th day after single whole body x-radiation. Mean thickness in epidermis in face was $40.32 \pm 0.32 \mu\text{m}$ as shown in table 1. The mean thickness of epidermis in Abdomen was $40.08 \pm 0.17 \mu\text{m}$ as shown in table 2. The mean thickness of epidermis was in Back was $58.04 \pm 0.29 \mu\text{m}$ as shown in table 3.

Treated group B:

Group B1: The animals of group B1 were ill looking, the skin of the face, abdomen and back appeared thin and dehydrated, patches of alopecia of varying sizes were scattered all over the skin. Skin showed varying degree of hyperemia and showed number of layers which were reduced to half and there was desquamation of surface epithelium.

Table No.2: Mean Thickness of Epidermal of Abdomen of Guinea Pigs

Groups	Subgroups	Thickness of epidermis of abdomen in micron at the sacrificial time		
A (Control)	(n=15)	48 hours	15th day	45th day
		--	--	40.08±0.17
		--	--	
B (Treated)	B1(n=5)	29.80±0.38		
	B2(n=5)	--	49.36±0.47	
	B3(n=5)	--	--	48.94±0.73

Table No. 3: Mean Thickness of Epidermal of Abdomen of Guinea Pigs

Groups	Subgroups	Thickness of epidermis of back in micron at the sacrificial time		
A (Control)	(n=15)	48 hours	15th day	45th day
		--	--	58.04±0.29
		--	--	
B (Treated)	B1(n=5)	29.80±0.38		
	B2(n=5)	--	57.84±0.41	
	B3(n=5)	--	--	57.76±0.26

The mean thickness of epidermis in, face was: $21.36 \pm 0.32 \mu\text{m}$ as shown in table 1. The mean thickness of epidermis in abdomen was: $29.80 \pm 0.38 \mu\text{m}$ as shown in table 2. The mean thickness of epidermis in back was $29.80 \pm 0.38 \mu\text{m}$ as shown in table 3. A decrease in thickness in group B1 was noted in all sites and when compared with group A it is highly significant ($P < 0.001$) result.

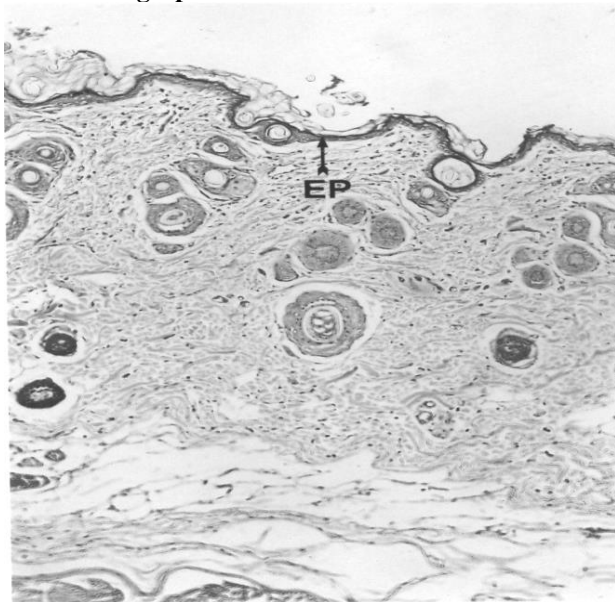
Group B2: The animals of group B2 were ill looking. The skin appeared thin and dehydrated, wide patches of alopecia were scattered all over, and showed varying

degree of hyperemia. In face abdomen and back number of cell layers were reduced to half but thickness of epidermis was near to control due to hyperkeratinization. The mean thickness of epidermis in face was: $39.92 \pm 0.26 \mu\text{m}$ as shown in table 1.

Figure No.1: H & E stained 5 μm thick longitudinal sections of face skin showing epidermal thickness (Ep) in control guinea pig. Photomicrograph x100.



Figure No.2: H & E stained, 5 μm thick longitudinal section of the face skin showing desquamation and the reduced thickness of the epidermis after 48 hours treatment with x-radiation in guinea pigs. Photomicrograph x100.



The mean thickness of epidermis in abdomen was: $49.36 \pm 0.47 \mu\text{m}$ as shown in table 2. The mean thickness of epidermis in back was $57.84 \pm 0.41 \mu\text{m}$ as shown in table 3. A slight decrease and increase in the thickness of epidermis in all three sites was noted. When compared with group A insignificant ($P > 0.05$) result was observed.

Group B3: The skin of face, abdomen and back regained its thickness, hairs were very sparse, patches of alopecia were scattered all over the skin and the hyperemia was diminished considerably.

In all three sites the epidermis showed increased number of cell layers as near to control and keratinization was also decreased. The mean thickness of epidermis in, face was: $40.28 \pm 0.47 \mu\text{m}$ as shown in table 1. The mean thickness of epidermis in abdomen was $48.94 \pm 0.73 \mu\text{m}$ as shown in table 2. The mean thickness of epidermis in back was $57.76 \pm 0.26 \mu\text{m}$ as shown in table 3. A slight decrease and increase in thickness in group B3 when compared with group A which was insignificant ($P > 0.05$).

DISCUSSION

All mammalian cells are affected by ionizing radiation; moderate variability exists among different cell types and tissue with respect to their susceptibility to specific effect such as cell death¹.

Exposure to both ionizing radiation and the certain transition metals can increase cellular formation of free radicals, under aerobic conditions. This can lead to formation of reactive oxygen species, reactivity of these oxyradicals lead to deleterious changes in living cell including DNA strands and breaks, protein oxidation and membrane damage⁹.

X-rays are widely used for both imaging and therapeutic purposes; our knowledge about their possible injuries effects on the skin is incomplete. Previous studies are based on the morphological X-rays induced skin changes. The present study was designed to observe the morphometric changes in skin of different locations induced by X-rays. Guinea pigs were taken as experimental animals because radio sensitivity of these laboratory animals is close to humans and these experimental animal were exposed to single whole body irradiation in dose of 5 GY^{10,11}.

The gross examination of treated animals of Group B show hair loss in face, abdomen and back. This finding was supported by similar observation made by Song and Lambert who found that after exposure of mice to 5 GY of ionization radiation, cell in the matrix of hair follicle under went apoptosis but not growth arrest. These findings are in agreement with Hopewell and Malkinson, they observed that loss of hair occurred after treatment with relatively low doses of radiation

indicating that hair follicles are highly sensitive to ionizing radiation^{11, 12, 13}.

In the present study the animals of group B1 with the dose of 5 GY radiation the thickness of epidermis in all three sites i.e. face, abdomen and back was reduced to half as compare with control, due to decrease in number of cell layers in stratum spinosum, stratum granulosum and stratum corneum this was probably due to growth arrest of epidermal cells. This finding was in agreement with the observation of Hussein et al who observed in their study that in X rays irradiated skin the stratification of epidermis was reduced to one layer each of basal, spinous and granular as well as few layer of corneocytes.

These findings are further supported by study of Song and Lambert et al, who observed the epidermal cells, responded to radiation by under going growth arrest. Growth arrest was more severe in 24 hours after (5 GY) irradiation¹¹.

Decrease in thickness of epidermis was in agreement with the observations by John et al in which degenerative phase of radiation effects consists of lost in prickle cells and basal cell layer. This loss is maximum or complete by day 21. The mitotic index falls to zero¹⁴.

In the group B2 the thickness of epidermis was near to control due to increase in the thickness in stratum corneum. The increase in thickness in stratum corneum was due to increase in ratio of cell loss in pathological states. This observation was in agreement with the observation of Berry, et al, Dechatterjee et al, Landthaler et al. They observed the morphologically X-radiation can produce epidermal loss and hyper keratinization^{15,16}.

In the group B3 thickness of epidermis in all three location i.e. face abdomen and back was near to control, this is because the cells of stratum basale shows the mitotic activity. This finding was in agreement with the observation of Hopewell, in which there is recovery of epidermis occurs as a result of proliferation of surviving clonogenic basal cells form with in the irradiated area. Furthermore, these finding were in agree with in the observation of Song and Lambert, in which epidermal cells respond to radiation undergoing growth arrest, not the apoptosis.

CONCLUSION

The study concludes that X-radiation produce deterministic damaging effects on epidermis in guinea pigs in 3 sites i.e. face, abdomen and back.

REFERENCES

1. Anderson RE, Berthrong M, Fajardo LF. Radiation injury. In: Ivan Damjonov, James Linder, editors. *Anderson's pathology*. 10th ed. St. Louis: the CV Mosby Company: 1990. p. 485-512.
2. Bradychiev MS, Peteric VD, Krasnov AS. Comparative Cellular and Species Radio sensitivity. *Med. Radiol* 1982;6: 7-11.

3. Moskolev Yu. I. Remote effects of ionizing radiation. *Med Radiol* 1991;4:20-23.
4. Hussein MR, Eman E, Dief-Abu, Mohammad H, Raheem AE, Abdel-Rehman, Ali Abdel. Rahman. Ultrastructural evaluation of the radioprotective effects of melatonin against x-ray induced skin damage in albino rats. *Int. J. Exp Path* 2005;86: 45-55.
5. Berry RJ, Mole RH. Skin response to x-irradiation in guinea pig. *Int J radiat Biol Relat Study Phys Chem Med* 1976;30:535-41.
6. Koeing TR, Wolff D, Mettler FA, Wagner LK. Skin injuries from fluoroscopically guided procedure; characteristics of radiation injury. *Am J Roentgenol* 2001;3-11.
7. Behrens CF, King ER, Carpender JW. The pathological anatomy of total-body irradiation. In: Upton AC, Lushbaugh CC, editors. *Atomic medicine*. 5th ed. New York: Williams and Wilkins: 1969. p.236-245.
8. Shope TB. Radiation induced skin injuries from fluoroscopy. *Radiographics* 1996; 16:1195-99.
9. Halliwell B, Gutteridge JMC. *Free radicals in biology and medicine*. Oxford: Clarendon Press: 1989.
10. Melchikov AS, Ryzhov AI, Medredev MA. Morphological changes in epidermal basal cells of different location induced by x-rays. *Bull Experimental Biol Med* 2003;136: 224-27.
11. Song S, Lambert PF. Different responses of epidermal and hair follicular cells to radiation correlate with distinct patterns of p53 and p21 induction. *Am J Pathol* 1999;155:1121-27.
12. Hopewell JB. The skin in its structure and ionizing radiation. *Int J Radiat Biol* 1990;57: 751-73.
13. Malkinson FD. Some principles of radiology: A selective review. *J Invest Dermatol* 1981;77: 32-38.
14. John O. Archambeau, Gerber A, Ayoub R, Harry J. Brenneis. Epidermal cell population changes produce by exposure to 2, 300R. *Radiol* 1972;103:199-196.
15. De Chatterjee. Low level x-ray exposure on rat skin, hyperkeratization and concomitant changes in biometal concentration. *Biol Trace Elem Res* 1984; 46:203-10.
16. Landthaler M, Hagspiel HJ. Late irradiation damage to skin caused by soft x-radiation therapy of cutaneous tumour. *Arch Dermatol* 1995; 131: 182-86.

Address for Corresponding Author:

Dr. Farrukh Mustafa Memon
Assistant Professor of Anatomy,
DMC, DUHS Karachi.
CELL # 0333-2185465

Original Article

Infant Mortality and its Causes in Three Different Districts of Punjab, Pakistan

1. Muhammad Saleem Rana 2. Asma Abdul Latif 3. Noreen Zafar 4. Muhammad Abdullah Zafar

1. Assoc. Prof. Health Services Academy, Islamabad 2. Senior Lecture, Lahore College for Women University, Lahore 3 & 4. Consultants Girls and Women Health Initiative Lahore.

ABSTRACT

Background: Maternal and newborn mortality rates remain unacceptably high, especially where the majority of births occur in home settings or in facilities with inadequate resources.

Objectives: This study was conducted to estimate the Infant Mortality Rate (IMR), reporting percentage and to identify the risk factors for infant mortality in Punjab, Pakistan.

Study Design: Retrospective Study.

Place and Duration of Study: This study was conducted in the Directorate General, Health Services Punjab, Lahore from 01-07-2007 to 30-06-2008.

Materials and Methods: Community-based cross-sectional survey was conducted during July to September 2009. Interviews of female family heads were conducted by the trained researchers.

Results: Deaths of 786 infants were reported in three districts, verbal autopsy of all cases was done to find out the causes of deaths during infancy. World Bank (2010) reported IMR of Pakistan 71/1000 live birth (estimated infant's deaths 9811), which is very high from this study (6/1000 live birth). Major Causes of infant mortality were found malnutrition 194(24.6%), Acute Respiratory Infections (ARI) 188(23.9%), and Diarrheal Diseases 161(20.4%).

Conclusion: Mortality due to said diseases can be reduced by improving childbearing and childrearing practices, equitable distribution of good standard health care facilities, safe drinking water and individual attention.

Key words: Infant mortality, social conditions, socioeconomic factors, Punjab.

INTRODUCTION

More than half a million maternal deaths, over 3 million stillbirths and 3 million early neonatal deaths occur each year worldwide, the majority in South Asia and sub-Saharan Africa¹⁻⁴. Delivery complications (pro-longed labor, preeclampsia, maternal infection and obstetric hemorrhage) are responsible for half of all maternal deaths, one-third of stillbirths and one-quarter of neonatal deaths⁵⁻⁹. Despite established interventions, the majority of maternal and neonatal deaths occur due to a lack of access to life-saving services^{10, 11}. The introduction of child survival interventions, immunization and oral rehydration, has resulted in a sustained decline of infant and child mortality in some areas of the developing world but consequently of this decline is that an increasing proportion of infant deaths occur during the neonatal period¹². However, there is limited epidemiological information on levels and clinical causes of neonatal and post neonatal death, infant mortality is sum of neonatal mortality and post neonatal mortality. Neonatal deaths are generally associated with elements linked to maternal care during pregnancy and delivery, while socio-environmental factors become more important

determinants of infant survival during the post-neonatal period. It is estimated that neonatal deaths can account for nearly 50–60% of all infant deaths in developing countries¹². Approximately 30–40% of all neonatal deaths are explained by neonatal infections, amounting to approximately 1.5–2 million neonatal deaths per year¹³. WHO has estimated that approximately 400 000 cases of neonatal tetanus occur annually, the vast majority in a limited number of developing countries, resulting in an annual toll of 340 000 neonatal tetanus deaths¹⁴, estimated 130 million infants born each year worldwide¹⁵, 4 million die in the first 28 days of life. Three-quarters of neonatal deaths occur in the first week, and more than one-quarter occur in the first 24 hours^{15,16}. Two-thirds of the world's neonatal deaths occur in just 10 countries, mostly in Asia. Pakistan is number three among these countries, with an estimated 298 000 neonatal deaths annually and a reported neonatal mortality rate of 49 per 1000 live births, Pakistan accounts for 7% of global neonatal deaths¹⁵⁻¹⁹. Infection (36%), preterm birth (28%) and birth asphyxia (23%) account for 87% of neonatal deaths worldwide^{15, 16, and 20}. Since causes of neonatal deaths vary by country and with the availability and quality of health care, understanding neonatal mortality in

relation to these factors is crucial¹⁶. Given the paucity of reliable population-based information in Pakistan, this study was undertaken to examine the prevalence, sex distribution, timing and causes of neonatal death in a population-based pregnancy cohort in urban Pakistan. We hypothesized that the neonatal mortality rate in urban population, with relatively good access to obstetric care and timely Caesarean section, would be substantially lower than that generally reported for Pakistan. This study examines delivery outcomes in pregnant women with reasonably good access to professional health care that were enrolled at 20 to 26 weeks' gestation and followed with their infants to 28 days postpartum²¹.

MATERIALS AND METHODS

This study was conducted from 01-07-2007 to 30-06-2008. The inclusion criteria were neonates died within one year of their birth. The record was collected from the hospitals, chowkidars, lumberdar, district national programme units and secretary union councils. Information obtained was the deceased age, antenatal care, level of cure, wealth, child-rearing (weaning) & childbearing practices (spacing), health care facilities, immunization, safe drinking water. The source of information were mothers or direct relatives of the deceased.

Comparing three districts (Sialkot, Chakwal and D.G.Khan) of Punjab, all have different economic situations. Sialkot is rich, Chakwal is in the middle range and D.G. Khan is an economically poor district of the Punjab. This study was planned to assess the infant mortality rates and its causes in correlation with economic indicators. Positive association between high infant mortality and income inequality is still present after controlling for other factors such as education, medical personnel, and fertility. The positive association of infant mortality and the income of the rich suggest that measured real incomes may be a poor measure of social welfare.

This study also examined factors associated with infant survival in Pakistan. Data of National Programme for family planning and primary health care of the districts was collected. Survey was conducted by the trained staff of the project funded by the United Nation Family Planning Association (UNFPA).

The infant mortality rate was still very high in Pakistan until the early 1990s, at 100 deaths per 1000 live births. Large differentials in infant survival by socio-economic factors and access to water and sanitation indicate that social and gender inequities are the underlying cause of the stagnation of infant mortality in Pakistan. Economic and social policies of earlier decades have resulted in tremendous disparities in wealth and access to resources in Pakistan. The low social, economic and

legal status of women is intimately tied to the well-being of their children. Health interventions in Pakistan should be designed to reach the most under-served: women and children. Systematic evaluations of health interventions will be necessary to make informed decisions about health investments in the future.

This paper generated and analyzed the survey data on inequalities in mortality among infants aged less than one year in Punjab, Pakistan. Mortality rates were estimated directly where complete fertility histories were available and indirectly otherwise. Mortality distributions were compared between districts, gender and different age groups by means of percentage.

RESULTS

786 infants of the age 0 hour to 11 months and 29 days found died during study period from 01-07-2007 to 30-06-2008. One of the objective of the study was to see the reporting percentage, which was found only 8% overall, which is significantly poor reporting. In different districts reporting ranges between 4-13% (Table No.1).

Table No.1: District wise infant mortality rate in Punjab, Pakistan

	Sialkot	D.G. Khan	Chakwal	Total
Population	2734481	1643118	1083725	5461324
Birth rate (world Bank)	25.3	25.3	25.3	25.3
Live births	69182	41571	27418	138171
Infants estimated deaths if IMR is 71 (World Bank)	4912	2951	1947	9811
Infants reported deaths	414	116	256	786
%age reporting	8	4	13	8

Out of 786 deceased only 432(55%) were reported by district national programme for family planning and primary health care, research teams traced 354(45%) more cases (Table No.2). Highest number 414 cases were found from Sialkot. From Chakwal 256 and from D.G.Khan 116 cases were recorded.

Table No.-2: Infant's Deaths reported by research team and National Programme (NP) of family planning and primary health care

Reported by	Sialkot (%age)	D.G.Khan (%age)	Chakwal (%age)	Total (%age)
Research team	187 (45)	42 (36)	151 (59)	354 (45)
National programme	227 (55)	74 (64)	105 (41)	432 (55)
Total	414 (53)	116 (15)	256 (32)	786

Female infants 550(69.97%) died more as compared to males 236(30.03%), same trends were found in all districts. Highest number infants 409(52.2%) died in the age of 1-10 days (Table No.3).

highest 69(27.0%) and in Sialkot highest deaths were noted by malnourishment 113(27.3%). Highest causes of deaths were found malnourishment 194(24.6%) and ARI 161(20.4%) as shown in Table No.4.

In D.G.Khan undiagnosed deaths recorded were found highest 30(25.9%), in Chakwal ARI was recorded

Table No.3: Gender and Age wise infant mortality in Punjab, Pakistan

Pakistan; Birth Rate 2010-25.3/1000 population, IMR 2010-71(World bank), 65.3(Pakistan website)				
	Sialkot (%age)	D.G.Khan (%age)	Chakwal (%age)	Total (%age)
Population	2734481	1643118	1083725	5461324
Study subjects	414	116	256	786
IMR	6	3	9	6
Gender				
Male	82(19.81)	55(47.41)	99(38.67)	236(30.03)
Female	332(80.19)	61(52.59)	157(61.33)	550(69.97)
Age				
<1day	86(20.67)	12(10.34)	45(17.58)	137 (17.4)
1-10 days	257(61.78)	73(62.93)	114(44.53)	409(52.2)
11-29 days	3 (0.72)	14(12.07)	18(7.03)	44(5.6)
1-2 months	39(9.38)	12(10.34)	30(11.72)	93 (11.8)
3-5 months	20(4.81)	1(0.86)	31(12.11)	65(8.3)
6-9 months	10 (2.40)	4(3.45)	14 (5.47)	30(3.8)
10-11 months	1(0.24)	0(0.00)	4(1.56)	8(0.9)

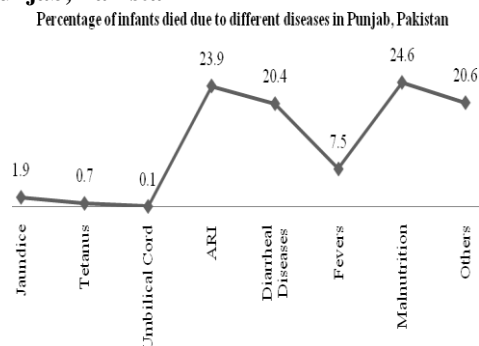
Table No.4: Area wise causes of infant mortality in Punjab, Pakistan

Clinical cause	Sialkot # (%age)	D.G.Khan # (%age)	Chakwal # (%age)	Total # (%age)
Jaundice	4(1.0)	3(2.6)	8(3.1)	15(1.9)
Tetanus	4(0)	1(0)	1(0)	6(0.7)
Umbilical Cord	0(0)	0(0)	1(0)	1(0.1)
ARI	96(23.2)	23 (19.8)	69(27.0)	188(23.9)
Diarrheal Diseases	95(22.9)	17(14.7)	49(19.1)	161(20.4)
Fevers	15(3.6)	17(14.7)	27(10.5)	59(7.5)
Malnutrition	113(27.3)	25(21.6)	56(21.9)	194(24.6)
Others	87(21.0)	30(25.9)	45(17.6)	162(20.6)
Total # (%age)	414(52.67)	116 (14.76)	256(32.57)	786

DISCUSSION

In total study area highest cause of infant mortality is shown in Figure-1, which is malnutrition (24.6%).

Figure No.1- Diseases wise infant mortality in Punjab, Pakistan



The death of infants is also tragedy, like death of mothers during delivery. It is a huge burden of grief and pain. Infant mortality in Pakistan is high at about 125-140/1000, for a country with mid-level per capital income²². Maternal education is a strong indicator of survival, much more so than paternal education. Similarly, female heads of households increased survival, probably because they control financial allocations. The study suggested that rather solely concentrating to eliminate poverty overall, improvements in maternal education, nutrition, health care facilities and ease of access to their use could be more helpful. Childbearing and child-rearing methods would do more to improve child survival in Pakistan. Present study results also agree with the author suggestions²², about the maternal education, nutrition,

health care facilities and their use, and childbearing and child-rearing methods would be more important interventions to decrease the IMR in Pakistan.

Between 1985 and 1987, a community-based case-management programme for acute lower respiratory infection (ALRI) was conducted in a rural district of Abbotabad, in northern Pakistan. The impact on infant and child mortality of this programme, which included active case-finding and maternal health education, was evaluated and found that the total child mortality rate in the control villages declined by 29% to 27.8 per 1000 children per year ($P = 0.09$). Similar intervention-associated declines in the infant mortality rate were also observed²³. Present study also suggested that ARI is high cause of mortality but with good intervention can be reduced.

It is concluded that existing health services must be improved and emergency obstetric care should be available to all women and children round the clock. Provision of antenatal care should be uniform and optimal. Nutritional status of infants should be improved to discourage rise in infant mortality. Referral system should be properly organised so that delay in seeking help could be avoided. Socio-economic status of community needs to be improved to avoid hindrance of high cost of care and poverty. Health care should be free for all infants. Non-governmental organizations should expand their services in rural areas to upgrade infant health status. It is global issue but more prevalent in developing countries. By strengthening of safe motherhood including antenatal care, clean safe delivery and essential obstetrical care, careful use of drugs to control ARI and breast feeding with appropriate diet can decrease the infant mortality in Pakistan. Mothers' training on home management of ARI, DD and malnourishment can play a significant role to reduce IMR in Pakistan.

Acknowledgement

We cordially thank to Ms. Aashifa Yaqoob and Mr. Mudassar Mushtaq faculty of Health Services Academy Islamabad for their value able inputs to analyze the data. We also wish to express our gratitude to UNFPA and MNCH programme of Punjab for their support to complete this study.

REFERENCE

1. Ronsmans C, Graham WJ. Maternal mortality: who, when, where, and why. *Lancet* 2006; 368:1189-1200.
2. Stanton C, Lawn JE, Rahman H, Wilczynska-Ketende K, Hill K. Stillbirth rates: delivering estimates in 190 countries. *Lancet* 2006; 367:1487-1494.
3. Lawn JE, Cousens S, Zupan J. 4 million neonatal deaths: When? Where? Why? *Lancet* 2005; 365:891-900.
4. Hyder AA, Wali SA, McGuckin J. The burden of disease from neonatal mortality: a review of South Asia and Sub-Saharan Africa. *BJOG* 2003; 110:894-901.
5. McClure EM, Goldenberg RL, Bann CM. Maternal mortality, stillbirth and measures of obstetric care in developing and developed countries. *Int J Gynaecol Obstet* 2007; 96:139-146.
6. World Health Organization: Perinatal mortality: a listing of available information. FRH/MSM.96.7 Geneva: WHO; 1996.
7. National Health Survey of Pakistan: Health profile of the people of Pakistan. Islamabad, Pakistan: Pak Med R Council 1998.
8. Sibley LM, Sipe TA, Brown CM, Diallo MM, McKatt K, Habarta N. Traditional birth attendant training for improving health behaviors and pregnancy outcomes (review). *Cochrane Database of Systematic Review* 2007; CD005460.
9. Lawn J, Shibuya K, Stein C. No cry at birth: global estimates of intrapartum stillbirths and intrapartum-related neonatal deaths. *Bull World Health Organ* 2005; 83:409-417.
10. Manandhar DS, Osrin D, Shrestha BP, Mesko N, Morrison J, Tumbahangphe KM, et al. Effect of a participatory intervention with women's groups on birth outcomes in Nepal: cluster-randomized controlled trial. *Lancet* 2004; 364:970-979.
11. Jokhio AH, Winter HR, Cheng KK. An intervention involving traditional birth attendants and perinatal and maternal mortality in Pakistan. *N Engl J Med* 2005; 352:2091-2099.
12. Perera T. Perinatal morbidity and mortality trends in South-East Asia. ASEAN Pediatric Federation; 1983.
13. Perinatal mortality: a listing of available information. Geneva: World Health Organization; 1996. Unpublished document WHO/FRH/MSM/96.7.
14. Eliminating neonatal tetanus: How near, how far? Geneva: World Health Organization; 1996. Unpublished document WHO/EPI/GEN/96.01.
15. World health report: Make every mother and child count. Geneva: WHO; 2005.
16. Lawn JE, Cousens S, Zupan J. 4 million neonatal deaths: When? Where? Why? *Lancet* 2005; 365:891-900.
17. Neonatal and perinatal mortality: country, regional and global estimates. Geneva: WHO; 2006.
18. Bhutta ZA. Maternal and child health in Pakistan: challenges and opportunities. Oxford University Press; 2004.
19. Jalil F. Perinatal health in Pakistan: a review of the current situation. *Acta Paed*. 2004; 93:1 273-1279.
20. Lawn JE, Cousens SN, Wilczynska K. estimating the causes of four million neonatal deaths in the year 2000. The world health report. Geneva: WHO; 2005.
21. Darmstadt GL, Bhutta ZA, Cousens S, Adam T, Walker N, Bern L, et al. Evidence-based, cost-effective interventions: how many newborn babies can we save? *Lancet* 2005; 365:977-988.
22. Sathar ZA. Seeking explanations for high levels of infant mortality in Pakistan. *Pak Dev Rev* 1987; 26(1):55-70.
23. Khan JA, Khan M, Akbar DG. *Bull World Health Organ* 1990; 68(5): 577-585.

Original Article

Outcome of Early Appendicectomy in Appendicular Mass Versus Conservative Approach

1. Muhammad Qasim Mallah 2. Ubedullah Shaikh 3. Sikander-e-Azam
4. Qambar Ali Laghari

1..Sr. Registrars, Surgical Unit-IV, LUMHS, Jamshoro 2. PG Student of Surgery, Surgical Unit-IV, LUMHS, Jamshoro 3. Sr. Registrar of Surgery, Miminal Invasive Surgical Centre, LUMHS, Jamshoro 4. Sr. Registrars, Surgical Unit-IV, LUMHS, Jamshoro

ABSTRACT

Aim: The objectives of the study are to compare the outcome of early appendicectomy in appendicular mass versus conservative approach.

Study Design: Experimental Study.

Place and Duration of Study: This study was carried out in Surgical Unit-IV, Liaquat University Hospital Hyderabad, from January 2008 to December 2009.

Materials and Methods: This study consisted of hundred patients were divided in two groups. Group A for early appendicectomy and group B traditional conservative treatment, each group consist of 50 patients admitted through the outpatient department, as well as from casualty department of Liaquat University Hospital Jamshoro/Hyderabad. Data was analyzed through SPSS software.

Results: In conservative management (CM) group 36(72%) were male and 14(28%) female. Ratio male:female ratio of 2.25:1. In immediate surgery (IS) group 34(68%) were male and 16(32 %) female with male:female ratio of 2.1:1. There was wide variation of age ranging from a minimum of 10 year to 50 year in both group. The mean age was 22.3 ± 3.30 years for CM group and 23.4 ± 3.50 years for IS group.

Pain in right iliac fossa were found in all patients in both groups , vomiting was seen 42(84%) patients in CM group and 43(86%) patients in IS group , nausea was seen 17(34%) patients in CM group and 18(36%) patients in IS group, fever was 42(84%) patients in CM group and 44(88%) patients in IS group, diarrhea was 4(8%) patients in both groups, anorexia was seen 35(70%) patients in CM group and 37(74 %) patients in IS group, constipation were 9(18%) patients in both groups and urinary complains was 8(16%) patients in CM group and 9(18%) patients in IS group.

Ultrasound findings revealed was inflamed appendix with omentum adherent in 10(20%) patients of CM group and 9 (18%) patients of IS group where as inflamed appendix with omentum and abscess formation in 17(34%) patients of CM group and 19 (38%) patients of IS group, and edematous appendix with fecolith and omentum adherent in 23(46%) patients of CM group and 22(44%) patients of IS group. Operative time in both groups was recorded. Operative time range 30 minutes to 90 minutes in both groups. The mean time in CM group was 60.10 ± 11.90 minutes and IS group was 45.30 ± 7.96 minutes.

Conclusion: The early appendectomy in appendicular mass is a safe alternate to conventional way of managing this problem. Hence, it obviates the need of a second admission and provides curative treatment during the index admission whereby minimizing total expenses.

Key words: Early appendicectomy , Appendicular mass , Conservative approach , Appendix, Complications of appendix.

INTRODUCTION

Acute appendicitis is one of the commonest surgical emergency requiring surgery ¹. No age is immune, but the highest incidence is seen during the second decade of life with a slight male dominance ².

Patient presenting late in the course of acute appendicitis usually present with a palpable mass in the right iliac fossa. This mass is composed of inflamed appendix, omentum, loop of small bowel and oedematous caecum. The surgical management of acute appendicitis presenting with appendicular mass remains

controversial³ but traditionally these patients are dealt with conservatively by putting them on the well known Ochsner Sherren regimen believing that surgery in these patients is hazardous, time consuming and has greater morbidity and mortality. The conservative management involves a long hospital stay and comprises, hospitalization, broad spectrum antibiotic cover, intravenous fluids and continuous monitoring of the vital signs ⁴.

Patients who respond well to this conservative treatment are usually re-admitted for an interval appendectomy after a period of 6-8 weeks. This

conservative treatment is needed for 1-2 weeks and thus causes a lot of economical burden on the patient. In addition, it demands a second admission for appendectomy and may need to be stopped in case of failure. Keeping in view all these facts, we carried out this study to find out the benefit of early appendectomy in terms of economical loss and undue and prolonged hospitalization.

MATERIALS AND METHODS

This study was carried out in Surgical Unit-IV, Liaquat University Hospital Hyderabad, from January 2008 to December 2009. This study consisted of hundred patients were divided in two groups. Group A for early appendectomy and group B traditional conservative treatment, each group consist of 50 patients admitted through the outpatient department, as well as from casualty department of Liaquat University Hospital Jamshoro/Hyderabad.

A detailed history was recorded on specially prepared proforma. Thorough physical examinations including abdominal and rectal examination were done in every patient. Cardiovascular, respiratory and central nervous system were examined for evidence of any concomitant disease.

All patients underwent for base line and relevant investigations investigation like complete blood picture, urine detailed report. X-ray abdomen erect and supine posture, ultra sound abdomen was performed to help diagnosis.

Inclusion criteria Patients with clinically palpable appendicular lump or detected on ultra sound will be included in this study regardless of their age and sex.

Exclusion criteria Patients

with malignant lump or iliocaeal tuberculosis mimicking appendicular lump assessed clinically or on operative findings will be excluded from the study. Data was analyzed through SPSS software version 16.0.

RESULTS

This study was carried out in the General surgical department at Liaquat University Hospital Hyderabad, Sindh, Pakistan from 2008 to 2009. This study consisted of 100 patients of appendicular mass diseases were admitted and divided into two groups.

In conservative management (CM) group 36(72%) were male and 14(28%) female. Ratio male:female ratio of 2.25:1. In immediate surgery (IS) group 34(68%) were male and 16(32%) female with male:female ratio of 2.1:1. There was wide variation of age ranging from a minimum of 10 year to 50 year in both group. The mean age was 22.3 ± 3.30 years for CM group and 23.4 ± 3.50 years for IS group.

Symptoms of patients in both groups were almost same. Pain in right iliac fossa were found in all patients in

both groups, vomiting was seen 42(84%) patients in CM group and 43(86%) patients in IS group, nausea was seen 17(34%) patients in CM group and 18(36%) patients in IS group, fever was 42(84%) patients in CM group and 44(88%) patients in IS group, diarrhea was 4(8%) patients in both groups, anorexia was seen 35(70%) patients in CM group and 37(74%) patients in IS group, constipation were 9(18%) patients in both groups and urinary complains was 8(16%) patients in CM group and 9(18%) patients in IS group.

Clinical examinations of patients (signs) in both groups were not so much different in percentage wise. In conservative management (CM) group tenderness at Mc Burney's was present in 50(100%) patients, guarding was present in 47(94%) patients, rebound tenderness was present 41(82%) patients, Rovsing's sign was present in 23(46%) patients and cough sign was present in 44(88%) patients. Where as in immediate surgery (IS) group, tenderness at Mc Burney's was present in 50(100%) patients, guarding was present in 46(92%) patients, rebound tenderness was present 42(84%) patients, Rovsing's sign was present in 24(48%) patients and cough sign was present in 45(90%) patients.

Ultrasound findings revealed was inflamed appendix with omentum adherent in 10(20%) patients of CM group and 9 (18%) patients of IS group where as inflamed appendix with omentum and abscess formation in 17(34%) patients of CM group and 19 (38%) patients of IS group, and edematous appendix with fecolith and omentum adherent in 23(46%) patients of CM group and 22(44%) patients of IS group.

In CM Group Leucocyte count (n=50) more than $>11000/\text{cu mm}$ were seen in 49(98%) patients and $<11000/\text{cu mm}$ was only in 1 (2%) patient, where as in IS group (n=50) leucocyte count more than $>11000/\text{cu mm}$ were in 50(100%) patients and $<11000/\text{cu mm}$ was not only in single patient.

37(74%) patients out of 50 patients were mass completely resolved on conservative treatment and 13(26%) patients there was no response on conservative treatment and conversion to surgery.

The duration of hospital stay varied. Total hospitalization period in immediate surgery group was 4 days to 8 days and average time was 6 days. In conservative management of mass plus interval appendectomy after 6-8 weeks, minimum times was 5 days, maximum time were 12 days and average time were 8.5 days.

Post operative complications in immediate surgery group was pain in 40(80%) patients, vomiting in 25(50%) patients, fever 24(48%) patients, wound infection 24(48%) patients, wound dehiscence 3(6%) patients and paralytic ileus in 7(14%) patients. While in conservative management group (interval

appendicectomy n=22) pain in 16(72.7%) patients, vomiting in 4(18.18%) patients, fever 5(22.72%) patients, wound infection 5(22.72%) patients and paralytic ileus in 1(4.54%) patients.

Return to normal activity in immediate surgery group was 12 days minimum to 25 days maximum and average time was 18.5 days. Where as in conservative management group was 18 days minimum to 28 days maximum and average time was 23 days.

Variable	Treatment				
	Conservative Management		Early Appendicectomy		
	Number of Patients	%age	Number of Patients	% Age	
Gender					Male : Female Ratio CM 2.25:1 IS 2.1:1
<ul style="list-style-type: none">MaleFemale	36 14	72% 28%	34 16	68% 32%	
Age					Mean Age : CM 22.3±3.30 years IS 23.4±3.5 years
<ul style="list-style-type: none">10-20 years21-30 years31-40 years41-50 years	4 26 10 8	8% 52% 20% 16%	5 22 13 10	10% 42% 26% 20%	
Presenting Complaints					
<ul style="list-style-type: none">Pain in right iliac fossaVomitingNauseaFeverDiarrhea	50 42 17 42 4	100% 84% 34% 84% 8%	50 43 18 44 4	100% 86% 36% 88% 8%	

DISCUSSION

The treatment of appendicular mass is taking a turn from the traditional approach of initial conservative treatment followed by interval appendicectomy to immediate appendicectomy^{5,6}. However this change is not widely accepted and the appendicular mass is traditionally treated by a conservative treatment (The Ochsner Sherren regimen) followed by interval appendectomy 6-8 week later. This comprises of hospitalization, broad spectrum antibiotics, Metronidazole and closed monitoring of the general health and vitals of the patients. Large number of surgeons still continue to adopt the same traditional approach^{7,8,9}. The rational of this study to early appendicectomy in patients presenting with appendicular mass, so as to reduce hospital stay, cut short the over all expenses and to ensure an early return to work.

In our study male to female ratio seen in CM group was 2.25:1 as compared to IS group where it was 2.1:1. However the male to female ratio given by Malik AM¹⁰ is 2.3:1 and Choudry ZA¹¹ is 2.2:1. The age ranged from 10 to 50 years in both groups with mean age was 22.3± 3.30 years for CM group and 23.4±3.50 year for IS group. The peak age of presentation in our

study is 15 to 30 years which is comparable to other study where peak age group presented 27.3 year¹⁰.

In our study the Pain in right iliac fossa was the commonest presentation (100%) followed by vomiting 84%, anorexia 70% and fever 84% in both group. However in study of Evan P¹¹ and Bor FS¹² the patients presented with vomiting 79%, anorexia 65% and fever 80%. In our study tenderness in right iliac fossa were 100% in both groups, guarding (CM=94% vs IS= 92%), rebound tenderness (CM=82% vs IS= 84%), and cough sign (CM=88% vs IS= 90%).

The clinical parameters were further supported by ultrasound examination which revealed inflamed appendix with omentum in (CM=20% VS IS= 18%), inflamed appendix with omentum and abscess in (CM=34% VS IS=38%) cases and inflamed appendix with fecolith and omentum in (CM=46% VS IS= 44%). Ultrasound finding given by Johansson EP¹³ and David R¹⁴ in their study supported these results. In the study of Young HR¹⁵ showed leucocyte counts high in all cases where as in our study leucocyte count >11000 in all cases.

In conservative treatment mass were resolved in 74%, but 26% patients did not respond on conservative treatment and needed immediate surgical intervention. Same is supported by other international studies^{4,16}. In

our study 30% patients did not report for interval appendectomy. Study of Gahukamble DB⁷ reported 27.7% not reported for interval appendectomy. In our study postoperative complications was found in IS group. The wound sepsis were observed in 48% patients, paralytic ileus in 4.5% patients, pain, fever and vomiting in 18-20% patients. Similar studies nearer to this data^{17,18}. The hospital stay in this study ranged from 1 to 10 days in both groups with mean length of hospitalization as 7 ± 1.5 days in CM and 5 ± 1.5 days in IS group. It is comparable to other studies given by different authors like 5 days in CM¹⁹ and 3 days in IS²⁰.

In our study mean period return to normal activity were 18.5 days in IS group and in CM group were 23 days (conservative management + interval appendectomy). Similar studies also favour this^{4,6,19}. The early operation has an edge of being curative in the index admission and ensures early return to work and high compliance.

CONCLUSION

The early appendectomy in appendicular mass is a safe alternate to conventional way of managing this problem. Hence, it obviates the need of a second admission and provides curative treatment during the index admission whereby minimizing total expenses.

REFERENCES

1. Choudry ZA, Sayed AS, Mishra P, Early exploration of appendicular mass. *Pak J Surg* 1996;12(2):64-66.
2. Simpson J, Scholefield JH, Acute appendicitis. *Surg Int* 2005;70:15-18.
3. Senapathi PS, Bhattacharya D, Ammori BJ. Early laparoscopic appendectomy for appendicular mass. *Surg Endosc* 2003;16(12):1783-85.
4. Samuel M, Hosie G, Holmes K. Prospective evaluation of nonsurgical versus surgical management of appendiceal mass. *J Pediatr surg* 2002;37(6):882-6.
5. Kumar S, Jain S. Treatment of appendiceal mass: Prospective, randomized clinical trial. *Indian J Gastroenterol* 2004;23:165-67.
6. Arshad M, Laghari A Aziz, Mullah QM, Altaf K. Early appendectomy in appendicular mass-A Liaquat University Hospital Experience. *JAMC* 2008; 20(1):70-72.
7. Gahukamble DB, Gahukamble LD. Surgical and pathological basis for interval appendectomy after resolution of appendicular mass in children. *J Pediatr Surg* 2002;35(3):424-7.
8. Erdogan D, Karaman I, Narci A, et al. Comparison of two methods for the management of appendicular mass in children. *Pediatr Surg Int* 2005; 21(2):81-3.
9. Eriksson S, Styrd J. Interval appendectomy. A retrospective study; *Eur J surg* 1998;164(10): 771-74.
10. De U, Ghosh S. Acute appendectomy for appendicular mass: A study of 87 patients. *Ceylon Med J* 2002;47(4):117-8.
11. Evan P, Nadler, Kimberly. Predictor of outcome with perforated appendicitis initially treated with non operative management. *Surgical infections. Mary Ann Liebert Inc* 2004;5(4):349-356.
12. Bor FS, Te FC, Jih CC, Meno ST. Risk factors associated with perforated appendicitis in elderly patients presenting with signs and symptom of acute appendicitis. *ANZ J. Surg* 2007;77:662-66.
13. Johansson EP, Rydh A, Riklund KA. Ultrasound, computed tomography and laboratory findings in the diagnosis of appendicitis. *Acta Radiol.* 2007; 48(3):267-73.
14. David R, Anthony FT, Kevin C. Radiological imaging to improve the emergency department diagnosis of acute appendicitis. *Emergency Medicine Australasia* 2004; 16:410-416.
15. Young HR, Wang YC, Chung PK, Chen WK et al. Laboratory test in patients with acute appendicitis. *ANZ J Surg* 2006;76(1-2):71-74.
16. Erdogan D, Karman I, Narci A. Comparison of two methods for the management of appendicular mass in children. *Pediatr Surg Int* 2005; 21(2):81-3.
17. Behrouz B, Saeed Al-H, Michael R. Laparoscopic Appendectomy with Appendix Mass in Children. *Pediatric Endosurgery & Innovative Techniques* 2004;8(1):25-30.
18. Gillick J, Velayudham M, Puri P. Conservative management of appendix mass in children. *BJS* 2001;88(11):1539-42.
19. Siddiqui AH, Afzal S. Perforated appendicitis, accuracy of ct diagnosis and correlation of ct findings with the length of hospital stay. *JCPS Pak* 2007; 17(12):721-25.
20. Liu ZF, Yu JC, Hsieh HF. Perforated appendicitis: urgency or interval surgery? *Zentralbl chir* 2007; 132(6):539-41.

Address for Corresponding Author:

Dr. Muhammad Qasim Malah
Banglow No. 105, Happy Homes
Near Citizen Colony Hyderabad Sindh.
Mobile :- 03003025573
Email:- drqasim_14@hotmail.com

Original Article

Comparison of Fissurectomy VS Lateral Internal Sphincterotomy in Chronic Anal Fissure Surgery

1. Khush Mohammad Sohu 2. Roshan Ali Solangi 3. A. Malik Sangri 4. G.Hyder Rind
5. S. Qarib Abbas 6. Faiza Abro

1. Asstt. Prof: of Surgery 2.Assoc. Prof: of Surgery 3.Asstt. Prof: of Surgery 4.Assoc. Prof: of Surgery 5. Prof: of Surgery 6.House Surgeon, Ghulam Mohammad Mahar Medical College Sukkur.

ABSTRACT

Background: Chronic anal fissure is the most common cause of anal pain associated with internal anal sphincter hypertonia. Although lateral internal sphincterotomy (LIS) is an effective treatment of chronic fissure in ano, it has the potential to cause serious complications, the most distressing of which is incontinence to flatus and fecal soiling. We proposed fissurectomy (F) as an alternative surgical treatment.

Study Design: Experimental and Comparative Study.

Place of Study: This study was conducted at Surgical Department, Ghulam Mohammad Mahar Medical College Sukkur.

Patients and Methods: one hundred twenty four patients, divided into two groups. Sixty patients underwent fissurectomy and 64 underwent lateral internal sphincterotomy. After a median follow-up of 18 months, we compared the results of the two procedures. In addition to frequent visits on a predetermined basis, a telephone inquiry into fissure recurrence and continence status was made.

Results: All patients in either group were pain-free and without bleeding within one week. In both groups, urinary retention was noted in two patients. Incontinence to flatus occurred in four patients (6.2%) in the LIS group, but no incontinence was noted in the F group. There were two patients (3.1%) with fissure recurrence in the LIS group, but no one in F group. No patient in either group was afflicted with anal stenosis or perianal infections. All wounds healed within 6 to 8 weeks. 58 patients (96.6%) in the F group and 56 (87.5%) in the LIS group reported satisfactory results.

Conclusion: In surgical treatment of chronic anal fissures not responding to conservative management, fissurectomy may be a sphincter-sparing alternative and perhaps a preferable surgical technique.

Key Words: Fissurectomy, Sphincterotomy, Chronic Anal Fissure

INTRODUCTION

An anal fissure is a crack or tears in the skin of the anal canal. Anal fissures may be noticed by bright red anal bleeding on the toilet paper, sometimes in the toilet. The etiology of this disease is in doubt up to now but mucosal ischemia secondary to sphincter spasm is an acceptable etiology. Spasm of the internal anal sphincter plays a central role in the pathogenesis of the disease^{1, 2, 3}. Despite the advent of new modalities in the conservative treatment of chronic fissures, such as nitric oxide donors, they frequently need surgical treatment. Lateral internal sphincterotomy (LIS) heals chronic fissures in ano in over 90 percent of cases, but it is associated with potential long-term complications^{4, 5, 6, and 7}. Incontinence to flatus and fecal soiling are distressing complications of sphincterotomy that may occur in up to 35 per cent of patients^{8, 9, 10}. Surgical techniques that preserve the anal sphincters should reduce the possibility of postoperative fecal incontinence. This study was designed to study the hypothesis that chronic anal fissures unresponsive to conservative treatment may be regarded as unstable

scar tissue. Fissurectomy or fissure excision to create a fresh surgical wound might then allow stable wound healing.

PATIENTS AND METHODS

One hundred- twenty four consecutive patients with chronic anal fissures not responding to conservative treatment were included in this study to compare the results of LIS versus fissurectomy (F). The patients were divided into two groups. In view of the distribution of age, sex and intervening variables, including the location of the fissure and other associated disorders such as hemorrhoids, there was a desirable matching between the two groups [tables 1-3]. Out of 124 patients, 60 underwent fissurectomy and 64 underwent LIS. 74 patients (59.6%) were male and 50 (40.3%) were female. The mean age was 34 years, ranging from 24-52. Location of the fissure was posterior in 112 (90.3%) and anterior in 12 (9.7%) patients. Considering associated anorectal disease, 1st degree hemorrhoids were noted in 4 (3.2%) patients. All patients had classical symptoms of a chronic anal

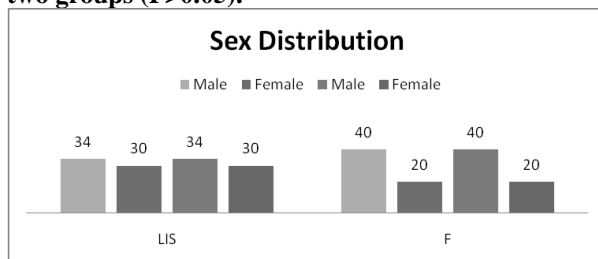
fissure unresponsive to medical treatment for at least 3 months. All patients had skin tags or sentinel piles. Patients with multiple fissures were not included in the study. Irrespective of the method of surgery, prior to operation, we drew up a questionnaire for patients, including specifications of the patient, pre- and postoperative symptoms, and postoperative complications. First, those items related to preoperative time were recorded in the questionnaire, and then we proceeded with the operation (fissurectomy or LIS).

Fissurectomy was performed by a single surgeon under spinal anesthesia in the lithotomy position. Excision of the fissure complex with a margin of healthy mucosa and scar tissue down to the level of the internal sphincter was carried out. Sphincterotomy was not conducted. As such, a fresh ulcer without any fibrous and scar tissue was established to precipitate its healing capacity. All wounds were left open. The day after surgery, the patients were discharged with warm sitz bath and bulking agents for at least 2-3 weeks. The second group of patients underwent the traditional approach of LIS and was discharged the day after with the above-mentioned recommendations. The first visit was scheduled within one week, the others within 1 and 2 months and the last one at the end of the follow-up period. Furthermore, patients were told that they would be contacted subsequently by telephone regarding symptoms and postoperative continence. The median follow-up was 18 months (range 14-22). At the end of the follow-up the rest of the questionnaire concerning postoperative complications and symptoms was filled out.

RESULTS

During follow-up all patients got rid of pain and bleeding within one week of the operation. In both groups, transient urinary retention was noted in two patients. Incontinence to flatus was seen in the LIS group in 4 patients (6.2%) but no incontinence was noted in the fissurectomy group. There was two patients (3.1%) with fissure recurrence in the LIS group after 20 months, but no one in the fissurectomy group ($P>0.05$).

Table No. 1: Sex distribution of the patients in the two groups ($P>0.05$).



No patient in either group suffered from anal stenosis or perianal infections. In patients who underwent

fissurectomy only two cases were affected with complications (3.3%) but in the LIS group 6 patients (9.3%) developed complications ($P>0.05$). In the fissurectomy group, 58 patients (96.6%) and in the LIS group, 56 patients (87.5%) described their operation as satisfactory ($P>0.05$). All wounds were healed within 6-8 weeks.

Table No. 2: Age distribution of the patients in the two groups ($P>0.05$).

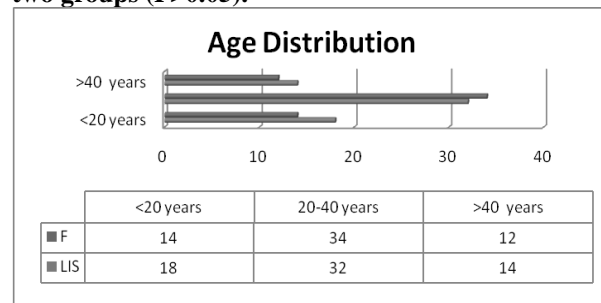
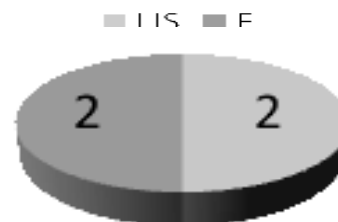


Table No. 3: Distribution of associated diseases in the two groups ($P>0.05$).

Associated Disorders (Hemorrhoids)



Operation	LIS	F
Associated disorders (hemorrhoids)	2	2

Table No. 4: Postoperative complications in F and LIS patients

Complication/ Operation	F	LIS
Persistence of pain	Nil	Nil
Persistence of bleeding	Nil	Nil.
Urinary retention	2(3.1%)	2(3.1%)
Incontinence of flatus or fecal soiling	Nil	4(6.2%)
Anal stenosis	Nil	Nil
Infection (abscess or fistula)	Nil	Nil
Total Complications	2(3.3%)	6(9.3%)

DISCUSSION

This study has shown that fissurectomy is a safe sphincter-sparing alternative in the treatment of chronic fissures in ano not responding to conservative treatment. Recent studies have shown that lateral

internal sphincterotomy is detrimental to the continence mechanism¹⁰. As long as the patient is willing to accept the risk of fecal incontinence, we can justify the gold standard therapy (LIS) as the 1st line treatment of chronic anal fissure¹¹. The length of the sphincterotomy and whether an open or closed technique is used are related to the incidence of incontinence. Given that surgical estimate of the length of the sphincterotomy is not always correct, lateral internal sphincterotomy is not as standardized a procedure as might otherwise be thought¹².

To examine the more sparing surgical technique, it is important to look at the etiology of chronic fissure in ano. Both hypovascularization and hypo perfusion occur in the posterior anal commissure in approximately 85% of normal people. Combination of these factors with internal anal sphincter hypertonia, causing ischemia, explains the poor wound healing and pain associated with chronic anal fissure^{13, 14, 15}. It does not explain why anterior chronic fissure in ano occurs in at least 10% of female patients and why pain of ischemic in nature occurs only for a certain period after defecation. Also the actual causative or initiating mechanism is unknown and the mechanism of the transition from acute to chronic fissure remains obscure. Repetitive trauma for example large diameter of fecal bolus may cause defects in the anal lining that heal poorly leading to unstable scar tissue and a defect termed chronic anal fissure. The central hypothesis in this study was that chronic fissure in ano is unstable scar tissue with a central defect in a hemodynamically unfavorable location.

Another aspect of our study is that it is a single procedure without any combination with other modalities such as topical isosorbide dinitrate or injection with botulinum toxin. Both techniques have been used in recent studies in combination with fissurectomy to cause temporary chemical sphincterotomy and to improve tissue perfusion^{4,5}. However, in other studies such as that by Meier et al. in Germany in 2001, fissurectomy has been used as a separate procedure in the treatment of chronic anal fissure with favorable results. Again in other studies, fissurectomy has been combined with posterior midline sphincterotomy^{16, 17, 18, 19, 20, 21, 22}. The main disadvantage of this latter procedure is keyhole deformity which may lead to fecal soiling. When fissurectomy is not combined with a midline sphincterotomy, wound dehiscence and keyhole deformities such as those that occur after anal fistulotomy do not occur.

All patients eventually were pain free within one week of operation. To emphasize the results, no patient in the fissurectomy group suffered from incontinence to flatus. There was no fissure recurrence in this group during the follow-up period. Totally, 58 patients

(96.6%) reported satisfactory results with their operation.

Statistical examinations reveal no significant difference between the two groups of patients; this may be due to the small numbers of patients, and larger series are needed to accurately compare these two different techniques. However, incontinence as a complication of LIS operation is so disabling that even small differences between two methods of surgery seem to be significant.

CONCLUSION

Finally, we concluded that given the lower rate of distressing complications (especially incontinence) and greater satisfaction of patients, fissurectomy could be considered as an alternative sphincter-saving and perhaps preferable approach in the surgical management of chronic anal fissures. However, much remains to be done regarding its long-term results through more extensive and larger clinical trials.

REFERENCES

1. Golfam F, et al. The effect of topical Nifedipine in treatment of chronic anal fissure. *Acta medica Iranica* 2010;48(5):295-299
2. Zarin M, et al Treatment of ch: fissure in ano with glyceryl trinitrate. *J Med Sci* 2010;18(3):123-25.
3. Massoud BW. Botulinum toxin injection versus internal anal sphincterotomy for the treatment of ch: anal fissure. *Ann Saudi Med* 2005;25(2) 2005: 140-142
4. Lindsey I, Cunningham C, Jones OM, et al. Fissurectomy- botulinum toxin: a novel sphincter-sparing procedure for medically resistant chronic anal fissure. *Dis Colon Rectum* 2004;47(11): 1947-52.
5. Engel AF, Eijssbouts QA, Balk AG. Fissurectomy and isosorbide dinitrate for chronic fissure in ano not responding to conservative treatment. *Br J Surg* 2002;89(1):78-83.
6. Meier Z, Eissen J. Chronic anal fissure therapy. *Kongressbd. Dtsch Ges Chir Kongr* 2001;118: 654-6.
7. Richard CS, Gregoire R, Plewes EA, et al. internal sphincterotomy is superior to topical nitroglycerin in the treatment of chronic anal fissure: Results of a randomized controlled trial by the Canadian Colorectal Surgical Trials Group. *Dis Colon Rectum* 2000;43:1048-58.
8. Rakinic J. *Anal Fissure. Clinics in colon & Rectal surgery.* 2nd ed. 2007.
9. Garcia J, Belmonte C, Wong WD, et al. Open vs. closed sphincterotomy for chronic anal fissure. Long-term results. *Dis Colon Rectum* 1996;39:440-3.

10. Khubchandani IT, Reed JF. Sequelae of internal sphincterotomy for chronic fissure in ano. *Br J Surg* 1989;76:431-4.
11. Mariusz H, Madalinski. Identifying the best therapy for chronic anal fissure. *WJGPT* 2011;6(2): 9-16.
12. Nelson RL. Meta-analysis of operative techniques for fissure-in-ano. *Dis Colon Rectum* 1999;42:1424-8.
13. Sultan AH, Kamm MA, Nicholls RJ, et al. Prospective study of the extent of internal anal sphincter division during lateral sphincterotomy. *Dis Colon Rectum* 1994;37:1031-3.
14. Gibbons CP, Read NW. Anal Hypertonia in fissures: cause or effect? *Br J Surg* 1986;73:443-5.
15. Abcarian H, Lakshmanan S, Read DR, et al. The role of internal sphincter in chronic anal fissures. *Dis Colon Rectum* 1982;25(6):525-8.
16. Lund JN, Scholefield JH. Etiology and treatment of anal fissure. *Br J Surg* 1996;83:1335-44.
17. Di Castro A, Biancari F, Andrea V, et al. Fissurectomy with posterior midline sphincterotomy and anoplasty in the management of chronic anal fissures. *Surg Today* 1997;27(10):975-8
18. Nahas SC, Sobrado CW, Araujo SE, et al. Chronic anal fissure: results of the surgical treatment of 220 patients. *Rev Hosp Clin Fac Med Sao Paulo* 1997;52 (5):246-9.
19. Saad AM, Omer A. Surgical treatment of chronic fissure-in-ano: a prospective randomized study. *East Afr Med J* 1992;69(11):613-5.
20. Hsu TC, Mackeigan JM. Surgical treatment of chronic anal fissure. A retrospective study of 1753 Cases. *Dis Colon Rectum* 1984;27(7):475-8.
21. Bode WE, Culp CE, Spencer RJ, et al. Fissurectomy with superficial midline sphincterotomy. A viable alternative for the surgical correction of chronic fissure-in-ano. *Dis Colon Rectum* 1984;27(2):93-5.
22. Abcarian H. Surgical correction of chronic anal fissure: results of lateral internal sphincterotomy vs. fissurectomy- midline sphincterotomy *Dis Colon Rectum* 1980;23(1):31-6.

Address for Corresponding Author:

Khush Mohammad Sohu,
Asstt. Prof: of Surgery,
Ghulam Mohammad Mahar Medical College,
Sukkur.

Original Article

Diurnal Variations in the Levels of Progesterone During Late Pregnancy

1. Shahnaz Nadir 2. Zafarullah Khan 3. Shahid Jamil 4. Mir Hassan Khan

1. Asstt. Prof. of Gyne & Obs, KMC, Peshawar 2. Asstt. Prof. of Entomology, BMC, Quetta

3. Assoc. Prof. of Medicine, KMC, Peshawar 4. SRO, PMRC, KMC, Peshawar

ABSTRACT

Background: Progesterone is a C-21 steroid hormone, plays a major role in the occurrence, maintenance and termination of pregnancy.

Objective: To study the diurnal variations in the levels of progesterone at the start and end of the day during late pregnancy in women having different life set ups.

Study Design: Experimental and Observational Study.

Place of Study: This study was conducted at the Department of Gynae and Obs., Khyber Medical College, Peshawar.

Materials and Methods: Blood samples of 50 women between 26-40 weeks of gestation were collected at two different intervals with a gap of 12 hours. Progesterone level was estimated by Serozyme EIA method.

Results: The concentration of progesterone was found low in the early morning and high in the late evening in our population. Besides, the magnitude of fluctuations in the samples of two different intervals declined with progress of age and weeks of gestation.

Conclusion: Our findings support the recommendation of restricting progesterone measurements to morning hours at all ages particularly during late pregnancy which is important information for clinicians at the time of interpretation of results.

Key Words: Progesterone, diurnal variations, late pregnancy.

INTRODUCTION

Progesterone is the first biologically active compound in the steroid biosynthetic pathway, formed in the adrenal cortex, the testes in males and the ovaries and foeto-placental unit in females. The same hormone has also been called the female's reproductive hormone as it regulates the accessory organs during the menstrual cycle and prepares the uterus for implantation of blastocyst. Some research workers demonstrated that due to luteal phase deficiencies, 64% women had infertility¹. Besides, the said hormone helps in maintaining pregnancy and prepares breasts for lactation.

The measurement of progesterone is important to confirm ovulation, luteal phase defect, to evaluate patients at risk from spontaneous abortion and to monitor replacement therapy². Its therapy is advised for breast cancer, breast pain, child spacing, withdrawal bleeding, Pre-Menstrual Syndrome, poor endometrial receptivity, post menopausal complications and when the level is low during pregnancy³.

Due to principle role of this hormone in pregnancy and substantial variations during reproductive life of women, it should be estimated in different racial groups. An experimental study on animals described circadian variations in plasma progesterone in the morning and night samples⁴. The diurnal variation of

testosterone hormone also has been well documented⁵. A previous study showed diurnal variation in the level of cortisol hormone, maximum concentration was found early in the morning and then declined throughout the whole day and reached to minimum level at the evening⁶.

In our early study, we found peak level of the progesterone in the second trimester which again declined in the last trimester⁷. While Burtis and Ashwood got peak concentration of hormone in the last trimester of pregnancy⁸. These conflicting observations also created our interest to study the level of progesterone two times a day i.e. in the early morning and at late evening particularly during late pregnancy in women having different nutrition, life style and environment.

MATERIALS AND METHODS

A total of 50 women (30 multiparas and 20 primiparas) in between 26 and 40 weeks of gestation from three villages of District, Nowshera were selected for this study. All of them had moderate socio-economic background and age range from 18 and 42 years. The participants had regular menstrual cycles, normal obstetric history, and had never used any hormonal medications or contraceptives. A scrutiny was done to exclude women with poor general health, had HIV/AIDS, polycystic ovarian diseases, congenital

abnormalities and those who did not give birth to live, healthy, singleton infants at term.

All the women were also subjected to a questionnaire including family income, family members, status and occupation, living condition and personal history like age, height, weight, dietary history, history of ailment and medication, onset of puberty, menses frequency, age at marriage, age at first delivery, history of lactation, history of delivery, parity, history of twins, gestation procedure, gestation period and previous laboratory investigation. Then objective of the study was explained to the enrolled women in the mother language, Pashto and written consent was obtained.

Five milli litre fasting blood samples were collected between 08 and 09 a.m; and 08 and 09 p.m. for three consecutive days/ nights from each woman. The blood was allowed to clot at room temperature for 30-45 minutes. Then it was centrifuged at 3000 rpm for at least 10 minutes. The serum was kept at -20°C until used for analysis. Progesterone was determined by Serozyme EIA method using blood employing polyclonal antibodies against P-7 carboxy-ethyl-thioether-BSA as the antigen⁹. Statistical examination of the data was performed accordingly.

RESULTS

The results of our analysis as given in tables 1&2 highlighted a significant diurnal variation in the levels of progesterone during pregnancy. In almost all the cases, the mean level was found low in the early morning and high in the late evening.

Table No.1 describes that the overall mean concentration of progesterone during the start of the day was 110.1 ng/ml and start of the night 122.7 ng/ml ($P < 0.05$). Besides, the differences in concentrations in the two samples of different intervals declined with age of pregnant women.

Table No.2 describes that the overall mean levels of the hormone was 107.8 ng/ml in the early morning and 123.9 ng/ml during the late evening ($P < 0.05$). The maximum difference (20.8 ng/ml) in the levels of the two samples was observed during 26-30 weeks and minimum (12.1ng/ml) during 36-40 weeks of gestation in our population.

Table No.1: Progesterone level (Mean \pm SD) during late pregnancy.

Age of women (In years)	Morning Level (ng/ml)	Evening Level (ng/ml)	P. Value
18-22	106.6 \pm 4.8	124.5 \pm 6.1	$P < 0.01$
23-27	108.2 \pm 4.9	123.7 \pm 6.1	$P < 0.01$
28-32	110.5 \pm 4.9	122.4 \pm 5.9	$P < 0.05$
33-37	111.9 \pm 5.0	121.8 \pm 6.0	$P < 0.05$
38-40	113.1 \pm 5.1	120.9 \pm 5.8	$P < 0.05$

Table No.2: Progesterone level (Mean \pm SD) during gestation.

Weeks of Gestation	AM level (ng/ml)	PM level (ng/ml)	P. value
26-30	105.4 \pm 5.1	126.2 \pm 5.7	$P < 0.01$
31-35	108.2 \pm 5.6	123.6 \pm 5.4	$P < 0.05$
36-40	109.7 \pm 5.9	121.8 \pm 5.3	$P < 0.05$

DISCUSSION

The measurement of progesterone in maternal blood is essential for the maintenance / care of pregnancy. In our previous published article, we investigated the concentrations of the same hormone during three trimesters of pregnancy⁷. We observed quite different values in the third trimester from the already reported data⁸. Because of the conflict findings in the third trimester, this study was designed to determine the levels of progesterone twice a day at two different intervals during late/third trimester of pregnancy.

In the present work, we found same figures in our morning samples as observed in our previous study⁷. But we got significantly higher figures ($P < 0.05$) during the late evening. The cause of this conspicuous diurnal pattern is not known. Similar fluctuations in the concentrations of progesterone were reported in an early experimental study on animals⁴. A significant variation/rise in the level of testosterone from 08 am to 08 pm was also documented in men⁵. Other workers observed circadian variations in the levels of cortisol, and got maximum values early in the morning and minimum values at the late evening⁶. In contrast to our work, Dame et al found no consistent diurnal variations in the level of progesterone at any gestation¹⁰. Other researchers also demonstrated negative fluctuations in the same hormone during the luteal phase in heifers¹¹. Hence, further work is needed to exploit more the pattern of variations of this important hormone throughout the day during the reproductive age of women.

Besides, the values of the two tables showed that the differences in the samples of two intervals were high at the young age and 26-30 weeks of gestation but later presented progressive decline in both groups. The possible reason for the decline may be the body's homeostatic mechanism for the adjustment of precursors as needed to placenta for the production of this hormone. But still there is major difference even at 36-40 weeks of gestation and in the last age group. This warrants that if one has to advise/measure progesterone level for diagnostic or prognostic purposes, he should be aware of the idea of diurnal variations during late pregnancy and hence appropriate to extract the blood samples in the morning hours.

REFERENCES

1. Gul Y, Ali A, Tayyeb M. Role of progesterone in infertility. *Biomedica* 2006;22(1):241-44.
2. Khan MH, Khan JA, Shah SH, Rahim R. Serum progesterone and cholesterol levels in pregnant women in Pakistan. *PJMR* 1999; 38 (2): 69-71.
3. Baber MJ, Khan MH. A two way action of progesterone in fertility management. *JPMI* 2003; 17(2): 231-234.
4. Steintetz BG, Goldsmith LT, Hassan LH. Diurnal variations of serum progesterone in the pregnant bitches. *Endocrinology* 1998;127(3):1057-63.
5. Donald JB, Alvin MM, John BM. The effect of diurnal variation on clinical measurement of serum testosterone and other sex hormone level in men. *J Clin Endocrinology* 2009;94(3):907-13.
6. Aron DC, Tyrell JB. Gluco-corticoides and adrenal androgens. In: Greensoan FS, Baxter JD, editors. *Basic and clinical endocrinology*. 4th ed. USA: Appleton and loge;1994.p.307-346.
7. Khan MH, Khan JA, Mabood SF, Begum N. Hormonal profile in pregnant women. *PJMR* 2002; 41(4):159-161.
8. Burtis CA, Ashwood ER. *Teitz textbook of clinical Biochemistry*. 2nd ed. Philadelphia: WB Saunders company; 1994.p.2203-4.
9. Serono Diagnostics SA. Serozyme immunoenzymetic assay, Determination of hormone in serum or plasma. Switzerland. 1992.
10. Dame FJ, McGarrigle HHG, Gillian CLL. Diurnal variations of plasma progesterone and cortisol in late pregnancy. *Eu J Obstet and Gyne* 1989;32(2): 57-66.
11. Hannan MA, Fuenzalida MJ, Siddique MAR. Diurnal variation in LH and progesterone during the luteal phase in heifers. *J Theriogenology* 2010; 74(8):1491-98.

Address for Corresponding Author:

Shahnaz Nadir,
Asstt. Prof. of Gyne & Obs,
Khyber Medical College,
Peshawar.

Original Article

Frequency and Type of Stroke in Hypertensive Patients

1. Rafique Ahmed Memon 2. Amir Hamzo Dahri 3. Shahzad Memon

1. Assoc. Prof. of Medicine 2. Assoc. Prof. of Pathology 3. Registrar of Medicine,
Peoples Medical College / Hospital, Nawabshah.

ABSTRACT

Objective: To describe the frequency and type of stroke in hypertensive patients

Study Design: Descriptive study.

Place and Duration of Study: This study was conducted in the carried out in the Department of Medicine (ICU) at Peoples Medical College / Hospital Nawabshah, from 1st September 2008 to 28th February 2009.

Patients and Methods: A total of 100 patients were admitted to the ICU of medicine department. Relevant investigations like CT Scan brain, ECG and routine investigations like blood CP, Serum cholesterol and random blood sugar were done. Data was retrieved from the files on a structured performa.

Results: 65 were male and 35 female with ratio of 1.8:1. Mean age was 60.58 ± 4.25 years for male and 59.22 ± 3.25 for female. Ischemic stroke were 73% cases while 27% cases were recurrent hemorrhagic stroke. In ischemic stroke uncrossed hemiplegia occurred in 69(94.5%) cases and crossed hemiplegia occurred in 4(5.5%) cases while all hemorrhagic stroke patients suffered from uncrossed hemiplegia (100%).

Conclusion: Frequency of ischemic stroke was more common then hemorrhagic stroke in hypertensive patients.

Key words: Frequency, Stroke, ischemic stroke, hemorrhagic stroke.

INTRODUCTION

Cerebrovascular disease is the third most common cause of death in developed world and the second most common cause of death worldwide^{1,2}. According to World Health Organization (WHO) 5.5 million people died of stroke in 2002 and roughly 20% of these deaths occurred in South Asia³. Although since past three decades there is a decline in the incidence of the disease in the Western population¹, but the burden of the disease has increased in South Asian countries (India, Pakistan, Bangladesh, and Sri Lanka), and is expected to rise⁴.

Two thirds of all deaths due to circulatory disorders (stroke and ischemic heart disease) occur in developing world. In white people, 80-85% of strokes are ischemic in origin but In Asians and blacks the proportion is 60-70%⁵. Stroke is common complication of hypertension and may be due to cerebral hemorrhage or cerebral infarction. Carotid atheroma and transient cerebral ischemic attacks are more common in hypertensive patients. Hypertension is major risk factor for ischemic as well as hemorrhagic strokes. Hypertension is found in 72-81% of patients with intracerebral hemorrhage⁷. 80% of patients with diagnosis of acute stroke are hypertensive on admission to hospital and although the elevated blood pressure levels spontaneously decline over subsequent 7-10 days, 30% of patients still may be classified as hypertensive (B.P more than 169/95mmhg) at long term follow up⁸.

Stroke occurs mostly in middle aged subject (45 to 69years), and occurring in developing region⁹. Acute stroke is characterized by the rapid appearance (usually over minutes) of a focal deficit of brain function, most commonly a hemiplegia with or without signs of focal higher cerebral dysfunction (such as aphasia), and hemi sensory loss and visual field defect or brainstem deficits¹⁰. Computerized Tomography (C.T) is very sensitive and specific for hemorrhage within first eight days of stroke only, in general strategies in which most patients were scanned immediately cost least and achieved the most qualities as cost of providing C.T, (even out of hours) was less than cost of in patient care¹¹.

PATIENTS AND METHODS

This case series study was carried out in the Department of Medicine (ICU) at Peoples Medical College / Hospital Nawabshah, from 1st September 2008 to 28th February 2009. 100 patients history of hypertension associated with acute stroke or after 24 hours of stroke and patients having infarction or haemorrhage stroke diagnosed on CT scan of the brain were included. Exclusion criteria were subarachnoid hemorrhage, syncopal attack, neurological deficit secondary to epilepsy or an infective, metastatic etiology and blood dyscrasias.

Detailed History was taken from all the patients regarding to hypertension, duration of hemiplegia, headache, vomiting, symptoms of higher cerebral dysfunction (such as aphasia), hemisensory loss and visual field defect and physical examination regarding

record of blood pressure, pulse, neurological and cardiovascular examination done. Relevant investigations like CT scan brain, ECG and routine investigations like blood CP, Serum cholesterol and random blood sugar were done. Results were prepared with help of tables and graphs. Data was analyzed through SPSS v.16 software.

RESULTS

100 consecutive patients with ischemic and hemorrhagic stroke were admitted. 65 were male and 35 female with ratio of 1.8:1. There was wide variation of age ranging from a minimum of 31 years to 80 years with mean age was 60.58 ± 4.25 years for male and 59.22 ± 3.25 years for female.

The stroke was more common in married 92% than unmarried 8% (Chart 1). Majority of the ischemic strokes were newly onset strokes 73% cases while 27% cases were recurrent hemorrhagic strokes. In ischemic stroke uncrossed hemiplegia occurred in 69(94.5%) cases and crossed hemiplegia occurred in 4(5.5%) cases while all hemorrhagic stroke patients suffered from uncrossed hemiplegia (100%).

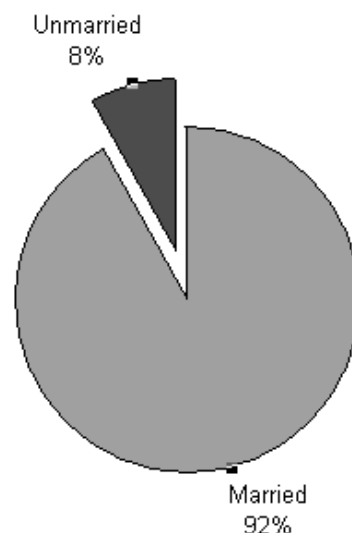
Table No.1:

Variable	Number of Patients	Percentage
Gender		
• Male	65	65%
• Female	35	35%
Type of Stroke		
1. Ischemic stroke	73	73%
• Lacunar	25	34%
• Putaminal	15	20%
• Thalamic	8	10%
• brain stem	4	5%
• Cerebellar	4	5%
• Unlocalized	17	23%
2. Hemorrhagic stroke	27	27%
• Putaminal	10	37%
• Thalamic	5	18%
• Brain stem	4	14%
• Cerebellar	3	11%

Out of 73 patients with ischemic stroke, the frequency of patients in descending order regarding territorial distribution were lacunar 25(34%) cases, putaminal 15(20%) cases, thalamic 8(10%) cases, brain stem 4(05%) cases, cerebellar 4(05%) cases and unlocalized 17(23%) cases while out of 27 in hemorrhagic stroke frequency were putaminal 10(37%) cases, thalamic

5(18%) cases, brain stem 4(14%) cases and cerebellar 3(11%) cases (Table No.1).

Chart No.1



DISCUSSION

Stroke is very common disorder in Pakistan and is one of the major causes of mortality and morbidity after ischemic heart disease and cancer. Studies show stroke to be the third commonest cause of death in developed countries and second most common cause of death worldwide^{1,2}. Stroke according to WHO classification stroke is "A focal (or at times global) neurological impairment of sudden onset, and lasting more than 24 hours (or leading to death), and of presumed vascular origin"^{10,12}.

In our study the hypertensive stroke was found more common in male with male:female ratio was 1.8:1. However the male to female ratio given by Portugal¹³ is 1.2:1. However another studies conducted at Poland¹⁴ and Taiwan¹⁵ population showed male:female ratio of 1.6:1 and 1.4:1 respectively which are quite different from present study, because of lesser number of female patients who smoke and take alcohol in Pakistan while study conducted at Poland showed regular smoking and alcohol used by women. The study conducted by Javed MA et al. showed ratio of 1.9:1 in Pakistan¹⁶. The age ranged from 31 to 80 years with mean age was 60.58 ± 4.25 years for male and 59.22 ± 3.25 for female which is comparable to other study Fonesa et al where mean age are 68 years¹³ and Mexican American population a relatively young mean age was found 58 years, which they attribute to high prevalence of Diabetes Mellitus in their population¹⁷. Similar observations were reported by All-Rajeh et al in Saudi Arabia¹⁸.

In the present study we had 73% of infarctive stroke and 27% hemorrhagic stroke. Compared to study conducted at Japanese population showed an incidence of infarctive stroke to be 56%¹⁹. Brazilian population showed an incidence of 73% for cerebral infarction, 19% for cerebral hemorrhage and 8% for subarachnoid hemorrhage²⁰. However American population showed an incidence of infarctive stroke to be 78%²¹. Only 9 out of 55 patients of age more than 61 years suffered cerebral hemorrhage in our study. This shows that not only the incidence of stroke increases with age but also shows that the incidence of cerebral infarction increases with age as compared to cerebral hemorrhage. Similar observation was made by Davis et al in the United States where 88% of stroke in the elderly hypertensive patients were found to be infarctive²². This fact is probably related to increase thromboembolism due to atrial fibrillation, carotid stenosis and left ventricular failure in elderly patients.

Crossed vs uncrossed hemiplegia was compared in our study 94.5% patients with infarctive hypertensive stroke had uncrossed hemiplegia, whereas 5.5% of the infarctive hypertensive stroke patients had crossed hemiplegia. All hemorrhagic stroke patients were found to have uncrossed hemiplegia. This observation is also seen in the study conducted by Geffier D et al, in the United States²³.

Regarding the territorial distribution of hypertensive strokes in our study was commonest site of infarction was to be lacunar 34.25% followed by second most common site of infarction in hypertensive stroke was putaminal lesion 20.5% and 23.25% patients exact site of lesion in infarctive hypertensive stroke could not be localized probably because of early CT scan intervention done in these patients, in which it is some times difficult to exactly localize the lesion.

Similar observation is also made by Mast H et al in Germany²⁴ in a study which was conducted on hypertensive diabetes patients in which lacunar infarction was found in 30% of the cases and putaminal infarction in 22% of the cases and in another study of Fonesca reported an incidence of 34% of lacunar infarction and 18% for putaminal infarction in the study conducted only on hypertensive patients¹³.

Out of the 22 hemorrhagic hypertensive strokes the commonest site of bleed was putamin 35% in our study. This fact is also observed by Davis BR et al in a study conducted at Houston United States, in which putaminal hemorrhage was found more commonly 31% in hypertensive patients²².

CONCLUSION

Frequency of ischemic stroke is much greater and related with disability then hemorrhagic stroke due to

less public awareness regarding outcome of hypertension.

REFERENCES

1. American Heart Association: Heart Disease and stroke statistic 2007 update. Dallas: USA, American Heart Association; 2007.
2. Sarti C, Rastenyte D, Cepatitis Z, Tuomilehto J. International trends in mortality from stroke, 1964 to 1994. *Stroke* 2000;31:1588-1601.
3. World Health Organization (WHO). The Atlas of heart Disease and stroke. http://www.who.int/cardiovascular_diseases/resources/atlas/en/ (Accessed December 18, 2007).
4. Bulatao RA, Stephens PW. Global estimates and projections of mortality by cause. Washington DC: Population, Health and Nutrition Department; World Bank, pre working paper 1992;1007.
5. Shah FU, Salih M, Saeed MA, Tarique M. Validity of Sirraj stroke scoring. *JCPSP* 2003;13:391-93.
6. Bloomfield P, Bradburg A, Grubb NR, Newby DE. Cardiovascular disease. In: Boon NA, Colledge NR, Walken BR, Hunter JAA, editors. *Davidson's Principles and Practice of Medicine*. 20th ed. Edinburgh: Churchill Livingstone; 2006.p.519-646.
7. Khealani BA, Syed NA, Maken Sabeen, Mapari VU, Hameed B, AH S, et al. Predictors of ischemic versus hemorrhagic strokes in hypertensive patients. *JCPSP* 2005; 15; 22-25.
8. Danson SL, Manklelon BN, Robinson TG, Panerac RB, Potter JF. Which parameters of beat to beat blood pressure and validity best predict early outcome after acute ischemic stroke? *Stroke* 2000; 31 463-68.
9. Lanes CMM, Bennelt DA, Feigen VL, Eodges A. Blood pressure and stroke, an overview of published reviews. *Stroke* 2004; 35; 1024-1033.
10. Allen CMC, Luke CJ, Denis M. Neurological disease. In: Boon NA, Colledge NR, Walken BR, Hunter JAA, editors. *Davidson's principles and practice of Medicine*. 20th ed. Edinburgh. Churchill Livingstone; 2006.p.1145-1256.
11. Waldlaw JM, Keir SL, Seymor J, Lewis S, Sander cock PA, Denis MS, et al. What is best imaging strategy for acute stroke. *Health technol acces* 2004; 8; 1-180.
12. World Health Organization: The WHO Stepwise approach to stroke surveillance. Geneva: WHO; 2005.
13. Klimowicz-Mlodzik I, Pietrzykowska I, Chodakowasa-Zebrowska M, Cegielska J. Cigarette smoking and alcohol abuse effects on stroke development. *Neurol Neurochir Pol* 1995;29(2):151-8.

14. Jeng JS, Lee TK, Chang YC, Huang ZS, Ng SK, Chen RC, et al. Subtypes and case fatality rates of stroke: a hospital based stroke registry in Taiwan. *J Neurol Sci* 1998;156(2):220-6
15. Javed MA, Malik SA, Khursid K. Cerebrovascular accident pattern and distribution of different types based on computed tomography. *Pak J Surg* 1995;11(4):213-15.
16. Al Rajeh S, Awada A, Niazi G, Larbi G. Stroke in Saudi Arabian National Guard Community . Analysis of 500 consecutive cases from a population based hospital. *Stroke* 1993;24(11):402-6.
17. Fonseca T, Cortes P, Monteiro J, Salgado V, Ferro J, Franco AS. Acute cerebrovascular disorder and arterial hypertension. Prospective study with 48 patients. *Rev Port Cardiol* 1996;15(7):565-73.
18. Suzuki K, Vultsuzawa T, Takita K. Clinico epidemiological study of stroke in Akita, Japan *Stroke* 1987;18:402-6.
19. Cabral NL, Longo AL, Moro Ch, Amaral CH, Kiss HC. Epidemiology of cerebrovascular disease in Joinville, Brazil. An institutional study. *Arq Neuropsiquiatr* 1997;55(3A):357-63.
20. Schmidt EV, Smirnov VE, Ryabun US. Results of seven years prospective study of stroke patients. *Stroke* 1998;19:942-9.
21. Bamford J, Sandercock P, Dennis M, Burn J, Warlow C. A prospective study of acute cerebrovascular disease in the community stroke project 1981-86. Incidence, case fatality rate and overall of one year cerebral infarction. Primary intracerebral and SAH: *J Neurology* 1990;54(1):16-22.
22. Davis BR, Vogt T, Frost PH. Risk factors for stroke and type of stroke in persons with isolated systolic hypertension. Systolic hypertension in the elderly program cooperative research group. *Stroke* 1998;29:1333-40.
23. Bonita R. Epidemiology of stroke. *Lancet* 1992;339:342-4.
24. Mast H, Konnecke HC, Hartmann A, Staph C, Marx P. Association of hypertension and diabetes mellitus with microangiopathic cerebral infarct patterns. *Nervenarzt* 1997;68(2):129-4.

Address for Corresponding Author:

Rafique Ahmed Memon

Associate Professor Medicine Unit III

PUMHS, Nawabshah.

Cell # 03013818053

Original Article

Complications of Pre-Term Infants in the Neonatal Unit

1. Aneela Shaheen 2. Saima Batool 3. M. Arshad Mahmood 4. Muhammad Naeem
5. Abdul Raheem

1. Assoc. Prof. 2. Asstt. Prof. Dept. of Pediatrics, The University of Lahore 3. Asstt. Prof. of Ophthalmology, SSTH, Lahore 4. 2. Asstt. Prof. Dept. of Pediatrics, The University of Lahore 5. Medical Officer Shaikh Zayed Hospital, Lahore.

ABSTRACT

Objective: To assess the complications of preterm infants in neonatal intensive care unit and compare that with those faced by preterm infants in western neonatal intensive care unit.

Study Design: A prospective comparative study

Place and Duration of Study: This study was conducted at Paediatrics Department, Shaikh Zayed Hospital Lahore from 1st December 1997 to 30th November 1998.

Patients and Methods: All neonates delivered before 37 weeks and admitted to the neonatal Intensive care unit (NICU, SZH) were included in the study. It was a prospective study conducted over a period of one year from 1st December 1997 to 30th November 1998. The study population included 170 preterm neonates. For the purpose of study, these infants were divided into three gestational age groups i.e. < 30 weeks gestational age, 30 to 35 weeks gestational age, and > 35 weeks gestational age. These neonates were then prospectively followed till discharge from NICU.

Results: Out of the 170 preterm infants admitted to NICU, 128 infants survived and were discharged under stable conditions, while 42 infants expired.

Conclusion: Maximum number of complications and highest mortality i.e. 87% was seen among the most premature group, i.e. below 30 weeks gestational age. Mortality in the gestational age group 30 to 35 weeks was 43%, while it was 9% in the gestational group >35 weeks.

Key Words: Pre-term infants, Neonatal, Perinatal mortality, Infant morbidity.

INTRODUCTION

A premature infant is defined as a live born infant delivered before 37 weeks from the 1st day of the last menstrual period. Although rapid advance in perinatal & neonatal medicine has improved survival of preterm infants, however prematurity still carries high morbidity and mortality especially in developing countries like Pakistan. The only solution to this problem is to provide best of neonatal care to these tiny infants and improve their survival. Premature infants are prone to certain complications because of their low birth weight and also because of the immaturity of their various organ systems. Recently there has been found that morbidity as well as mortality relates more to gestational age than to weight at birth.¹ Preterms make a large share to the total number of admissions to NICU. In one analysis of 4 years admission to NICU in Peshawar, it was seen that 39.4% admissions were of preterms.² Even after discharge from Nursery, preterms require rehospitalization more than the term infants.³ Infants born preterm are at increased risk for Sudden Infant death Syndrome, hypoglycemia, hypothermia, hypocalcaemia preterms are also reported to be at highest risk for developing intraventricular hemorrhage,

ischemic brain injury, retinopathy of prematurity as well as developmental disabilities.⁴ Thus prematurity is a major cause of perinatal mortality and infant morbidity.⁵ So measure should be done to improve our neonatal services. In Pakistan facility of well-equipped NICU is available in very few tertiary centers.

PATIENTS AND METHODS

This study was carried out at the neonatal intensive care unit (NICU) in Sheikh Zayed Hospital, Lahore. It was a prospective study conducted over a period of one year from 1st December 1997 to 30th November 1998. All preterm neonates admitted to Intensive care unit Sheikh Zayed Hospital were included, 170 preterm neonates. For the purpose of study, these neonates were divided into three groups according to gestational age group, i.e. below 30 weeks, 30-35 weeks and 35-37 weeks. A detailed antenatal record of each patient was obtained and a detailed physical examination was carried out within twenty-four hours of birth. Based upon this examination, each child was assigned initial diagnosis at the time of admission to NICU. Each baby was followed closely till discharge and the complications, the outcome developed by neonate was also recorded.

Relevant laboratory tests were also recorded. Later this information was correlated to assess the course & outcome of preterms in our set up. For retinopathy of prematurity infants were assessed and followed up by department of ophthalmology.

RESULTS

Out of the total 170 patients included in our study 16 (9%) belonged to gestational age group of less than 30 weeks, 56 (33%) patients belonged to gestational age group 30-35 weeks, 98 (58%) were more than 35 weeks gestational age, 47% were male, and 53% were females. 138 preterm neonates (81%) were delivered in SZH, and 32 (19%) were delivered elsewhere and referred to NICU Shaikh Zayed Hospital. 148 (87%) infants in our study population were appropriate for gestational age, (AGA), 7 (14%) infants were large for gestational age (LGA), while 15 (9%) were small for gestational age. (SGA). Analysis of the study population showed, that 50 (29%) preterm infants had the primary diagnosis of sepsis, 15 (9%) infants had

RDS, 8 (5%) infants had birth asphyxia, 5 (3%) infant where cases of meconium aspiration 3 (2%) infants had jaundice neonatorum, and 1% had multiple congenital anomalies while 88 (51%) infants were otherwise healthy, at the time of admission and were admitted for preterm care and observation. The incidence of complication among our study population and their distribution among these gestational age groups. As for as outcome of our study infant related to gestation age is concerned, a total of 128 (75%) infants survived and Discharged under stable condition. while 42 (25%) infant expired. Mortality in the gestational group < 30 weeks was 87% (14 infants died). 43% (24 infants) in gestational group 30 to 35 weeks survived and 4% infants mortality was observed in gestational group more than 35 weeks. Septic shock, disseminated intravascular coagulation, intracranial hemorrhage, hypoxic ischemic encephalopathy and Respiratory Distress Syndrome were among the common causes of death in our study group (Table No. 1).

Table No. 1: Frequency of complications according to age

Complications	Total (n = 170)		<30 weeks (n = 16)		30 – 35 weeks (n = 56)		>35 weeks (n = 98)	
	No.	%	No.	%	No.	%	No.	%
Sepsis (presumed)	73	43.0	16	100.0	37	66.0	20	20.0
RDS	15	9.0	7	44.0	8	14.0	-	-
Apnea	12	7.0	5	31.0	7	12.0	-	-
Pulmonary hemorrhage	8	5.0	4	25.0	4	7.0	-	-
Meconium aspiration	5	3.0	-	-	-	-	5	5.0
Pneumothorax	4	2.0	2	12.5	2	4.0	-	-
PDA	7	4.0	4	25.0	3	5.0	-	-
Anemia	23	14.0	12	75.0	11	20.0	-	-
Jaundice Neonatorum	124	73.0	16	100.0	45	80.0	63	64.0
DIC	14	8.0	7	44.0	5	9.0	2	2.0
Necrotizing enterocolitis	11	6.0	4	25.0	06	11.0	1	1.0
Hypoglycemia	19	11.0	7	44.0	9	16.0	3	3.0
Hypothermia	12	7.0	8	50.0	4	7.0	-	-
Hypocalcemia	55	32.0	13	81.0	27	48.0	15	15.0
Hyponatremia	6	4.0	4	25.0	1	2.0	1	1.0
Intraventricular Haemorrhage	22	13.0	9	56.0	10	18.0	3	3.0
Hypoxic ischemic encephalopathy	6	4.0	-	-	3	5.0	3	3.0
Neonatal Seizures	13	8.0	7	44.0	5	9.0	1	1.0

DISCUSSION

During the past few decades improvement in the neonatal intensive care has led to marked improvement in neonatal mortality.⁶ A large share of improved neonatal mortality is due to the increasing survival among premature infant. Unfortunately reduced mortality among preterm infants is accompanied by increase in morbidity. So the emphasis has now been shifted from concerns of mortality towards a better understanding of the scope and nature of morbidity.

Results of our study showed that the prominent group of patients admitted to NICU was more than 35 weeks gestation age and very few preterm i.e. 9% with gestational age less than 30 weeks were brought to NICU. This could be partly due to improved obstetrical strategies to prevent or at least delay preterm labor and the other reason might be that in our setup mortality increases sharply below 30 weeks gestation. Analysis of our study reveal that 51% preterms were brought to NICU for care and monitoring, while 29% had the

primary diagnosis of sepsis. Among the other infant admitted prominent diagnosis was RDS 9% , birth asphyxia 5%, JNN 2% , meconium aspiration 3%, and multiple congenital anomalies 1% .During stay in NICU 43% infants had presumed sepsis either as a primary diagnosis or after wards (Culture proven 32%). The highest incidence of sepsis was seen in the gestational group <30 weeks i.e. 100%. This high percentage can be explained on the fact that suspicion of early onset of sepsis is almost universal to the very low birth weight preterm infants.⁷

The over all incidence of RDS was found to be 9%, it was 44% in infants below 30 weeks, which compares favorably to the incidence of RDS given 60-80% below 28 weeks gestational age and 15-30% below 32 –36 weeks.⁸ The overall mortality for preterms with RDS was quite high i.e. 9%. The results of our study showed 5% incidence of pulmonary hemorrhage and 2% incidence of pneumothorax with the highest incidence again seen in infants below 30 weeks gestational age i.e. 25% and 12% respectively. The incidence of anemia was 14% among our study population and about 75% infants below 30 weeks gestational age developed anemia requiring blood transfusion. 8% infant developed disseminated intravascular coagulation, which proved fatal in all the infants.

A total of 22(13%) infants developed intraventricular hemorrhage, however an other study conducted in Pakistan codes an overall incidence of 75% PVH-IVH in infants less than 34 weeks gestation⁹, which is very high as compared to our study.

The overall mortality of our study infants was 25% as expected max. survival was seen among infants more than 35 weeks gestational age i.e. 96% and survival was lowest among infants less than 30 weeks gestational i.e. 13%. While survival rate for infants 30-35 weeks gestational age was 55% this survival rate is quite low when we compare it with study conducted in The West. One study has given 95% survival rate for 30-31 weeks gestation¹⁰ another study has coded 25% mortality for infants less than 32 weeks gestation¹¹, which is in sharp contrast to our study which showed a 87% mortality in infants below 30weeks gestation and 45% mortality at 30-35 weeks gestation.

There are a number of factors that contribute to the marked difference observed in mortality of preterm infants between our hospitals and the west. Umbilical and arterial catheterization and central venous lines are used in the west for providing nutrition, as well as for taking blood samples, which may minimize infection. However in our set up peripheral veins and small arteries are used for the purpose of phlebotomy tests and for providing nutrition, repeated pricking leads to increased chances of infection. The nurse to neonate ratio works to a disadvantage when compared to the developed countries thus septicemia remains a major

cause of neonatal morbidity and mortality in the developing world.^{12,13}

The important inference from our study is that a premature baby is a catastrophe emotionally for the parents, psychologically for the Obstetrician, economically for the nation and challenge for the paediatrician. Shorter gestational age is usually associated with a need for invasive procedures, mechanical ventilation and prolonged hospital stay. More immature the infant, greater are the chances of developing complications like RDS, IVH, sepsis and NEC etc. All these factors contribute to high morbidity and mortality seen among the preterms. Another important inference from our study is the high incidence of sepsis which as already discussed is due to the lack of resources, limited number of nursing staff and very frequently done arterial pricks and putting intravenous branulas daily or every second or third day. Thus we need to improve the quality of our neonatal intensive units and neonatal services in order to reduce the high morbidity and mortality associated with prematurity.

CONCLUSION

Maximum number of complications and highest mortality i.e. 87% was seen among the most premature group, i.e. below 30 weeks gestational age. Mortality in the gestational age group 30 to 35 weeks was 43%, while it was 9% in the gestational group >35 weeks.

REFERENCES

1. Wariyar U, Richmond S, Hey E. Pregnancy outcome at 24-31 weeks gestation: neonatal survivors. *Arch Dis Child* 1989; 64: 678-86.
2. Mehr TR, Tufail M. Neonatal disease profile in NWFP. An analysis of four year admission 1977-1980. *Pak Pediatr J* 1983; 11: 7-22.
3. Cunningham CK, McMillan JA. Rehospitalization for respiratory illness in infants of less than 32 weeks gestation. *Pediatrics* 1991; 88: 527-32.
4. Msall ME, Buck C, Roger BT, et al. Risk factors for the major development impairment and need for special education resources in extremely premature infants. *J Pediatr* 1991;119:606-14.
5. Papernick E, Baryer J, Dreyfus J, et al. Prevention of preterm births. A perinatal study in Haguenau, France. *Pediatrics* 1985; 76: 154 8.
6. Richardson DK, Gray JE, Gortmaker SL, Goldmann DA, Pursley DM, McCormick MC. Declining severity adjusted mortality: evidence of improving neonatal intensive care. *Pediatrics* 1998; 102: 893-9.
7. Stoll BJ, Gordon T, Korones SB, et al. Early onset sepsis in very low birth weight neonates: a report from the National Institute of Child Health and

- Human Development neonatal Research, New York. J Pediatr 1996; 129: 72-80
8. Kliegman RM. Respiratory tract disorders: hyaline membrane disease. In: Behrman RB, Kliegman RM, Arvin AM, editors. Nelson text book of pediatrics. 15th ed. Philadelphia: WB Saunders Company;1996.p.478-84.
 9. Mahfooz-ur-Rehman, Rasul G, Khan HI. Prevalence of periventricular intraventricular hemorrhage in premature and low birth weight infants. Pak Pediatr J 1998; 22: 145-7.
 10. Cartilidge PH, Stewart JH. Survival of very low birth weight infants in a geographically defined population. Scta Paediatr 1997; 86 : 105-10.
 11. Thea M, VanZeban Van der AA, Verloove-Vanhorick PS, Jan RH. Child Health Morbidity of very low birth weight infants at corrected age of two years, in a geographically defined population. Lancet 1989; 4: 253-5.
 12. Ashiq B, Jamil M. A study of neonatal aerobic bacterial septesemia. JCPSP 1996; 6: 18-21
 13. Bhutta ZA, Yousf K. Neonatal sepsis in Karachi: Factors determining outcome and mortality. J Trop Pediatr 1997; 43: 65-70.

Address for Correspondence Author:

Aneela Shaheen,
Associate Professor,
Department of Pediatrics,
Faculty of Health Sciences,
The University of Lahore.

Original Article

Alfagin: A herbal product beneficial in Hypercholesterolemia

1. Fareeda Islam 2. M. Iqbal Ahsun 3. S. M. Shamim

1, Prof. of Pharmacology, KM&DC, Karachi 2. Sr. Registrar of Anesthesia, KM&DC, Karachi

3. Prof. of Pharmacology, Baqai Medical University, Karachi.

ABSTRACT

Objective: To determine the effects of herbal drugs in Hypercholesterolemia.

Study Design: Experimental Study.

Place and Duration of Study: This study was conducted in the Department of Pharmacology, University of Karachi from Jan. 2007 to Dec. 2008.

Materials and Methods: In the present study experiments regarding lipid profile were performed on rabbits of either sex, the calculated dose was administered for 30 days and 60 days (High dose and low dose group).

Results: Alfagin possess wide therapeutic range and is comparatively safe, animals of neither group showed no gross toxicity. No death occurred in control and test animals.

Discussion: Alfagin has been shown having, lowering capability of cholesterol.

Conclusion: It has been concluded that Alfagin is beneficial in hypercholesterolemia.

Keywords: Alfagin, Hypercholesterolemia, Herbal Drug.

INTRODUCTION

Herbal remedies and extracts are traditionally being used and available world wide for the treatment of many diseases, since natural products have played and continue to play an invaluable role in the process of drug development^(1,2,3). The use of plants in drug discovery and development is less time consuming and cheaper^(4,5). The term herb is used to refer not only herbaceous plants but also to bark roots, leaves, seeds flowers and fruits of trees⁶. Among the first active principles to be isolated were strychnine, morphine, atropine, papaverine and colchicines⁽⁷⁾. Herbal drugs have been extensively used in developed countries as well because patients are now looking for alternative and less invasive approaches to health care⁸. Currently about 122 clinically useful prescription drugs derived from 94 plant species are used worldwide for the treatment of diseases⁹. Plants have been used for the development of herbal remedies as alternative therapy e.g. cranberry Echinacea, few garlic, ginko, St. John's Wort, Saw Palmetto, Valerian Goldenseal, Ginseng.^{9,10,11}

Today the use of herbs and herbal extracts for the treatment of disease is an established therapeutic modality although much of the science behind it is still in its infancy nevertheless, modern medicine also benefited from the plants of therapeutic importance and many drugs are derived from natural resources.

Alfagin (Herbal Product)

Alfagin is a unique preparation of an original formulation composed solely of bioactive medicinal herbs, free of any synthetic chemicals and developed in the laboratories of Herbiion.

Alfagin increases muscle strength, physical work capacity and helps in overcoming fatigue by enhancing oxygen metabolism, due to its powerful adaptogenic properties, it provides resistance against stress and strain. It is also used in mental exhaustion, nutritional deficiencies, geriatric disorders, convalescence and anorexia.

Alfagin also simulates and stabilizes the central nervous system; it improves adaptability increases tolerance against infections and promotes self-recovery against disease, the composition of Alfagin is Ginseng (*eluthrococcus senticosus*), *Medicago sativa* (alfalfa), *Embilica officinalis* (*emibilica myrobalan*) and *Trigonella foenum gracum* (fenugreek). Each 5ml elixir contains

S. No.	Name of Ingredients	Quantity	
	Extract of:		
01	Ginseng	125.00	mg
02	Medicago Sativa	250.00	mg
03	Embilica Officinalis	400.00	mg
04	Trigonella	250.00	mg
	Excipients:		
01	Sucrose	3.50	gm
02	Glycerin	0.05	ml
03	Citric Acid	6.00	mg
04	Malt extract	500.00	mg
05	Methyl paraben	5.00	mg
06	Propyl paraben	1.00	mg
07	Propylene glycol	0.0012	ml
08	Essence of orange No. 9627	0.003	ml
09	Essence of Strawberry	0.003	ml
10	D.I. Water q.s.	5.00	ml

MATERIALS AND METHOD

This study was carried on 54 healthy white rabbits of either sex weighing from 1800 to 2000 grams. All animals were equally divided into six groups two group served as control while other four received normal and high doses of Alfagin syrup, before administration of drug apparent health of these animals was monitored during the conditioning period under laboratory environment for a week specifically noting loss of hair, diarrhea, edema, ulceration and lack of activity. All animals were given standard diet prepared in the laboratory and water.

Dosing: Alfagin was administered in the normal dose of 0.25 ml/kg (prescribed dose 10ml) twice a day and 0.5 ml / kg high dose for a period of 30 and 60 days orally, the control group received saline orally.

Sample Collection: Blood samples of about 7 C.C. were collected from these animals through cardiac puncture technique after completion of dosing period on 30th day and in other group on 60th days to perform various biochemical tests.

Assessment of Gross Toxicities: The gross toxicities were observed every one week after the administration of the drug. The number of animals died during there intervals was also noted.

Autopsy was performed after random selection after the completion of dosage. The remaining survived animals were left to observed changes after drug free interval of 15 days.

Biochemical Testing: Serum were immediately separated out by centrifuging (Heraeus Christ LaboFuge A) blood samples at 4000 upon for about 8 minutes and parameter were analysed within three hours of sample collection on vital lab eclipse automatic analogue (Merk) at 37°C.using standard reagent kits supplied by Merk.

Lipid profile including cholesterol, triglycerides, HDL, VLDL, LDL, were estimated as mentioned in the table No. 1 and No.2.

RESULTS

Lipid Profile

Table No. 1 reveals the comparison of cholesterol, triiglycerides, HDL, VLDL and LDL following 30 days administration of Alfagin syrup in normal and high doses. Animals of both groups showed highly significant decrease in cholesterol i.e. 40.44 ± 1.4 mg/dl and 40.89 ± 1.2 mg/dl respectively as compare to control animals i.e. 55.44 ± 2.42 mg/dl, however decrease in triglycerides was insignificant in both animal groups. Animals kept at high dose showed significant decrease in HDL i.e. 12.68 ± 0.045 mg / dl as compared to animals of control group i.e. 12.56 ± 0.80 mg/dl. The changes in VLDL and LDL level in

both animal groups were insignificant in comparison to control.

Table No. 1: Comparison of lipid profile following Administration of alfagin syrup in Normal and high dose for 30 days

Parameters mg/dl	Animals Groups		
	Control	Alfagin-Nd	Alfagin-Hd
Cholesterol	55.44 ± 2.42	$40.44 \pm 1.40^{**}$	$40.89 \pm 1.20^{**}$
Triglycerides	67.56 ± 3.30	61.11 ± 1.20	65.89 ± 4.30
HDL	12.56 ± 0.80	12.78 ± 0.46	12.68 ± 0.045
VLDL	13.51 ± 0.75	12.22 ± 0.24	13.18 ± 0.86
LDL	25.33 ± 1.85	24.00 ± 1.10	24.22 ± 0.8

n = 9

Average values \pm S.E.M

*p <0.05 significant as compared to control

**p <0.005 highly significant as compared to control

Table No. 2: Comparison of lipid profile Following administration of alfagin syrup in Normal and high dose for 60 days

Parameters mg/dl	Animals Groups		
	Control	Alfagin-ND	Alfagin-HD
Cholesterol	86.89 ± 3.20	$56.22 \pm 2.20^{**}$	$46.56 \pm 1.20^{**}$
Triglycerides	35.78 ± 0.66	34.56 ± 1.40	34.8 ± 1.20
HDL	17.11 ± 0.63	16.44 ± 2.0	14.44 ± 0.88
VLDL	7.16 ± 0.15	6.91 ± 0.29	6.53 ± 0.23
LDL	16.00 ± 0.58	14.33 ± 1.10	$13.89 \pm 0.25^*$

n = 9

Average values \pm S.E.M

*p <0.05 significant as compared to control

**p <0.005 highly significant as compared to control

Table No. 2 shows the comparison of lipid profile following 60 days of drug administration in normal and high doses. Animals of both groups showed highly significant decrease in cholesterol i.e. 56.22 ± 2.20 mg / dl and 46.56 ± 1.20 mg/dl respectively as compared to control animals i.e. 86.89 ± 3.26 mg / dl. There was no significant change in triglycerides at normal dose i.e. 34.56 ± 1.40 mg / dl and at high dose 34.8 ± 1.20 mg/dl as compared to control i.e. 35.78 ± 0.66 mg/dl. Animals of both groups normal and high dose revealed no significant change in HDL i.e. 16.44 ± 2.00 mg/dl and 14.44 ± 0.88 mg/dl. as compared to animals of control group i.e. 17.11 ± 0.63 mg/dl. 7.16 ± 0.15 mg / dl.

Similarly VLDL of both dose groups remains unchanged. Animals at normal dose showed insignificant decrease in LDL i.e. 14.33 ± 1.10 mg/dl and animals at high dose revealed a highly significant decrease in LDL i.e. 13.89 ± 0.28 mg/dl with respect to control value i.e. 16.89 ± 0.58 mg/dl.

DISCUSSION

Alfagin is a unique preparation composed of bioactive medicinal herbs including ginseng, alfalfa, embilica officinalis and triognella graecum this product is free of any synthetic chemicals. Animals of neither group showed gross toxicities at any time during the total period of experiment. Increase in weight might be due to ginseng a bioactive herb which contain a mixture of steroids¹¹. Similarly Raltan reported that ginseng improved health and prevent aging¹² this was further supported by other studies¹³. Increase in weight of animals might be due triogonella foerum graecum which has protein concentrate¹⁴.

Table 1 shows the comparison of cholesterol, triglycerides, HDL, VLDL and LDL after the administration of Alfagin for 30 days. Animals at both doses normal and high showed highly significant decrease in cholesterol i.e. 40.44 ± 1.40 mg/dl and 40.89 ± 1.20 mg/dl respectively as compared to control other parameters such as triglycerides. VLDL and LDL did not show any significant change.

Table 2 shows lipid profile following 60 days of drug administration, animals of both groups on Alfagin showed highly significant decrease in cholesterol i.e. 56.22 ± 2.20 mg/dl and 46.56 ± 1.20 mg/dl as compared to control while a significant decrease in LDL i.e. 13.88 ± 0.28 mg/dl was found at high dose as compared to control. These findings support that Alfagin possess hypocholesterolemic activity.

Studies done by Mailnow et al in 1976 also showed cholesterol lowering activity of alfalfa^{15,16}. Studies by Morley and Molgard revealed that alfalfa binds to bile acids required for cholesterol absorption from gut^{17,18} Emblica officailis also has a significant role in lowering serum lipid levels^{19,20,21}.

CONCLUSION

Alfagin (a herbal product) has been formed to effect lipid profile. It is a helpful drug to lower raised blood cholesterol, however, further studies and recommended. The data collected showed be verified in humans also.

REFERENCES

1. Balandrin MF, Klocke JA, Wurtele ES, Bollinger WH. Natural plant chemicals. Sources of Industrial and medicinal materials Science. 1985.p.1154-1160.

2. Strohl WR. The role of natural products in modern drug discovery program. Drug Discovery Today 2000; (5):39-41.
3. Neamati and Barchi Jr. New paradigms in drug design and discovery. Current topics in Medicinal Chemistry 2002;2(3):211-27.
4. Soejarto DD. Biodiversity prospecting and benefit sharing: perspectives form the field. J of Ethnopharmacol 1996;(51):1-15.
5. Schiemeier. Traditional owners should be paid. Nature 2002;(6906):419-23.
6. Barrette B, Kiefer D, Rabago D. Assessing the risks and benefits of herbal medicine. An over view of scientific evidence. Altern Ther Health 1999;5(4):40-49.
7. Newman DJ. Cragg GM, Snader KM. The influence of natural produc suon drug discovery Natural Product report 2000; (17):215-34.
8. Elsenberg DM, Davis RB, Etter SL, Susan L, et al. Trends in alternative medicine use in the United States,1990-1997.results of a follow- up national survey. JAMA 1998;280:1569-1575.
9. Fabricant DS, Fransworth NR. The value of plants used in traditional medicine for drug discovery. Environmental Health Perspectives 2001;(109): 69-75.
10. Marc, Bent S. An evidence-based review of the 10 most commonly used herbs. Western J of Medicine 1999; 171 (3):168-71.
11. Evans WC. Saponins cadioactive drugs and other steroids. Cited from the book Trease and Evans pharmacognosy 2002;289-298.
12. Rattan SI. Is gene therapy for possible. Indian J of Experimental Biology March 1998; 36(3): 233-6.
13. Ferrerick. Functional foods, herbs and nutraceuticals towards biochemical mechanism of healthy aging; Biogastroentology 2004;5(5): 275-89.
14. Nazar A, Nasri El, Tinay AHE. Functional properties of fenugreek (Trigonella foenum graecum) protein concentrate; Food Chemistry 2007;(103):582-59.
15. Malinow MR, McLaughin P, Papworth L, Stafford. Effect of Alfalfa Saponins an intestinal cholesterol absorption in rats. Am J of Clin Nut 1977; (30) 2061-67.
16. Malinow M, McLaughlin P, Papworth L. Hypocholesterolimic effect of alfalfa in cholesterol fed monkeys IVth International Symposium on Tokyo, Japan Atherosclerosis 1976.
17. Morley JE. Food peptides. A new class of hormones? JAMA.1982; 247(17) 2379-80.
18. Molagard J, Von Schenk H, Olsson AG. Alfalfa seed slower density lipoprotein cholesterol and apolipoprotein concentrations in patients with type

- II hyperlipoproteinemia. Atherosclerosis. 1987; 65 (1-2):173-79.
19. Mathur R, Sharma A, Dixit AP, Varma A. Hypolipdemic effect of fruit juice of *Emblica officinalis* in cholesterol fed rabbits. J of Ethnopharmacol 1996;50 (2):61-68.
 20. Augusti KT, Arathy SL, Asha R, Ramakrishnan J, Zaira J, Lekha V, et al. A comparative study on the beneficial effects of garlic (*Allium Sativum* Linn) amla (*Emblica officinalis* Gaerten) and onion (*Allium Cepa* Linn) on the hyperlipidemia induced by butter fat and beef fat in rats. Indian J Exp Biol 2001;39 (8):760-66.
 21. Anila, Alakshmi V, Flavonoids from *Emblica officinalis* and *Mangifera indica* effectiveness for dyslipidemia. J of Ehnopharmacol 2007;(79): 81– 87.

Address for Corresponding Author:

Dr. Fareeda Islam

Professor of Pharmacology.

Karachi Medical and Dental College,
Karachi.

E.mail: dr.fareedaislam@hotmail.com

Cell No.0333-2194990

Original Article

Desarda Repair - A new method of tension free repair for Inguinal Hernia - Experience of 77 cases at DHQ Hospital Abbottabad

1. Asif Saeed 2. Muhammad Nawaz 3. Samson Griffin 4. Saleem Akhtar

1. Asst. Prof of Surgery 2. Assoc. Prof of Surgery 3. Prof of Surgery 4. Assoc. Prof of Radiology,
Women Medical College, Abbottabad.

ABSTRACT

Objective: To determine the frequency of patients with inguinal hernia in whom Desarda repair can safely be accomplished and study the morbidity and mortality in such cases.

Background: Inguinal hernia is a common disorder in males which requires corrective surgery to lead a comfortable life. Tension free surgery is aim of the surgeon to avoid recurrence of the disorder. Mesh repair has been the most widely performed surgery for inguinal hernia. A new technique of inguinal hernia repair has been developed which utilizes the normal tissue of the patient to create a tension free repair.

Study Design: A prospective study.

Place and Duration of Study: This study was conducted at DHQ Hospital Abbottabad from September 2009 – June 2011.

Patients and Methods: A prospective study was conducted at DHQ Hospital Abbottabad on 77 patients having inguinal hernia. All patients above the age of 15 years were included. Patients having recurrent inguinal hernia were excluded from study. Most common age group was (56-65 yrs). Out of 77 patients 64% were of indirect inguinal hernia while 36% were of direct inguinal hernia. Common age group with direct hernia was above 50 years.

Results: Post operative complications, hospital stay and return to routine activities were evaluated. Hematoma formation and wound infection in two cases were only complications noted. Patients were free of post operative pain.

Conclusions: Desarda repair is simple, very safe technique of inguinal hernia repair free from any complications.

Keywords: Inguinal hernia, Tension free repair, Mesh repair, Desarda repair.

INTRODUCTION

Inguinal hernia is a common disorder in males which requires corrective surgery to lead comfortable life. Dragging pain and discomfort are major complaints of uncomplicated hernia. Obstruction and strangulation are major complications which require urgent surgery. Hernia, which may descend into the testis, hinders daily routine activities. Inguinal hernia repair remains still a problem because of high recurrence rate, risky dissection of inguinal floor in Bassini's / Shouldice repair. Tension free surgery is aim of the surgeon to avoid recurrence of the disorder. Mesh repair has been the most widely performed surgery for inguinal hernia. Infection, chronic pain and foreign body reaction are common complications of mesh repair which may require removal of mesh in some cases. The cost of mesh may not be afforded by poor patients. Desarda repair consists of construction of firm and dynamic post. wall of the inguinal canal with the help of external oblique aponeurosis which remains undetached from its origin. The procedure is free from complications and can be performed as a day case surgery.

PATIENTS AND METHODS

This study was conducted at DHQ Hospital Abbottabad from Sept 2009-June 2011. Total of 77 patients having inguinal hernia were subjected to surgery. Patients of all ages above 15 years were included in this study. Patients having recurrent inguinal hernia were excluded from study. All patients having reducible and irreducible hernia were included in the study. All patients were investigated with Blood Complete Picture, ECG, X-ray Chest and Ultrasound abdomen. Patients having Enlarged Prostate associated with inguinal hernia were operated first for Enlarged Prostate and then Desarda Repair done. Patients were divided into six age groups. Common age group was (56-65yrs) 25%. All patients were male and no female patient above 15 years reported with inguinal hernia. All operations were done under General Anaesthesia or Spinal Anaesthesia. Average operation time was 25 minutes. All patients were followed up as out patients for complications. Maximum follow up of the patients is about 02 years. Out of 77 patients 45(58%) had Rt sided hernia and 32(42%) had Lt sided hernia. In 28 patients (36%), it was direct hernia while in 49(64%) it

was of indirect type. Out of 28 patients having direct hernia 22(79%) patients were between 50-70 years. In indirect type out of 49 patients 33(67%) were below 50 years. Anaesthesia administered was general anaesthesia in 34(44%) patients and spinal in 43(56%) patients. Incision made was inguinal incision. Repair was done with prolene 2/0 and skin closed with interrupted silk sutures.

RESULTS

Repair was done by suturing an undetached strip of external oblique aponeurosis with inguinal ligament and conjoint muscle. Prolene 2/0 suture was used for repair. Average operation time was 25 minutes. Post operative recovery was very good and mean hospital stay was 01 day. All the patients were pain free and were mobilized after the effects of anesthesia were over. The reason for hospitalization was that we operated all patients under G/A or Spinal Anaesthesia. The patients were discharged next day. Only 01 patient had hematoma formation at operation site which resolved itself without any intervention and 01 patient had mild wound infection which was treated successfully. Patients were followed up in OPD and no recurrence has been reported so far after follow up for about 02 years.

Table No. 1: Age Distribution

Age (years)	No: of Cases	Percentage
15-25	07	9%
26-35	17	22%
36-45	11	14%
46-55	15	20%
56-65	19	25%
66-75	08	10%

Table No.2: Various Parameters of Inguinal Hernia

Parameter		No of patients	Percentage
Side of Hernia	Rt side	45	58%
	Lt side	32	42%
Type of Hernia	Direct hernia	28	36%
	Indirect hernia	49	64%
Anaesthesia	GA	34	44%
	Spinal	43	56%
Complications	Heamatoma	01	1.3%
	Wound infection	01	1.3%

DISCUSSION

Inguinal hernia is a common disorder in males which requires corrective surgery to lead comfortable life. Inguinal hernia repair remains still a problem because of high recurrence rate, risky dissection of inguinal

floor in Bassini's / Shouldice repair. Tension free surgery is aim of the surgeon to avoid recurrence of the disorder. Mesh repair has been the most widely performed surgery for inguinal hernia. Infection, chronic pain, foreign body tissue reaction, migration of mesh and recurrence of hernia are common complications with mesh repair. The cost of mesh may not be afforded by some patients. Anterior posterior compression of the inguinal wall is lost due to loose and adynamic post. inguinal wall. Wear and tear with aging leads to weak and loose posterior inguinal wall and is the cause of direct inguinal hernia in elderly. Providing a strong and physiologically dynamic post. inguinal wall is essential to restore anterior posterior compression. Absent aponeurotic extension in the post. wall are replaced with an aponeurotic structure. Additional muscle strength of the external oblique muscle helps the weakened muscle arch to keep the newly formed post wall.

Desarda repair is the new method of tension free repair for inguinal hernia. Dr. Desarda introduced this tension free repair for inguinal hernia in 2001. In this technique a strip of undetached external oblique aponeurosis is used to construct firm and dynamic post. inguinal wall. It can be safely done under local anaesthesia as a day care surgery.

This avoids unnecessary dissection of the posterior wall as in shouldice repair. The complications of mesh repair such as post operative pain, infection, F/body reaction are avoided. It is very cost effective as cost of mesh and hospital stay is reduced. In our study, all the patients were operated under GA/ Spinal anaesthesia so they had to be admitted to hospital and discharged next day when the effects of anaesthesia were over. During the follow up of the patients 01 patient had slight superficial wound infection and 01 patient had mild hematoma formation. No other complication was noted. No recurrence has been reported so far in our patients.

CONCLUSION

Inguinal hernia is a common disorder in males which requires corrective surgery to lead comfortable life. Inguinal hernia repair remains still a problem because of high recurrence rate, risky dissection of inguinal floor. Desarda repair is simple, very safe technique of inguinal hernia repair free from any complications. It avoids all the complications of mesh repair. The recurrence rate is zero.

REFERENCES

1. Deveney KE. Hernias and other lesions of the abdominal wall. In: Doherty GM, Way LW, editors. Current Surgical Diagnosis and Treatment.

- 12th ed. New York: Lange Medical Books/McGraw-Hill; p.765-773.
2. Harmon JW, Wolfgang CL. Hernias of the groin and abdominal wall. In: Fiebach NH, et al, editors. Principles of Ambulatory Medicine. 7th ed. Philadelphia: Lippincott Williams and Wilkins; p. 1673-1681.
 3. Fitzgibbons RJ, et al. Inguinal hernias. In: Brunickardi FC, et al, editors. Schwartz's Principles of Surgery. 8th ed. New York: McGraw-Hill; p. 1353-1394.
 4. Agrawal A, Avill R. Mesh migration following repair of inguinal hernia: a case report and review of literature. *Hernia* 10:79–82.
 5. Desarda MP. New method of inguinal hernia repair. A new solution. *ANZ J Surg* 2001;71: 241-44
 6. Griffith CA. Inguinal hernia: An anatomic surgical correlation. *Surg Clin North America* 1959; 39: 531.
 7. Anson BJ, McVay: Surgical anatomy. 5th ed. Philadelphia: WB Saunders;1971.
 8. Desarda MP. Surgical physiology of inguinal hernia repair. A study of 200 cases. *BMC surg* 2003;3:2
 9. Amid PK. Driving after repair of groin hernia. *BMJ* 321:1033–1034.
 10. Chuback JA, Singh RS, Sills C, Dick LS. Small bowel obstruction resulting from mesh plug migration after open inguinal hernia repair. *Surgery* 127:475–476.
 11. Taylor EW, Dewar EP. Early return to work after repair of a unilateral inguinal hernia. *Br J Surg* 70:599–600.
 12. Farquharson EL. Early ambulation; with special reference to herniorrhaphy as an outpatient procedure. *Lancet* 269:517–519.
 13. Gallegos NC, Dawson J, Jarvis M, Hobsley M. Risk of strangulation in groin hernias. *Br J Surg* 78:1171–1173.
 14. Ramyil VM, Ognonna BC, Iya D. Patient acceptance of outpatient treatment for inguinal hernia in Jos, Nigeria. *Cent Afr J Med* 45:244–246.
 15. Amid PK, Shulman AG, Lichtenstein IL. Open “tension-free” repair of inguinal hernias: the Lichtenstein technique. *Eur J Surg* 162:447–453.
 16. Bay-Nielsen M, Knudsen MS, Christensen JK, Kehlet H. Cost analysis of inguinal hernia. Surgery in Denmark. *Ugeskr Laeger* 161:5317–5321.
 17. Bay-Neilson M, Perkins FM, Kehlet H. Danish Hernia Database. Pain and functional impairment 1 year after inguinal herniorrhaphy nationwide study. *Ann Surg* 2001;233:1-7
 18. Taylor SG, O'Dwyer PJ. Chronic groin sepsis following tension free inguinal hernioplasty. *Br J Surg* 1999;86:562-5
 19. Anson BJ, Morgan EH, McVay CB. Surgical anatomy of the inguinal region based upon a study of 500 body-halves. *Surg Gynaecol Obstet* 1960;111:707
 20. Kark AE, Kurzer MN, Belsham PA. Three thousand one hundred seventy-five primary inguinal hernia repairs: Advantages of ambulatory open mesh repair using local anaesthesia. *J Am Coll Surg* 1998; 186:447-55.

Address for Corresponding Author:

Dr. Asif Saeed

H No: 113 Street No: 10

Jinnahabad Township

Abbottabad

Ph: 92-992-380372

Mob: 0333-5037702

E-mail: aasif_saeed@yahoo.co.uk

Original Article

Patterns of Refractive Errors at Independent Medical College, Teaching Hospital, Faisalabad

1. Muhammad Ahmed 2. Sohail Rasheed 3. Faheem Ahmed Chaudhry 4. M. Sultan Mahmood 5. Mushtaq Ahmed Cheema

1, 2, 3, Asstt. Profs. Islam Medical College Pasroor Sialkot 4. Prof. of Ophthalmology, Punjab Medical College, Faisalabad 5. Prof. of Ophthalmology, Independent Medical College, Faisalabad.

ABSTRACT

Objective: To determine the patterns (Frequency and types) of refractive errors, affecting different age groups of our population and to suggest glasses for huge functional improvement of individuals.

Study Design: Descriptive Study

Place and Duration of Study: This conducted at Independent University Hospital Faisalabad in collaboration with Allied Hospital (Punjab Medical College) Faisalabad from 15 March 2010 to 31 March 2011.

Materials and Methods: Patients of all age groups presented in Eye OPD with the complaint of visual acuity having less than 6/12, were underwent history and detailed examination (Including retinoscopy, autorefraction and cycloplegic refraction in children less than 8 years).

Exclusion criteria: Patients with corneal opacity, glaucoma, penetrating trauma, cataract, aphakia, macular or retinal diseases were excluded.

Results: Out of 8215 OPD patients 658 (8%) had refractive error. Mean age was 31 years. Age varied from 5 to 66 years. New patients were 533 (81%), while patients required refinement of refraction, were 125 (19%). Individuals up to the age of 15 years were 119 (18.08%), between 16 to 29 years were 196 (29.79%), 30 to 40 years were 151 (22.95%) and above 40 years were 192 (29.17%). It was found that male were 260 (39.51%) while female 398 (60.49%). Myopia was 381 (57.90%) hypermetropia was 122 (18.54%) while astigmatism was 155 (23.56%). Myopic astigmatism was 114 (17.33%) and hyperopic astigmatism was 41 (6.23%). All individuals showed improvement with glasses.

Conclusion: Refractive error is very common in our population. Female are affected more commonly than males. Myopia is more frequent. Astigmatism also affects almost every fifth patient with refractive error.

Key Words: Refractive error, Myopia, Hypermetropia, Astigmatism.

INTRODUCTION

Vision is a gift of God. Blindness is curse. It is estimated that 2.3 billion people worldwide have refractive errors; out of which 1.8 billion have access to adequate eye examination and affordable corrections leaving behind 500 million people, mostly in developing countries with uncorrected error causing either blindness or impaired vision.¹

The World Health Organization introduced the global initiative for elimination of avoidable blindness by the year 2020 known as "Vision 2020 initiative". Refractive errors are one of the priority areas for vision 2020 initiative as they are common and because corrective spectacles provide a remedy that is cheap, effective and associated with huge functional improvement. Refractive errors which account mostly for low vision and visual handicap are the third largest cause of preventable/curable blindness in Pakistan.²

In Pakistan 11.4% of the blindness is due to uncorrected refractive errors including that is caused by aphakia (natural lens extraction during cataract surgery).³ In one study it was found that the refractive errors account

for 8% cases of unocular blindness in NWFP.⁴ School children are considered to be high risk group because uncorrected refractive errors can seriously affect their learning abilities⁵, their physical and mental development⁶, on the other side young and adults cannot perform well due to uncorrected refractive errors.

The objectives of the study were to determine the types and frequency of refractive errors in different age groups and to suggest the required glasses to improve their functional efficiency.

MATERIALS AND METHODS

This descriptive study was conducted at eye department Independent University Hospital Faisalabad. Six hundred and fifty eight patients out of 8215 OPD cases were included in the study. Over a period of one year from 16th March 2010 to 15th March 2011 was included in the study. Patients having previous ocular surgery with corneal opacity, glaucoma, penetrating trauma, cataract, aphakia, macular or retinal diseases were excluded from this study. Patients of all age groups presented in Eye OPD with the complaint of

visual acuity having less than 6/12, were underwent history and detailed examination (Including retinoscopy, autorefraction and cycloplegic refraction in children less than 8 years with 1% cyclopentolate eye drop three times with 10 minute interval), ocular motility with cover test for near and distance for children, papillary reaction, direct ophthalmoscopy and examination of anterior segment with slitlamp and detailed fundus examination as required. Visual acuity was measured with Snellen's chart, E-chart or Lea charts. For every patient visual acuity was tested without correction, pinhole and with correction. Objective refraction was determined using a Topcon autorefractometer. Appropriate spectacles wearing guidance was provided to all patients and refinement of refraction (and glasses) six monthly or annually according to age, advised to all individuals. The data was processed by the computer special package for social sciences (SPSS).

RESULTS

Out of 8215 OPD patients 658 (8%) had refractive error. Mean age was 31 years. Age varied from 5 to 66 years. Individuals up to the age of 15 years were 119 (18.08%), between 16 to 29 years were 196 (29.79%), 30 to 40 years were 151 (22.95%) and above 40 years

were 192 (29.17%). It was found that male were 260 (39.51%) while female 398 (60.49%). Myopia was 381 (57.90%) hypermetropia was 122 (18.54%) while astigmatism was 155 (23.56%). Myopic astigmatism was 114 (17.33%) and hyperopic astigmatism was 41 (6.23%). All individuals showed improvement with glasses. Patients were divided into four major groups according to age. In age group 1 (5 to 15 years) and Group 2 (16 to 29 years) myopia is significantly higher than other refractive errors. As the age advances, prevalence of myopia decreases while that of hypermetropia increases also shown in table 2 (Tables No. 1-2)

Table No. 1: Distribution of patients according to age (n=658)

Age Group	No. of Patients	Percentage
Group 1 (5 -10 years)	119	18.08
Group 2 (16 to 29 years)	196	29.79
Group 3 (30 to 40 years)	151	22.95
Group 4 (>40 years)	192	29.17

Table No. 2: Gender and refractive error pattern distribution of age in all groups

Group	Total (%)	Males (%)	Females (%)	Myopic (%)	Hypermetropia (%)	Astigmatism (%)
1	119 (100%)	44 (36.9%)	75 (63.1%)	79 (66.4%)	12 (10.1%)	28 (23.5%)
2	196 (100%)	76 (38.7%)	120 (61.3%)	143 (72.9%)	18 (9.2%)	35 (17.9%)
3	151 (100%)	72 (47.7%)	79 (52.3%)	76 (50.4%)	27 (17.8%)	48 (31.8%)
4	192 (100%)	68 (35.4%)	124 (64.6%)	83 (43.3%)	65 (33.8%)	44 (22.9%)

DISCUSSION

This study was designed to determine the types and frequency of different refractive errors among different age groups (5 to 66 years) in our population presented in our hospital. A population based survey should have been conducted but due to limited resources and different other reasons it was not possible. However, the individuals presented with refractive errors were divided into four age groups for the purposes of comparison of the patterns of refractive error to other studies. Refractive errors are among the leading causes of visual impairment worldwide and are responsible for high rates of low vision and blindness in certain areas⁷. In younger age group (up to 15 years), the refractive error study in children in China⁸, Chile⁹ and Nepal¹⁰ is the first multicountry population based assessment of

refractive errors in children. The data reveals that there are significant and large geographic differences in the prevalence of refractive errors and that uncorrected refractive errors are very common. The prevalence of refractive error of 18% in our study is higher than the percentage of refractive error in China⁸ 11.3%, in Chile⁹ 9.8%, in Southern Ethiopia¹¹ 11.8%, in Tanzania¹² 6.1%, in Turkey¹³ 11% and Baltimore¹⁴ 8.2%.

In our study the prevalence of myopia was 66.4%, hypermetropia 10.1% and astigmatism 23.5%. The study done among school children in Dezful, Iran revealed overall rate of myopia in students 15 years of age and younger as 3.4%, hyperopia 16.6% and astigmatism 18.7%¹⁵. The study done by Mingguing et al showed prevalence of myopia was 3.3% in 5 years old. Hyperopia measured with retinoscopy was present

in 16.7% of 5 years old. Astigmatism was present in 33.6% of children¹⁶. According to Tehran eye study the age and gender-standardized prevalence of myopia based on manifest refraction was 21.8% (95% confidence interval (CI), 20.1 to 23.5) and that for hyperopia was 26.0% (95% CI, 24.5 to 27.6). Prevalence of myopia and hyperopia differed significantly among the age and gender groups ($P < 0.001$). Astigmatism of 0.75 dioptre cylinder or greater was present in 29.6% (95% CI, 28.5 to 31.1) of right eyes with manifest refraction and in 30.3% (95% CI, 28.5 to 32.1) with cycloplegic refraction. Among the study population, 6.1% (95% CI, 5.3 to 6.8%) had anisometropia of 1 dioptre or more¹⁷.

In our study it was found that 44 (37%) patients were male while 75 (63%) were female. This is not different to multicountry survey of refractive error in children in China⁸, Chile⁹ and Nepal¹⁰ where both myopia and hyperopia were significantly higher in females than males. In a study conducted in China⁸ it was found that the myopia of -0.5D or less in either eye was essentially absent in 5 years old children, but increased to 36.7% in male and 55% in females by age of 15. Over the same age range, hypermetropia of 2 dioptres or greater was from 8.8% in males and 19.6% in females to less than 2% in both sexes. Similar results were found in refractive error study in children from La Florida Chile⁹.

In the study done at Mayo Hospital Lahore showed errors of refraction were the third common disorders, affecting 494 children, of which the majority, (63%) were above the age of five, 30% in the one to five age group and only 7% were under the age of one. In the gender distribution major bulk of the cases was males. The cases in this category comprised of hypermetropia (82%), Myopia (13%) and astigmatism (5%). The majorities of the children, (54%) were males between the ages of five and fifteen and were affected by hypermetropia¹⁸. In a study done at Department of Ophthalmology, Jinnah Postgraduate Medical Centre Karachi, Pakistan showed that refractive error of 2% was found to be the cause of primary ocular morbidity in children 5-15 years of age.¹⁹ Refractive errors are significant cause of visual disability in school children. While primary vision screening by teachers tremendously decreases the workload of ophthalmic staff. Teachers can effectively identify those children with poor vision for refraction and corrective spectacles.

In our study, age group 2 (16 to 29 years) has the similar pattern of refractive errors to first younger age group (5 to 15 years). Myopia, hypermetropia and astigmatism was 72.91%, 9.18 % 17.86 % respectively. Only myopia worsens with the advancement of age which probably shows the increased visual activity like intensive study and near work in this age group.

Myopia is strongly associated with literacy and young had the highest rate of literacy (if used as proxy for near work) our finding provide some support towards the "use/abuse" theory of myopia.²⁰ The high prevalence of myopia in the age group (30 to 39 years) provides some support for a cohort effect in the young.²¹

In age group 3 (30 to 40 years) myopia gradually decreases (50.33%) in severity and it still continue to decrease (43.23%) in above 40 years, while hypermetropia increases with advancement of age (Table 2). In our study, adult age group 3 (30 to 40 years) myopia, hypermetropia and astigmatism were 50.33%, 17.88% and 31.79% respectively, while in adult age group 4 (above 40 years) these errors were 43.23%, 33.85% and 22.92% respectively which are similar to the results of a study conducted in the adult Pakistani population, the crude prevalence of myopia, hypermetropia and astigmatism was 36.5%, 27.1%, and 37%, respectively.²²

The prevalence of myopia in this study was significantly higher than in a national survey in Bangladesh²³ but similar to that reported from Southern India (≥ 40 years, 36.5%)²⁴ but lower than among Singaporean Chinese (38.7%).²⁵

Refractive error has variable pattern in different age, sex, geography and races. Refractive blindness is a major cause of morbidity in our population. It shows inadequacy of eye care services in general, perhaps treatment of refractive error is simple and effective that is in the form of glasses. Vision screening programme should be started at national level to detect individuals suffering from refractive blindness. In this context an adequate infrastructure should be developed at the level of rural health centre with trained personnel to perform reasonable quality of refraction. An affordable, reasonable-quality spectacle should be provided to the individuals with refractive blindness. All the individuals with refractive error should be advised to undergo refinement of refraction once or twice annually to improve the functional efficiency of life.

CONCLUSION

Refractive error is very common in our population which contributes to the third major cause of preventable blindness in Pakistan. It affects all age groups, in children it interferes with the learning abilities; in young and adults, it impairs the learning skills and functional efficiency. Females are affected more commonly than males 6:4. Myopia is more frequent (57.90% $n=381$). Astigmatism also affects almost every fifth patient with refractive error (23.56% $n=155$). It should be diagnosed and treated at an early stage especially in children so that a clear vision can be restored to achieve maximum learning abilities. Glasses remain the mainstay of treatment which is highly cost

effective. All the individuals with blurred vision should be educated to undergo refraction and refinement six monthly or annually according to age group.

Suggestions

- A comprehensive eye care programme should be started at national level so that individual with refractive errors should be corrected with glasses at appropriate age.
- It should be diagnosed and treated at an early stage especially in children so that a clear vision can be restored to achieve maximum abilities. Glasses remain the mainstay of treatment which is highly cost effective. All the individuals with blurred vision should be educated to undergo refraction and refinement annually.

REFERENCE

1. Holden BA, Sulaiman S, Knox K. The Challenge of providing Spectacles in the Developing World. *J of Community Eye Health* 2000; 13 (33): 9-10.
2. Parajasegram R. Vision 2020. The Right to Sight: from strategies to action. *Am J Ophthalmol* 1999; 128: 359- 60.
3. National Committee for Prevention of Blindness, Ministry of Health, Special Education and Social Welfare, Islamabad, Pakistan, National Programme for Prevention of Blindness: First five year Plan 1994-98.p.24.
4. Resnikoff S, Pascolini D, Mariotti SP, Pokharel GP. Global magnitude of visual impairment caused by uncorrected refractive errors in 2004. *Bull WHO* 2008; 86:63–70.
5. Negrel AD, Maul E, Pakharel GP. Refractive error study in children: sampling and measurement methods for a multicountry survey. *Am J Ophthalmol*. 2000; 129:421-6.
6. Gilbert C, Foster A. Childhood blindness in context of vision 2020 – the right to sight. *Bull WHO* 2001; 79:227-32.
7. Dandona R, Dandona L. Refractive error blindness. *Bull WHO* 2001;79: 237-43
8. Zhao J, Pan X, Sui R, Munoz SR, Sperduto RD, Ellwein LB, et al. Refractive error study in children: results from shunyi district, China. *Am J Ophthalmol* 2000; 129:427-35.
9. Maul E, Barroso S, Munoz SR, Sperduto RD, Ellwein LB. Refractive error study in children: results from La Florida, Chile. *Am J Ophthalmol* 2000; 129:445-54.
10. Pakharel GP, negrel AD, Munoz SR, Ellwein LB. Refractive error study in children: results from Mechi Zone, Nepal. *Am J Ophthalmol* 2000;129: 436-44.
11. Worku Y, Bayu S. Screening for ocular abnormalities and subnormal vision in school children for Batayira Town, Southern Ethiopia. *Ethop J of Health and Develop* 2002; 16:165-171.
12. Wedner SH, Rose DA. Myopia in School students in Manza city, Tanzania; The need for national screening programme. *Br J Ophthalmol* 2002; 86:1200-6.
13. Lewellen S, Lowdon R, Countright P, Mehl GL. Population based survey of prevalence of refractive error in Malawi; *Ophthalmic Epidemiol* 1995; 3: 145-9.
13. Preselan MW, NW A. Baltimore screening project. *Ophthalmology* 1998; 105:150-3.
14. Fotouchi A, Hashemi H, Khiabazkhoob M, Mohammad K. The prevalence of refractive errors among school children in Dezful, Iran. *Br J Ophthalmol* 2007; 91:287-92.
15. Mingguang H, Janwer Z, Yizhi L, Jingjing X, Gopal P, Pokarel, et al. Refractive error and visual impairment in Urban children in southern China. *Inves Ophthalmol and Vis Sci* 2004; 45:793-9.
16. Hashemi H, Fatouchi A, Mohammad K. The age and gender specific prevalence of refractive errors in Tehran: The Tehran Eye Study. *Ophthalmic Epidemiology* 2004; 11:213-25.
17. Bile ZK, Ahmad S, Khan AA. Spectrum of ophthalmic diseases in children at a referral hospital. *Pak J Ophthalmol*. 2007; 23:33-7.
18. 19 Shaikh SP, Aziz TM. Pattern of eye diseases in children of 5-15 years at Bazzertaline area (South Karachi) Pakistan. *J CPSP*. 2005;15:291-4.
19. Park DJ, Congdon NG. Evidence for an "epidemic" of myopia. *Ann Acad Med Singapore* 2004; 33(1):21–6.
20. Angle J, Wissmann DA. The epidemiology of myopia. *Am J Epidemiol* 1980; 111:220–8.
21. Shaheen P, Shah I, Mohammad Z, Jadoon, et al. Refractive Errors in the Adult Pakistani Population: The National Blindness and Visual Impairment Survey *Ophthalmic Epidemiology* 2008;15(3):183–190.
22. Bourne RR, Dineen BP, Ali SM, Noorul Huq DM, Johnson GJ. Prevalence of refractive error in Bangladeshi adults: Results of the National Blindness and Low Vision Survey of Bangladesh. *Ophthalmology* 2004;111(6):1150–60.
23. Dandona R, Dandona L, Srinivas M, Giridhar P, McCarty CA, Rao GN. Population-based assessment of refractive error in India: the Andhra Pradesh Eye Disease Study. *Clin Experiment Ophthalmol* 2002;30(2):84–93
24. Wong TY, Foster PJ, Hee J, Ng TP, Tielsch JM, Chew SJ, et al. Prevalence and risk factors for refractive errors in Adult Chinese in Singapore. *Invest Ophthalmol Vis Sci* 2000;41(9):2486–94.

Address for Corresponding Author:

Muhammad Ahmed,
Islam Medical College,
10-Kilometer Pasroor Road,
Sialkot e-mail:786ahmed2000@gmail.com.

Original Article

A Hospital Based Study of Frequency, Intensity and Impact of Premenstrual Syndrome Symptoms on Female Patients

1. Irum Sohail 2. Arifa Bari

1.Assoc. Prof. 2. Senior Registrar, Dept of Gyne & Obst., Foundation University Medical College Rawalpindi.

ABSTRACT

Objective: To study the frequency, intensity of the premenstrual symptoms and its impact on the women reporting to the hospital with other complaints.

Study Design: Observational Study.

Place and Duration of Study: This study was conducted at the Outpatient Department of Gyne & Obst. Unit, Fauji Foundation Medical College / Hospital, Rawalpindi from 1st June 2008 to 31st December 2008.

Patients and Methods: We had total 224 women who were included in this study. These women were included in this study because they were menstruating regularly for the last six months. They were not suffering from any surgical, medical or psychiatric illness and were not pregnant. These women were interviewed by trained personnel and all the symptoms with their intensity were entered into the specially designed proformas. Only those symptoms were given importance which was present in the preceding at least three menstrual cycles.

Results: Out of total 224 women only 34% of the women had any awareness regarding the presence of these symptoms in relation to menstruation. Lethargy was the commonest symptom found in 74% of women with mild intensity (51.9%). Least common symptom was negative thoughts present in 16% of the women. 50% of the women reported that their daily activities were affected by the presence of these symptoms. For the relief of these symptoms the commonest drug used was ponston(39.7%). The age group mostly affected in our study was from 36 to 50 years.

Conclusion: The awareness regarding premenstrual syndrome associated symptoms is very low and especially amongst women belonging to rural background with low educational status. Health providers should be actively involved in providing information and therapies to these women so that they do not suffer in silence.

Key Words: premenstrual syndrome, Pakistani rural women, awareness.

INTRODUCTION

Premenstrual syndrome (PMS) is defined as a group of symptoms that include physical, cognitive, effective and behavioral, which occur during the luteal phase of the menstrual cycle and are resolved with the onset of menstruation.¹

Most of the women will notice some changes in mood or may develop physical symptoms during the time preceding menstruation. These changes are however minor and the symptoms are considered important if they interfere with routine activities at work, school or in social events.²

The American College of Obstetricians and Gynecologists (ACOG) has defined ten diagnostic criteria for PMS. The person fulfills these criteria if she suffers from one of the six affective and one of the four somatic symptoms in the days preceding menstruation in the three prior menstrual cycles and these ceased within four days of onset of menses.³

The etiology of premenstrual syndrome is still unclear and many causes have been proposed which include hormonal disturbances, abnormal serotonin function,

interaction of endorphins and prostaglandins with GABA, cholecystokinin and the renin- angiotensin-aldosterone system.⁴

As the etiology of premenstrual symptom has remained unclear therefore a range of treatment modalities have been employed in the management of PMS. Among these the most common ones are oral contraceptives, progesterone, bromocriptine, prostaglandin synthetase inhibitors (especially mefenamic acid), and danazol⁵. Amongst herbal treatments the trials have shown some benefit of chaste berry (vitex agnus castus)⁶ and evening primrose oil (Oenothera biennis)⁷. Amongst these the most promising treatments that have been found out to be effective are those which suppress ovulation.⁸

We have conducted this study to find out the frequency, intensity and impact of premenstrual syndrome symptoms in our patients. As most of our patients belong to the low socioeconomic status with lack of primary education we wanted to find out what was the awareness level of PMS amongst them and if they were suffering from any symptoms of PMS, what treatments were used to relieve these symptoms.

PATIENTS AND METHODS

This study was conducted in the out patient department of Obstetrics and Gynaecology unit of Fauji Foundation Hospital Rawalpindi over a period of six months from 1st June 2008 to 31st December 2008 where 15672 patients attended the outdoor clinic of Gyne and Obst. Unit. The hospital is a tertiary care unit where all referred patients from rural areas of Punjab and adjacent areas come. The study was approved by hospital ethical committee and then a questionnaire was developed for the interview of the patients. The doctors on duty in the outdoor were trained to fill the questionnaire under supervision of a senior doctor. Only those women were interviewed who were in their reproductive age group and were not suffering from any medical, surgical or menstrual problem. All the pregnant women and patients having psychiatric problems were also excluded from the study. We had a total of 224 women who agreed to give the interview who were menstruating regularly for the last six months thus they were fulfilling the inclusion criteria.

The data was entered into the SPSS version 15 and then analysis was done. Descriptive statistics were used to describe the data i.e mean and standard deviation (SD) for quantitative variables while frequency and percentages for qualitative variables.

RESULTS

Out of total 224 patients we had only 78(34%) women who were aware that the presence of these symptoms prior to menses was due to some problems in the body caused by menstruation but none had any awareness of the exact relationship with the menstrual cycle. Approx 10%(n=24) of patients had less than three symptoms in the preceding menstrual cycles while rest were complaining of three or more than three symptoms in their preceding menstrual cycles for the last three cycles. The mean age of these patients were 32 years (13-52) and we had 65%(n=146) of women married while 34% (n=78) were unmarried. The mean parity of married women were 3.6 children (0-11). 86% (n= 194) of the women belonged to low socioeconomic status i.e their monthly income was below Rs. 5000/- while the rest were from middle class. Regarding the educational status only 6%(n=15) women were educated till middle class while 25(11%) had only education till primary level. The most common symptom was lethargy which was present in 74% of women and the severity was mild in 59%. After this the next common symptom was headache in about 62% of the women and mostly was of the minor degree i.e. 51%% (Table I). The least common symptom was negative thoughts which was only present in 40 of women and which was also in mild severity 62.5%.

Table No.1: Premenstrual symptoms in order of their Frequency and Intensity

Sr. No.	Symptom	Yes	Mild	Moderate	Severe
1	Lethargy	181 (74%)	94 (51.9%)	75 (41.4%)	12 (6.6%)
2	Headache	152 (62%)	79 (57.9%)	58 (38%)	15 (9.8%)
3	Irritability	142 (58%)	80 (56%)	47 (33%)	15 (10%)
4	Poor concentration	112 (45%)	87 (77.6%)	23 (20%)	2 (1.7%)
5	Nausea	99 (40.5%)	71 (71.7%)	26 (26%)	2 (2%)
6	Social withdrawal	93 (38%)	39 (41%)	45 (48%)	9 (9.6%)
7	Sadness	88 (36%)	64 (72.7%)	22 (25%)	2 (2.2%)
8	Appetite change	87 (35%)	51 (58%)	27 (31%)	9 (10%)
9	Mood changes	85 (34.8%)	55 (64%)	29 (34%)	1 (1.1%)
10	Depression	79 (32%)	56 (70%)	22 (27%)	1 (1.2%)
11	Insomnia	55 (22.5%)	28 (50%)	22 (40%)	5 (9.09%)
12	Bloating	54 (22%)	37 (68%)	17 (31%)	0
13	Hostility	47 (19%)	23 (48%)	17 (36%)	7 (14%)
14	Mastalgia	44 (19.6%)	22 (50%)	18 (40.9%)	4 (9.09%)
15	-ive thoughts	40 (16.3%)	25 (62.5%)	13 (32%)	2 (5%)

If we see for the level of awareness amongst different age groups then the most educated was the age group of 36-50 years in which 34 (44%) of the women knew something regarding the cyclical changes while the next aware group was 25 women(32%) who belonged to the 26-35 years group (Fig.A). Among the rest of the age groups 19%(n=15) women belonged to 20-25 years while below 20 years were only 3% of the girls who

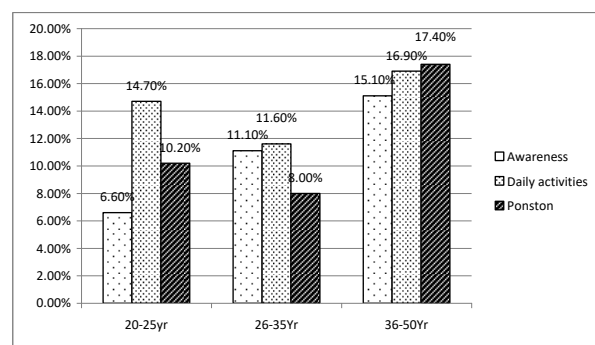
had awareness. There were no women in the 50 years age group with any information regarding these changes. 93 of the women stated that during this specific time because of the symptoms they withdrew from all the social activities while 58% said that these symptoms were not affecting their social activities. On the other hand 50% of the women commented that the daily activities were being affected due to these

symptoms. The age group which was more aware had the maximum number of the women who had limitation in their daily activities i.e. 38 women (33%).

Table No.2: Different Treatments used for Premenstrual Symptoms

Sr. No.	Treatment	Yes	No
1	Ponston	89 (39.7%)	135 (60.3%)
2	Panadol	33 (14.7%)	191 (85.3%)
3	Nicotine	25 (11.2%)	199 (88%)
4	Vitamins	22 (9.8%)	202 (90%)
5	Injectables	7 (3.1%)	217 (97%)
6	Homeopathic	4 (1.8%)	220 (98.2%)
7	Exercise	4 (1.8%)	220 (98.2%)
8	COC	4 (1.8%)	220 (98.2%)
9	Anxiolytics	3 (1.3%)	221 (98.7%)

Figure A: Level of awareness, Daily activities and use of ponston in different age groups



As the awareness regarding the etiology of these symptoms was low therefore mostly tablet ponston was being employed for the relief of these symptoms i.e. 89 pts were using it (Table II). Tablet panadol was the next commonest drug being used by 33(14.7%) women, Nicotine by 25(11.2%) and Vitamins by 22 (9.8%) women. 3.1% (n=7) of the women were using injections of unknown nature for the relief of these symptoms. The least common used medication was anxiolytic i.e. 1.3 % while combined oral contraceptives, homeopathic treatments and exercise was used by 1.8% of women each. The use of tablet ponston along with maximum awareness was seen in the 36-50years age group i.e. the use was 17.40% while the total number of women were 34 (15.10%) (Fig.A). This group also complained of maximum limitation of daily activities 16.90%. In 20-25 years age group the awareness was only 6.6% (n=15) while the use of tablet ponston was also 10%. The women in 26-35 years age group although had a high awareness level than their younger counterparts i.e. 11.10% (n=25) but the use of medication was the lowest i.e. 8% only with limitation of daily activities in 11.6% cases.

DISCUSSION

In our present study we had included only those women who had come for other ailments than menstrual irregularities and were not suffering from any surgical, medical or psychiatric problem therefore a true frequency rate of PMS could not be given as there is no control group. Different studies done in the region state prevalence as 33%⁹ to 51%¹⁰. In our study we have tried to find out the frequency, intensity of different premenstrual symptoms which can have an impact on a healthy women's life.

As most of our women belonged to the rural background they had a low literacy rate with poor socioeconomic status therefore the awareness was present in only 34% and that too in the age group which was more affected i.e. 36-50 years. This is true as stated in the study by Hylan TR, et al¹¹ that the women who experience more impairment will believe that no treatment is available. We had 100% of the patients reporting at least one of the premenstrual symptoms in their previous menstrual cycle and this is same in study by Cleckner-Smith¹² in 1998 which showed 100% of the adolescents in the study suffering from one of the premenstrual symptoms.

The most frequently occurring symptom was lethargy, in 79% of women which has also been stated as 84%¹³ in an Iranian study on female university students. Most of the other studies have found irritability as being the commonest symptom i.e. 71.4%¹⁴, 80%¹¹ and 37%¹⁵ and in our study it was present in 58% of our patients and mostly experienced it to the mild severity. Loss of concentration was reported in 45% of our patients which was 48.3%¹⁵ in female medical students in Saudi Arabia. In our study group the somatic symptoms were of less frequency i.e. abdominal bloating (22%), mastalgia(19.6%) and headache in 62% only, while in comparison with the females in Saudi Arabia those had it in 75%, 64%, and 44% respectively¹⁵.

The impact on daily activities were worse as 50% of the women stated that this was affected while social withdrawal was only in 41% while in Saudi women the daily chores were affected in 41.6%¹⁵.

The frequency distribution of PMS symptoms showed that most of our patients had mild form of symptoms i.e. 51%-77%, moderate were 20%-48% while the severe intensity was reported in a range of none to 14%. This frequency of symptoms is same as in the study by Balaha¹⁵ as 45% was mild, 32% moderate and 22% was severe. We had less number of patients who reported with severe symptoms and this corresponds with the study by Abulhashim¹⁶ et al and Nisar¹⁰ et al where the severe cases were 5.8% and 4.4% respectively.

For the relief of these symptoms tablet ponston (mefenamic acid) was the commonly used drug i.e. 39.7%. Prostaglandin synthetase inhibitor have been

shown to be beneficial in managing both dysmenorrheal and premenstrual symptoms like headache, depression, tension and irritability⁵. The next common used medications were multivitamin tablets (9.8%) although only pyridoxine 80mg was found to be superior in relieving anxiety and mood and has no effect on physical symptoms¹⁷. Similarly 1.8% of the women were using combined oral contraceptives, exercise and homeopathic form of treatments. Some studies have showed that some premenstrual symptoms may improve by doing regular exercise¹⁸ while combined oral contraceptives have been advocated to play a definitive role in ovulation suppression thus causing a decrease in the premenstrual syndrome¹⁴. The most important contraceptive pill which has some role in the symptoms of PMS is that constituting of drospirenone 3mg but unfortunately it is still unavailable in Pakistan. A qualitative study done in 1998 in Ireland²⁰ stated that the term premenstrual syndrome is understood by women differently than it is represented by medical researcher and text book authors thus clearly indicating that it was women's own perception that whether she was suffering from PMS symptoms or not and it was very difficult for anyone to judge it in her place. Therefore making it mandatory that the most common symptom of PMS should be made publically aware so that the women do not suffer in silence.

CONCLUSION

Although most of the women are suffering from different symptoms associated with premenstrual syndrome, their awareness regarding the etiology is very low. The intensity of these symptoms might be mild but these do affect their daily activities therefore awareness should be made common to healthcare providers first so proper therapies can be provided along with counseling of these women coming from rural background with low education. Further studies on large sample of general population need to be conducted to confirm the frequency of PMS and also to plan out strategies for better detection of this disease to find the exact burden. The introduction of reproductive health education at some level of education can also help in providing information, education and support to the young girls suffering from PMS.

REFERENCES

1. Braverman PK. Premenstrual Syndrome and Premenstrual Dysphoric Disorder. *J Pediatr Adolesc Gynecol* 2007; 20(1): 3-12.
2. Johnson SR. The epidemiology and social impact of premenstrual symptoms. *Clin Obstet Gynecol* 1987; 30(2): 367-76.
3. American College of Obstetrics and Gynecology. ACOG practice bulletin: premenstrual syndrome. Washington, DC: ACOG; 2000 April.p.15.
4. Halbreich U. The atiology, biology and evolving pathology of premenstrual syndromes. *Psychoneuroendocrinology* 2003; 28(suppl 3): 55-99.
5. O'Brien PMS. The premenstrual syndrome. A review. *J Reprod Med* 1985; 30: 113-126.
6. Schellenberg R. Treatment for the premenstrual syndrome with agnus castus fruit extract: a prospective, randomized, placebo controlled study. *BMJ* 2001; 322: 134-7.
7. Kleijnen J. Evening primrose oil. *BMJ* 1994; 309: 824-5.
8. Kouri EM, Halbreich U. Hormonal treatments for premenstrual syndrome. *Drugs Today* 1998; 34: 603-610.
9. Shershah S, Morrison JJ, Jafarey S. Prevalance of premenstrual syndrome in Pakistani women. *J Pak Med Assoc* 1991; 41: 101-3.
10. Nisar N, Zehra N, Haider G, Munir AA, Sohoo NA. Frequency, intensity and impact of premenstrual syndrome in medical students. *J Coll Physicians Surg Pak* 2008 18(8): 481-4.
11. Hylan TR, Sundell K, Judge R. The impact of premenstrual symptomtology on functioning and treatment-seeking behavior: experience from the United States, United Kingdom and France. *J Womens Health Gend Based Med* 1999; 8: 1043-52.
12. Cleckner-Smith CS, Doughty AS, Grossman JA. Premenstrual symptoms. Prevalence and severity in an adolescent sample. *J adolesc Health* 1998; 22: 403-8.
13. Bakhshani N, Mousavi M, Khodabandeh G. Prevalence and severity of premenstrual symptoms among Iranian female university students. *J Pak Med Assoc* 2009;59(4): 205-8.
14. Longo DA, Silva CM, Gigante DP, Carret ML, Fassa AG. Population study of premenstrual syndrome. *Rev. Saude Publica* 2006;40(1).
15. Balaha MH, Amr MA, Moghannum MS, Muhaidab NS. The phenomenology of premenstrual syndrome in female medical students: a cross sectional study. *Pan Afr Med J* 2010; 5:4.
16. Abu-Hashem H, Amr M, Allam AF, Yousef H, Nemar A. Premenstrual syndrome(PMS) in a sample of Egyptian adolescents. *J Egy Soc Obstet Gynecol* 2006; 32: 417-18.
17. Kashanian M, Mazinani R, Jalalmanesh S. Pyridoxin (vitamin B6) therapy for premenstrual syndrome. *Int J Gynecol Obstet* 2007; 96: 43-4.
18. Pearlstein T. Nonpharmacologic treatment of premenstrual syndrome. *Psychiatric Annals* 1996; 26(9): 590-4.

19. Yonkers KA, Brown C, Pearlstein TB, et al. Efficacy of a new low dose oral contraceptive with drospirenone in premenstrual dysphoric disorder. *Obstet Gynecol* 2005; 106: 492-501.
20. Reilly J, Kremer J. A qualitative investigation of women's perceptions of premenstrual syndrome: implications for general practitioners. *Br J of GP* 1999;49:783-786.

Address for Corresponding Author:

Dr Irum Sohail
Associate Professor Department of Gynae/Obs
Foundation University Medical College
Rawalpindi

Original Article

Association Between Hypomagnesaemia and Foot Ulcers in Type II Diabetes Mellitus

1. Ashok Kumar 2. M. Saleem Faiz Bhatti 3. Anwer Jamli 4. Ubedullah Shaikh

1. Asstt. Prof. of Medicine 2. Assoc. Prof. of Medicine 3. PGR 4. PG Student of MS, General Surgery, Peoples University of Medical & Health Sciences Hospital, Nawabshah

ABSTRACT

Objective: The aim of the study was to seek the association between hypomagnesaemia and foot ulcers in type II diabetes mellitus and to verify the effect of age, sex, grades of ulcer, duration of ulcers and duration of diabetes and presence of hypomagnesaemia in the association with type 2 diabetes mellitus.

Study Design: cross sectional study.

Place and Duration of Study: This study was carried out in the indoor, setting of Medical Department Peoples Medical College Hospital Nawabshah from September 2009 to May 2010.

Samples: The subjects were divided into two groups. One was with Grade-I Diabetic foot ulcer and the other with Grade-II diabetic foot ulcers with type II diabetes mellitus. Both the groups contained 50 subjects each and were selected according to the inclusion and exclusion criteria.

Materials and Methods: After a brief interview of 100 patients regarding age, sex, duration of Type II diabetes mellitus, duration of foot ulcer and grade of foot ulcer, both groups underwent fasting serum Magnesium level and categorized on the basis of foot ulcers Grade-I and Grade-II according to Wagner's classification of diabetic foot ulcers.

Results: Chi – square test was applied to see the association and then odds ratio was calculated to check the strength of association. Out of 100 Type II diabetic patients, hypomagnesaemia was detected in 20 with grade I diabetic foot ulcer and in 37 patients with grade II diabetic foot ulcers having chi-square value of 13.071 and significance of 0.000 with likelihood ratio 13.554.

Conclusion: There is strong association between hypomagnesaemia in foot ulcers with Type II diabetes mellitus.

Key Words: Hypomagnesaemia, Type II diabetes mellitus, Foot ulcers.

INTRODUCTION

Diabetes is a common metabolic disorder that constitutes a major health problem in the world. Accurate diagnosis and appropriate management can greatly reduce the morbidity and mortality rate in the world.

The name "diabetes" comes from the Greek word for "siphon." Evidence from an Egyptian papyrus suggests that the ancient Egyptians were aware of an illness associated with the passage of much urine. The association of diabetes with its hallmark symptom captured the attention of medical investigators for centuries¹.

Diabetes mellitus is a syndrome with disordered metabolism and inappropriate hyperglycemia due to either a deficiency of insulin secretion or to a combination of insulin resistance and inadequate insulin secretion to compensate. Type II diabetes is the more prevalent form and results from insulin resistance with a defect in compensatory insulin secretion². The number of people with diabetes mellitus is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity.

In Pakistan there were 5.2 million cases in the year 2000 and it is estimated to be 13.9 millions in 2030³.

Diabetes is a common disorder with changing diagnostic criteria with clear objective measurements, approached easily, accurately that can confirm the diagnosis based on the patients history, clinical examination and laboratory evidence. Magnesium (Mg) ion is an essential element and is a cofactor in both glucose transporting mechanism of cell membranes and various enzymes which plays an important role in carbohydrate oxidation⁴. Hypomagnesemia occurs at an incidence of 13.5 to 47.7% among patients with Type II diabetes. Hypomagnesemia has been linked to poor glycemic control, coronary artery diseases, hypertension, diabetic retinopathy, and nephropathy, neuropathy, and foot ulcerations.

In the present era of high technological advances and increasing approach to disease complexity of medical knowledge it is very much necessary for all of us to explore the all aspect of the disease and the factors affecting it for the patient welfare. This study will help in future to manage the patients properly by reducing the risks of complications, treating the complications, avoiding the complications by giving the additional supplements of Magnesium as primary step to manage

the diabetes by adding the basic element to diet and as drug supplements.

MATERIALS AND METHODS

This cross-sectional study was conducted at Medicine Department at Peoples Medical College Hospital, Nawabshah, from September 2009 to May 2010. All patients of uncontrolled Type II diabetes mellitus with foot ulcers were included in this study. Detailed history was taken from all the patients regarding diabetes mellitus. Detailed clinical examination of the patients was done.

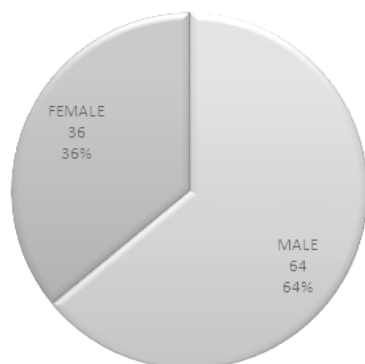
The venous blood were drawn after the admission of all patient in fasting state and sent to PMCH Nawabshah laboratory for analysis of serum Magnesium level by using Xylidyl Blue method with 3338 Merck test Kit (Merck). Level below <1.5 meq/l were labeled as hypomagnesaemia.

Inclusion criteria were all uncontrolled DM type II male/female patients of ≥ 45 years age, with diabetic foot ulcers patients associated grade-I foot ulcers and grade-II foot ulcers. Exclusion criteria were patients with acute complication of diabetes mellitus (such as diabetic keto-acidosis, lactic-acidosis, hypoglycemia, hyperosmolar non ketotic coma. Patients with gestational DM), cerebrovascular accidents, patients on dialysis with renal failure, patients on drugs like diuretics or containing Magnesium, patients on extra supplementation of Magnesium, foot ulcers other than type 2 DM and ulcers other than grade I and grade II.

RESULTS

One hundred cases of Type -II DM with foot ulcer were admitted during the study period. Out of 100 total patients 50 cases were Grade-I and 50 cases were Grade-II. 64(64%) were male and 36(36%) female with male female ratio of 1.7:1 (Chart No.1). There was wide variation of age ranging from a minimum of 45-70 years with mean age of 57.31 ± 6.18 years.

Chart No 1



The education level was 30 un-educated, 53% primary, 15% middle and 02% patients were only matriculation pass. By occupation; male patients were 25% farmers, 26% laborers, 02% drivers in 11% patients were without any current occupation and all 36% female patients were housewives.

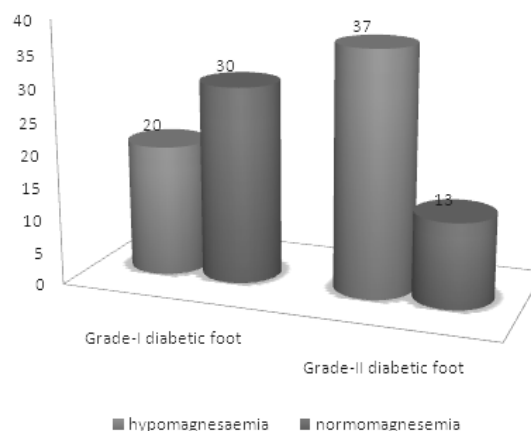
Duration of disease 30% patients had duration of less than 05 years, 39% had duration of 5-10 years and 31% patients had duration of more than 10 years.

After the analysis of serum Magnesium level out of 100 patients 57% were with low serum magnesium and 43% were with normal magnesium level and as the grade of foot ulcer increases the frequency of hypomagnesaemia also increases as in majority of the cases.

Out of 57 patients the duration of disease <05 years were in 15 cases, 05-10 years were in 14 cases and >10 years were in 28 cases associated with hypomagnesaemia, while remaining 43 patients the duration of disease < 05 years in 15 patients, 05-10 years in 25 patients and 03 with duration > 10 years were with normal serum magnesium level.

Duration of diabetic foot ulcer and duration of diabetes has a co-relation, as the duration of type II DM increases the risk of hypomagnesaemia also increases that was statistically significant with p -value <0.001 and simultaneously as the grade of foot ulcer progresses the risk of hypomagnesaemia also increases. In Grade-I diabetic foot ulcer patients 20(40%) have hypomagnesaemia and 30(60%) have normomagnesaemia and in Grade II 37(74%) patients have hypomagnesaemia and 13(26%) patients normomagnesaemia that was statistically significant with p -value <0.001 (Chart No.2).

Chart No.2



DISCUSSION

Diabetes mellitus is a major health problem and hypomagnesaemia represents an important issue in its management. It is matter of intensive research in

western countries. A comprehensive study of the problem should be based upon clinical assessment as well as biochemical and laboratory investigations, including co-relation of blood glucose concentrations with levels of insulin and counter-regulatory hormones like glucagon, adrenaline, cortisol, and many other important substances like trace elements like copper, zinc, magnesium and other trace elements.

There are lot of studies about the diabetes and its complications but there is limited data available in our setup. The data collected in these patients indicates that in adult practice problem of hypomagnesaemia is more pronounced in Type II diabetics with its chronic complication like foot ulcers. In my study the hypomagnesaemia is a common finding in two sub groups of diabetic foot ulcer (grade-I and grade-II). Out of 100 patients there 64(64%) were male and 36(36%) female with male female ratio of 1.7:1. In our study there were decreased ratio of females as compared with males, the possibility of our social back ground low level of education are important factors to influence it. There was wide variation of age ranging from a minimum of 45-70 years with mean age of 57.31 ± 6.18 years. However the male to female distribution given by Kaur T⁵ are 203 male and 197 female with male female ratio is 1:1.03 and age range between 30 to 70 years.

Some previous decades, the interest of health professionals towards the importance of education concerning self management of type II diabetes has been rapidly increased. The final goal of educating patients with diabetes mellitus type II is to accomplish changes of the human behavior through acquisition of knowledge and understanding of the disease⁶. In our study education level was 30 un-educated, 53% primary, 15% middle and 02% patients were only matriculation pass. By occupation; male patients were 25% farmers, 26% laborers, 02% drivers in 11% patients were without any current occupation and all 36% female patients were housewives.

In our study normomagnesemia were 43% and hypomagnesaemia were out of 57%; while some other studies reported were hypomagnesaemia in patients type I and type II diabetes mellitus, with an incidence of 25%–39%^{7,8,9}.

Diabetes mellitus is one of the most common causes of magnesium deficiency¹⁰. Hypomagnesaemia is related to poor metabolic control, which is attributed to increase in urinary magnesium losses¹¹ and although we did not determine glycosylated hemoglobin levels in our patients, poor diabetic control might be an additional factor for their hypomagnesemia. Other factors, however including vomiting, diarrhea, low sodium intake and diuretic use may play a role in magnesium deficiency in diabetes. Recent evidence suggests that insulin enhances the transport of

magnesium into cells; thus, lack of insulin may result in an intracellular magnesium deficit^{12,13}. In our study showed hypomagnesemia with the duration of disease <05 years were in 15 cases, 05-10 years were in 14 cases and >10 years were in 28 cases associated with hypomagnesaemia, while remaining 43 patients the duration of disease < 05 years in 15 patients, 05-10 years in 25 patients and 03 with duration > 10 years were with normal serum magnesium level. While the study of Ankush RD showed Decreased levels of plasma magnesium, erythrocyte reduced glutathione and erythrocyte superoxide dismutase activity while increased levels of plasma lipid peroxides, nitric oxide end products and erythrocyte membrane lipid peroxides were observed in patients with type-2 diabetes mellitus¹⁴.

The diabetic state interferes in the maintenance of the normal concentrations on body Mg, being able to trigger hypomagnesemia easily, mainly in poor metabolic control, which leads more spontaneously the outcome of diabetic chronic complications.

In our study results showed Grade-I diabetic foot ulcer patients 20(40%) have hypomagnesaemia and 30(60%) have normomagnesemia and in Grade II 37(74%) patients have hypomagnesaemia and 13(26%) patients normomagnesemia that was statistically significant with p-value <0.001. However study of Moran R¹⁵ suggested that hypomagnesemia may be associated with an increased risk of diabetic foot ulcers. Indeed, they observed a higher incidence of hypomagnesemia among their patients with diabetic foot ulcers compared with those without the condition (93.9% of the 33 patients with diabetic foot ulcers compared with 73.1% of the 66 patients without diabetic foot ulcers; p value 0.02)¹⁶.

As such, extrapolations to Mg deficiency should be viewed with caution because in our setup male mostly do the strenuous daily rough work and are more prone to get injuries which are not noted as in routine deal as simple injury.

CONCLUSION

The diabetic condition interferes in the maintenance of the normal Mg concentrations, which leads more spontaneously the conclusion of chronic complications associated with Type II DM with foot ulcers. Diabetic foot ulcers in 57% of patients as concluded from my study.

Recommendations

I therefore emphasize that serum magnesium be routinely included for the analysis and early correction be made so that DM with the complication of foot ulcer can be prevented and controlled accordingly.

We recommend periodic determination of magnesium levels and appropriate magnesium replacement. To

examine the effect of magnesium replacement on outcomes, a long-term prospective study is needed.

REFERENCES

1. Dineen SF. What is diabetes? Diabetes basic facts. Medicine Int Number 2006;6(1);45-46.
2. Masharani U. Diabetes mellitus & hypoglycemia. In: Tierney JR, McPhee SJ, Papadakis MA, editors. Current medical diagnosis & treatment. 47th ed. New York: McGraw-Hill; 2008.p.1142-90.
3. Sarah W, Gojka R, Anders G, Richard S, Hilary K. Global Prevalence of Diabetes. Diabetes Care 2004;27:1047-53.
4. Shafique M, Ahmed M, Fayyaz KM, Hussain S. Beneficial effects of magnesium supplementation in diabetes mellitus – an animal study. Pak J Med Res 2002;41(2):73-76.
5. Kaur T, Bishnoi D, Badaruddoza. Effect of sex on prevalence of type II diabetes mellitus (T2DM) with respect to blood pressure, BMI and WHR among Punjabi population. Int J Med & Med Sci 2010;2(9):263-270.
6. Polikandrioti M. Editorial Article: The role of education in diabetes mellitus type II management. J Health Sci 2010;4(4):200-201.
7. De Valk HW. Magnesium in diabetes mellitus. Neth J Med 1999;54(4):139-46.
8. Rude RK. Magnesium deficiency and diabetes mellitus: causes and effects. Postgraduate Medicine 1992;92(5):217–224.
9. Nadler JL, Rude RK. Disorders of magnesium metabolism. Endocrinol Metab Clin North Am 1995;24(3):623–641.
10. McNair P, Christensen MS, Christiansen C, Madsbad S, Transbol I. Renal hypomagnesemia in human diabetes mellitus: Its relation to glucose homeostasis. Eur J Clin Invest 1982;12(1):81–85.
11. Djurhuus MS, Skott P, Vaag A, et al. Hyperglycemia enhances renal magnesium excretion in type 1 diabetic patients. Scan J Clin Lab Invest 2000; 60(5):403–409.
12. Barbagallo M, Gupta RK, Resnick LM. Cellular ionic effects of insulin in normal human erythrocytes: a nuclear magnetic resonance study. Diabetologia 1993;36(2):146–149.
13. Seyoum B, Siraj ES, Saenz C, Abdulkadir J. Hypomagnesemia in Ethiopians with diabetes mellitus. Ethnicity & Disease Spring 2008;18:147-151.
14. Ankush RD, Suryakar AN, Ankush NR. Hypomagnesaemia in type-II diabetes mellitus patients: A study on the status of oxidative and nitrosative stress. Indian J of Clin Biochemistry 2009;24(2):184-189.
15. Rodríguez- Morán M, Guerrero-Romero F Low serum magnesium levels and foot ulcers in subjects with type II diabetes. Arch Med Res. 2001; 32(4):300-3.
16. Corsonello A, Lentile R, Buemi M, Cucinotta D, Mauro VN, Macaione, S et al. Serum ionized magnesium levels in Type II diabetic patients with microalbuminuria or Clinical proteinuria. Am J Nephrol 2000;20:187–192.

Address for Corresponding Author:

Dr.Ashok Kumar

Asstt. Prof. of Medicine,
Peoples University of Medical & Health Sciences
Hospital, Nawabshah.
Flat No: 1 Pak Plaza Trunk Bazar/ Moni Bazar,
Nawabshah.
Email address: drashokfcps@yahoo.com
Cell # 03003025348

Original Article

CNS Stimulant Activity of Qurs Saffron (A Herbal Medicine) in Experimental Animal Models

1. Naveed Ullah 2. Mir Azam Khan 3. Huma Waqas 4. Afraseyab Ali Shah
5. Ghayour Ahmed 6. Nouman Altaf

1. Ph.D. Student Pharmacy Dept, University of Malakand 2. Assoc. Prof. of Pharmacy, University of Malakand
3. Asstt. Prof. of Paediatrics, WMC, Abbottabad 4. Lecturer of Pharmacology, FMC Abbottabad 5 & 6 M.Phil
Students, Pharmacy Dept, University of Malakand.

ABSTRACT

Objective: To confirm the safety and efficacy of the product for human health due to its wide use and to explore its effects on CNS.

Study Design: Experimental and observational

Place and Duration of Study: This study was conducted at Frontier medical college Abbottabad Pakistan in March 2011.

Materials and Methods: Thirty rabbits divided into five groups were administered Qurs saffron at the dose of 50, 100 and 200 mg/kg, Caffeine 100mg/kg orally and the last group was taken as control group, received normosaline. The animals were observed for behavioral changes at 30 min intervals.

Results: At 50mg/kg of the drug were found to have mild stimulant activity, while 100mg/kg were found to have a moderate CNS stimulant properties same like caffeine at a dose of 50mg/kg. While at a dose of 200mg/kg Qurs saffron were found to have a strong stimulant properties.

Conclusion: From the current study it can be concluded that the product have dose dependent CNS stimulant effects.

Key Words: Qurs saffron, Caffeine, CNS stimulant effects.

INTRODUCTION

Nature has been a source of medicinal agents and a large number of drugs are isolated from natural sources. Medicinal plants have a great value in the field of health. From the very past the use of herbal medicine have been very important, and fulfills the primary health care needs of about 80% of the world population¹.

Qurs saffron (herbal tablets) is used as an analgesic for the treatment of all body pain, especially it is prescribed for the treatment of arthritis. It claimed to have the following plant extracts. I.e. Meadow saffron, Colchicum, Murdannia, Asparagus, Pellitory, China root, Mace, Dill, Peppermint, Fennel fruit, Horse radish, Kala dana, Black pepper, Long pepper and Coral.

Colchicum autumnale (meadow saffron), are well known, preparations traditionally used as medication against gout². Asparagus officinalis is a spring vegetable, a flowering perennial³, plant species in the genus Asparagus, eaten raw as a component of a salad. Dill (Anethum graveolens) is a short-lived perennial herb. In Arabic, dill seed is called ain jaradeh (means cricket eye) used as a spice in cold dishes like fattosh and pickles. In Lao cuisine and parts of northern Thailand and Vietnam, dill is known in English as Laotian coriander⁴. Horseradish (Armoracia

rusticana, syn. Cochlearia armoracia) is a perennial plant of the Brassicaceae family. Known to have diuretic properties, the roots have been used to treat various minor health problems, including urinary tract infections, bronchitis, sinus congestion, ingrowing toe nails and coughs. Compounds found in horseradish have been found to kill some bacterial strains⁵. Peppermint has promising radio protective effects for cancer patients undergoing cancer treatment⁶. Peppermint oil has a high concentration of natural pesticides, mainly menthone⁷. Saffron is a spice derived from the flower of the saffron crocus (Crocus sativus). Crocus is a genus in the family Iridaceae. Saffron has many medicinal uses⁸. A 2010 double-blind, placebo-controlled study found saffron helped mild to moderate Alzheimer's disease⁹. Crocetin, an important carotenoid constituent of saffron, has shown significant potential as an anti-tumor agent in animal models and cell culture systems¹⁰.

As arthritis is a most common disease in the old age, and most of the people believed that, herbal medicine have a great effect in this disease, rather than allopathic medicines. Qurs saffron tablets (herbal product) widely used for the treatment of gout and other body pain. And an observation from the users that the drug has alertness properties, therefore the current study was designed with a view to confirm and explore the CNS stimulant activity of the product.

MATERIALS AND METHODS

Drug Material

The fresh formulated drug (Qurs saffron) was purchased from local market of Taxila Pakistan. The specimen pack, marked with a number 1821 has been deposited in Pharmacology Museum, Frontier Medical College Abbottabad Pakistan.

Preparation for tests

Isotonic solution of Qurs saffron tablets and Caffeine tablets were prepared by dissolving in sufficient quantity of normo-saline to prepare 50mg/ml, 100mg/ml, and 200mg/ml of Qurs saffron and 100mg/ml of Caffeine.

Experimental Animals

Rabbits of either sex were breed locally. Their average weight was in the range of 1.5 – 2.0 kg. They were maintained at the “Animal House of Frontier Medical College Abbottabad” as per Byelaws of Scientific Procedures. Animals were given free access to standard diet along with fresh water.

Experimental Protocol

Evaluation of general behavioral profiles was performed by the method of Dixit and Varma¹¹. Thirty rabbits of either sex were taken and divided into five groups. Each group contained six animals. Qurs saffron was administered to the first three groups of animals at the dose of 50, 100 and 200 mg/kg orally. One group was administered Caffeine 100mg/kg orally and the last group was taken as control group, received normosaline in the same amount as that to the others.

The animals were under observation for their behavioral changes, if any, at 30 min intervals in the first one hour and at the hourly intervals for the next 4 hour for the following parameters. The alertness was recorded by visual measure of the animal's response. The normal behavior at resting position was scored as; No activity (-)

Little activity (+)

Moderate activity (++)

Strong response (++++)

RESULTS

The qualitative CNS stimulant activity of Qurs saffron revealed that, this herbal drug has a strong stimulant effect on central nervous system, and was found to be dose dependant. Further their stimulant effect was compared with caffeine, which was found to be approximately same as that of caffeine as given in table 1. *Qurs saffron* at a dose of 50mg/kg were found to have mild CNS stimulant activity, while caffeine at a dose of 50mg/kg showed moderate stimulant effect. A moderate CNS stimulant effect were also noted at a dose of 100mg/kg of *Qurs saffron*, and this effect were found so severe in the experimental animals that were

administered with a dose of 200mg/kg of this particular drug.

Table No.1: CNS stimulant effect of Qurs saffron

Type of Extract	Quantity & Extant of alertness and Visual behavioral changes in Animals No.						
	1	2	3	4	5	6	Cumulative
<i>Qurs saffron</i> 50 mg/kg	+	+	++	+	+	+	+
<i>Qurs saffron</i> 100mg/kg	++	++	++	++	++	++	++
<i>Qurs saffron</i> 200mg/kg	++	++ +	++ +	++ +	++	++ +	+++
Caffeine 50mg/kg	++ +	++	++	++	++	++ +	++
Isotonic solution	-	-	-	-	-	-	-

+++ excess (Present)

++ Moderate (present)

+ Mild (present)- Absent

DISCUSSION

Group-1 received *Qurs saffron* at a dose of 50mg/kg showed a mild CNS stimulant activity. Group-2 received *Qurs saffron* at a dose of 100mg/kg showed a moderate stimulant activity. Group-3 received *Qurs saffron* at a dose of 200mg/kg showed a strong CNS stimulant activity. Group-4 received Caffeine at a dose of 50mg/kg showed a moderate CNS stimulant activity. Group-5 received only normosaline did not show a measurable CNS stimulant activity. As *Qurs saffron* *claimed* to have the following plant extracts. I.e. Meadow saffron, Colchicum, Murdannia, Asparagus, Pellitory, China root, Mace, Dill, Peppermint, Fennel fruit, Horse radish, Kala dana, Black pepper, Long pepper and Coral. MacLagan reviewed the published experience with colchicum, which is also present in this particular drug; he described his own clinical studies¹². He found colchicum useful as a diuretic in dropsy following scarlet fever, especially when the urine was suppressed and signs of coma were present. He recommended colchicum as an anti-inflammatory drug in acute gout, in acute articular rheumatism, and in urticaria. Maughan and Griffin reported that Caffeine has diuretic properties when administered in sufficient doses to subjects who do not have a tolerance for it⁸. So both the drugs were reported to have diuretic properties.

Haden, in 1820 published a monograph on the use of colchicum as a general remedy in the treatment of acute and chronic inflammatory diseases¹³. His father has begun the use of colchicum in gout after want's report he extended the use of the remedy from gout to rheumatism.

Armstrong considered colchicum a medicine of considerable benefit in inflammatory fever; He recommended it especially in acute or sub-acute rheumatism, and in internal serous inflammation, particularly of the arachnoids or of the pleura for the treatment of dropsy¹⁴. From these it can be concluded that the alkaloids colchicines may be present in excess in the drug which have more potent anti-inflammatory activities responsible for anti-gout effects. And has also had some chemical constituents which have strong CNS stimulant properties like Caffeine etc, and need to have a quantitative study of the drug.

REFERENCES

1. World Health Organization. General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine WHO Geneva: Switzerland; 2001.p.10.
2. Klintschar M, Beham Schmidt C, Radner H, Henning G, Roll P. Colchicine poisoning by accidental ingestion of meadow saffron (*Colchicum autumnale*): pathological and medicolegal aspects, 1999; 106(3): 191-200.
3. Grubben GJH, Denton OA, editors. Plant Resources of Tropical Africa 2. Vegetables. PROTA Foundation, Wageningen; Backhuys, Leiden; CTA, Wageningen. 2004.
4. Davidson A. Seafood of South-East Asia, 2nd edition. Ten Speed Press. 2003.
5. Barbara P. Horseradish. Mother Earth News. 2003
6. Baliga MS, Rao S. Radioprotective potential of mint: A brief review. J Cancer Res Ther 2010; 6 (3): 255-262.
7. Krieger RI. Handbook of Pesticide Toxicology: Principles. Academic Press, 2001. p. 823.
8. Maughan RJ, Griffin J. Caffeine ingestion and fluid balance: a review. Journal of Human Nutrition and Dietetics 2003;16 (6): 411-20.
9. Akhondzadeh S, Sabet MS, Harirchian MH, Togha M, Cheraghmakani H, Razeghi S, et al. Saffron in the treatment of patients with mild to moderate Alzheimer's disease: A 16-week, randomized and placebo-controlled trial". J of Clin Pharmacy and Therapeutics 2010; 35(5):581-588.
10. Gutheil WG, Reed G, Ray A, Dhar A. Crocetin; an Agent Derived from Saffron for Prevention and Therapy for Cancer. Curr Pharm Biotechnol 2011.
11. Dixit VK and Varma KC. Effects of essential oil of leaves of *Blumea*. Indian J Pharmacol 1976; 18, 7-11
12. MacLagan JM. On the *Colchicum autumnale*, chiefly with reference to the growth of the plant, and it's physiologic and therapeutic actions. Monthly J Med Sci (Edinburgh) 1852;14:1-33
13. Haden CT. Practical observation on the colchicum autumnale as general remedy of great power London, Burgess and Hill. 1820.
14. Armstrong J. Lectures on the Morbid Anatomy, Nature and Treatment of Acute and Chronic Diseases. Philadelphia: Haswell & Barrington; 1837.p. 293.

Address for Corresponding Author

Dr. Naveed Ullah

Ph.D. Student Pharmacy Dept,

University of Malakand.

Tel: 0092-992-511020

Cell: 0092-345-5910522

E-mail: naveedjia@yahoo.com

naveedullahpharmacist@gmail.com

Original Article**Etiology of Hepatomegaly in Balochistan****1. Esaa KhanTareen 2. Haroon Ishaq 3. Muhammad Atif 4. Wasim Baig**

1. Asstt. Prof. of Medicine 2 & 3. PGRs / MOs of Medicine
4. Chief Pharmacist, Sandeman (P) Hospital / Bolan Medical College, Quetta.

ABSTRACT

Aim of study: The aim of our study was to find out the definite diagnosis of hepatomegaly and the prevalence of various causes of hepatomegaly in Balochistan.

Study Design: Experimental and Observational study.

Place and Duration of Study: This study was conducted in the Medical Unit-III, Bolan Medical College, Quetta from April 2009 to December 2010.

Patients and Methods: 105 patients were admitted in our medical unit III with the clinical presentation of hepatomegaly. Patients were the age group 10 years to 85 years, 73 patients were males and 23 patients were females. Patients with congestive hepatomegaly were excluded from this study and methods used in this study were history, clinical examination, LFTs and liver biopsy.

Results: The incidence of various common causes of hepatomegaly in Balochistan are amoebic liver abscess 12%, hydatid disease of liver 13%, hepatocellular carcinoma 15%, hepatitis 17%, obstructive jaundice 9% & normal 9%.

Conclusion: The most common causes of Hepatomegaly in Balochistan are amoebic liver abscess, hydatid disease of liver, hepatocellular carcinoma, viral hepatitis, obstructive jaundice. This study has shown that percentage of hydatid disease of liver, fatty liver and lymphoma, as compared to Durban study was higher. This study will help in managing and understanding various causes of hepatomegaly in field of Therapeutics and Research, especially in Balochistan.

Key Words: Hepatomegaly, Liver abscess, Amoebic liver abscess, Hepatocellular carcinoma.

INTRODUCTION

Since the recommendation of World Health Organization in 1985, to use ultra sound equipment it has become readily available for diagnostic imaging, in the developing countries. The use of ultrasound for definite diagnosis of hepatomegaly has increased. The list of causes of hepatomegaly is long, but there are certain etiologies peculiar to each area, with the aim in mind we devised a study to find out the most common causes of hepatomegaly encountered in Balochistan, as all the patients of the province are referred to Civil Hospital Quetta for investigations and treatment. The most common causes of hepatomegaly in Balochistan are amoebic liver abscess, hydatid disease of liver, hepatitis, obstructive jaundice and hepatocellular carcinoma. The increased incidence of viral hepatitis and amoebic liver abscess secondary to amoebic colitis is due to poor sanitary conditions and inadequate availability of pure drinking water. Hydatid disease of liver is more common because the occupation of the majority of the people of Balochistan is farming and they are in close association with the dogs used for the herding sheep, goats and cattle, the reservoir of infection, thus completing the life cycle of hydatid disease. Hepatocellular carcinoma is a common

neoplasm world wide and a relation between this neoplasm and infection with hepatitis B virus and hepatitis C virus has been described.

PATIENTS AND METHODS

Hepatomegaly is one of the common causes of admission of patient in medical wards.

105 patients were admitted in our medical unit III with the clinical presentation of hepatomegaly. Patients were the age group 10 years to 85 years, 73 patients were males and 23 patients were females. Patients with congestive hepatomegaly were excluded from this study. In order to reach the definite diagnosis the following parameters were utilized 1)History 2)Clinical examination 3)Liver function test 4) HbsAg, HBe Ag, HBV DNA Polymerase 5)Anti HCV Anti body, HCV RNA by PCR 6)Ultra sound scanning 7)Liver biopsy 8)Needle aspiration of liver abscess 9)Hepatic surgery for hydatid liver disease and subdiaphragmatic abscess. Liver biopsy was done with the trucut needle. The biopsy specimen was sent to the laboratory in formalin. Tissue piece after sectioning and fixation was stained with haematoxylin and eosin. Indirect haemagglutination test was carried out for hydatid disease of liver.

RESULTS

The incidence of various common causes of hepatomegaly in Balochistan are amoebic liver

abscess 12%, hydatid disease of liver 13%, hepatocellular carcinoma 15%, hepatitis 17%, obstructive jaundice 9% & normal 9%.

Table No.1: Percentage of different diseases in different age groups of male and female.

Total number of cases.....105

Sr.No.	Diagnosis	No. of Cases %	Age Limit (Years)	Sex
1	Amoebic liver abscess	12	24-85	All Male
2	Hepatocellular carcinoma	15	34-60	All Male
3	Viral Hepatitis	17	24-56	10M 10 F
4	Fatty Change	05	35-52	03M 02F
5	Hydatid disease	13	30-60	10M 03F
6	Obstructive jaundice	09	44-52	04M 05F
7	Lymphoma	05	32-45	03M 02F
8	Metastasis	51-85	51-85	04M 01F
9	Thalasemia	03	13-17	03M 0 F
10	Subdiaphragmatic abscess	03	17-35	02M 01F
11	Hepatic Tuberculosis	02	10-15	01M 01F
12	Chronic Lymphocytic Leukemia	02	35-46	01M 01F
13	Sarcoidosis	01	56	Male
14	Visceral Leishmaniasis	01	17	Male
15	Glycogen Storage Disease	02	10-12	01M 01F
16	Primary Biliary Cirrhosis	01	50	Female
17	Normal	09	12-60	05M 04F

DISCUSSION

The study which we carried out included 105 patients which were admitted in the year April 2009 to December 2010 in Medicine unit III of Civil Hospital Quetta. In this study patients included from Quetta and all the referred patients from peripheral hospitals of Urban & Rural areas of Balochistan. In Table No.1, the incidence of amoebic liver abscess as a cause of hepatomegaly was 12%. All the patients were male and belong to age group 24 - 85 years. The importance of ultrasound in the diagnosis and management of liver abscess has been emphasized by Berry et al in 1986⁴.we were able to localize the amoebic liver abscess and drain it by needle aspiration with the help of ultrasonography in all cases. One case presented as obstructive jaundice due to huge size of amoebic liver abscess. Hydatid cyst as a cause of hepatomegaly was found in 13% of patients. This incidence of hydatid disease of liver is much higher than the study of Maharaj et al in 1985⁵, where an incidence of less than 0.5% has been reported. Hepatocellular carcinoma was diagnosed in 15% of the patients. All the patients were male, the age group of patients was from 34-60 years. This male preponderance in hepatocellular carcinoma has been reported from Africa and the orient with male to female ratio of 6:1⁶.The oncogenic role of hepatitis B virus and hepatitis C virus in hepatocellular carcinoma

is particularly important in countries with a high prevalence of HBV infection⁷. obstructive jaundice was diagnosed in 9% of patients with hepatomegaly. Four of these patients had gall stones in common bile duct, 3 patients had carcinoma common bile duct and 2 patients had carcinoma of head of pancreas. In a similar study of the etiological diagnosis of extrahepatic cholestasis, 31% of patients had gall stones in common bile duct, 28.5% of patients had carcinoma pancreas and 5.7% of patients had bile duct tumor as cause of extrahepatic cholestasis⁸. 17 patients with hepatomegaly were diagnosed as to have viral hepatitis. Patients were of the age group 24 to 56 years. Six patients were HbsAg positive, out of which 2 had hepatitis more than 6 months duration and they were HBe Ag and HBs DNA Polymerase their liver biopsies showed chronic hepatitis. Liver metastasis was diagnosed by ultrasound and liver biopsy in 5% of patients. Two patients had metastasis from carcinoma colon. One female patient had carcinoma breast with liver metastasis. In two cases the primary malignancy could not be traced. About 50% of all carcinoma originating from the splanchnic area and about 35% of these arising outside the portal venous drainage area eventually spread to the liver⁶. We have found ultrasound to be very sensitive in detecting hepatocellular carcinoma and early metastasis in liver⁹. With the help of ultrasound the site and depth of focal lesion can be measured and needle liver

Table No.2: Percentage of different diseases in two cities.

<u>Sr.No.</u>	<u>Diagnosis</u>	<u>Durban Study</u>	<u>Quetta Study</u>
<u>1</u>	Amoebic liver abscess	12.7%	12%
<u>2</u>	Hydatid disease	0.5%	13%
<u>3</u>	Hepatocellular carcinoma	15.7%	15%
<u>4</u>	Hepatitis	18.0%	17%
<u>5</u>	Fatty change	02.0%	05%
<u>6</u>	Metastasis	12.0%	05%
<u>7</u>	Lymphoma	0.6%	05%
<u>8</u>	Chronic Lymphocytic Leukemia	0.0%	02%
<u>9</u>	Hepatic Tuberculosis	04.5%	02%
<u>10</u>	Thalassaemia	0.0%	03%
<u>11</u>	Sub diaphragmatic abscess	0.0%	03%
<u>12</u>	Alcoholic Hepatitis	03.8%	0.0%
<u>13</u>	Obstructive jaundice	0.0%	09%
<u>14</u>	Schistosomiasis	04.5%	0.0%
<u>15</u>	Normal	17.0%	09%

biopsy taken accurately from site of lesion, increasing the diagnostic accuracy of needle biopsy¹⁰. This makes ultrasound and liver biopsy as supplementary to each other, rather than substitutes. Hepatic tuberculosis was diagnosed by liver biopsy in two cases, one patient was female aged ten years and second patient was male aged 15 years. Ultrasound is of little value in the diagnosis of hepatic tuberculosis¹². Hepatic biopsy is the only method to confirm the diagnosis of hepatic tuberculosis. Hepatomegaly due to fatty infiltration of the liver was diagnosed in 5% of patients. 55 patients have diagnosed to have Non-Hodgkin lymphoma upon liver biopsy. The patients with hepatomegaly were diagnosed to have chronic lymphocytic leukaemia in peripheral blood smear and bone marrow aspiration biopsy. Three male patients who presented with hepatosplenomegaly were diagnosed as thalassaemic upon haemoglobin electrophoresis. Three patients who presented with hepatomegaly were diagnosed to have subdiaphragmatic abscesses upon ultrasound examination which were later drained surgically. In 9 cases with hepatomegaly, liver histology was normal upon liver biopsy. Patients with glycogen storage disease were members of the same family. In Table No.2, the comparison of this study with a similar study in 1986 by Maharaj et al. 5 in Durban reveals both similarities and differences in the prevalence of various causes of hepatomegaly. The percentage of hydatid disease of liver, fatty liver and lymphoma was higher in our study. No case of chronic lymphocytic leukaemia, thalassaemia, obstructive jaundice and sub-diaphragmatic abscess as a cause of hepatomegaly was reported in the Durban study. No case of schistosomiasis and alcoholic hepatitis is reported in our study. The detail comparison given in the Table No.2.

CONCLUSION

The most common causes of Hepatomegaly in Balochistan are amoebic liver abscess, hydatid disease of liver, hepatocellular carcinoma, viral hepatitis, obstructive jaundice. This study has shown that percentage of hydatid disease of liver, fatty liver and lymphoma, as compared to Durban study was higher. This study will help in managing and understanding various causes of hepatomegaly in field of Therapeutics and Research, especially in Balochistan.

REFERENCES

1. Palmer PES. Diagnostic imaging for developing countries. WHO Chron 1985;39:143-48.
2. Nelson GS. Hydatid disease, Medicine International, 3rd ed. Pakistan: 1988.p.2267-69.
3. Munoz N, Bosch X. Epidemiology of Hepatocellular carcinoma. In: Okuda K, Ishak KG, editors. Neoplasms of the Liver. Tokyo: Springer-Verlag;1987.p.3.
4. Berry M, Bazaz R, Bhargava S. Amoebic liver congenic diagnosis and management, Clin ultrasound 1986;14;39-42.
5. Maharaj B, Coops RM, Maharaj RJ, et al. Causes of hepatomegaly at kind Edward VIII Hospital, Durban a Prospective study of 240 black patients. S Afr Med J 1986;183-84.
6. Kew MC. Hepatic Tumours, Medicine International 1986;Vol 2 (10) 1201-05 Beasley RP. Hepatitis B virus as the etiological agent in hepatocellular carcinoma, epidemiologic considerations, hepatology 1982;2(Suppl):21-265.
7. Amouyal P, Palazzo I, Amouyal G, Ponsot PE. Endosonography: promising method for diagnosis

- of extrahepatic cholestasis. *Lancet* 1989;(I): 1195-98.
8. Sheu GC, Sung JL, Chen BS, et al. Early detection of hepatocellular carcinoma by real time ultrasonography: a Prospective study. *Cancer* 1985;56:660-66.
 9. Jennings PE, Donald GT, Coral A, et al. Ultrasound guided core biopsy 1989;11369-71.
 10. Ceelege G, Savarino V, Piceitte V, Piceiotte A, Mangnolia MR, et al. Is hepatic ultrasonography a valid alternative tool to liver biopsy? Report on 507 cases studied with both techniques. *Gig Dis Sci* 1988;33:467-71.
 11. Mahraj B, Leary WP, Pudifin DJ. A prospective study of hepatic tuberculosis in 41 black patients. *Q J Med* 1987;68:517-22.
 12. James OF, Day CP. Non-alcoholic steatohepatitis (NASH): a disease of emerging identity and importance *J Hepatol* 1998; 29:495–501.
 13. Shimano H, Horton JD, Hammer RE, Shimomura I, Brown MS, Goldstein JL. Overproduction of cholesterol and fatty acids causes massive liver enlargement in transgenic mice expressing truncated SREBP-1a. *J Clin Invest* 1996; 98: 1575–1584.
 14. Weltman MD, Farrell GC, Liddle C. Increased hepatocyte CYP2E1 expression in a rat nutritional model of hepatic steatosis with inflammation. *Gastroenterology* 1996; 111: 1645–1653
 15. Leclercq IA, Farrell GC, Field J, Bell DR, Gonzalez FJ, Robertson GR. CYP2E1 and CYP4A as microsomal catalysts of lipid peroxides in murine nonalcoholic steatohepatitis. *J Clin Invest* 2000; 105: 1067–1075.
 16. Matloff DS, Selinger MJ, Kaplan MM. Hepatic transaminase activity in alcoholic liver disease. *Gastroenterology* 1980; 78: 1389–1392.
 17. Aoyama T, Peters JM, Iritani N, Nakajima T, Furihata K, Hashimoto T, et al. Altered constitutive expression of fatty acid-metabolizing enzymes in mice lacking the peroxisome proliferator-activated receptor alpha (PPARalpha). *J Biol Chem* 1998; 273: 5678–5684.
 18. Zeledon R, Hidalgo H, Viquez A, Urbina A. Atypical cutaneous leishmaniasis in a semiarid region of northwest Costa Rica. *Trans R Soc Trop Med Hyg* 1989;83:786
 19. Murray HW. Treatment of visceral leishmaniasis (kala-azar): a decade of progress and future approaches. *Int J Infect Dis* 2000;4:158-77.
 20. Kattan YB. Hydatid cyst in pancreas. *Br Med J* 1975;4:729-30.
 21. Faucompret S, Farthouat P, Sainton T, Breda Y. Complicated hydatid cyst of the pancreas after needle biopsy. *Ann Chir* 2001;126:491-2.
 22. Abdel-Wahab MF, Esmat G, Farrag A, El-Boraey Y, Strickland GT 1993. Ultrasonographic prediction of esophageal varices in schistosomiasis mansoni. *Am J Trop Med Hyg* 88: 560-563

Address for Corresponding Author:**Esaa KhanTareen**

Asstt. Prof. of Medicine, BMC, Quetta

E.Mail: dr.essakhan@yahoo.com

Cell No. 0333-7816475

