

Recognized by PMDC

CONTENTS

Recognized by HEC

**Editorial**

1. **Smoking Shisha or Cigarette – Dangerous for Human Health – Different Studies** \_\_\_\_\_ 1  
*Dr. Azhar Masud Bhatti*

**Original Articles**

2. **Screening of some Herbal Medicines for Psychopharmacological Activity** \_\_\_\_\_ 3  
*1. Saima Ahmed 2. Muhammad Asadullah*
3. **Renal Outcome in Women with Preeclampsia and Eclampsia at Presentation and Six Months Post Delivery** \_\_\_\_\_ 8  
*1. Mirza Muhammad Ilyas Baig 2. Aftab Haider Alvi 3. Shabnum Tahir 4. Omer Sabir*
4. **Effect of Lemon Grass and Green Tea on Blood Pressure and Heart Rate** \_\_\_\_\_ 11  
*1. Naveed Ullah 2. Amir Nazir 3. Sadaf Anwar 4. Nouman Altaf 5. Abdullah 6. Maqsood ur Rehman*
5. **Juvenile Nasopharyngeal Angiofibroma, Experience of 35 Cases with Different Surgical Approaches** \_\_\_\_\_ 14  
*1. Masood Akhtar 2. Mohammad Saleem Sheikh*
6. **Comparison of Ondansetron and Metoclopramide in the Prevention of Nausea and Vomiting after Laparoscopic Cholecystectomy Under General Anaesthesia** \_\_\_\_\_ 18  
*1. Noor Hussain 2. Dur-i-Shahwar 3. Madiha Malik 4. Shaheen Mahmood*
7. **Glycation Pattern of Captopril in diabetics** \_\_\_\_\_ 24  
*1. Samina Kousar 2. Mahboob Bari 3. Nighat Naeem 4. Munir A. Sheikh*
8. **The Incidence of Weapon used in Medicolegal Cases of Urban Area of Abbottabad** \_\_\_\_\_ 29  
*1. Nighat Seema 2. Iftikhar Ahmad 3. Mohammad Saleem 4. Saleem Afzal*
9. **Frequency of Fetal Anomalies in Polyhydramniotic Patients Through Antenatal Ultrasound in Radiology Department of PIMS** \_\_\_\_\_ 33  
*1. Nuwayrah Jawaid 2. Shahla Zameer 3. Aliya Ahmed*
10. **Co-relation of thyroid function test with the clinical presentation** \_\_\_\_\_ 37  
*1. Tariq Saeed 2. Shahid Mahmood 3. Muhammad Taimur 4. Sadaf Faisal Bhopal*
11. **Presentation and Outcome of Surgical Management of Strangulated Inguinal Hernia at Liaquat University Hospital Hyderabad** \_\_\_\_\_ 41  
*1. Sikander-e-Azam 2. Ubedullah Shaikh 3. Muhammad Qasim Mallah 4. Qambar Ali Laghari*
12. **The Effects of Saturated and Unsaturated Fat Diets on the Histology of Adrenocortical Cells of Albino Rats - A Comparative Study** \_\_\_\_\_ 45  
*1. Iram Quddus 2. Ghulam Mujtaba Kolachi 3. Rais Ahmad 4. Furrukh Mustafa*
13. **A Qualitative Study to Assess the Awareness Level of Diabetes Mellitus in Patients Coming to JPMC** \_\_\_\_\_ 49  
*1. Shaheen Akbar Agha 2. Muhammad Akbar Agha 3. Ruma Ashraf 4. Fareeha Khan 5. Tooba Chohan 6. Yusra Azhar*

**Review Article**

14. **Significant Reduction of Malaria in the Punjab, Pakistan after Introduction of Roll Back Malaria Strategy In 2003** \_\_\_\_\_ 54  
*1. Muhammad Saleem Rana, 2. Akhtar Tanveer, 3. Asma Abdul Latif, 4. Ammara Hassan Tahir*

**Case Report**

15. **Rhino-Sino-Orbito-Cerebral Mucormycosis, a case report and literature review** \_\_\_\_\_ 60  
*1. Azhar Mehmood Javed 2. Malak Hassan Alawi 3. Farhad Hussain Mir 4. Abdul Hafeez Alawi*

**Seminar Report**

16. **Efforts Urged for Drug free Lahore** \_\_\_\_\_ 63  
*Mohsin Masud Jan*

**Editorial**

# Smoking Shisha or Cigarette – Dangerous for Human Health – Different Studies

**Dr. Azhar Masud Bhatti**

A. Director Health Services, EPI Punjab, Lahore

&  
Editor in Chief

## Smoking shisha: how bad is it for you?

Shisha, the origins of which are disputed (some say India, others Persia or Turkey) in a glass bottomed water pipe in which fruit-flavoured tobacco is covered with foil and roasted with charcoal. The tobacco smoke passes through a water chamber and is inhaled deeply and slowly; the fruit-flavoured tobacco tastes smooth and smells sweet, enthusiasts say, making it an enjoyable and unrushed experience.

Rezavi, a student from London, tried his first shisha when he was 16. He began smoking regularly five years ago and helped his father establish a shisha café. The café closed down after the smoking ban came into effect in 2007, but Rezavi still smokes six times a week, either at home or at one of his favourite shisha bars with friends. “It’s part of my routine. It’s just nice to have it bubbling in the background when I am studying.”

And he’s not alone, usually shared between friends Shisha is now associated with Middle Eastern café culture, but has become increasingly popular in the UK in recent years with cafes popping up in cities across the country. It’s a phenomenon that has worried Primary Care Trusts across the UK, which think that, unlike cigarette smokers, Shisha user are unaware of the health risks.

Earlier this year, Leicester Primary Care Trusts stop smoking service said it had seen an alarming rise in the number of teenagers in the city smoking Shisha. And this summer, Birmingham’s three Primary Care Trusts will launch a city wide tobacco control strategy which includes increasing the awareness of Shisha smoking. Meanwhile, the Niche Tobacco Advisory Group (NTAG) for North England recently introduced an educational campaign on Shisha smoking.

Dr. Khalid Anis, chairman of NTAG in Manchester, says “There’s a misconception that Shisha is not as bad for you as cigarettes, because the tobacco in flavoured and passes through water first. But the carcinogens and nicotine are still there. So a regular Shisha smoker can expect to be at risk to the similar health problems that cigarette smokers face, whether that’s respiratory heart disease or Cancer. As with any other tobacco product, I expect regular shisha smokers will find it addictive, to the point that they may need it every day.”

According to research carried out by the World Health Organization (WHO), the volume of smoke inhaled in an hour long Shisha session is estimated to be the equivalent of smoking between 100 and 200 cigarettes. The estimated findings go on to show that, on average, a smoker will inhale half a litre of smoke per cigarette, while a Shisha smoker can take in anything from just under a sixth of a litre to a litre of smoke per inhale.

But NTAG, a tobacco experts from London suggests the WHO findings are “alarmist”, pointing out that there’s not yet been enough research into the long term of effects of Shisha smoking. Dr. Kamal Chaouachi, a tobacco expert who teaches at Paris IX University and has researched Shisha for 15 years, says comparing Shisha with cigarettes “amounts to comparing oranges to apple.”

According to Chaouachi, studies led by independent researchers at the Royal University of Saudi Arabia have shown that Shisha smoke is 30 times less concentrated in chemicals than cigarette smoke, contradicting the WHO’s warning. “It is ludicrous and anti scientific to claim that hookah or Shisha smoke is 200 times more toxic than cigarette smoke,” he says, “while about 5,000 chemicals have been identified so far in cigarette smoke, chemists and pharmacologists from Saudi Arabia only found 142 chemicals in Shisha smoke. Also, a medical team in Pakistan found that Shisha smoke can be much less carcinogenic and radioactive than cigarette smoke.”

In previous days, the BBC issued a news story claiming that GPs in Leicester are seeing an increase in teenagers with health problems linked to Shisha pipe smoking.”

## Even one cigarette can prove lethal

As little as one cigarette a day, or even just inhaling smoke from someone else’s cigarette, could be enough to cause a heart attack and even death, warn a report by US Surgeon General, Dr. Regina M. Benjamin.

“The chemicals in tobacco smoke reach your lungs quickly every time you inhale causing damage immediately,” Benjamin said in a statement, “Inhaling even the smallest amount of tobacco smoke can also damage your DNA, which can lead to cancer.”

And the more you are exposed, the harder it is for your body to repair the damage. Smoking also weakens the immune system and make it harder for the body to

respond to treatment if a smoking linked cancer does arise.

It is a really good thing when the Surgeon General comes out and gives a wide scope to the dangers of smoking.” Said Dr. Len Horovitz, a pulmonary specialists with Lenox Hill Hospital in New York City. They are looking at every small mounts of smoke and this is dramatic. It’s showing the effect is immediate and does not take very much concentration. In other words, there is no safe level of smoking. It is a zero tolerance issue.”

A report of the Surgeon General: How Tobacco Smoke Causes Disease . The Biology and Behavioral Basis for smoking attributable disease, is the first tobacco report from Surgeon General Benjamin and the 30<sup>th</sup> since the landmark 1964 surgeon general’s report that first linked smoking to lung cancer. More so than previous reports, this one focused on specific pathways by which smoking does its damage. Some 70 of the 7,000 chemicals and compounds in cigarettes can cause cancer, while hundreds of the others are toxic, inflaming the lining of the airways and potentially leading to chronic obstructive pulmonary disease (COPD), a major killer, in the United States. The chemicals also corrode blood vessels and increase the likelihood of blood clots, upping the risk for heart conditions.

Smoking is responsible for about 85 percent of lung cancers in the United States. But this report puts more emphasis on the link between smoking and the nation’s no. 1 killer, heart disease. This report went way beyond pulmonary issues, which people are all too familiar with but got into cardiovascular risks.”

Horovitz said.

“We have known that even a few cigarettes a day could triple your risk of heart disease. If you have a 3 percent risk of cardiac issues as a light smoker you could have 9 or 10 percent. That’s significant, it’s a little Russian Roulette.”

And the problems don’t stop there, the report stated. Smoking cigarettes can interfere with blood sugar control for Diabetes and can help spur a range of pregnancy and Birth related problems such as Miscarriage, Low birth weight and sudden infant death syndrome (SIDS).

**Original Article**

# Screening of Some Herbal Medicines for Psychopharmacological Activity

1. Saima Ahmed 2. Muhammad Asadullah

1. Asstt. Prof. Faculty of Pharmacy, Hamdard University, Karachi 2. Asstt. Prof. of Pharmacology, Hamdard College of Medicine & Dentistry, Hamdard University, Karachi.

## ABSTRACT

**Objectives:** In our present study, we evaluate the effectiveness of these drugs as Psychotropic agents and accessed by biochemical-parameters.

**Study Design:** Experimental and Observational Study.

**Place and Duration of Study:** This Study was conducted at the Faculty of Pharmacy, Hamdard University, Karachi from Jan 2009 to June 2009.

**Materials and Methods:** Study on Mice [Part-A]: Rats (weighing 180-250g) and Mice (22-32g) either sex were used in this study. One group was kept as control for both drugs. Mice were kept under room temperature. Part B: Study on Rats: The effect of herbal medicine and homeopathic drugs are investigated on psychotropic parameters of rats. Doses were given according to the body weight of rats.

**Results:** Screening of herbal medicine as psychotropic drugs has strong modulating effect on brain and behavior. Majority of Pakistani population lives in far-flung rural area where modern medicines are not easily available, so they rely on traditional herbal medicines for relief. This signifies the importance of Eastern system of medicine in our society and stresses the need of research on herbal medicines like. Some of the herbal drug Reserpine, Nux-Vomica, Anacardium and Chlorpromazine with a wide range of pharmacological actions. Among these, Strychnos Nux-Vomica has strong action on cholinergic system, CNS activity and observed as a antispasmodic. Rauwolfia serpentina is an active alkaloid particularly present in reserpine are used to treat essential hypertension and in certain neuropsychiatry disorders. It has a sedative and tranquilizing effects, as it depletes catecholamine from the central nervous system.

**Conclusion:** Keeping in view, the medicinal importance of these herbs, our present study was designed to screen these herbs as for CNS activity on Albino mice and rats.

**Key words:** Herbal Medicines, Psychotropic drugs, Mices and Rats.

## INTRODUCTION

Products based on herbal medicine are one of the major frontiers of research. The apparent simplicity of herbal-product after experimental studies proved to be deceptive. Central nervous system effects have been studied more extensively because of its easy availability and its involvement in many symptoms such as depression, cataplexy, convulsions and coma etc. Depression is one of the most common public health problem of developing countries<sup>1</sup>,

Depression is one of the major nervous system problem in Pakistan. Majority of Pakistani people are hypertensive and most of them have certain neuropsychiatric disorders. Many new structural-analogues are being developed in the management of psychiatric illnesses and effect memory. In our study, the effects of some herbal medicine were observed for psychopharmacological profile. Chemical investigation of the herbal drugs help us in exploring another use of these herbs / alkaloids and / or better understanding of adverse effects that could be seen by the use of these herbal-products<sup>2</sup>.

Nux-Vomica is the dried ripe seed of *strychnos nux-vomica* Linne belongs to (Family-Loganiaceae). *Strychnos* is the Greek name for a number of poisonous plants. Nux-vomica derived from two Latin words that means a nut that causes vomiting<sup>3</sup>.

Nux-vomica tree is about 12 meters tall, grows in Sri Lanka, India and North Australia<sup>4</sup>. The seeds, bark and leaves of *strychnos nux-vomica* contain strychnine, a highly poisonous substance that seriously damages the nervous system<sup>5</sup>.

Strychnine in minute doses has a beneficial effect on body, supporting the digestive system and improves urination. In high doses, strychnine is extremely toxic as a CNS stimulant<sup>6</sup>. The alkaloid produces excitation of all parts of the CNS and blocks inhibitory spinal impulses at the postsynaptic level. This results in toxic convulsions. Brucine is less toxic than strychnine and is used commercially as an alcohol denaturant<sup>7</sup>.

*Rauwolfia-Serpentina* is a snake root plant belongs to the Apocynaceae. *Rauwolfia*s are evergreen shrubs and trees. Extracts of *rauwolfia-serpentina* have been used. Primarily as Ayurvedic medicine for a variety of conditions including snakebite, hypertension, insomnia

and insanity<sup>8</sup>. The active constituents of rauwolfia-serpentina are indole alkaloids such as reserpine, rescinnamine, yohimbine, ajmaline and serpentine. In 1940, Indian physician had recognized two distinct properties of rauwolfia, one as a hypotensive effect and other as a sedative effect. They began using the agent for clinical-purpose<sup>9</sup>. After the isolation of reserpine in 1952, it was used to lower high blood-pressure, and its property of producing severe depression as a side-effect also made it useful in psychiatry to use it as a tranquilizer in the control of agitated psychotic-patients<sup>10</sup>.

Reserpine produces its antihypertensive effects through depletion of catecholamine (adrenaline and noradrenaline) from peripheral sites. The hypotensive effect is mainly due to a reduction in cardiac output and peripheral resistance. Large doses cause hypothermia and respiratory depression. The cardiovascular effect of reserpine includes hypotension, reduced heart rate and cardiac output. The hypotensive response of the drug is due to impairment of adrenergic-transmission results in increased parasympathomimetic effects including increased gastric acid secretion, G.I hypermotility and miosis<sup>11</sup>.

Anacardium is the marking nut of the Semecarpus Anacardium, a small tree belonging to the Anacardiaceae. A tincture is prepared from the crushed seeds (marking nut). The anacardium patients suffer from a very peculiar and contradictory state of mind such as laughing at serious matters and serious over trifling things. They also suffer from fixed ideas as their mind and body is separate; they suspect everybody and everything around them. They are also subject to illusions of hearing and smell. Anacardium patients have a peculiar sensation of a hook or a pin on the surface of the body as also a sensation of a plug causing a pressing penetrating pain. These sensations whenever present and in whatever ailment will make it a first rare, remedy<sup>12</sup>.

Chlorpromazine is a classical neuroleptic. It acts on particular areas of brain to decrease dopaminergic neuronal firing. It is used as a standard psychotropic<sup>13</sup>.

## MATERIALS AND METHODS

### Study on Mice [Part-A]

Rats (weighing 180-250g) and Mice (22-32g) either sex were used in this study. One group was kept as control for both drugs. Mice were kept under room temperature. Tap-water was allowed ad-libitum. Following drugs and corresponding doses were used:

#### Animals

Animals were observed during and after 21 days. Tablets crushed in 10ml of water 1cc was given. Screening methods used were: Head dip, Open field,

Home cage activity, Stationary-Rod & Swimming induced-despair.

**Table 1.1:**

S. No.	Drug	Dosage
1	Reserpine	0.06 mg
2	Nux-Vomica	0.07mg.
3	Anacardium	0.08mg
4	Chlorpromazine	100mg /60 kg

**Table 1.2: Table of Behavioural Pattern of Animals (Mice)**

S. No	Drug	Dosing				
		1	2	3	4	5
1	Control	-	-	-	-	-
2	NUX-VOMICA	0.06	0.06	0.07	0.08	0.09
3	Reserpine	0.06	0.06	0.07	0.08	0.09
4	Anacardium	0.06	0.06	0.07	0.08	0.09
5	Chlorpromazine	0.06	0.06	0.07	0.08	0.09

**Table 1.3: Table of Significant and Non Significant Effect of Drugs**

S. No	Drug	Head Dip	Open Field	Stationary Rod	Home Cage Activity	Swimming Induced Despair
1	Control	↑↑	↑↑	↑↑	↑↑	↑↑
2	NUX-VOMICA	↑↑	↓↓	↓↓	↑↑	↑↑
3	Reserpine	No Significant Effect	Not Much Effect	↓↓	No Significant Effect	No Significant Effect
4	Anacardium	↓↓	↓↓	↓↓	↓↓	↓↓
5	Chlorpromazine	↓↓	↓↓	↓↓	↓↓	↑↑

**Table 1.4: Table of Behavioural Pattern of Animals (Rat)**

S. No.	Drug	DOSING				
		1	2	3	4	5
1	Control	-	-	-	-	-
2	NUX-VOMICA	0.2	0.2	0.3	0.4	0.5
3	Reserpine	0.2	0.2	0.3	0.4	0.5
4	Anacardium	0.2	0.2	0.3	0.4	0.5

### Part B: Study on Rats

The effect of herbal medicine and homeopathic drugs are investigated on psychotropic parameters of rats. Doses were given according to the body weight of rats.

All these animals were fasted for 24 hours then they were trained on different models. Different doses were given to them for 21 days. After 21 days of dosing, the activity is seen on different models.

**Table 1.5: Table of Significant and Non Significant Effect of Drugs**

S. No	Drug	Open field	Swimming induced despair	Light and dark box	Home cage activity	Radial maze
1	Control	↑↑	↑↑	↑↑	↑↑	↑↑
2	NUX-VOMICA	↓↓	No Effect	No Effect	↓↓	↓↓
3	Reserpine	No Significant Effect	No Effect	↓↓	No Significant Effect	No Significant Effect
4	Anacardium	↓↓	No Effect	No Effect	↓↓	↑↑

**Effect of herbal drugs on exploratory activity**

1. **Open Field:** Significant reduction of exploration on open field activity was noted as compared to control rats.
2. **Swimming Induced Despair:** There was no effect on swimming induced despair. There was no effect on food and water intake.
3. **Light And Dark Box:** There was significant effect of reserpine on light and dark box activity. Significant decreases in time spent by “reserpine treated rats” in light box was observed. No effect was observed on light and dark activity box in other medicines treated rats.
4. **Cage Crossing (Home Cage Activity):** There was no effect on home cage activity by any of the herbal medicine used in the experiment.
5. **Radial Maze:** There was significant reduction of exploration **observed** due to the nux vomica and reserpine in the radial maze. Anacardium did not produce significant reduction of exploration as compared to control.

**Table : 1.6: Effect Of Herbal Drug On Exploratory Activity Of Mices**

Treatment	Head Dip	Open Field	Cage Crossing	Stationary Rod
Control	70.±6.35	205±3.7	108.6±5.84	0.70±0.46
Reserpine	*62.2±43.4	197. ±168.8	102.8±92.4	0.63±0.47
Nux-Vomica	*39.8±28.8	167.2±160.4	103±90.8	5.2±5
Anacardium	*37.2±28.6	160.4±216.6	86.6±61.8	4.2±4.4
Chlorpromazine	39.4±32.4	*207±169.4	90.8±74.8	2.62±1.7

Values are mean ± S.E.M. (n=5) significant differences by student t-test \* P<0.05, \*\*P<0.1 as compared to control

**Table : 1.7: Effect of Herbal Drug On Exploratory Activity of Rats**

Treatment	Open Field	Radial Maze	Cage Crossing
Control	80.4±43.3	2.6±5.11	27.8±14.27
Nux-Vomica	54.8±50.8	4.6±3.6	40.2±29.8
Reserpine	76.2±130.4	*2.2±1.2	22.6±36.6
Anacardium	70.2±104	1.38±1.46	*43.6±40.6

Values are mean ± S.E.M. (n=5) significant differences by student t-test \* P<0.01 as compared to control.

**RESULTS****Part A: Study on Mices****Effect of herbal drugs on exploratory activity:**

1. **Head Dip:** Significant reduction of exploration on Head Dip was noted.
2. **Open Field:** Nux-vomica, Anacardium and Chlorpromazine produced a significant reduction of exploration but reserpine did not produce effect on open field activity.
3. **Home Cage Activity:** Reserpine Anacardium and Chlorpromazine decreased the activity of cage crossing but increased Nux-vomica.
4. **Stationary Rod:** Reserpine Anacardium and Chlorpromazine impaired the stationary rod response but no change was observed on stationery rod by Nux-vomica
5. **Swimming Test:** Reserpine and Anacardium decreased the activity of swimming. Chlorpromazine produced no effect on swimming

induced stress but Nux-vomica produced excitation on swimming.

## DISCUSSION

This study is aimed to evaluate different behavioral changes produced by the healing properties of herbs that are at last being scientifically investigated. There are two main focuses of this research. One, is the examination and other was the evaluation of the effectiveness of some herbal extracts using assessment tools for behavior. This research provided a scientific basis for the comparison of herbal and homeopathic remedies. The other direction of research is the search for the newer drugs among known plants or in new plant species<sup>14</sup>. To establish herbalsim on scientific grounds, Psychopharmacological screening must be carried out. Psychopharmacological screening generally turned so as to indicate simply the presence or absence of a response. Thus, the fundamental elements of a drug discovery program are the bioassays used to detect substances with biological activities. The CNS screening included Open field activity, Cage crossing, Swimming induced depression, Radial-maze. There was a group in which 6 per group and one group was kept as control. They were provided with food and water ad-libitum and different CNS screening tests were performed. During the course of present study, three herbs Rauwolfia-Serpentina, Nux-Vomica and Anacardium were studied. Pharmacological screening of Reserpine, Nux-Vomica, Chlorpromazine and Anacardium was carried out. Rauwolfia-Serpentina has been used since centuries in folk medicine in East India. Reserpine is now used as antihypertensive and tranquilizer in western medicine<sup>15</sup>. Chronic reserpine treatment showed a non significant effect on water intake. Previously, it was reported that reserpine increased water intake in the light phase and the animal consumed less water in the dark phase. Other herbal drugs such as Nux-vomica and Anacardium did not produce remarkable effect<sup>16</sup>.

In the present study, motor activity is significantly decreased in an open field. Reserpine treatment induced hypo locomotion mediated by nigral dopaminergic dysfunction<sup>17</sup> producing few affect on peripheral movements, rearing, grooming, immobility and defecation<sup>18</sup>. Nux-vomica and anacardium did not show significant effects. In conclusion, the present results show that oral intake of rauwolfia serpentina in rats and mice's brings about behavioral changes. Reserpine affects feeding behavior and body weight.

## CONCLUSION

Keeping in view, the medicinal importance of these herbs, our present study was designed to screen these herbs as for CNS activity on Albino mice and rats.

## Acknowledgement:

This paper is dedicated to Late Prof. Dr. Shahida P. Ahmad, University of Karachi under whose guidance this project was completed.

## REFERENCES

1. Reynolds GS. Behavior Contrast. J Exp Anal-Behav 1961;4:57-71.
2. Baumeister AA, Francis JL. Historical development of the doamine hypothesis of schizophrenia. Hist. Neurosci 2002;113(9):265-277
3. Cai BT, Nagasawa, et al. Processing of Nux Vomica. VII. Antinociceptive effects of crude alkaloids from the processed and unprocessed seeds of Strychnos nux-vomica in mice. Biological and Pharmaceutical Bulletin. Japan 1998;19(1): 127-131.
4. Bandyopadhyay JB. Presence of Vomisine in callus cultures of Strychnos nux-vomica. India J Botany 1995;66(2):183.
5. Balakrishma P, Raman A. Cecidogenesis of leaf galls of Strychnos nux vomica (Loganiaceae) induced by the jumping plant louse species Diphoria truncate. Madras India 1992;17(4): 285-292.
6. Bisset NG, Choudhury AK, et al. Phenolic glycosides from the fruit of Strychnos nux vomica. J Phytochemistry 1995;28(5):1553-1554.
7. Sha D, Dou. Studies on the relationship between alkaloids in semen strychnine and its processing. China J Chinese Materia Medica 1989;14(1):22-24.
8. Janscar SM, Leonard BE. Behavioural and neurochemical interactions between chronic reserpine and chronic antidepressants. A possible model for the detection of a typical antidepressants. Biochem Pharmacol 1983; 3210(15):1569-71
9. Benjamin BD, Roga G, Heble MR. India J Phytochemistry 1990;35(2):381-3.
10. Goodman and Gillman. The Pharmacological basis for therapeutics. 10<sup>th</sup> ed. 2001.p.448-450 and 474-476.
11. Epstein M, Oster JR. Hypertension. A Practical approach, Saunders. Philadelphia; 1984.p.116-117.
12. Chopra RN, Nayar SI, Chopra IC. Glossary of Indian Medicinal Plants. CSIR Publication, New Delhi 1956;11.
13. Finger FW. Measuring behavioural activity. In: Myers RD, editor. Method in Psychobiology. 2<sup>nd</sup> ed. Academic Press: New York; 1972.p.1-18.
14. Ghosh B. Some unreported medicinal uses of Plants used by the tribals of District. Begusarai, Bihar (India). J Economic and Taxonomic-Botany 1987;10(1):187-190.
15. Haq, Nazmul. Breeding and improvement of medicinal and aromatic plants 6-30. Medicinal and

- aromatic plants in Asia, Oxford and IBH: New-Delhi; 1995.p.534-538.
16. Seiden LS, Hanson LCF. Reversal of the reserpine induced suppression. Conditioned avoidance response. *Psychopharmacologia* 1964;6:239-244.
  17. Shiozaki S, Ichikawa S, Nakamura J, Klitama S, Yamada K, Kuwana Y. Actions of adenosine A2A receptor antagonist KW-6002 on drug-induced catalepsy and hypokinesia caused by reserpine or MPTP. *Psychopharmacology Berl* 1999;147:1: 90-5.
  18. Angrini M, Leslie JC, Shephard RA. Effects of Propranolol, buspirone, PCPA, reserpine, and chloridiazepoxide on open-field behavior. *Pharmacol Biochem Behav* 1998;59:2 387-97.

**Address for Corresponding Author:**

Saima Ahmed,  
Asstt. Prof. Faculty of Pharmacy,  
Hamdard University. Karachi.  
Cell No. 0301-2949182



**Original Article**

# Renal Outcome in Patients with Pre-eclampsia and Eclampsia at Presentation, Three and Six Months Postpartum

1. Mirza Muhammad Ilyas Baig 2. Talat Manzoor 3. Shabnum Tahir Saleem 4. Aftab Alvi  
5. Omer Sabir

1. Asstt. Prof. of Medicine, FMMC, Lahore 2. Asstt. Prof. of Gyne/Obs, FMMC, Lahore 3. Asstt. Prof. of Gyne/Obs, CPMC, Lahore 4. Asstt. Prof. of Gastroenterology, FMMC, Lahore 5. Senior Registrar, FMMC, Lahore

## ABSTRACT

**Objectives:** To assess the natural history of Renal Disease in patients with Pre-eclampsia or Eclampsia.

**Study design;** It was an observational study.

**Place and Duration of study:** This study was conducted simultaneously at two tertiary care hospitals: Fatima Memorial Hospital, Lahore and Bhatti International Teaching Hospital, Kasur from March 2009 to January 2011.

**Patients and Methods;** women presented with pre-eclampsia or/ and eclampsia were consecutively selected for the study fulfilling the inclusion criteria. A total number of 220 patients were enrolled in this study. All parameters required for the study were done carefully as blood pressure, proteinuria, renal function tests, urinary creatinine, weight, primary or multiparous, any previous history of pre-eclampsia. These parameters are checked at three and then six months post delivery.

**Results:** Among 220 patients, 140 (63.6%) were primigravida and 80 (36.4%) were multigravida. Blood pressure was from 140/90 to 210/110mmHg average blood pressure was 175/100. 195 (88.63%) patients had deranged renal function tests and 215 (97%) patients had proteinuria >2+. At Three months post-delivery 151(68.6%) patients achieved normal blood pressure and 190 (86.3%) had normal serum creatinine i.e < 1.4.

At six months 161 (73.8%) got adequate control of blood pressure, 59 (26.81%) had blood pressure > 140/90. Serum creatinine became in normal range in 195 (88.63%). Acute renal failure was observed in 6 patients who were put on renal replacement therapy.

**Key words:** Pre-eclampsia, Eclampsia, Proteinuria, Serum creatinine.

## INTRODUCTION

Pre-eclampsia is a disorder of widespread vascular endothelial malfunction and vasospasm that occurs after 20 weeks gestation and can present as late as 4-6 weeks postpartum. The renal involvement in pre-eclampsia is characterized by hypertension and proteinuria that have to present after twentieth weeks of gestation to fulfil the clinical diagnosis. Pre-eclampsia and Eclampsia results in multiorgan failure, effects every organ but kidneys being highly vascular bears the major burnt of the disease. Renal outcome of patients with Pre-eclampsia is generally good but it needs careful monitoring and adequate control of hypertension, can reduce renal failure and even may lead to complete recovery of renal functions. Only few patients develop renal failure upto a level where they need renal replacement therapy.

## PATIENTS AND METHODS

An observational study was conducted to assess the prevalence and natural history of renal disease in patients with Preeclampsia and Eclampsia. This study was conducted simultaneously at two tertiary care hospitals: Fatima Memorial Hospital, Lahore and Bhatti

International Teaching Hospital, Kasur. The study was conducted from March 2009 to January 2011. A total of 220 consecutive patients admitted with preeclampsia or eclampsia were included in the study. Initial evaluation included a detailed history to document age, parity and to rule out other common causes of renal disease i.e. diabetes, hypertension, connective tissue disorders and autoimmune diseases. A physical examination was done in every patient to assess weight, pulse and blood pressure and to rule out complications of increased blood pressure. Baseline investigations included serum creatinine, urine for proteinuria and protein – to – creatinine ratio and ultrasonographic scan of the abdomen and pelvis. The patients were followed up at 3 and 6 months post-delivery and repeat assessments was made.

## RESULTS

A total of 220 patients were enrolled in this study, out of whom 140 (63.6 %) patients were primigravida and 80 (36.4%) patients were multigravida. Age of participating patients ranged from 19 years to 41 years. The average age of the participating patients was 31 years. Weight of the patients varied from 60 to 105 Kg.

200 (90%) patients weighed 60 to 90 Kg, whereas 20 (10%) patients weighed more than 90 Kg. 217 (98.63%) patients had a single fetus while 3 (1.5%) patients had twin pregnancy.

At presentation: Blood pressure ranged from 140 / 90 mmHg to 210 / 110 mmHg with an average blood pressure of 175 / 100 mmHg. 195 (88.63%) patients had a serum creatinine value ranging from 0.7 to 1.4 mg/dL whereas 25 (11.37%) patients had a baseline serum creatinine value from 1.5 to 2.7 mg/dL. In 215 (97%) patients 2+ proteinuria was seen while 5 (3%) patients had proteinuria less than 2+.

The patients were followed up AT THREE MONTHS when it was seen that normal blood pressure (less than 140/90 mmHg) had been achieved in only 151(68.6%) patients and was more than 140/90 mmHg in 69(31.3%) patients. Serum creatinine was normal i.e. less than 1.4 mg/dL in 190 (86.3%) patients and more than 1.4 mg/dL in 30 (13.63%) patients. 22 (10%) patients were dipstick negative for proteinuria, 90 (40.9%) patients had a proteinuria of 1+, 56 (25.4%) patients had proteinuria of 2+ and 42 (19%) patients had proteinuria of 3+.

At six months, blood pressure was less than 140/90 mmHg in 161 (73.18%) patients and more than 140/90 mmHg in 59 (26.81%) patients. Serum creatinine was normal i.e. less than 1.4 mg/dL in 195 (88.63%) patients and more than 1.4 mg/dL in 25 (11.3%) patients. 68 (30.9%) patients were dipstick negative for proteinuria, 70 (31.8%) patients had a proteinuria of 1+, 47 (21.3%) patients had proteinuria of 2+ and 35 (15.9%) patients had proteinuria of 3+.

Recurrence of Pre-eclampsia was seen in 28 (12.72%).

Acute Renal Failure with uraemic syndrome was observed in 6 patients who were put on Renal Replacement Therapy with Haemodialysis.

One patient with tachycardia proved to have Hyperthyroidism.

## DISCUSSION

Pre-eclampsia and eclampsia are recognized cause of renal function abnormalities during pregnancy<sup>1,2</sup>. This study was designed to assess the renal outcomes in patients with preeclampsia and eclampsia post-delivery. Preeclampsia/eclampsia is more likely to occur in women at either extreme of reproductive life. A young nulliparous woman is more likely to experience the condition. Similarly, a multiparous woman older than 35 years is more likely to be affected<sup>3</sup>.

Obesity has been known to increase the risk of preeclampsia and eclampsia. Maternal obesity is a risk factor for severe preeclampsia<sup>4</sup>. It has not been demonstrated that maternal weight has an independent effect on the genesis of preeclampsia or the renal outcomes<sup>5</sup>. Our study was not powered sufficiently to

assess any independent effect of weight on the development of preeclampsia or renal outcomes.

Almost two thirds of the patients in our study were primiparae. This finding is consistent with the published studies. The incidence of pre-eclampsia was 9.3%, being significantly higher in primiparae (14.1%) than multiparae (5.7%).<sup>6</sup>

Controlled cohort studies showed that the risk of pre-eclampsia is increased in women with a previous history of pre-eclampsia<sup>7</sup>. In our study 26 (13%) patients were found to have recurrence of preeclampsia in the present pregnancy.

Pre-eclampsia is associated with later kidney disease. In one study it was determined that the lower renal function in middle-aged formerly preeclamptic women does not result from accelerated age-dependent renal function loss, but from an already reduced renal function relative to parous controls at young age<sup>8</sup>.

Women with a history of preeclampsia have an increased risk of microalbuminuria with a prevalence similar to the published prevalence in patients with type 1 diabetes mellitus<sup>9</sup>. In our study 56 (25.4%) patients had proteinuria of 2+ and 42 (19%) patients had proteinuria of 3+ at three months after delivery and 47 (21.3%) patients had proteinuria of 2+ and 35 (15.9%) patients had proteinuria of 3+ at six months after delivery. These findings are compatible with the international data<sup>10</sup>.

A longer follow up will be required to see the complete resolution of proteinuria in participants of this study.

Hypertension also needs time to resolve in patients with preeclampsia and eclampsia. At three months post-partum 69 (31.36%) patients were still having blood pressures of more than 140/90 mmHg. At the end of 6 months 59 (27%) patients were hypertensive. These figures are similar to the published data<sup>10</sup>.

Berks D. et al found that at the end of three months 39% of the women still had hypertension. At the end of two years this figure had dropped to 18%. It is also known that previously preeclamptic women are at a higher risk of developing hypertension up to 10 years after pregnancy<sup>11</sup>.

At six months post-delivery 25 patients had elevated renal function tests (blood urea and serum creatinine). Interestingly all of these patients were also hypertensive as well. This is well documented that resolution of hypertension in pre-eclamptic women also depends upon complete resolution of kidney injury<sup>12</sup>. As of now these women are having a regular follow up and we intend to observe the pattern of renal disease in these patients. Another study gave similar results<sup>13</sup>.

Acute renal failure developing in pregnancy can be due to pre-eclampsia. In one study, 12% of patients with acute renal failure had preeclampsia<sup>14</sup>.

In our study 6 (2.72%) patients developed acute renal failure consequent upon pre-eclampsia. It is possible that if the blood pressures are controlled vigorously at the onset of preeclampsia, this threatening complication can be avoided.

## CONCLUSION

Preeclampsia is an important cause of renal disease in pregnant females. The manifestations of hypertension and renal diseases may take a sub-acute course and take time to resolve.

## REFERENCES

1. Ansari MR, Laghari MS, Solangi KB. Acute renal failure in pregnancy: One year observational study at Liaquat. *J Pak Med Assoc* 2008;58(2):61-4.
2. Khalil MA, Azhar A, Anwar N, et al. Aetiology, maternal and foetal outcome in 60 cases of obstetrical acute renal failure. *Acta Obstet Gynecol Scand* 2010;89(9):1202-5.
3. (<http://emedicine.medscape.com/article/1184270-overview>)
4. Martin JN, May WL, Rinehart BK, et al. Increasing maternal weight: a risk factor for preeclampsia/eclampsia but apparently not for Hellp syndrome. *South Med J* 2000;93(7):686-91
5. Easterling TR, Schmucker BC, Selke S, et al. Maternal Weight, Hemodynamics and Preeclampsia; 16<sup>th</sup> ed. 1997.p.(3) 379-388
6. Long PA, Abell DA, Beischer NA. Parity and pre-eclampsia. *Aust N Z J Obstet Gynaecol* 1979; 19(4):203-6.
7. Duckitt K, Harrington D. Risk factors for pre-eclampsia at antenatal booking: systematic review of controlled studies. *BMJ* 2005;330:565.
8. Spaan JJ, Ekhardt T, Spaanderman ME, et al. Reduced renal function after preeclampsia does not result from accelerated age-dependent renal function loss. *Acta Obstet Gynecol Scand* 2010; 89(9):1202-5.
9. McDonald SD, Han Z, Walsh MW, et al. Kidney disease after preeclampsia: a systematic review and meta-analysis. *Am J Kidney Dis* 2010;55(6): 1026-39
10. Berks D, Steegers EA, Molas M, et al. Resolution of hypertension and proteinuria after preeclampsia. *Obstet Gynecol* 2009;114(6):1307-14.
11. Shammass AG, Maayah JF. Hypertension and its relation to renal function 10 years after pregnancy complicated by pre-eclampsia and pregnancy induced hypertension. *Saudi Med J* 2000; 21(2):190-2.
12. Ndayambagye EB, Nakalembe M, Kaye DK. Factors associated with persistent hypertension after puerperium among women with pre-eclampsia/eclampsia in Mulago hospital, Uganda. *BMC Pregnancy Childbirth* 2010;12(10):12.
13. Khalil MA, Azhar A, Anwar N, Aminullah. Aetiology, maternal and foetal outcome in 60 cases of obstetrical acute renal failure. *Acta Obstet Gynecol Scand* 2010;89(9):1202-5.
14. Sibai BM, Villar MA, Mabie BC. Acute Renal failure in hypertensive disorder of pregnancy. Pregnancy outcome and remote prognosis in thirty one consecutive cases. *Am J Obstet Gynecol* 1990;162(3):777-83.

### Address for Corresponding Author:

Dr. Mirza Muhammad Ilyas Baig,  
Asstt. Prof. of Medicine,  
Fatima Memorial Medical College /  
Hospital, Lahore  
Cell # 0300-4100388

**Original Article**

# Effect of Lemon Grass and Green Tea on Blood Pressure and Heart Rate

1. Naveed Ullah 2. Amir Nazir 3. Sadaf Anwar 4. Nouman Altaf 5. Abdullah  
6. Maqsood ur Rehman

1. Sen. Lecturer of Pharmacology, FMC, Abbottabad 2. Lecturer of Physiology, AMC, Abbottabad 3. Lecturer of Pathology, AMC, Abbottabad 4, 5 & 6. PG Students of M.Phil, Pharmacology, University of Malakand.

## ABSTRACT

**Objective:** Lemon grass and Green tea are the herbal products, widely used, next to that of water. Because of their common use, it is so much necessary to find their effects on all the body functions. In the current study its effects of blood pressure and heart rate of human male has been evaluated.

**Study Design:** Observational study.

**Place of Study:** This study was conducted at Pharmacy Department, University of Malakand.

**Materials and Methods:** Seventy two male volunteers for each tea had been selected and the blood pressure before and after giving one cup of each tea to each individual was evaluated by using sphygmomanometer and stethoscope.

**Results:** A minor increase in blood pressure was noted in the volunteers taken green tea. On other hand a moderate decrease in the systolic blood pressure and mild increase in the diastolic blood pressure were noted in the case of lemon grass. Also, great decreases in the heart rate of individuals taken lemon grass, and a moderate increase in the heart rate of individuals taken green tea were observed.

**Conclusion:** From the current study it can be concluded that the Male heart patients are on the high risk to the use of either type of tea, so they have to take care while using either type of tea in excess quantity.

**Keywords:** Lemon grass, Green tea, Blood pressure, Heart rate.

## INTRODUCTION

*Cymbopogon citratus* (Lemon grass) is an aromatic perennial tall grass with rhizomes and densely tufted fibrous root. As a medicinal plant, lemon grass has been considered a carminative and insect repellent. Studies on extracts from *Cymbopogon citratus* leaves have demonstrated anti-inflammatory, vaso-relaxing, diuretic and valuable remedy in treating ringworm as local application. Lemongrass oil was claimed to have anti-helminthic activity<sup>1</sup>.

Lemongrass oil is used as a pesticide and a preservative. Research shows that lemongrass oil has anti-fungal properties<sup>2</sup>. *Cymbopogon citratus* is consumed as a tea for anxiety in Brazilian folk medicine<sup>3</sup>, but a study in humans found no effect<sup>4</sup>. The tea caused a recurrence of contact dermatitis in one case<sup>5</sup>. The researchers observed that citral induces programmed cell death in the cancerous cells, while the normal cells were left unharmed<sup>6</sup>.

The leaves of *Camellia sinensis* is used as green tea, which have undergone minimal oxidation during processing. Green tea originates from China<sup>7</sup> and has become associated with many cultures in Asia. According to a survey released by the United States Department of Agriculture in 2007<sup>8</sup>, the mean content of flavonoids in a cup of green tea is higher than that in the same volume of other food and drink items. Flavonoids are a group of phytochemicals in most plant

products that are responsible for such health effects as anti-oxidative and anticarcinogenic functions<sup>8</sup>. Green tea contains salubrious polyphenols, particularly catechins and has more potent antioxidant than black tea<sup>9</sup>. Types of tea are commonly graded depending on the quality, parts of the plant used and how they are processed<sup>10</sup>. After water, tea is the most widely consumed beverage in the world<sup>11</sup>. In a study of the eating habits of 2,018 women, consumption of mushrooms and green tea was linked to a 90% lower occurrence of breast cancer<sup>12</sup>. The green tea extract may play a role in the control of body composition via sympathetic activation of thermogenesis, fat oxidation, or both<sup>13</sup>. It has also been presented that epigallocatechin-3-gallate (a component of green tea) can be used in prevention or treatment of inflammatory processes<sup>14</sup>. However, pharmacological and toxicological evidence does indicate that green tea polyphenols can in fact cause oxidative stress and liver toxicity<sup>15</sup>. Other evidence presented in the review cautions against the drinking of green tea by pregnant women<sup>16</sup>. It "suggested that the oral intake of L-Theanine (a chemical found in green tea) could cause anti-stress effects via the inhibition of cortical neuron excitation<sup>17</sup>. Daily consumption of tea containing 690 mg catechins for 12 wk reduced body fat, may be useful in obesity<sup>18</sup>. Green tea also has a role in the treatment and prevention of cancer<sup>19</sup> and to treat multiple sclerosis<sup>20</sup>.

As Lemon grass and Green tea is widely used throughout the Asia. Therefore the current study was designed with a view to confirm and explore the effects of these plants materials on the blood pressure and heart rate, whether the decoction of these plants i.e. tea are beneficial for high blood pressure or it may lead to high blood pressure, to stop drinking by volunteers' have routine high blood pressure.

## MATERIALS AND METHODS

### Plant Material

The fresh dried leaves of *Cymbopogon citratus* and *Camellia sinensis* were purchased from local market Abbottabad, Pakistan. The specimen packs was marked with number 1622 and deposited in the Pharmacy Museum University of Malakand, Pakistan.

### Preparation of Decoction

02 grams of dried plant material for each subject were weighed and soaked in 150 ml (cup) of boiling water for 03 minutes. 10 grams of sugar were added as a sweetening agent in each cup.

### Experimental protocol

The basis for this investigation was blood pressure and heart rate of 3<sup>rd</sup> year and 4<sup>th</sup> year male students of Frontier medical College Abbottabad Pakistan. Subjects were selected on the basis of four primary criteria. These include age, sex, health and Physical body status. The research specifically targets individuals between 21 and 23 years of age. One hundred and forty-four male students (seventy-two for each tea), who fulfilled the above criteria, were selected for the study. They were first provided a thorough explanation of the research effort, its benefits and the potential risks to subjects.

Blood pressure and heart rate were noted in all the volunteers by using aneroid sphygmomanometer with stethoscope before and after the drinking of one cup of each tea. I.e. Before, at 0min and after 30 & 60 minutes of taking the decoction. Cumulative results were calculated by using formula;

Cumulative (systolic/ diastolic/ Heart rate) =

$$\frac{\text{Sum of all systolic / diastolic / heart rate}}{\text{total number}(72)}$$

## RESULTS

A total seventy two individuals for each tea were selected in the current study, and a cumulative result was shown in table 1. An acute decrease in the heart rate was observed after taking a cup of hot decoction of lemongrass tea. In the first half hour a maximum decrease had been noted, while in the next half hour no further significant decrease had been observed. From this it can be concluded that *Cymbopogon citratus* has an effect on heart rate, i.e. it quickly decreases the heart rate in normotensive individuals. A decrease in the

systolic blood pressure was also noted, while a minor increase in the diastolic blood pressure was also found. From this it can be concluded that, drinking of *Cymbopogon citratus* as a tea by the males may have risk of bradycardia.

In the case of *Camellia sinensis* a great increase in the heart rate was observed as; in the first half hour a little increase in the heart rate, but in the next half hour a great increase in the heart rate had been noted. From this it can be concluded that *Camellia sinensis* has a strong effect on heart rate, i.e. it increases the heart rate in normotensive male individuals opposite to that of lemon grass, which decreases the heart rate. It was also noted a minor increase in the systolic and diastolic blood pressure.

**Table.No.1: Cumulative result of seventy two male subjects for each tea**

Decoction	Timing	Systolic Blood Pressure	Diastolic Blood Pressure	Heart Rate
Lemon grass	Initial Reading	115 mmHg	74 mmHg	81/min
	After 30 minutes	108 mmHg	75 mmHg	65/min
	After 60 minutes	103 mmHg	78 mmHg	63/min
Green tea	Initial Reading	120 mmHg	80 mmHg	75/min
	After 30 minutes	121 mmHg	80 mmHg	77/min
	After 60 minutes	124 mmHg	84 mmHg	85/min

## DISCUSSION

As Carbajal et al<sup>21</sup> reported that *Cymbopogon citratus* leaves have dose related hypotensive effects in rats. But the current study was performed in human (male) revealed that the decoction of *Cymbopogon citratus* has a moderate decrease in systolic and minor increase in diastolic blood pressure effects.

Gazola et al<sup>22</sup> reported an in-vitro study of aqueous extract of *Cymbopogon citratus*, showed a significant decrease in the heart rate of rats. Same was the outcomes of the current study (in-vivo) as; effect of *Cymbopogon citratus* oral decoction on human (male) was found a significant decrease in the heart rate.

Anigbogu, C.N and Olayeni<sup>23</sup> reported that *Cymbopogon citratus* has a little or no effect on blood pressure except in high doses, and also have no effect on heart rate, but in the current study a great decrease in the heart rate was noted.

According to Hodgson et al<sup>24</sup>, Drinking of green tea leads to acute increase in systolic and diastolic blood pressure at 30 min after drinking. But in the current study, no significant increase was noted at 30 minutes but minor increase was noted after 60 minutes.

Seifert et al<sup>25</sup> reported that, Green tea extract in a short-term dosing schedule similar to that commonly used with dietary supplements did not result in alterations in heart rate or blood pressure, while in the current study it was found that each cup of green tea have a minor increase in systolic and diastolic blood pressure. Also a great increase in heart rate had been noted unlike lemon grass. So it is recommended for heart patients to take care of drinking green tea and lemon grass.

## CONCLUSION

From the current study it can be concluded that, excess drinking of Lemon grass tea by the males may have risk of bradycardia, while Green tea were found to increase the heart rate in normotensive male individuals i.e. opposite to that of lemon grass.

## REFERENCES

- Kokate CK, Varma KC. Anthelmintic activity of some essential oils. *Indian J Hosp Pharm* 1971; 8:150-151.
- Shadab Q, Hanif M, Chaudhary FM. Antifungal activity by lemongrass essential oils. *Pak J Sci Ind Res* 1992;35:246-249.
- Blanco MM, Costa CA, Freire AO, Santos JG, Costa M. Neurobehavioral effect of essential oil of *Cymbopogon citratus* in mice. *Phytomedicine* 2009;16(2-3):265-70.
- Leite JR, Seabra Mde L, Maluf E. Pharmacology of lemongrass (*Cymbopogon citratus* Stapf). Assessment of eventual toxic, hypnotic and anxiolytic effects on humans. *J Ethnopharmacol* 1986;17 (1): 75-83.
- Bleasel N, Tate B, Rademaker M. Allergic contact dermatitis following exposure to essential oils. *Australas J Dermatol* 2002; 43(3): 211-3.
- Dudai N, Weinstein Y, Krup M, Rabinski T, Ofir R. Citral is a new inducer of caspase-3 in tumor cell lines. *Planta Med* 2005;71 (5): 484-8.
- The Tea Guardian. Quality Basics 1: Various Plants, Various Qualities. Retrieved 20 December 2010.
- USDA Database for the Flavonoid Content of Selected Foods, Release 2.1; 2007.
- Cabrera C, Artacho R, Giménez R. Beneficial effects of green tea--a review. *J Am Coll Nutr* 2006; 25 (2): 79-99.
- Heiss Mary Lou Heiss, Robert J. The story of tea: a cultural history and drinking guide. 2007. p.179-185
- Macfarlane A, Macfarlane I. The Empire of Tea. The Overlook Press. 2004. p.32
- Zhang M, Huang J, Xie X, Holman CD. Dietary intakes of mushrooms and green tea combine to reduce the risk of breast cancer in Chinese women. *Int J of Cancer* 2009;124 (6): 1404-8
- Dulloo AG, Duret C, Rohrer D. Efficacy of a green tea extracts rich in catechin polyphenols and caffeine in increasing 24-h energy expenditure and fat oxidation in humans. *Am J Clin Nutr* 1999; 70 (6): 1040-5
- Rodríguez-Caso C, Rodríguez-Agudo D, Sánchez-Jiménez F, Medina MA. Green tea epigallocatechin-3-gallate is an inhibitor of mammalian histidine decarboxylase. *Cell Mol Life Sci* 2003; 60 (8): 1760-3.
- Lambert JD, Sang S, Yang CS. Possible controversy over dietary polyphenols: benefits vs risks. *Chem. Res Toxicol* 2007; 20 (4):583-5
- Strick, Strissel PL, Borgers S, Smith SL, Rowley JD. Dietary bioflavonoids induce cleavage in the MLL gene and may contribute to infant leukemia. *Proc Natl Acad Sci USA* 2000; 97 (9): 4790-4795.
- Kimura K, Ozeki M, Juneja LR, Ohira. L-Theanine reduces psychological and physiological stress responses". *Biol Psychol* 2007; 74 (1): 39-45
- Nagao T, Komine Y, Soga S. Ingestion of a tea rich in catechins leads to a reduction in body fat and malondialdehyde-modified LDL in men. *Am J Clin Nutr* 2005; 81(1): 122-9
- Sartippour MR, Pietras R, Marquez-Garban DC. The combination of green tea and tamoxifen is effective against breast cancer. *Carcinogenesis* 2006; 27 (12): 2424-33
- Sueoka N, Suganuma M, Sueoka E. A new function of green tea: prevention of lifestyle-related diseases. *Ann N Y Acad Sci* 2001; 928: 274-80
- Carbajal D, Casaco A, Arruzazabala L, Gonzalez R, and Tolon Z. Pharmacological study of *Cymbopogon citratus* leaves. *J of Ethno pharmacology* 1989; (25)1:103-107.
- Gazola R, Machado D, Ruggiero C, Singi G, Macedo Alexandre M. Lippia alba, Melissa officinalis and *Cymbopogon citratus* effects of the aqueous extracts on the isolated hearts of rats. *Pharmacol Res* 2004; 50(5):477-80.
- Anigbogu CN, Olayeni A. Cardiovascular function in normotensive rats following administration of *Cymbopogon citratus* and *Ocimum gratissimum* The FASEB J 2007;21:582.50.
- Hodgson JM, Puddey IB, Burke V, Beilin LJ, Jordan N. Effects on blood pressure of drinking green and black tea. *J Hypertens* 1999; 17(4): 457-63.
- Seifert JG, Nelson A, Devonish J, Burke ER, Stohs SJ. Effect of Acute Administration of an Herbal Preparation on Blood Pressure and Heart Rate in Humans. *Int J Med Sci* 2011; 8:192-197.

**Original Article**

# Juvenile Nasopharyngeal Angiofibroma, Experience of 35 Cases with Different Surgical Approaches

1. Masood Akhtar 2. Muhammad Saleem Sheikh

1 & 2. Asstt Profs, ENT, Quaid-e-Azam Medical College, B.V. Hospital Bahawalpur.

## ABSTRACT

**Objective:** 1) To study the clinical presentation. 2) To study the outcome regarding recurrence, prognosis and complications of different surgical approaches of juvenile nasopharyngeal angiofibroma.

**Study design:** Observational study.

**Place and duration of study:** The study was conducted at department of Ear, Nose, Throat. Head & Neck Surgery, Quaid-e-Azam Medical College and Bahawal Victoria Hospital Bahawal Pur, from March 2005 to February 2009.

**Patients and methods:** All young male patients presenting in ENT OPD/COD with complaint of recurrent nose bleeding, nasal obstruction and nasopharyngeal mass were admitted in ward. Detailed history was taken and thorough clinical examination done. Routine investigations and CT scan done in all cases. Staging done according to Fisch staging systems. Sufficient quantity of blood arranged and patient prepared for surgery. Specimen removed was sent for histopathological examination to confirm clinical diagnosis. Follow up was done for 12-18 months to see the recurrence and complications.

**Results:** Total 35 young male patients clinically diagnosed as JNA and postoperatively confirmed by histopathology were included in the study. Age range was between 10-25 years, majority were between 12-20 years (n-31). All patients were male. All patients presented with epistaxis, nasal obstruction and nasopharyngeal mass. Other presenting symptoms were, anemia (n-29), nasal mass (n-27), ear blockage (n-27), nasal discharge (n-25), headache (n-22), snoring (n-15), speech defect (n-11) and proptosis (n-6). All patients under went surgery. Seventeen patients were approached through lateral rhinotomy, 12 through transpalatal approach and 06 through Weber Furguson approach. In 05 patients recurrence occurred and in 11 patients postoperative complications occurred.

**Conclusion:** Meticulous surgical approach depending on the stage of JNA reduces the risk of recurrence and complications.

**Key words:** Angiofibroma, Lateral rhinotomy, Transpalatal, Weber Furguson, Recurrence..

## INTRODUCTION

Recognized since ancient time by Hippocrat, Juvenile nasopharyngeal angiofibroma (JNA) is a benign vascular tumour, constitute less than 0.5% of all head and neck tumours<sup>1</sup>. Although histologically benign but is locally aggressive tumour, which arise from posterolateral wall of nasopharynx, found exclusively in adolescent male but in literature female patients have been reported<sup>2</sup>. The exact site of origin is sphenopalatine foramen<sup>3</sup>.

Classical presentation is adolescent male with recurrent epistaxis, nasal obstruction, nasal mass and chronic anaemia. The voice acquires a nasal intonation and if the swelling is large enough to force the soft palate down there may be an added plummy quality to it. Other presentations like proptosis, cheek swelling, visual impairment, hearing loss, tinnitus or neurological symptoms may be present in advanced cases. Failing vision has been reported<sup>4</sup> indicating tenting of the optic nerve.

Diagnosis is made on history and clinical examination. Angiography, CT scan and MRI are done to see the

feeding vessel and extent of tumour. Pre operative biopsy is not recommended due to intractable bleeding<sup>5</sup>.

Surgery is the treatment of choice for JNA. Selection of proper surgical approach depends primarily upon the extension of tumour<sup>6</sup>. Radiotherapy is reserved for advanced tumour<sup>7</sup>.

## PATIENTS AND METHODS

This observational study was conducted at department of ENT and Head & Neck Surgery Quaid-e-Azam Medical College / B.V. Hospital Bahawal Pur from March 2005 to February 2009. All the adolescent male patients presenting in ENT OPD or in casualty with history of epistaxis, nasal obstruction were admitted in ward. Proper history and clinical examination done. Routine investigations carried out. Those patients who were having nasopharyngeal mass were sent for CT scan and included in the study. Staging of tumour done according to Fisch staging system. Surgery was planned in all cases after arranging sufficient quantity of blood. Stage I tumour under went transpalatal approach, stage II tumours by lateral rhinotomy approach and stage III tumour by Weber Furguson approach. Specimen

removed was sent for histopathological examination. Patients were followed up for 12-18 months postoperatively, recurrence and complications were noted.

Those patients who were having postoperative histological diagnosis other than JNA were excluded from the study. Advance stage IV JNA patients and recurrent cases were also excluded from the study.

## RESULTS

Total 35 young male patients clinically diagnosed as JNA and postoperatively confirmed by histopathology were included in the study. Age range was between 10-25 years with mean age of 16.7 years, majority (n-31) were between 12-20 years, 88.57%. One patient was below 12 years (02.85%) and 03 (08.57%) were above 20 years age. (Table No. I).

**Table No.I: Age Wise Distribution**

Age (years)	No. of cases	Percentage
<12	01	02.85
12-20	31	88.57
>20	03	08.57
Total	35	100

All patients were male, no female patient was reported. All patients presented with recurrent epistaxis, nasal obstruction and nasopharyngeal mass. Other presenting symptoms were, anemia 29 patients (82.85%), nasal mass in 27 patients (77.14%), ear blockage in 27 patients (77.14%), nasal discharge in 25 patients (71.42%), headache in 22 patients (62.86%), snoring in 15 patients (42.85%), speech defect in 11 patients (31.42%) and proptosis in 06 patients (17.14%) (Table No.2).

**Table No.2: Clinical Presentation**

Symptoms / signs	No. of cases	Percentage
Recurrent epistaxis	35	100
Nasal obstruction	35	100
Nasopharyngeal mass	35	100
Anemia	29	82.85
Nasal mass	27	77.14
Ear blockage	27	77.14
Nasal discharge	25	71.42
Headache	22	62.86
Snoring	15	42.85
Speech defect	11	31.42
Proptosis	06	17.14

Twelve patients (34.29%) presented in stage I, 17 (48.57%) in stage II and 06 patients (17.14%) presented in stage III (Table No.3).

**Table No.3: Staging of the Cases**

Stage	No. of cases	Percentage
Stage I	12	34.29
Stage II	17	48.57
Stage III	06	17.14
Total	35	100

All patients under went surgery. Seventeen patients (48.57%) were approached through lateral rhinotomy, 12 (34.29%) through transpalatal approach and 06 (17.14%) through Weber Furguson approach (Table No.4).

**Table No.4: Surgical Approaches**

Approach	No. of cases	Percentage
Lateral rhinotomy	17	48.57
Transpalatal	12	34.29
Weber Furguson	06	17.14
Total	35	100

Patients were followed up for 12-18 months postoperatively. In 05 patients (14.29%) recurrence occurred, and they underwent revision surgery. Twelve patients (34.28%) developed postoperative complications. Cheek anesthesia due to section of the infra orbital nerve occurred in all 06 patients (17.14%) operated by Weber Furguson approach, which decreased with the passage of time. Four patient (11.43%) developed post operative wound infection which was dealt with intravenous antibiotics. Palatal fistula was observed in 02 cases (05.71%), which was repaired secondarily. (Table No.5).

**Table No.5: Recurrence / Complications**

Recurrence / complications	No. of cases	Percentage
Recurrence	05	14.29
Cheek anesthesia	06	17.14
Wound infection	04	11.43
Palatal fistula	02	05.71



Juvenile Nasopharyngeal Angiofibroma removed after surgery



## DISCUSSION

JNA is a benign but locally aggressive, highly vascular tumour of nasopharynx found exclusively in adolescent male. It constitute less than 0.5% of all head and neck tumours. Its incidence is more in subcontinent as compared to Europe and America. Midilli<sup>2</sup> found incidence of 02 patients per year in his study with mean age of 16. He also reported a female patient. Witt<sup>8</sup> found 01 patient per year and all were male. While Muhammad<sup>9</sup> described same incidence with age and sex but 12.5 cases per year. Marfani<sup>10</sup> described 08 cases per year, all were male with age range 12-17 and mean age 15.4 years. Our study shows 8.8 cases per year with age range 10-25 and mean age 16.7 years which is near to local studies.

Although it is a unilateral tumour and arises from the posterolateral wall of nasopharynx, but in literature bilateral cases of JNA<sup>11</sup> has been reported. Rarely they originates outside the nasopharynx. Reports of primary extranasopharyngeal angiofibroma have appeared sporadically in the literature. One such unusual case of an angiofibroma arising from middle turbinate has been reported by Huang<sup>12</sup>. In our study all cases were arising from the nasopharynx and no extra nasopharyngeal origin was noted. Exact site of origin of JNA has been under discussion for the long time but with advancement of imaging techniques, most researchers agree that it arises from sphenopalatine foramen and from here it goes medially to nasopharynx, forward into the nose and paranasal sinuses. Growth in lateral direction invade pterygopalatine fossa, infratemporal fossa, superior orbital fissure, eyes and cranial cavity.

Clinical presentation of adolescent male with recurrent epistaxis, nasal obstruction and nasal mass is so typical that clinician has no hesitation to make its diagnosis. Other presentations may be like deafness, nasal discharge, headache, change of voice or proptosis. In our study recurrent epistaxis, nasal obstruction and nasopharyngeal mass were present in 100% cases. Other presenting symptoms were, anemia 29 patients (82.85%), nasal mass in 27 patients (77.14%), ear blockage in 27 patients (77.14%), nasal discharge in 25 patients (71.42%), headache in 22 patients (62.86%), snoring in 15 patients (42.85%), speech defect in 11 patients (31.42%) and proptosis in 06 patients (17.14%), which is almost same as studies conducted by Mohammad<sup>9</sup> and Marfani<sup>10</sup>

Preoperative biopsy is contraindicated for fear of bleeding. Postoperatively the tissue removed is sent for histopathology to confirm the clinical diagnosis. CT scan and MRI are needed to see the extent of tumour for staging. Carotid angiography is done to see the feeding vessel and its embolization. In our centre the facility of carotid angiography is not available, so no comments can be given about the feeding vessels.

We staged the tumour after clinical examination and CT scan and / or MRI. In our study stage I tumours were found 34.29%, stage II tumours 48.57% and stage III were 17.14%. According to Marfani<sup>10</sup>, 04% cases were in stage I, 24% in stage II and 74% in stage III. While according to study conducted by Mohammad<sup>9</sup>, 08% were in stage I, 24% in stage II and 48% in stage III and 20% were in stage IV. The difference observed in stages of the tumour may be due to geographical variation and early or late presentation of the patient.

JNA has always presented management challenges to ENT surgeons because of its vascular nature, site of occurrence and local tissue destruction. Surgery, radiotherapy, chemotherapy and hormone therapy are different treatment modalities for JNA, but surgery is the treatment of choice. Different surgical approaches are used for its resection. These approaches are, lateral rhinotomy, transpalatal, Weber Furguson, midfacial degloving, maxillary swing and infratemporal approach.. We used only three approaches in our study i.e. lateral rhinotomy, transpalatal and Weber Furguson approaches. Pre operative angiography and arterial embolization of feeding vessel 24-72 hours prior to resection has significantly reduced intraoperative blood loss and facilitate resection of large tumours due to shrinkage<sup>13</sup>. We did not have the facility of angiography, so we did not use embolization.

Recent advancement in endoscopic surgery also gave concept of this type of surgery in resection of JNA, but this approach is reserved for tumours involving nose and paranasal sinuses with minimal extension into pterygopalatine fossa<sup>14</sup>, but Onerci<sup>15</sup> has tried endoscopic approach for tumours with minimal intracranial extension with minimum morbidity and low recurrence rate. As we do not have the facility of endoscopic surgery, so we only used three classical surgical approaches in our study. These classical surgical approaches are still practiced with good results for larger tumours and where endoscopic facility is not available. By using these approaches we have recurrence rate of almost 14.2%, while Hirani<sup>16</sup> has shown recurrence rate of 9.4% in his study, and Witt<sup>8</sup> has shown recurrence rate of 14% and Marfani<sup>10</sup> 7% with surgery in his study. Variation in recurrence rate may be due to difference in stage of tumour, surgical approach, experience of surgeon and facilities available.

In our study complications occurred in 11 (31.42%) cases. Cheek anesthesia seen in 06 (17.14%) cases, wound infection in 03 (08.57%) and palatal fistula in 02 (05.71%) cases. Main complication was cheek anesthesia which was due to section of infraorbital nerve, which is inevitable in Weber Furguson approach. In our study palata fistula occurred in 02 patients out of 12 cases (16.66%) who were operated by transpalatal approach, while Hassan<sup>17</sup> in his study has shown palatal

fistula in 01 case out of 03 (33.33%) cases. This difference may be due to correction of preoperative anemia and better management of palatal wound. Wound infection in our study is 11.43% which is comparable to other sinonasal surgery.

## CONCLUSION

Nasopharyngeal angiofibroma is not uncommon in our region. Angiofibroma should be suspected whenever adolescent male present with nasal obstruction epistaxis and nasopharyngeal mass. Surgery is the treatment of choice. Surgery of JNA is always a challenge due to its vascularity and recurrence. Classical surgical approaches are best to combat this challenge. Pre operative CT scan and / or MRI of paranasal sinuses helps in staging of the tumour. Meticulous surgical approach is planned according to the stage of tumour and it reduces the rate of complication and recurrence. We recommend these approaches for operable cases.

## REFERENCES

1. Waldman SR, et al. Surgical experience with nasopharyngeal angiofibroma. *Arch otolaryngol* 1981;107(11):677-82.
2. Midilli R, Karci B, Akyildiz S. Juvenile nasopharyngeal angiofibroma: Analysis of 42 cases and important aspects of endoscopic approach. *Int Journal of Pediatric Otolaryngol*. Mar 2009; 73: 401-8.
3. Lloyd G, et al. Imaging for juvenile angiofibroma. *J Laryngology Otolaryngology* 2000; 114(9): 727-30.
4. Sheen OH. Angiofibroma. In: John Hibbert, editor. *Scott Brown's Otolaryngology Head and Neck Surgery*. 6<sup>th</sup> ed. London:1997.
5. Gleeson M. Juvenile Angiofibroma. In: Edward Arnold, editor. *Scott Brown's Otolaryngology Head and Neck Surgery*, 7<sup>th</sup> ed. London: 2008. p.2438.
6. Tyagi, Syal R, Goyal A. Staging and surgical approaches in large juvenile angiofibroma-study of 95 cases. *Isha Int J of Pediatric Otolaryngol* 2006; 70:1619-27.
7. Reddy KA, et al. Long term results of radiation therapy for juvenile nasopharyngeal angiofibroma. *Am J of Otolaryngol* 2001; 22:172-5.
8. Witt TR, Shah JP, Sternberg SS. Juvenile nasopharyngeal angiofibroma: A 30 year clinical review. *The Am J of Surgery* 1983; 146: 521-5.
9. Mohammad S, Mohammad A. Nasopharyngeal Angiofibroma. *The Professional* 2002;9:111-5.
10. Marfani MS, Mutiullah S, Ahmed Z, Danish-ur-Rahim, Zahid T. Frequency, Presentation and management of juvenile nasopharyngeal angiofibroma. *Pak J of Otolaryngol Head & Neck Surgery* 2009;25:35-8.
11. Rha KS, Byun SN, Kim TH, Kim YM. Bilateral juvenile nasopharyngeal angiofibroma. *Otolaryngol Head and Neck Surgery* 2003; 128: 891-3.
12. Huang RY, Damrose EJ, Blackwell KE, Cohen AN, Calcaterra TC. Extranasopharyngeal angiofibroma. *Int J of Pediatric Otorhinolaryngol* 2000; 56: 59-64.
13. Ahmad R, Ishlah W, Azilah N, Rehman JA. Surgical management of juvenile nasopharyngeal angiofibroma without angiographic embolization. *Asian J of Surgery* 2008;31: 174-8.
14. Mitskavich MT, Carrau RL, Snyderman CH, Weissman JL, Fagan JJ. Intranasal endoscopic excision of a juvenile angiofibroma. *Auris Nasus Larynx* 1998; 25: 39-44.
15. Onerci TM, Yucel OTK. Endoscopic surgery in treatment of juvenile nasopharyngeal angiofibroma. *Int J of Paed Otolaryngol* 2003; 67: 1219-25.
16. Hirani I, Muhammad IA, Farrukh S, Alam J. Is Lateral Rhinotomy, an Adequate Surgical Approach for Juvenile Naso-pharyngeal Angiofibroma. *Pak J of Otolaryngol Head & Neck Surgery* 2009; 25: 3-5.
17. Hassan S, Abdullah J. Critical Appraisal and the Surgical Technique of Maxillary Swing Approach for Advance Stage Juvenile Nasopharyngeal Angiofibroma. *Pak J of Otolaryngol Head & Neck Surgery* 2008;24:60-65.

### Address for Corresponding Author:

Dr. Masood Akhtar.

14-C Medical Colony Bahawalpur.

E.mail: entdrmasood@yahoo.com

**Original Article**

# Comparison of Ondansetron and Metoclopramide in the Prevention of Nausea and Vomiting after Laparoscopic Cholecystectomy Under General Anaesthesia

1. Noor Hussain 2. Dur-i-Shahwar 3. Madiha Malik 4. Shaheen Mahmood

1. Prof. of Anaesthesia 2. Asstt. Prof of Anaesthesia 3. Demonstrator of Pharmacology 4. PG Trainee Anaesthesia, Foundation University Medical College / Fauji Foundation Hospital, Rawalpindi.

## ABSTRACT

**Objective:** To evaluate and compare the antiemetic efficiency of ondansetron with metoclopramide when administered prophylactically for the prevention of post operative nausea and vomiting after laparoscopic cholecystectomy.

**Study Design:** Prospective, Randomised, Comparative study.

**Place and duration of study:** The study was conducted at the department of Anaesthesia Fauji Foundation Hospital, Rawalpindi from Sep 2010 to may 2011.

**Patients and Methods:** Total 90 ASA grade-I and ASA grade-II patients, sex female, and age 35 – 70 years undergoing elective laparoscopic cholecystectomy were included in the study. Patients were randomly divided into three groups, 30 in each group. Group-I received 4 mg intravenous ondansetron, group-II received 10 mg, Intravenous metoclopramide and group-III received intravenous 0.9% normal saline 2 minutes prior to induction of anaesthesia. They received standard General Anaesthesia for surgery. Post operative analgesia was provided with intravenous ketorelac 30 mg. There was no difference among the groups in patient characteristics and risk factors for PONV. Patients were observed for 24 hours after operation for occurrence of nausea and vomiting and requirement of rescue antiemetic. Efficiency of the drug was evaluated as (a) complete response- no nausea and no vomiting. (b) Mild response – Nausea with no vomiting (c) Moderate response – 1-2 vomiting episodes / moderate nausea (d) Severe response - > 3 vomiting episodes /severe nausea.

**Results:** During 1st 24 hours after operation incidence of nausea and vomiting was 77% in patients in placebo group, was 33% in patients in the ondansetron group and 53% in patients in the metoclopramide group. The incidence of PONV was significantly lower in patients who received ondansetron ( $P < 0.05$ ) as compared to metoclopramide or placebo. Complete response with no nausea and vomiting was higher in patients who received ondansetron (66 %) than in patients who received metoclopramide (46 %) or placebo (23 %). The incidence of nausea with vomiting (moderate to severe response) was significantly lower with ondansetron (20 %) as compared to metoclopramide (34 %) and placebo (60 %). There was no need for another rescue antiemetic in (80 %) patients, with ondansetron (67%) with metoclopramide, (40 %) with placebo.

**Conclusion:** Single intravenous dose of 4 mg ondansetron when administered prophylactically is more effective than 10 mg intravenous metoclopramide in the prevention of PONV after laparoscopic cholecystectomy. Single 4 mg IV dose of ondansetron reduces the incidence and severity of PONV and also requirement of rescue antiemetic in the Post operative period.

**Key Words:** Ondansetron, Metoclopramide, Laparoscopic Cholecystectomy.

## INTRODUCTION

Post operative nausea and vomiting (PONV) are distressing and frequent adverse events after general anaesthesia & surgery (<sup>1,2</sup>). A number of factors which include age, sex, obesity, history of motion sickness, operative procedures, anaesthetic techniques and post operative pain are considered to increase the incidence of these symptoms post operatively (<sup>3</sup>). laparoscopic cholecystectomy is associated with shorter post operative hospital stays, overall less expensive, less

morbidity, less post operative pain and has become a widely used surgical technique (<sup>4</sup>). It has been reported that the incidence of nausea & vomiting is as high as 60 -70% following laparoscopic cholecystectomy (<sup>5,6,7,8</sup>). Antiemetic prophylaxis is justified in patients undergoing laparoscopic cholecystectomy. There are several classes of drugs that constitute the mainstay of antiemetic therapy. These drugs range from older drugs like droperidol, metoclopramide to 5 HT antagonists. Ondansetron, a 5 hydroxytryptamine antagonist with selectivity for type 3 (5-HT) receptors has been

introduced as a new class of antiemetics. It acts probably on both peripheral and central sites with little or no clinically relevant effects on dopamine or other receptors<sup>9</sup>. Recent studies suggest that ondansetron is effective in the prevention of PONV in patients undergoing anaesthesia<sup>(10,11)</sup>. Metoclopramide is a procainamide derivative and a benzamide prokinetic agent with dual site of action, blocking D2 receptor in the periphery (GI tract) and centrally (CTZ and area postrema, vomiting centre). It is effective for the treatment of post operative nausea and vomiting<sup>(12)</sup>.

In the present study we have compared in our population the efficacy of 4 mg IV ondansetron with that of 10 mg IV metoclopramide for prevention of PONV in Female patients undergoing laparoscopic cholecystectomy. Both drugs were administered prophylactically two minutes prior to induction of anaesthesia. For this the study was designed to evaluate and compare the antiemetic efficiency of ondansetron and metoclopramide by observing incidence and severity of nausea and vomiting and requirement of rescue antiemetic in the 1st 24 hours after operation.

## PATIENTS & METHODS

This randomized, prospective comparative clinical study was carried out at the department of Anaesthesia, Fauji Foundation Hospital Rawalpindi from Sep 2010 to May 2011. 90 ASA grade-I and ASA grade-II patients, Sex female age 35 – 70 years (Table-1) undergoing elective laparoscopic cholecystectomy under general anaesthesia were included in the study. Patients with gastro enteritis, intestinal disease, history of motion sickness, previous PONV, pregnancy, or those who had taken antiemetics within 24 hours before operation were excluded from the study. After pre-anaesthesia check up, all the patients were kept NPO after mid night.

On arrival in operation theatre intravenous line was established on the dorsum of hand. Routine monitoring devices were attached and continuous monitoring of ECG, NIBP, Heart rate, SPO2 and End tidal CO2 was done during the surgical procedure.

Patients were randomly divided into three groups, thirty patients in each group.

Group-I received inj. Ondansetron (4 mg) intravenously, group-II received inj metoclopramide (10 mg) intravenously and group –III (placebo) received. 0.9 % normal saline. All drugs were administered prophylactically two minutes prior to induction of Anaesthesia. The Anaesthetists, nurses and surgeons caring the patients were blinded to the studied drugs.

The standard Anaesthetic technique was used for all patients. Inj Midazolam 3 mg IV and nalbuphine 0.1mg/kg was given intravenously to all patients

immediately before induction of Anaesthesia. Anaesthesia was induced with propofol 1.5 to 2 mg/kg and tracheal intubation was facilitated with atracurium 0.5 mg/kg intravenously. Anaesthesia was maintained with Isoflurane 0.7 % to 1 % (inspired concentration), nitrous oxide 50 % in oxygen. Ventilation was controlled mechanically with tidal volume and respiratory rate adjusted to maintain End tidal CO2 between 30 – 35 mm Hg. Neuromuscular blockade was maintained with incremental dose of IV atracurium. After tracheal intubation a nasogastric tube was placed and suction was applied to empty the stomach of air and other contents.

Patients were placed in supine position on operating table. Abdominal insufflation for the laparoscopic procedure was achieved with CO2 and intra- abdominal pressure was maintained between 10 -15 mm Hg. Reverse trendelenburg position 15 to 20 degree tilt was made in the beginning of laparoscopic procedure. At the end of surgery residual neuromuscular block was reversed with IV inj atropine 0.02/kg and IV inj neostigmine 0.05 mg/kg. The nasogastric tube was removed at the end of procedure and the trachea was extubated. IV Ringer's lactate was given as maintenance fluid to each patient during the laparoscopic surgery. After operation all the patients were transferred to recovery room. During their one hour stay in the recovery room oxygen was given via face mask. All the vital signs, oxygen saturation, ECG and Blood pressure were monitored. After one hour in recovery the patients were transferred to post operative ward for observation.

Inj Ketorolac 30 mg IV was given for postoperative analgesia.

### Collection of Data

Patients were observed for 24 hours after operation for incidence and severity of nausea and vomiting and also requirement of rescue antiemetic. The anaesthesiologist or ward sister registered whether vomiting had occurred and asked the patients whether they felt nauseated. The number of vomiting episodes were counted. Rescue antiemetic was given if vomiting occurred. Efficacy of the drug was evaluated as (a) complete response no nausea, no vomiting and no rescue antiemetic. (b) Mild response, nausea, no vomiting, no rescue antiemetic (c) Moderate Response – 1-2 vomiting episodes / moderate nausea, rescue antiemetic received. (d) Severe Response (Failure) vomiting episodes >3/ severe, nausea, rescue antiemetic received.

### Statistical Analysis

Data was analyzed using SPSS version 10.0. Mean, standard deviation, standard error of mean (SEM) and percentages were calculated. The statistical analysis was done by student's t-test and P- value less than 0.05 was considered significant.

## RESULTS

The data collected from 90 patients were analyzed. The patients characteristics, Age, weight, sex, duration of Anaesthesia, surgery, and CO<sub>2</sub> insufflation were similar among the groups (Table No.1). During 24 hours post operative observation period, arterial blood pressure, heart rate and respiration were stable and were not significantly different among groups.

In 1st 24 hours, PONV was seen in 23 (77 %) of 30 women in the placebo group (Figure No.1).

10 (33 %) 30 women in the ondasteron group (P-0.04) and 16 (53 %) 30 women in the metocolopramide group (P- 0.529). The incidence of PONV was significantly decreased in the ondasteron group as compared to metocolopramide and placebo group.

**Table No.1: Patient Demographics and Operative Characteristics (n=90)**

Variable	Group I Ondasteron 4 mg IV	Group II Metoclopra- mide 10 mg IV	Group III Saline Placebo
No of patients (n)	30	30	30
Age (yrs)	44 ± 13	51 ± 12	47 ± 13
Weight (kg)	65 ± 12	68 ± 12	66 ± 12
Sex , F	30	30	30
ASA grade 1: 2	26 : 4	22: 8	24: 6
Duration of Anaesthesia (min)	77 ± 21	92 ± 28	82 ± 21
Duration of Surgery (min)	63 ± 20	76 ± 27	66 ± 21
Duration of CO <sub>2</sub> Insufflation	51 ± 18	60 ± 24	55 ± 20

All values are expressed as mean ± SD.

The efficacy of study drug was assessed in each group 24 hours after operation. Complete response with no PONV was observed in 20 patients (66 %) in group-I, in 14 patients (46 %) in group-II, and in 7 patients (23 %) in group - III, placebo (Table No.2 Figure No.2). Patients experiencing only mild nausea (mild response) was noted in 4 (13 %) patients in group - I, in 6 (20 %) patients in group -II, in 5 (17 %) patients in group III, Moderate response, nausea with vomiting episodes 1-2 was noted in 4 (13 %) patients in group-I, 5 (17 %) patients in group-II in 10 patients (33 %) in group -III. Severe response, nausea with vomiting. Episodes > 3 was seen in 2 patients (7 %) , in group I, 5 patients (17 %) , in group II and 8 patients (27 %) , in group III, (Table-2, Figure-1). The rescue antiemetic was given to

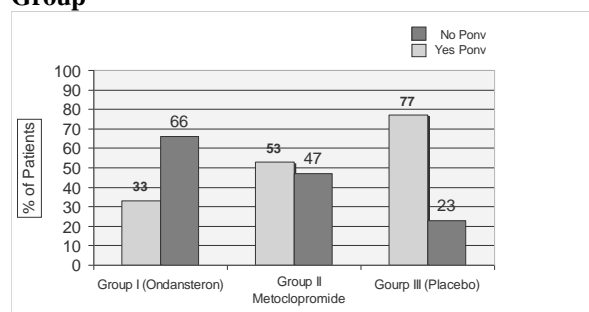
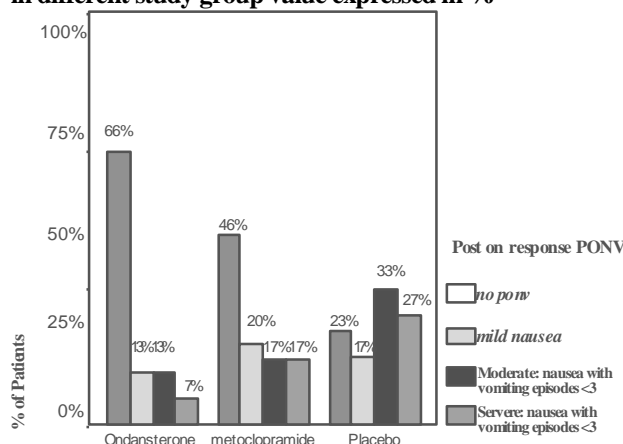
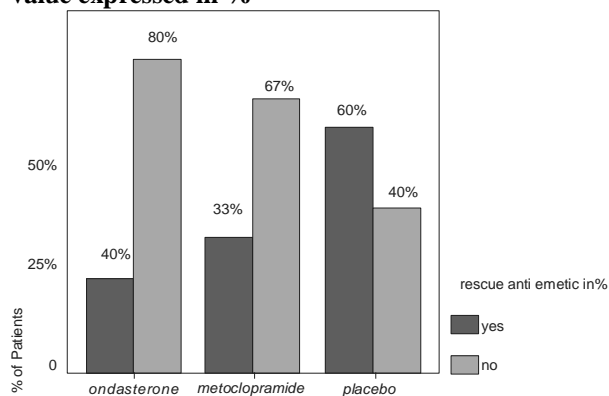
6 (20 %) patients in group-I (P value 0.032) to (33 %) patients in group-II (P- 0.445) and to 18 (60 %) patients in group-III (Figure No.3, Table No.2).

**Table No.2. The evaluation of post operative nausea and vomiting (PONV) 0 - 24 hours after laparoscopic cholecystectomy (n=90).**

Variable	Group I Ondansetron 4 mg	Group II Metoclopr- amide 10 mg	Group III Saline
1. No of patients	30	30	30
2. No (%) of patients experiencing no PONV (complete Response).	20 (66 %)	14 (46%)	7 (23 %)
3. No of (%) of patients experiencing nausea only (mild Response).	4 (13 %)	6 (20%)	5 (17%)
4. No of (%) of patients experiencing nausea with vomiting episodes < 3 (moderate Response).	4 (13 %)	5 (17%)	10 (33%)
5. No of (%) of patients experiencing nausea with vomiting episodes > 3 (severe Response).	2 (7%)	5 (17%)	8 (27%)
6. No of (%) of patients experiencing (PONV).	10 (33 %)	16 (53 %)	23 (77 %)
7. Rescue Antiemetic	6 (20 %)	10 (33%)	18 (60 %)

## DISCUSSION

PONV is the most common complication following anaesthesia and surgery with a selectively high incidence after laparoscopic cholecystectomy. Better anaesthetic technique, identification of precipitating factors, use of new generation of antiemetics and improvement in operative techniques reduce the incidence and severity of PONV. Despite these changes, there is still unacceptable frequency of PONV with incidences up to 85 % reported in some studies (13).

**Figure No.1: Incidence of PONV in different Study Group****Figure No.2: Post operative response of nausea vomiting in different study group value expressed in %****Figure No.3: Rescue anti emetic in different group value expressed in %**

This problem is multifactorial in origin, including the patient demographics, the nature of underlying disease, the duration of surgery, anaesthetic technique and post operative care<sup>(14)</sup>. The main patient related factors are age, sex, obesity, history of motion sickness and / or previous PONV. Surgical factors also include the effects of intraperitoneal

CO<sub>2</sub> insufflation on residual stretching and irritation of the peritoneum<sup>(15)</sup>. In this study, however the treatment groups were similar with respect to patient characteristics, surgical procedures, anaesthetics drugs

administered and analgesia used post operatively (Table No. 1). Therefore, the difference in the incidence of PONV between the patients who had received ondansetron and those who had received metoclopramide or placebo can be attributed to the differences in these agents tested.

Both ondansetron and metoclopramide were given at the time of induction of anaesthesia to evaluate their antiemetic efficacy. In our study the incidence of PONV in group-I was 33 %, in group-II 53 % and in group-III 77 % during 1st 24 hours after operation (Table No.2, Figure No.1). The study demonstrated lower incidence of PONV (33 %) with ondansetron ( $P=0.04$ ) compared with metoclopramide (53 %). The difference is statistically significant with ondansetron ( $P < 0.05$ ). The incidence of PONV was very high (77 %) in patients, who did not receive antiemetic drugs prophylactically. (Figure No.1)

The treatment with metoclopramide ( $P=0.529$ ) did not significantly decrease the incidence of PONV. Recent studies have shown that although popular metoclopramide performs poorly in well controlled clinical trials and our findings confirm this for women undergoing laparoscopic cholecystectomy (16,17).

In our study complete response with no nausea and vomiting was significantly higher in patients who received ondansetron (66 %) than those who received metoclopramide (46 %) or placebo 23 % (Figure No.2 Table No.2). Mild response, nausea with no vomiting was observed in group-I (13 %), in group-II (20 %) and in group-III (17 %). There was no significant difference among the groups. Moderate response, nausea with vomiting episodes 1 -2 was (13 %) in group -I, 17 % in group-II and 33 % in group-III. Severe response (Treatment failure) nausea with vomiting episodes > 3 was observed in 7 % in group-I, 17 % in group-II and 27 % in group -III. Incidence of nausea with vomiting was significantly lower with ondansetron 20 % as compared to metoclopramide (34 %) or placebo (60 %). Study demonstrated very high incidence and severity of vomiting in patients who had not received antiemetic drug prophylactically. In the present study 20 % patients in group-I, 33 % patients in group-II and 40 % patients in group-III required another rescue antiemetic medication (Figure No.-3). The requirement of another rescue antiemetic medication was significantly lower with ondansetron ( $P=0.032$ ) as compared with metoclopramide. The difference is statistically significant with ondansetron

( $P < 0.05$ ). The antiemetics commonly used e.g droperidol and metoclopramide, have limited efficacy and are associated with a variety of side effects. Droperidol even at a low dose, has been described as being associated with excessive sedation and extrapyramidal reactions<sup>(18)</sup>. Also, adverse reactions involving the nervous system after small doses of

metoclopramide have been described in the literature 18. Ondansetron lacks the sedative, dysphoric and extrapyramidal symptoms associated with other antiemetics.

Several recent studies <sup>(9, 19, 20)</sup> have shown that a single intravenous dose of ondansetron

4 mg, the dose chosen in this study, is an optimal dose and is effective at preventing PONV after a variety of surgical procedures. The majority of studies comparing the antiemetic efficacy and safety of ondansetron with other currently used antiemetics have been performed in patients undergoing gynaecological procedures under general anaesthesia. None has been performed in female patients in our population undergoing laparoscopic cholecystectomy under general anaesthesia. The findings in this study are in agreement with Raphael and Norton who showed that preoperative prophylactic intravenous ondansetron 4 mg was superior to metoclopramide 10 mg in preventing PONV after general anaesthesia for day case gynaecological laparoscopic surgery <sup>(21)</sup>. In another study of patients undergoing therapeutic abortion, ondansetron 8 mg resulted in a significantly lower incidence of postoperative vomiting (13%) compared with metoclopramide 10 mg (54 %) <sup>(22)</sup>.

Scuderi and coll. demonstrated that there is a difference in outcomes when routine antiemetic medication with ondansetron is administered versus simply treating PONV when the symptoms occur. Moreover, Scholz and coll demonstrated that the ondansetron reduces the incidence of PONV in patients undergoing laparoscopic cholecystectomy as well as major gynaecological surgery <sup>(23)</sup>. Our data support the prophylactic use of intravenous 4 mg Ondansetron for PONV.

## CONCLUSION

From the results of study it is obvious that prophylactic intravenous 4 mg ondansetron reduces the incidence & severity of PONV and also the requirement of rescue antiemetic in the post operative period. The ondansetron is more effective than metoclopramide in preventing post operative nausea & vomiting in patients undergoing laparoscopic cholecystectomy.

It is concluded that pre-anaesthesia intravenous 4 mg ondansetron is superior to intravenous 10 mg metoclopramide as a prophylactic antiemetic in patients undergoing laparoscopic cholecystectomy under general anaesthesia.

The prophylactic use of intravenous 4 mg ondansetron is recommended for preventing post operative nausea & vomiting in patients undergoing laparoscopic cholecystectomy under general anaesthesia.

## REFERENCES

1. Watcha MF, White PF. Postoperative nausea and vomiting its etiology, treatment and prevention. *Anesthesiology* 1992;77:162-84.

2. Rowbotham DJ, Smith G. Introduction to (Suppl.) on postoperative nausea and vomiting. *Br J Anesth* 1992; 69 (Suppl.1) : IS
3. CM Ku, BC Ong. Postoperative nausea & vomiting: A Review of Current Literature. *Singapore Med J* 2003;44 (7):366 -374
4. Reddick EL, Olsen DO. Laparoscopic laser cholecystectomy: A comparison with mini-lap cholecystectomy. *Surgical Endoscopy* 1989;3: 131-3.
5. Litomi T, Toriumi S, Kondo A, Akazawa T, Nakahara T. Incident of nausea and vomiting after cholecystectomy performed via laparotomy or laparoscopy. *Masui* 1995;44:1627-31.
6. Sanatoua JM. Anaesthesia for laparoscopic cholecystectomy. *Anaesthesia* 1991;46:317 (letter)
7. Biswas BN, Rudra A. Comparison of granisetron and granisetron plus dexamethasone for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. *Acta Anaesthesiologica Scandinavica* 2003; 47:79-83.
8. Hofer CK, Zollinger A, Buchi S, et al. Patient well-being after general anaesthesia: a prospective, randomized, controlled multi-centre trial comparing intravenous and inhalation anaesthesia. *Br J Anesth* 2003;91: 631-6.
9. Butler A, Hill JM, Ireland, SJ, et al. Pharmacological properties of GR 38032F, a novel antagonist at 5-HT<sub>3</sub> receptors. *Br J Pharmacol* 1988; 94: 397 -412
10. Gan TJ, Collis R, Hetreed M. Double-blind comparison of ondansetron, Droperidol and saline in the prevention of postoperative nausea and vomiting. *Br J of Anesth* 1994;72:544-7.
11. Pearman MH. Single dose intravenous ondansetron in the prevention of postoperative nausea and vomiting. *Anesthesia* 1994; 49 (Suppl.):11 -5.
12. Henzi I, Walder B, Tramer MR. Metoclopramide in the prevention of postoperative nausea and vomiting: a quantitative systematic review of randomized, placebo- controlled studies. *Br J Anesth* 1999; 83:761-71.
13. Hernandez Conte AT. Postoperative nausea and vomiting: a review of antiemetic pharmacological interventions. *Anesth Pharmacol Physiol Rev* 1996; 4: 57-65.
14. Watcha M, White PF. Postoperative nausea and vomiting. Its etiology, treatment and prevention. *Anesthesiology* 1992; 77: 162 – 184.
15. Fujii Y, Saito Y, Tanaka H, Toyooka H, Effective dose of granisetron for the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy. *Eur J Anesth* 1998; 15: 287 -291.
16. Malins AF, Field JM, Nesling PM, Cooper GM. Nausea and vomiting after gynaecological

- laparoscopy: comparison of premedication with oral ondansetron, metoclopramide and placebo. Br J of Anesth 1994; 72: 231-3.
17. Rowbotham DJ. Current management of postoperative nausea and vomiting. Br J of Anesth 1992; 69 (Suppl.1) : 46S-59S.
  18. Madej TH, Simpson KH. Comparison of the use of domperidone, droperidol and metoclopramide in the prevention of nausea and vomiting following gynaecological surgery in day cases. Br J of Anesth 1986; 58: 879 -83.
  19. Tang J, Watcha MF, White PF. A comparison of costs and efficacy of ondansetron and droperidol as prophylactic anti-emetic therapy for elective outpatient gynaecologic procedures. Anaesthesia and Analgesia 1996; 83: 304-13.
  20. Koivuranta MK, Laara E, Ryhanen PT. Anti-emetic efficacy prophylactic ondansetron in laparoscopic cholecystectomy. A randomised, double-blind, placebo controlled trial. Anaesthesia 1996; 51: 52-5.
  21. Raphael JH, Norton AC. Anti-emetic efficacy of prophylactic ondansetron in laparoscopic surgery: Randomized, double –blind comparison with metoclopramide. Br J of Anesth 1993; 71: 845-8.
  22. Alon E, Himmelseher S. Ondansetron in the treatment of postoperative vomiting: A randomised, double- blind comparison with droperidol and metoclopramide. Anaesthesia and Analgesia 1992;75: 561-5.
  23. Scholz J, Hennes J, Steinfath M, Farber L, Scwhwiger C, Dick W, et al. Tropisetron or ondansetron compared with placebo for prevention of postoperative nausea and vomiting. Eur J Anesth 1998; 15: 676-685.

**Address for Corresponding Author:**

Brig (Retd) Dr Noor Hussain,  
Professor of Anaesthesia  
Foundation University Medical College /  
Fauji Foundation Hospital,  
Rawalpindi.  
Tele: +92- 051- 5472678  
Cell: 0336-5134143  
Email: drnoorhussain47@ hotmail.com



**Original Article**

## Glycation Pattern of Captopril in Diabetics

1. Samina Kousar 2. Mahboob Bari 3. Nighat Naeem 4. Munir A. Sheikh

1. Asstt. Prof. of Biochemistry 2. Prof. of Biochemistry, University College of Medicine and Dentistry, The University of Lahore 3. Asstt. Prof. of Biochemistry, Independent Medical College, Faisalabad 4. Prof. of Biochemistry, University of Agriculture, Faisalabad.

### ABSTRACT

**Objective:** Captopril is a chemical which acts as vasodilator and angiotensin- I converting enzyme inhibitor. The present attempt is to study the glycation inhibition pattern of captopril in diabetics and normals.

**Study Deign:** Experimental Study.

**Place and Duration of Study:** This study was conducted at the Research Lab., Department of Biochemistry, University of Agriculture, Faisalabad from May 2006 to February 2007.

**Materials and Methods:** The study was designed on blood plasma from apparently healthy non-diabetic and diabetic persons. Plasma samples with different concentrations of glucose and that of captopril were prepared, followed by incubation for 5 weeks at 37 °C temperature. Glucose was estimated by glucose oxidase method before and after dialysis. Glycation level was measured by TBA and Periodate assays.

**Results:** Increased glycation was observed from 1<sup>st</sup> to 3<sup>rd</sup> week of incubation while it decreased after 5<sup>th</sup> week due to the formation of advanced glycation end products. 10 mM concentration of captopril showed fairly good response to decrease glycation as compared to its other two concentrations.

**Conclusions:** Highest concentration of captopril produced overall good enough of inhibition. Periodate borohydride appeared to be more reliable and sensitive glycation assay as compared to TBA.

**Key Words:** Glycation, Diabetes, Maillard reaction, Captopril, TBA, Periodate

### INTRODUCTION

Diabetes is characterized by hyperglycaemia resulting in various short-term metabolic changes in lipid and protein metabolism and long-term irreversible vascular changes<sup>1</sup>. Diabetes and its complications are rapidly becoming the world's most significant disease epidemic<sup>2</sup>. The morbidity caused by diabetes has traditionally been classified into macro vascular complications including, atherosclerosis leading to heart disease, stroke, peripheral vascular disease and micro vascular complications like retinopathy, nephropathy and neuropathy. The same disorders are also two to five times more prevalent in diabetic as compared to normal subjects<sup>1</sup>. Chronic hyperglycemia is a major threat to diabetic microvascular complications. According to Matthew and George,<sup>3</sup> glucose is utilized in a variety of diverse metabolic pathways; hence, chronic hyperglycemia can induce multiple cellular changes leading to various complications.

The adverse effects of high plasma glucose depend upon the type of the cells. Cells which express a high level of the glucose transporter 1 (GLUT1), are unable to regulate intracellular glucose concentrations and are thus very susceptible to hyperglycemia-induced damage<sup>4</sup>. The *in vivo* formation of non-enzymatic glycated compounds were first detected in 1969 from studies on chromotagenic mobilities of fast moving, minor hemoglobin from diabetic patients, in particular

HbA1C, now used as a clinical tool in the management of glycaemic control in diabetic patients<sup>5</sup>. Reaction of glucose with proteins is called Maillard reaction. The Maillard reaction has three stages. The early reactions results in the formation of a Schiff base and Amadori products. Then rearrangements of chemical groups take place resulting in the formation of classical Maillard browning products known as AGEs<sup>6</sup>. Non-enzymatic glycation of proteins have now been implicated in the pathogenesis of different diseases like diabetes, renal failure and aging<sup>7</sup>.

Living system has devised various defense mechanisms to protect the tissues against deleterious effects of advanced glycation end products. These include glyoxylase system (I and II) having oxaldehyde reductase and aldose reductase that catalyze the deglycation and detoxification of methylglyoxal, the most common reactive intermediates of AGEs to D-lactate<sup>8</sup>.

Now it is the need of the day to develop or isolate new compounds either from plants or synthetically to control diabetes and other age accelerating diseases. Aminoguanidine (AG) is the first compound that has been extensively studied *in vitro* and *in vivo*, to be a powerful glycation and AGE inhibitor<sup>9</sup>. AG is a nucleophilic compound that traps reactive carbonyl intermediates partially inhibiting carboxy methyl lysine and carboxy ethyl lysine<sup>10</sup>. Hammes et al.<sup>11</sup> showed that oral benfotiamine supplementation in diabetic rats could effectively block the formation and accumulation

of AGEs and prevent the development of experimental diabetic retinopathy and nephropathy. The major objective of this study was to investigate the glycation inhibition level of captopril in normal and diabetic human plasma and secondly to compare the sensitivities of Thiobarbituric Acid (TBA) with that of Periodate method.

## MATERIALS AND METHODS

### Experimental concentration and conditions

Four different concentrations of glucose i.e ( $G_1=500$  mM,  $G_2=250$  mM,  $G_3=50$  mM and  $G_4=5.5$  mM) were prepared. Blood plasma samples were collected from diabetic (Type II) patients as well as from normal/ healthy male and females. Samples were stored at  $-20^\circ\text{C}$  till use. At the time of use, all plasma were pooled together. Thereafter, separately both in normal as well as in diabetics the required sample volume for experiments were obtained. Then all plasma samples were diluted so as to have protein concentration range up to 20mg/mL. Glycation level was assessed by two different methods. Proteins were estimated by Biuret method<sup>12</sup> before and after dialysis of plasma samples. Three different concentrations of captopril, the inhibitor ( $I_1= 10$  mM,  $I_2= 5$  mM and  $I_3 = 1$  mM) were used in this experimental study.

### Selection of Combinations

To study the effect of captopril, sixteen combinations with normal ( $P_N$ ) and diabetic ( $P_D$ ) plasma were made. All were placed simultaneously for five weeks at  $37^\circ\text{C}$  (Table No.1).

**Table No. 1: Different combinations for Plasma glycation inhibition**

S#	Combinations for Normal/ Diabetic Plasma	S#	Combinations for Normal/ Diabetic Plasma
1	$G_1 + P_{N/D}$	9	$G_3 + P_{N/D}$
2	$G_1 + P_{N/D} + I_1$	10	$G_3 + P_{N/D} + I_1$
3	$G_1 + P_{N/D} + I_2$	11	$G_3 + P_{N/D} + I_2$
4	$G_1 + P_{N/D} + I_3$	12	$G_3 + P_{N/D} + I_3$
5	$G_2 + P_{N/D}$	13	$G_4 + P_{N/D}$
6	$G_2 + P_{N/D} + I_1$	14	$G_4 + P_{N/D} + I_1$
7	$G_2 + P_{N/D} + I_2$	15	$G_4 + P_{N/D} + I_2$
8	$G_2 + P_{N/D} + I_3$	16	$G_4 + P_{N/D} + I_3$

### Glycation of Plasma

All plasma combinations with four different concentrations of glucose were incubated for 1-5 weeks at  $37^\circ\text{C}$ . Plasma samples after incubation were dialyzed to remove free glucose, as free glucose is the major hindrance in ascertaining the glycation level. Glucose was again estimated after dialysis by glucose oxidase method in order to see whether the concentration of glucose is decreased or not.

### Glycation inhibition of plasma

Different concentrations of glucose and that of captopril were incubated at  $37^\circ\text{C}$  for 1-5 weeks.

### Thiobarbituric Acid (TBA) Colorimetric Technique

Enzymatic and non-enzymatic glycation was determined by TBA technique. This method is based on the reaction between fructose, amino acids and weak acid that will yield 5-hydroxymethyl furfural (HMF) compound.<sup>13</sup>

Non enzymatic glycation was determined as follows.

NE Glycation = (C Glycation + E Glycation) - E Glycation

NE =Non Enzymatic, E= Enzymatic, C =Collective

### Periodate Borohydride Assay

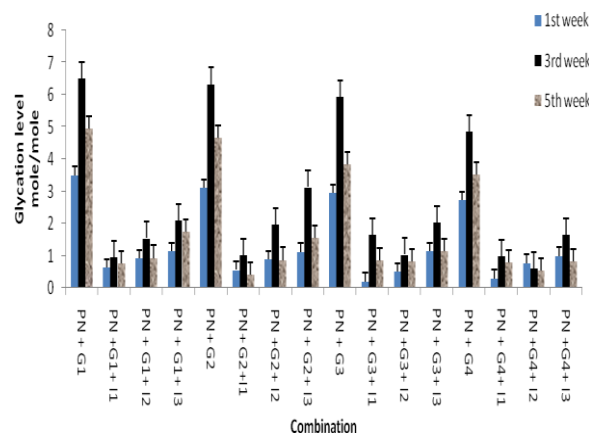
This test is based on the formation of formaldehyde by periodate oxidation of cis-diol, aminol, ketol or ketoamine structures. Two moles of formaldehyde are formed from hexose sugar. The amount of formaldehyde produced was quantified as fluorescent adduct formed by condensation of formaldehyde with acetyl acetone and ammonia.<sup>14,15</sup>

## RESULTS

### Effect of Captopril on glycation level with normal human plasma

The results obtained from captopril in normal human plasma showed that 500 mM ( $G_1$ ) concentration of glucose had maximum glycation level with value 6.507mole/mole after 3<sup>rd</sup> week of incubation and it was minimum after 1<sup>st</sup> week of incubation with  $G_4$  (5.5 mM) glucose concentration (Figure No.1). TBA technique showed that 10 mM ( $I_1$ ) concentration of captopril was more active to inhibit glycation while 5 mM ( $I_2$ ) gave variable response and 1 mM ( $I_3$ ) concentration exhibited least glycation inhibition effect.

**Figure 1: Effect of Captopril on glycation level with TBA in normal human plasma**



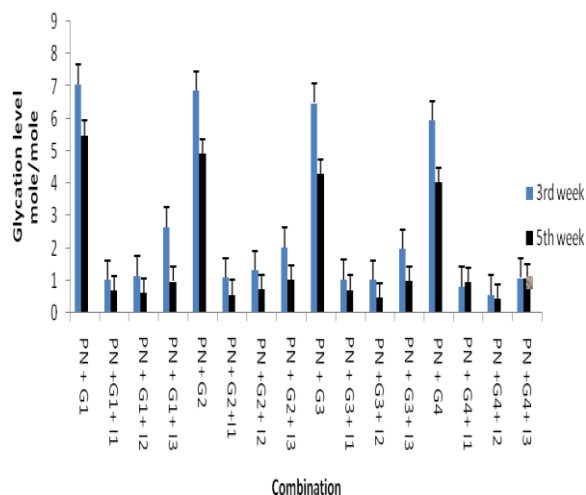
Normal plasma protein ( $P_N \approx 20$  mg/mL) was incubated with all glucose concentrations ( $G_1= 500$  mM,  $G_2= 250$  mM,  $G_3= 50$  mM &

$G_4=5.5\text{ mM}$ ) and three concentrations of captopril ( $I_1=10\text{ mM}$ ,  $I_2=5\text{ mM}$  &  $I_3=1\text{ mM}$ ) in  $0.075\text{ M}$  PBS. Reaction mixtures were incubated at  $37^\circ\text{C}$  for 5 weeks at the same time. Samples were analysed after 1<sup>st</sup>, 3<sup>rd</sup> and 5<sup>th</sup> week and glycation level was measured in mole\ mole (glucose\ protein).

\* Values were the average of experiments carried out at  $n=3$

With Periodate borohydride assay, maximum glycation response i.e. 7.053 mole/mole was observed after 3<sup>rd</sup> week with  $G_1$  concentration of glucose which dropped to 2.960 mole/mole with  $G_4$  glucose concentration in 1<sup>st</sup> week of incubation (Figure No.2). Different concentrations of captopril showed comparable inhibitory responses i.e.  $10\text{ mM}$  ( $I_1$ ) produced maximum inhibition with  $G_1$  and  $G_2$  concentration of glucose. Likewise,  $5\text{ mM}$  ( $I_2$ ) concentration of captopril also exhibited maximum inhibitory response against  $G_3$  and  $G_4$  glucose concentrations.

**Figure 2: Effect of Captopril on glycation level with Periodate borohydride assay in normal human plasma**

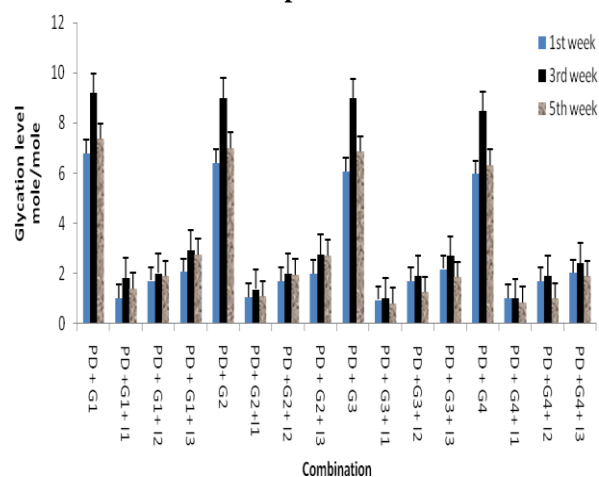


Normal plasma protein ( $P_N \approx 20\text{ mg/mL}$ ) was incubated with all glucose concentrations ( $G_1=500\text{ mM}$ ,  $G_2=250\text{ mM}$ ,  $G_3=50\text{ mM}$  &  $G_4=5.5\text{ mM}$ ) and three concentrations of captopril ( $I_1=10\text{ mM}$ ,  $I_2=5\text{ mM}$  &  $I_3=1\text{ mM}$ ) in  $0.075\text{ M}$  PBS. Reaction mixtures were incubated at  $37^\circ\text{C}$  for 5 weeks at the same time. Samples were analysed after 1<sup>st</sup>, 3<sup>rd</sup> and 5<sup>th</sup> week and glycation level was measured in mole\ mole (glucose\ protein).

\* Values were the average of experiments carried out at  $n=3$

Results in Figure No. 3, are of diabetic human plasma which showed that  $G_1$  concentration of glucose showed maximum glycation (9.195mole/mole) after 3<sup>rd</sup> week of incubation with TBA test. Minimum glycation i.e. 5.966 mole/mole was observed after 1<sup>st</sup> week of incubation with  $G_4$  concentration of glucose. Maximum glycation inhibition response was reflected in  $10\text{ mM}$  ( $I_1$ ) concentration of captopril while  $5\text{ mM}$  ( $I_2$ ) and  $1\text{ mM}$  ( $I_3$ ) had variable response towards inhibition

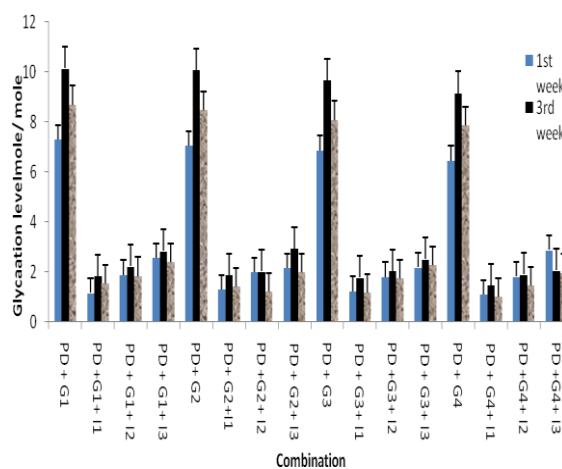
**Figure 3: Effect of Captopril on glycation level with TBA in diabetic human plasma**



Normal plasma protein ( $P_D \approx 20\text{ mg/mL}$ ) was incubated with all glucose concentrations ( $G_1=500\text{ mM}$ ,  $G_2=250\text{ mM}$ ,  $G_3=50\text{ mM}$  &  $G_4=5.5\text{ mM}$ ) and three concentrations of captopril ( $I_1=10\text{ mM}$ ,  $I_2=5\text{ mM}$  &  $I_3=1\text{ mM}$ ) in  $0.075\text{ M}$  PBS. Reaction mixtures were incubated at  $37^\circ\text{C}$  for 5 weeks at the same time. Samples were analysed after 1<sup>st</sup>, 3<sup>rd</sup> and 5<sup>th</sup> week and glycation level was measured in mole\ mole (glucose\ protein).

\* Values were the average of experiments carried out at  $n=3$

**Figure 4: Effect of Captopril on glycation level with periodate borohydride assay in diabetic human plasma**



Normal plasma protein ( $P_D \approx 20\text{ mg/mL}$ ) was incubated with all glucose concentrations ( $G_1=500\text{ mM}$ ,  $G_2=250\text{ mM}$ ,  $G_3=50\text{ mM}$  &  $G_4=5.5\text{ mM}$ ) and three concentrations of captopril ( $I_1=10\text{ mM}$ ,  $I_2=5\text{ mM}$  &  $I_3=1\text{ mM}$ ) in  $0.075\text{ M}$  PBS. Reaction mixtures were incubated at  $37^\circ\text{C}$  for 5 weeks at the same time. Samples were analysed after 1<sup>st</sup>, 3<sup>rd</sup> and 5<sup>th</sup> week and glycation level was measured in mole\ mole (glucose\ protein).

\* Values were the average of experiments carried out at  $n=3$

With periodate borohydride assay, maximum glycation i.e. 10.138 mole/mole was measured after 3<sup>rd</sup> week with  $G_1$  concentration which dropped to minimum i.e. 6.453 mole/mole with  $G_4$  after 1<sup>st</sup> week of incubation (Figure No.4). Overall maximum glycation inhibitory effect of

captopril was seen in  $I_1$  concentration. One exception was observed where  $I_2$  showed maximum response.

## DISCUSSIONS

The results reflected that overall  $G_1$  (500 mM) concentration of glucose exhibited maximum glycation impact while  $G_2$  (250mM) has almost similar trend as  $G_1$  at many points. 10 mM concentration of captopril showed maximum glycation inhibitory response in both normal and diabetic condition (Figures 1-4). These results are comparable with Mariee et al. studies,<sup>16</sup> who studied comparative inhibitory pattern of captopril and aminoguanidine (AG). Our results also corroborates with report by Jakus et al.<sup>17</sup> as they concluded that captopril decreases AGEs formation. Huang et al. findings are also in conformity with our results as they studied the role of captopril in the pathogenesis of diabetic nephropathy and found dose-dependent inhibition by antisense RAGE oligodeoxynucleotide and captopril.<sup>18</sup>

Glycation assays: TBA and Periodate almost showed same trend of glycation measurement but periodate proved to be more sensitive and affective method to measure glycation level. Our results are also in harmony with Jakus et al.<sup>17</sup>. It can be inferred that periodate glycation assay measurement of Amadori product was more convenient.

It can be conclude ed from the present study that glycation increased from 1<sup>st</sup> to 3<sup>rd</sup> week of incubation and slight decline in glycation level was seen after 5<sup>th</sup> week of incubation. This possibly could be due to formation of advanced glycation end products. It was also seen that  $G_1$  and  $G_2$  concentrations of glucose produced maximum glycation as compared to its other concentrations.

## CONCLUSIONS

- Glucose concentrations 500mM and 250 mM can produced maximum glycation
- 10 mM concentration of captopril can produce fairly good response to decrease glycation both in normal and diabetics.
- Periodate borohydride technique seems to be more affective and sensitive as compared to TBA test.

## REFERENCES

1. Zimmet PZ, Alberti KG. The changing face of macrovascular disease in non-insulin-dependent diabetes mellitus: an epidemic in progress. *Lancet* 1997; 350 (Suppl 1): I1-I4.
2. Forbes JM, Soldates G, Thomas MC. Advanced glycation end products (AGEs) That Detour "around the Side" Is HbA1c not an accurate

enough predictor of long term progression and glycaemic control in diabetes? *Clin Biochem Rev* 2005; 26(4): 123- 134.

3. Matthew JS, George LK. Molecular Understanding of Hyperglycemia's Adverse Effects for Diabetic Complications. *J Am Med Assoc.* 2011; 305(12): 1165-1256.
4. Heilig CW, Concepcion LA, Riser BL. Overexpression of glucose transporters in rat mesangial cells cultured in a normal glucose milieu mimics the diabetic phenotype. *J Clin Invest* 1995; 96(4): 1802-1814.
5. Rahbar S, Blumenfeld O, Ranney HM. Studies of unusual hemoglobin in patients with Diabetes mellitus. *Biochem Biophys Res Commun* 1969; 36(5):838-843.
6. Singh R, Barden A, Mori T, Beilin L. Advanced glycation end-products: a review. *Diabetologia* 2001; 44: 129-146.
7. Schleicher ED, Wagner E, Nerlich AG. Increased accumulation of the glycoxidation product N(epsilon)-(carboxymethyl)lysine in human tissues in diabetes and aging. *J Clin Invest* 1997; 99(3):457-468.
8. Szweggold BS, Howell S, Beisswenger PJ. Human fructosamine- 3 kinase: purification, sequencing, substrate specificity and evidence of activity in vivo. *Diabetes* 2001; 50(9): 2139- 2147.
9. Brownlee M. Glycation and diabetic complications. *Diabetes* 1994; 43(6): 836- 841.
10. Bolton WK, Cattran DC, Williams ME, Adler SG, Appel GB, Cartwright K, et al. Randomized trial of an inhibitor of formation of advanced glycation end products in diabetic nephropathy. *Am J Pathol* 2004; 24(1): 32-40.
11. Hammes, HP, Du X, Edelstein D. Benfotiamine blocks three major pathways of hyperglycemic damage and prevents experimental diabetic retinopathy. *Nat Med* 2003; 9(3): 294-299.
12. Gornall AG, Bardawill CS, David MM. Determination of serum proteins by means of biuret reaction. *J BioI Chem* 1949; 177(2): 751-766.
13. Furth AJ. Methods for assaying non enzymatic glycosylation: a review. *Anal. Biochem.* 1988; 175(2): 347- 360.
14. Gallop PM, Fluckiger R, Hanneken A, Mininshon MM, Gabbay KH. Chemical quantitation of hemoglobin glycosylation: fluorometric detection of formaldehyde released upon periodate oxidation of glycoglobin. *Anal Biochem* 1981; 117(2): 427-432.

15. Zhang EY, Swaan PW. Determination of Membrane Protein Glycation in Diabetic Tissue. AAPS Pharm Sci 1999; 1(4): 20- 24.
16. Mariee AD, Shabanah O. Protective ability and binding affinity of Captopril towards serum albumin in an in vitro glycation models of diabetes mellitus. J Pharm Biomed Anal 2005; 12: 25-31. (www.sciencedirect.com)
17. Jakus V, HrnEiarova M, Sky J, Krahulec B, Rietbrock N. Inhibition of nonenzymatic protein glycation and lipid peroxidation by drugs with antioxidant activity. Life Sci 1999; 65 (18-19): 1991-1993.
18. Huang JS, Guh JY, Hung WC. Role of the Janus kinase (JAK)/signal transducers and activators of transcription (STAT) cascade in advanced glycation end-product-induced cellular mitogenesis in NRK-49F cells. Biochem J 2001; 342(Pt 1): 231-238.

**Address for Corresponding Author:**

Samina Kousar  
Assistant Professor,  
Department of Biochemistry,  
University College of Medicine and Dentistry,  
University of Lahore. 1-KM Defense Road,  
OFF Raiwaind Road, Lahore, Pakistan.  
Email: samphdbio@gmail.com,  
Mobile # 03064822900,  
Office: 04235321457 Ext.116

**Original Article**

# The Incidence of Weapon used in Medicolegal Cases of Urban Area of Abbottabad

1. Nighat Seema 2. Iftikhar Ahmad 3. Muhammad Saleem 4. Saleem Afzal

1. Asstt. Prof. of Forensic Medicine, AMC, Abbottabad 2. Asstt. Prof. of Forensic Medicine, AMC, Abbottabad  
3. Asstt. Prof. of Forensic Medicine, PGMI, Lahore 4. Assoc. Prof. of Medicine, AMC, Abbottabad.

## ABSTRACT

**Objectives:** the objective of this study was to compare the use of weapon of offence in medico legal cases in urban area with the use of weapon in rural area in such cases.

**Study Design:** Comparative study.

**Place and Duration of Study:** A medico legal centre of an urban area of Shaheed Benazir Hospital Abbottabad was selected. The record of recorded cases was taken, researched and record was formed on Performa's, the total time interval of the recorded cases in Performa's was of two months (February to March 2011).

**Materials and Methods:** It is also a record based research retrospectively like the study of rural area, 55 cases recorded in a MLC centre of urban area of Abbottabad were recorded from the previously registered cases consecutively on designed Performa, Data of weapon used along with preliminary data was recorded of these registered cases and analysed.

**Results:** Among the 55 cases the weapon of offence used was Blunt, Sharp, Pointed, Fire Arm, RTA and others means thermal or chemical etc. The blunt weapon was used 33 ( 60% )cases, Sharp edged light weapon was used in 3 ( 5.5% ) cases, pointed weapon was used in 2 (3.6%) cases, Fire Arm in 8 (14.5%) cases, RTA cases were 8 (14.5%) and others in 1 (1.8%) cases.

**Conclusions:** The study represents the true picture of the province and society, being a comparative study it shows that there is not much difference in the society as a whole, in urban study no female was victimized among these 55 cases, the perpetrator used weapon only against male victims, which again shows less involvement of female population in daily disputes like rural area, the incidence of using Blunt weapon was higher, and the cases suffering from FAI and RTA were equal.

**Keywords:** FAI, RTA, MLC,

## INTRODUCTION

Before defining the term weapon, it is necessary to define certain other things ,which will not only be made to understand themselves, but they will also help us to create some idea about the weapon which have compulsory role in their infliction .Wound, means a solution or disruption of the anatomical continuity of any tissue of the body.<sup>1</sup> Injury, is defined as any harm whatever illegally caused to any person in the body, mind, reputation or property, and injuries caused by application of physical violence or force to the body are known as mechanical injuries.<sup>1</sup> Hurt; in law means, causing of pain, harm, disease, infirmity, injury or impairing , disabling or dismembering any organ of the body or part thereof without causing death, and they are classified on the bases of part of the body involved and manner of infliction.<sup>2</sup>

The wound, bodily injuries and hurt are caused by the application of force directly or indirectly along with other contributory factor e.g. the specific effect of the force, area over which the force act and the time taken over which the Kinetic energy is transferred.<sup>3,4</sup>

The attempt to apply force or to offer threat to the body of another one is termed in law as Assault while the

Battery is the term used when the force is actually applied to the body of another one e.g. punching some one or plucking of cloths.<sup>1</sup>

Weapon by definition is any instrument or object which when used is likely to cause injury, wound or hurt which may or may not lead to death, but if it causes the death or likely to cause the death of the victim then it is termed as dangerous weapon.<sup>5</sup> The weapon of offence is one which is used when the offence is committed, in committing crimes different things or weapon are used, they may be punch, shoe, stick, knife, needle, firearm, transporting machine, heat or chemical or fire, electricity, radiation and even water. All these things can be said the weapon of daily utility, but they are termed weapon of offence when offence is committed by use of any of them. The common dangerous weapon of offence among blunt weapon are stick, stone etc among sharp weapon are light weapons with sharp cutting edge e.g. knife and razor etc, and heavy weapons with sharp cutting edge e.g. hatchet, axe etc, among pointed weapons are dagger, ice pick etc, and firearms may be smooth or rifled bore.

It is possible to infer the type of weapon used in the assault or crime from an examination of wound, injury

pattern and findings in cloths. The hard blunt object can cause abrasions, contusions, lacerations and fractures either singly or in combination depending on the surface of the object, severity of blow and the part of the body struck. The surface of the weapon of offence coming in contact with the body may some time bear the pattern and give a clue to the weapon used e.g. chain, hammer etc. Some time the injury caused by blunt force or object may resemble incised wound caused by sharp weapon, but careful examination with magnifying lens will reveal the true nature of laceration caused by blunt weapon. Similarly the wound caused by sharp cutting weapon have clean cut edges and one caused by jagged edges of metal or glass will resemble this but on examination it will have irregular and bruised edges. The wound caused by heavy weapon with sharp edges will cause chop wounds and the edges will show bruising and marked destruction of under lying tissue, the dimension of such wound will correspond with the cross section of penetrating blade of the weapon. The pointed weapons cause specific wounds called penetrating or perforating wounds the weapon give specific shape to it, and if the wound is caused by fall on sharp pointed object, the broken pieces of it may be detected by magnifying lens in the depth of wound.<sup>6-8</sup> The fire arm wound also have there characteristic pattern by which the weapon can be identified whether it is smooth bored or rifled, So the injury pattern is playing important role in the identity of weapon of offence like in self inflicted wounds and defence wounds.

It is the duty of the medical examiner to identify the weapon of offence, Some time the weapon is brought by police along with victim or later during investigation, so he should ascertain, if the injuries could have been caused by the kind of weapon and in the manner as alleged by police or victim. The kind of weapon used can be judged from an examination of weapon for its appearance, weight, dimension and tip etc with special reference to the wound e.g. size, shape, margins, edges and direction etc. The weapon must also be examined for certain relevant things e.g. stain from victim or perpetrator, The wound for broken pieces of weapon in it, Cloths for tear or hole and blackening and its correspondence or correlations with injury and shape of weapon.

The medical officer, if convinced that the injuries are such as could not have been caused by the kind of weapon and in the manner suggested by police or the victim, he should record it so as to avoid unnecessary cross examination at the time of evidence and to withstand justice. The weapon should be described and labelled in such a way that, it is identifiable during evidence, Should be covered with cloth and sealed, signed, The signature of the constable should also be taken who receive it.<sup>9,11</sup>

The use of weapon also has relation with demography, customs, religion and circumstances. Different people use different weapons, it also varies in different areas, different customs, and in different circumstances e.g. Bandsola or fire Arm in war situations.<sup>12-13,19</sup>

## MATERIALS AND METHODS

A medico legal centre of an urban area of shaheed Benazir hospital Abbottabad was selected. The record of recorded cases was taken, researched and record was formed on Performa's, the total time interval of the recorded cases in Performa's was of two months (February to March 2011). The research was done on cases recorded consecutively; a questionnaire was formed in the Performa to record preliminaries and opinion about the type of weapon of offence, researched and data of the recoded information were made from the MLC register. Such register were available for the memory of MLO and judicial matters. The collected data was subjected to analysis; results were interpreted and compared with our previous study about the use of weapon of offence in cases of a rural population sample of victims.

## RESULTS

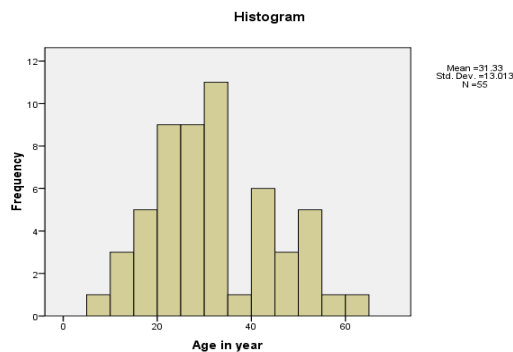
From the previously recorded MLC, cases of an urban area, 55 cases were selected, 100% were males and no female victim was there, the mean age of male was  $31.33 \pm 13.013$ , the occupation of most of the victims was in group of other type making 20 (36.4%), salaried were 14 (25.5%), businessman 11 (20%), manual workers were 6 (10.9%), professionals were 3 (5.5%) and the least sufferer was class of formers making 1 (1.8%).

The victims of other class had their mean age as  $27.50 \pm 15.969$ , the mean of age of salaried was  $33.71 \pm 11.405$  and those of business man were  $36.45 \pm 9.533$ .

The use of blunt weapon of offence was most common, making its use in 33 (60%) cases the age of most of them was between 15 and 35 years, the use of fire arm and road traffic accident were same making 8 (14.5%) and their age range was between 25 and 45 years, the sharp weapon was used in 3 (5.5%) cases their age group was 26–35 years and pointed weapon in 2 (3.6%) cases.

**Table No.1: Type of Weapons used**

Weapons	Frequency	Percent	Mean $\pm$ SD
Blunt	33	60.0	31.61 $\pm$ 14.029
Sharp Edged Light	3	5.5	31.00 $\pm$ 2.646
Pointed	2	3.6	27.00 $\pm$ 21.213
Firearm	8	14.5	31.62 $\pm$ 8.943
RTA	8	14.5	29.38 $\pm$ 14.947
Others	1	1.8	45.00 $\pm$ 0
Total	55	100.0	31.33 $\pm$ 13.013

**Figure No.1: Age in Years****Table No.2: Occupation**

Occupation	Frequency	Percent
Farmer	1	1.8
Manual Worker	6	10.9
Professional	3	5.5
Salaried	14	25.5
Business	11	20.0
Others	20	36.4
Total	55	100.0

**Table No.3: Types of Weapon used \* Age Group Cross tabulation**

Types of Weapon used	Age Group (Years)					Total
	5-15	16-25	26-35	36-45	>45	
Blunt	3	10	10	4	6	33
Sharp Edged Light	0	0	3	0	0	3
Pointed	1	0	0	1	0	2
Firearm	0	2	4	2	0	8
RTA	1	2	3	0	2	8
Others	0	0	0	1	0	1
Total	5	14	20	8	8	55

**Table No.4: Types of Weapon used \* Occupation Cross tabulation**

Types of Weapon used	Occupation						Total
	F	MW	P	S	B	O	
Blunt	0	5	3	9	3	13	33
Sharp Edged Light	1	0	0	2	0	0	3
Pointed	0	0	0	0	1	1	2
Firearm	0	1	0	1	4	2	8
RTA	0	0	0	2	2	4	8
Others	0	0	0	0	1	0	1
Total	1	6	3	14	11	20	55

F= Former, MW=Manual Worker, P=Professional, S=Salaried,  
B=Business, O=Other

The mean age of victims against whom blunt weapon was used by perpetrators was  $31.61 \pm 14.029$ , mean age of victims of sharp weapon was  $31.00 \pm 2.646$ , and mean

of age of victims of pointed weapon was  $27.00 \pm 21.213$ , that of victims of fire arm was  $31.62 \pm 8.943$

## DISCUSSION

This is a comparative study to our previous study about the use of weapon of offence in medico legal cases in a rural area of province of KPK, and was also compared with a national level study of urban area done in King Edward medical college Lahore. The results of our study were representing the true picture of society which is male dominated, in this study there were no female victim while in the study of rural area a small group of female which was 12.7% were victimized by the use of weapon, The victims of this study were 100% male, that of rural area 87.3% and of urban study of Lahore 85.44%.<sup>12</sup>

The mean age of victims of this study was  $31.33 \pm 13.013$ , while in that of rural area study mean age was  $37.73 \pm 13.661$ .<sup>14</sup> The mean age of rural study, on whom blunt weapon was used  $31.61 \pm 14.029$ , the sharp weapon was used in the group of mean age  $31.00 \pm 2.646$  years, pointed weapon was used on group of mean age  $27.00 \pm 21.213$  and the mean of age of victims of FA was  $31.62 \pm 8.943$ .<sup>14</sup> In this urban study the age group involved mostly was between 25 and 35 years and in rural area 62% were of age 30 years.

The occupation of victims in this study mostly was in other group e.g. students, making 20 (36.4%), salaried 14 (25.5%), business 11 (20.0%) and the least involved were former about 1.8%, while in rural study the formers were 23 (47.9%), salaried and manual worker 7 (14.6%), business man 5 (10.4%) and least has occupation as vocational.<sup>14</sup> This also shows the true difference in both areas working fields.

The weapons of offence used in this urban study of our is as, the blunt weapon was used in 33 (60.0%) cases, sharp in 3 (5.5%), pointed in 2 (3.6%), FA and road traffic accidents had 8 (14.5%) victims and others victims were 1.8%. The rural study had victims of blunt weapon about 31 (64.6%), sharp weapon 4 (8.3%), FA 3 (6.2%), RTA 10 (20.8%).<sup>14</sup> In comparison to our urban study the urban study of Tajammal N, *et al*<sup>12</sup> and Sultana K *et al*<sup>17,18</sup>, shows use of Fain 26.76% victims, 17.85% victims were due to RTA, and 10.80% victims were due to use of sharp weapon.

## CONCLUSION

In both of our studies the true picture of the province is presented and compared with the national scenario, The true difference between urban and rural attitude toward the use of weapon has been reflected, Due to the less involvement of female in life matters and less exposure to routine disputes, less time weapon has been used against them. The type of weapon mostly used was blunt, and the age group mostly involved in crime is



between 20 and 40 years and dangerous weapons were used by the perpetrators of age between 25 and 35 years.

## REFERENCES

1. Simpson K, Knight B. Forensic Medicine, London: Edward Arnold Publisher Ltd; 1985.
2. Qisas and Dyat Ordinance 1991, amended 1997. Government of Islamic Republic of Pakistan.
3. Awan NR. Principles and practice of Forensic Medicine, 1<sup>st</sup> ed. Lahore Pakistan: Sublime Arts; 2004.
4. Mason JK, editor. The Pathology of Violent Injury, 2<sup>nd</sup> ed. London: Edward Arnold; 1994.
5. Camps FE, editor. In: Gradwohl's legal Medicine, 2<sup>nd</sup> ed. Bristol UK: John wright & sons Ltd; 1968.
6. Di Maio D, Di Maio, V. Forensic Pathology. New York: Elsevier; 1989.
7. Shepherd JP, Shapland M, Pearce NX, Scully C. Pattern, severity and aetiology of injuries in victims of assault, Roy soc Med 1990;83:75–8.
8. Camps FE. Recent advances in forensic pathology. London: J & A Churchill Ltd; 1969.
9. Knight B. The Post-Mortem Technician's Handbook: A Manual of Mortuary Practice. Oxford: Blackwell Scientific Publications; 1984.
10. Walls HJ. Forensic Science: An introduction to scientific crime detection, 2<sup>nd</sup> ed. London: Sweet & Maxwell; 1974.
11. Boorman KE, Dodd BE, Lincoln PJ. Blood Group serology: Theory, Techniques, Practical applications, 5<sup>th</sup> ed. Edinburgh: Churchill Livingstone; 1977.
12. Tajammul N, Chaudhry TH, Hanif S, Bhatti MA. Profile of Medicolegal cases at Jinnah Hospital Lahore. Ann King Edward Med Coll 2005;11: 332–5.
13. Rao NG. Text book of Forinsic Medicine, 2<sup>nd</sup> ed. Japanese Brothers; 2010.p.
14. Ahmad I, Seema N, Humayun M, Raja Alvina. Weapon of offence used in bodily medicolegal injuries in a rural area. Med Forrum 2011; 22(5): 51–3.
15. Blood Group serology: Theory, Techniques, Practical applications, Kathleen e. Boorman, Barbara E. Dodd, P J Lincoln, 5<sup>th</sup> ed. Edinburg: Churchill Livingstone; 1977.
16. Krogman WM editors. The Human skeleton in Forensic Medicine. Springfield: Charles C. Thomas Publisher; 1962.
17. Sultana K, Anwer MA, Faizuddin. Trend of Medicolegal cases and their Postmortem Examination at Accident and Emergency Department of Jinnah Postgraduate Medical Centre, Karachi. Ann Abbasi Shaheed Hosp Karachi Med Dent Coll 1999;4:143–5.
18. Sultana K, Faizuddin, Ahsan R. Pattern of injuries during the last eight years (1991 - 1998) cases reported to Medicolegal Section JPMC, Karachi. Ann Abbasi Shaheed Hosp Karachi Med Dent Coll 1999;4:155–6.
19. Seema N, Ahmad I, Mughal S, Khan D, Khan O. Frequency and types of bodily medico-legal injuries in a rural area. J Ayub Med Coll Abbottabad 2010;22(2):93–5.

### Address for Corresponding Author:

Iftikhar Ahmad,  
Assistant Professor,  
Department of Forensic Medicine,  
Ayub Medical College,  
Abbottabad, Pakistan  
Cell: +92-300-5613983  
Email: doctor\_ia@yahoo.com

**Original Article**

# Frequency of Fetal Anomalies in Polyhydramniotic Patients Through Antenatal Ultrasound in Radiology Department of PIMS

1. Nuwayrah Jawaid 2. Shahla Zameer 3. Aliya Ahmed

1. Radiologist, Dept. of Radiology, FFM College / Hospital, Rawalpindi 2. Assoc. Prof. Dept. of Radiology, PIMS, Islamabad 3. Radiologist, PIMS, Islamabad

## ABSTRACT

**Objective:** To evaluate frequency of fetal anomalies in polyhydramniotic patients through antenatal ultrasound in Radiology Department of Pakistan Institute of Medical Sciences (PIMS).

**Study Design:** Cross Sectional Observational study

**Place and Duration of Study:** This study was conducted at the Mother and Child Health (MCH) Centre, Pakistan Institute of Medical Sciences (PIMS), Islamabad from January to December, 2003.

**Patients and Methods:** All women coming for antenatal ultrasound scan during the period January – December 2003 were included in this study. The ultrasound scans were done by the Radiology resident and confirmed by a single consultant radiologist. The data obtained was entered on a proforma.

**Result:** A total of 42(0.79%, n=5260) women were found to have polyhydramnios, out of which 11(26%) had associated fetal anomalies. Among all (11) anomalies detected, there were 5 cases (45.45 %) of anencephaly, 3 cases (27.27 %) of hydrocephalus, one of which had associated meningocele, and 01(9%) case each of omphalocele, spinal anomaly and skeletal dysplasia. 3 (27.27 %) women had concurrent disease.

**Conclusion:** Expert antenatal ultrasound is recommended to assess the presence of polyhydramnios and any associated fetal anomalies. Amniocentesis, glucose tolerance test or HbA1c levels are advisable when the suspicion of associated fetal anomalies is high.

**Key Words:** Polyhydramnios, Antenatal ultrasound, Amniotic fluid.

## INTRODUCTION

Polyhydramnios is defined as excessive amount of amniotic fluid surrounding the fetus.<sup>1</sup> It is both a symptom and a threat, occasionally associated with fetal or maternal abnormalities<sup>2</sup>. Its significance is also due to the fact that even if it is idiopathic it can lead to premature rupture of the membranes, premature labour and premature delivery.<sup>3,4,5</sup> Hence, this study was conducted to evaluate all women coming for antenatal ultrasound, and to identify the occurrence of concurrent abnormalities.

Assessment of liquor volume is usually subjective. However, the following parameters for its assessment have been developed. Firstly, an amniotic fluid index (AFI) greater than 24, AFI (measured in cm) being the sum of the single deepest pocket of amniotic fluid in each of the 4 quadrants.<sup>6</sup> Secondly, largest fluid pocket greater than 8 cm is indicative of polyhydramnios. Thirdly, if the fetus does not fill the AP diameter of the uterus, it is considered to be polyhydramnios.<sup>3,7</sup>

The incidence of the major groups of causes is idiopathic causes 60%, maternal causes 20% and fetal causes 20%.<sup>7,8,9</sup>

Maternal causes include diabetes mellitus, hypertension, obesity, rhesus incompatibility, anemia, congestive cardiac failure and syphilis.

Fetal causes encompass lesions, malformations and abnormalities of the CNS, gastrointestinal tract, thorax, heart, musculoskeletal system and urinary tract. Other conditions causing polyhydramnios include twin-twin transfusion, fetal hydrops, infections, metabolic and chromosomal disorders, various neck masses and other miscellaneous conditions.

CNS lesions include neural tube defects like anencephaly, hydrocephalus, holoprosencephaly, encephalocele, hydranencephaly, meningocele, Dandy Walker malformation, agenesis of the corpus callosum and lissencephaly.

Obstructive malformations of the gastrointestinal tract comprise tracheoesophageal fistula, esophageal, duodenal and jejunal atresias, congenital pancreatic cysts, annular pancreas, gastroschisis, meconium peritonitis, bowel perforation, and hepatic tumours<sup>10</sup>.

Thoracic abnormalities include cystic adenomatoid malformation, primary pulmonary hypoplasia, diaphragmatic hernia, congenital chylothorax, mediastinal and lung masses like teratoma, tracheal atresia and pulmonary sequestration.

Cardiac causes of polyhydramnios are arrhythmias, myocardial disorders, ventricular septal defects, coarctation of aorta, interruption of fetal aorta, truncus arteriosus, ectopia cordis and high output states like teratoma

Musculoskeletal abnormalities include achondroplasia, osteogenesis imperfecta, hypophosphatasia, platyspondyly, and camptomelic and thanatophoric dwarfism

Urinary tract anomalies e.g. vesicoureteric reflux, ureteropelvic junction obstruction, congenital mesoblastic nephroma

Infections like toxoplasmosis and cytomegalovirus; metabolic disorders such as Gaucher's disease and mucopolysaccharidosis; and chromosomal anomalies like trisomies 18, 21 and 13-15 and Turner's syndrome can also cause polyhydramnios.

Other causes include neck masses that cause extrinsic compression of the esophagus and impairment of swallowing like cystic hygroma and congenital goiter and miscellaneous conditions such as sacrococcygeal teratoma and ovarian cyst.<sup>11</sup>

## MATERIALS AND METHODS

**Subjects:** All pregnant women coming for antenatal ultrasound were included in this study irrespective of their age or the presence or absence of systemic diseases or risk factors.

**Apparatus:** Schimadzu ultrasound machine was used for doing the ultrasound scans and all positive cases were further evaluated and reported by a single consultant radiologist.

**Method:** This was a cross sectional observational study conducted at the Mother and Child Health (MCH) Centre, Pakistan Institute of Medical Sciences (PIMS), covering the period January to December, 2003.

All women presenting for antenatal ultrasound were included in the study. All records were scrupulously maintained on a proforma, and the presence of polyhydramnios and any associated fetal or maternal abnormalities was recorded meticulously.

## RESULT

A total of 5260 women were included in the study. of these, 42 were found to have polyhydramnios (Figs Nos. 1,2,3 ), out of which 11 women had associated fetal anomalies (Table No.1).

Out of a total of 42 women showing polyhydramnios, 11 were found to have associated fetal anomalies. Of these 11 patients, 5 had anencephaly, 2 hydrocephalus alone, and one each of hydrocephalus with meningocele, omphalocele, spinal anomaly and skeletal dysplasia. Three women had associated maternal problems, two being diabetic and one hypertensive.

## DISCUSSION

The purpose of this study was to analyze the prevalence of polyhydramnios, which is a problem seen quite regularly in a tertiary care hospital like PIMS. In addition, the association of polyhydramnios with fetal anomalies was also assessed.

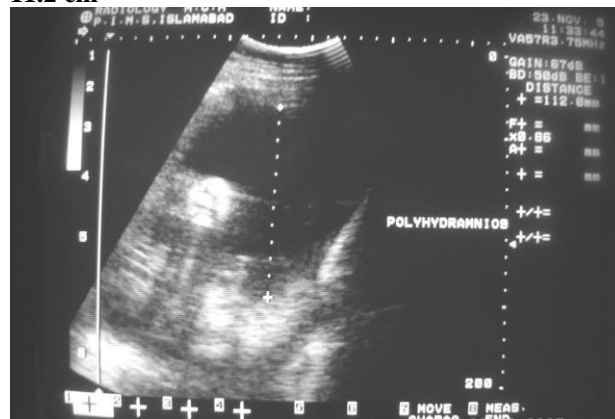
**Table I: Number of patients with polyhydramnios and fetal anomalies**

Month	Total antenatal ultrasound	No. of polyhydramnios	No. of fetal anomalies
January	404	6	1
February	622	4	Nil
March	500	3	1
April	266	2	1
May	513	9	4
June	597	4	Nil
July	620	2	Nil
August	308	2	Nil
September	372	4	1
October	353	4	1
November	352	2	2
December	353	Nil	Nil
<b>Total</b>	<b>5260</b>	<b>42</b>	<b>11</b>

**Figure No.1: Anencephalic fetus with polyhydramnios**



**Figure No. 2: Polyhydramnios with a large pocket of 11.2 cm**



**Figure No. 3: Fetus with polyhydramnios**

The incidence of polyhydramnios in our study was 0.79%, which is less than the internationally published value of 1.1-3.5%,<sup>7</sup> or 2% from another source<sup>12,13</sup>.

In our study, the anomalies detected were anencephaly, hydrocephalus alone and with meningocele, omphalocele, spinal anomaly and skeletal dysplasia. The commonest association detected was with anencephaly of which five cases were seen,<sup>17</sup> 11.9% of the total. This corresponds to the published value of 9-16% for neural tube defects.<sup>7</sup> Anencephaly is the single most common fetal anomaly causing hydrocephalus.<sup>11</sup> Next in order of frequency was hydrocephalus with meningocele, 7.1 % of the total.

Omphalocele comprised 2.38% of the total anomalies detected which compares with 2.5% reported in the Indian literature<sup>18</sup>. Spinal anomalies also comprised 2.38% which is much less than the 7.5% reported<sup>18</sup>. Skeletal dysplasia again comprised 2.38% of the total cases of polyhydramnios.

Maternal causes were seen in 7.14% of the patients, 4.76% having diabetes, and 2.38% being hypertensive. In published data, maternal causes account for 20%, of which 5% are diabetic.<sup>7</sup> The percentage of diabetics with polyhydramnios in our study corresponds to the published data<sup>7</sup>. Other studies report an incidence of 10.8%<sup>14</sup> and 14%<sup>15</sup>.

In 66.7% of our cases of polyhydramnios, no maternal or fetal cause could be ascertained. This is slightly more than the 60% reported in the literature.<sup>7,8,16</sup> The reported incidence of fetal anomaly was 18.9 % in international literature.<sup>2,6</sup>

In view of our population characteristics that generally diseases and anomalies of all types are more common in our set up, it is surprising that the incidence of polyhydramnios in our setup was found to be lower than in Western literature. This raises certain questions:-

(i) Are we following the same criteria when diagnosing polyhydramnios?

(ii) Should we, being an Asian set up, be following the same criteria or should we be using a different set of criteria for evaluating polyhydramnios?

As Pakistani/Asian babies tend to be smaller, the normal upper limit of AFI may generally be smaller in such pregnancies. Hence many pregnancies may be found to have polyhydramnios if a lower set of values is taken as normal.

(iii) Incidentally, the association of maternal problems with polyhydramnios was found to be lower in our study.<sup>11</sup> Are we evaluating for diabetes and hypertension according to set criteria or is our pregnant population younger than in other countries and such problems have not yet developed in them? For evaluation of diabetes mellitus, glucose tolerance test is advisable<sup>19,20</sup>, which recommendation is not routinely followed and only random glucose level assessment is performed. Alternatively, HbA1c level on a single fasting sample is advisable and less cumbersome than glucose tolerance test.<sup>21</sup>

## CONCLUSION

Antenatal ultrasound by an expert in the field is recommended to assess the presence of polyhydramnios and any associated fetal anomalies. Amniocentesis, glucose tolerance test or HbA1c levels are to be performed as an adjunct in diagnosis when the index of suspicion of associated fetal anomalies is high.

## REFERENCES

1. Hart JA. Medical Encyclopedia: Polyhydramnios. 2004 Jan [cited 2005 Nov]. Available from: URL:<http://www.nlm.nih.gov/medlineplus/ency/article/003267.htm>
2. Mazor M, Ghezzi F, Maymon E, Shoham-Vardi I, Vardi H, Hershkowitz R, et al. Polyhydramnios is an independent risk factor for perinatal mortality and intrapartum morbidity in preterm delivery. Eur J Obstet Gynecol Reprod Biol 1996 ;70:41-7.
3. "Pregnancy" Encyclopedia Britannica from Encyclopedia Britannica Premium Source [cited 2005 Dec]. Available from: URL:<http://www.britannica.com/eb/article?tocId=76099>
4. Chen KC, Liou JD, Hung TH, Kuo DM, Hsu JJ, Hsieh CC, et al. Perinatal outcomes of polyhydramnios without associated congenital fetal anomalies after the gestational age of 20 weeks. Chang Gung Med J 2005;28:222-8.
5. Phelan JP, Park YW, Ahn MO, Rutherford SE. Polyhydramnios and perinatal outcome. J Perinatol. 1990 ;10:347-50.
6. Thompson O, Brown R, Gunnarson G, Harrington K. Prevalence of polyhydramnios in the third trimester in a population screened by first and

- second trimester ultrasonography. J Perinat Med 1998;26:371-7.
7. Dahnert W. Radiology review manual. 5<sup>th</sup> ed. Philadelphia: Lippincott Williams & Wilkins 2003.p.989-90.
  8. Kahn CE. Polyhydramnios 2002 [cited 2005 Nov]. Available from: URL:<http://chorus.rad.mcw.edu/to-go/00329.html>
  9. Nabeela Waheed, Mussarat Ashraf. Fetal outcome in pregnancies with Polyhydramnios. J Rawal Med Coll 2003;7:73-6.
  10. Dashe JS, McIntire DD, Ramus RM, Santos-Ramos R, Twickler DM. Hydramnios: anomaly prevalence and sonographic detection. Obstet Gynecol 2002 ;100:134-9.
  11. Bisset RAL, Khan AN, Thomas NB, editors. Differential diagnosis in obstetric and gynecologic ultrasound. 2<sup>nd</sup> ed. London: Elsevier Science Limited; 2002.p.64-70.
  12. Medical references: Amniotic fluid abnormalities 2005 [cited 2005 Nov]. Available from: URL:[http://www.marchofdimes.com/printableArticles/681\\_4536.asp](http://www.marchofdimes.com/printableArticles/681_4536.asp)
  13. Mathew M, Saquib S, Rizvi SG. Polyhydramnios. Risk Factors and outcome. Saudi Med J 2008;29: 256-60
  14. Chetrit AB, Celnikier DH, Ron M. Hydramnios in the third trimester of pregnancy. A change in the distribution of accompanying fetal anomalies as a result of early ultrasonographic prenatal diagnosis. Am J Obstet Gynecol 1990; 162: 1344-5.
  15. Carlson DE, Platt LD, McDearis AL. Quantifiable polyhydramnios. Diagnosis and management. Obstet Gynecol 1990; 75: 989-93.
  16. Panting-Kemp A, Nguyen T, Chang E, Quillen E, Castro L. Idiopathic polyhydramnios and perinatal outcome. Am J Obstet Gynecol 1999 Nov;181 (5 Pt 1):1079-82
  17. Desmedt EJ, Henry OA, Beischer NA. Polyhydramnios and associated maternal and fetal complications in singleton pregnancies. Br J Obstet Gynaecol. 1990 ;97:1115-22
  18. Clinical and ultrasonographic evaluation of polyhydramnios [cited Dec 2005]. Available from: URL:[http://www.journal\\_obgyn\\_india.com/articles/issues\\_march\\_april2003/o\\_papers\\_145.asp](http://www.journal_obgyn_india.com/articles/issues_march_april2003/o_papers_145.asp)
  19. Polyhydramnios and oligohydramnios [cited Dec 2005]. Available from: URL:<http://www.emedicine.com/ped/topic1854.htm>
  20. Gestational diabetes mellitus – management and guidelines [cited Apr 2008]. Available from: URL:<https://www.mja.com.au/public/issues/jul20/hoffman/hoffman.html>
  21. Gestational diabetes screening of a multiethnic, high-risk population using glycat proteins[cited Apr 2008]. Available from: URL:<http://linkinghub.elsevier.com/retrieve/pii/S0168822700002060>

#### Address for Corresponding Author:

Dr. Nuwayrah Jawaid  
Radiologist,  
Dept. of Radiology, FFM College / Hospital,  
Rawalpindi.  
Ph # 0345-5058426  
Email: nuwayrah@gmail.com

S

**Original Article**

# Co Relation of Thyroid Function Test with the Clinical Presentation

**1. Tariq Saeed 2. Shahid Mahmood 3. Muhammad Taimur 4. Sadaf Faisal Bhopal**

1. Consultant Surgeon, FFH, Rawalpindi 2. Assoc. Prof. of Surgery, FUMC, Rawalpindi 3. Registrar of Surgery, FUMC, Rawalpindi 4. Medical Student, Wah Medical College, Wah Cantt., Rawalpindi

## ABSTRACT

**Objective:** To correlate the biochemical thyroid profile with the clinical presentation of the patient and decision about the time of surgery.

**Study Design:** It is an analytical cross sectional study.

**Place & Duration of Study:** This study was carried out in the Department of Surgery, Fauji Foundation Hospital, Rawalpindi from 1<sup>st</sup> January 2010 to 31<sup>st</sup> March 2011

**Patients & Methods:** Thirty patients were included in this study after taking consent & approval from the ethical committee of the hospital. All of them were females. Age ranges between 13 to 45 with mean of 22.26 years. These patients presented with a swelling in front of neck with or without signs of hypothyroidism or hyperthyroidism. Trial of 6 to 12 months given to every patient to bring the TFT's within normal range. Only those patients were included in the study who took the medicines regularly. Mode of presentation was out door department of Fauji Foundation Hospital Rawalpindi. Patients were examined clinically by surgeon and anesthetist for risk assessment. Routine laboratory investigations including thyroid function test were requested and analyzed by operating surgeon. TFT's were co-related with the clinical signs and symptoms of the patients. Patients were divided into two groups. Group one includes clinically euthyroid patients with TFT's within normal range. Group two again include clinically euthyroid patients but abnormal TFT's.

**Results:** A total of 30 patients were included in this study. All of them were females & clinically euthyroid. Mode of presentation was the outdoor patient department of Fauji Foundation hospital. Presenting complaint was swelling in front of neck. 23 out of 30 patients (66.6 %) had normal TFT's & clinically euthyroid. 7 out of 30 Patients (33.3%) shows variation between their thyroid profile and clinical presentation. Sub or near total thyroidectomy was done in all the patients. Recovery was un-eventful.

**Conclusion:** Operation on thyroid gland is a major undertaking & decision should be taken by senior surgeon. Ideally TFT's should be within normal range as well as patient should be euthyroid clinically in order to avoid post operative complications. In those cases where patient is clinically euthyroid but biochemically status is either hyper or hypo thyroid, surgery can be done after clinical trial of at least six months with thyroxin or anti thyroid drugs with a view to bring the TFT's within normal range. We can conclude that although the biochemical profile of the patients with thyroid disease is important but in country like Pakistan where thyroid hormonal assay is not easily available the surgery can be done by careful clinical assessment, keeping in view compliance of patient, regularity of taking medicine, clinical status & side effects of medical treatment.

**Keywords:** Thyroidectomy, thyroid function test, Hyperthyroidism, hypothyroidism.

## INTRODUCTION

The mountain regions in north-west of Pakistan & Kashmir are probably the worst affected areas in the World<sup>1-2</sup>. These areas are labeled as goiter belt due to high incidence of the disease in the area<sup>3</sup>. Through the incidence of goiter is remarkably decreased all over the world in the last 30 years due to introduction of iodinated salt but the situation is otherwise here. Commonest source of water in the hilly areas of Pakistan is obtained from fountains which is very deficient in iodine & fails to meet the daily requirements. The recommended daily allowance of iodine is about 100 nanogram per day<sup>2</sup>. The deficiency of iodine can cause a lot of complications like goiter,

mental retardation, cretinism, high infant mortality rate, decreased fertility rate & increased perinatal death rate<sup>4</sup>. The iodine deficiency goiter starts as diffuse involvement of the gland due to raised levels of TSH. Later on, the diffuse enlargement develops nodularity due to fluctuating level of TSH & unequal sensitivity of thyroid cells to the stimulating hormone. Multinodular goiter is the most common presentation of thyroid disease in these areas. The female preponderance is well known & is due to increase requirement of iodine at the age of puberty (puberty onset goiter). Another situation when females require extra iodine is during pregnancy as discuss in detail by M A Zahid et al in Annals of PIMS (January 2006).

Thyroid is a Greek word means "shield" after the shape of the related thyroid cartilage. The most common problem of the thyroid gland is enlargement of gland which is known as goiter. It can be multi nodular, which is the commonest variety seen in our country or diffusely enlarge. Clinically patient can be euthyroid, hyperthyroid or hypothyroid. Graves disease, named after Graves<sup>5</sup> who first time described it in 1935, is a triad of hyperthyroidism with diffuse enlarge thyroid, ophthalmopathy with exophthalmos & pretibial myxedema. It usually occurs in young females & there is production of auto antibodies that act on TSH receptors. Hypothyroidism may occur as a result of congenital thyroid abnormalities, autoimmune disorders such as Hashimoto's thyroiditis (which is common in females of above 40), iodine deficiency (commonest cause in Pakistan) or the removal of the thyroid following surgery.

A number of studies have sought to determine age related changes in thyroid profile<sup>6</sup>. It was found that lower serum T3 levels and higher rT3 levels were detected in the institutionalized elderly adults. Probably, these changes occur in thyroid profile are due to non thyroidal illness. Two studies that evaluated thyroid hormone profiles in healthy adults have clarified this issue. One study that measured T3 and free T3 levels in healthy adults aged 65 and older determined that while levels of these hormones were lower than in younger adults, they fell well within the limits of reference ranges<sup>7</sup>. Another study of thyroid hormone profiles in a range of healthy adults who were not taking prescribed medications determined that there were no significant differences in T4, free T4, T3 & free T3 levels between groups stratified by age<sup>8</sup>.

Abnormalities in thyroid profile can complicate Hyponatremia, Hyperlipidemia, myopathy with increased creatine phosphokinase levels, hypo chromic microcytic anemia (up to 15% in primary hypothyroidism<sup>24</sup>) increased homocysteine and lipoprotein levels with primary hypothyroidism, potentially contributing to an increased risk of atherosclerotic disease<sup>9</sup> are few examples of complicate thyroid physiology.

## PATIENTS & METHODS

Thirty patients were included in this study after taking consent & approval from the ethical committee of the hospital. All of them were females. Age ranges between 13 to 45 with mean of 22.26 years. These patients presented with a swelling in front of neck with or without signs of hypothyroidism or hyperthyroidism. Trial of 6 to 12 months given to every patient to bring the TFT's within normal range. Only those patients were included in the study who took the medicines regularly. Mode of presentation was out door

department of Fauji Foundation Hospital Rawalpindi. Patients were examined clinically by surgeon and anesthetist for risk assessment. Routine laboratory investigations including thyroid function test were requested and analyzed by operating surgeon. TFT's were co-related with the clinical signs and symptoms of the patients. Patients were divided into two groups. Group one includes clinically euthyroid patients with TFT's within normal range. Group two again include clinically euthyroid patients but abnormal TFT's.

### Inclusion Criteria

Age between 12 to 45, clinically euthyroid with normal or abnormal levels of T3 & T4 and ASA1 were included in the study. Patients who showed poor compliance with irregular medication were excluded from the study.

## RESULTS

All 30 patients were females & clinically euthyroid. Youngest patient was 13 years old while oldest one was 49 with a mean of 22.26 years. On admission vitals were noted. Average pulse was 74 beat per minute while blood pressure was 125/85. No other co-morbid factors present & all the patients ranked as ASA 1 by anesthesiologist. 8 out of 30 give H/O dysphagia while 9 out 30 complaint of difficulty in breathing at night. 13 patients were worried about their cosmetic problem.

**Table No.1 showing presenting complaints.**

Total	30
Dysphagia	8
Difficulty in breathing	9
Cosmetic problem	13

7 (33.3%) patients out of 30 showed variation between their biochemical thyroid profile and clinical presentation. Two (6.6%) patients showed elevated levels of T3 and T4 and decreased levels of TSH. Two (6.6 %) patients had T3 & T4 below normal levels & raised TSH. 2 patient showed normal level of T3, T4 but decreased level of TSH. One patient (3.3%) showed elevated levels of T3 and normal level of T4 and decreased level of TSH. 22 out of 30 patients had subtotal while 8 had near total thyroidectomy. As thyroid surgery is a safe surgery if done by an experienced surgeon. Very few complications were noted which were given in table 2. Hoarseness of voice settles in 2 weeks while symptoms of hypoparathyroidism disappeared within 5 days.

**Table No. 2: Showing complications of thyroidectomy.**

Total	Hoarseness of voice	Symptoms of hypoparathyroidism	Blood transfusion	Skin infection
30	2	1	7	1

Seven patients required blood transfusion pre or post operatively. Nine patients had tachycardia of 96 beat per minute on first post op day which settles completely on second post op day. Tachycardia was attributed to anemia, pain, anxiety & other post op factors. Drain was removed on first or second post op day. Recovery was un-eventful. All the patients discharged on 2<sup>nd</sup> post op day. Skin stitches were removed on 5<sup>th</sup> day & TFT's repeated after 1, 3 & 6 months as a policy of the department. Interestingly after 3 months, clear cut correlation was seen between TFT's & clinical status of the patients.

## DISCUSSION

Most of the studies published all over the world shows that thyroid disease is a predominant disease of female gender<sup>10-11</sup>. In our study, all the 30 patients were female.

Another point noted by the team of surgeons in our department is 7 patients (33 %) presented with abnormal TFT's but they were euthyroid clinically. The interpretation of thyroid function test profiles in hospitalized patients must be tempered by an understanding of how non thyroidal illnesses may produce changes in TSH and thyroid hormone levels. The direction and extent of changes observed may depend on the severity of an underlying illness and the point in the course of recovery at which thyroid function tests are measured<sup>12</sup>. Longitudinal studies have demonstrated that early on in the course of severe illnesses or protracted procedures, TSH levels in euthyroid patients may decline to levels that fall below the lower limits of normal reference ranges<sup>13</sup>. This change may be paralleled by a decline in T4 and T3 levels that may be particularly pronounced in elderly patients. One study demonstrated that 59% of elderly patients known to be euthyroid had documented low T3 levels measured during a course of hospitalization, whereas another demonstrated that changes in T3 levels detected in elderly hospitalized patients were more closely correlated with the severity of each underlying illness than with advanced age itself<sup>14</sup>. In our study, 6.6 % of patients had below normal T4 levels with raised TSH though T3 was normal. Another 6.6 % had both below normal T4 & T3 levels with raised TSH.

Although data from the NHANES III study has established that median TSH levels appear to increase with advancing age, the normal upper limit of established reference range may still be used as a cutoff to confirm the diagnosis of primary hypothyroidism in most elderly patients. While a blood spot TSH level has been shown to be an adequate screening test for the detection of overt primary hypothyroidism in the elderly, it may not be sensitive enough to detect cases of subclinical hypothyroidism characterized by elevated

serum TSH levels with normal T4 or free T4 levels<sup>15</sup>. One study has determined that there may be a negative correlation between age and the degree to which TSH levels are elevated in elderly patients presenting with primary hypothyroidism<sup>16</sup>. In cases of suspected secondary hypothyroidism that may result from disruption of the anatomy or function of the hypothalamic-pituitary axis, the TSH level may not be relied upon as an accurate index of thyroid function. In this setting the free T4 level may serve as more reliable measure of thyroid hormone production.

Current data indicates that the normal or low TSH levels found in the presence of low T4 and T3 levels in the setting of nonthyroidal illness likely reflect the combined effects of central hypothyroidism and reduced peripheral generation of T3, effectively representing a deficiency of thyroid hormone. Whether this condition should be treated with administration of thyroid hormone preparations remains controversial. Some observers argue in favor of thyroid hormone replacement, while others weigh against it, without conclusive data to support either viewpoint<sup>17</sup>.

In cases where changes in TSH and thyroid hormone levels may be plausibly ascribed to nonthyroidal illness, the patient's thyroid function tests should be reassessed one to two weeks later to see if observed changes are resolving. One study completed 24 years ago that tracked thyroid function test profiles in hospitalized elderly female patients showed that while 14% of the subjects had increased TSH levels and decreased T4 and T3 levels on initial assessment, only 2% were proven to have evidence of underlying primary hypothyroidism in follow up<sup>18</sup>.

Estimates of subclinical hypothyroidism range between 3–8%. Incidence is more common in women than in men<sup>19</sup>. A 2007 meta-analysis by the Cochrane Collaboration found no benefit of thyroid hormone replacement except in some parameters of lipid profiles and left-ventricular function

We can see that there are many factors in the body which can change the levels of T3, T4 & TSH levels and it is not easy to interpret the thyroid profile co relating with the clinical status of the patient. So clinical thyroid status is very important to decide about the time of surgery in conditions where ambiguity exists and hormonal assay does not relate with the clinical status of the patient. The physiology of thyroid gland is very complex. The production, conversion and uptake of thyroid hormone in the body involve several steps. A malfunction in any of these steps can cause hypothyroid symptoms, but may not show up on standard lab tests<sup>20</sup>. It's incorrect and even negligent to assume that all cases of hypothyroidism share the same cause and require the same treatment. Subclinical hypothyroidism occurs when thyrotropin (TSH) levels are elevated but thyroxine (T4) and triiodothyronine (T3) levels are



normal. The levels of the active hormones will be within the laboratory reference range. About three percent of the general population has hypothyroidism<sup>21</sup>.

## CONCLUSION

We concluded that although the biochemical profile of the patients with thyroid disease is very important factor but clinical signs and symptoms of the patients have come out to be other important criteria. 33.3 % of the total patients had clinical presentation different from biochemical profile and decision about the time of surgery was planned on their clinical status. Patient remained well during and after the surgery. So it is recommended in country like Pakistan where thyroid hormonal assay is expensive, not easily available, laboratory error, compliance of patients e.t.c, the decision about surgery should be taken as last step if clinically patients are euthyroid & no other risk factors are present.

## REFERENCES

1. Sooch SS, Deo MG, Karmarker MG. Prevalence of endemic goiter with iodized salt. Bull WHO 1973; 49:307
2. Zafar A. Survey of school going children in Murree for prevalence of goiter. J Surg PIMS 1993;(3): 62-5
3. Zahid MA. Role of thyroid scan in the management of thyroid disorders. Annal of PIMS 2006;2(1).
4. Delang F. The disorders induced by iodine deficiency thyroid. 1994;4(1):107-28.
5. Robbins and Cotran. Pathologic Basis of Disease. 8<sup>th</sup> ed. Philadelphia: W B Saunders; 2011.p.1117.
6. Yalcin B, Ozan H. "Detailed investigation of the relationship between the inferior laryngeal nerve including laryngeal branches and ligament of Berry". J Am College of Surgeons 2006;202(2): 291-6.
7. Venturi S, Donati FM. "Environmental iodine deficiency: A challenge to the evolution of terrestrial life?" Thyroid. J American Thyroid Association 2000;10 (8): 727-728
8. Küpper FC, Carpenter LJ, McFiggans GB, et al. "Iodide accumulation provides an inorganic antioxidant impacting atmospheric chemistry" Proceedings of the National Academy of Sciences of the United States of America 2008;105(19): 6954-8.
9. Venturi S; Bégin ME. "Thyroid Hormone, Iodine and Human Brain Evolution". Environmental Influences on Human Brain Evolution. John Wiley & Sons 2010.p.105-124.
10. Klofanda J. Thyroid surgery at the first surgical clinic of the first medical school of Charles University and Genetic Medical School Hospital in Prague; Review of Problems.1998;77(10):435-40.
11. Korcen N, Asci C, Yilmazlem T. Total thyroidectomy or lobectomy in benign nodular disease of thyroid. Int Surg 1997;82 (4):417-9
12. Brown-Grant. "Extrathyroidal iodide concentrating mechanisms". Physiol Rev 1961;41:189.
13. Spitzweg C, Joba W, Eisenmenger W, Heufelder AE. "Analysis of human sodium iodide symporter gene expression in extrathyroidal tissues and cloning of its complementary deoxyribonucleic acid from salivary gland, mammary gland, and gastric mucosa". J Clin Endocrinol Metab 1998;83:1746.
14. Banerjee RK, Bose AK, Chakraborty TK, Datta AG. "Peroxidase catalysed iodotyrosine formation in dispersed cells of mouse extrathyroidal tissues". J Endocrinol 1985;2:159.
15. Eugster, Erica A, Pescovitz, Ora Hirsch. Pediatric endocrinology. Mechanisms, manifestations and management. Lippincott Williams & Wilkins 2004. ISBN 0-7817-4059-2.
16. Zoeller RT. "Transplacental thyroxine and fetal brain development". J Clin. Invest 2003;111 (7): 954-956
17. Berbel P, Navarro D, Ausó E, Varea E, Rodríguez AE, Ballesta JJ, et al. Role of late maternal thyroid hormones in cerebral cortex development, an experimental model for human prematurity. Cereb Cortex 2010;20(6):1462-75.
18. Don F, Ronald J. Bloom & Fawcett's Concise Histology. New York: Arnold Publishers; 2002.p.257-258.
19. Yamamoto M, Shibuya N, Chen LC, Ogata E. "Seasonal recurrence of transient hypothyroidism in a patient with autoimmune thyroiditis". Endocrinol. Jpn 35 (1):135-42.
20. Hidaka Y, Amino N, Iwatani Y, Itoh E, Matsunaga M, Tamaki H. "Recurrence of thyrotoxicosis after attack of allergic rhinitis in patients with Graves' disease". J Clin Endocrinol Metab 77 (6):1667-70.
21. Nussey S, Whitehead S. Thyroid Gland Endocrinology: An Integrated Approach. Published by BIOS Scientific Publishers Ltd. 2001.

### Address for Corresponding Author:

Dr Tariq Saeed,  
Consultant Surgeon,  
Fauji Foundation Hospital Rawalpindi  
Mobile: 0321-5871036  
E- mail: surgeontariq@ yahoo.com

**Original Article**

# Presentation and Outcome of Surgical Management of Strangulated Inguinal Hernia at Liaquat University Hospital Hyderabad

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

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

## ABSTRACT

**Aim:** The objectives of the study are to determine the incidence of strangulated inguinal hernia in patients presenting with irreducibility and obstruction, evaluate the age and sex incidence, see the duration of hospital stay in our setup and see the post operative morbidity and mortality.

**Study Design:** Experimental Study.

**Place and Duration of Study:** This study was carried out in Surgical Unit-IV, Liaquat University Hospital Jamshoro, from 2007 to 2009.

**Materials and Methods:** 100 cases of obstructed hernia were selected out of which 85 with strangulation were included in this study. These patients were admitted through the outpatient department, as well as from casualty department of Liaquat University Hospital Jamshoro/Hyderabad. All these patients were admitted in emergency. Results were prepared with help of tables and graphs. Data was analyzed through SPSS software.

**Results:** 140 patients presenting with obstructed hernia were selected of which 85 were found to have strangulated hernia. There was wide variation of age ranging from a minimum 15 to 70 years with the mean age 42 years. 55 patients had Right sided hernia 64.7% and 30 patients had Left sided hernia 35.2% and no patient with bilateral strangulated inguinal hernia reported 0%. During surgery of 60 patients (70.5%) had gangrenous omentum while 23 cases (27%) ileum was non viable so we had to resort to resection and anastomosis, two cases (2.3%) Ileum was so much contaminated so we had to resort to Ileostomy and two case (2.3%) sigmoid colon was involved so we had to resort to colostomy.

Postoperatively majority of them developed wound infection 14 (16.4%) followed by chest infections 10 (11.7%) Haematoma formation was reported in 5 (5.8%) and retention of urine in 3 patient (3.5%).

**Conclusion:** Good pre-operation assessment and early management will decrease the morbidity and mortality in strangulated inguinal hernia.

**Key Words:** Strangulated Inguinal Hernia, irreducibility & obstruction, Ileostomy, colostomy.

## INTRODUCTION

A hernia is the protrusion of part of the abdominal contents beyond the normal confines of the abdominal wall<sup>1</sup>. The word "hernia" is derived from a Greek word "hernios" which means "branch or off shoot"<sup>2</sup>.

Hernia is a common condition afflicting both men and women since time immemorial. Inguinal hernia is protrusion of abdominal contents through 4 cm long inter muscular slit lying above the medial half of inguinal ligament called inguinal canal. It may be direct (i.e. defect in the transverses abdominus aponeurosis and transversalis fascia) or indirect (i.e. protrusion through and opening in the internal ring)<sup>3,4,5</sup>. A hernia, from which a contained organ cannot be reduced, is said to be irreducible or incarcerated; if in addition to incarceration there is a compromise of the blood supply of the contained organ, than this hernia is said to be strangulated. Strangulated hernias are particularly

dangerous because they lead to tissue necrosis and can progress to severe complications like perforation, sepsis and even death. So it's a surgical emergency.

Diagnosis of hernia is purely clinical but there is long list of surgical methods available for the management of strangulated inguinal hernia and techniques are improving day by day. It depends on the surgeon's choice that what method he prefers to manage the condition.

Different surgical methods are performed all over the world for the management of strangulated hernia and the techniques are improving day by day. The less the post-surgical complication related to the procedure more would be the preference for management.

Constipation, abdominal distension, absent bowel sounds and redness of swelling are important pre-operative findings associated with morbidity and mortality<sup>7</sup>.

Object of this study will reflect the presentation, surgical management and outcome of surgical management of strangulated inguinal hernia in our setup.

## MATERIALS AND METHODS

This study was carried out in the General surgical department at Liaquat University Hospital Hyderabad, Sindh, Pakistan from 2007 to 2009. This study consisted of 140 patients of diagnosed case of obstructed hernia were admitted. 140 patients selected out of which 85 with strangulation were included in this study. All these patients were admitted in emergency.

Patients whose hernias were reduced spontaneously and those in whom gut was not strangulated during operation were excluded from study. In each case relevant printed Performa was filled, which included detailed clinical history of patient, physical examination, clinical findings and clinical diagnosis. All patients underwent for base line investigations.

Resection was restored to end to end anastomosis was done when the gut was found to be gangrenous. In recurrent cases especially very elderly, consent was obtained for orchidectomy before surgery.

## RESULTS

140 patients presenting with obstructed hernia were selected of which 85 were found to have strangulated hernia. There was wide variation of age ranging from a minimum 15 to 70 years with the mean age 42 years.

55 patients had Right sided hernia 64.7% and 30 patients had Left sided hernia 35.2% and no patient with bilateral strangulated inguinal hernia reported 0% (Table 1). The majority of patients in our series were farmers 41 (48.2%) and labourers 24 (28.23%) other professions include drivers 6 (7%), railways coolies 9 (10.5%), teacher 2 (2.3%) and carpenter 3 (3.5%) (Chart 1).

All the patients underwent surgery. During surgery of 60 patients (70.5%) had gangrenous omentum while the rest of the gut was normal. Hence omentectomy was done.

In 23 cases (27%) ileum was non viable so we had to resort to resection and anastomosis, two cases (2.3%) Ileum was so much contaminated so we had to resort to Ileostomy and two case (2.3%) sigmoid colon was involved so we had to resort to colostomy.

Complications were also reported in our series of the patients. Majority of them developed wound infection 14 (16.4%) followed by chest infections 10 (11.7%) Haematoma formation was reported in 5 (5.8%) and retention of urine in 3 patient (3.5%) (Table 2).

The mortality rate in our series was 3.5%. 3 patients died. Patients were above 60 years of age with history

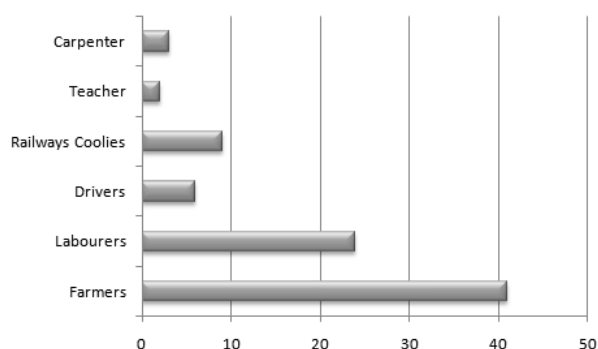
of comorbid disease. One died on 5th post operative day due to chest infection while two died on 10th post operative day due to cardiac arrest. Hence delayed presentation and age were common factors responsible for mortality

The duration of hospital stay varied from 7 to 30 days. Duration of stay was longer in those patients who had developed complications.

**Table No.1:- Side of Hernia**

Side	No. of Patients	Percentage
Right sided	55	64.7%
Left sided	30	35.2%
Bilateral	0	0
Total	85	100%

**Chart No.1:- Occupation of Patients**



**Table No.2:- Postoperative Complication**

Complications	No. of Patients	Percentage
Wound infection	14	16.4 %
Chest infection	10	11.7%
Haematoma	5	5.8%
Retention of urine	3	3.5%
	32	37.4%

## DISCUSSION

Inguinal hernia is one of the common surgical emergencies in third world countries. The rate of strangulation of bowel is very high with late presentation and ignorance of already existing inguinal hernias<sup>8</sup>. Therefore strangulated inguinal hernia is a common surgical emergency with life threatening consequences<sup>9</sup>.

The results of this study show that inguinal hernias are more common in men and found rarely in women. In this study, 55 patients (64.7%) had right sided hernia compared to 30 patients (35.2%) who had left sided indicating the incidence of strangulated inguinal hernia is more on right side. Compared to study conducted by Manzar Salim which shows ratio of 66 to 34% respectively<sup>10</sup>.

According to our study, the majority of the patients were farmers 41 (48.2%) followed by labourers 24 (28.23%) compared to the study conducted by Kangsk Burnettca which shows hernia incidence about 95% in labourers who do heavy work <sup>11</sup>. In our country the ratio of farmers is high due to agricultural background and most of our patients come from rural areas. So strangulated inguinal hernia is more common in lower socioeconomic group or we can say that it is the disease of poor people <sup>12</sup>.

The morbidity and mortality of strangulated inguinal hernia depends on the presentation of patients. If patients present early and operation is conducted soon than bowel can be saved or only omentectomy is done and rest of the gut is given a chance of viability by applying warm packs <sup>13</sup>.

In this study 60 patients (70.5%) went for omentectomy and rest of viable gut was returned to abdominal cavity, on the contrary 23 patients (27%) who presented late i.e. beyond 72 hours have to undergo resection. Ileal resection done and end to end anastomosis performed and these patients were kept N.P.O for 72 hours. Ileum was the second most common part of the gut after omentum which is affected in strangulated inguinal hernia <sup>14</sup>. This is to be compared to Mrihedioh and Alina study which shows that 12 out of 15 strangulated hernias presented with small bowel obstruction <sup>15</sup>.

In cases where patients present late and the peritoneum is contaminated than stoma formation is the only option <sup>16</sup>. In this study ileostomy was therefore done in 2 cases (2.3%) due to late presentation and contamination. Sigmoid colon is also the part of the hernial sac in some cases but it doesn't happen very often. In this study only two cases was reported in which colostomy was done compared to the study conducted by Tufnellml Abraham that shows perforated diverticulum of sigmoid colon is a rare finding in strangulated inguinal hernia <sup>17</sup>. Strangulated inguinal hernia can present as acute pancreatitis<sup>18</sup> or it can present as diverticular abcess as a part of sac<sup>19</sup> but it happens very rarely. Primary omental liposarcoma has also been reported to be part of hernia sac in strangulated hernia <sup>20</sup>.

Repair of strangulated inguinal hernia depends how early patient reports to the hospital and facilities available there. In this study all hernias were repaired with Bassini's technique i.e. by interrupted sutures connecting inguinal ligament with conjoint tendon. In all cases repair was done with prolene one as recommended by latendicum standard<sup>21</sup>.

There is also incidence of higher rate of wound infection and other complications with leichtenstein tension free repair in the management of strangulated inguinal hernia. <sup>22,23</sup>.

There are studies which have proposed that TAPP procedure can also be used for emergency treatment of strangulated inguinal hernia. But it can be done by

experienced and trained laparoscopic surgeon <sup>24</sup>. In our set up where the facilities are not available and the patients present late only Bassini's repair would be a standard technique to repair strangulated hernia. In this study, there was incidence of wound infection in 14 patients (16.4%) followed by chest infection 10 (11.7%) compared to a case study published by Mr. Coskun and Deamir regarding necrotic soft tissue infection in strangulated inguinal hernia <sup>25</sup>.

Three patients in our study died due to cardio-respiratory failure. Hence mortality rate was 3.5%. Patients were above the age of 60. Hence late presentation and old age are the main cause of morbidity and mortality in strangulated inguinal hernia. But in comparison to femoral hernia which has more tendency to strangulate is rare in comparison to inguinal hernia <sup>26</sup>.

## CONCLUSION

Good pre-operation assessment and early management will decrease the morbidity and mortality in strangulated inguinal hernia.

Inguinal hernia should be operated as soon as it is reported and people should be told to get their hernias repaired early to avoid complications like obstruction and strangulation.

## REFERENCES

1. Snell RS. Clinical anatomy for medical student. 6<sup>th</sup> ed. USA: Lippincott, William and Wilkins; 2006.p. 175-177.
2. Sinnatamby CS. Last's Anatomy Regional and Applied. 10<sup>th</sup> ed. UK: Churchill Livingstone; 1999.p.211.
3. Raftery A T. Churchill's pocket book of Surgery. 2<sup>nd</sup> ed. UK: Hartcourt Publishers limited; 2001.p. 196-199.
4. Nirula R. High-yield surgery. 2<sup>nd</sup> ed. USA: Lipincott, Williams and Wilkins; 2000.p.69.
5. Chung K W. Gross Anatomy Board Review Series. 4<sup>th</sup> ed. USA: Lippinkott, Williams & Wilkins; 2000.p.182-183.
6. Farooq O, Rehman B, Batool Z, Prolene Darn. Safe and effective method for primary inguinal hernia repair. J Coll Physicians Surg Pak 2005;15(6):358 – 361.
7. Ahmad M, Niaz WA. Polypropylene Mesh Repair of incisional Hernia. J Coll Physicians Surg Pak 2003;13(8): 440-442.
8. Abbas H. Outcome of strangulated inguinal hernia. Pak J Med Sci 2005;21(4): 445-450.
9. Ahmed. A Fibrous Stricture of small intestine following strangulated inguinal hernia. Anal Af Med 2006;5(1): 56-58.

10. Manzar S. Hernia is more common on right side. Pak J Surg Jan-March 1992;1:65-66.
11. Kangsk BC, A Freau de Sesitoj. Hernia is it a work – related condition. AM J Int Med 1999;36(6): 638-644.
12. Mazdak H, Shekoofeh. Herinal sac lithiasis a rare presentation of inguinal hernia. JRMS 2007;12(1): 49-51.
13. Kumar SD. Intestinal Gangrene due to mesenteric vascular occlusion masquerading as strangulated inguinal hernia. Hernia 2008;12:195-197.
14. Dakubo JCB. Ileal stricture following strangulated inguinal hernia. Tropical doctor 2007;37: 260-262.
15. Alaina I. Hernias are the most common causes of strangulation in patients presenting with small bowel obstruction. Hernia Aug 2006;10(4):338-340.
16. Fevang BT, Fevang M. Delay in operative treatment among patients with small bowel obstruction. Scandinavian J Surg 2003;92:131-137.
17. Abraham T. A perforated diverticulum of the sigmoid colon found with in strangulated inguinal hernia. Hernia Aug 2008;12 (14):421-427.
18. Nazar MA, D'souza FR. Unusual presentation of acute pancreatitis; an irreducible inguinoscrotal swelling mimicking a strangulated hernia. Abdom imaging 2007;32: 116-118.
19. Andrabi SI, Pitale A. Diverticula abcess presenting as strangulated inguinal hernia. Ulster Med Jan 2007;76(2):107 – 108.
20. Millic DJ, Mrajkovic M. Primary Omental Liposarcoma presenting as an strangulated inguinal hernia. Hernia 2005; 9: 88-89.
21. Lazaridis BP. Tension free versus modified Bassini's Technique for strangulated inguinal hernia. Hernia 2005; 92: 156-159.
22. Bessa SS, Katri KM. Early results from the use of Lichtensin repair in the management of strangulated inguinal hernia. Hernia 2007; 11: 239-242.
23. Liangxiao, Caixiv JW. Strangulated bowel obstruction from mesh repair. Chinese Med J 2008; 121: 183-184.
24. Legnani GL, Rasini M. Laproscopic Trans peritoneal hernioplasty (TAPP) for acute management of inguinal scrotal hernias. Hernia 2008; 12: 185-188.
25. Nowak DD, Chin A. Large scrotal hernia a complicated case of mesh migration as cited and bowel strangulation. Hernia 2005;9:96-99.
26. Golu OA, Kaya B. Femoral Hernia overview of 3 cases. Hernia 2006;10:70-73.

**Address for Corresponding Author:**

Dr. Sikander-e-Azam,  
Senior Registrar of Surgery,  
Miminal Invasive Surgical Centre,  
LUMHS, Jamshoro.

**Original Article**

# The Effects of Saturated and Unsaturated Fat Diets on the Histology of Adrenocortical Cells of Albino Rats - A Comparative Study

**1. Iram Quddus 2. Ghulam Mujtaba Kolachi 3. Rais Ahmad 4. Furrukh Mustafa**

1. Lecturer of Anatomy, SMC (DUHS), Karachi 2. Asstt. Prof. of Anatomy, DMC (DUHS), Karachi  
3. Asstt. Prof. of Anatomy, SMC (DUHS), Karachi 4. Asstt. Prof. of Anatomy, DMC (DUHS), Karachi

## ABSTRACT

**Objectives:** High fat diet stimulates Hypothalamic -pituitary- adrenal (HPA)axis activity and enhances the release of corticosteroids from adrenal gland which in turn contributes to metabolic syndrome by producing insulin resistance. Present study objectives are to compare the effects of two different types of fat that is saturated and polyunsaturated on the histology of adrenal gland with respect to its activity.

**Study Design:** Prospective experimental.

**Place and Duration of Study:** Department of Anatomy BMSI, JPMC August – October: 2008

**Materials and Methods:** A total of 30 adult male albino rats weighing 200-240 gm, aged 190 days were divided into three groups. group 'A' received standard laboratory diet and group 'B' received high saturated fats in the form of unsalted butter as 20% added fat of the total calories. Group 'C' received high unsaturated fats in diet i.e. 20% fat added in the form of corn oil of the total calories. Each group was subdivided according to their time of sacrifice i.e. 4 and 8 weeks respectively. Animals were sacrificed at the end of their respective periods by ether anesthesia. Adrenal glands were dissected out, weighed and processed for paraffin embedding and sectioned at 4µm thickness to be stained with H&E, for cell count and cell diameter in the 3 cortical zones.

**Result:** Observations on adrenal gland weight /100gm of body weight of butter and corn oil treated groups revealed moderately significant decrease in weight in corn oil treated group at 4 weeks while there was insignificant difference at 8weeks when compared to butter treated group. There was insignificant difference in cell count in the three zones between butter and corn oil treated groups. Cell diameter in zona fasciculata was significantly increased in butter treated groups at 8weeks when compared to corn oil treated group.

**Conclusion:** Insignificant differences were found in most of the observation between the 2 fat groups. Insignificant difference in adrenal gland weight /100gm body weight between butter and corn oil treated groups at 8 weeks was because of less marked increase in body weight in corn oil treated group. Zona fasciculata showed increase cell size in butter treated group reflecting increased stress hormone release.

**Key Words:** Adrenal gland, zona fasciculata, high fat diet, HPA axis.

## INTRODUCTION

High fat diet has been reported to adversely affect the health of human and animal species<sup>1</sup>. High dietary fat stimulates HPA axis activity<sup>2,3,4</sup>, inducing both hyperplasia and hypertrophy of adrenal cortex<sup>5,6</sup>. Resultant glucocorticoid excess has been linked to obesity, hypertension, hyperlipidemia and glucose intolerance<sup>7</sup>.

Disorders characterized by insulin resistance are associated with specific fatty acid pattern of serum lipids with increased proportion of palmitic and palmitoleic acid (saturated fatty acids) and reduced levels of linoleic acid which is a polyunsaturated fatty acid<sup>8</sup>. Myristic and palmitic acids (saturated fatty acids) are also more potent in increasing serum cholesterol. Butter is one of the sources of saturated fatty acids<sup>9</sup>.

Diets high in polyunsaturated fatty acids (PUFAs) are negative regulator of lipogenesis that exert their effect

primarily at the level of transcription<sup>10</sup>. Corn oil which contains PUFAs, has hypocholesterolemic action<sup>11</sup>.

Adrenal gland is an essential stress response organ that is part of HPA axis<sup>12,13</sup>. Diet high in saturated fat increases circulatory corticosteroid levels from adrenal gland in addition to changes in glucose homeostasis<sup>14</sup>. Cultured adrenocortical cells were experimentally stimulated by unsaturated fatty acids i.e. oleic acid and to lesser extent linoleic acid to produce increased levels of glucocorticoids<sup>15</sup>. Oxidized derivatives of linoleic acid also have the potential to stimulate corticosteroid production<sup>16</sup>.

A lot had been said about the comparison between saturated and unsaturated fats and the beneficial effect of unsaturated fats with respect to their effect on obesity and cardiovascular diseases. Adrenal gland which is the ultimate organ of stress axis has an established role in obesity and metabolic syndrome. How saturated and unsaturated fats affects the histology

of adrenal gland is of interest as it seems to play a decisive role and the impact of each type of fat on the development of metabolic syndrome through adrenal gland is the area for more research.

Most studies focused on the effects of variable amount of high fat diet with one or different types of fats on adrenal activity. But mostly they were assessed by the biochemical parameters. In present study a comparison of two types of fat in terms of their effect on the histological parameters was done.

## MATERIALS AND METHODS

Thirty male adult albino rats aged around 190 days weighing 200-240 gm were taken and kept on standard laboratory diet for one week observational period (12 hrs dark and light cycle) before study.

The animals were divided into group, A, B, C according to the diet they received. Group 'A' received normal diet, group 'B' received high fat diet (20 gram unsalted dairy butter/100 grams of normal diet, Lurpak, Denmark) and group 'C' received high unsaturated fat diet (20 ml of corn oil /100 gm of normal diet, Coroli-Cebag, Abu Dhabi). Animals were then subdivided into subgroups A1, A2, B1, B2, C1 and C2 according to their time of sacrifice i.e. 4 and 8 weeks. Each subgroup comprised of 5 animal

Animals were individually housed after weighing in plastic cages, and were kept on 12:12 hrs light-dark cycle. Given food and water ad libitum. At the end of respective study period animals were weighed and anaesthetized with ether. Adrenal glands were excised after dissection and weighed and fixed in 10% buffered neutral formalin for 24 hours. After fixation they were processed in ascending grades of alcohol (70-100), cleared with xylene and infiltrated in paraffin. 4µm thick sections were cut with rotatory microtome and stained with H&E for morphometric study.

The cell count in the three cortical zones was done under 8 x ocular and 100 x oil immersion objective with counting reticule in randomly selected 3 fields from each cortical zone of each animal. Cell diameter was measured by randomly selecting ten cells per field in each zone with ocular micrometer scale under 8 x ocular and 100 x oil immersion objective.

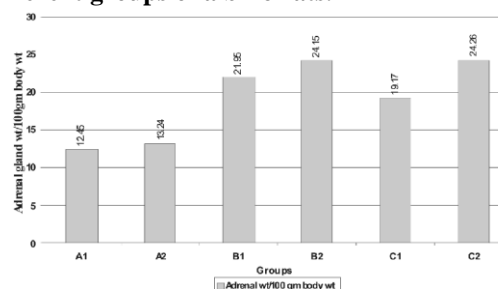
The statistical analysis was done by student's 't' test and P-value less than 0.05 was considered as significant. Calculations were done by utilizing computer software SPSS version 13.

## RESULTS

Observations of adrenal gland weight per 100 gm of body weight of different groups revealed that group 'B' animals showed highly significant ( $P<0.001$ ) increase at 4 and 8 weeks when compared to control group. Group 'C' animals, at 4 and 8 weeks also showed highly

significant ( $P<0.001$ ) increase in adrenal gland weight per 100 gm of body weight, when compared to control. Comparison of the two fat groups revealed that Corn oil treated animals showed moderately significant ( $P<0.01$ ) decrease in weight at 4 weeks while insignificant ( $P>0.05$ ) difference at 8 weeks, when compared with butter treated group as shown in (Graph No. 1).

**Graph No.1: Adrenal Gland wt/100gm body wt in different groups of albino rats.**



**Table No.1: Mean number of cells (per unit area) in three cortical zones in different groups of albino rats**

Groups	Sub-groups	Zona Granulosa	Zona Fasciculata	Zona Reticularis
A	A1	45±0.44	22±1.00	46±2.30
	A2	44±1.30	23.8±0.40	47±1.87
B	B1	39±0.63	17±0.70	47±0.70
	B2	32±1.58	17±0.83	48±0.70
C	C1	40±0.70	18±0.31	46±2.91
	C2	35.2±0.66	18±1.04	47±0.54

\*Mean±SEM

**Table No. 2: \*Mean diameter of cells (µm) in three cortical zones in different groups of albino rats**

Groups	Sub-groups	Zona Granulosa	Zona Fasciculata	Zona Reticularis
A	A1	13.60±0.20	11.50±0.19	7.80±0.26
	A2	13.62±0.50	12.50±0.18	7.90±0.09
B	B1	14.70±0.21	13.10±0.25	7.82±0.13
	B2	15.00±0.35	16.60±0.26	8.00±0.28
C	C1	14.00±0.28	12.30±0.22	7.81±0.25
	C2	14.50±0.17	15.50±0.19	8.20±0.21

\*Mean±SEM

Cell count per unit area (Table-1) in different groups revealed that in group 'B' animals moderately significant ( $P<0.01$ ) decrease in cell count in zona glomerulosa was found at 4 and 8 weeks when compared to control. Cell count in zona fasciculata showed moderately significant ( $P<0.01$ ) decrease at 4 and 8 weeks, and zona reticularis showed insignificant ( $P>0.05$ ) difference in count.

Group 'C' animals, when compared with control group showed moderately significant ( $P<0.01$ ) decrease in cell count in zona glomerulosa at 4 and 8 weeks. Zona fasciculata showed significant ( $P<0.05$ ) decrease in cell

count at both 4 and 8 weeks. Zona reticularis showed insignificant ( $P>0.05$ ) difference.

When group 'B' and group 'C' were statistically compared insignificant ( $P>0.05$ ) difference in cell count was found at both 4 and 8 weeks in the three cortical zones.

Cell diameter observed in different groups revealed that group 'B' animals when compared to control showed moderately significant ( $P<0.01$ ) and significant ( $P<0.05$ ) increase in cell diameter in zona glomerulosa at 4 and 8 weeks respectively. Moderately significant ( $P<0.01$ ) and highly significant ( $P<0.001$ ) increased diameter was seen in zona fasciculata at 4 and 8 weeks respectively. Zona reticularis showed insignificant ( $P>0.05$ ) change.

Group 'C' animals when compared to control group showed insignificantly ( $P<0.05$ ) increased cell diameter in zona glomerulosa at 4 and 8 weeks. Significant ( $P<0.05$ ) and highly significant ( $P<0.001$ ) increase in diameter in zona fasciculata was found at 4 and 8 weeks respectively. Zona reticularis showed insignificant ( $P>0.05$ ) change.

Statistical comparison of group 'B' and group 'C' revealed insignificantly ( $P>0.05$ ) increased diameter of cells in Group 'B' at both 4 and 8 weeks in zona glomerulosa when compared to group 'C'. In zona fasciculata insignificantly ( $P>0.05$ ) increased and significantly ( $P<0.05$ ) increased diameter was observed at 4 and 8 weeks respectively in group 'B' animals. Insignificant differences in diameter were observed in zona reticularis between the 2 groups.

## DISCUSSION

Virtually every metabolic disorder characterized by elevated plasma free fatty acid levels is also associated with hypercorticism<sup>15</sup>. The pattern of effect of high fat diet is similar to that after chronic stress<sup>2</sup>. Long term stimulation of adrenal cortex by adrenocorticotrophic hormone (ACTH) not only increases secretory activity but also causes hypertrophy and hyperplasia of adrenocortical cells<sup>12</sup>. ACTH increases synthesis of low density lipoprotein (LDL) and high density lipoprotein (HDL) receptors on adrenocortical cells. LDL and HDL deliver cholesterol to the adrenal gland.<sup>5</sup> Both saturated fat<sup>14</sup> and polyunsaturated fat<sup>16</sup> affects the activity of adrenal gland. Present study observations focus on the histological differences in their effect on adrenal cortex. In present study adrenal gland weight per 100 gm of body weight increased in both fat treated groups. Butter treated group (Group 'B') revealed more weight increase at 4 weeks compared to corn oil treated group (Group 'C') while at 8 weeks both fat groups had equal weight because the body weight increment was less in corn oil treated group. Neilly et al (2009) used saturated

fat and observed increased adrenal weight, which is in conformity with the present study observations. Kronenberg et al (2008) explained increase in adrenal gland weight after ACTH stimulation due to chronic stress as a result of hypertrophy and hyperplasia. Gotohda et al (2005) observed increased adrenal gland weight in response to toluene inhalation stress, the body weight decreased due to the stress while the organ weight increased due to hypertrophy.

Cell count in zona glomerulosa of both butter and corn oil treated groups showed decrease in cell number per unit area as the size of the cell increased at 4 and 8 weeks period. Difference in cell count in between the two fat groups was insignificant. In zona fasciculata the decrease in cell count /unit area was more evident in case of butter treated groups at 4 and 8 weeks compared to control and less in case of corn oil treated group when compared to control, but statistical comparison of the two fat groups showed insignificant difference.

Tannenbaum et al (1997) and La Fleur et al (1995) used unsaturated and saturated fat respectively in their study and observed and assessed the activity of gland by biochemical parameters, in response to restraint stress and found exaggerated response by increased hormonal levels. Legendre and Harris (2006) used a mixture of corn oil and coconut oil equals to 40% of total calories and observed the activity of gland in response to mild stress and found similar results. Lai et al (2006) observed adrenocortical hyperplasia in response to chronic variable stress, the findings correlates well with present study observations as the decrease in count per unit area is relative due to increase in size.

Cell diameter was increased in butter treated groups both at 4 and 8 weeks period, in zona glomerulosa and zona fasciculata cells. In corn oil treated group increase in size of cell was only appreciable in zona fasciculata. Comparing the two fat groups there wasn't much difference in cell size in zona glomerulosa and reticularis, only in the longer duration (8 week) butter treated animals showed increased cell size in zona fasciculata compared to corn oil treated group. Gotohda et al (2005) observed increased cell size in response to toluene induced stress. Lai et al (2006) observed both hyperplasia and hypertrophy in response to chronic variable stress which involved zona fasciculata mainly, which in accordance with present study results.

## CONCLUSION

Despite of all the debate which proves that polyunsaturated fats are superior or less harmful in excess, to saturated fats, present study observations indicated that no remarkable difference was found related to stressful effects on adrenal gland in between two types of fat.



## REFERENCES

1. Sreekumar R, Unnikrishnan J, Fu A, Nygren J, Short KR, Schimke J, et al. Impact of high-fat diet and antioxidant supplement on mitochondrial functions and gene transcripts in rat muscle. *Am J Physiol Endocrinol Metab* 2002;282:1055-1061.
2. Tannenbaum BM, Brindley DN, Tannenbaum GS, Dallman MF, McArthur MD, Meaney MJ. High-fat feeding alters both basal and stress-induced hypothalamic-pituitary-adrenal activity in the rat. *Am J Physiol Endocrinol Metab* 1997;273:1168-1177.
3. La Fleur SE, Houshyar H, Roy M, Dallman MF. Choice of lard, but not total lard calories, damps adrenocorticotropin responses to restraint. *Endocrinology* 2005;146: 2193-2199.
4. Legendre A, Harris RB. Exaggerated response to mild stress in rats fed high-fat diet. *Am J Physiol Regul Integr Comp Physiol* 2006; 291: 1288- 1294.
5. Kronenberg HM, Melmed S, Polonsky KS, Larsen PR. *Williams textbook of endocrinology*. 11<sup>th</sup> ed. Philadelphia: Saunders Elsevier;2008.
6. Gotohda T, Tokunaga I and Kubo S. Toluene inhalation-induced adreno-cortical hypertrophy and endocrinological changes in rat. *Life Sci* 2005;76: 1929-37.
7. Wang M. The role of glucocorticoid action in the pathophysiology of the metabolic syndrome. *Nutrition & metabolism* 2005;2:1172-1178.
8. Vessby B. Dietary fat and insulin action in humans. *Br J Nut* 2000; 83: 91-96
9. Champe PC, Harvey RA, Ferrier DR. *Lippincott's Illustrated Reviews: Biochemistry*. 4<sup>th</sup> ed. Philadelphia: Lippincott Williams and Wilkins; 2008.
10. Cruz MR, Tovar AR, Gonzalez BP, Prado MD , Torres N. Synthesis of long-chain polyunsaturated fatty acids in lactating mammary gland: role of  $\Delta^5$  and  $\Delta^6$  desaturases, SREBP-1, PPAR $\alpha$ , and PGC-1. *J of Lipid Res* 2006;47:553-560.
11. Mooradian AD, Haas MJ, Wong NC. The effect of select nutrients on serum high-density lipoprotein cholesterol and apolipoprotein A-1 levels. *Endocrine Reviews* 2005;27: 2-16.
12. Guyton AC, Hall JE. *Textbook of medical physiology*. 11th ed. Philadelphia: Saunders Elsevier; 2006.
13. Lai YM, Figueiredo HF, Ostrander MM, Choi DC, Engeland WC, Herman JP. Chronic stress induces adrenal hyperplasia and hypertrophy in a subregion-specific manner. *Am J Physiol Endocrinol Metab* 2006;291: 965-973.
14. Neilly AM, Williamson R, Balfour D, Sutherland C, Stewart C. Adrenal hypertrophy occurs in concert with insulin resistance following high fat feeding of two different strains of rat. *Endocrine Abstracts* 2009; 19: 133.
15. Widmaier EP, Margenthaler J, Sarel I. Regulation of pituitary- adrenocortical activity by free fatty acids in vivo and in vitro. *Prostaglandins Leukot Essent Fatty Acids* 1995; 52:179-83
16. Bruder ED, Ball DL, Goodfriend TL, Raff H. An oxidized metabolite of linoleic acid stimulates corticosterone production by rat adrenal cells. *Am J Physiol Regul Integr Comp Physiol* 2003;284: 1631-1635.

### Address for Corresponding Author:

Dr. Iram quddus  
Lecturer of Anatomy  
Sindh Medical College,  
DUHS Karachi  
Cell No: 0333-3865001

**Original Article**

# A Qualitative Study to Assess the Awareness Level of Diabetes Mellitus in Patients Coming to JPMC

1. Shaheen Akbar Agha 2. Muhammad Akbar Agha 3. Ruma Ashraf 4. Fareeha Khan  
5. Tooba Chohan 6. Yusra Azhar

1. Asstt. Prof. of Community Medicine, SMC / DUCH Karachi 2. Asstt. Prof. of Haemtology, DIMC, DUHS, Karachi 3,4,5 & 6 House Officers of JPMC.

## ABSTRACT

**Objective:** The study was conducted to assess the awareness level about diabetes in patients coming to JPMC and to initiate steps to increase their knowledge and clear misconceptions.

**Study Design:** Descriptive Cross-Sectional Study.

**Place and Duration of Study:** This study was conducted in JPMC hospital from April 2008 to October 2008.

**Materials and method:** A non- probability convenience sampling technique was applied in a population aged  $15 < n < 80$  ( $n=230$ ) through which both diabetics and non-diabetics were interviewed after taking informed consent using a pre-structured questionnaire. Details regarding awareness about diabetes in relation to their knowledge on diabetes, causes, signs and symptoms, complications, treatment, diet, physical activity, degree of diabetes in the patient and measures to enhance their knowledge and health on the subject were accordingly marked. The data has been analyzed using SPSS 10.0.

**Results:** In this study, 230 subjects irrespective of gender and age were assessed. 15% of the subjects were diabetics and most of them were unaware of the cause of the disease as well as of its complications, while the remaining 85% also had very little knowledge about diabetes and issues related to it.

**Conclusion:** The level of awareness was generally low amongst the general population. The study reveals the essential need for strategies to create awareness regarding diabetes in the lower socio economic group. Diabetic patients were well informed about the disease they were suffering from.

**Keywords:** Diabetes, Awareness, Knowledge, Health Education.

## INTRODUCTION

“Diabetes mellitus is not a single disease entity, but rather a group of metabolic diseases sharing the common underlying feature of hyperglycemia. Hyperglycemia in diabetes results from defects in insulin secretion, insulin action, or most commonly both.”<sup>1</sup> Physiologically the blood glucose levels are closely regulated by the pancreatic insulin. “Blood glucose values are normally maintained in a very narrow range, usually 70-120mg/dL.”<sup>1</sup> The diagnosis of the available experimental and clinical evidence suggests that the complications of diabetes are a consequence. DM is recognized by the increased blood glucose levels, classical signs and symptoms, by either random glucose level ( $>200\text{mg/dL}$ ), fasting glucose level ( $>126\text{mg/dl}$ ) or an abnormal oral glucose tolerance test (OGTT) ( $>200\text{mg/dL}$ ).<sup>1</sup> The net effect is a chronic disorder of carbohydrate, fat, and protein metabolism with long term complications affecting the microvascular and macrovascular systems of the body including blood vessels, cardiovascular system, kidneys, eyes, and nerves.

Risk factors of diabetes include certain medications, sedentary lifestyle, race, stress, pregnancy, hypertension, high cholesterol, obesity, age (65+), and

family history. The onset is marked by polyuria, polydipsia, polyphagia, and in certain extreme cases can lead to ketoacidosis. The contradiction of polyphagia and weight loss is paradoxical and should always raise the suspicion of diabetes.<sup>1</sup>

Presently Pakistan contributes 6.2 million diabetics in the global pool of diabetes and if strategies for prevention are not taken the predictive figures for the year 2025 will jump to 11.6 million that is double the current figures. According to WHO, annual 2% reduction in chronic disease death rates in Pakistan would provide an economic gain of 1 billion dollars over the next 10 years.<sup>2</sup> According to a WHO report mortality rate due to diabetes may double in the next decade if neglected.<sup>3</sup>

Due to rapid increase in the incidence of diabetes in Pakistan, preventive strategies are needed to be targeted towards a healthy population. Preventive programs targeted towards general population show greater benefits in this situation rather than targeting only high risk and diseased population. However, it has been known that knowledge alone is not sufficient to bring about behavioral change in population. Lifestyle modification and/or medication (e.g., metformin) are cost-effective in reducing the incidence of T2DM. However, their application is not yet routine practice.<sup>4</sup>

Consumption of healthy food concept is not clear among the general population, requiring assessment of public knowledge and awareness about healthy diet.<sup>5</sup> During the past ten years there is an innovation in the diet and nutrition pattern in diabetes. Today nutritionist advises a strict restriction of fat intake and allows a lot of fiber and complex carbohydrates.”<sup>6</sup>

The present research paper focuses on the awareness level of diabetes amongst the patients coming to JPMC, and to increase the knowledge of diabetes in the community. The study aims to elicit information that will aid in the development for future research on the subject and on enlightening the community of the potential risks of diabetes and how it can be prevented.

## MATERIALS AND METHODS

In order to gather baseline measures of public awareness and attitudes towards diabetes mellitus a descriptive cross-sectional study was conducted in JPMC hospital from April 2008 to October 2008. In a population aged 15<n<80 comprising of both males and females, diabetics and non-diabetics, 230 individuals were interviewed after taking their informed consent using a pre-structured questionnaire. The patients coming to the different wards and OPD were selected by a non-probability convenience sampling technique coming to the different Wards and O.P.D.

A three sheet questionnaire was prepared for participants asking for open-ended responses to the questions. Details regarding awareness level about diabetes, in relation to their knowledge on diabetes, causes, signs and symptoms, complications, treatment, diet, physical activity, regarding personal associations with the disease were asked. Each participant was interviewed individually with the questionnaire and the answers were ticked appropriately. The resultant computer database was analyzed using the Statistical Package for the Social Sciences (SPSS) version 10.0.

## RESULTS

The overall awareness level was low with misconceptions prevailing in communities probably due to inadequate knowledge. However behavioral change is not solely dependent on information and knowledge rather is influenced by various social, cultural, socio-economic and health factors.

Statistical analysis has shown that sixty nine percent responded diabetes as a ‘disease’ and didn’t know beyond and the rest thirty percent didn’t know at all. Among the interviewees 14.8% were diabetic whereas 40% had never tested for diabetes.

24% believed that DM is contagious whereas 54% were aware of the fact that it is the fastest growing non-infectious disease in the world. 67% assumed that people having family history of DM were more prone

to developing the disease. Only 52% knew that it has no cure once developed and 82% believed that blood sugar levels can be controlled by a balanced diet.

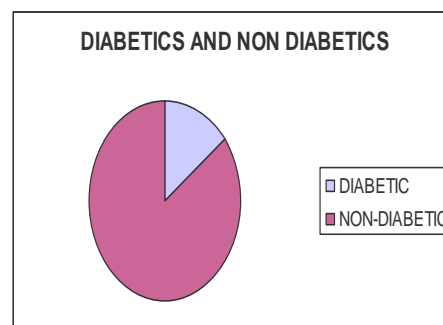
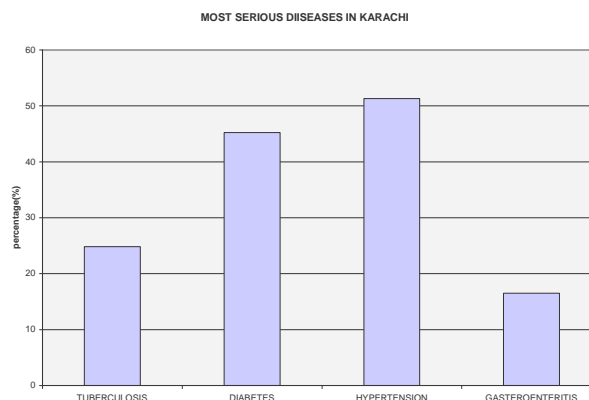
**Table No.1:**

Statements	%
<b>Dm is caused by:</b>	
• Eating too many sweets	66.5
• Pregnancy	23.0
• Insulin imbalance(some endocrinal disorder)	20.0
• Use of certain drugs	13.9
• Infection	19.1
• Supernatural/ god’s curse	20.0
• Don’t know the causes	14.3

**Table No.2:**

Statements	%
• Sedentary life style	41.3
• Smoking	32.6
• High fat diet	32.6
• Obesity	57.0
• Stress	67.0

**Illustration No. 1**



### Factors responsible for diabetes mellitus:

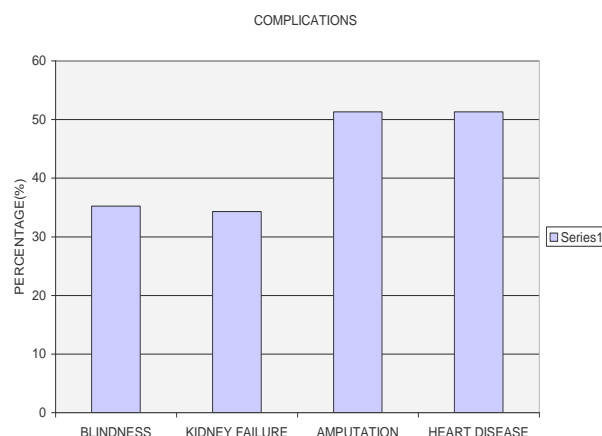
When asked about the source of information 18.7% read it from newspapers, 43.9% heard it from people, 24.8% got the information from a doctor, and 11.3%

had never heard of it. When inquired about family member being diabetic 45.2% replied in affirmative. 45.7% often suffered from tingling or burning pain in feet or toes.

**Table No.3:**

Statements	%
Polydypsia	41.7
Polyphagia	34.3
Polyuria	43.0
Decreased desire for water	4.8
Decreased appetite	6.5
Decreased micturation	3.0
Weight loss	36.1
Weight gain	10.4
I don't know	32.2

**Illustration No. 2**



The table No. 3 and the Illustration No 2 present the results of the symptoms and complications of Diabetes Mellitus patients in the patients coming to JPMC

## DISCUSSION

Educating the masses about diabetes is widely acknowledged as being vital to initiating diabetes therapy. The study conducted gave an insight into the level of awareness present amongst people about this disease. The study found that the majority of the individuals had never received education on diabetes, as can be seen in various other studies.<sup>7,8,9</sup>

The data from a study done in rural Islamabad grossly indicates that a significant number of the population have little or no awareness of Diabetes Mellitus. Amongst those familiar with the disease labeled it as 'sugar' instead of 'diabetes'. Information about the disease was not through any health education program but rather through affected relatives,<sup>10</sup> similar findings are further validated in this study.

It is interesting to know that majority responded that it is a 'disease' and did not know beyond. The rest were

not even aware of the fact that Diabetes Mellitus is a disease. Of the people asked, very few were actually diabetic but the level of awareness amongst those individuals about the disease and its complications was comparatively high which is in contradiction to a study done in Nepal that revealed a low level of knowledge, attitude and practice even amongst diabetic patients.<sup>11</sup> However, the overall knowledge about the disease and its complications was low among the study participants, which is in accordance with other studies.<sup>12,13</sup>

Many myths and misconceptions regarding diabetes are prevalent in our society which is not surprising considering the fact that the vast majority of the population is illiterate. The most common one being that eating too many sweets causes Diabetes.<sup>14</sup> Other myths include diabetes being considered a contagious disease and that spiritual factors like witchcraft and super natural causes lead to DM.

A sizable portion of the people interviewed stated that they were unaware of early signs and symptoms. This is an alarming situation as most of the DM early symptoms are non-specific and the complications of this emergent disease can only be controlled by an early diagnosis and proper treatment and personal care. It has been stressed in one study that there is a need to enhance the basic health need assessment in communities on a large scale with the view to deal emerging health issues of diabetes. Health education programs with facilities and training in regional languages for better compliance is the need for the hour.<sup>15</sup>

An increasingly sedentary lifestyle partly due to the over dependence on technology and poor eating habits have contributed to the concurrent escalation of diabetes and obesity worldwide. A study done recently in China clearly shows that lifestyle interventions could decrease the risk of diabetes mellitus, help their transferring into normal blood glucose, and improve diabetic measures for the IGR population in Shanghai urban communities.<sup>16</sup>

In this study, most of the participants believed that obese people had a higher risk of developing diabetes than non-obese individuals. Globally the prevalence of obesity is increasing dramatically, so much so that in some countries, all most half of the people are overweight. With a 34% prevalence of hypertension, an aging population, high prevalence of obesity, and a sedentary lifestyle, there is an estimation of a rise in 85% of the prevalence of diabetes in South-America, for the next decades.<sup>17</sup> A number of studies have shown the beneficial effect of weight reduction in helping to control and prevent Diabetes. One such article went on to conclude that obesity in Type 2 diabetic individuals should be given prime importance and weight reduction as a necessary step.<sup>18</sup>

Undoubtedly stress has major effects on metabolic activity of the body. According to this study, a majority of subjects interviewed had the same opinion. When one is stressed, the blood sugar levels rises. A research conducted by the American psychosomatic society highlighted that one of predisposing factor of chronic hyperglycemia in diabetes is stress, although its exact mechanism is ambiguous.<sup>19</sup>

When asked about the complications, less than half of the participants knew about all the complications. Diabetes brings with it several life-threatening complications if not properly treated, which can be prevented if detected early. A research study on the association of diabetes and cardiac manifestation it was found out that, the relative risk of a heart attack in type 2 diabetics is more than double than non diabetics where as the absolute risk of diabetic patients without a history of myocardial infarction seems to be equal to risk in non diabetics with an episode of previous infarction.<sup>20</sup>

“About 20-40% of diabetics are reported to have neuropathy of which almost 50% are likely to develop symptomatic peripheral vascular disease within twenty years of diagnosis”.<sup>21</sup> In diabetics ulcers of the foot are common when treated there is a chance of reoccurrence, diabetic foot effects the quality of life, may be fatal or lead to amputation of the limb. “the life time risk for any diabetic patient is up to 15%”.<sup>22</sup>

Generally people with diabetes suffer tingling, pins and needles, burning or pain or loss of sensations in feet, toes or lower limb. Nearly half the people claimed to have experienced such sensations, which shows that these people might have an underlying disease, for which they might have not been tested. The association of Diabetes with myocardial infarction and stroke is sixth on the mortality list. Furthermore the incidence of blindness in the age group 20-74, the lower limb amputation due to diabetic neuropathy and 43% all end-stage renal failures are due to diabetic kidneys related to diabetes.<sup>23</sup>

The source of information plays a very important role in the awareness of the disease. In our study, a large percentage of people received information about the disease from an affected family member or friend, while very few seemed to have information from the media or newspapers. Diabetes is a multifactorial disease its socio-cultural effects demands the need and support of the family, friends and diabetic clubs.

It is important to educate people about the spread of the disease, and for that community's participation is equally needed. One such study is focused on health promotion and primary health care approach which can address the issues of health education and counseling programs to deal with the apprehensions and phobias which stigmatize the diabetics so that they can lead

satisfactory lives through change in behavior and attitude.<sup>24</sup>

Prevention is better than cure. According to our study, a significant number of participants believed that blood sugar levels could be controlled by taking a balanced diet, indicating their high level of awareness regarding the importance of diet in relation with DM. Although there is no special diet for DM, but a healthy balanced diet, low in fat and rich in fiber is the key to a healthy life. An “evidence-based review using meta-analyses techniques largely support the strong majority recommendations of the international diabetes community. Strong RCTs support these recommendations: intake of carbohydrate of  $\geq 55\%$  or 55–65% of energy, dietary fiber intakes of 25–50 g/d (15–25 g/1000 kcal), total fat intakes of  $<30\%$  of energy and incorporation of the glycemic index into diabetes counseling. There is very strong support for the recommendation that diabetic individuals achieve and maintain a desirable body weight with a BMI  $\leq 25$  kg/m<sup>2</sup>”.<sup>25</sup>

## CONCLUSION

The study reveals the essential need for research based health promotion programs to create awareness about diabetes in the lower socio economic strata of the city. Diabetics require a complete change in life style in relation to diet and exercise.

In conclusion, JPMC a tertiary care hospital in Karachi demonstrated that the level of awareness about diabetes mellitus is low amongst the community who are not suffering from the disease, whereas the diabetic patients are well informed about the disease which reflected in their approach towards the disease.

## Acknowledgement

We highly appreciate and acknowledge the efforts and contribution made in data analysis during September 2008-December 2008 at the Department of Community Medicine by Dr.Farah Zaki, Dr Rabiya Fazal Dad, Dr.Mehren Iqbal and Dr. Abya Fatima, Ex Students of Sindh Medical College, Dow University of Health Sciences. Karachi.

## REFERENCES

1. Kumar, Abbas, Fausto. The endocrine system. In: Robbins, Cortan, editors. Pathologic Basis of Disease. 8<sup>th</sup> ed. Philadelphia: W B Saunders; 2011.p.1197.
2. WHO Report. Diabetes kills without distinction. 26 Feb 2006. <http://www.idf.org/home/index.cfm?unode=DE93DC2D-468B-4C75-91DA-69314504BD0E>
3. Hashmi NR, Daud S, Manzoor I. Diabetes Mellitus; Awareness among individuals attending

- outpatient department of Ghurki Trust Teaching Hospital. Prof Med J 2008; 15(1):96-100.
4. Echouffo-Tcheugui JB, Ali MK, Griffin SJ, Narayan KM. Screening for Type 2 Diabetes and dysglycemia. Epidemiol Rev 2011;30(5).
  5. Groi ME, Halabi VT, Gerstenbluth JF, Alberts JF, O'Neil J. Lifestyle in Curacao. Smoking, alcohol consumption, eating habits and exercise. West Indian Med J 1997;46:8-14.
  6. Pennock T. Diabetes and nutrition: the latest thinking on dietary management. Prof Nurse 2005; 20: 27-30.
  7. Adil MM, Alam AY, Jaffery T. Knowledge of Type 2 Diabetic Patients about their illness: Pilot project. JPMA 55:221;2005.
  8. Nisar N, Khan IA, Qadri MH, Sher SA. Knowledge and Risk assessment of diabetes mellitus at primary care level: A Preventive approach required combating the disease in a developing country. Pak J Med Sci 2008; 24(5): 667-72.
  9. Rafique G, Azam SI, White F. Diabetes knowledge, beliefs and practices among people with diabetes attending a university hospital in Karachi, Pakistan. Eastern Mediterranean Health J 2006;12(5).
  10. Ulvi OS, Chaudhary RY, Ali T, Khan MFA, Khan M, Malik FA, et al. Investigating the awareness level about Diabetes Mellitus and associated factors in Tarlai (Rural Islamabad). JPMA 2009;59:98.
  11. Sivagnanam G, Namasivayam K, Rajasekaran M, et al. A comparative study of the knowledge, beliefs, and practices of diabetic patients cared for at a teaching hospital (free service) and those cared for by private practitioners. Ann N Y Acad Sci 2002 958:416-9.
  12. Gruesser M, Bott U, Ellermann P, Kronsbein P, Joergens V. Evaluation of a structured treatment and teaching program for non-insulin-treated type II diabetic outpatients in Germany after the nationwide introduction of reimbursement policy for physicians. Diabet Care 1993;16:1268-75.
  13. Simmons D, Meadows KA, Williams DR. Knowledge of diabetes in Asians and Europeans with and without diabetes: the Coventry Diabetes Study. Diabetes Med 1991;8(7):651-6.
  14. Rai M, Kishore J. Myths about diabetes and its treatment in North Indian population. Int J Diabetes Dev Ctries 2009;29(3):129-32.
  15. Iqbal F, Naz R. Patterns of diabetes mellitus in Pakistan: An overview of the problem. Pakistan J Med Res 2005;44(1).
  16. Zhou J. Life style interventions study on the effects of impaired glucose regulations in Shanghai urban communities. Wei Sheng Yan Jiu 2011; 40(3):331-3.
  17. Ardiles L, Mezzano S. Diabetic renal disease: the World Kidney Day in Chile. Rev Med Chil 2010;138(4):397-400.
  18. Anderson JW, Kendall CW, Jenkins DJ. Importance of weight management in type 2 diabetes: review with meta-analysis of clinical studies. J Am Coll Nutr 2003;22(5):331-9.
  19. RS Surwit, MS Schneider. Role of stress in the etiology and treatment of diabetes mellitus. Psychosomatic Medicine 55(4):380-393.
  20. Haffner SM, Lehto S, Ronnema T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. The New Eng J of Medicine 1998; 339: 229-34.
  21. Jawaid SA, Jawaid M. Management of diabetic foot ulcers: some bitter facts and harsh realities. P J Med Sci. 2006; 22( 1)  
<http://www.pjms.com.pk/issues/octdec06/article/page1.html>
  22. Reiber GE, Lipsky BA, Gibbons GW. The burden of diabetic foot ulcers. Am J Surg 1998;176 (2A Suppl):5S-10S.
  23. Purdy M. Diabetic tissue damage may be explained by controversial theory. Nov 2004. <http://mednews.wustl.edu/news/page/normal/4169.html>
  24. Rafique G, Shaikh F. Identifying needs and barriers to diabetes education in patients with diabetes. J Pak Med Assoc. 2006;56(8):347-52.
  25. Anderson JW, Randles KM, Kendall CWC, Jenkins DJA. Carbohydrate and Fiber Recommendations for Individuals with Diabetes: A Quantitative Assessment and Meta-Analysis of the Evidence. J Am Coll Nutr 2004; 23(1):5-17.

#### Address for Corresponding Author:

Shaheen Akbar Agha  
202-B. Amber Towers  
Plot No. 22-A, Main Sharea Faisal  
Block-6. PECHS  
Karachi-75400  
Phone: 0333-2215280, 0333-2112930  
E.mail: dr\_s\_gha@yahoo.com

**Review Article**

# Significant Reduction of Malaria in the Punjab, Pakistan after Introduction of Roll Back Malaria Strategy in 2003

1. Muhammad Saleem Rana 2. Akhtar Tanveer 3. Asma Abdul Latif  
4. Ammara Hassan Tahir

1. Assoc. Prof., Health Services Academy, Islamabad 2. Prof. of Parasitology, Punjab University, Lahore  
3. Asstt. Prof. of Zoology, Women College University, Lahore 4. Asstt. Prof. of Medicine, AIMC, Lahore.

## ABSTRACT

**Aims of Study:** The purpose of this study was to understand the malarial situation in Punjab, Pakistan.

**Place and Duration of Study:** In this study, the data was collected from different health facilities, malaria control programme offices, reference laboratories and field stations of 91 districts from 2005 to 2009.

**Materials and Methods:** The data of past five years (2005-2009) from health facilities, malaria control programme offices, reference laboratories and field stations was collected. An excel databank was created and analysis was done by using SPSS. Out of the total of 123 districts, 91 districts (86.7%) were endemic for malaria in Pakistan. Balochistan and FATA (Federally Administered Tribal Areas) had highest malaria incidence, while Sind and KPK (Khyber Pakhtoon Khah) had moderate. The lowest malaria incidence was confined to Punjab and AJK (Azad Jammu Kashmir). In Punjab the maximum API (Annual Parasitic Incidence) was noted 0.04 in 2005 and 0.05 in 2009. The incidence of cases in south Punjab was more than central and north Punjab, 82% of indigenous cases were of *Plasmodium vivax*, 18% were of *P.falciparum*, *P.ovale* & *P.malariae* or mix infection was not reported. In Punjab malaria has reduced significantly ( $p=0.028$ ) and fully qualifies the embarkation of malaria elimination strategy. Prioritizing to target *P.falciparum* first and subsequently eliminate the *P.vivax* malaria. KAP (Knowledge, Attitudes and Practices) study is required before initiating malaria elimination in Punjab, Pakistan.

**Key Words:** Malaria, Roll back, elimination, Punjab, Pakistan.

## INTRODUCTION

Since ancient times, humankind has had to struggle against the pathogenic microorganisms, among which *plasmodium* is still the most important causing malaria worldwide<sup>1</sup>. Malaria is a major public health problem, both treatment and control are hampered by the spread of resistance to common antimalarial drugs which is highly prevalent<sup>2</sup>. *Plasmodium falciparum* (*P.falciparum*) resistance to 4-aminoquinolines (chloroquine etc) contributes to increase the malarial morbidity and mortality<sup>3</sup>. Cerebral malaria was reported among 4% and severe anaemia due to malarial was found among 17% of Afghan population admitted in hospitals<sup>4</sup>. Anatoly 2008<sup>5</sup> reported that available data for 1963 to 2007 reveal that malarial endemicity in the Punjab province of Pakistan fluctuated between hypo-to-meso levels during “normal” years and was subjected to “regional” malaria epidemics with periodicity of 5-8 years. Although this classic pattern was altered by the activities of the National Eradication Programme, this trend was traced during subsequent years. Thus, the highest malaria incidence was reported in 1974 (API 9.44), reducing to very low level in

1984(0.47). Next increase in malaria incidence occurred in 1984 (1.35) and then in 1992 (0.99), thereafter and up to now the incidence was demonstrating steady declining trend, reaching API 0.02 in 2006.

Malaria is quite common in Pakistan but epidemiological data is insufficient to exactly evaluate the incidence<sup>6,7,8</sup>. Malaria is accountable for every fifth person in D.I.Khan<sup>9</sup>. The PCR analysis confirmed 83.3% *P.vivax* and 24.6% *P.falciparum* malaria in Bannu, Pakistan<sup>10</sup>. In Punjab ME (Malaria Eradication) programme worked from 1960-1970, since 1971 MC (Malaria Control) programme is working till to date with RBM (Roll Back Malaria) strategy from 2003. RBM strategies are well tuned to the principles of the Global RBM strategy<sup>11</sup>. RBM strategies aiming for early detection and prompt treatment at the health facilities and in the community, reduced reliance on the use of insecticide by restrict selective deployment of the IRS (In Door Spray) in well defined malaria endemic areas, strengthening of disease surveillance and malaria outbreaks response and BCC (Behavior Change Communication). Laboratory confirmed positive cases treatment as per national treatment guidelines. API (Annual Parasite Incidence), SPR (Slide Positive Rate),

ABER (Annual Blood Examination Rate), MBER (Monthly Blood Examination Rate), Percentage *P.falciparum* cases and vector density per room in sentinel sites of areas under IRS were important indicators for performance and diseases incidence evaluation.

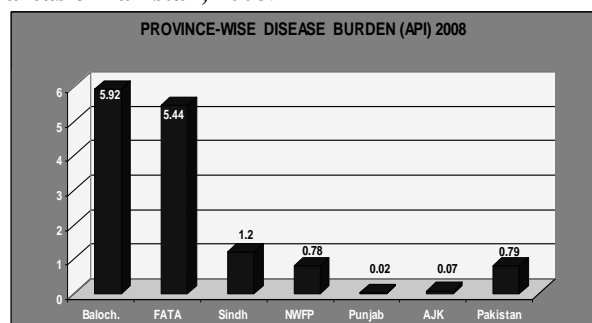
## MATERIALS AND METHODS

This study was planned to review the malaria situation in Punjab, Pakistan. Data collection tools of programme were used. Subjects of the study were laboratory confirmed positive human malaria cases for *P.falciparum* and *P.vivax*. Data was collected from the provincial malaria control programme Punjab, national malaria control programme Pakistan, reference laboratories and field stations for the year 1963 to 2009. Statistical analysis was done by using SPSS program and significance of different variables and correlation was calculated. All positive cases of *P.falciparum* and *P.vivax* were treated with 4-aminoquinoline (chloroquine etc) and 8-aminoquinoline (primaquine) from 1963 to 1996. Later *P.falciparum* cases were treated with sulphadoxine-pyrimethamine up to 2007. Since 2007 all *P.falciparum* cases are being treated with ACT (Artemisinin Combination Therapy). For vector control IRS was started with DDT (dichlorodiphenyltrichloroethane) in 1963 against which vector became resistant and new group of insecticide OP (organophosphorus) compound was introduced in 1976. 1992 vector also became resistant against OP compounds; hence, presently use insecticide of pyrethroid (deltamethrin) group was launched and used very carefully by observing scientific techniques. This data was also collected and analyzed.

## RESULTS

Province wise malaria situation in Pakistan is presented in the figure 1<sup>12</sup>. It can be seen that, the lowest malaria incidence was confined in two provinces, Punjab and AJK with combined population of more than 56% of total population of the country Figure 1

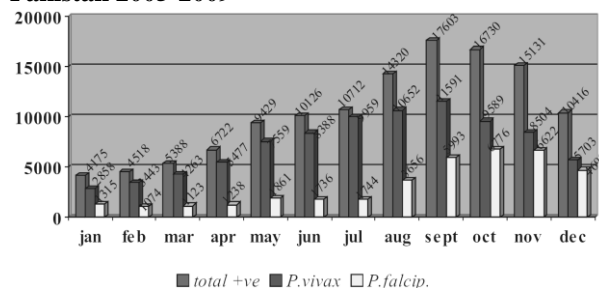
**Figure No.1: Occurrence of malaria in different areas of Pakistan, 2008.**



Malaria incidence less than 1 case per thousand populations per year indicates that malaria is not no more major public health problem in the in the area. However, malaria indicators demonstrate that the system of anti malarial activities carried out during the last few years appears to reach the ceiling of its efficacy, thus necessitating the decision on further course of action.

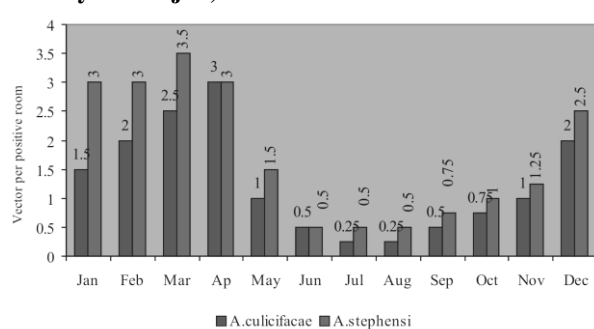
There is a well established seasonal pattern of malaria with the peak of *P.vivax* transmission during July to October soon after moon soon and that of *P.falciparum* during October to December as given in figure 2. This pattern showed that during rainy season vector density increases and disease transmission started but in winter season how transmission of *P.falciparum* occurs. The resistance of *P.falciparum* is because of recrudescence during this low temperature season.

**Figure No.2: Seasonal Pattern of Malaria in Punjab, Pakistan 2005-2009**



In Punjab the major malaria vectors were found *A.culicifacies* and *A.stephensi*, while mosquitoes of the anopheles genus *A.fluviatilis* and *A.superpictus* were also noted. Seasonal trends of major vectors *A.culicifacies* and *A.stephensi* in the province are given in figure 3. *A.stephensi* is represented by both type forms<sup>13</sup>. *A.culicifacies* and *A.stephensi* found susceptible to deltamethrin and resistant to Malathion & DDT.

**Figure No.3: Seasonal Trend of Malaria Vectors Density in Punjab, Pakistan 2005-2009**



In Punjab province data from 1963 to 2009 (Figure 4), reveal that malaria endemicity in the province fluctuated between hypo to meso levels during "normal" years and was subjected to "regional" malaria

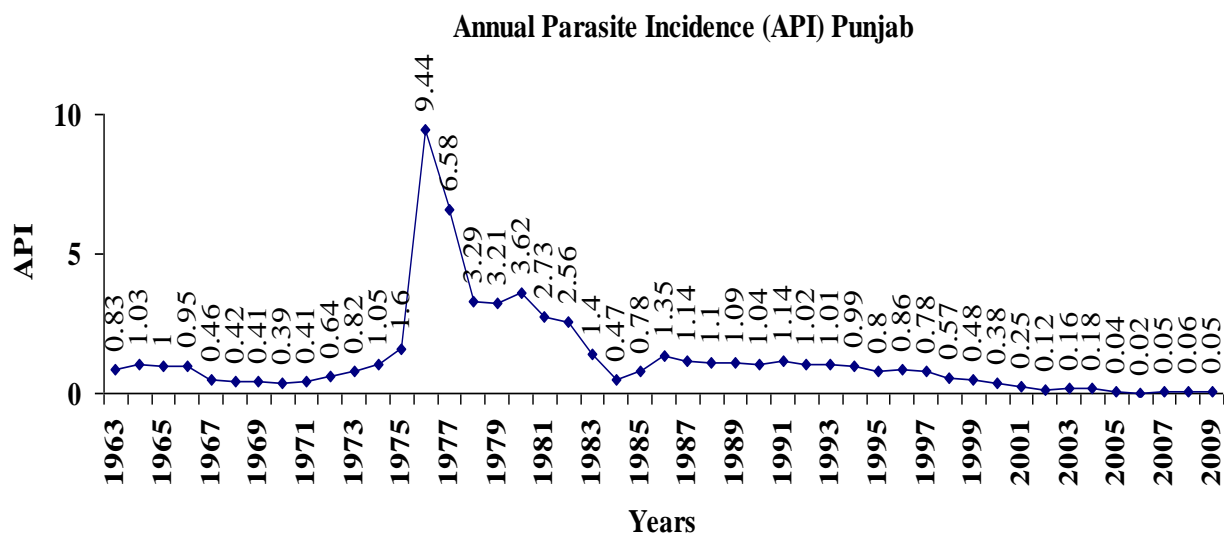


epidemics with periodicity of 5-8 years<sup>14</sup>. Although this classic pattern was altered by the activities of the

National Eradication Programme, its trend was traced during subsequent years in Malaria Control.

**Figure No. 4: Annual Parasite Incidences (API) in Punjab from 1963 to 2009**

(Curtsy of Malaria Control Programme Punjab, Pakistan (2009))



Thus, the highest malaria incidence was reported in 1976 (API 9.44%), reducing to low level from 1984(0.47) and thereafter up to now the incidence was demonstrating steady declining trend, reaching API 0.05% in 2009. Overall objective of the programme is to reduce malaria morbidity and eliminate malaria mortality by keeping malaria under effective control so that it does not become a major public health and socio-economic problem.

**Table No.1: Results of Drug Monitoring (Chloroquine) in Punjab, Pakistan 2004**

	M/garh	D.G.Khan	Rajanpur	Total	%age
Total Subjects	200	200	200	600	100
Lost and Withdrawal	1	10	2	13	2
Analyzed	199	190	198	587	98
LCF	64	59	51	174	29
EPF	22	18	16	56	9
LPF	76	69	71	216	36

**LCF;** Late Clinical Failure, **EPF;** Early Parasitic Failure, **LPF;** Late Parasitic Failure

Targets to keep malaria under control are incidence less than 2 per 1000 population per year and to have halved by 2015 (which has been already achieved). Thus, it appears that the goal of malaria control programme in Punjab Province (malaria incidence less than 2 per thousand populations) has been achieved since last several years. With malaria incidence less than 1 case per thousand population malaria has ceased to be a major Public health problem in the Province. However,

malaria indicators demonstrate that the system of anti malarial activities carried out during the last few years appears to reach the maximum of its efficacy, thus necessitating the decision on further course of action. Local strains of *P.falciparum* resistant to chloroquine were reported<sup>15</sup> as given in table No.1.

In 2004, Out of the total of 105 districts, 91 districts (86.7%) had been affected by malaria as given in table No.2.

Two provinces, namely Balochistan and FATA reported highest malaria incidence, while Sind and KPK provinces reported moderate. *P.vivax* was predominant malaria species. Highest *P.falciparum* malaria proportion was reported in Balochistan and Sind, although it did not exceed 35%. In 2007, out of the total reporting 123 districts, malaria was present in 114 districts (93%). Most remarkable reduction of malaria incidence was shown in Punjab province (almost three times less as compared with 2004); reduction was not observed in other provinces (able No.3).

Data of 2004 and 2007 was analyzed and compared; statistical findings calculated by SPSS-16 are given in table 4. It showed highly significant (p value =0.001) decrease in API of Punjab only by applying paired T-test. In Sind and KPK API decreased but difference was not significant. In all other areas including Pakistan, FATA and Balochistan API was increased significantly. In AJK increase in API was found not significant.

### Findings

It appears that the goal of malaria control programme in Punjab Province (malaria incidence less than 2 per thousand populations per year) has been achieved. Malaria incidence reduced in the province after introduction of RBM strategy and has reached its ever

lowest level. This level of incidence fully qualifies for strategy in Punjab Pakistan. embarkation on implementation of malaria elimination

**Table No.2: Malaria Situation in Different Provinces of Pakistan, 2004**

(Curtsy of Directorate of Malaria Control Pakistan (2008))

Province	Population (000)	Total cases	P.v	P.f	P.f (%)	ABER (%)	SPR (%)	Parasite Incidence	Districts	
									Total	Affected
Punjab	86 157	4 413	3 558	855	19.0	1.72	0.30	0.05	34	33
Sind	36 032	36 447	24142	12207	33.0	3.84	2.63	1.01	16	15
KPK	21 445	23 834	21218	2 221	9.0	1.87	6.04	1.13	24	18
F A T A	3 765	14 665	12327	2 528	17.0	3 66	10.78	3.95	8	8
Balochistan	7 488	31 685	20987	10731	34.0	3.76	11.27	4.23	23	17
A J K	3 424	547	495	58	11.0	4.97	0.32	0.16	NA	NA
Pakistan	158 011	111 781	82727	28600	25.6	2.44	2.90	0.71	105	91

**Table No.3: Malaria Situation in Different Areas of Pakistan, 2007**

(Curtsy of Directorate of Malaria Control Pakistan (2008))

Province	Population (000)	Total Cases	P.v	P.f	P.f (%)	ABER (%)	SPR (%)	Parasite Incidence	Districts	
									Total	Affected
Punjab	92 040	1 903	1 534	369	19.0	2.14	0.1	0.02	35	29
Sind	41 142	29 330	19 604	9 728	33.0	2.89	2.4	0.71	23	23
KPK	21 806	17 451	13 794	1 664	10.0	2.77	2.8	0.80	24	24
F A T A	3 757	23 234	19 455	3 773	16.0	5.70	10.8	6.19	7	7
Balochistan	8 829	55 908	29 801	24314	43.0	7.46	8.4	6.33	30	27
A J K	3 496	744	724	20	2.0	7.88	0.2	0.21	4	4
F A N A	1 375	-	-	-	-	-	-	-	-	-
I C T	1 056	-	-	-	-	-	-	-	-	-
Pakistan	173 500	128 570	84 912	39856	31.0	2.83	2.6	0.74	123	114

**Table 4-Data Analysis by SPSS 16 and Significance of Annual Parasite Incidence (API) for the Year 2004 and 2007 Calculated by Paired T-test**

Area	Paired Differences in API			
	2004 Mean $\pm$ SD	2007 Mean $\pm$ SD	differe nce	P-value
Punjab	0.53 $\pm$ 0.05	0.24 $\pm$ 0.03	0.29	0.001*
Sind	1.01 $\pm$ 1.89	0.71 $\pm$ 0.89	0.30	0.329
KPK	1.13 $\pm$ 1.84	0.80 $\pm$ 0.94	0.33	0.260
FATA	3.95 $\pm$ 0.26	6.19 $\pm$ 0.61	-2.24	0.000
Balochistan	4.22 $\pm$ 2.59	6.33 $\pm$ 1.27	-2.11	0.001
AJK	0.16 $\pm$ 0.09	0.20 $\pm$ 0.08	-0.04	0.350
Pakistan	1.60 $\pm$ 2.35	2.08 $\pm$ 2.80	-0.48	0.007

\*highly significant

## DISCUSSION

Data of all provinces and Pakistan for the year 2004 was compared with data for the year 2007 which gave very complex picture of Sind and KPK. In Sind 15 districts were endemic out of total 16 districts in 2004 and 23 districts were found endemic out of 23 in 2007. Number of positive cases for all types of malaria was 36447 in 2004 and reported 29330 in 2007 with p value 0.563. This situation showed horizontal increase of cases and vertically there is decreasing trend but this result is not showing significant statistical values. In KPK 18 districts were endemic out of total 24 districts 2004 and 24 districts were found endemic out of 24 in 2007. Number of positive cases for all types of malaria

was 23834 in 2004 and reported 17451 in 2007 with p value 0.380. There is same observation on data of KPK. In Punjab 33 districts were endemic out of total 34 districts 2004 and 29 districts were found endemic out of 35 in 2007. Number of positive cases for all types of malaria was 4413 in 2004 and reported 1903 in 2007 with p value 0.028. In Punjab disease incidence decreased horizontally and vertically with significant statistical values. In Pakistan 91 districts were endemic out of total 105 districts 2004 and 114 districts were found endemic out of 123 in 2007. Number of positive cases for all types of malaria was 111781 in 2004 and reported 128570 in 2007 with p value 0.000. Pakistan data also showed horizontal and vertical increase of disease incidence with significant p value. Hence, on the data of Punjab any future decision can be safely made.

Therefore possibility of malaria elimination in Punjab Province is a reality, providing that additional efforts and inputs in terms of resources both financial and human are made available. Ecological changes favoring reduced level of malaria transmission "Green revolution" in agriculture through improved water management due to scarcity of water, resulting in drastic reduction of breeding sites, introduction of practices of intermittent irrigation for rice, leveling of rice and cotton fields, cementing of edges of irrigation canals preventing water leakages, introduction of high-yielding varieties of cotton and rice with the large-scale deployment of pesticides and alike. There is an abundance of eucalyptus trees (known for its ability to extract water from underground thus reducing water table) and neem trees (known for its leaf mosquito repellent action) throughout the province, on which local industry of paper mills is based. Literacy rate of population of Punjab province is higher than in any other province of Pakistan, which could be beneficial for implementation of the awareness campaign particularly in pre-elimination stage of malaria elimination programme. Socio-economic status of population of the Province is somewhat superior to any other province, allowing the local population to allocate more money for purchasing individual means of protection from mosquito bites.

## CONCLUSION

It is concluded that factors are favoring malaria elimination in the province of Punjab, Pakistan because there is a strong political commitment on the part of the provincial and federal Governments, efficient and motivated staff of the malaria control programme in the province is available, reliable malaria diagnosis service at various levels of the malaria control programme is existed and recently highly efficacious tools of treatment "ACT for *P.falciparum* and 14-day

primaquine for *P.vivax* has been introduced. Provincial malaria control programme is capable to almost immediately respond to emergency situation and has already demonstrated success in dramatic reduction of overall malaria incidence during the last few years. Hence, programme should adapt the elimination strategy to target the *P.falciparum* malaria first and subsequently eliminate *P.vivax*.

## 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 national and provincial malaria control programmes of Pakistan for their cooperation to complete this study.

## REFERENCES

- Schlitzer M. History of antimalarial drug development, currently used therapeutics and drugs in clinical development. *Chem Med Chem* 2007;2(7):944-986.
- Touré AO, Koné LP, Jambou R, Konan TD, Demba S, Beugre GE. In vitro susceptibility of *Plasmodium falciparum* isolates from Abidjan (Côte d'Ivoire) to quinine, artesunate and chloroquine. *Sante* 2008; 18(1):43-47.
- Ogunbamigbe TO, Ojurongbe O, Ogunro PS, Okanlawon BM. Chloroquine resistant *Plasmodium falciparum* malaria in Nigeria: efficacy of amodiaquine + sulfadoxine-pyrimethamine and chloroquine + chlorpheniramine for treatment. *Mem. Inst. Oswaldo. Cruz* 2008; 103(1):79-84.
- Okiro EA, Al-Ta'iar A, Reyburn H, Idro R, Berkley JA, Snow RW. Age patterns of severe paediatric malaria and their relationship to *Plasmodium falciparum* transmission intensity. *Malar J* 2009; 8:4-6.
- Anatoly K. Situation analysis of malaria situation in the province of Punjab, Pakistan 2008; 16-21.
- Khadim MT. Malaria a menace at Zhob Garrison. *Pak Armed Forces Med J* 2002; 52: 203-207.
- Muhammad N, Husain A. Prevalence of malaria in general population of district Bunir. *J Post grad Med Inst* 2003; 17: 75-80.
- Murtaza G, Mammon A, Norani AK. Malaria prevalence in Sind. *Med Channel* 2004; 10:41-42.
- Khan HU, Aziz MK, Khan MH, Mahsud IU, Shah SH. A study of prevalence of malaria in adult population of D.I. Khan Pakistan. *Biomedica* 2006; 22:99-105.
- Lubna K, Frederick NB, Mariangela B, Salman A M, Guiyun Y. Short Report: Prevalence of antimalarial drug resistance mutations in *Plasmodium vivax* and *Plasmodium*

- falciparum from a malaria endemic area of Pakistan. *Am J Trop Med Hyg* 2009; 81(3): 525-528.
11. National Strategic Plan for malaria control in Pakistan 2004; 12-18.
  12. Directorate of malaria control programme Islamabad Pakistan. Annual report of malaria control programme 2009; 7-12.
  13. Ramachandra R. The Anopheline of India. *Trans Roy Soc Trop Med and Hyg* 1984; 78-85.
  14. Malaria Control Programme Punjab, Pakistan. Annual report of malaria control programme 2010; 5-11.
  15. Rana MS, Tanveer A. Chloroquine resistance and *Plasmodium falciparum* in Punjab, Pakistan during 2000-2001. *Southeast Asian J Trop Med Public* 2004; 35(2):40-43.

**Address for Corresponding Author:**

Muhammad Saleem Rana,  
Associate Professor,  
Health Services Academy,  
Islamabad.

**Case Report**

# Rhino-Sino-Orbito-Cerebral Mucormycosis, a Case Report and Literature Review

1. Azhar Mehmood Javed 2. Malak Hassan Alawi 3. Farhad Hussain Mir  
4. Abdul Hafeez Alawi

1. Asstt. Prof. of Radiology, ICH, Multan 2 & 3. Consultant Radiologists, King Abdul Aziz Hospital, Makkah, Saudi Arabia 4. Consultant Radiologist, Al-Noor Specialist Hospital, Makkah, Saudi Arabia.

## ABSTRACT

Mucormycosis is rare, life threatening infection, especially in diabetic with ketoacidosis. The infection is caused by a group of saprophytic fungi of class phycomycetes rhizomucor, rhizopus and mucor are more common fungi. The diagnosis is based on high clinical suspicion, CT / MRI imaging and histopathological confirmation. We present a 50 years, diabetic female, with history of mainly left sided facial pain, swelling is recent decreased left eye movement as well. High suspicion of Mucormycosis on CT which confirmed on histopathology later on.

Patient responded well clinically with amphotericine B posaconazole & endoscopic debridement. Patient was discharged 10 days later with followed up MRI and antifungal treatment for 6 month.

**Key Words:** Mucormycosis, Diabetes, Paranasal sinuses, Orbits Brain, Immunosuppression, Computerized Tomography (CT), Magnetic Resonance Imaging (MRI).

## INTRODUCTION

Mucormycosis, also called Zygomycosis or phycomycosis, was described by Paull Tauf in 1885<sup>(1)</sup>. Paranasal mycosis usually Mucor or Rhizopus<sup>(2)</sup>, manifests as two distinct entities, a benign or non invasive infection and a relatively serious, invasive infection which usually occurs in immunocompromised individuals<sup>(3)</sup>. Invasive form causes vascular thrombosis and tissue necrosis with signs and symptoms due to involvement of nose, PNS, orbits or central nervous system. The risk factors include ketoacidosis and hematologic malignancies. The prognosis is poor, especially in presence of severe sequelae resulting in high mortality even in patients with prompt diagnosis and correct treatment<sup>(4)</sup>.

## CASE REPORT

We present 50yrs old house wife, came in medical OPD in King Abdul Aziz Hospital Makkah (Saudi Arabia) for nasal swelling, pain and swelling of left maxilla with recent onset of restricted left eye movement & ptosis. Patient was known diabetic, but not ketoacidotic with poor oral antidiabetic control, on external examination showed left sided nasal / cheek skin involvement and ptosis of left eyelid with provisional diagnosis of fascitis, mainly left sided (Fig1). Laboratory findings revealed increased neutrophils (14500 / mm<sup>3</sup>), blood glucose level 360g/100ml. normal electrolytes and renal parameters. Liver enzymes and coagulation profiles were in normal limits. Left eye examination revealed minimal painful restriction of movement and redness which aggravated

though blood sugar was controlled and antibiotics were given. After two days, suppuration from her left nostril appeared, with some black material in it. So suspicion of Mucormycosis was made. CT PNS and brain was recommended along with histopathology after incisional biopsy of left nasal cavity mass. Amphotericin B therapy was started. CT study showed opacification of sinuses, more on left side with medial wall of orbit destruction and intracranial extension in left basifrontal region (Fig 2 a & b). Histopathology also revealed aspetate hyphae with right angle branching, which are typical for mucormycosis (Fig 03). She recovered completely after endoscopic sinus / nasal debridement and antifungal treatment. Patient remained well after two month follow up with no residual left eye damage, this all was due to early diagnosis of mucormycosis with diagnostic support of imaging studies.

## DISCUSSION

Mucormycosis is commonly caused by Rhizopus, absidia, Mucor, Rhizomucor species, however different fungi (Cunningamella, Saksenala, Syncephala strum, Cokeromy, Mortiella) can also be found. Few cases reported in medical literature are caused by apophytomyces, usually in healthy individuals with traumatic inoculation<sup>05</sup>. Fungi usually acts as opportunistic infection, may be present in solid, decaying organic debris and bread moulds. The predisposing factors are diabetes mellitus and hematologic malignancies with neutropenia. The risk factors are chronic steroid intake, organ transplant,

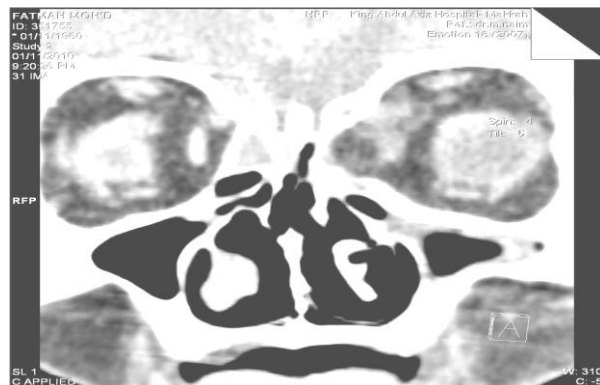
chronic renal insufficiencies, chemotherapy, ferrum intoxicity and tooth extraction.



**Figure No.1: Nasal / left maxillary swelling with color changes and left eye ptosis**



**A**

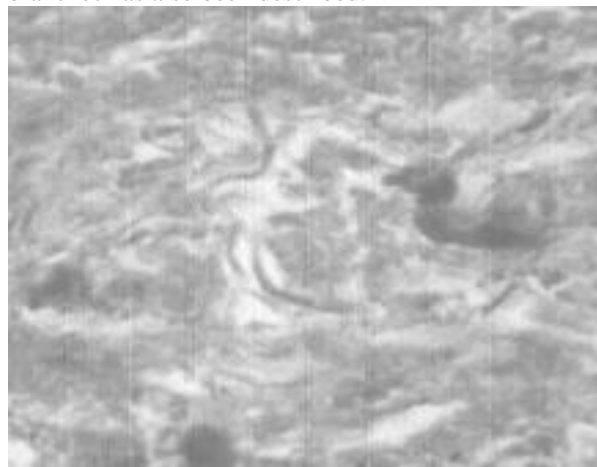


**B**

**Figure No.2: A, B CT Coronal images showing involvement of basifrontal, both ethmoids, left maxillary and left orbital regions.**

Different forms seen by intalation / inoculation of spores, these include, rhino, orbital, respiratory, gastrointestinal, cutaneous and mixed. Only in advanced disease, symptoms become more specific otherwise in initial stages, may be difficult to detect. Necrosis is present in 20-40% of cases and is considered bad prognostic sign. CNS is affected

through orbital apex while orbit is involved by nasolacrimal duct, medial wall dehiscences or the anterior and posterior ethmoidal orifices. The fungus adheres to blood vessel wall, leading to ischemia and necrosis. Perineural spread through the trigeminal branches has also been described.



**Figure No.3: Aseptate hyphae, branching at right angle, typical form Mucormycosis.**

The diagnosis is usually made by clinical suspicion, imaging findings and histopathology. Clinically, fever is the most common early symptom (44% cases) <sup>6</sup>, followed by nasal ulceration or necrosis, periorbital or facial swelling and decreased vision (33% cases), 80% may develop necrotic lesions on nasal or oral mucosal later on. Imaging findings may be non specific initially however later on polyridal mucosal thickening and hyperdense foci in affected sinuses / nose are highly suggestive of fungal disease on CT<sup>3</sup>. MRI gives a better visualization of brain, orbits, perineural invasion and vascular obstruction. It is usually preferred choice because of use of nephrotoxic drugs and presence of compromised renal function.

## CONCLUSION

In conclusion the early diagnosis is imperative in management and reduction in bad sequelae in invasive Rhino, Orbito, sinocerebral mucormycosis as in this case, The treatment should be focused on proper antifungal (amphotericine B and Posaconazole) and surgical debridement. Follow up is by clinical examination and MRI. The prognosis has improved dramatically, with a mortality rate of 85% in 1960 to 30-35% in 2010 <sup>1</sup>.

## REFERENCES

1. Gonzalez Martin Moro J, Lopez- Arcas- Calleja JM, Burgueno-Garcia M, Cebrian- Carretero JL, Garcia-Rodriguez J. Rhino-orbito-cerebral mucormycosis: A case report and literature

- review. Med Oral Patol Oral Cir Bucal 2008; 13 (12):792-5.
2. Khan AR, Khan MU, Ullah S, et al. Rhinocerebral mucormycosis. J coll physician surg Pak 2002;12:639-41.
  3. Wg Cdr A Alam, Gp Capt BN Chander, Wg cdr GS SabhiKhi, Sq ldr M Bhatia. Sinonasal mucormycosis; diagnosis using computerized Tomography (CT) MJAFI 2003;59:243-245.
  4. Auluck A. Maxillary necrosis by mucormycosis, a case report and literature review. Med Oral Patol Oral Cir Bucal. 2007;12(5):360-4.
  5. Liang KP, Tleyjeh IM, Wilson WR, Roberts GD, Temesgen Z. Rhino-Orbital mucormycosis caused by Apophysomyces elegans. J Clin Microbiol 2006;44(3):892-8.
  6. SPS Yadav, Anuj Kumar Goel. Rhino-Orbital mucormycosis- A case report. Int J of paed otorhinolaryngology extra 2010;5:9-12.

**Address for Corresponding Author:**

1. Dr. Azhar Mehmood Javed,  
+9203087949542;  
azharmjaved-g@hotmail.com.
2. Dr. Malak Hassan Alawi  
+966557235911;  
m6alawi@hotmail.com

**Seminar Report****Efforts Urged for Drug free Lahore****Mohsin Masud Jan****Editor**

Every individual, collective political will, every institution, role of a female, civil society and media are required to create clean and healthy drug free atmosphere in Lahore.

This was stated by Federal Secretary Anti Narcotics Control Chaudhry Iftikhar Ahmad during a seminar. The seminar titled "Free Drug Lahore, How and Why" was held at a hotel by Mir Khalil-ur-Rehman Memorial Society (MKRMS) with the collaboration of the Ministry of Narcotics Control and Anti Narcotics Force. Speakers from various walks of life spoke on the occasion and highlighted the causes of effects of drugs and preventive measures to stop their spread. They all agreed that the education, awareness, planning, treatment, political and civil society can help make Lahore a drug free city. Chaudhry Iftikhar, who was the chief guest on the occasion said that this was the time when everyone would not only have to come forward but share his or her commitment and cooperation to make the project successful. He urged the leadership of all political parties to add drug free project into their manifestos. He said that as family was a key component of a social mobilization, it should play its part to create a drug free atmosphere in the city and added that without the participation of NGOs, Civil Society and the Media, the goal could not be achieved.

Anti Narcotics DG Major General Shakil Hussain said that it was need of the hour to educate young generation in colleges and universities as they are falling victim to the menace. He asked the rich to come forward and play their role by helping the poor addict financially.

Anti Narcotics Control Deputy Director, Altaf Qamar said that 600,000 people were taking to addiction every year so we all should stand up by joining hands to root out the menace from country. Ex-Secretary Excise and Taxation Shumail Ahmad Khwaja said the government was ready to include a chapter on narcotics in the curriculum in this regard.

Muhyyuddin Wani, Secretary Information, Culture and Youth Affairs said that religious leaders should also be on board in the critical matter. He said social networking sights like the face book and twitter and celebrities could be used effectively to draw the public attention to the harms of drugs. Prof. Khalida Tarin said economic division was the main cause of promotion of drugs as people used them to get some satisfaction.

Dr. Azhar Masud Bhatti, Director Health Punjab said a committee should be constituted in every town and government should facilitate it overcome drug dealing.

Punjab University VC, Dr. Mujahid Kamran, Dr. Aslam, Dr. Zahid and Mian Zahid said that our youth had become a major victim of addiction and a major strategy needed to chalk out to save our youth as well as our future. Shahzad Ali Malik, President LCCI Lahore, offered his and his office bearer's financial and social help for making the city drug free. Wasif Nagi described the history of drug use in the world. Chief Executive of the Guard Group of Companies Iftikhar Ali Malik, members from civil society, NGOs, government officials, officers and media persons attended the seminar.