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**Editorial Alzheimer's could be stopped from Progressing****Dr. Azhar Masud Bhatti**

Editor in Chief

Alzheimer's disease spreads in a predictable pattern like an infection, going from one brain cell to another along linked circuits known as synapses, researchers say.

The findings, published in the online journal PloS One, suggest that blocking the process early on may keep the disease from spreading.

'This is a phenomenon that is increasingly recognised and potentially very important,' said Dr Samuel Gandy, of the Mount Sinai Alzheimer's Disease Research Center in New York.

'If we understood this process, we could potentially arrest progression at an early stage.'

Imaging studies in people have suggested that Alzheimer's spreads from region to region in the brain rather than popping up spontaneously in different areas, but the evidence was not strong enough to say for sure.

'Everyone talks about Alzheimer's 'spreading', but there really has not been a standard theory,' study authors Dr Karen Duff and Dr Scott Small from the Columbia University Medical Center in New York, said.

'In the past, we have asked many of our colleagues in the field of Alzheimer's research what they mean when they say 'spread'. Most think that the disease just pops up in different areas of the brain over time, not that the disease actively jumps from one area to the next,' they said.

'Our findings show for the first time that the latter might be true.'

More than five million Americans and 465,000 people in the UK suffer from Alzheimer's, a brain disease that causes dementia.

Despite costly efforts, no drug has been found that can keep the disease from progressing.

There is currently no cure for Alzheimer's, which is a progressive condition and most common in people over 65.

For their study, the team used mice that were genetically engineered to accumulate deposits of tau in a key memory center of the brain known as the entorhinal cortex, which is where that toxic protein starts to deposit in people.

Their aim was to map the progression of tau, an abnormal protein that forms tangles of protein fibers in the brains of people with Alzheimer's disease. The team analysed the brains of the mice periodically over a period of 22 months to see how the disease progressed.

They found that as the mice aged, the abnormal human tau spread along a linked pathway, traveling from the entorhinal cortex to the hippocampus to the neocortex, areas of the brain needed to form and store memories. That pattern closely follows the progression of Alzheimer's as it passes through various stages in people, Dr Duff said.

The team also saw signs that tau moved from brain cell to brain cell across synapses, connection points that allow nerve cells to communicate.

The researchers think those findings suggest new strategies for diagnosing and treating Alzheimer's disease.

'First, it would suggest that imaging tools that can detect entorhinal cortex dysfunction will be particularly helpful in diagnosing the earliest stages of the disease,' they said.

'More importantly, it might suggest ways of improving treatment.

'The implication of our study is that if it were possible to 'treat' Alzheimer's when it was first detected in the entorhinal cortex, this would prevent spread,' they said. They likened the approach to treating cancer early, when it is still in one spot, and not waiting until it has spread.

The study may bring a new focus to diagnostics and treatments that focus on tau, rather than amyloid, the protein that causes plaques to form in the brain. Current imaging agents used with PET scanners can identify amyloid deposits in the brain, but not tau. Most late-stage Alzheimer's drugs, including Eli Lilly and Co's solanezumab, and Johnson & Johnson and Pfizer's bapineuzumab, take aim at amyloid, which accumulates silently 15 to 20 years before signs of dementia appear.

# Magnesium Sulphate Therapy in Pre-Eclampsia and Eclampsia: One Year Experience

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## ABSTRACT

**Objective:** To study the efficacy of Magnesium Sulphate Therapy for prevention and control of fits in patients with preeclampsia and eclampsia

**Study Design:** Interventional Study.

**Place and Duration of Study:** This Study was conducted at the Department of Obstetric and Gynecology Unit II, Mother and Child Health Centre, Pakistan Institute of Medical Sciences, Islamabad from April 2002 to March 2003.

**Materials and Methods:** Total 50 women with preeclampsia / imminent eclampsia and eclampsia fulfilling the study criteria were admitted in HDA, adjacent to labour ward. Magnesium Sulphate therapy started after complete evaluation of the patients according to the study protocol. Patients monitored carefully for any side effects of magnesium therapy and occurrence of convulsions. Primary outcome measures were development of eclampsia or recurrent seizures in patients with eclampsia, neonatal morbidity and mortality. **Secondary outcome measures** were serious maternal morbidity, magnesium toxicity and other side effects of  $MgSO_4$  and complications of labour and delivery.

**Results:** Total 50 women were entered into the study over a period of one year. Out of these 12 (24%) women presented with eclampsia, 5 (10%) had imminent eclampsia and 33 (66%) were diagnosed as pre-eclampsia. Of the 12 women with eclampsia, none had recurrent seizures. Out of 38 women with pre-eclampsia and imminent eclampsia, only one (2%) woman developed eclampsia. There was no case of magnesium toxicity. Overall 12 (24%) of the babies were delivered with poor Apgar score. Two babies were expired within five minutes of delivery while 5 babies expired in NICU. There were 6 intrauterine deaths and 4 intrapartum deaths.

**Conclusion:** Magnesium sulphate is an effective anticonvulsant for the treatment and prevention of eclampsia when used judiciously. In the dosage used it does not have any substantive harmful effects on women and their babies.

**Key Words:** Eclampsia, Magnesium Sulphate, Convulsions.

## INTRODUCTION

Pre-eclampsia/eclampsia is an unpredictable multiorgan disorder unique to human pregnancy. The international society for the study of hypertension in pregnancy (ISSHP) currently defines PE as the occurrence of hypertension in combination with proteinuria, developing after 20 weeks gestation in a previously normotensive, non-proteinuric patient.<sup>1</sup> PE is a pregnancy specific syndrome of reduced organ perfusion secondary to vasospasm and endothelial activation. It complicates around 2-8% of pregnancies.<sup>2-4</sup> Although outcome is often good PE is a major cause of maternal and fetal morbidity and mortality worldwide<sup>5</sup> and it accounts for around 16% of maternal deaths in UK (mortality rate 0.9/100,000 maternities).<sup>6</sup> Mortality from hypertensive disorders is much higher in developing countries reaching rates of 70-120/100,000 maternities.<sup>6</sup> The risk of eclampsia in women with severe PE appears to be 1-2%.<sup>6</sup>

Currently eclampsia is defined as "the occurrence of generalized convulsion(s) associated with signs of PE during pregnancy, labor, or within 7 days of delivery and not caused by epilepsy or other convulsive disorders." Of seizures 44% occur postnatally, the remainder being antepartum (38%) or intrapartum

(18%).<sup>6</sup> Almost without exception, PE precedes the onset of eclamptic convulsions.

In developed countries eclampsia is rare, affecting around 1 in 2000 deliveries,<sup>7</sup> while in developing countries estimates vary from 1 in 100 to 1 in 1700.<sup>8-11</sup> In Pakistan, an analysis of 644 maternal deaths in hospital of four provinces showed hypertensive disease, mostly eclampsia, to be the second most common cause (18.6%) preceded only by hemorrhage (21%).<sup>12</sup> Worldwide cerebral infarction and haemorrhage is the principal cause of death<sup>13,14</sup> although in the UK pulmonary complications have now superseded cerebral causes.<sup>6</sup>

Although hypertension is a requisite to diagnosing PE it may not be central to the pathogenesis of PE. Thus eclampsia is not prevented simply by adequate BP control.<sup>15</sup> The main objectives<sup>1</sup> in the management of PE are prevention of convulsions, complications such as pulmonary edema, renal failure, cardiovascular accidents and abruptio placentae and delivery of a healthy neonate with minimal maternal morbidity. So Anticonvulsants are important in the management of PE and eclampsia in addition to antihypertensive therapy. For well over half a century, magnesium sulfate ( $MgSO_4$ ) has been advocated for seizure prophylaxis in PE and eclampsia, yet its use remained controversial.<sup>16</sup>

Although MgSO<sub>4</sub> is being used effectively worldwide, it is not being used in most of the obstetric units of our country for eclampsia and pre eclampsia. The burden of this disease, however, occurs in poor countries and majority of significant morbidity and mortality associated with the disease also occur in these countries. It is therefore more important for developing countries like ours' to establish whether the benefits of administering MgSO<sub>4</sub> to all women with PE and eclampsia outweigh the risk. The purpose of this study is to know the safety and efficacy of MgSO<sub>4</sub> in reducing the risk of eclampsia or to arrest the recurrent seizures in eclampsia.

## MATERIALS AND METHODS

This single centre based interventional study was conducted over a period of one year from April 2002 to March 2003, at department of Obstetric and Gynecology Unit II, Mother and Child Health Centre, Pakistan Institute of Medical Sciences, Islamabad, a postgraduate teaching institution that provides tertiary level care. Fifty women with severe pre-eclampsia and eclampsia who received MgSO<sub>4</sub> Therapy fulfilling the study inclusion criteria were studied.

Women with severe pre-eclampsia where decision for delivery had been made, Imminent eclampsia (e.g. aura, headache, nausea, vomiting, epigastric pain, visual disturbances) and women with eclampsia were included in the study. The criteria for severe pre-eclampsia included:

- Diastolic BP  $\geq$  110 mm Hg on two occasions at least 6 hours apart
- Significant proteinuria (> ++)

Women with mild hypertension, and other neurological disorders causing convulsions were excluded from the study. All women with severe pre-eclampsia and eclampsia were admitted in high dependency area (HDA) adjoining the labour ward. Before starting magnesium sulphate therapy, it was confirmed that the knee jerk or other tendon reflexes were present, the respiratory rate was normal (> 16 resp/min), and urine output was 100ml or more during last 4 hours, or greater than 30ml/h. Magnesium sulphate therapy then started.

**Loading dose:** 4gm of MgSO<sub>4</sub> (8ml of 50% solution) given i.v slowly over 10-15 minutes followed immediately by 6gm i.m given as 3gm (6ml of 50% solution) in the upper and outer quadrant of each buttock.

**Maintenance therapy:** 2.5gm (5ml of 50% solution) given deep intramuscular every 4 hours in the alternate buttocks.

Clinical monitoring of the women continued throughout the treatment with particular attention to BP levels, urine output and development of symptoms. Once stabilized, women not in labour either had their labour induced or were delivered by caesarean section where

indicated. MgSO<sub>4</sub> therapy was continued until 24hours after delivery or last convulsion whichever was later. Therapy stopped early if there were any side effects or urine output dropped below 30 ml/hour because of the risk of toxicity.

**Primary outcome measures** were development of eclampsia or recurrent seizures in patients with eclampsia, neonatal morbidity (poor apgar score, intubation at place of delivery, and admission to neonatal intensive care unit (NICU) and neonatal mortality.

**Secondary outcome measures** were serious maternal morbidity (respiratory depression, respiratory arrest, cardiac arrest, coagulopathy, renal failure, liver failure, pulmonary oedema, and cerebral haemorrhage), magnesium toxicity (need for calcium gluconate, stopped or reduced treatment due to side effects or toxicity), and other side effects of MgSO<sub>4</sub> (nausea, vomiting, flushing of skin, drowsiness, abscess), and complications of labour and delivery (caesarean section, retained placenta, blood loss and transfusion).

Women were retained in HDA until the completion of MgSO<sub>4</sub> therapy and then shifted to postnatal ward. Follow up of women and their babies was until discharge from hospital. The data of all women was recorded on a predesigned Performa which was filled at the time of discharge. Data was entered and analyzed on SPSS. As this was a descriptive study, data are expressed as frequencies, mean with standard deviation and median with range.

## RESULTS

Total 50 women were entered into the study over a period of one year. Out of these 12 (24%) women presented with eclampsia, 5 (10%) had imminent eclampsia and 33 (66%) were diagnosed as pre-eclampsia. 40% of these patients were booked and 60% were non-booked.

**Table No.1: Maternal Demographic Indicators (n=50)**

Variable	Mean	Range	S.D
Age (years)	26.3	18-40	4.3
Gestation (weeks)	34.1	26.6-41	3.8
Hospital stay (days)	6.8	2-15	3.2

**Table No.2: Maternal Complications**

Complication	Number	Percentage
Eclampsia	1	2%
HELLP Syndrome	2	4%
Low platelet count	2	4%
Impaired renal function	2	4%
PPH	2	6%
Need for transfusion	4	8%
Hypotension	1	2%

The characteristics of the study population are shown in Table 1. The maternal demographics show that mean age was 26.3 years (SD=4.3 years). The mean

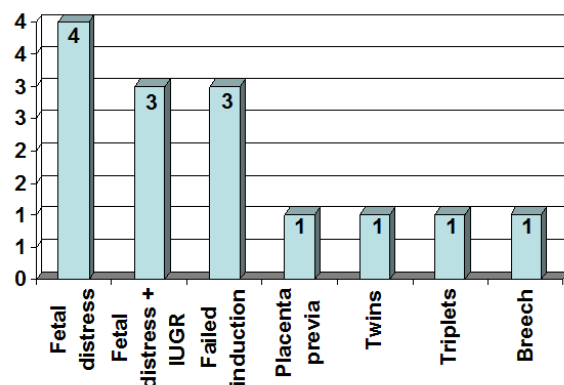
gestational age at admission was 34 weeks and 1 day (range 26.6-41 weeks). The mean number of days spent by the women in the hospital were 6.8 days (SD of 3.2 days). Primigravidae comprised the bulk of the group (54%) followed by multigravidae (34%) and grandmultigravidae (12%)

**Table No.3: Side Effects of Magnesium Sulphate Therapy (n=6)**

Side effect	Number
Respiratory depression	1
Absent tendon reflexes	3
Pain at injection site	2

**Table No.4: Neonatal Outcomes (n=50)**

	Number	Percentage
<b>Live born</b>	<b>40</b>	<b>80%</b>
<b>a) NICU admission</b>	<b>13</b>	<b>26%</b>
- prematurity	6	
- prematurity+IUGR	2	
- IUGR	2	
- Neonatal sepsis	3	
<b>b) Neonatal mortality</b>	<b>7</b>	<b>14%</b>
- prematurity	5	
- prematurity+IUGR	2	
<b>Still born</b>	<b>10</b>	<b>20%</b>
<b>a) IUD</b>	<b>6</b>	<b>12%</b>
<b>b) Intrapartum deaths</b>	<b>4</b>	<b>8%</b>
- prematurity	2	
- prematurity+IUGR	2	



**Figure No.1: Indications For LSCS (n=14)**  
EL=3 EM=11

The major maternal complications that occurred in women receiving magnesium sulphate are shown in Table 2. Of the 12 women with eclampsia who received magnesium sulphate therapy none had recurrent seizures. Out of 38 women with pre-eclampsia and imminent eclampsia, only one (2%) woman developed eclampsia after receiving magnesium sulphate therapy. At admission 2 women were diagnosed to have HELLP syndrome. Low platelet count and impaired renal

functions were present in 2 women each. 72% of the patients delivered vaginally and 28% women had caesarean section. The various indications for caesarean section are shown in Figure 1.

Mean duration of magnesium sulphate therapy was 29.2 hours (SD 12.3 hours). Side effects of magnesium were observed in 6 (12%) of the patients (Table 3). There was no case of magnesium toxicity. In 2 women the magnesium sulphate was discontinued due to prolonged therapy and oliguria.

9 (18%) of the women were diagnosed to have IUGR. The mean birth weight was 1700 g (SD 700g). The mean Apgar score at 1 and 5 minutes was 4.7 and 6.6 respectively. Overall 12 (24%) of the babies were delivered with poor Apgar score and needed intubation at the place of delivery. Neonatal outcomes are shown in table 4. 13 (26%) of the babies were admitted to NICU. The main reasons for admission were prematurity and IUGR. Two babies were expired within five minutes of delivery while 5 babies expired in NICU with severe hyaline membrane disease and sepsis related complications being the most common problems. In all of these neonatal deaths the fetal birth weight was less than 1500 grams. There were 6 intrauterine deaths and 4 intrapartum deaths. All of these deaths occurred between birth weight of 900 and 1200 grams and no operative interventions were done on fetal grounds due to extremely high mortality in infants weighing less than 1500 grams in our nursery.

## DISCUSSION

Every minute, a woman dies in pregnancy or child birth, and 99 out of every 100 of these women live in developing countries.<sup>17</sup> Among deaths from causes other than abortion which are directly attributable to the complications of pregnancy, about quarter are associated with pre-eclampsia / eclampsia. As the aetiology of the syndrome has remained obscure, many different approaches have been used to prevent and manage it. One of these—magnesium sulphate as an anticonvulsant—was introduced to obstetric practice in the USA almost a century ago. However, the drug was mainly used in USA until recently. One reason that magnesium sulphate did not initially gain universal acceptance was the lack of reliable empirical evidence of its effects from controlled trials. While another reason was that some critics maintained that no theory existed to explain how magnesium sulphate could be helpful in eclampsia.

The women in this study represented a high risk group. They presented at early gestational age (mean 34 weeks) with high blood pressure values, often suffering from headache. Most of these pregnancies were terminated for maternal reasons or due to intrauterine deaths. This study shows that magnesium sulphate in the dosage used is effective in treatment of eclamptic convulsions and it considerably reduces the risk of

eclampsia in women with severe pre-eclampsia. However the routine use of magnesium sulphate in all cases of pre-eclampsia is not justified as the incidence of eclampsia is likely to be lower in milder cases than those with a severe disease.<sup>18</sup>

The most significant randomized clinical trial on the subject of anticonvulsants in eclampsia was the Collaborative Eclampsia Trial.<sup>19</sup> The study concluded that there was compelling evidence in favour of magnesium sulphate rather than phenytoin or diazepam for the treatment of eclampsia. Chein et al<sup>20</sup> carried out an over view of the evidence from randomized trials of magnesium sulphate in the treatment of eclampsia and pre-eclampsia and concluded that there was strong support for the use of magnesium sulphate in preventing recurrent seizures in eclampsia. Duley and Johanson<sup>21</sup> also agreed with this view.

Lucas et al<sup>22</sup> conducted a prospective study comparing magnesium sulphate to phenytoin in the prevention of eclampsia. In their study no woman receiving magnesium sulphate developed eclampsia, while 10 women randomized to the phenytoin group had convulsions. A systematic review<sup>23</sup> of evidence from controlled trials involving women with pre-eclampsia showed that magnesium sulphate was the most promising among the alternative anticonvulsants studied. The Magpie Trial<sup>24</sup>, which involved 10141 women with pre-eclampsia and their carers in 175 hospitals in 33 countries, shows that magnesium sulphate reduces the risks of eclampsia among women with pre-eclampsia.

In patients with HELLP syndrome or deranged renal profile at admission no deterioration in renal functions or coagulation profile was found on subsequent investigations during magnesium sulphate therapy. Similar results were observed in The Magpie Trial.<sup>24</sup> Roberts<sup>25</sup> suggested that there are other beneficial effects of magnesium sulphate in addition to prevention of convulsions in pre-eclampsia.

The mean duration of magnesium sulphate therapy in this study was 29.2 hours. One of the concerns about magnesium sulphate has been the risk of respiratory depression. In our study only one patient had respiratory depression while there was no case of magnesium toxicity or respiratory arrest. However problems at injection site were observed in 2 women. In one woman the i.m regimen was then stopped and maintenance i.v infusion of magnesium sulphate started at 1gm/hour. Absent tendon reflexes were observed in 3 women. These side effects were not life threatening and observed in few patients. It is of note that there were no adverse effects attributable to the use of magnesium sulphate in the Collaborative Eclampsia Trial.<sup>19</sup>

14 (28%) of the women had caesarean section. In Magpie Trial<sup>24</sup> there was 5% increase in the relative risk of caesarean section but this increase was related to other factors. One of the beliefs supporting the

unevaluated use of magnesium sulphate over many decades has been that it improves the outcome for the child. Recent support for this belief has come from case control studies, suggesting that in-utero exposure to magnesium sulphate might reduce the risk of cerebral palsy for low birth weight (<1500grams) babies.<sup>26,27</sup> In our study out of 40 live born babies 16 had a birth weight less than 1500grams. Of these 16 babies only 7 expired later while 9 babies survived. There was no neonatal death in birth weight > 1500 grams. These findings indicate relatively good neonatal outcome in women with eclampsia and pre-eclampsia who received magnesium sulphate.

## CONCLUSION

Magnesium sulphate is an effective anticonvulsant for the treatment and prevention of eclampsia when used judiciously. In the dosage used it does not have any substantive harmful effects on women and their babies. As it is an inexpensive drug, it is especially suitable for use in low income countries. Serum monitoring is not necessary. So consideration should be given to the administration of magnesium sulphate to all women with severe pre-eclampsia and eclampsia, together with adequate antihypertensive therapy and early delivery.

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# The Effects of X-Rays on the Hair Follicles, Blood Vessels, Collagen and Elastic Fibers, of the Skin of Guinea Pigs and the Role of Vitamin C, A Morphological Study under Light Microscope

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## ABSTRACT

**Objective:** To observe the effects of x-rays on hair follicles, blood vessels and collagen and elastic fibers of the skin and role of vitamin C.

**Study Design:** A prospective experimental study.

**Place and Duration of Study:** This Study was conducted at the Department of Anatomy, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre Karachi from 2008 to 2009.

**Materials and Methods:** Twenty seven animals were taken and were divided in to three groups. Each group was further subdivided into three subgroups containing three animals each according to the time of sacrifice i.e. 48 hours, 15<sup>th</sup> day and 45<sup>th</sup> day respectively. A single whole body x-irradiation in a dose of 5 Gy was given. Group C animals were also given injection of vitamin-C intraperitoneally in the dose of 1 mg/G/day. Animals were sacrificed under ether anaesthesia after completion of their respective periods. Tissues were processed and 4-5 micron thick paraffin embedded sections were cut and stained with Hematoxylin and eosin for morphology of hair follicles and blood vessels, Masson's trichrome for study of collagen and Van Geison for elastic fibers.

**Results:** Group A served as control. In Group 'B' hair follicles were reduced in size and number of cells per bulb was also reduced, blood vessels were dilated their endothelial cells were swollen lumen was narrow and vessel wall was sclerosed, collagen and elastic fibers were reduced in amount. In group 'C' early effects of x-rays subsided to great extent in less than 15 days but there was no sign of improvement in elastic fibers.

**Conclusion:** X-rays have hazardous effects on hair follicles, blood vessels and collagen fiber elastic fiber. Vitamin C minimizes these hazardous effects.

**Key Words:** Hair follicle, Masson's trichrome, Van Gieson.

## INTRODUCTION

The ever increasing use of radioactive substances both in industry and medicine has made the study of radiation damages, of great practical importance (Walter and Talbot, 1996). Irradiation has been reported to produce multiple negative effects on wound healing process inhibits inflammatory reaction, connective tissue proliferation, maturation of granulation tissue, transcription of mRNA, secretion of collagen and neovascularization (Gu et al., 1998; Bernstein et al., 1993). Different components of skin react to radiation with different sensitivities, loss of hair occur after treatment with relatively low doses of radiation indicating that hair follicles are highly sensitive to ionizing radiation (Malkinson 1981, Prasad 1995). Hair loss or alopecia is one of the earliest responses following exposure to ionizing radiation (Hopewell 1990). This observation suggests that hair follicles are sensitive to radiation, induced damage (Song and Lambert 1999).

Vascular damage is extremely important consequence of irradiation (Anderson 1999). In acute radiodermatitis

capillary endothelium may be hypertrophic and congested; hemorrhages and thrombosis are often observed (Spittle 1998).

Irradiation of animals caused a significant reduction in collagen synthesis with heavy dose of radiation there is decrease in proliferation of fibroblasts which is responsible for collagen synthesis, a direct negative impact of ionizing radiation on fibroblast proliferation (Grant et al., 1973, javanovic, 1993). In irradiated skin fibroblasts were relatively small in size and had few branches; their nuclei were hyperchromatic (Hussein 2005). Cell culture studies of fibroblasts exposed to ionizing radiation have demonstrated that irradiated fibroblasts has a significant prolonged generation time when compared to normal fibroblast (Rudolph 1988).

Ascorbic acid treatment has been reported to confer protection against radiation in vitro and in vivo (Nevas et al 1993; Barerstock, 1979) and it has beneficial effects on the course of radiation-induced skin injuries (Decosse, 1988). Ascorbic acid plays an important role in the maintenance of collagen (Naidu, 2003). Treatment with ascorbic acid before irradiation enhanced the synthesis of collagen hexosamine



(Jagetia et al., 2003). The use of natural radio protector/antioxidants to overcome direct negative effect of ionizing radiation and for targeting reactive oxygen species could be an important therapeutic strategy to improve healing of irradiated wounds (Cabbabe and Kroack 1986). Therefore keeping in mind the radioprotective role of ascorbic acid we designed this study to observe these effects on hair follicles, blood vessels and collagen and elastic fibers.

## MATERIALS AND METHODS

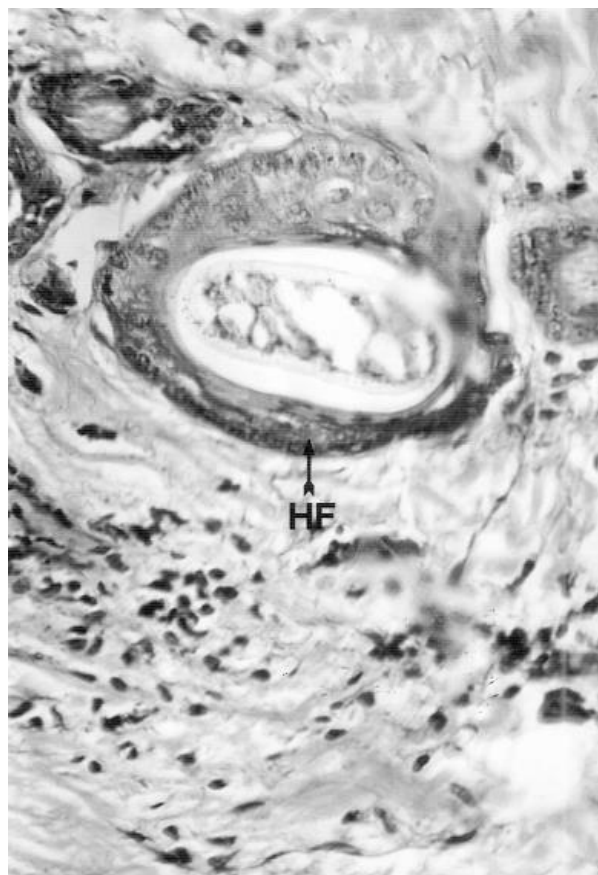
This study was conducted in The Department of Anatomy, Basic Medical Sciences Institute Jinnah Postgraduate Medical Center Karachi where 27 adult male Guinea pigs weighing 400 to 450 G were taken and were divided into three groups, A, B and C. each group was further sub-divided into three sub-groups containing three animals each according to the time of sacrifice, i.e. 48 hours, 15<sup>th</sup> and 45<sup>th</sup> day. Group-A served as control. Group-B received whole body X-irradiation in dose of 5 Gy at Karachi Institute of Radiotherapy and Nuclear Medicine. Group-C received whole body X-radiation in dose of 5 Gy and injection of vitamin-C intraperitoneally in the dose of 1 mg/G/day (Injection vitamin-C manufactured by Shanghai Medicines and Health Products Shanghai, China).

The animals (Guinea pigs) were sacrificed at their respective time of treatment under the ether anaesthesia. The skins of Guinea pigs were shaved and skin fragment (size one centimeter square in shape) from face, back and abdomen were collected at 48 hours, 15<sup>th</sup> and 45<sup>th</sup> day. Skin fragment from each side was fixed in 10% formalin and 10% buffered neutral formalin for 12-18 hours. After that tissues were processed in ascending strength of alcohol, cleared in xylene and infiltrated and embedded with paraffin. Five micron thick vertical sections were cut at rotatory microtome and floated in hot water bath and were placed on glass slide and stained with Hematoxylin and eosin for morphology of skin and Masson's trichrome for study of collagen fibers, and with Van Geison stain for study of elastic fibers. The condition of hair follicle was observed in 40x objective and 8x ocular under light microscope (by observing the size of hair follicle and number of cells per bulb and pyknosis to assess the degree of apoptosis). The changes in blood vessels were assessed by visualizing the size of lumen, size of endothelial cells and sclerosis of the vessel wall. The arrangement of collagen fibers were observed in 10x objective and 8x ocular under light microscope. Elastic fibers were observed to assess the degeneration of these fibers in 10x objective and 8x ocular under light microscope.

## RESULTS

In control group the hair follicles were scattered through the dermis and consisted of three to four

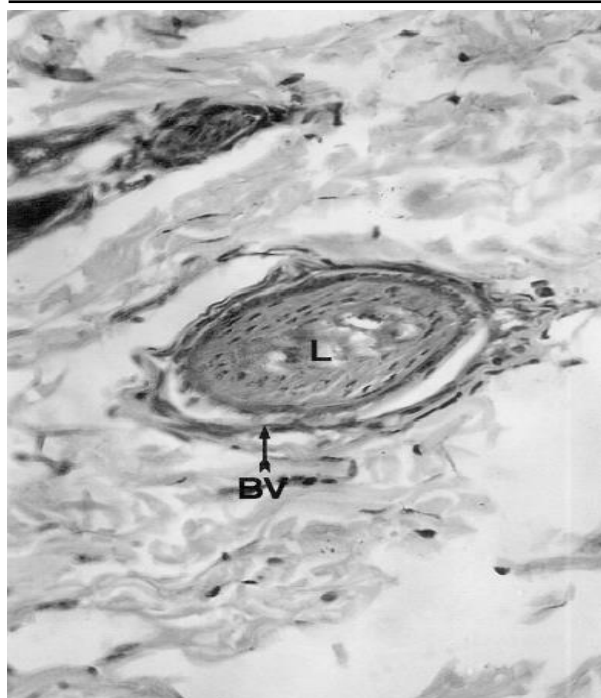
concentric layers of epithelial cells with rounded nucleus at its base hair bulb was also seen with hair matrix. Blood vessels were seen at the junction of papillary and reticular layer of dermis with adequate lumen and endothelial cells. Collagen fibers were blue in colour and arranged irregularly in the form of extensive network just beneath the epidermis. Elastic fibers appeared black against red stained collagen, in papillary layer they were thin and scanty, and in reticular layer they were long, thick and followed the course of collagen bundle.



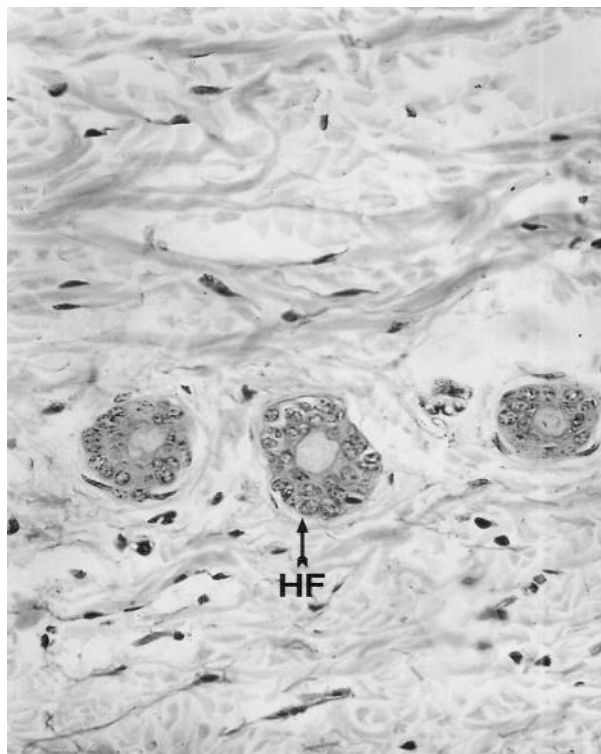
**Figure No.1: H&E stained, 5µm thick longitudinal section of back skin showing blood Vessel (BV) swelling of endothelial cells and narrowing of lumen (L) 48 Hours after treatment with X-radiation in Guinea pig Photomicrograph x 400.**

In group 'B1' the hair follicles were reduced in size. Follicular matrix was smaller and total numbers of cells per bulb were 20-30% less than the control. The nucleus of the cell was pyknotic fig-1.

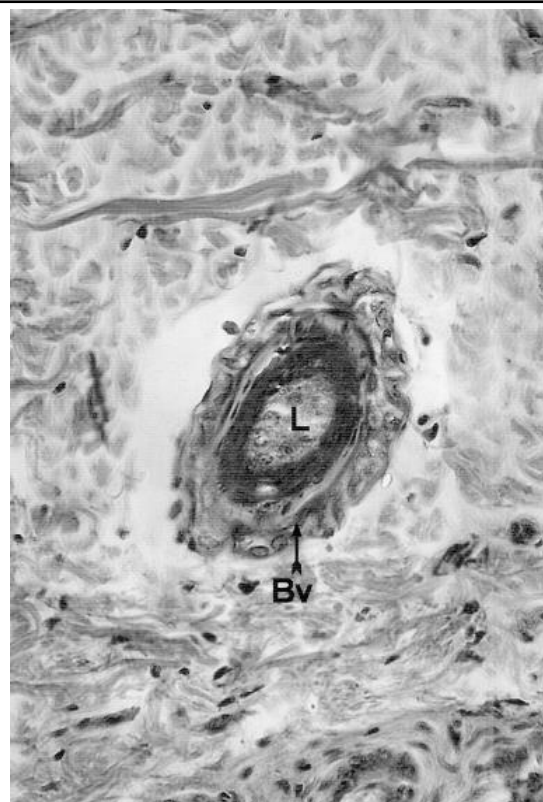
Blood vessels were seen dilated, their endothelial cells were swollen and lumen was narrower than control and there was also sclerosis of vessel wall fig-2. There was no change in collagen and elastic fibers compared with control. Group B2: The hair follicles were reduced in size and follicular matrix was smaller and total numbers of cells per bulb were less than the control and the nucleus of the cell was pyknotic fig-3.



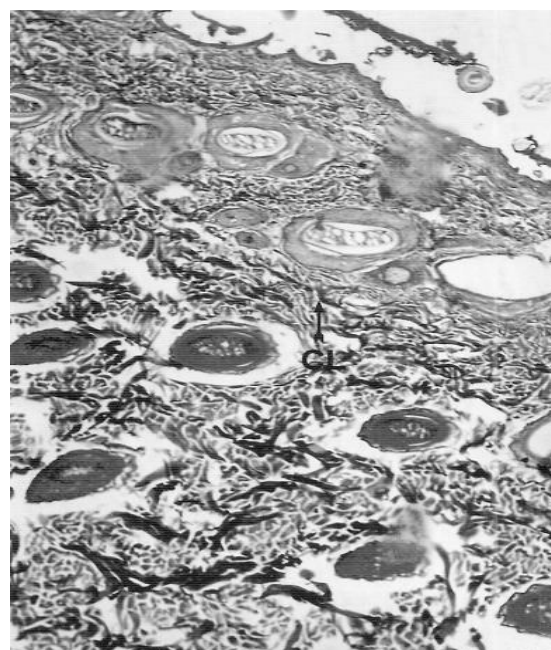
**Figure No.2:** H&E stained 5  $\mu\text{m}$  thick longitudinal section of back skin showing Blood vessels (BV) swelling of endothelial cells and narrowing of lumen (L) After 48 hours of treatment with X-radiation in Guinea pigs. Photomicrograph x 400.



**Figure No.3:** H&E stained 5  $\mu\text{m}$  thick longitudinal section of back skin showing hair follicle (HF) decrease size and total number of cells per bulb with pyknotic nucleus after 15 days treatment with x-radiation in guinea pig. Photomicrograph x400.



**Figure No.4:** H&E stained, 5  $\mu\text{m}$  thick longitudinal section of back skin showing blood vessel (BV) decreased swelling of endothelial cells and increase lumen (L) size after 45 days treatment with x-radiation in guinea pig Photomicrograph x400



**Figure No.5:** Masson's trichrome stained, 5  $\mu\text{m}$  thick longitudinal section of back skin showing thinning and reduced amount of collagen fibers (CL) after 15 days treatment with x-radiation in guinea pig. Photomicrograph X 100.



**Figure No.6: Elastic Von Geison stained 5 µm thick longitudinal section of back skin showing thinning of elastic fiber (EL) after 15 days treatment with x-radiation in guinea pig. Photomicrograph x 100.**

Blood vessels were seen dilated and their endothelial cells were swollen and lumen was narrower than control with sclerosis of vessel wall fig-4. Collagen fibers were thin and reduced in amount fig-5. Elastic fibers became thinner than control showing degeneration fig-6. Group B3: The hair follicles were reduced in size, follicular matrix was smaller and total numbers of cells per bulb were less than the control. Dilatation of Blood vessels was reduced and swelling of endothelial cells was subsided lumen was like control. Collagen fibers were thin and reduced in amount. Elastic fibers were thinner than control showing degeneration.

Group C1: Hair follicles were reduced in size. Follicular matrix was smaller and total numbers of cells per bulb were less than control, and nucleus of the cell became pyknotic. The blood vessels were seen dilated and their endothelial cells were swollen and lumen was narrower than control. There was also sclerosis of vessel wall. Collagen fibers were blue in colour (in Masson's trichrome stain) there was no change in collagen than control. Elastic fibers appeared black against red stained collagen there was no change in elastic fibers than control. Group C2: Hair follicles were reduced in size. Follicular matrix was smaller and total numbers of cells per bulb were less than control, nucleus of the cell became pyknotic. The dilatation of

the blood vessels was reduced and swelling of endothelial cells was subsided. Lumen was wide like control the sclerosis of vessel wall was very much reduced. The collagen fibers were thicker and elastic fibers became thin than control. Group C3: Hair follicles were reduced in size. Follicular matrix was smaller and total numbers of cells per bulb were less than control. The dilatation of the blood vessels was reduced and swelling of endothelial cells was subsided and lumen was wide like control. The collagen fibers were increased and thicker and elastic fibers became thin than control.

## DISCUSSION

In present study as mentioned was designed to observe the radioprotective role vitamin C on hair follicles, blood vessels, collagen and elastic fibers. Vitamin C was chosen in injectable form to attain high serum concentration level rapidly and adult male Guinea pigs were selected because radiosensitivity is close to humans (Bardychew et al 1982) these both were in also agreement with the selection criteria of Raziq and Jafarey (1987) and Melchikov et al (2003). Hair loss (reduced hair follicles) was seen in all three sites, i.e. face, abdomen and back. This finding was supported by similar observation made by song and Lambart (1999) who found that after exposure of mice to 5 Gy of ionizing radiation, cell in the matrix of hair follicle underwent apoptosis but not growth arrest. The above findings were also in agreement with Hopewell (1990) and Malkinson and Prasad (1995). They observe loss of hair occurs after treatment with relatively low doses of radiation, indicating that hair follicles are highly sensitive to ionizing radiation.

In the x-irradiated groups the blood vessel were seen dilated, endothelium cells were swollen then control, and the lumen was narrower and sclerosis of vessel wall was present, this is due to post irradiation inflammatory response called radio-dermatitis these findings were in accordance with Anderson,(1990) in which early after irradiation the vascular dilatation may cause skin erythema and regressive changes, including swelling and vacuolization of endothelium and necroses of vessel wall and some time haemorrhage. Hussein et al (2005) reported that in irradiated skin under electron microscope the endothelial cell had marked irregularly of their luminal surface, hetrochromic nuclei, numerous pinocytotic vesicles and widening of intercellular spaces.

In X- irradiated groups B2, B3 and the collagen fibers became thin in all sites and irregularly arranged this finding was in agreement with the Walter and Talbot (1996) according to it irradiation of animals caused a significant reduction of collagen synthesis, both newly formed and original collagen became hyalinized. In groups-B1, B2, B3 the elastic fibers became thinner

indicating the sign of degeneration which is in agreement with the observations of Robbins, 1994. In group C2 and C3 the amount of collagen was increase near to control this is because vitamin 'C' improves the collagen deposition and reduce the hyalinization and increases the vascularity and fibroblast density. These finding were in agreement with the observation of Frie et al (1989) and Navas et al (1994) in which indicated the beneficial effects of ascorbic acid on wound healing through changes in cell regeneration and collagen synthesis. These observations were further supported by the observations of Frie., et al (1989), Navas .,et al (1994) who mentioned in there studies that beneficial effect of ascorbic acid on wound healing through changes in cell regeneration and collagen synthesis. Jagetia et al (2004) also observed that ascorbic acid inhibited the radiation induced decrease in collagen syntheses.

## CONCLUSION

The study concludes that the damaging effects of x-rays on hair follicle, blood vessels and collagen and elastic fibers (of the skin) could be minimized by the treatment of vitamin C.

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# Spectrum of Thyroid Gland Disorders in Karachi-DDRRL Experience

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## ABSTRACT

**Objective:** To find out the spectrum of thyroid gland disorders in association with age and gender and to identify histological types of thyroid lesions.

**Study Design:** Descriptive Study.

**Place and Duration of Study:** This study was carried out at the Department of Histopathology, DOW University (OJHA campus) Karachi from 1<sup>st</sup> Jan 2010 to 31<sup>st</sup> Dec 2011.

**Materials and Methods:** The record of total 208 specimens, were reviewed from the department of Histopathology, DOW University (OJHA campus) Karachi throughout the period from 1<sup>st</sup> Jan 2010 to 31<sup>st</sup> Dec 2011. The specimens were received in 10% buffered formalin and processed as per routine laboratory procedure and then embedded in paraffin for block preparation. The sections were stained with the routine haematoxylin and eosin method and were studied and diagnosed by a consultant histopathologist. Difficult cases were discussed in Departmental Consultation Committee.

**Results:** Total 208 cases were studied, there was a female predominance 184 (88.5%) and among them majorities were in 3<sup>rd</sup> decade of life. Males were 24 (11.5%) commonly seen in 4<sup>th</sup> decade of life. The ages ranged from 15-75 years, mean age is 30 years. Nodular hyperplasia was the commonest thyroid lesion found.

**Conclusion:** The information in the present study may be considered as a baseline data of thyroid diseases in Karachi and a more elaborate prospective study carried out on a large scale in this country will contribute more to make the things clearer.

**Key Words:** Nodular hyperplasia, Follicular adenoma, Papillary carcinoma, Hashimoto thyroiditis.

## INTRODUCTION

The most common worldwide non-neoplastic lesion in thyroid is due to iodine deficiency, which is assessed to have emotional impact around three-quarters of a billion people<sup>1</sup>. The Diseases of thyroid gland are the second most common endocrine disorder, after diabetes around the globe<sup>2</sup>. The significance of thyroid disorders to oral pathology and oral and maxillofacial surgery lies in potential of carcinoma of thyroid to metastasize to mandible, maxilla and cervical chain of lymph nodes<sup>3-7</sup>. The incidence of thyroid cancer in USA is increasing approximately 1 in 13 or 7.35%<sup>8</sup>. The prevalence of thyroid disease increases with age; it is 60% in 80-yr-old persons. The number of diagnosed small thyroid cancers and occult thyroid cancer will be head to head, up to 36%<sup>9</sup>. Thyroid abnormalities are quite shared in senile individuals without known thyroid dysfunction; therefore thyroid screening is advisable for women over 50 and at least every five years beginning at the age of 35 in adults<sup>10</sup>.

In Pakistan Goiter is prevalent in the north-west areas. The prevalence of cancerous change in thyroid nodules is indefinite in our country due to lack of nationwide data and study<sup>11</sup>. The general incidence of non-neoplastic lesions and neoplastic lesions are 89% and 11% respectively in Pakistan. Papillary carcinoma is the

most common malignant thyroid lesion about 60% of all thyroid malignancies in Pakistan<sup>12</sup>.

The most common etiology encountered in different countries of the world is an iodine deficiency and exposure to radiation hazards. Most of the reported thyroid nodules are either cystic or due to neoplastic change<sup>13</sup>.

The thyroid gland is palpable in about 50% of women and 25% of men. The thyroid gland synthesizes and secretes two hormones: Thyroxine (T<sub>4</sub>), Tri-iodothyronine (T<sub>3</sub>)<sup>2</sup>. Both these hormones are under the control of thyroid stimulating hormone (TSH) of anterior pituitary gland which in turn is controlled by thyrotrophin releasing hormone (TRH) from hypothalamus<sup>14</sup>. The uniqueness of thyroid gland is the storage of thyroid hormone in an extracellular compartment. Two-Three months' supply of thyroid hormone is stored within the follicles, and this delays the onset of symptoms in deficiency diseases. Thyroid disease ranges from the production of too much or too little of the thyroid hormones, to the development of neoplastic lesion. The main groups of thyroid gland disease are hyperthyroidism (excess of thyroid hormone production), hypothyroidism (deficiency of thyroid hormone production), goiter formation, adenoma (benign growths) of the thyroid, and carcinoma of the thyroid<sup>2</sup>.



The perseverance of this study was to observe the frequency and prevalence of various thyroid disorders in different age and sex groups in population of Karachi and to detect a number of histological types of thyroid lesions in specimens sent to the DOW laboratory for histopathology.

## MATERIALS AND METHODS

In the present study, 208 thyroid specimens, from the department of Histopathology, DOW University (OJHA campus) Karachi during the period from Jan 2010 to Dec 2011 have been investigated. The specimens were received in 10% buffered formalin and processed as per routine laboratory procedure and then embedded in paraffin for block preparation. The sections were stained with the routine haematoxylin and eosin method and were studied and diagnosed by a consultant histopathologist. Difficult cases were discussed in Departmental Consultation Committee.

## RESULTS

The data was evaluated to find out the frequency of various thyroid disorders and it was further separate out into sub-groups of age and sex to govern the prevalence of the disorders accordingly. The comparative frequencies and ratios were calculated for each group of disorders by entering the data in SPSS version 16. Frequency bar chart and tables were arranged using Microsoft excel software program.

**Table No.1: Histological Types Of Lesions.**

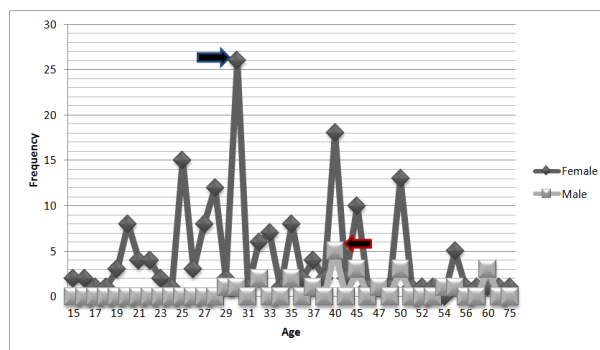
Histopathological Diagnosis	Number	%age
Nodular hyperplasia	145	69.7
Hashimoto thyroiditis	12	5.8
Lymphocytic thyroiditis	9	4.3
Chronic granulomatous inflammation	3	1.4
Follicular adenoma	19	9.1
Papillary carcinoma	14	6.7
Follicular carcinoma	3	1.4
Insular carcinoma of thyroid	1	0.5
Metastatic Well differentiated squamous cell carcinoma	2	1.0
Total	208	100.0

Among 208 cases studied, there was a female predominance 184 (88.5%) and majorities were in the 3<sup>rd</sup> decade of life. Males were 24 (11.5%) commonly in the 4<sup>th</sup> decade of life. The ages ranged from 15-75 years, mean age was 30 years as shown in figure 1. Nodular hyperplasia was the commonest thyroid lesion found in 145 cases, followed by follicular adenoma 20 cases, papillary carcinoma 14 cases, Hashimoto thyroiditis 12 cases, lymphocytic thyroiditis 9 cases, follicular carcinoma and chronic granulomatous inflammation 3 cases each, well differentiated squamous cell carcinoma in 2 cases and insular

carcinoma of thyroid was found in a female of 55 years. Papillary carcinoma was the most common thyroid malignancy. The overall incidence of malignancy was 9.6%. as shown in table 1 and figure 2. Ratio of hyperplasia to inflammation is 4.8:1, ratio of hyperplasia to benign tumor is 7.2:1, ratio of hyperplasia to malignant tumors 7.2:1, ratio of inflammation to benign tumor is 1.5:1, ratio of inflammation to malignant tumor is 1.5:1, ratio of benign to malignant tumors 1:1, Female to male ratio in hyperplasia is 8.6:1, female to male ratio in inflammation is 29:1, female to male ratio in benign tumor is 19:1 and female to male ratio in malignant tumor is 1.8:1 as shown in table 2

**Table No.2: Ratios in Thyroid Disorders**

Ratio of Thyroid Disorders	No. of Subjects	Ratio
Ratio of hyperplasia to inflammation	145/30	4.8 : 1
Ratio of hyperplasia to benign tumors	145/20	7.2 : 1
Ratio of hyperplasia to malignant tumors	145/20	7.2 : 1
Ratio of inflammation to benign tumors	30/20	1.5 : 1
Ratio of inflammation to malignant tumors	30/20	1.5 : 1
Ratio of benign to malignant tumors	20/20	1 : 1
Female to male ratio in hyperplasia	130/15	8.6 : 1
Female to male ratio in inflammation	29/1	29 : 1
Female to male ratio in benign tumors	19/1	19 : 1
Female to male ratio in malignant tumors	13/7	1.8 : 1

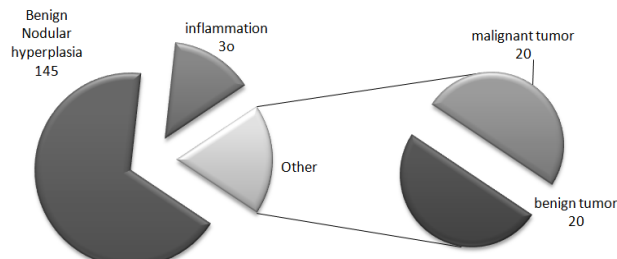


**Figure No.1: Bar Chart showing Gender Distribution**

## DISCUSSION

Thyroid disorder is the commonest endocrine system malfunction<sup>13</sup>. The most common form of hyperthyroidism in aged females is Graves' disease (F: M, 8:1), while hypothyroidism effects 1/100

females and 1/500 males. It is very challenging to differentiate between benign and malignant lesions clinically<sup>2</sup>. In this study there was also female predominance 184 out of 208 cases and majority were in their 3<sup>rd</sup> decade of life. The rest were males in 4<sup>th</sup> decade of life. The ages ranged were 15 to 75 years.



**Figure No.2: Pie Chart showing Spectrum of Thyroid Disorders**

The overall frequency of non-neoplastic lesions in this study was 69.7% as compared to 9.6% of neoplastic lesions. The commonest non neoplastic lesion in this study was nodular hyperplasia; which constituted 145 out of 208 of the thyroid specimens including diffuse (139) cases and multi-nodular goiters (6) cases. Mean age in females was 30 years (130/145) cases. This is constant with some native studies in which multinodular goiter and diffuse colloid goiters were found to be the commonest pathologies of the thyroid lesions<sup>10-12</sup>. The second common thyroid lesions were inflammatory 30 out of 208 cases. Among them 15 cases were of Hashimoto's thyroiditis, 8 cases of lymphocytic thyroiditis, 4 cases of chronic granulomatous inflammation, and 3 cases of follicular thyroiditis. Females were affected more (29 out of 30) cases. Follicular adenomas were seen in 20 cases (9.6%) of the specimens, female: male ratio is 19:1. There were 20 cases of malignant tumors of thyroid. In this study papillary carcinoma was the most common malignant thyroid lesion observed in about 6.7% (13 out of 20) lesions, followed by 4 cases of follicular carcinoma, 2 cases of well differentiated squamous cell carcinoma, and 1 case of insular carcinoma. However in distinction to Mofti et al; stating higher incidence of thyroid malignancies (29%) in a study of 158 patients<sup>15</sup>. In the present study the incidence of carcinoma thyroid in females were 13 cases out of 20. Female to male ratio was (1.8:1). Thyroid tumors are rare in children and they increase in frequency with the advancing age<sup>12</sup>. Even though patients of both gender and any age group may be affected, and individuals in the third to fifth decade of life<sup>15</sup>. In this study the age range of malignant thyroid lesions was second to sixth decade of life. The reason might be increased prevalence of thyroid disorders in certain areas of Pakistan. The overall incidence of malignancy in USA was 5.8%, in Libya 9.7% and in South Africa 5.4%<sup>2, 11,14,15</sup>. This study showed the malignant lesion of about 9.6% and

these findings were similar to the finding of Libya resulted in 9.7% of malignant lesions. The studies from Riyadh stated an extremely high incidence of thyroid malignancy ranging from 21% to 29% as papillary carcinoma (66.6%), Follicular carcinoma (22%) and medullary carcinoma (4%)<sup>13</sup>. Other studies from different parts of the world also exhibited a similar pattern with thyroid carcinoma being more prevalent (62%-81%) in females.<sup>11,16,18,20</sup> Similarly in the present study, Colloid goiter is the most common benign lesion of the thyroid gland while papillary carcinoma is the most common malignant lesion of thyroid gland than the follicular carcinoma which is in agreement with the printed data.<sup>2, 10,13,17,18,19,20</sup>

## CONCLUSION

The present study may be well thought-out as a baseline data of thyroid diseases in Karachi and a more elaborative and prospective study need to be carried out on a large scale nationwide will contribute further to make the things clearer. Evaluation of thyroid status may help in early detection and possible treatment of thyroid diseases.

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# Frequency of Low Serum Magnesium Level in Diabetic and non- Diabetic Patients compared with other Risk Factors of Cardiovascular Diseases

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## ABSTRACT

**Objective:** To assess the frequency of serum magnesium level in heart failure patients with and without diabetes mellitus.

**Study Design:** Cross Sectional Study.

**Place and Duration of Study:** This study was conducted at Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Centre (JPMC), Karachi, in collaboration of National Institute of Cardiovascular Diseases (NICVD) Karachi, from April 2003 to December 2003.

**Materials and Methods:** A sample size of 45 was drawn through convenient sampling, between the age group of 35-65 years. Serum magnesium, glucose levels were estimated, using Kit method, data was analyzed on the SPSS 11 for statistical significance.

**Results:** Out of 45 cases of heart failure, 15 were diabetic with low level of serum magnesium (1.67mg/dl) as compared to 30 non-diabetics with significantly high level of serum magnesium (1.75mg/dl)

**Conclusion:** This study concluded, in heart failure patient with diabetes mellitus had low serum magnesium level and was at increased risk of complications related to magnesium.

**Key Words:** Diabetes Mellitus, Heart Failure, Magnesium, Risk Factors.

## INTRODUCTION

Magnesium is very important, necessary for mechanism of glucose transport through the cell membranes, cofactor of various enzymes involved in carbohydrate oxidation<sup>(1,2,3)</sup>. Magnesium is second most plentiful cation present in serum, normal level is 1.8 to 3.0 mg/dl<sup>(4,5)</sup>. Diabetes mellitus is declared when fasting blood glucose level is 126mg/dl or more random blood glucose level is 200 mg/dl, in already diagnosed cases or taking hypoglycemic drugs<sup>(6)</sup>. Diabetes mellitus is the most common chronic disease associated with secondary magnesium deficit. In humans insulin is responsible for transfer of magnesium through the cellular membrane, regulates intracellular magnesium. Increased insulin resistance has been found in patients with compressed free magnesium levels. Increased glucagon stimulation, decreased insulin secretion, reduced insulin uptake with magnesium deficiency have also shown in animal studies. Insulin-dependent, non-insulin-dependent diabetic patients have low serum, intracellular levels of magnesium, due to increased urinary losses of magnesium caused by osmotic diuresis<sup>7</sup>. Cardiovascular diseases risk factors such as smoking, diabetes mellitus are threat factors of the progress of heart failure<sup>(8)</sup>. Fewer intakes of dietary magnesium, abnormalities in magnesium metabolism play important roles in different types of heart diseases such as ischemic heart disease, congestive heart failure,

atherosclerosis, ventricular complications in diabetes mellitus<sup>(9)</sup>. Plenty of magnesium is available on the earth and in living tissue, it is extremely easy to build up a magnesium deficiency due to comparatively poor magnesium absorption, fast turnover of the magnesium pools, related to the continued life reliant biochemical pathways<sup>(10)</sup>. People with diabetes mellitus are at larger risk for cardiovascular disease (CVD) comparative to those devoid of diabetes mellitus<sup>(11)</sup>. The aim of this study was to determine the serum magnesium level in heart failure patients with diabetes mellitus to diagnose deficiency, maintain magnesium status by supplementation.

## MATERIALS AND METHODS

The study comprised 45 diagnosed cases of heart failure with, without diabetes mellitus between the age group of 35-65 years. Study included the patients with major risk factors of heart failure; hypertensive, diabetics, smokers, family history of heart diseases. Patients receiving drugs diuretics, digoxin along with other cardiovascular medication were included. Samples were collected with antiseptic measures. Serum glucose level was determined by enzymatic colorimetric (GOD PAP) method, using kit, Lot No. B02868. Serum magnesium was determined by colorimetric method using kit Cat No.0137. The results were calculated as frequencies, percentages for qualitative data whereas mean and standard deviation was used for quantitative data. For

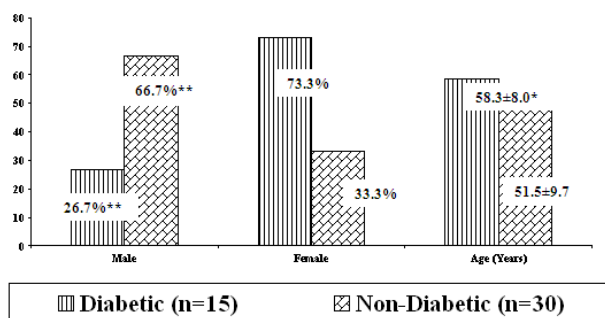
comparison between diabetic and non diabetic, test of proportion was used for qualitative data and student t-test was used for Quantitative data. In all statistical analysis p-values < 0.05, 0.01, and 0.001 were considered significant.

### Data Analysis

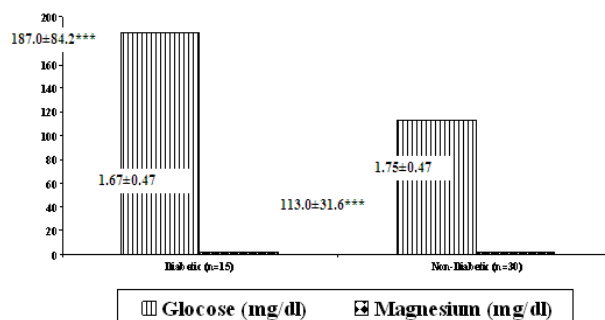
The study was completed in nine months from 1<sup>st</sup> April 2003 to 31<sup>st</sup> December, 2003. The significance of the data was determined by using Statistical Package of Social Sciences software (SPSS, Version 11.0). Confidence interval of 95% was taken with margin of error 5% and p-value of 0.05.

## RESULTS

The study compared the demographic distribution of diabetic and non-diabetic with heart failure. patients with diabetes were seen to be of a significantly older age. It was assessed that female patients with diabetes were significantly ( $P < 0.01$ ) higher in percentage.



**Fig. 1. Distribution of Diabetic and Non-Diabetic in Heart Failure Patients**

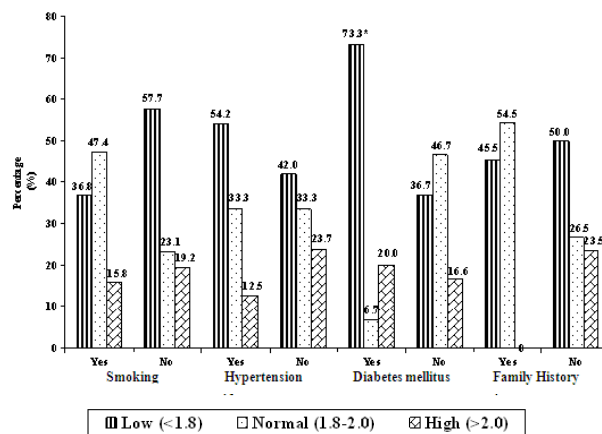


**Fig.2: Glucose (mg/dl) and Magnesium (mg/dl) Level in Diabetic and Non-Diabetic Heart Failure Patients.**

In Biochemical comparison of diabetic, non-diabetic patients it was assessed that patients with diabetes had a significantly higher serum glucose level ( $187 \pm 84.2$ ). The serum magnesium in diabetics was lower than the non-diabetics.

The values of serum magnesium were compared with other risk factors of heart failure, Patients were classified on the basis of their serum magnesium level, as low magnesium group was defined as having a level ( $< 1.8$  mg/dl), and the high magnesium group was

defined as having a level ( $> 2.0$  mg/dl) and normal having serum magnesium of ( $1.8 - 2.0$  mg/dl).



\*  $P < 0.05$  = Significant when compared Diabetes mellitus with other risk factors

**Fig. 3. Comparison of Risk Factors in Heart Failure Patients with Serum Magnesium Level (mg/dl)**

## DISCUSSION

Magnesium is the next (after calcium) plentiful intracellular cat ion acting a key role in cellular metabolism<sup>(12)</sup>. Curiosity in this element drives from its key function in glucose metabolism, insulin homeostasis, hypertension, inflammation, cardiovascular disease. In recent times, biochemical function, effect of trace elements in preventing, treating disease is extensively studied. Its insufficiency has a negative effect on post receptor signaling of insulin, impair insulin-mediated glucose uptake, glucose-induced insulin secretion, and produce hyperglycemia. In human, sugar load causes loss of magnesium in urine, possibly converting a marginal intake to a scarce one. Previous studies showed magnesium metabolism is distorted in patients with diabetes mellitus. In type II diabetic patients, hypomagnesaemia can be a result or reason of increased insulin resistance. The constant magnesium supplements in diabetic patients improve both islets beta cell response, insulin resistance in these patients<sup>(13)</sup>. Domanski et al (2003)<sup>(14)</sup>, reported diabetes mellitus is related with increased unfavorable cardiovascular transactions with myocardial infarction (MI), chronic heart failure (CHF) stroke. Diabetes is also linked with structural, metabolic abnormalities that can harmful effect on myocardial function. Diabetes has been related with reduced serum, tissue magnesium myocardial magnesium concentration. The study of Shafique M., Fayyaz KM, Nazir S. accomplished magnesium supplementation improves metabolic homeostasis and useful adjuvant to the standard hypoglycemic agents in the treatment of non insulin reliant subjects. The interrelationship among magnesium, carbohydrate metabolism has regained significant attention more than the previous years.

Magnesium deficiency results in impaired insulin secretion magnesium substitute restore insulin secretion. Experimental magnesium insufficiency reduces the tissues sensitivity to insulin. Sub clinical magnesium insufficiency is common in diabetes. It results from both insufficient magnesium intakes, increase magnesium losses; in the urine <sup>(15)</sup>. Grundy et al. (1999) <sup>(16)</sup> noticed that cigarette smoking is a leading risk factor of cardiovascular disease. Diabetes mellitus is single most endocrine disorders associations with disturbance in electrolytes metabolism. Magnesium scarcity is a disorder of metal metabolism in diabetes mellitus. In this study, hypomagnesaemia, alterations biochemical homeostasis in diabetic heart failure patients have been evaluated. Prelude proof insulin sensitivity, hyperglycemia, diabetes mellitus, left ventricular hypertrophy, and dyslipidemia may be better with amplified magnesium intake <sup>(17)</sup>. Gottlieb et al. study (1990) <sup>(18)</sup> aberration of serum magnesium concentration are not laboratory interest but have significant clinical implications.

## CONCLUSION

This study concluded patients with diabetes mellitus had low serum magnesium level and were at increased risk of complications related to magnesium. In light of these impending complications, periodic determination of serum magnesium levels and appropriate magnesium replacement should be considered.

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# Port Site Complications in Patient after Laproscopic Cholecystectomy

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## ABSTRACT

**Objective:** To assess the frequency of port site complications in patient after laproscopic cholecystectomy.

**Study Design:** Observational study.

**Place and Duration of Study:** This study was carried out in the Department of Minimal Invasive Surgical Centre (MISC) at Liaquat University of Medical & Health Sciences Jamshoro Pakistan, from Oct 2009 to 31st May 2011.

**Materials and Methods:** This study consisted of Four hundred & fifty patients, admitted for laparoscopic cholecystectomy. Base line and specific investigations were done in all patients, especially ultrasound of abdomen for assessment of gallstone disease. Inclusion criteria were that all patients diagnosed as case of gallstone disease on the basis of history, clinical examination and investigations specially ultrasound of abdomen. Exclusion criteria included complicated gallstone disease, unfit patients for general anesthesia, pregnant ladies due to risk of foetal loss, patients with carcinoma of gall bladder, patients with acute pancreatitis and patients with obstructive jaundice. Postoperatively the patients were followed for up to 6 month and observed port site complications. Results were prepared with help of tables and graphs. Data was analyzed through SPSS software.

**Results:** 315(70%) were female and 135(30%) male. Ratio male: female ratio of 1:2.3. Age ranging from a minimum of 20 year to 65 year with mean age was 38+ 3.4 years. Complications were port site infection in 4 (0.88 %) cases, followed by port site bleeding in one (0.22 %) case and epigastric port site diathermy burn in one (0.22 %) case.

**Conclusion:** In conclusion, we recommend all 10 mm trocar sites be closed care fully. Over stretching of infra / supra umbilical port should be avoided. Gallbladder should be removed in endo- bag.

**Key Words:** Gall Stone, Laproscopic cholecystectomy, Port site complications.

## INTRODUCTION

Nowadays surgery is modernized into minimally invasive techniques, at present laparoscope is a tool used by almost in every surgical field<sup>1</sup>. History of laparoscopic surgery is attractive and long. In late 1980, Kelling invented a main computerized camera chip, which is use in laparoscopic surgery<sup>2</sup>. Open cholecystectomy has long been accepted as gold standard treatment of gallstones<sup>3</sup>. Changing in the treatment of gallstones came in 1987 when first laparoscopic cholecystectomy was performed by Carl August Langerbach<sup>4</sup>. Nowadays laparoscopic cholecystectomy has become a reputable practice due to less pain, short hospital stay, minimum morbidity and accelerating postoperative recovery<sup>5,6</sup>.

Laparoscopic cholecystectomy though superior than open cholecystectomy but is still not free from complications and can be responsible for various minor to major problems. Port-site complications associated with laparoscopic cholecystectomy are intraoperative and post operative i.e bleeding, haematoma, wound infection, painful scar, hernia and metastatic malignancy<sup>7</sup>. In surgery wound infection is common complication reported all around the world. Some studies have reported frequency varied from 5% to

6.3% of port site infection in Laparoscopic Cholecystectomy procedure<sup>8</sup>. Port site bleeding may be present as very slow ooze or frank bleeding if major vessel is damaged during LC procedure. It can be seen on the overlying dressing or can present as concealed internal bleeding postoperatively<sup>7</sup>. Port site hernia is a type of incisional hernia that occurs at port or trocar site after laparoscopic surgery. It is usually seen at the site of 10 mm port in umbilical region. It is rarely found in 5 mm cannula site. Incidence of port site hernia varies from 1% to 6 %<sup>9</sup>. Port-site tuberculosis following laparoscopic cholecystectomy is rare.

The current study was aimed to evaluate various port related complications encountered during laparoscopic cholecystectomy.

## MATERIALS AND METHODS

This case series study was carried out in minimal invasive surgical centre at Liaquat University of Medical & Health Sciences Jamshoro Pakistan, from Oct 2009 to 31st May 2011. This study consisted of Four hundred & fifty patients, admitted through the outpatient department, as well as from casualty department of Liaquat University Hospital Jamshoro/Hyderabad for laparoscopic cholecystectomy.

Base line and specific investigations were done in all patients, especially ultrasound of abdomen for assessment of gallstone disease. Inclusion criteria were that all patients diagnosed as case of gallstone disease on the basis of history, clinical examination and investigations specially ultrasound of abdomen. Exclusion criteria included complicated gallstone disease, unfit patients for general anesthesia, pregnant ladies due to risk of foetal loss, patients with carcinoma of gall bladder, patients with acute pancreatitis and patients with obstructive jaundice. Postoperatively the patients were followed for up to 6 month and observed port site complications. Results were prepared with help of tables and graphs. Data was analyzed through SPSS software.

## RESULTS

The 450 cases of gallstone were admitted. 315(70%) were female and 135(30%) male. Ratio male: female ratio of 1:2.3 (Chart No.1). There was wide variation of age ranging from a minimum of 20 year to 65 year with mean age was  $38 \pm 3.4$  years.

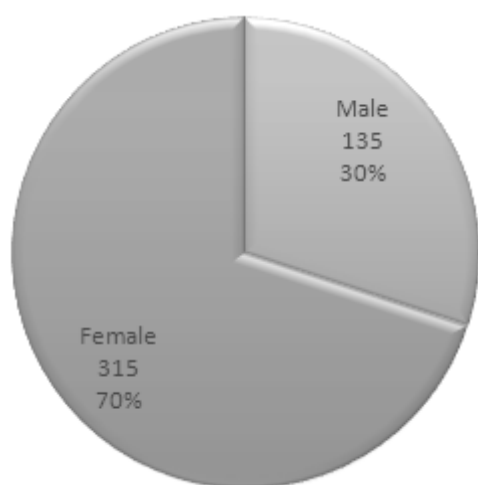


Chart No.1: Distributions of Gender

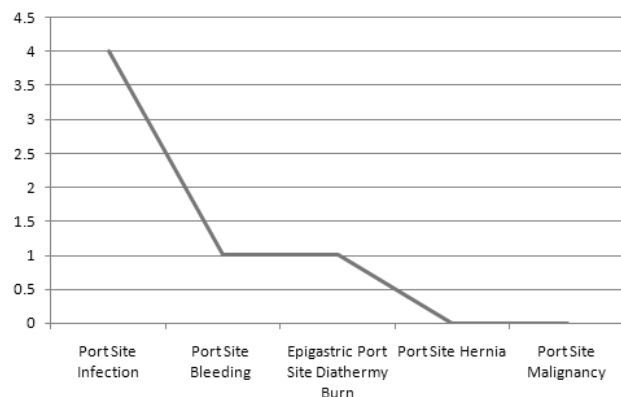


Chart No. 2: Complications at Port Site

The common complications seen in this study were port site infection in 4(0.88 %) cases, followed by port site bleeding in one (0.22 %) case and epigastric port site diathermy burn in one (0.22 %) case. Port site hernia and metastatic malignancy were not reported in our study (Chart No. 2).

## DISCUSSION

In recent times laparoscopic gastrointestinal surgery has become established among general surgeons. Since 1980, once first laparoscopic cholecystectomy was performed, there is continuous decrease in numbers of port site complications due to increased surgeons skills and techniques<sup>10</sup>.

The present study elaborates the experience of 450 patients underwent laparoscopic cholecystectomy in terms of port site complications. In our study female was dominant over the male and ratio of male to female ratio was 1:2.3. However the male to female ratio given by Siddiqui K<sup>11</sup> is 1:5.2 which is quite different from present study. The age of the patients ranged from 20-65 years with the maximum number in the 4th decade with mean age was  $38 \pm 3.4$  years. Which is comparable to other study where the age range was 16-59 years with mean  $37 \pm 10$  years<sup>12</sup>.

Laparoscopic Surgery associated with certain conditions that may influence surgical infection are use of antibiotic prophylaxis, impact on the immune system, influence of pneumoperitoneum and technical aspects related to sterilization of instruments<sup>11</sup>. In our study we observed the frequency of port site infection in 4(0.88 %) cases, while in study of Shindholimath VV et al<sup>13</sup> reported wound site infection was 6.3% which is quite higher and Den Hoed PT et al reported 5.3% port site infection in 1998<sup>14</sup>.

Surgeons encountered complication of port site bleeding if major vessel is damaged during the insertion of Veress needle or trocar. Our study shows port site bleeding in one (0.22 %) case, this result is compared with study of Malik AM<sup>15</sup> reported port site bleeding in 13(0.5%) cases. Veress needle remains the important cause of port site bleeding due to access blindly peritoneal cavity as reported by some authors<sup>16,17</sup>. In our study also reported epigastric port site diathermy burn in one (0.22 %) case.

Postoperative at port site hernia is a rare and incisional type of hernia after laparoscopic surgery. It is usually seen at the site of 10 mm port in umbilical region<sup>18</sup>. In our study no case was reported for post operative laparoscopic port site hernia even after one year follow up, but several other studies have reported trocar site hernia 1 in 500 cases<sup>19</sup>, 3 in 1983 cases<sup>20</sup>, 1 in 800 cases<sup>21</sup>, 11 in 1300 cases<sup>22</sup> and 10 in 1453 cases<sup>23</sup>.

## CONCLUSION

Port site hernia at 10 mm or larger size 12 mm site is rare but still experienced by both the patient & surgeon.

We recommend all 10 mm trocar sites be closed carefully. Over stretching of infra / supra umbilical port should be avoided. Gallbladder should be removed in endo-bag. Factors causing delayed wound healing i.e. malnutrition, poor blood supply, anemia, connective tissue disorder be carefully taken into consideration pre-operatively so that this unkind complication of such artistic technique (Laparoscopy) for both patient & surgeon be avoided.

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## Original Article

# Significance of Gram's stain in the diagnosis and management of Lower respiratory tract infections

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## ABSTRACT

Respiratory tract infections are one of the leading causes of ill health worldwide. For the diagnosis of LRTI, expectorated sputum is the most commonly used specimen.

**Objective:** To establish the importance and relationship of Gram's staining and positivity of sputum culture in lower respiratory tract infections

**Study Design:** Experimental study.

**Place and Duration of Study:** This study was carried out in the Dept. of Microbiology Basic Medical Sciences Institute, Jinnah Postgraduate Medical Center, from January 2001 to September 2001.

**Materials and Methods:** Sputum sample of one hundred clinically suspected cases of lower respiratory tract infections attending OPD or admitted in the wards were included in the study. Early morning sputum samples were collected in sterile container. Gram's staining culture and sensitivity were carried out according to the standard methods.

**Results:** It was very interesting to note that a direct relationship exists between Gram's staining and positivity of culture. Number of pus cells seen per HPF was directly proportional to the isolated bacterial pathogen. <15 pus cells/HPF had 13.2% cases positive for bacterial pathogen. Pus cells 15- 20/HPF had 54.5% cases positive for bacterial pathogen and specimens in which there were >20 pus cells/HPF, 90% cases were positive for bacterial pathogen.

**Conclusion:** Gram's staining is a simple and cost effective method that could provide a basis for culture positivity of the specimen. Higher the number of pus cells in sputum sample greater was the culture positivity. Based on Grams staining results it would be possible to start empiric therapy and alter the therapy after the sensitivity of isolates if needed.

**Key Words:** Gram stain, Pus cells, Sputum, H.influenzae, S.pneumoniae.

## INTRODUCTION

Although LRTIs were a major cause of morbidity and mortality, diagnosis of these infections was often complicated by the contamination of specimens with upper respiratory tract secretions during collection. Gram's staining could provide a basis for determining the extent to which identification and susceptibility testing of organism recovered from specimen.<sup>1</sup>

Despite remarkable advances in the identification of new microbial pathogens and antimicrobial agents, a few diseases were so characterized by disputes about diagnostic evaluation and therapeutic decisions.<sup>2</sup>

Identifying the etiologic agents responsible for pneumonia remained a challenge, primarily because of difficulty in obtaining adequate samples for culture and in differentiating infection from colonization and lack of reliable diagnostic methods.<sup>3</sup>

The diagnostic value of Gram's staining and culture of expectorated sputum had been debated for more than two decades. The value of bacteriological assessment of sputum was controversial during lower respiratory tract infections.<sup>4</sup>

In addition, recommendations had been made that sputum culture results be correlated with direct Gram's stain results in order to provide more clinically relevant information.<sup>5, 6, 7</sup>

Finally, the Gram's stain was a useful tool in laboratory quality assurance. Comparison of Gram's stain and culture results could reveal errors in procedure, specimen collection and/or transport issues, or specimen identification and tracking errors.<sup>8</sup>

Treatment of LRTI could be very simple and cost effective if etiological agent was isolated accurately. Unfortunately neither a standardized laboratory method nor a standard timing for the collection of sample exists. Because of easy availability of Gram's staining and culture rather than blood culture, antigen detection, or nucleic acid amplification, Gram's staining could be a better alternative.<sup>9</sup> The sensitivity of Gram's staining was between 50-96% and specificity from 12 to 100% (Rein et al; 1978)<sup>10</sup>.

## MATERIALS AND METHODS

This study was conducted in the Department of Microbiology, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi, from January 2001 to September 2001. During this period sputum samples were analyzed. Samples were collected from clinically diagnosed cases of lower respiratory tract infections (LRTI)

Patients above 14 years of age were included in the study. Early morning Sputum was collected in a sterile



container, Patients on antibiotics and samples that contained only saliva were excluded from the study.

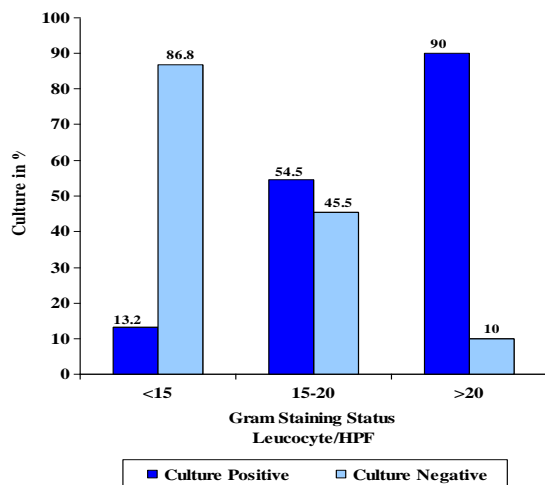
**Macroscopic examination:** Samples collected were observed by naked eye and were described as purulent, muco-purulent, mucoid and muco-salivary.

**Microscopic examination:** Expecterated sputa were screened microscopically before inoculation. Gram's staining smear from purulent portion of the specimen was done and observed under low power magnification to determine the number of epithelial cells and or neutrophils. Samples containing more than 10 squamous epithelial cells were discarded.<sup>11, 12, 13</sup> Three categories were made for neutrophil count i.e. neutrophil count < 15 /HPF, 15-20 /HPF and >20 /HPF. Ziehl Neelsen staining was done routinely to see any probable association of tuberculosis along with LRTI.

**Culture:** To obtain as pure culture as possible and to reduce the number of commensals, washing of purulent part of the sputum was done in 5ml of sterile physiological saline. Sputum was inoculated on Blood, Chocolate and Mac Conkey's agar. *S.pneumoniae* was further confirmed by Optochin sensitivity and *H.influenzae* by applying factor X, V and XV discs. Sensitivity to antibiotics was observed by standard methods.

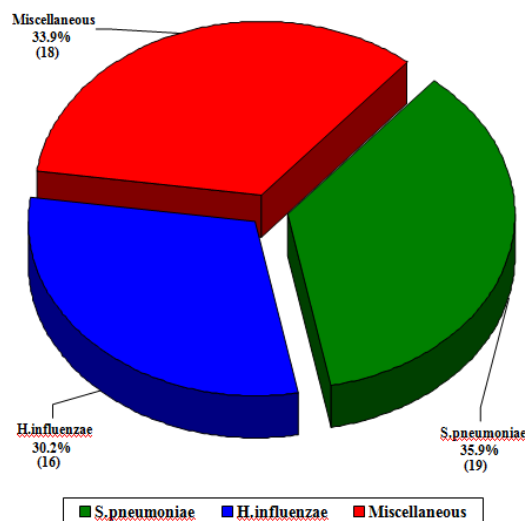
## RESULTS

Relationship between pus cells/HPF and culture positivity for bacterial pathogen was seen and Gram's staining results were divided in to three categories, specimen having <15 pus cells/HPF, 15-20 pus cells/HPF and >20 pus cells/HPF and it was observed that in sputa which contained <15 pus cells/HPF had 13.2% cases positive for bacterial pathogen, specimen which had pus cells between 15 and 20/HPF had 54.5% cases positive for bacterial pathogen and specimens in which there were >20 pus cells/HPF, 90% cases were positive for bacterial pathogen.

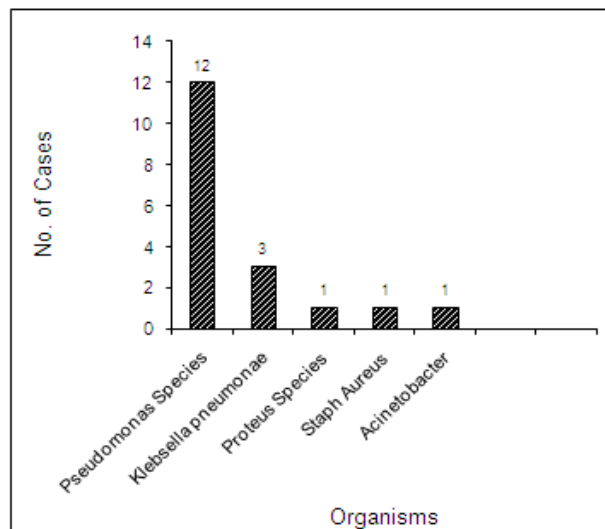


\* Statistically significant

**Figure No.1: Relationship between number of pus cells and culture positivity**



**Figure No.2: Distribution of 53 lower respiratory tract bacterial pathogens**



**Figure No.3: Distribution of miscellaneous organisms (n=18)**

It was observed that higher the number of pus cells/HPF better was the yield for culture positivity (Fig1).

Of 53 positive cultures 19 (35.9%) were *S. pneumoniae*, 16 (30.2%) were *H. influenzae* and 18(33.9%) were miscellaneous organisms (Fig-2)

Of the miscellaneous pathogens, 12 were Pseudomonas species, 3 were Klebsiella pneumoniae, and one each was Proteus species, Staphylococcus aureus and Acinetobacter Fig-3

## DISCUSSION

For the diagnosis of LRTI, expecterated sputum remained the most commonly used sample which could be obtained easily and non- invasively.<sup>9</sup>



Clinical laboratory had an important role in the diagnosis of LRTI because of diverse etiological agents, contamination of the oral flora and complex pathophysiology of respiratory system.

Sputum microscopy suggested that presence of pus cells was a good indicator for LRTI. There was direct relationship between pus cells per HPF and isolated pathogen. Only 13% of sputa showed culture positivity in samples who had < 15 pus cells/HPF as opposed to those who had 15-20 pus cells/HPF, and more than 20 pus cells/HPF, 54.4% and 90% culture positivity respectively. Higher the number of pus cells greater was the rate of LRTI as it was observed by Niederman et al.<sup>14</sup>(1993) in their study. Bartlett and Mundy (1995)<sup>2</sup> in their work had mentioned that Gram's stain showing multiple pus cells with large numbers of bacteria that had the morphologic characteristics of likely pulmonary pathogens were an appropriate basis for making initial therapeutic decisions. Roson B et al (2000)<sup>13</sup> in their study mentioned that specimen possessed more than 25/HPF leucocytes were considered as good quality sputum samples, on the other hand Buenviaje MB (1989)<sup>15</sup> did not show any correlation between number of pus cells and quantitative colony counts. Nihan Ziyade and Aysegul Yagci (2010)<sup>9</sup> in their study reported the comparable results to present study, he mentioned that higher the leucocytes count greater was the culture positivity of sputum. Culture positive sputum in leukocyte count less than 10/HPF were 16.7%, while positivity was 88% in specimen which had leukocyte count greater than 25/HPF. Roch N (2007)<sup>16</sup> also suggested that leucocytes count and direct sputum examination should be performed routinely.

Of the positive cultures, 19 (35.9%) had grown *S.pneumoniae*, 16 (30.2%) *H.influenzae* and 18 (33.9%) were miscellaneous organisms.

Amongst miscellaneous group the commonest was *Pseudomonas* Sp., 12 cases; next to it was *Klebsella* species, 3 cases and one each *Proteus* species, *Staphylococcus aureus*, and *Acinetobacter*. Fang et al (1990)<sup>17</sup> studied 359 cases collected from multiple centers and described that the 32.9% were miscellaneous organisms which was comparable to present study. Macfarlane et al (1993)<sup>18</sup> in data of 206 patients, in 113 (54.8%) bacterial pathogens were isolated and 30% were *S.pneumoniae* which was comparable to our data they found *Haemophilus influenzae* in 7.7% cases and viruses were seen in 4.3% cases. Viruses were not seen in our study. Allegra L (2005)<sup>19</sup> in their study mentioned growth of Gram positive organisms in 38% of cases expectorated purulent sputa. Lloveras J J et al (2010)<sup>4</sup> reported 57% culture positivity in their study, this data was comparable to our results however the most commonly found organism in their study was *Staphylococcus aureus* this showed the known variability in the spectrum of micro-organism in different parts of the

world. *H. influenzae*, *Pseudomonas aeruginosa* and *Streptococcus pneumoniae* were the most common micro organisms reported by Ziyade N and Yagei A (2010)<sup>9</sup> in their study. Same study endorsed the usefulness of Gram's stain and culture in diagnosis of LRTI.

## CONCLUSIONS

Higher the number of pus cells in sputum, greater was the culture positivity. Gram's staining was a simple and cost effective method that could provide a basis for culture positivity in patients of LRTI.

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# Pattern of Cigarette Smoking among College Students of Quetta

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## ABSTRACT

**Background:** Cigarette smoking habit is developed more at the young age, hazardous to health and causes premature mortality.

**Objective:** To determine the pattern of cigarette smoking and factors contributing to the said habit among college students of Quetta.

**Study Design:** Randomized study.

**Place and Duration of Study:** This study was conducted at the Bolan Medical College, Quetta during the academic year 2010-2011.

**Materials and Methods:** A total of 850 students from different colleges of Quetta were randomly selected during the academic year 2010-2011. Prevalence and influence of factors associated with the cigarette smoking were recorded on a predesigned questionnaire. The collected data was analyzed with the help of statistical procedures.

**Results:** Out of the total, 122 students were smokers, 23 ex-smokers and 705 non-smokers. Smokers had the habit for charm and relaxation. While non-smokers and ex-smokers avoided cigarettes use due to family blame, religion and its adverse effect on health. Besides, the habit was found more common among students whose fathers and brothers were smokers. Majority of them knew the hazards and very little number was smoking in the public places.

**Conclusion:** Young age and transition period from school to college is a critical time to adopt the habit of cigarette smoking, hence needs an immense attention of the authority designing tobacco control policies. Healthy recreational activities, awareness programs related to its hazards, non-smoking home environment, increased tax and ban on its advertisements are the essential measures, which can minimize the habit. In addition, the present basic work would serve as a template to conduct further advanced studies on this line.

**Key words:** Cigarettes smoking, associated factors, college students of Quetta.

## INTRODUCTION

Smoking is not only socially unacceptable but also hazardous to human health. Its smoke as produced from combustion of tobacco contains Tar, Nicotine and carbon monoxide. Tar component coats lungs like soot in a chimney, paralyzing the cilia and causes carcinoma of the lungs. Whereas Nicotine when reaches the brain, makes the heart to beat faster, also constricts the blood vessels and hence increases the blood pressure. These effects in combination with the stress produced by carbon monoxide in the smoke of cigarette caused 120,000 heart attacks in the United States<sup>1</sup>. Not only smokers are facing the complications of tobacco use but also non smokers are affected through indoor pollution. Some scientists demonstrated that bronchitis is easily developed in young children of smoking parents<sup>2</sup>. In a study in Japan, the risk of lungs cancer was found significantly higher among non smoking wives married to heavy smokers as compared to those married to non smokers<sup>2</sup>.

A study showed that cigarette smoking leads to decrease HDL and increase LDL by extra secretion of catecholamine, which is a well known cause of Coronary artery disease<sup>3</sup>. Apart from carcinogenic and cardiovascular diseases, tobacco use is responsible for diseases of breasts, teeth, prostate, pancreas and

kidneys<sup>2</sup>. In women, smoking during pregnancy affects fertility, birth outcomes, lactation, foetal development, causes cancer of reproductive system and increases perinatal mortality<sup>4</sup>. A report highlighted that the smoking women have link with early onset of menopause and their babies born have increased levels of carboxyhaemoglobin in the blood<sup>4</sup>. In males, heavy smoking is associated with impaired spermatogenesis, abnormal sperm morphology, lower androgen secretion and erectile dysfunction<sup>5</sup>. About one million premature deaths occurred annually worldwide among which fifty thousand are due to passive smoking<sup>6</sup>. In Cuba, smoking related diseases account for over 30 % of all the deaths and in the United Kingdom for about 15-20%<sup>2</sup>. If special attention is not given to this particular issue, the death rate will jump to about 10 million deaths by the year 2030<sup>7</sup>.

As per WHO figures, 47% of men and 121% of women smoke worldwide<sup>6</sup>. Among them 70 % live in developing countries<sup>6</sup>. The national health survey of Pakistan reported a prevalence of 13.7% among adolescents and 5% among women of rural areas<sup>8</sup>. Despite know how of hazards, 21.3% medical students were found smokers in Sind medical college, Pakistan<sup>9</sup>. The habit of tobacco use is developed easily in the younger age group and with the change in life style from school to college. Hence, it should be observed

and modified/stopped with basic education. Therefore, the present study was designed to determine the percentage of smokers, ex-smokers and non smokers among college students of Quetta. Contributing factors will also be identified regarding this habit so that effective intervention program for the control may be suggested.

## MATERIALS AND METHODS

Six colleges in Quetta were selected for this study. Information regarding personal, contributing and smoking habit was recorded in the predesigned questionnaire. A smoker is defined as one who smokes at least one cigarette per day for 30 days and ex-smoker who had previously smoked at least one cigarette per day for 30 days but does not smoke now. The personal information included age, sex, and education level, whether urban or rural, boarder or day scholar, monthly income, total family number, smoking history of family, peak time/ places of smoking, ailment history, sources of hazards awareness, duration of smoking, number of cigarettes smoked per day, reason for smoking, not smoking and quitting the habit.

Volunteers were taken from each class and they distributed the questionnaire among the students. A lecture to explain the purpose of the study and how to fill the questionnaire was given to the students. Then written consent was obtained from the participants as well as district education officer. The code of confidentiality was kept throughout the study and the students were also assured that the responses will not be disclosed to any college authority. A total of 850 students (Males 832 and females 18) had filled and returned the questionnaires (Table-1). The SPSS version 10 program was used for entering the data and statistical analysis.

**Table No.1: Distribution of participants of the study**

Name of College	Number of students
Bolan Medical College (BMC), Quetta	340
Government Degree College (GDC), Quetta	202
Government Science College (GSC), Quetta	129
Tameere Nou Public College (TNPC), Quetta	76
Musa Public College (MPC), Quetta	55
Law college (LC), Quetta	48
<b>Total</b>	<b>850</b>

## RESULTS

The results of our survey are described in tables 2-4. Out of the total, 122 (14.4%) were found smokers, 23(2.7%) ex-smokers and 705 (82.9%) non-smokers. The prevalence of high smokers was found in

Government degree college (16.8%) followed by Musa public college (14.6%). Ex-smokers were predominantly observed in Law College (4.2%) and Bolan medical college (3.2%). Most of the students of Government Science College (84.5%) and Tameer nou public college (84.2%) were non smokers. Among 18 female students from Bolan medical college, no one was found smoker or ex- smoker.

Day scholar's students and those living in the rural area were found light smokers. 30% had smoker fathers and 43% were brothers of smokers, and 11% fathers and 16% brothers of ex-smokers were also smokers. Majority of the smokers stated that they are doing so to reduce tension and for maintaining good personality/ charm as shown in the advertisement of cigarettes by different media. Though very less number did not hesitate to smoke in the public places but their peak time of smoking was at the night. 58% students started the habit between the ages of 16-23. Almost 60% knew about the hazards either from TV, radios, newspapers, teachers or doctors.

About 53.3% ex-smokers had stopped smoking due to it adverse effect on health and 30% because of family pressure. Most (46.2%) of the non smokers stated that they were not smoking due to its harmful effect and 40.4% has considered it as addiction and prohibited by Islam. Only three smokers have complaint of nocturnal cough and one ex-smoker has diagnosis of ischemic heart disease.

**Table No.2: Findings of the survey, number (%age)**

Name of College	Smokers	Ex-smokers	Non-smokers	Total
BMC, Quetta	48 (14.1%)	11 (3.2%)	281 (82.7%)	340
GDC, Quetta	34 (16.8%)	03 (1.5%)	165 (81.7%)	202
GSC, Quetta	16 (12.4%)	04 (3.1%)	109 (84.5%)	129
TNPC, Quetta	10 (13.2%)	02 (2.6%)	64 (84.2%)	76
MPC, Quetta	08 (14.6%)	01 (1.8%)	46 (83.6%)	55
LC, Quetta	06 (12.5%)	02 (4.2%)	40 (83.3%)	48
<b>Total</b>	<b>122 (14.4%)</b>	<b>23 (2.7%)</b>	<b>705 (82.9%)</b>	<b>850</b>

**Table No.3: Ex- Smokers: Reason for Quitting the habit**

Reason	Number	Percentage
Health effect	16	53.3
Waste of money	03	10.0
Loss of charm	01	3.3
Family blame	09	30.0
Friend advise	01	3.3
Brand not available	-	-

**Table No.4: Non smokers: Reason for not smoking**

Reason	Number	Percentage
Religion	301	40.4
Health hazards	344	46.2
Waste of money	49	6.6
Non smokers society	14	1.9
Family blame	17	2.3
No charm	09	1.2
No tension	11	1.5

## DISCUSSION

Tobacco is used worldwide in different brands and its introduction to any country is associated with immense health problems. China is the top consumer as one of the three cigarettes in the world today is smoked there<sup>10</sup>. In developing countries, its prevalence is also increasing. In Bangladesh, 15 million males and 0.5 million females were found smokers in a population of 110 millions<sup>11</sup>. In our study, we got 14.4% prevalence rate in college students of Quetta. An early study conducted in USA showed a prevalence of 14% among college students<sup>12</sup>. While another study in Karachi reported, the prevalence of smoking to be 13.7% in school going adolescents<sup>8</sup>.

Besides, we found that smoking was more common in GDC and less common in GSC. There are multiple possible reasons for the different pattern like environment, knowledge of health hazards, depression etc. Lack of knowledge and depression are well known risk factors for smoking and increase the danger of starting the habit at young age. Some scientists gave possible explanation that science students are more cared and restricted, and more recreational activities are provided in their colleges<sup>13</sup>.

In the present attempt we also observed that father and brothers of most of the smokers were also smoking. This means that family has strong influence on the habit of the individual. 46.2% students in colleges of Quetta were not smoking because of its harmful effect thus indicating that the majority of students are familiar about smoking related complications. However, 40.4 students gave the reason that they did not smoke for the religious reasons.

Some of the students had left smoking due to family reasons and its adverse effect on health. The advice of the doctor in this regard will be more effective if he/she himself/herself is not smoking. A researcher demonstrated that people who smoke mainly for stimulation, handling and pleasure could easily stop smoking as compared to those who have the habit to reduce tension<sup>14</sup>. Quitting smoking is a long term process requiring a great deal of unconscious, constructive and painful conflict, but one can stop smoking if he is guided regularly and should keep him busy in some beneficial alternative activities. Besides, the harmful effects of smoking should be advertized, discussed and included in dramas on radio and

television as well as through the press. Like us, an early study reported that advertisement-showing charm in smoking is a major promoter of teenage smoking<sup>3</sup>. In addition, increased tax, ban on tobacco advertisement and seminars on subjects such as "Health or Tobacco" are other beneficial measures which may help to minimize the habit.

## CONCLUSION

Young age and transition period from school to college is a critical time to adopt the habit of cigarette smoking, hence needs an immense attention of the authority designing tobacco control policies. Healthy recreational activities, awareness programs related to its hazards, non- smoking home environment, increased tax and ban on its advertisements are the essential measures, which can minimize the habit. In addition, the present basic work would serve as a template to conduct further advanced studies on this line.

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# Prevalence of Dengue Fever in Rawalpindi, Islamabad - A Cross Sectional Study

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## ABSTRACT

**Background:** Dengue is an important vector borne viral disease of public health significance. Dengue fever is on the rise in Pakistan with considerable morbidity and mortality in recent outbreaks. We undertook the study to analyze the prevalence of Dengue fever in Rawalpindi and Islamabad region.

**Objectives:** The object of our study was to estimate the burden of dengue fever in Rawalpindi and Islamabad region. Another aim of our study was to evaluate and if possible alleviate the anxiety associated with dengue fever. We wanted to find out the factual prevalence of the disease. We aimed to determine the most common age group and gender of the illness as well.

**Study Design:** Cross Sectional Study.

**Place and Duration of Study:** This study was conducted in Benazir Bhutto Hospital (BBH) and Pakistan Institute of Medical Sciences (PIMS) in Rawalpindi and Islamabad from 1<sup>st</sup> September to 15<sup>th</sup> November 2011.

**Materials and Methods:** People of all ages and both sexes with suspicion of Dengue were included in the study.

**Results:** A total of 16616 people turning up at these hospitals were tested for Dengue virus. Only 2269 were positive for disease (13.6%). Male to female ratio came out to be 2.1:1 and maximum number of cases belonged to age group 21-30 years.

**Conclusion:** The number of cases turning up with Dengue suspicion is out of proportion to actual disease burden. Thus we need to alleviate the anxiety associated with the disease. There is a genuine need for strict adherence to preventive control measures and research needs to be undertaken in order to reduce the mortality and morbidity associated with the Dengue.

**Key Words:** Dengue Fever, Prevalence, Aedes Aegypti.

## INTRODUCTION

Dengue is the most important arthropod-borne viral disease of public health significance. Dengue infection is one of the most rapidly expanding diseases known to mankind with an estimate of 50 million new cases worldwide annually.

The first definitive case of dengue fever was reported by Benjamin Rush in 1789 and he called it the break bone fever. However it was first recognized in its present day form as the dengue fever caused by dengue virus in 1950s.<sup>1</sup> WHO currently estimates there may be 50 million dengue infections worldwide every year.<sup>2</sup> It is currently endemic in more than 100 countries.

The principal vector for DEN is *Aedes aegypti*, a highly urbanized, daytime biting mosquito that breeds in stored water<sup>3</sup>. These mosquitoes normally bite during daylight and take multiple blood meals from one or more human subjects. These vectors are very efficient in transmitting dengue virus because of their breeding sites, which are the houses or outdoor places including artificial containers and construction sites.

Dengue infection can cause a spectrum of illness ranging from mild, undifferentiated fever to illness up to 7 days' duration with high fever, severe headache, retro-orbital pain, arthralgia and rash, but rarely causing death. Dengue Haemorrhagic Fever (DHF), a deadly complication, includes haemorrhagic tendencies,

thrombocytopenia and plasma leakage. Dengue Shock Syndrome (DSS) includes all the above criteria plus circulatory failure, hypotension and low pulse pressure. Dengue fever (DF) is an arthropod-borne disease caused by any of the four serotypes of dengue virus (DEN), a member of the family Flaviviridae. Dengue virus (DV) is an envelope, single-stranded, positive RNA virus<sup>4</sup>. There are four dengue viruses designated as DENV-1, -2, -3 & -4 which are serologically related but are antigenically and genetically distinct<sup>5</sup>. In South East Asia, the average number of cases of DHF per year has increased from 10,000 in the 1950s to over 200,000 in the 1990s.

Thus, dengue virus remains a major cause of morbidity and mortality in tropical areas<sup>6</sup>. WHO declares dengue and dengue haemorrhagic fever to be endemic in South Asia. Dengue outbreaks with multiple serotypes can lead to dengue shock syndrome as well.<sup>7</sup> DF outbreaks have been reported from Pakistan in 1994, 1995, and 1997<sup>8-10</sup>. Thereafter, few sporadic cases were reported until the winter of 2006 when an outbreak occurred, followed by another from September to November in 2007 that caused significant morbidity and mortality.

Evidence suggests that the overall burden of disease, as well as its severity, is on the rise in Pakistan. In Asian countries where DHF is endemic, the epidemics have become progressively larger in the last 15 years. In 2005, dengue was the most important mosquito-borne

viral disease affecting human<sup>11-13</sup>. Since dengue virus is endemic in Pakistan, circulating throughout the year with a peak incidence in the post monsoon period, we undertook our research in the same period. This would enable us to study the illness when it is at its peak.

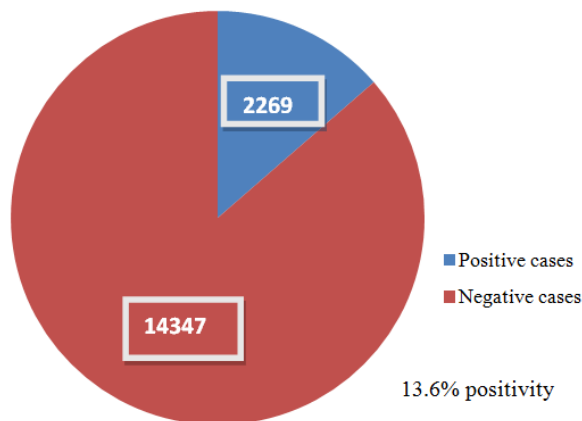
## MATERIALS AND METHODS

People of all ages and both sexes turning up at Benazir Bhutto Hospital (BBH) Rawalpindi and Pakistan Institute of Medical sciences (PIMS) Islamabad with Dengue suspicion were included in the study. The criteria for positivity was serum IgM, serum IgG levels along with clinical symptomatology. Temperature changes on monthly basis were also recorded.

## RESULTS

A total of 16616 people turning up at the hospital were tested for dengue virus. However only 2269 were positive for the disease. Out of these, 12938 turned up in Rawalpindi region (BBH) and only 3678 were from Islamabad (P.I.M.S). These figures show that the turn out and prevalence of dengue in Rawalpindi is higher than that in Islamabad. BBH (Pindi) was also catering for Chakwal, and other suburbs. Percentage positivity of our study came out to be 13.6%. Using the seroprevalence data, the force of infection was estimated to be 11.7% per year in another study. These have been shown in a Pie chart figures:

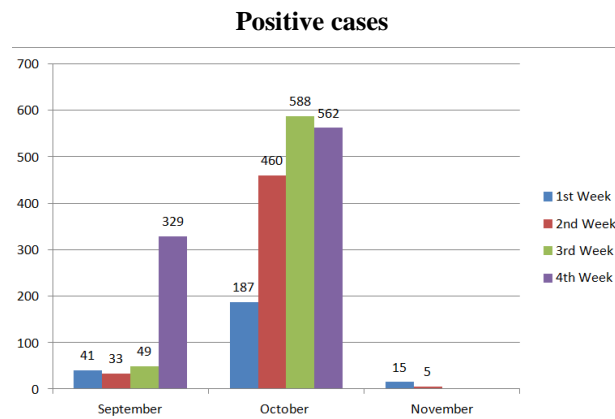
**Pie Chart No.1: Total cases = 16616**



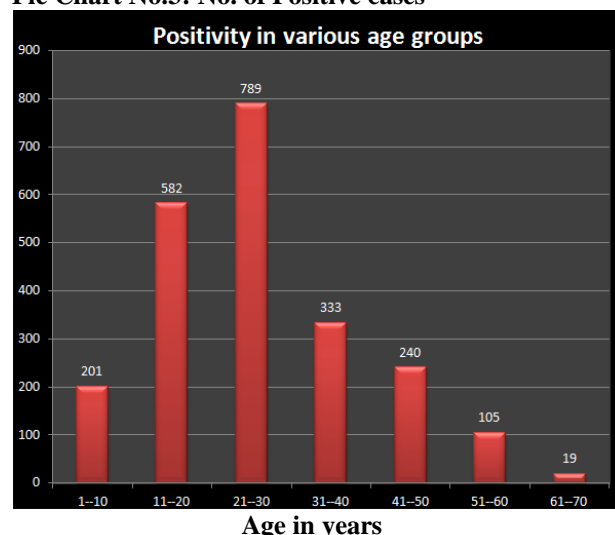
Maximum numbers of cases were seen in 3<sup>rd</sup> week of October 2011 shown graphically. The average temperatures recorded in September were 21-33 degrees Celsius, in October 15-31 degrees Celsius and in November 8-25 degrees Celsius. As the temperatures fell in November, the number of cases also reduced.

**Gender ratio:** Out of a total of 2269 patients 1544 were males and 725 were females. The ratio comes out to be 2.13:1. This fact is also supported by other studies conducted in South East Asia<sup>14</sup>.

**Pie Chart No.2: Week wise positivity of Dengue cases**



**Pie Chart No.3: No. of Positive cases**



Maximum number of cases were found in the age group 21-30 years, the second most frequent group was age 11-20 years.

## DISCUSSION

Pakistan experienced major epidemics of dengue fever last year thus it is imperative to evaluate the burden of disease. Our study shows 13.6 percent positivity, another researcher reports 11.7% positivity of the disease per year.<sup>15</sup>

Our study points out to another aspect of dengue fever. We conclude from our results that there is too much anxiety and panic associated with the disease because 16616 patients turned up with dengue suspicion and only 2269 were positive (so every fever is not dengue fever) and one should not panic too much.

During the past century, surface temperatures have increased by a global average of 0.75°C. Temperature increases of this magnitude may be associated with substantial increases in dengue epidemic potential<sup>16</sup>. In keeping with this study our results show that the

number of cases decreased with the fall in temperature in November when the number dropped to 20 only.

Since the epidemics of dengue have been commonly associated with the rainy season<sup>17</sup>.

We decided to undertake our study in the post monsoon period. Our study shows 452 cases in September, 1797 in October and with the fall in temperature there is a significant decrease in the number of dengue patients in November.

Our results show that maximum number of patients fall in the age range 21-30 years. In Singapore (1982) most of the patients were older than 15 years of age. In Indonesia (1975-1984) majority of patients were young adults. Bangladesh (2000) reports highest proportion of cases in the 18-33 years age group. Our results are comparable to the above mentioned studies. Since maximum number of patients were seen in the age group 21-30 years. However Puerto Rico (1995) shows 10-19 years to be the commonest age group<sup>18</sup>. There is an age shift from children to adults. Initially dengue fever was acknowledged to be a childhood disease but over time there is increasing evidence that older age groups are more commonly affected. Many studies in Southeast countries where dengue has been epidemic for several years show a clear cut age shift<sup>18</sup>.

One possible reason for higher incidence in this age group could be that repeated DEN infections lead to sequential augmentation of the immune system<sup>19</sup> so that the severe infections, more probable in older patients, are more likely to come to medical attention as opposed to milder ones in the younger age group.

Hospital-based studies have similarly reported increasing infection rates among adults, mentioning that it is contrary to the popular belief that dengue is a paediatric disease<sup>20,21</sup>. Our study shows a male predominance which is similar to the studies by other researchers who have reported male to female ratio of 1.9:1, 1:0.57, 2.5:1, 1:0.25, 1.5:1, 1.5:1 in south east asia.<sup>22,23</sup> However South American and a Mexican study shows that the disease is more common in females as compared to males<sup>24,25</sup>. Understanding male-female differences in infection rates and severity of disease is important for public health control programmes.

Studies by Kabra, Halstead and Shekhar show that the severity of the illness is higher among females despite higher incidence in males<sup>4</sup>.

Dengue virus infection is increasingly recognized as one of the world's emerging infectious diseases. About 50-100 million cases of dengue fever and 500,000 cases of Dengue Hemorrhagic Fever (DHF), resulting in around 24,000 deaths, are reported annually<sup>2</sup>.

Certain demographic and societal changes are thought to be associated with the reappearance of lethal dengue infection over the past 50 years<sup>26</sup>. The factors responsible for such an enormous expansion are rapid population growth, peri-urbanization with

inadequate public health systems, lack of vector control, climatic variability and rainfalls, and increased travel (especially air travel) to endemic areas<sup>27</sup>. Due to these factors, there is an increase in the reportable cases of dengue infection. Half the world's population lives in countries endemic for dengue, underscoring the urgency to find solutions for dengue control. The consequence of simple DF is loss of workdays for communities dependent on wage labour. The consequence of severe illness is high mortality rates, since tertiary level care required for DHF/DSS management is beyond the reach of most of the persons at risk.

## CONCLUSION

The number of cases turning up with Dengue suspicion is out of proportion to actual disease burden. Thus we need to alleviate the anxiety associated with the disease. There is a genuine need for strict adherence to preventive control measures and research needs to be undertaken in order to reduce the mortality and morbidity associated with the Dengue

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# Abdominal Pain: A Common Presentation of Dengue Fever

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## ABSTRACT

Dengue fever (DF) is a mosquito born viral disease caused by dengue virus and is endemic in large areas of southeast of Asia. Pakistan is an endemic country for dengue virus infection. Abdominal pain is a commonly reported symptom in dengue fever (DF). The most common causes of abdominal pain are acalculus cholecystitis, ascites, acute pancreatitis, acute hepatitis, pleural effusion and peptic ulcer disease.

**Study design:** A Case Series Study.

**Place and Duration of Study:** This study was conducted at Mayo and Lady Willingdon Hospitals, Lahore from September and October 2011.

**Materials and Methods:** 105 patients with fever and abdominal pain admitted to Mayo and Lady Willingdon Hospitals, Lahore during months of September and October 2011 were included in the study. A provisional diagnosis of dengue fever was made based on the presence of acute febrile illness and two of the following features :headache, retro orbital pain, myalgia, arthralgia , skin rash, hemorrhagic manifestations and leucopenia. The diagnosis was confirmed by enzyme immunoassay based serology. The cause of pain was determined by blood tests (Serum Amylase , serum lipase, liver function tests {LFTs} ) and radiology ( ultrasound, contrast enhanced CT {CECT} and chest xray {CXR} ) except for pregnant patients. 67 patient had dengue fever and 38 patient had other causes of fever and abdominal pain. In patient with dengue fever causes of abdominal pain were acalculus cholecystitis, ascites, acute pancreatitis, acute hepatitis, pleural effusion and peptic ulcer disease. Among 67 patients 2 were pregnant, one at 28 weeks and other at 32 weeks of gestation.

**Results:** Results of this study show that among 105 patients having fever and abdominal pain, 67 patients had serologically proven dengue fever. Table I shows that among patients with serologically proven dengue fever 29 had acalculus cholecystitis, 14 had ascites, 9 had acute pancreatitis, 11 had gastrointestinal disorder and 4 had bilateral pleural effusion. Among 3 patients with menorrhagia 2 had acalculus cholecystitis and 1 had gastrointestinal disorder. 2 patients were pregnant at 28 and 32 weeks of gestation. Both of them had peptic ulcer disease. Among 67 patients, 47 were male and 20 were female. Ages of patients range from 15 to 62 years. All patients had temperature ranging from 101°F to 104°F while mean duration of fever was 5 days.

In patient with dengue fever etiology of abdominal pain should be aggressively looked into for proper and better management.

**Conclusion:** If carefully looked into, the etiology of abdominal pain in dengue fever can be found and appropriately managed.

**Key Word:** Dengue Fever (DF), Abdominal Pain, Acalculus Cholecystitis, Ascites, Acute Pancreatitis, Pleural Effusion.

## INTRODUCTION

Dengue fever (DF) is a mosquito born viral disease caused by dengue virus and is endemic in large areas of southeast of Asia <sup>(1)</sup>. Pakistan is an endemic country for dengue virus infection. Dengue virus infection may be asymptomatic or present as undifferentiated fever: DF or dengue hemorrhagic fever (DHF) <sup>(2)</sup>. Dengue shock syndrome (DSS) may lead to hypovolemic shock. Abdominal pain is a frequently reported symptom in patients with dengue fever<sup>(3)</sup>. The protean character of dengue fever ranges from mild febrile illness to profound shock. The common symptoms in dengue infection are fever, malaise, headache, musculoskeletal pain, nausea, vomiting , bleeding , acute renal failure and seizure <sup>(4, 5)</sup>. Other complications include acute myocarditis<sup>(6, 7)</sup> , acute hepatic failure, ascites <sup>(8)</sup> ,

dengue encephalitis <sup>(9, 10)</sup> , acute pancreatitis<sup>(11)</sup>, acalculus cholecystitis and pleural effusion<sup>( 12)</sup>. In September 2011 Lahore faced a severe endemic of dengue infection with highest case level and deaths. In this endemic frequent occurrence of abdominal pain was noted in patients presented to Mayo and Lady Willingdon Hospitals Lahore, Punjab, Pakistan.

## MATERIALS AND METHODS

105 patients with abdominal pain and fever who presented to emergency and outdoor of Mayo and lady Willingdon Hospitals, Lahore in the month of September and October 2011 were included in the study and 67 patients had serologically proven DF. A provisional diagnosis of DF was made if the patient had acute febrile illness with two or more of the following manifestations : headache, retro orbital pain, skin rash,

myalgia, arthralgia, hemorrhagic manifestations and leucopenia<sup>(2)</sup>. The diagnosis was confirmed by presence of IgM antibodies against dengue virus using the immunocomb II dengue Bispot IgM and IgG test. This test is solid phase enzyme immunoassay, based on an immunocapture principle the sensitivity and specificity of the test is 97.5% and 97.7% respectively. Diagnosis of DHF was made if following features were present <sup>(1)</sup>: fever lasting 2 to 7 Day <sup>(2)</sup> hemorrhagic tendencies e.g; positive tourniquet test, petechiae, ecchymosis, bleeding from mucosa, gastrointestinal haematamesis or maleena, menorrhagia <sup>(3)</sup> thrombocytopenia (<100,000 platelets /mm<sup>3</sup>),<sup>(4)</sup> evidence of plasma leakage due to increased vascular permeability, manifested by either a rise in the haematocrit equal to or greater than 20% above average for age/sex or drop in the haematocrit following volume replacement and sign of plasma leakage such as pleural effusion, ascites or hypoproteinemia. All patients underwent abdominal ultrasound. CXR and CECT were done of every patient except pregnant patients. The platelet count of every patient was done at presentation and every alternate day. It was done every day in patients of DHF with thrombocytopenia. Among pregnant patients obstetrical complications were ruled out.

## RESULTS

Results of this study show that among 105 patients having fever and abdominal pain, 67 patients had serologically proven dengue fever. Table I shows that among patients with serologically proven dengue fever 29 had acalculus cholecystitis, 14 had ascites, 9 had acute pancreatitis, 11 had gastrointestinal disorder and 4 had bilateral pleural effusion. Among 3 patients with menorrhagia 2 had acalculus cholecystitis and 1 had gastrointestinal disorder. 2 patients were pregnant at 28 and 32 weeks of gestation. Both of them had peptic ulcer disease. Among 67 patients, 47 were male and 20 were female. Ages of patients range from 15 to 62 years. All patients had temperature ranging from 101°F to 104°F while mean duration of fever was 5 days.

Among rest of 38 patients presenting with abdominal pain and fever, 15 had cholelithiasis with acute cholecystitis, 9 acute viral hepatitis, 9 typhoid fever, 3 obstructive jaundice and 2 had amoebic hepatic abscess. 49 patients had hemorrhagic manifestations. Table 2 shows distribution of hemorrhagic manifestations in these patients.

**Table No.1: Causes of abdominal pain n=67**

Acalculus cholecystitis	29 (43.28%)
ascites	14 (20.89%)
GI disorders( peptic ulcer disease)	11 (16.41%)
Acute pancreatitis	9 (13.43%)
Bilateral pleural effusion	4 (5.97%)

While table 3 shows results of laboratory investigations in patients suffering from Dengue fever. Highest number of patients had thrombocytopenia while hypoproteinemia was least common.

**Table No.2: Hemorrhagic manifestations n= 49**

Tourniquet test	30(61.22%)
Bleeding from mucosa	5(10.20%)
Petechiae	4(8.16%)
GIT haematamesis/ maleena	4(8.16%)
Ecchymosis	3(6.12%)
Menorrhagia	3(6.12%)

**Table No.3: Laboratory investigations n= 67**

Thrombocytopenia	65 (97%)
IgM antibodies	65 (97%)
Rise in haematocrit	60(89.55%)
IgG antibodies	8(11.94%)
Hypoproteinemia	7(10.44%)

## DISCUSSION

Abdominal pain is a common feature in patient with DF<sup>(13, 14)</sup>. It needs to be differentiated from obstetrical complications among pregnant patients and dysmenorrhia in patients suffering from menorrhagia. Abdominal pain with fever may be caused by cholelithiasis, acute cholecystitis, acute viral hepatitis, typhoid fever and many other abdominal conditions. In patients with DF this abdominal pain could be attributed to acalculus cholecystitis, ascites, pancreatitis and GIT disorders. The pathogenesis of abdominal pain in dengue fever is not clearly understood however lymphoid follicular hyperplasia seems to play an important role and plasma leakage through damaged capillary endothelium had been proposed<sup>(15, 16)</sup>. It might be the possible cause of subserosal fluid collection and thickened gall bladder wall associated with dengue fever. The specific organ involvement in viral hepatitis, acute pancreatitis and gastrointestinal disorder can also produce abdominal pain.

## CONCLUSION

If carefully looked into, the etiology of abdominal pain in dengue fever can be found and appropriately managed.

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# Risk Factors Associated with Development of Post-Meningitic Hydrocephalus

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## ABSTRACT

**Objective:** To determine the frequency and risk factors associated with the development of post-meningitic hydrocephalus in children suffering from pyogenic meningitis.

**Study Design:** A descriptive as well as case control study.

**Place and Duration of Study.** Children admitted with the diagnosis of pyogenic meningitis from December 2010 to July 2011 in the Pediatric unit-2 of Bolan Medical Complex Hospital Quetta.

**Patients and Methods:** All the children admitted to the Pediatric Unit-2 of Bolan Medical Complex Hospital (BMCH) from December 2009 to July 2011 with the diagnosis of bacterial meningitis. The diagnosis of bacterial meningitis was based on history and examination suggestive of meningitis with at least one of the following items be present, positive CSF culture or positive gram stain (for hemophilus influenza, Streptococcus Pneumoniae, or Neisseria meningitidis.), or CSF TLC10/ML and positive blood culture for above mentioned organism or CSF culture and gram stain negative for the organism but CSF WBC100/ML with >50% polymorphonuclear cells. Patients below 2 month of age and patient with Tuberculous meningitis were excluded from the study. The data collected on a specific Performa having different variables such as age, sex, seizure, duration of treatment ect. Then the data was analyzed on Epi info version 6 simple frequencies were calculated for each variable. Chi square analysis was done to see any correlation between the risk factors and post-meningitic hydrocephalus. Odds ratio was calculated for the risk factors.

**Results:** The mean age of study subjects was 7.2 years with 60% males and 40% females. Gram stains were positive in 37.5% of patients, CSF culture was positive in 27.5% of the patients, in 17.5% of the patients hydrocephalus was the main complication of bacterial meningitis and 25% had other type of sequelae including seizures, hearing loss, hemiparesis etc. Significant association was found between seizure at admission (p-value<0.040), duration of illness (p-value<0.01%), age on admission (p-value<0.01). 68.8% patients came for follow up 2.5% patients left against medical advice (LAMA) and 2.5% expired.

**Conclusion:** The association was found between the development of post-meningitic hydrocephalus and variables such as seizure, duration of illness (patients having duration of symptoms like fever, headache, vomiting, cerebrospinal fluid leukocyte count and duration of antibiotic treatment.

**Key Words:** Pyogenic meningitis, Hydrocephalus, Computed tomography, Magnetic resonance imaging, Cerebrospinal fluid, Prognosis.

## INTRODUCTION

Fifty years after the advent of antibiotics for clinical use, bacterial meningitis remains an important cause of morbidity and mortality. As such, it represents a unique human infectious disease, because the pathophysiologic effects of the disease progression and sub-optimal outcomes occur despite bacteriologic cure of the infection.<sup>1</sup> Bacterial meningitis is the most destructive of acute infections in normal individuals. With the use of appropriate antimicrobials mortality from bacterial meningitis has been reduced from greater than 90% to less than 10%, although mortality in the neonate remains between 15 and 20%.<sup>2,3</sup> The three most common aetiologic bacteria, Hemophilus Influenza, Streptococcus Pneumoniae and Neisseriae Meningitidis account for 90% of reported cases occurring in infants and children more than 60 days of age.<sup>4,6</sup> Before the use of the Haemophilus conjugate vaccines, the annual incidence of bacterial meningitis in children 0 to 5

years of age was between 30 and 70 per 1000000.<sup>4,6-9</sup> However, because the morbidity and mortality of bacterial meningitis vary with etiologic organism, the substantial reduction in prevalence of meningitis caused by Haemophilus vaccine may not lead to as striking a reduction in the incidence of neurologic sequelae of this disease<sup>10-14</sup>. Meningitis is still the most serious infectious disease for many developing countries, including Pakistan. In a local study done at Sheikh Zayed Medical Institute Lahore, the incidence of pyogenic meningitis was 1.2% cases per 100 admissions.<sup>15</sup> In developed countries, the focus in managing bacterial meningitis has been shifted from reduction of mortality to reduction of sequelae<sup>16</sup>, but developing countries are still burdened by excessive mortality and sequelae rates<sup>17,18</sup>, compared with those in developed countries.<sup>1,4,16,19</sup> According to various studies done abroad, the incidence of post-meningitic hydrocephalus ranges from 21-41% in new born babies<sup>20,21</sup>, and 7-9% in infants and school age

children.<sup>23,24</sup> In two other studies done in Arizona and Canada the serious sequelae of pyogenic meningitis including hydrocephalus among the survivors were 44% and 33% respectively.<sup>24,25</sup>

In a local study done at Lahore (Mayo Hospital) the incidence of post-meningitic residual sequelae was 7% at the time of discharge and the most common residual defect was found to be hydrocephalus and deafness<sup>27</sup>. Several risk factors have been described to have association with the development of hydrocephalus in children suffering from pyogenic meningitis. These include age, coma, temperature, seizure at admission, duration of symptoms, type of organism, cerebrospinal fluids findings and gender<sup>22,27</sup>. Very few studies have been carried out on this subject. Furthermore, almost all the studies have been carried out in Europe and America, while local data is lacking in this regard. Thus this study will be of immense help to our clinicians to find out the magnitude of the problem and to predict the development of hydrocephalus in these children.

## PATIENTS AND METHODS

This study was conducted at the Department of Pediatrics Unit-2, Bolan Medical Complex Hospital (BMCH), Quetta. All the children (>2month age) admitted to the pediatric unit-2 ward of (BMCH) from December 2009 to July 2011 with the diagnosis of bacterial meningitis, were included in the study. The diagnosis of bacterial meningitis was based on history and examination suggestive of meningitis with at least one of the following three items should be present.

- Positive CSF culture, gram stains for Hemophilus Influenza, Streptococcus pneumoniae, Neisseria meningitides.
- If CSF Leukocyte counts 10/ml and blood culture positive by day three of admission for Hemophilus influenza, Streptococcus pneumoniae, Neisseria meningitides.
- If CSF culture and gram stain negative, but CSF Leukocyte count 100/ml with >50% polymorphonuclear cells and CSF glucose <50% of blood glucose or if no blood glucose, CSF glucose <30mg/dl; OR CSF Leukocyte>1000/ml with >50% polymorphonuclear cells.

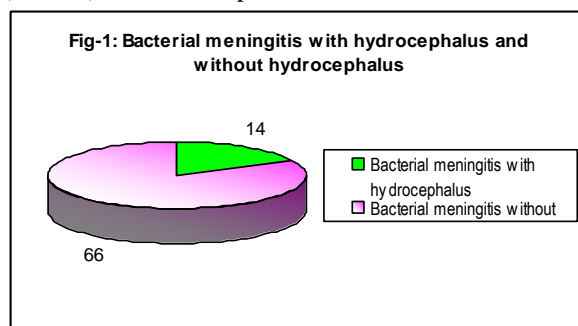
The diagnosis of hydrocephalus was based on increased fronto-occipital circumference, ultrasound head, computed tomography (CT) and Magnetic resonance imaging (MRI). The exclusion criteria were age<2mont and >15years, tuberculous meningitis, Arnold-chiari malformation, intraventricular tumours. During the study period, 87 patients were admitted to our ward with the diagnosis of bacterial meningitis. Out of these, seven patients were excluded based on the above mentioned criteria, leaving 80 patients. The mean age

of study subjects was 7.2 years with a range of 2months to 15 years. Males were 60 percent and females 40%.the data was collected on a performa noting, variables such as age, sex, duration of illness on admission (>3 or<3days), seizure on admission (present or absent), CSF examination, duration of antibiotic treatment, ultrasonography brain, CT and MRI brain. 42 out of 80 patients (52%) suffering from bacterial meningitis had no imaging done and therefore, were presumed to have no hydrocephalus. Outcomes were evaluated at the time of discharge from the Hospital and their follow-up at the out patient department (OPD). Outcome measures were described as follows; complete recovery, recovery with sequelae, such as, hydrocephalus, seizures, paresis, hearing loss and others and death

The data was analyzed on Epi info version 6. Simple frequencies were calculated for each variable. Chi square analysis was done to see any correlation between the risk factors and post-meningitic hydrocephalus. Odds ratio was calculated for the risk factors.

## RESULTS

The mean age of study subjects was 7.2 years with 60% males and 40% females. Gram stains were positive in 37.5% of patients, CSF culture was positive in 27.5% of the patients, in 17.5% of the patients hydrocephalus was the main complication of bacterial meningitis and 25% had other types of sequelae including seizures, hearing loss, hemiparesis ect. In 48% (32 patients) patients neuroimaging was done, ultrasonography was 1.3%, CT scan head was 41.3% and MRI head was 5.0%, in 63.2% patients, neuroimaging did not show any abnormality. In 68.8% patients only Ceftriaxone was given. Ceftriaxone and others antibiotics in combination were given in 25% of patients. Significant association was found between seizure at admission (p-value<0.040), duration of illness (p-value<0.01%), age on admission (p-value<0.01). 68.8% patients came for follow up. 2.5% patients left against medical advice (LAMA) and 2.5% expired.



**Table 1: Risk factors associated with post-meningitic hydrocephalus (n = 80)**

Variable	Hydrocephalus	No hydrocephalus	Odds ratio	95% CI	*P-Value
<b>Age</b>					
2 month-1year	12	15	20.4	3.6-149	<0.01
>1year – 15year	02	51			
<b>Duration of symptoms</b> (Fever, vomiting, headache, seizure)			06	1.2-42	<0.01
≥3days	12	33			
<3days	02	33			
<b>Seizure on admission</b>					
Present	07	15	3.4	0.89-13.2	<0.03
Absent	07	51			
<b>Cerebrospinal fluid, total leukocyte count (TLC)</b>					
<500 cells/cumm	09	26	2.7	0.73-10.8	<0.08
>500 cells/cumm	05	40			
<b>Duration of antibiotic</b>					
14 days	05	08	4.03	0.0-1.1	<0.02
7-10 days	09	58			

\*P-value determined by chi-square test.

## DISCUSSION

Bacterial meningit (BM) results in substantial morbidity and mortality. Hemophilus Influenza, Streptococcus pneumoniae and Neisseriae meningitides account for 90% of reported cases occurring in infants and children more than 60 days of age.<sup>4-6</sup> Hydrocephalus following bacterial meningitis is a common and major complication in children. It presents as a challenge for the physicians and has considerable effect on the effectiveness of the treatment and outcome of patients. Outcome of bacterial meningitis has significantly improved with advent of antibiotics. In spite of appropriate treatment with antibiotics some of the patients develop major as well as minor sequelae associated with bacterial meningitis. However, few of the studies have been done to find out the modalities to intervene in the pathophysiology of bacterial meningitis to decrease the worst outcome of bacterial meningitis. Studies also have been done to find out certain risk factors at the time of presentation of bacterial meningitis which could be associated with development of post-meningitic sequelae, including hydrocephalus, e.g. age, sex, seizure at admission, duration of illness, type of organism, type of antibiotic used. Therefore, we can predict the development of post-meningitic sequelae at the time of presentation and refer the patients to tertiary care hospital, our study shows a statistically significant correlation between certain risk factors such as seizure at admission (p-value 0.03) and duration of symptoms (p-value 0.01) with development of post-meningitic hydrocephalus, which is consistent with the results of the literature.<sup>23,28</sup> In our study frequency of post-meningitic hydrocephalus was much higher (17.5%) than reported in literature (7.9%)<sup>20,21</sup>, the reason of

which is difficult to explain. Even in a local study<sup>27</sup> done (at Mayo Hospital Lahore) the incidence of post-meningitic sequelae was much lower i.e. 7% than our study. However, other sequelae such as seizures, hemiparesis and hearing loss were less common in our study as compared to the reported from Arizona and Canada.<sup>24,25</sup>

In a meta analysis of prospective cohort studies from developed countries the least favorable outcome was with streptococcus pneumoniae meningitis, the most favorable with Neisseriae meningitides while outcome with Hemophilus influenza meningitis was intermediate.<sup>11</sup> According to our study post-meningitic hydrocephalus developed in 26.6%, 10% and 40% of patients with Streptococcus pneumoniae, Neisseriae meningitides and Hemophilus influenza meningitis respectively. As the wide spread use of Hemophilus conjugate vaccine results in the virtual elimination of meningitis caused by Hemophilus influenza type b, Streptococcus pneumoniae become the predominant cause of bacterial meningitis in developing countries. Our study shows that Hemophilus influenza is the predominant cause of post-meningitic sequelae following bacterial meningitis. This is probably due to the low use of Haemophilus vaccine in our country. Our study is mainly focusing on the development of post-meningitic hydrocephalus at the time of discharge. Another study needs to be done to look at the remaining post-meningitic sequelae (seizures, hearing loss, paresis) and the duration of cohort of patients with bacterial meningitis needs to be extended, because some of the post-meningitic sequelae in many patients improve with time and may resolve completely.<sup>28</sup> Feigin et al<sup>28</sup> reported that neurologic or audiometric abnormalities were present in 42% of children with

Hemophilus influenza meningitis at discharge, 38% at 1 month, 26% at 3 months, 13% at 6 months and 5% at 1 year. No child had developed late onset deafness or had a late recovery of Audiometry function.

## CONCLUSION

The association was found between the development of post-meningitic hydrocephalus and variables such as seizure, duration of illness (patients having duration of symptoms like fever, headache, vomiting, cerebrospinal fluid leukocyte count and duration of antibiotic treatment. We have also observed that the smaller the age of the patient the more he is prone to develop hydrocephalus and other post-meningitic sequelae

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# Parasitosis through the Food-Handlers and Food Samples of Lahore City

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## ABSTRACT

**Background:** Parasitosis” means infection or infestation with parasites. Parasites are responsible for significant morbidity and mortality worldwide. Various epidemiological studies indicate that the prevalence of intestinal parasites is high specially in developing countries.

**Objective:** To identify possible positive cases of intestinal parasitic infection among food handlers and also to determine the presence of intestinal parasitic cysts and ova in vegetables and meat.

**Study Design:** A co-relational descriptive study design.

**Place and Duration of Study:** Study was conducted in two randomly selected markets of Lahore from January 2009 to June 2009.

**Materials and Methods:** This study was designed to determine the association between various risk factors and the occurrence of intestinal parasites. Random sampling was done. Stool parasitological profile was done by direct smear and foramline-ethyl acetate sedimentation method. Both vegetables and meat samples were examined for the presence of intestinal parasitic cysts and ova by using centrifugal-flotation technique.

**Results:** 58% vegetables, 71.1% meat and 34.5% stool samples were found to be positive for intestinal parasites. Of the parasites detected, the most common parasites infecting the food handlers were *Entamoeba histolytica* and *Ascaris lumbricoides*. Whereas parasites were more in the meat samples that were not properly stored than those that were kept in refrigerator.

**Conclusion:** This study revealed that risk of intestinal parasites is in direct proportion to the poor sanitary conditions.

**Key Words:** Parasitosis, Food handlers, Food samples.

## INTRODUCTION

Parasites present a persistent and intolerable threat to the health of millions of people mainly in the tropics and subtropics.<sup>1</sup> Parasitic intestinal infection continue to be an important cause of morbidity and mortality in developing world.<sup>2-6</sup> The risk of intestinal parasitic infection is measured using the DALY (disability-adjusted life year) and one DALY represents the loss of one year of equivalent full health.<sup>7</sup> The resulting diseases have socioeconomic impact in terms of high treatment costs per DALY and hospitalization costs.<sup>8</sup> Globally millions of people suffer from parasitic infections such as *Ascaris lumbricoides* (1.2 billion), *Trichuris trichiura* (795 million), Hookworms-*Ancylostoma duodenale* (740 millions)<sup>9</sup>, *Entamoeba histolytica* (50 million), *Giardia lamblia* (2.8 million)<sup>11</sup> and *Taenia saginata* (3.2 million).<sup>12</sup> In man, intestinal parasites are significantly associated with diarrhea.<sup>8</sup> Most of the pathogenic organisms known to cause diarrhea are transmitted by the oro-faecal route<sup>13</sup>, environmental conditions like contamination of soil and water sources with human faeces and poor sewage disposal such as use of night soil as fertilizer.<sup>14</sup> When the soil becomes contaminated, the eggs in soil can be transferred onto vegetables then onto the hands and

transferred directly into the mouth<sup>15</sup> or ingested by eating raw vegetables.<sup>14</sup> Intestinal parasites have been found to adhere to vegetables, fruits, fingers, utensils, door handles and money.<sup>16</sup> Additionally, they can be transmitted through house-flies<sup>17</sup> and contaminated finger nails.<sup>18</sup>

Studies carried out in Lahore city during seventies reveal that intestinal parasitic infection was a significant health problem. A study was carried out by Ansari and Sapru<sup>19</sup> in conservancy staff of Lahore Municipal Corporation and rate of infestation was found to be 80.6%. Another study by Ansari and Naru<sup>20</sup> revealed that frequency of intestinal parasitic infection in 216 children of Lahore orphanage was 64.75%. In 1995, a study was carried out on school children belonging to urban areas of Lahore. The frequency of infection was observed to be 51.83%.<sup>21</sup> Recent studies carried out at various locations in Lahore city showed that there was high prevalence of many intestinal parasites such as *Ascaris lumbricoides*, *Entamoeba histolytica*, *Entamoeba coli*, *Ancylostoma duodenale*, *Trichuris trichiura* and *Taenia* among the food handlers at different locations in Lahore and also in different food samples.

## MATERIALS AND METHODS

This study was carried out from January 2009 to June 2009 in Lahore City. This study was designed to determine the association between various risk factors and the occurrence of intestinal parasites. Two markets were randomly selected. The sample size for food stuffs and food handlers was calculated on a prevalence of 10%,  $d = 0.05$ . Sampling was done under three categories; vegetables, meat and food handlers. Vegetables – each of the four varieties of vegetables commonly sold in the study area was selected by random sampling from vendors in the open air markets. Samples of vegetable leaves weighing 250 g for each variety – Saag (Mustard leaves), spinach, cabbage and Fenugreek (Methi) were collected each day from the vendors by random sampling. Meat – similarly thirty butcher shops were chosen randomly. The meat samples (chicken, mutton and beef) each weighing 250 g was collected from butcher shops selected, weekly. Food handlers – at the same time 200 food handlers from the sampled markets and butcheries were randomly selected for routine examination of stool parasitological profile. Each of the food handler selected was given a plastic stool container and asked to bring bean-sized stool sample within 24 hours.

A 250 g sample of each vegetable or meat sample was examined for intestinal parasitic profile.<sup>16</sup> The sample was washed in distilled water and the suspension was strained through a sterile sieve to remove undesirable materials. The filtrate was centrifuged and supernatant discarded while the deposit was suspended in magnesium sulphate floatation fluid of specific gravity 1.3 and recentrifuged. The floatation fluid was filled to the brim and a cover slip was superimposed. The cover slip was lifted and examined under a light microscope. The cysts and eggs of various parasitic species present were identified.<sup>22</sup> The food handling practices of the butcheries including the meat storage method, the handlers hygiene standards and the presence of house-flies on meat samples were observed using a check list and recorded during each sampling day. A direct saline smear preparation of the stool sample specimens obtained from the food handlers were prepared for examination of trophozoites, ova and cysts of intestinal parasites using Lugol's iodine solution and formaline-ethyl acetate sedimentation method.<sup>23</sup>

## RESULTS

A total of 100 vegetable samples comprising of 25 samples for each category were collected – saag, spinach, cabbage and Fenugreek (methi). In all 58 (58%) vegetable samples were infected with intestinal helminthes. Fourteen (56%) of saag, 17 (68%) of spinach, 12 (48%) of cabbage and 15 (60%) of Fenugreek tested positive. An average parasite score

density of 2.37 was observed in the vegetables (Table 1).

The relationship between risk factors for meat handling practices and prevalence of parasites was studied by observing independent variables (risk factors) influencing infection with intestinal parasites (dependent variables). Independent variables include meat storage methods, presence or absence of cashier and the presence or absence of house-flies on meat samples collected from 22 butcher shops. Parasites were significantly less likely to be present on meat that was refrigerated (7%) than meat that was displayed at ambient temperature (37.5%) [ $P=0.002$ ]. There was a significantly high prevalence of intestinal parasites in meat samples where there was no cashier (59.8%) than where the cashier was present (16.1%) [ $P0.000$ ]. The prevalence of parasites where there were house-flies on the meat samples collected was (71.1%) and that did not have house-flies was 7%. The average parasite score density in the meat samples was ranging from 1.40 to 2.83 (Table 2)

**Table No.1: The prevalence and density of intestinal parasites among vegetable food samples**

Sample	No.	Frequency of intestinal parasite (%)	Score of parasite density
Saag	25	14 (56%)	2.43
Spinach	25	17 (68%)	1.86
Cabbage	25	12 (48%)	2.57
Fenugreek	25	15 (60%)	2.62
Overall	100	58 (58%)	2.37

**Table No.2: The relationship between risk factors for meat handling practices and prevalence of intestinal parasites**

Risk factors	No. of samples	Frequency of intestinal parasite (%)	Score of parasite density
<b>Storage methods</b>			
Refrigerator	80	31 (7.0%)	1.40
Open surface	200	165 (37.5%)	1.87
Wire mesh	160	138 (31.4%)	1.63
<b>Cashier</b>			
Absent	300	263 (59.8%)	1.85
Present	140	71 (16.1%)	1.64
<b>House-flies</b>			
Present	360	313 (71.1%)	2.83
Absent	80	31 (7.0%)	1.64

Stool samples were collected from 200 food handlers. 87 (43.5%) were infected with one or more of intestinal parasites of whom 31 (15.5%) were infected with one species of protozoan, 49 (24.5%) were infected with one species of helminth, 7 (3.5%) had mixed infection. Of the most common intestinal parasites were *A. lumbricoides* 27 (13.5%) and *E. histolytica* 24 (12%). There was a statistically significant difference between

the number of various intestinal parasitic species among the food handlers ( $P < 0.010$ ). The parasite score density in the faecal specimens observed ranged between 1.67 for *Giardia lamblia* whilst highest parasitic score density was found among multiple infection with *Entamoeba histolytica* and *Ascaris lumbricoides* with 2.63 (Table 3).

**Table No. 3: Intestinal parasite distribution in stool samples of food handlers**

Parasites (single infection)	No. of infected Cases (n)	Infection rate (%)	% of those examined (N=200)	Score of parasite density
Protozoa				
<i>Entamoeba histolytica</i>	24	77.4	12.0	2.50
<i>Giardia lamblia</i>	7	22.5	3.5	1.67
Subtotal	31	100.0	15.5	
Helminths				
<i>Ascaris lumbricoides</i>	27	55.1	13.5	2.55
<i>Ancylostoma duodenale</i>	16	32.6	8.0	2.38
<i>Trichuris trichiura</i>	6	12.3	3.0	1.50
Subtotal	49	100.0	24.5	
Multiple infection				
<i>E. histolytica</i> + <i>A. umbricoides</i>	4	57.2	2.0	2.63
<i>E. histolytica</i> + <i>G. lamblia</i>	3	42.8	1.5	2.56
Subtotal	7	100.0	3.5	
Overall total	69		34.5	

## DISCUSSION

Despite of development in the delivery of health services, parasitic diseases remain as the most important public health problem in most countries, particularly the developing countries of the world.<sup>24</sup> This study showed high intestinal parasitic infestation of both meat and vegetable foodstuffs as 58% and 71.3% respectively. Additionally, the burden of infection with intestinal parasites among food handlers was 34.5% which is much higher than that reported in Sudanese food handlers which was 2.7%<sup>25</sup> and also much higher than reported by Al-Lahlam et al<sup>26</sup> who found that 13.5% of non-Jordanian food handlers working in Jordan were infected with intestinal helminthes. Whereas it was found to be 41% in a study carried out in Kenya<sup>27</sup> which is higher than our study. All the vegetable samples namely Saag, Spinach, Cabbage and Fenugreek were found to be highly contaminated with infestation by different parasites in percentages of 56%, 68%, 48% and 60% respectively. This is attributed to handling techniques of vegetables.<sup>14</sup> The risk of infection with intestinal parasites to the population is increased because these contaminated vegetables are sometimes eaten raw,

undercooked to retain the natural taste and preserve heat labile nutrients or unclean.<sup>28</sup>

The type of meat storage practice influenced the prevalence of intestinal parasites. Only 18.1% of butcher shops used refrigerators, whereas it is appropriate to use refrigerator for meat storage. Poor storage methods expose meat to mechanical vectors like house-flies, cockroaches and rats that transfer eggs and cysts of intestinal parasites to improperly stored meat.<sup>17</sup> The butcher shops where the handlers handled money while serving meat had 59.8% parasite prevalence while those where different personnel handled money and the meat serving had low prevalence 16.1%. This has been a major factor in acquiring intestinal parasites as shown in other studies.<sup>29,30</sup> The most common intestinal parasites affecting the food handlers were *A. lumbricoides* (13.5%) and *E. histolytica* (12%) as was observed in Kisii District.<sup>31</sup> This high prevalence is a risk to consumer especially if the food handlers fail to sanitize hands and other materials in their use.

## CONCLUSION

Thus this study has revealed that there is a high risk of infection with intestinal parasites in the sampled markets of Lahore. About half of the people surveyed (43.5%) had one or more parasitic infection. Furthermore, meat (71.36%) and vegetables (58%) sold at those markets were found to be contaminated with parasites. So it is required that food handlers and even the consumer should be properly educated about the food safety and improvement of sanitary conditions.

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# Cutaneous Leishmaniasis in Karachi

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## ABSTRACT

**Background** Cutaneous leishmaniasis (CL) is an infection caused by a protozoan parasite of the genus *Leishmania*, which is endemic in various parts of Sindh and Balochistan and is widely spreading day by day.

**Objective:** To know the frequency of Cutaneous Leishmaniasis in the dermatology OPD and ward of JPMC, Hospital, Karachi. These patients were sent to microbiology Department, Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Centre, Karachi, for observing Amastigotes (LD Bodies) by microscopy to diagnose the cases.

**Study Design:** Experimental study.

**Place and Duration:** This study was carried out in the Department of Microbiology at BMSI, JPMC, Karachi, from November 2003 to April 2004.

**Materials and Methods:** The suspected cases of Cutaneous Leishmaniasis on clinical ground were sent by the dermatology OPD and ward of JPMC, Hospital, wounds were cleaned by the alcohol (spirit) swab. The smear prepared from the skin ulcer tissues were stained with Field Stain A and B for microscopy to confirm the diagnosis by detecting Amastigotes (LD Bodies).

**Results:** The total of 67 suspected patients with skin lesions were examined and 42 were found to be suffering from CL, on the basis of observing Amastigotes (LD Bodies) by microscopy. Their ages ranges from 2 years to 58 years. Among these cases 29 (69.04%) were males and 13 (30.96%) were females. Multiple lesions were seen in 16 (38.10%) cases only. Size of lesion varies from 1-10 cms. Body distribution were 16 (38.10%) on upper limbs, 13 (30.95%) on lower limbs, followed by 2 (4.76%) head, 3 (7.15%) neck, 4 (9.53%) face and 2 (4.76%) nose, 1 (2.38%) trunk and abdomen 1 (2.38%). Morphological patterns seen were crusted plaques, non-healing ulcers, erythematous infiltrated nodules and papules. From above morphological forms 25 (59.14%) were wet type of lesions and 17 (40.86%) were dry type of lesions. Majority of the cases were from the rural area 32 (76.19%) as compared to 10 (23.81%) urban area of the city.

**Conclusion:** Cutaneous leishmaniasis is endemic and increasing in Karachi and its surrounding area.

**Key words:** Leishmaniasis, *Leishmania tropica*, Amastigotes (LD Bodies).

## INTRODUCTION

Cutaneous Leishmaniasis is a parasitic disease caused by haemoflagellate *Leishmania*<sup>1</sup>, an intracellular protozoan parasite, and it affects 12 million people worldwide, with 1.5-2 million new cases each year. The incidence of leishmaniasis has increased in recent years due to increased international leisure and military-related travel, human alteration of vector habitats, and also HIV infection and malnutrition. Cutaneous leishmaniasis (CL) is a rising epidemic in Pakistan<sup>3</sup>. It is a major public health problem in the country especially near Afghanistan border and cities that have had the maximum burden of refugees.<sup>2,3,4</sup> Postigo has lighted that Pakistan in particular has to focus both anthroponotic cutaneous leishmaniasis caused by *Leishmania tropica* (*L. tropica*) and zoonotic CL caused by *Leishmania major* (*L. major*) with epidemics occurring in various parts of the country. *L. tropica* is mostly seen in urban areas whereas *L. major* is more common in rural areas of the country. Disease that is responsible for cutaneous lesions which develops at the site of the insect bite, is usually noted on exposed parts of the body, mainly arms, face, and legs. The clinical manifestations are extremely diverse including unusual

sites and atypical morphologies.<sup>5,6,7,8</sup> It comprises a complex of diseases with an important clinical and epidemiological diversity. It has 3 clinical forms, visceral, mucocutaneous, and cutaneous.<sup>9,10</sup>

Cutaneous Leishmaniasis is largely diagnosed by its clinical appearance, in an endemic region. There is diagnostic problem when cases appear in non-endemic areas, particularly when the clinical picture is distorted, or any atypical variants are seen even in endemic area.<sup>11</sup> One of the most important causes of chronic ulcers in some parts of the tropical World are the protozoa belonging to the genus *Leishmania* causes Cutaneous Leishmaniasis (CL). It is classified on the basis of a variety of biochemical, immunological, and molecular criteria.<sup>12</sup> In Pakistan cutaneous leishmaniasis found sporadically throughout the year and various outbreaks are reported frequently. The disease, once endemic in Baluchistan, has become highly prevalent in Sindh, North West Frontier Province and parts of Punjab. The present survey was conducted after the outbreaks of cutaneous leishmaniasis in the mountainous belt of upper Sindh.<sup>13</sup> Movement of immigrants into the endemic areas, increase in tourism, decrease in the use of insecticides have all contributed to increase in the number of leishmaniasis cases estimated numbers will

exceed 500,000 new cases annually, only in visceral leishmaniasis. The prevalence of various types of leishmaniasis worldwide is more than 12 million cases.<sup>14,15,16</sup>

## MATERIALS AND METHODS

The 67 suspected cases of Cutaneous Leishmaniasis on clinical grounds were sent by the Dermatology OPD and ward of JPMC, Hospital, to Microbiology Department, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi. The skin specimens were obtained by standard procedure and wounds were cleaned by the alcohol (spirit) swab. The smear prepared from the skin ulcer tissues were stained with Field Stain A and Field Stain B for microscopy.

Out of 67 suspected cases, 42 cases of Cutaneous Leishmaniasis were diagnosed by observing Amastigotes (LD Bodies).

## RESULTS

The total of 67 suspected patients with skin lesions were examined and 42 were found to be suffering from CL, on the basis of observing Amastigotes (LD Bodies) by microscopy. Their ages range from 2 years to 58 years. Among these cases 29 (69.04%) were males and 13 (30.96%) were females. Multiple lesions were seen in 16 (38.10%) cases. Size of lesion varies from 1-10cms.

**Table No.1: Age and sex distribution of affected patients**

Age group	Male	%age	Female	%age	Total cases	%age
2-10	2	(4.76)	1	(2.38)	3	(7.14)
11-20	4	(9.53)	2	(4.76)	6	(14.28)
21-30	8	(19.04)	3	(7.15)	11	(26.19)
31-40	6	(14.28)	3	(7.15)	9	(21.42)
41-50	5	(11.90)	2	(4.76)	7	(16.67)
51-58	4	(9.53)	2	(4.76)	6	(14.28)
Total	29	(69.04)	13	(30.96)	42	(100)

**Table No.2: Distribution of lesion on the body parts**

No.	Body parts	Number of cases	percentage
1.	Upper limbs	16	(38.10%)
2.	Lower limbs	13	(30.95%)
3.	Head	2	(4.76%)
4.	Neck	3	(7.15%)
5.	Face	4	(9.53)
6.	Nose	2	(4.76%)
7.	Trunk.	1	(2.38%)
8	Abdomen 1(2.39%)	1	(2.38%)
Total	8	42	(100%)

Body distribution were 16 (38.10%) on upper limbs, 13 (30.95%) on lower limbs, 2 (4.76%) on head, 3 (7.15%)

on neck, 4 (9.53) on face and 2 (4.76%) on nose, (26.19%), on trunk (2.38%).and abdomen 1(2.38%), as shown in table 2. Morphologically, predominant patterns seen was erythematous infiltrated nodules and followed by crusted plaques. From above morphological forms 25 (59.14%) were wet type of lesions and 17 (42.86%) were dry type of lesions. Majority of the cases were from the rural area 32 (76.19%) as compared to 10 (23.81%) urban area of the city.

**Table No.3: Type of lesion in the patients with age groups**

Age group	Wet type of lesion	%age	Dry type of lesion	%age	Total cases	%age
2-10	2	(4.76)	1	(2.39)	3	(7.15)
11-20	4	(9.53)	2	(4.76)	6	(14.28)
21-30	5	(11.90)	6	(14.28)	11	(26.19)
31-40	5	(11.90)	5	(11.90)	9	(21.42)
41-50	4	(9.53)	2	(4.76)	7	(16.67)
51-58	5	(11.90)	1	(2.39)	6	(14.28)
Total	25	(59.14)	17	(42.86%)	42	(100)

## DISCUSSION

In more than 80 countries of the world cutaneous leishmaniasis is endemic. Endemic areas include Argentina, USA, Middle East, India, Pakistan, Iran and North & East Africa. In Pakistan, it has become a particular health problem in many parts of the country. It occurs with various presentations from the self-limited and even self-healing cutaneous forms to fatal systemic disease. Systemic leishmaniasis is not common in Pakistan and invariably fatal if not treated promptly.<sup>17</sup>

Cutaneous leishmaniasis is common in those areas of our country which are near to the Afghanistan border such as many villages and towns of Balochistan and Khyber Pakhtunkhwa (KPK) provinces north Waziristan and many districts and some cities of interior Sindh and Punjab.<sup>18,19,20</sup> Most lesions were present on an exposed area of the body.

In our studies the age groups affected were from 2 years to 58 years. But disease can affect at any age group depending upon the bite of insect. Multiple lesions were seen in 16 (38.10%) cases. Out of total 42 (100%) patients 29 (69.04%) were males and 13 (30.96%) were females. This finding is nearer previous study from Nawabshah by Rajpar GM (62.19%) and (38.8%) respectively, it shows little difference<sup>21</sup>, in a study from Iraq, 57% males were sufferers and It was found that 58% (62 cases) had multiple lesions, while 42% had a single lesion<sup>23</sup>. In a study by a Zubair Khan from Peshawar has also reported the majority of the male patients (72.7%) and females were (27.3%). He also mentioned 64% patients from rural areas, about 36% from urban areas. Majority of the cases were from the

rural area 32 (76.19%) of the city as compared to 10 (23.81%) urban area, there is a little difference between the two. Distribution of the sites of the lesions was as follows: 15 (35.71%) on upper limbs; 13(30.95%) on lower limbs, on head 2 (4.76%), on face; 4(9.53%) on nose 2 (4.76%). In a study from Iraq, distribution of the sites of the lesions was as follows: 57% on upper limbs; 25% on face; 15% on lower limbs; 2% on the scalp. This difference may depend the covering or uncovering of the body parts during sleeping time. In our study 25 (59.53%) were wet type of lesions and 17 (40.47%) were dry type of lesions, where as figures from Iraq shows while 63.5% were Wet type and 36.5% were Dry type. This little difference may be due individual body response or due to some environmental conditions.

## CONCLUSION

This study shows that Cutaneous leishmaniasis is endemic and increasing in Karachi and its surrounding areas. It is a major health problem in our country. This problem can be decreased by implementing precautionary measures including to improvement of hygienic condition s and public awareness programs.

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# Co-relation of Dietary and Circulatory Calcium on Bone Mineral Density in Female Population of Quetta

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## ABSTRACT

**Objective:** To determine the prevalence and severity of low bone density in the females of Quetta city and find out its co-relation with dietary factors and blood calcium level.

**Study Design:** Descriptive Corelation Study.

**Place and Duration of Study:** Two hundred women from all ethnic groups which included mixed population of Pathans, Balochi, and settlers (residing from last 30-65 years) of Quetta city were randomly enrolled in this study.

**Materials and Methods:** A sample of 200 adult healthy women, residents of Quetta city, aged 20-80 years were randomly selected to participate in the study. Blood calcium level was determined by Blood biochemical auto analyzer and bone mineral density of these subjects was measured by bonesonometer. A questionnaire was used to collect dietary, sociodemographic, age, dietary factors and other relevant detailed information affecting bone mineral density (BMD) status of women.

**Results:** Amongst all the subjects 66 (38%) were osteopenic, 17 (8.5%) and 117 (58.5 %) were normal. T-score was positively correlated with milk, ( $p < 0.01$ ) and negatively correlated to age ( $r = -0.61$ ,  $p < 0.01$ ), junk food and women bearing more than four children. BMD decreased with increasing age and low BMD was found to be more prevalent in women above 45.

**Key Words:** Dietary Calcium, Bone Mineral Density, T-score, Females.

## INTRODUCTION

Calcium plays an important role in building stronger, denser bones early in life and keeping bones strong and healthy later in life. Approximately ninety-nine percent of the body's calcium is stored in the bones and teeth. It plays an important role in many other cellular functions<sup>1</sup>. Calcium levels in mammals are tightly regulated with bone acting as the major mineral storage site. Calcium ions ( $\text{Ca}^{2+}$ ) are released from bone into the bloodstream under controlled conditions. When we do not eat enough calcium-rich food to meet the body's needs, the mineral is drawn from bones to maintain a relatively constant supply in the bloodstream. This, in turn, speeds up the loss of bone mass<sup>2</sup>. Throughout our life, old bone is constantly being broken down and removed, and new bone tissue is built to replace it. In a healthy adult, the bone cells osteoblasts synthesize the organic components of the bone matrix, which later mineralizes. Whereas, osteoclasts, break down or resorb bone<sup>3</sup>. Under normal homeostatic control, the amount of bone resorbed is roughly equal to the amount of new matrix formed. However, rate of bone-building changes as we age. Up to about age 35, new bone is added to the skeleton more rapidly than old bone is removed<sup>4</sup>. After that, bone is lost more quickly than it is built and, as a result, the skeleton becomes less dense. In Osteoporosis the normal architecture of bone is

disrupted and the matrix of bone is demineralized. The balance is disturbed and osteoclasts resorb bone faster than osteoblasts can replace it, reducing the bone strength<sup>5</sup>.

In this study the prevalence and severity of low bone density and its relationship with dietary factors as risk for Osteoporosis were accessed in females ranging from 20-80 years of age from Quetta.

## MATERIALS AND METHODS

Two hundred women from all ethnic groups which included mixed population of Pathans, Balochi, and settlers (residing from last 30-65 years) of Quetta city were randomly enrolled in this study. Participation in the study was entirely voluntary and there was no cost to the subject. All subjects were interviewed after obtaining verbal consent, by using a closed response questionnaire. Data collected from subjects included demographic information, self-reported age, language, household income, and consumption of dairy products/ other dietary habits.

Data from questionnaire was entered into Microsoft Access 2003 and then analyzed with SPSS 13.0 (SPSS Inc, USA). Anthropometric data included height, weight, subjects was also measured. to find out body mass index ( $\text{BMI} = \text{wt in kg/ht in m}^2$ ) of the subjects<sup>6</sup>.

Nutrition data was collected using a 24-hour dietary recall. Questionnaire was used to estimate dietary calcium. Dietary data was collected by a 24-hour

dietary recall method. During the interview, each subject was asked for number of servings per week on average they ate a given food item. Estimating a serving size for each food the amount of calcium per serving from tables of nutrient values was determined. These values were used to calculate calcium intake<sup>7</sup>.

Persons with fractures due to major trauma, patients with metabolic bone-related diseases or any treatment by bisphosphonate, calcium, and vitamin D3, were excluded from the study. Women taking Hormone Replacement Therapy (HRT) were also excluded from the study.

Venous blood samples were collected from women aged 20-80 years residing in Quetta city. The area of needle prick or skin was cleaned with 70% alcohol swab and allowed to dry before being punctured. Blood samples were collected through venapuncture using disposable syringes. About 2 ml blood was withdrawn from all the subjects.

Blood calcium analysis was done by Biochemical analyzer (Techno 786.) using calcium testing kit provided by Merck.

Bone mineral density of the same subjects was determined by Bone Sonometer (Hologic Inc. USA) to assess the strength of the predictive relationship of heel ultrasound, the T-score. All heel ultrasound measurements were made using the left heel and the results were interpreted according to the WHO classification of T-scores<sup>8</sup>.

-1 to +1 = Normal Bone density

-1 to -2.5 = Osteopenia

-2.5 onwards = Osteoporosis

SPSS 13 was used for data entry and analysis. Groups were compared by using Student's t test in parametric values which is significant at \*=significant ( $P < 0.05$ ) and \*\*=highly significant ( $P < 0.01$ ).

Any correlations between parameters were evaluated by using Spearman's Correlation Test. Correlation Statistics is significant at the 0.01 and 0.05 level (2-tailed). Results are given as percentages and mean  $\pm$  SD.

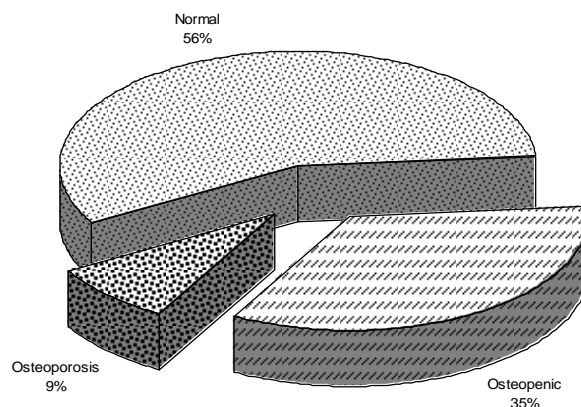
## RESULTS

Results of blood calcium analysis and bone mineral density data collected randomly from 200 women residing in Quetta city, who belonged to different ethnic groups which included mixed population of Pathans, Balochi, and settlers. Data collected from subjects including self-reported age, language, household income, and consumption of dairy products and other dietary habits.

The data were computed for means and standard deviations of means, student t-test and other statistical analysis to find the significant values. Pearson correlations were calculated among food groups and nutrients were correlated with T-score (BMD).

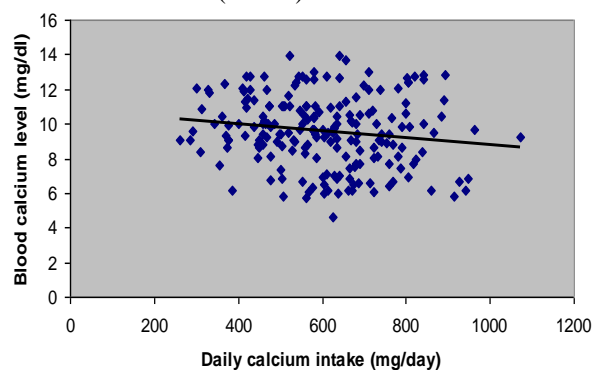
According to the BMD status of all the subjects studied

(Fig 1) 114 (57%) were normal, 69 (34.5%) women were osteopenic (i.e. T-score ranges from -1 to -2.5) and 17 (8.50%) had osteoporosis (T-score less than -2.5). Moreover, osteopenia and osteoporosis was found to be more prevalent in women bearing more than four children.



**Figure No.1: Distribution of female subjects according to bone mineral density.**

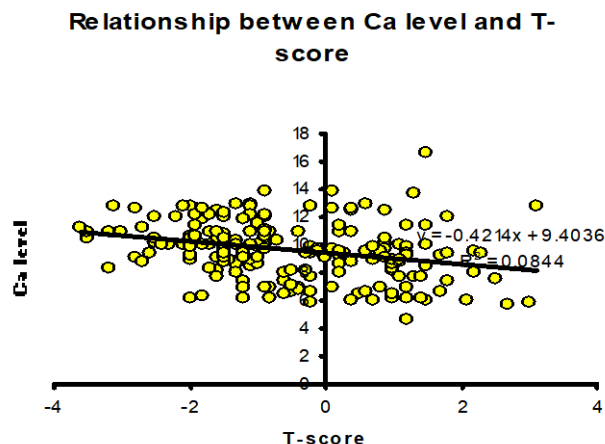
Blood calcium level was determined by Blood biochemical analyzer using kit method (Merck). Results of correlation of blood calcium level and daily calcium intake is shown in Fig 1. The mean calcium level and standard deviation of subjects was  $9.62 \pm 2.06$  mg/dl, with a maximum value of 12.5 mg/dl and a minimum level of 4.66 mg/dl. The normal range of blood calcium level is 9.00 -11.00 mg/dl. Low calcium level of about 4.50 - 8.50 mg/dl and below was present in 54 women (27%), while 81 (40.5%) women had a normal Ca level of about 8.51-10.50 mg/dl and a little above the normal range (10.51 mg/dl to 12.5 mg/dl) was observed in 65 (32.5%) women.



**Figure No. 2: Blood calcium level (mg/dl) and daily calcium intake of all subjects (N=200).**

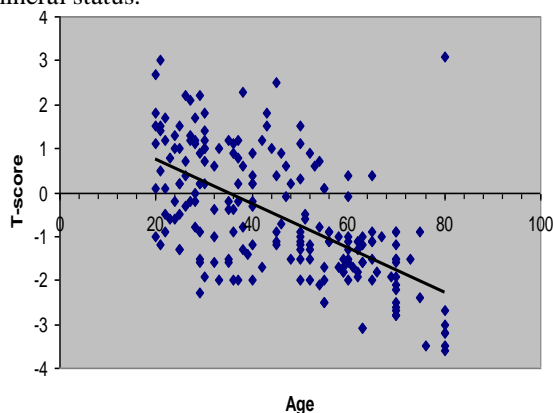
Respective T-scores were co-related with blood calcium levels of all the studied subjects were analyzed graphically and by Chi square test. However, no relationship in blood calcium level and T-score was established as shown in Fig 3 and Table 1. Relationship between Blood Ca level and BMD status

is analysed in Table 1. However, maximum number (114) subjects had normal BMD status.



**Figure No. 3: Calcium level and T-score of the studied subjects.**

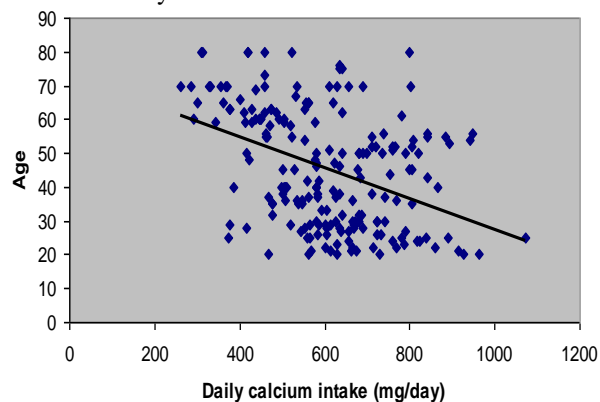
Although a large number of the subjects having normal blood calcium level lied in the range of normal bone mineral density (T-score more than -1), but low level (5-8 mg %) and higher levels of blood calcium (12-16 mgs %) were also observed in the subjects having normal bone mineral density (Fig 2). Further analysis by Chi square test (Table 2) also did not established any relationship between blood calcium level and bone mineral status.



**Figure No. 4: Age (years) and T-score of all subjects (N=200)**

The overall mean age and standard deviation of the subjects was  $45.6 \pm 17.2$  years. Youngest subject was 20 years old and maximum age was of 80 years. BMD and blood calcium level showed a negative correlation between T-score and age i.e.  $r = -0.61$ ,  $p < 0.01$  (Fig 4). BMD decrease with increasing age and low BMD was found to be more prevalent in women above 45<sup>9</sup>. Moreover, peak bone mass was observed in young adult women of 20-30 years of age.

Questionnaire data was used to estimate dietary calcium. Estimating a serving size for each food the amount of calcium per serving from tables of nutrient values was determined. These values were used to calculate calcium intake. From normal dietary routine of our subjects, daily calcium intake was estimated through calcium content (mg/ 100g) of different foods<sup>10</sup>. Mean calcium intake was 603.42 mg/100g of daily diet. Lowest calcium intake was 262mg/ day while highest calcium intake was 1071mg/100g of daily diet which is lower than recommended daily calcium intake for adults is 1000- 1300 mg/ day, Relating Fig 4 with Fig 5 it could be observed that a high dietary calcium intake is required for a healthy effect on bone mineral density<sup>11</sup>.



**Figure No. 5: Age (years) and daily calcium intake (mg/day) (N=200).**

**Table No. 1: Relationship between Blood Ca level and BMD status of the studied subjects.**

BMD status		Blood Ca_level (mg/100ml)			Total
		$\leq 8.50$	8.51 – 10.50	10.51+	
Normal	Count	44	43	27	114
	% within BMD status	38.6%	37.7%	23.7%	100.0%
Osteopenic	Count	9	32	28	69
	% within BMD status	13.0%	46.4%	40.6%	100.0%
Osteoporosis	Count	1	6	10	17
	% within BMD status	5.9%	35.3%	58.8%	100.0%
Total	Count	54	81	65	200
	% within BMD status	27.0%	40.5%	32.5%	100.0%

Chi square = 22.1201\*\*

BMD = Bone mineral density

Junk food consumption (Table 2) was calculated by estimating the serving size as done for assessment of dietary calcium. T- test was used to test the significance

of the results, alpha level was set at 0.05.

NS= non-significant ( $P>0.05$ ); \*= Significant ( $P<0.05$ );

\*\*= Highly significant ( $P<0.01$ )

n = Number of observations

**Table No. 2: T-Score of studied subject with respect to junk food (t-test).**

	Consumers/Non consumers	n	Percent	T.Score+Std. Deviation	P value
Cold Drinks	Drinking 1-2 bottles/wk	46	23.0	1.30±0.19	>0.05*
	Not Drinking	154	77.0	1.45±0.12	
Fast Food	Eating	15	7.5	-1.96±0.25	<0.01**
	Not consuming	185	92.5	1.42±0.10	
Chocolate	5-20 chocolates/wk	33	16.5	-1.24±0.22	<0.01**
	Not consuming	167	83.5	1.41±0.11	
Ice-cream	3-4 servings/wk	56	28	1.16±0.15	<0.01**
	Not consuming	144	72	1.42±0.12	

About 46 (23%) mostly young women consumed soft drinks, ice-cream and other junk food, while 154 (77%) mostly belonging to low income groups consumed simple diet and did not use junk food and soft drinks.

A small number of the subjects in our study consumed cola/carbonated drinks the average per week consumption was too low (1-2 glass/week). Thus, it correlation with blood calcium level, and T-score was not significant ( $P>0.05$ ). However, subjects consuming other junk food and chocolates were found to be osteopenic having T-score values of -1.96 and -1.24 respectively.

Subjects having ice cream in their diet (28%) had a mean T-score of  $1.16\pm0.15$  indicating normal BMD as compared to women not having ice cream, (two-tailed  $p<0.01$ ) providing evidence that there is significant difference between two groups.

## DISCUSSION

The study suggests that most of the subjects had 114 (57%) normal BMD, 69 (34.5%) women had a low BMD and were osteopenic (i.e. T-score ranges from -1 to -2.5) and only 17(8.50%) had severely low BMD and were suffering with osteoporosis (T-score less than -2.5). Moreover, osteopenia and osteoporosis were more prevalent in elderly women and amongst women bearing more than four children. T-score and age were negatively correlated ( $r = -0.36$ ,  $p<0.01$ ) reflecting bone mineral density decreasing (or bone loss) with increasing age. Young women of 20-30 years of age had Peak bone mass with a T-score of -1 to 3<sup>12</sup>. Age is a potentially confounding variable due to the decline that occurs in bone density with aging. Moreover, our study showed that women are only involved with home chores and have very little physical activities, which is further reduced after 60 years of age resulting in a low BMD. However, the significant positive effect of physical activities is observed on BMD as shown by Ferda et al.<sup>13</sup>. Gallacher<sup>14</sup> observed that in old age especially after 50 years of age bone becomes

incredibly fragile. Delaney<sup>15</sup> also reported that the lack of physical activity or weight bearing exercises is an important risk factor for osteoporosis.

In our study the lowest calcium intake was 262mg/ day, but the average intake was 603.42 mg/100g of daily diet. The dietary calcium intake of Indian women was only about 300mg /day, which is almost 700 mg less than the RDA in the West<sup>16</sup>. T-score of women having junk food was slightly reduced as observed earlier. However, a normal T-score (better BMD) as compared to women not having ice cream 144 (72%). Van der Hee et al<sup>17</sup> demonstrated that absorption of calcium from ice cream is no different than from low-fat milk. Ice cream as a potential bone health food, says a new study from Unilever. Typical ingredients and frozen format of ice cream do not negatively influence calcium absorption, wrote the researchers. In our study women also consumed junk food, but the consumption of such food is very low, thus, its relation with T-score was not significant i.e.,  $P>0.05$  in this study group.

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# Complications of Radical Neck Surgery for Squamous Cell Carcinoma

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## ABSTRACT

**Objective:** To determine the complications of the Radical neck surgery for oral squamous cell carcinoma.

**Study Design:** Cross-sectional Study.

**Place and Duration of Study:** This study was conducted in Dental Section, Mayo Hospital, Lahore from 1<sup>ST</sup> January to 31<sup>ST</sup> December 2001.

**Materials and Methods:** The study was conducted in dental section, Mayo hospital, Lahore. Fifteen patients of squamous cell carcinoma of the oral cavity were selected. All the patients underwent radical neck surgery. Postoperative complications were recorded at each follow up visit.

**Results:** Post operatively, secondary hemorrhage occurred in 40.0%, of the patients, delayed healing due to infection in 73.3 % of the patients. There was no recurrence after 1 month, 3 month and 6 month. After 9 months recurrence was noted in 6.7% of patients.

**Conclusion:** Complications occur after radical neck surgery. Recurrence however is lower with radical neck surgery.

**Key Words:** Oral squamous cell carcinoma, Radical neck surgery, Neck dissection

## INTRODUCTION

Oral squamous cell carcinoma is the 6<sup>th</sup> most common cancer world wide.<sup>1</sup> Head and neck malignancies also represent 7% of newly diagnosed cancers.<sup>2</sup>

The treatment of the neck in patients with squamous cell carcinoma of the head and neck region continues to be one of the most controversial issues in head and neck oncology. The evolution of the treatment of the neck is a good maximize tumor control and minimize morbidity to each patient with the passage of time.<sup>3</sup>

The radical neck dissection remains the basic tool for managing cervical metastasis.<sup>4</sup>

The radical neck dissection is defined as the en block removal of the lymph node bearing tissues for one side of the neck The resected specimen included the spinal accessory nerve, the internal jugular vein, and the sternocleidomastoid muscle.<sup>3</sup>

Removal of the primary tumor and the lymphatic system of the neck should be carried out to prevent further tumor dissemination to occur in any direction.<sup>5</sup>

radical neck dissection indicated when there are multiple clinically obvious cervical lymph node metastasis, particularly when involve the lymph nodes of the posterior triangle of the neck and these are found to be closely related to the spinal accessory nerve. It is also indicated when there is a large metastatic tumor mass or there is multiple matted nodes in the upper portion of the neck, In such instances it is unwise to preserve the sternocleidomastoid muscle or the internal jugular vein or to dissect the spinal accessory nerve and risk entering the tumor.<sup>5</sup>

Radical neck dissection carries a significant morbidity as many normal anatomical structures are sacrificed.<sup>5</sup>

The postoperative complications routinely included severe facial and cerebral edema, shoulder dysfunction, skin necrosis, and carotid rupture.

Spinal accessory nerve is removed to better ensure removal of all perineural lymphatics. Sacrifice of this nerve entails loss of function of the trapezius muscle and resultant debilitating "SHOULDER DROP".<sup>6</sup>

Leipzig et al. (1983) studied 109 patients, who had undergone various types of neck dissection, utilizing preoperative and postoperative observations of shoulder movement. They concluded that any that any type of Neck dissection may result in impairment of function of the shoulder.

They noted that dysfunction occurred more frequently among those patients in whom the spinal accessory nerve was extensively dissected or resected.<sup>7</sup>

Any type of neck dissection may result in impairment of function of the shoulder. Dysfunction occurs more frequently among those patients in whom the spinal accessory nerve was extensively dissected or resected.<sup>8</sup>

Byers RM (1985) concluded that obstruction of one or both jugular veins, particularly when combined with lymphadenectomy, results in lymph oedema of the face.<sup>9</sup>

Hirate RM, Jaques DA et al , (1975) concluded that the combination of infection and local ischemia of skin or mucosa may result in wound infection, suture line break and flap necrosis.<sup>10</sup>

## MATERIALS AND METHODS

This was a cross sectional study conducted in the department of oral and maxillofacial surgery, king Edward Medical College /Mayo Hospital, Lahore



Consecutive sampling was done to collect the sample. Fifteen patients were selected according to the set inclusion criteria from out patient department who presented with squamous cell carcinoma of oral cavity along with level I, II, III lymph node involvement. Patients with recurrent disease, evidence of distant metastasis, evidence of other malignancy along with oral tumor and those who were medically unfit for surgery were excluded from the sample so that bias in the study results can be controlled.

Informed consent from all patients was taken. The patients were ensured about the confidentiality of the information given by them. Radical neck dissection along with excision of tumorous mass was done. All cases in the study were followed up from 1<sup>st</sup> January 2001 to 31<sup>st</sup> December 2001 at intervals of one month, three months, six months and nine months. At each follow up visit complications in terms of infection, hemorrhage, recurrence, metastasis were checked and recorded.

## RESULTS

Over a period of one year from 1<sup>st</sup> January to 31<sup>st</sup> December 2001, total number of fifteen (15) patients were studied. Surgical excision of tumorous mass along with radical neck dissection was done. The mean age of patients studied was 49 years with SD of 11.8 years.(table-I) It was seen that 20.0% of the patients were female and 80.0% were male. All the patients were confirmed histopathologically and 100% of cases were proved as squamous cell carcinoma of the oral cavity. In the study group, 60.0% of the patients were in grad I, 20% in grad II and 20% in Grad III category (table-II). Post operatively, secondary hemorrhage occurred in 40.0%, (table-9), delayed healing due to infection occurred in 73.3% (Table-3). Follow up was done over a period of 1 year on quarterly basis. In group I and group II, there was no recurrence after 1 month, 3 Month and 6 month. After 9 month review recurrence was noted. It was 6.7% in group.

**Table No.1: Group undergoing radical neck dissection**

N	Mean age*	Std deviation
Radical neck 15 Dissection	49.1	11.8

**Table No.2: Category of tumors in patients of oral squamous cell carcinoma.**

Category	Number	Percentage
I	9	60.00%
II	3	20.00
III	3	20.00%

**Table No.3: Complications following selective and radical dissection of neck. Radical Dissection (n=15)**

Complications	Number	Percentage
Hemorrhage*	6	40.0
Delayed Metastasis after:	11	73.3
3 Months	0	0.0
6 Month	0	0.0
9 Month	1	6.7

## DISCUSSION

Fifteen patients of oral squamous cell carcinoma were enrolled for radical neck dissection along with surgical excision of tumorous mass.

The main purpose of this study was to determine the post operative complication like secondary haemorrhage, delayed healing, shoulder prop and recurrence in both surgical procedures and to find out the best surgical option for the management of cervical lymph node metastasis.

**Colemann JJ (1986) categorized the** Complications specific to surgical treatment of oral cavity cancer are:<sup>11</sup>

- Anatomic:** Injury to nerves or blood vessels with in the field of surgery.
- Physiologic:** The result of interference with blood or lymphatic supply to the area secondary to surgery.
- Technical:** Surgical rearrangement that result in secondary problems.
- Functional:** Derangements of normal behaviour secondary to therapy.

Byers RM, Maxmell PFel (1988) said that the accessory, marginal mandibular, mylohyoid and cervical plexus sensory branches are frequently sacrificed in neck dissection. Injuries caused by traction, electrocautry or other technical misadventure may affect hypoglossal, lingual, mandibular, vagus, phrenic, facial, recurrent laryngeal, motor branches to cervical plexus and cervical sympathetic chain.<sup>12</sup>

Spinal accessory nerve is removed in Radical Neck Dissection to better ensure removal of all perineural lymphatics. Sacrifice of this nerve entails loss of function of the trapezius muscle and resultant debilitating "SHOULDER DROP".<sup>6</sup> Leipzig et al. (1983) studied 109 patients, who had undergone various types of neck dissection, utilizing preoperative and postoperative observations of shoulder movement. They concluded that any type of Neck dissection may result in impairment of function of the shoulder.

They noted that dysfunction occurred more frequently among those patients in whom the spinal accessory nerve was extensively dissected or resected.<sup>7</sup>

In this study no complication related to shoulder was observed because in all the cases the accessory nerve was spared.

In our study there was no such complication like ischemia of skin or mucosa, flap necrosis. However delayed healing, due to infection, occurred in 73.3% of patients. Because of old age, malnutrition & long stay in hospital for post operative care.

In our study, there was no such complication like lymph oedema of the face due to the obstruction of the jugular vein however haemorrhage occurred in 40.0% of cases. This is perhaps due to infection of wound.



There are some limitation in our study like small sample size and short duration of the study. To further look into the matter we need large sample size and longer follow up duration to find exactly the late complications and recurrence in these patients.

## CONCLUSION

Complications occur after radical neck surgery. Recurrence however is lower with radical neck surgery.

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# Complications of Selective Neck Dissection for Squamous Cell Carcinoma of Head and Neck Region

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## ABSTRACT

**Objective:** To determine the complications of the selective neck surgery for oral squamous cell carcinoma.

**Study Design:** Cross-sectional Study.

**Place and Duration of Study:** This study was conducted in dental section, Mayo hospital, Lahore from 1ST January to 31ST December 2002

**Methods and Materials:** Fifteen patients of squamous cell carcinoma of the oral cavity were selected. All the patients underwent selective neck surgery. Postoperative complications were recorded at each follow up visit. The patients were kept under study for one year.

**Results:** Post operatively, secondary hemorrhage occurred in 26.7%, of the patients, delayed healing due to infection in 46.7 % of the patients. There was no recurrence after 1 month, 3 month and 6 month. However after 9 months recurrence was noted in 20% of patients.

**Conclusion:** Complications occur after selective neck surgery. Recurrence however is higher with selective neck surgery.

**Key Words:** Oral squamous cell carcinoma, Selective neck surgery, Neck dissection.

## INTRODUCTION

Oral squamous cell carcinoma is the 6<sup>th</sup> most common cancer world wide.<sup>1</sup> It is the most common oral malignant tumor i.e. 97% in head and neck region. Head and neck malignancies also represent 7% of newly diagnosed cancers.<sup>2</sup>

The treatment of the neck in patients with squamous cell carcinoma of the head and neck region continues to be one of the most controversial issues in head and neck oncology.

In most recent years, the decision regarding the management of the palpable cervical nodes is centered mostly around the method of treatment, either radical neck dissection or selective neck dissection. The decision of selection between these two is often dependent on the extent of regional disease or evidence of extra capsular spread of the tumor in to the adjacent structure.<sup>3</sup>

Radical neck dissection indicated when there are multiple clinically obvious cervical lymph node metastasis, particularly when involve the lymph nodes of the posterior triangle of the neck and these are found to be closely related to the spinal accessory nerve. It is also indicated when there is a large metastatic tumor mass or there is multiple matted nodes in the upper portion of the neck

Radical neck dissection carries a significant morbidity as many normal anatomical structures are sacrificed.<sup>4</sup>

Unlike that produced by the radical neck dissection, selective neck dissection produces minimum dysfunction of the trapezius muscle which is usually temporary and reversibl.<sup>5,6</sup>

Preservation of sternocleidomastoid muscle renders good soft tissue cover over carotid vessels and result in normal neck contours. Excision of internal jugular vein results in decrease in venous return and risk of secondary haemorrhage.

If these structures can be preserved with out compromising the disease control, the morbidity of surgery can be minimized.

Selective neck dissection is defined as en bloc removal of only those Lymph nodegroups which are most likely to contain metastasis depending on the location of the primary tumor.<sup>3</sup>

Although preservation of functional and cosmetically relevant structures were also primary goals in the development of these operation, their current use is predicated on the following concepts: en bloc removal of the nodes at highest risk from metastasis is anatomically justified; it has the same therapeutic vale and provides the surgeon with the same staging information as the more extensive radical and modified radical neck dissection and it is associated with less postoperative morbidity.<sup>7</sup>

This study is intended to determine the frequency of different complications of selective neck dissection. If the frequency of different complications especially of recurrence and metastasis is found to be then priority will be given to the selective neck dissection for the surgical treatment of oral carcinoma.

## MATERIALS AND METHODS

- This was a case series study. Fifteen patients of age 18 to 65 years age, with histopathologically confirmed squamous cell carcinoma of oral cavity, along with T2, T3, T4 and N1, N2 disease confined

to level I, II, III lymph node involvement, having received no treatment in the past were selected amongst those who presented in out patient department. All cases in the study underwent selective neck surgery and followed up from 1st January 2002 to 31st December 2002 at the department of oral and maxillofacial surgery, King Edward Medical College / Mayo Hospital, Lahore. Patients with recurrent disease, evidence of distant metastasis, evidence of other malignancy along with oral tumor and medically unfit for surgery were excluded from the sample because they will act as effect modifiers and if included in the study sample will result in bias in the study results. Written informed consent will be taken from the patients for inclusion in the study sample. The patients will be ensured for the confidentiality of their data.

Outcome in terms of control of cervical metastasis, recurrence and other post operative complications were evaluated. The patients were followed up for a period of one year after discharge.

At each follow up visit following were checked and recorded.

- Infection,
- Recurrence,
- Metastasis,
- Shoulder drop,
- Any other problem regarding the surgery.

Patient were examined at intervals of one month after getting discharged and then after three month, sixth month and nine month post operatively.

## RESULTS

- Over a period of one year from 1ST January to 31ST December 2002,
- fifteen(15) patients who underwent selective neck dissection were studied for the development of post operative complications, metastasis and recurrence of tumour. In all patients surgical excision of tumorous mass along with selective
- neck dissection was done .
- The age range of the patients included in the study was 33-47 year with a mean of 49 + 11.8 years. Female to male ratio was 1:4 as shown in table No.1.
- Histopathologically 100% of cases were diagnosed as squamous cell carcinoma of oral cavity .
- In the study sample 60.0% of the patients were in grad I, 20% in grad II and 20% in
- Grad III category shown in table No.2
- Post operatively, secondary hemorrhage occurred in 40.0% , delayed healing due to infection occurred in 73.3 %.
- Follow up was done over a period if 1 year on quaterly basis. There was no recurrence after 1 month, 3Month and 6 month.

- After 9 month review recurrence was noted in 6.7% of the patients. Frequency of different complications is shown in table No 3.

**Table No.1: Distribution of gender in the sample**

Gender	Frequency	percentage
Female	3	20.0
Male	12	80.0

**Table No.2: Distribution of respondents by grading of tumors.**

Category	Number	Percentage
I	11	73.33%
II	3	20.00%
III	1	6.67%

**Table No.3: Complications following selective and radical dissection of neck.**

**Complications Selective dissection (n=15)**

	Number	Percentage
Hemorrhage*	4	26.7
Delayed healing:	7	46.7
Metastasis after:		
3 Months	0	0.0
6 Month	0	0.0
9 Month	3	20.3

## DISCUSSION

Any type of neck dissection in cases of oral carcinoma may result in different complications depending upon the type of the neck dissection. Colemann jj categorized these complications following neck dissection as:

**Anatomic:** Injury to nerves or blood vessels with in the field of surgery.

**Physiologic:** The result of interference with blood or lymphatic supply to the area secondary to surgery.

**Technical:** Surgical rearrangement that result in secondary problems.

**Functional:** Derangements of normal behaviour secondary to therapy.<sup>8</sup>

They noted that dysfunction occurred more frequently among those patients who undergo radical neck dissection due to excision of different anatomical structures.

In 1985, Sobol et al. performed a prospective study in which preoperative and postoperative measures of shoulder range of motion were compared. Shoulder range of motion was better in patients who underwent a selective neck dissection than in patients who had a radical neck dissection.<sup>6</sup>

In our study there was no dysfunction of the shoulder movement as spinal accessory nerve was not sacrificed .

Byers RM (1985) concluded that obstruction of one or both jugular veins, particularly when combined with lymphadenectomy, results in lymph oedema of the face.<sup>9</sup>

In our study, there was no such complication like lymph oedema of the face due to the obstruction of the jugular vein because the jugular vein remain intact. Byers RM concluded that obstruction of one or both jugular veins, particularly when combined with lymphadenectomy, results in lymph oedema of the face<sup>9</sup>, which is usually seen in cases of radical neck dissection. However secondary haemorrhage occurred in 26.7% of the patients.

In our study there was no such complication like ischemia of skin or mucosa, flap necrosis except, delayed healing occurred due to infection in 46.7%. This is perhaps because of extent of surgery. However Hirate RM, Jaques DA et al, concluded that the combination of infection and local ischemia of skin or mucosa may result in wound infection, suture line break and flap necrosis.<sup>10</sup>

In our study, metastasis along with recurrence occurred in 3 patients out of 15 at the level IV 9 months after the surgery.

Casumano RJ, Persky MS concluded that the squamous cell carcinoma has a high recurrence rate. 89% of patients showed locoregional recurrence with in 2 years of therapy.<sup>11</sup> In our study the follow up period was up to one year therefore low recurrence rate was noted.

There are some limitation in our study like small sample size and short duration of the study. To further look into the matter we need large sample size and longer follow up duration to find exactly the late complications and recurrence in these patients.

## CONCLUSION

Complications occur after selective neck surgery. Recurrence however is higher with selective neck surgery.

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# Incidence of “Stress Syndrome” or Type A Personality in Medical Students

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## ABSTRACT

**Objective:** 1. To assess the frequency of type A personality in medical students  
2. To compare different personality types of medical students from 1st to final year.

**Study Design:** A cross sectional study.

**Place and Duration of Study:** This study was conducted at the Department of Community Medicine, SMC, DUHS, Karachi from 15th, May to 25th, November 2010.

**Materials and Methods:** A sample size of 140 students was drawn by using systemic random sampling; every 22nd student from each year was selected according to the roll numbers from first year to final year in Sindh, Dow Medical College and Karachi. Data was collected through a structured questionnaire.

**Three personalities (Type A, Type AB, Type B)**

Personality Types	Scores
• Type B	0 – 35
• Type AB	36 – 45
• Type A	46 – 80

**Results:** Out of 140 students, 42 were males, 98 were females. The results showed Type A personality was 82.9%, Type AB 16.4%, TYPE B was 0.7%. Students having type A personality in first year were 92.85%, in second year 100%, in third year 46.4%, in fourth year 85.7%, in final year 89.2%. Type A personality in males were found to be 92.30% as compared to females 83.67%. Students who took their task very seriously 45%, easily got Irritated 51.4%, Restless during studies 32.1%, dissatisfied with task performed 49.3%, Work conscious 43.6%. On the basis of these results majority of the medical students fall in the category of type A personality, surprisingly 100% students of 2nd year fall in type A category.

**Conclusion:** The study proved major population of medical students had Type A personality which showed they were tensed, impatience, aggressiveness, time conscious, concerned about their studies, highly competitive, ambitious, vulnerable to stress related diseases.

**Key Words:** Type A personality, Personality, Stress, Behavior Pattern, Medical students.

## INTRODUCTION

Every person in this world has their unique personality which they adopt during the course of life and merge it with their natural instincts and ways so that they complement each other. That is how every person is just suited to the life he/she leads as his/her personality gets perfectly molded in it to work best for him/her in this world that strictly follows the rule of 'survival of the fittest'. 'Impatient', 'time conscious', 'workaholics' and not to forget, 'the nerds' were the immediate responses of the general public when we asked them to consider the word 'medical student'. The Type A personality has been defined by Meyer Friedman and Ray Rosen man as "a behavior pattern associated with individuals who are highly competitive and work compulsively to meet deadlines".<sup>(1)</sup> Their lives are governed by unrealistic ambition that constantly keeps them on the go as they tend to be impatient and the

sense of urgency incorporates aggressiveness in their character.<sup>(2)</sup> On the other side of the personality spectrum, is Type B personality, which in striking contrasts with the type A is displayed by individuals who are calm, easy going relaxed and satisfied. Some people share the mixed characteristics of both personality types and cannot be clearly classified into any one are included in type AB personality. 'Stress syndrome' 90% students fell under type A personality. The stress levels progressively increased during the clinical years.<sup>(3)</sup>

## MATERIALS AND METHODS

A cross-sectional study was done on students of Sindh, Dow Medical Colleges. Sample size of 140 was drawn using systematic random sampling method. 28 students were selected from each class from 1st year to final year M.B.B.S. Every 22nd student was selected from roll number list from each class. Structured

questionnaire was distributed among the students with their consent.

Three personalities (Type A, Type AB and Type B) were divided by scoring method out of 80 with following limits:

Type of Personality	Scoring Limits
Type A	46-80
Type AB	35-45
Type B	0-34
Total Scoring	80

Data Analysis: The significance of the data was determined by using Statistical Package of Social Sciences software (SPSS, Version 16.0). Confidence interval of 95% was taken with margin of error 5% and p-value of 0.05. The study was completed in six months from 15th, May, 2010 to 25th, November, 2010. The required permission was obtained from the administrators of various departments prior to study. Data was collected, analyzed on Statistical Package of Social Sciences (SPSS) of version 17.0.

## RESULTS

The study assessed Type A personality in medical students of Dow and Sindh Medical College from 1st year to Final year. 28 students were selected from each year. Sample size of 140 was drawn through systematic random sampling; every 22nd student from each class was selected. Out of 140, 42 males were and 98 females. Overall results showed Type A personality to be 82.9%, Type AB personality 16.4% and Type B personality 0.7%. This proved majority of the students belonged to Type A personality. Students with type A personality in first year were 92.85%, second year 100%, third year 46.4%, fourth year 85.7%, final year 89.2%.

**Table No.1: Frequencies of Personality Type in Medical Students**

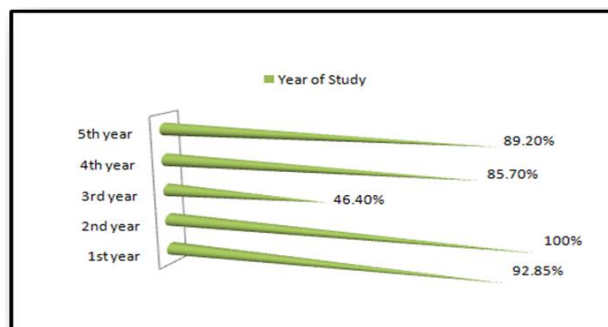
Personality type	Frequency	Percent
Type A	116	82.9
Type AB	23	16.4
Type B	1	0.7
Total	140	100.0

**Table No.2: Frequencies of positive and negative result for Personality Type in medical students**

Questions asked	A % Agreed	B %Disagreed
Task seriously	45%	4.3%
Easily Irritated	51.4%	10.7%
Restless	32.1%	15.7%
Dissatisfaction	49.3%	11.4%
Work conscious	43.6%	3.6%

Students who took their task very seriously 45%, easily got Irritated 51.4%, Restless during studies 32.1%, dissatisfied with task performed 49.3%, Work conscious 43.6%. On the basis of these results majority

of the medical students fall in the category of type A personality, surprisingly 100% students of 2nd year fall in type A category.



**Figure 1: Comparison of Type A personality of 1st to 5th Year Medical Students.**

## DISCUSSION

Prevalence of Type A behavior was found to be significantly high among the students of first year and second year. Surprisingly, drop in Type A personality with concomitant rise in AB was observed in the initial clinical year, i.e. third year. The stress levels went on a high again with increase in Type A as the clinical exposure takes the front seat in fourth year, final year. The appealing traits of being competitive, task oriented and time conscious have always been a source of pride for the medical students. The present literature review revealed high prevalence of type A personality among medical students correlating with stress levels. The factors leading to stress are many, academic being the most important. <sup>(4)</sup> Friedmann studied this relationship. The results proved that the psychosocial factors of type A behavior did proceed onto the development of cardiovascular complications later in life. <sup>(2)</sup> As conducted by Contrada the undergraduate students examined for the systolic and diastolic blood pressures and the hardness was analyzed as the indicator of the strength of the heart, the differences were modest but reliable. <sup>(5)</sup> In Wolf study Type A personality decreased in initial years. Type A scores showed a significant increase over the first 3 years of the course, followed by a drop to approximately second-year levels by the end of the 5-year period. <sup>(3)</sup> Study by Zeppa compared the performances of students under stress after clinical clerkships. The unfavorable stress leads the students to external control and low self-esteem, along with poor performance <sup>(6)</sup> Study by Lebanon analyzed the relationship between the personality and performance on written and clinical skills. Type A students performed well on written examinations, although no difference noted on the clinical grounds. <sup>(7)</sup> Type A personality is also a known risk factor for cardiovascular diseases, <sup>(8)</sup> Another study by Firth on fourth year students revealed the levels of stress comparatively higher than general population. <sup>(9)</sup> Such

individuals are driven by the excessive drive of competition and the need for control.<sup>(10)</sup>

## CONCLUSION

Type A and Type B personality type theory describes a behavior pattern characterized by tenseness, impatience, aggressiveness, often resulting in stress-related symptoms such as insomnia, indigestion, increasing the risk of heart disease. The study proved major population of medical students had Type A personality which showed they were tensed, impatience, aggressiveness, time conscious, concerned about their status, highly competitive, ambitious, vulnerable to stress related diseases. Teachers and Parents both should make the students comfortable, talk to them more often, try to solve their problems, reassure them frequently, keep a hawk eye for change in behavior.

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# A Prospective Randomized Trial Comparing the Spinal and General Anesthesia in Lumbar Disc Surgery: A Study of 44 Cases

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## ABSTRACT

**Objective:** General anesthesia is most frequently used for lumbar disc surgery despite the evidence that spinal anesthesia is as safe and may offer some additional advantages. The purpose of this study was to compare the intraoperative parameters and postoperative outcome after spinal and general anesthesia in demographically well matched patients undergoing elective lumbar Decompressive surgery.

**Study Design:** Prospective randomized controlled study

**Place and Duration of Study:** This study was carried out at DHQ Hospital Mirpur AJK from January 2007 and May 2010.

**Materials and Methods:** In this randomized controlled study we analyzed the outcome obtained in 44 patients in whom either spinal or general anesthesia was induced for lumbar disc surgery. The variables recorded were anesthesia related class, surgical diagnosis, disc levels operated and pre, peri and postoperative measurements of variables like BP, and heart rate. All aspects of surgery, recovery, post anesthesia care and pain management were same irrespective of anesthetic type. The narcotic and antiemetic requirement and length of stay in the hospital and incidence of urinary retention were also recorded in the post operative course.

**Results:** Demographically both groups were well matched. Anesthesia time was longer in patients receiving GA with increased heart rate and MABP perioperatively. There was more nausea and greater requirements for antiemetic and analgesics in patients receiving

GA (p value < 0.05). Perioperative heart rate and MABP was on normal side and there was no urinary retention in patients who received spinal anesthesia.

**Conclusion:** Spinal anesthesia was as safe and effective as GA for patients undergoing lumbar Decompressive surgery. Spinal anesthesia had added advantages of short anesthesia duration, decreased antiemetic and analgesic requirements.

**Abbreviations:** GA general anesthesia, HR heart rate, I/V intravenous, MAP mean arterial pressure, PACU post anesthesia care unit, RCT randomized controlled trial, SA spinal anesthesia

**Key Words:** Laminectomy. Spine surgery. Spinal anesthesia. Spinal stenosis.

## INTRODUCTION

Spinal and general anesthesia have both been used for lumbar Decompressive surgery but general anesthesia is used far more widely and almost exclusively in many practices. This preference may be due to greater acceptance by the patients, the ability to perform longer operations,<sup>1</sup> and anesthesiologist feeling more comfortable with secured airway in prone position.<sup>2</sup>

On contrary some anesthesiologist prefer spinal anesthesia for lumbar disc surgery because they believe it is accompanied by less blood loss<sup>3</sup>, less hemodynamic instability<sup>4,5</sup>. An additional advantage is the patient ability to reposition the extremities and chest to avoid nerve injury or pressure necrosis to either the face or chest wall.<sup>6,2</sup>

Spinal anesthesia also reported to have reduce incidence of pulmonary complications compared with

GA<sup>7,8</sup>. There have been few RCTS regarding the subject in the literature.<sup>9,10,11,12</sup>

The purpose of this study to conduct RCT to compare the intraoperative parameters and postoperative outcome after spinal and general anesthesia.

## MATERIALS AND METHODS

All the patients awaiting for lumbar Decompressive surgery for single or two levels between January 2007 to May 2010 at DHQ Hospital Mirpur AJK were enrolled for the study. After verbal and written informed consent a total number 42 patients of ASA physical status 1 and 2 undergoing either single or double level laminectomy or fenestration for lumbar discectomy were admitted during this period. Patients were excluded if they had severe cardiac, renal or hepatic disease. Patients with coagulation abnormalities,

or infectious conditions that would contraindicate spinal block were also excluded. If patients had any changes in surgical technique or massive bleeding during operation which needed blood transfusion, were also excluded from the study. Eligible candidates were given written informed consent. All the operations were done by the same surgeon. Patients were divided into two groups either GA or SA by randomization.

Patients in GA group were taken to the operation theater on a stretcher and monitors were attached. Baseline NIBP, pulse, SPO<sub>2</sub> and ECG were recorded. Patient were then given midazolam 2mg and 10 mg nalbuphine intravenously(IV) at pre induction. Patient was induced with propofol 2mg/kg. Intubation was facilitated with atracurium 0.6mg/kg. Anesthesia was maintained with 1.2% Isoflurane and Nitrous Oxide 50% in Oxygen. Muscle relaxant was repeated after every 20 min, 10 mg till the surgery was finished. Monitors were detached and patients were then log rolled on to the operating table on a prone position frame. Arms were positioned with shoulders perpendicular to the body and arms flexed 90 degrees at the elbow resting on arm board in front of the patient. The arms were padded and head was positioned on a pillow and head ring with padding for eye and nose to avoid any injury. Ventilator settings were adjusted to maintain end tidal CO<sub>2</sub> of 30-35. ECG, NIBP, pulse oximetry and end tidal CO<sub>2</sub> were continuously monitored and recorded every 10 minutes. At completion of operation the anesthetics were discontinued and patients were given 100% oxygen. Patients were then rolled back into supine position and reversal of atropine 0.02mg/kg and neostigmine 0.04mg/kg was administered. The patients were extubated and when appropriate were shifted to PACU.

In the SA group patients with already explained procedure were taken to operation table and preloaded with ringer lactate 15 ml/kg in 10-15 minutes. Baseline NIBP, ECG and pulse oximetry were done. Patient were cleaned draped in sitting position and injection xylocain 2% 2ml were given in L3-4 or L4-5 interspace for skin infiltration. Injection bupivacain 0.75%, 15mg was injected with 25 G Quincke spinal needle after aspiration of free CSF. Patient was then shifted to supine position. When a spinal level between T6 and T10 was achieved (approximately after 10 min) the patient was rolled on to the prone position on laminectomy frame. The patient was allowed to self position until comfortable. The head of patient was elevated to provide surgical field that is approximately at the same level as heart. The monitors were reattached and oxygen was supplied with oxygen mask at 4L/minute. Injection midazolam 0.1-0.2mg/kg given IV for sedation. ECG, NIBP and pulse oximetry were recorded at 10 minutes interval. At the completion of surgery the patient was rolled from prone position on a bed and transferred to PACU.

Age and ASA status along with HR and MAP were recorded at time of entering operation theater. Total anesthesia (time patient entered the operating room until PACU admission) and surgical time (incision to placement of surgical dressing) were also documented. During course of anesthesia for episodes of bradycardia (heart rate less than 60 per minutes) or hypotension (systolic blood pressure less than 90 mmHg), 0.5 mg Atropine or 5 mg ephedrine were administered.

In immediate post operative period the variables recorded include HR and MAP on admission in PACU and every 10 min for the first hour. Severity of pain and nausea were recorded using VAS scale where 100 = maximum and 0 = no pain or nausea. Postoperative analgesic use and total administered dosage of nalbuphine were recorded till 24 hours after surgery. If the VAS score was more than 50, then 5mg of nalbuphine was given intravenously and, if the score did not reduce within 10 minutes, an additional 2mg IV was administered and the total nalbuphine consumption was recorded. Intravenous Metoclopramide at 0.1 mg/kg IV was administered to patients with vomiting and for nausea with a score more than 50.

If patients were awake and had no pain, nausea, vomiting, or hemodynamic instability, they were discharged from PACU in Group GA. In Group SA, when patients had no pain, nausea, vomiting, and at least two segment regression of spinal block, they were discharged from the PACU.

Over next 24 hours occurrence of vomiting and VAS score for nausea and pain were recorded. Metoclopramide was given if score was more than 50. Need for analgesia was also recorded and additional dose of nalbuphine 5mg given IV was given if score is more than 50 otherwise mild discomforts were controlled by oral acetaminophen. Occurrence of urinary retention requiring catheterization were also noted in both groups.

## RESULTS

Forty two patients were enrolled in the study. Demographic characteristics, ASA classification, diagnosis, number of involved vertebrae, surgical procedure preop heart rate and preop MABP did not differ significantly between two groups. (table 1)

Per operative Heart rate, and anesthesia time was longer in patients receiving GA but surgery time and MABP did not differ significantly. (Table 2)

During recovery heart rate remained elevated in patients in patients receiving GA with significantly increased antiemetic and narcotic requirements. (table 3) Postoperatively two patients receiving general anesthesia had urinary retention there were no pulmonary complications in either group. There were no spinal headache or retention of urine in patients receiving spinal anesthesia.

The mean postoperative hospital stay in the patients receiving GA (4.6 days) was less than receiving spinal anesthesia (5.1 days) which was not statistically significant (p value.058).

**Table No.1 Preop variables**

Variables	Spinal Anesthesia	General Anesthesia	P value
Mean age in years	36.50	36.72	0.389
Sex			0.500
Male	13	12	
Female	9	10	
Diagnosis			0.627
Disc prolapsed	15	15	
Spinal stenosis	7	7	
Operation Levels			0.500
Single	21	20	
Double	1	2	
ASA class			0.500
1	18	17	
2	4	5	
Preop baseline heart rate	80.2 (73-87)	80.4 (72-88)	0.51
Preop MABP	95.8 (89-101)	96 (87-105)	0.82

**Table No.2: Intraoperative parameters**

Variables	Spinal Anesthesia	General Anesthesia	P value
Mean anesthesia time in minutes	115.22	164.04	0.001
Std Deviation	12.48	19.48	
Mean operation time in minutes	75.22	81.09	0.454
Std. Deviation	12.48	14.10	
Mean intraoperative BP	88.04	90.72	0.487
Std.Deviation	3.76	5.65	
Mean intraoperative Heart rate	67.45	85.18	0.003
Std.Deviation	3.97	7.29	

## DISCUSSION

Both spinal and general anesthesia have been used in patients undergoing lumbar disc surgery but only few controlled studies are available to suggest whether either of these techniques is superior to other.<sup>10,11,9 13</sup> Several studies have compared SA and GA in lumbar disc surgery and many of which have concluded SA as preferred method<sup>8,10,11,12</sup>, whereas Sadrolsadat et al<sup>13</sup> are in the opinion that SA had no advantages over GA.

Our current prospective randomized controlled study although composed of very small number of patients supported spinal anesthesia as a safe and effective alternate to GA in these patients. Our results confirm the clinical impression that spinal anesthesia is comparable to general anesthesia with some additional advantages.

**Table No.3: Post op recovery Data**

Variables	Spinal Anesthesia	General Anesthesia	P value
Mean heart rate	76.25	88.21	0.003
MABP	88.52	102	0.00
Narcotic Requirements			0.00
None	19	0	
One dose	3	15	
Two doses	0	7	
Antiemetic requirements			0.00
None	19	2	
One dose	3	11	
Two doses	0	9	

All of our patients were treated in the same operating room by one surgeon and same anesthesia team.

In this study spinal anesthesia reduced anesthesia time significantly (p value <0.05) where as operation time did not differ in both groups. Shorter operation time has been reported in some studies<sup>10</sup> due to less bleeding in patients receiving SA. It has been suggested that patients receiving SA bleed less in lower extremity surgery as compared to GA.<sup>14,15,16,17,10</sup> They are in the opinion that reduced blood loss was due to the combination of sympathetic blockade and lower intrathoracic pressure when patients were allowed to breath spontaneously.<sup>18</sup> The reduced bleeding in previous reported cases might be due to reasons because spinal anesthesia inhibit surgically induced stress levels to a greater degree than GA.<sup>19,20,21</sup>

In our study mean intraoperative BP remained comparable in both groups but intraoperative mean heart rate remained significantly high in patients receiving GA. Blood loss in both groups remained minimal.

Our patients receiving spinal anesthesia experienced less post operative pain as well as fewer episodes of nausea and vomiting comparable to other studies.<sup>10,12</sup> Heart rate and MABP remained physiologically more stable in these patients during recovery reflecting lower levels of systemic stress and pain. The increased incidence of nausea and vomiting in patients receiving GA was most likely due to anesthetic method itself. Nitrous oxide has been reported as a cause of postoperative emesis.<sup>1-2</sup> General anesthesia has also been reported to impair gastric emptying.<sup>22,23</sup>

Two of patients who received GA developed retention of urine were catheterized in the ward. Our patients receiving SA did not have spinal headaches or retention of urine. Urinary retention has been reported more in spinal anesthesia in some studies<sup>24</sup>, Jellish et al<sup>10</sup> found no difference whereas McLain et al had more urinary retention in patients receiving GA in their studies. We did not have any other complications in either group. Postoperative hospital stay was comparable in both groups.

## CONCLUSION

Our results support the conclusion in the literature that spinal anesthesia was as safe and effective as GA for patients undergoing lumbar spine surgery. Spinal anesthesia had the added advantages of short anesthesia time, decreased postoperative analgesic and antiemetic requirements.

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# Abdominal Tuberculosis: Varied Presentations

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## ABSTRACT

**Objective:** To study various clinical presentations and out come of management of abdominal tuberculosis.

**Study design:** Prospective cross-sectional study.

**Place and Duration of Study:** This study was conducted at the Surgical Unit-1 Ghulam Mohammad Maher Medical College Hospital Sukkur and Al-Khair Hospital Sukkur from January 2007 to December 2010.

**Patients and Methods:** The 65 patients admitted throughout patient department and emergency with abdominal catastrophes. Ages ranged between 14 to 70 years. Out of 65 patients 37 were males and 28 were females. All the patients were evaluated with history, examination & investigations. 34 patients were operated & the resected tissue sent for histopathology to conform the diagnosis of tuberculosis.

**Results:** Out of 65 cases of abdominal tuberculosis, 37 were male and 28 female. The mean age was 30.9 years with SD 14.19 years (range 14 to 70 years). The mean duration of symptoms at presentation was 6 months (range 1 month to 24 months).

34 (52.3%) out of 65 patients were admitted with different complications in which 10 (29.4%) presented with peritonitis due to gut perforation, 9 (26.5%) with sub-acute intestinal obstruction, 8 (23.5%) with abdominal mass, 5 (14.7%) with acute appendicitis and 2(5.9%) with umbilical fistula. Surgery was performed in all these patients, Strictureplasty done in 13 (38.3%), Ileostomy in 8 (23.5%), resection anastomosis in 5(14.7%), Right Hemicolectomy in 5 (14.7%) and adhesionolysis and biopsy in 3 (8.8%) patients. Diagnosis in these patients was confirmed with biopsy. Morbidity and mortality in this group was 40.2% and 17.6% respectively.

**Conclusion:** Early diagnosis of the abdominal tuberculosis is possible only by the specific investigations like PCR. As these are not available in the remote areas of sindh so the general surgeons in the peripheral tertiary care hospitals have to face such patients with complications. Early diagnosis of ATB can be made by high index of clinical suspicion to symptoms of abdominal pain, weight loss, low grade fever and vague ill health of more than one month duration and refractory to conventional treatment associated with raised ESR, positive Montoux test. To above symptomatology if empirical ATT is started early many of the complications of ATB can be avoided.

**Key Words:** Abdominal Tuberculosis, Complications, Presentations.

## INTRODUCTION

Tuberculosis is still a major problem in Asia. According to World Health Organization (WHO) approximately one-third of the world's population is under the risk of acquiring tuberculosis and more than 30 million deaths occurred due to tuberculosis in 1990's, especially in Africa and Asia.<sup>i</sup> In an other report from WHO, incidence of tuberculosis in Pakistan is 181 cases per 100,000 population per year and estimated mortality is 40 deaths per 100,000 population per year.<sup>ii</sup> In 2000-2020, an estimated one billion people estimated to be infected, 200 million will become sick and 35 million will die from tuberculosis.<sup>iii</sup> Abdomen is involved in 11% of patients with extra-pulmonary tuberculosis.<sup>iv</sup> Mycobacterium tuberculosis found to be cause of abdominal tuberculosis (ATB) in most countries but M-bovis is also reported from some countries.<sup>v</sup> ATB remains a diagnostic problem for surgeons because the signs and symptoms are non-specific and there is no specific diagnostic test.<sup>vi</sup> Insidious onset and non-specific clinical and radiological findings of ATB mimics several diseases.<sup>vii</sup>

ATB continues to challenge the diagnostic acumen and therapeutic skills of all clinicians due to protean clinical features and varied complications.<sup>viii</sup> The accurate diagnosis of ATB usually takes a long time and requires a high index of suspicion in clinical practice.<sup>ix</sup> In addition to other ancillary investigations, ultrasound is helpful in showing the intraabdominal fluid, lymph nodes (matted or discrete), bowel wall thickening & pseudo kidney sign.<sup>10,11</sup> All the complications of this potentially curable disease can be avoided if diagnosis is made early and anti-tuberculous therapy started in time. We, therefore, present a prospective study of various clinical presentations and outcome of management of abdominal tuberculosis to assist the management of ATB in a hope to eradicate this disease from world.

## PATIENTS AND METHODS

This prospective, case series study was carried out in Surgical Unit-1 at Ghulam Mohammad Maher Medical College Teaching Hospital (GMCH) and Al-Khair Hospital Sukkur from January 2007 to December 2010. Seventy patients of ATB were selected for study but

five patients, belonging to remote areas of Balouchistan, were lost to follow up were excluded from study therefore 65 patients were finally included in study. Detailed information regarding patient's demographics, symptoms/signs, past history of tuberculosis, family history of tuberculosis, investigations, management, morbidity and mortality was recorded on specially designed proforma.

Patients who came in OPD or emergency with some complication were admitted in hospital and operated after necessary investigations and pre-operative treatment, and diagnosis confirmed by histopathology of resected specimen of intestine or involved lymph node or omentum. Diagnostic tests done in this group were: Complete blood Picture and ESR, Blood Urea, Serum Electrolytes, CXR, Plain X-Ray Abdomen (in Erect and Supine positions), Barium Follow-through / enema in selected cases, Ultra-Sound Abdomen and Biopsy of material obtained on laparotomy. Sputum test for AFB was done in those patients in whom CXR was showing some abnormality. Overall morbidity was 41.2% and mortality was 17.6% in these cases.

All the patients received a nine months course of ATT. (Rifampicin, Ethambutol, INH, and Pyrazinamide for first four months and followed by Rifampicin and INH for last five months)

## RESULTS

In this study of 65 cases of ATB, 37 (56.9%) were male and 28 (43.1%) were female. The mean age was 30.9 years SD  $\pm 14.19$  (from 14 to 70 years). The mean duration of symptoms at presentation was 6 months (range 1 month to 24 months). 31 patients were kept on antituberculous drugs and kept the record of follow-up and surveillance.

Thirty four (52.3%) out of sixty five patients were admitted in hospital with different complications (Table-1). Amongst the 34 patients, 25 were admitted through Casualty department and 9 were admitted through OPD. Family and past history of tuberculosis was present in 13 (38.2%) and 8 (23.5%) patients respectively. Most of the patients in this group were anemic with raised ESR. Five patients proved to be diabetic. Chest X-Ray done in all patients showing: free air under right dome of diaphragm in 10, active pulmonary lesions in 13 (Sputum AFB +ve), old healed lesions in 6 and normal in 15 patients. Barium follow-through was done in two patients showing multiple strictures with dilated segments of small intestine. Barium enema done in three patients showing: sub-hepatic distorted caecum in two patients and was inconclusive in one patient. All patients in this group were surgically explored and dealt accordingly (Table-2). The mean hospital stay of patients was 13.2 days (range 8 to 32 days). Fourteen patients out of thirty four (41.2%) developed different post operative complications; Wound Infection in 10 (29.4%), Wound

Dehiscence in 3 (8.8%), Faecal Fistula 01 (2.9%) patients. Six patients out of thirty four (17.6%) died. Out of 6 died patients, three had miliary tuberculosis, two had jumbled mass of intestine riddled with tubercles and one old man with severe peritonitis secondary to ilial perforation died due to septicemia (Table-3).

**Table No.1: Presentation of Patients (n=34)**

Presentation	No. of Patients	Percentage
Peritonitis secondary to gut perforation	10	29.4
Sub-acute intestinal obstruction	9	26.5
Abdominal Mass	8	23.5
Right Iliac Fossa pain mimicking acute appendicitis	5	14.7
Umbilical fistula	2	5.9
Total	34	100

**Table No.2: Surgical Procedures done (n=34)**

Presentation	No. of Patients	Percentage
Stricturoplasty	13	38.3
Ileostomy	8	23.5
Resection anastomosis	5	14.7
Limited Right Hemicolectomy	5	14.7
Adhesionolysis and Biopsy	3	8.8
Total	34	100

**Table No.3: Postoperative Complications (n=14)**

Complications	No. of Patients	Percentage
Wound infection	10	29.4%
Wound Dehiscence	03	8.8%
Faecal Fistula	01	2.9%
Expired	06	17.6%

## DISCUSSION

Abdominal tuberculosis can occur at any age but is predominantly a disease of young adults with the mean age of patients being 30-40 years.<sup>x, xi</sup> The mean age of patients in this study was 30.9 SD  $\pm 14.19$  years which coincide with previous study. The prevalence of disease is approximately equal among males and females.<sup>12</sup> The male to female ratio in our study was 1.3:1. Baluch N et al<sup>xii</sup> has reported in their study of 30 cases a male to female ratio of 2:1, while many other investigators has shown a female predominance.<sup>xiii, xiv, xv</sup> The mean duration of symptoms at presentation, in our study, was six months. Bolukbas et al<sup>9</sup> who enrolled 88 patients of ATB, has reported mean duration of disease at presentation 10.4 months which is higher than present study. In another study from Iran, Abbasi et al<sup>12</sup> has

reported, duration of symptoms of ATB were predominating one month to one year before the diagnosis.

ATB is characterized by different modes of presentation i.e., chronic, acute on chronic, acute or it may be an incidental finding at laparotomy for some other disease.<sup>13</sup> The awareness of clinical presentation of ATB shortens its diagnostic time and improves its management.<sup>16</sup> In our series 31 (47.7%) patients presented with non-specific abdominal symptoms. The most common symptoms/signs in these patients were abdominal pain, low grade fever, malaise, weight loss, vomiting and abdominal tenderness which is in accordance with other studies<sup>xvi, 14, 15</sup>. Family history of tuberculosis was present in 32.2% of patients and previous history of same was present in 19.3% of patients. Chong VH and Rajendran N<sup>18</sup> have reported past history of tuberculosis in 30% of their patients which is higher than our finding. Bolukbas et al<sup>9</sup> has reported in their study family and past history of tuberculosis in 8.3% and 16.7% of patients respectively, in non specific symptoms group which is lower than our study. The majority of cases of peritonitis result from the reactivation of latent tuberculous foci.<sup>3</sup> These foci follow hematogenous dissemination from the primary disease in the lung and remain latent.<sup>xvii</sup> Eighty percent of patients in Group-1 were managed conservatively and 6 (19.4%) patients developed recurrent episodes of intestinal obstruction under went laparotomy. Out of six operated patients 3 had multiple strictures in terminal part of ileum, two had bands arising from caseous lymph nodes and one had mass/stricture in Ileo-caecal area. Tuberculous strictures heal by fibrosis on ATT this could be a reason that these patients developed intestinal obstruction.<sup>9, xviii</sup> No morbidity and mortality seen in this group. The reason of zero morbidity and mortality could be early presentation, elective operation and patients were already on ATT.

Thirty four out of sixty five patients were admitted in hospital with different complications. The most common presentations were peritonitis secondary to small gut perforation 29.4%, Sub-acute intestinal obstruction 25.5% and Abdominal mass 23.5% which concurs with that reported by Baloch NA et al.<sup>15</sup> Five patients presented with acute appendicitis in which appendectomy and biopsy of mesenteric lymph node done. Ohene et al<sup>xix</sup> has reported four case of abdominal tuberculosis presented as acute appendicitis in their study which concur with our finding. In our series two patients presented with umbilical fistula while Agarwal P et al<sup>13</sup> has reported three cases of entero-umbilical fistula in their series. In group-2 patients Stricturoplasty and Ileostomy were most common done in 38.3% and 23.5% of patients. The resection and anastomosis and limited right Hemicolectomy was done in 14.7% of patients each.

The adhesiolysis and biopsy was done in 8.8% of patients. These results confirm to the findings of the other studies<sup>14,15,16,21</sup>. The overall morbidity and mortality, in patients who presented with complications, (Group-2) was 41.2% and 17.6% respectively in our study. Agarwal P et al<sup>13</sup> has reported post operative complication rate of 58% which is higher than our study. The mortality rate of 15.3% is reported by Shaikh R et al<sup>16</sup> in their study is closest to our finding of 17.6%.

## CONCLUSION

Early diagnosis of the abdominal tuberculosis is possible only by the specific investigations like PCR. As these investigations are not available in the remote areas of Sindh, early diagnosis of ATB can be made by high index of clinical suspicion to symptoms of abdominal pain, weight loss, low grade fever and vague ill health of more than one month duration and refractory to conventional treatment associated with raised ESR, positive Montoux test. To above symptomatology if empirical ATT is started early many of the complications of ATB can be avoided.

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# The Role of Vitamin 'C' on the Thickness of the Epidermis after X-Irradiation of the Guinea Pigs a Morphological Study under Light Microscope

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## ABSTRACT

**Objective:** To study the role of vitamin 'C' on X-irradiated epidermis of Guinea pigs under light microscope.

**Study Design:** A prospective experimental study.

**Place and Duration of Study:** This study was conducted at the Department of Anatomy, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre Karachi 2008 to 2009.

**Materials and Methods:** Twenty seven animals were taken and were divided in to three groups. Each group was further subdivided into three subgroups containing three animals each according to the time of sacrifice i.e. 48 hours, 15<sup>th</sup> day and 45<sup>th</sup> day respectively. A single whole body x-irradiation in a dose of 5 Gy was given. Group C animals were also given injection of vitamin-C intraperitoneally in the dose of 1 mg/G/day. Animals were sacrificed under ether anaesthesia after completion of their respective periods. Tissues were processed and 4-5 micron thick paraffin embedded sections were cut and stained with Hematoxylin and eosin

**Results:** Decrease in epidermal thickness was observed in Group B1 animals. Which is highly significant ( $P < 0.001$ ) when compared to control. Results of animals of Group B2, and B3 were non significant ( $P > 0.05$ ) when compared to control. Non significant results were obtained when Group C was compared to control group.

**Conclusion:** X-irradiation damages the epidermis and vitamin 'C' minimizes the damaging effects.

**Key Words:** X-ray radiation, Gy, Epidermis, Vitamin 'C'.

## INTRODUCTION

Life on earth has evolved in the presence of ionizing radiation. The natural or background radiation is derived from three major sources, cosmic rays from sun and outer space, radium and other radioactive elements contained in the earth crust and Potassium-40 and other naturally occurring radionuclides (Anderson, 1990). The ever increasing use of radioactive substances both in industry and medicine has made the study of radiation damages, of great practical importance. On human body its effects vary from local tissue necrosis to genetic damage, cancer and death (Walter and Talbot, 1996). In humans (first of all skin) is exposed to the radiation during medical examination (Andronov et al 1988; Bardychev et al, 1982).

Use of nutritional factors in the reconstruction of radiation induced cell injury is an attractive proposition (Jagetia et al., 2003). Vitamin-A supplementation has been reported to ameliorate the acute radiation induced skin injuries (Gavenson et al., 1984). Vitamin-E treatment has also been reported to normalize the breaking strength of wounds that receive pre-operative radiation (Taren et al., 1987). Vitamin-C (a reactive oxygen scavenger) is considered to be a dietary radio-protective agent and acts as an anti-oxidant to protect DNA damage from ionizing radiation (Cai et al., 2001). L-ascorbic acid ( $C_6H_8O_6$ ) is the trivial name of vitamin-C. The chemical name is 2-oxo-L-threo-Hexano-1, 4-lactone-2, 3-enediol L-ascorbic and

dehydro-ascorbic acid are the major dietary forms of vitamin-C (Moser and Bendian, 1990) The radio-protective effects of ascorbic acid seen to result from the interaction of ascorbic acid with radiation-induced free radicals (Duschesne et al., 1975).

The pre-treatment of mice with ascorbic acid improved the collagen synthesis, and increased vascularity and fibroblast density in radiated animals (Naidu, 2003). Furthermore, ascorbic acid has found to be a good anti-oxidant and radio-protective agent (Frie et al., 1989; Navas et al., 1994). Ascorbic acid treatment has been reported to confer protection against radiation in vitro and in vivo (Barerstock, 1979) and it has beneficial effects on the course of radiation-induced skin injuries (Decosse, 1988). Keeping in mind the above facts this study was planed to observe protective role vitamin C in relation to x-irradiation.

## MATERIALS AND METHODS

This study was conducted in the Department of Anatomy, Basic Medical Sciences Institute Jinnah Postgraduate Medical Center Karachi where 27 adult male Guinea pigs weighing 400 to 450 G were taken from Animal House. The animals were divided into three groups, A, B and C containing nine animals each and were further sub-divided into three sub-groups containing three animals each according to time of sacrifice, i.e. 48 hours, 15<sup>th</sup> day and 45<sup>th</sup> day. Group-A served as control. Group-B received whole body X-radiation in dose of 5 Gy at Karachi Institute of

Radiotherapy and Nuclear Medicine Karachi. Group-C received whole body X-radiation in dose of 5 Gy and injection of vitamin-C intraperitoneally in the dose of 1 mg/G/day. [Injection vitamin-C manufactured by Shanghai Medicines and Health Products Shanghai, China].

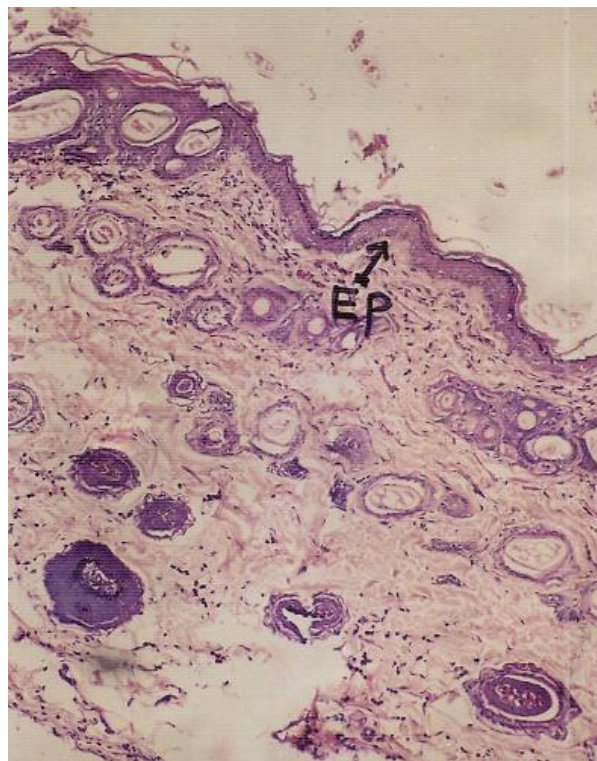
The animals (Guinea pigs) were sacrificed at the end of their respective period of treatment under the ether anaesthesia. The skins of guinea pigs were shaved and skin fragment (size one centimeter square in shape) from face, back and abdomen were collected. Skin fragment from each side was fixed in 10% formalin for 12-18 hours. After that tissues were processed in ascending strength of alcohol, cleared in xylene and infiltrated and embedded with paraffin. Five micron thick vertical sections were cut at rotatory microtome and floated in hot water bath and placed on glass slide and stained with Hematoxylin and eosin for morphology of skin. The thickness of epidermis was measured with the help of ocular micrometer scale in 10x objective and 8x ocular under light microscope. The statistical significance of difference of various quantitative changes between treated and control Guinea pigs were evaluated by student's t' test. The difference was regarded as statistically significant, if the P-value was equal to or less than 0.05. All calculations were done by utilizing computer software SPSS through Microsoft Excel in Windows 2000 XP.

## RESULTS

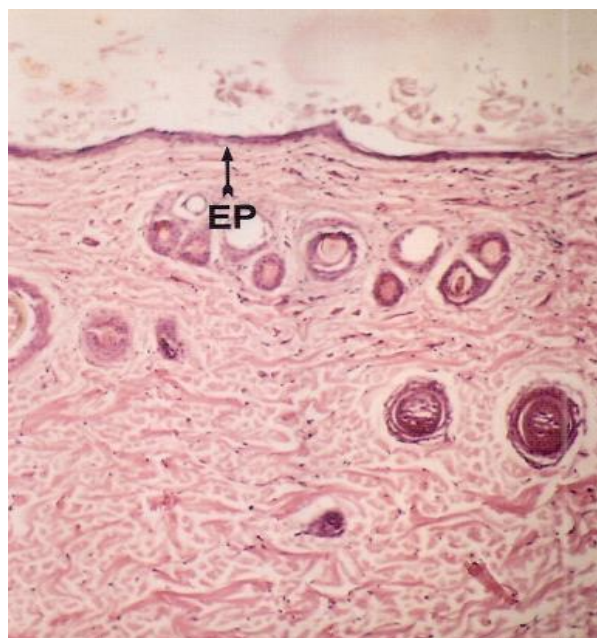
The epidermis of control group showed 5-6 varying layers of cells in addition to stratum corneum. All layer cells and their nuclei were visualized-Fig: 1. Mean thickness of epidermis was  $40.32 \pm 0.32 \mu\text{m}$ ,  $49.08 \pm 0.17 \mu\text{m}$  and  $58.04 \pm 0.29 \mu\text{m}$  in face, abdomen and back respectively.

The Group-B1 animals were ill looking. The skin appeared thin, dehydrated and hyperemic showing the patches of alopecia and cell layer were reduced to half with desquamation of surface epithelium Fig: 2 and 3. Mean thickness of epidermis was  $21.36 \pm 0.32 \mu\text{m}$ ,  $29.08 \pm 0.38 \mu\text{m}$  and  $29.80 \pm 0.38 \mu\text{m}$  in face, abdomen and back respectively. When compared with control results were highly significant ( $P < 0.001$ ). The skin of Group-B2 appeared thin and dehydrated with wide patches of alopecia. Epidermis showed reduced number of cell layers to half, but thickness of epidermis was near to control (due to hyperkeratinization) Fig.4, 5 and 6. Mean thickness of epidermis was  $39.92 \pm 0.26$ ,  $49.36 \pm 0.47$  and  $57.76 \pm 0.26$  in face, abdomen and back respectively. When compared with control results were insignificant ( $P > 0.05$ ). In Group B3 the hairs were very sparse but hyperemia of skin was diminished and numbers of cell layers were as near to control and keratinization was decreased. Mean thickness of epidermis was  $40.28 \pm 0.47 \mu\text{m}$ ,  $48.94 \pm 0.73 \mu\text{m}$  and  $57.76 \pm 0.26 \mu\text{m}$  in face, abdomen and back respectively.

When compared with control results were insignificant ( $P > 0.05$ ).



**Figure No. 1:** H&E stained 5µm thick longitudinal section of abdomen skin showing epidermal thickness (Ep) in control guinea pig. Photomicrograph X 100.

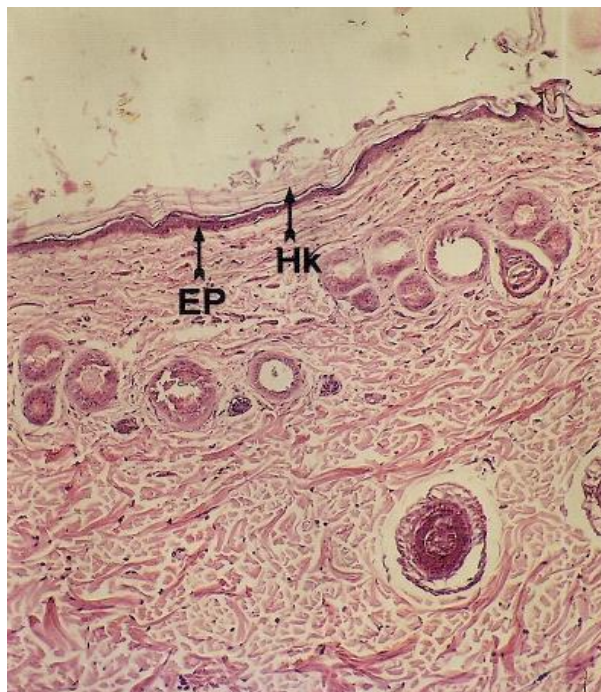


**Figure No.2:** H&E stained 5µm thick longitudinal section of abdomen skin showing desquamation and decreased thickness of epidermis (Ep) 48 hours after treatment with x-radiation in Guinea pig. Photomicrograph X 100.





**Figure No.3:** H&E stained 5µm thick longitudinal section of back skin showing desquamation and decreased thickness of epidermis (Ep) 48 hours after treatment with x-radiation in Guinea pig. Photomicrograph X 100.



**Figure No.4:** H&E stained 5µm thick longitudinal section of face skin showing increase in thickness of epidermis (Ep) to hyperkeratinization (Hk) after 15 days treatment with x-radiation in Guinea pig. Photomicrograph X 100.

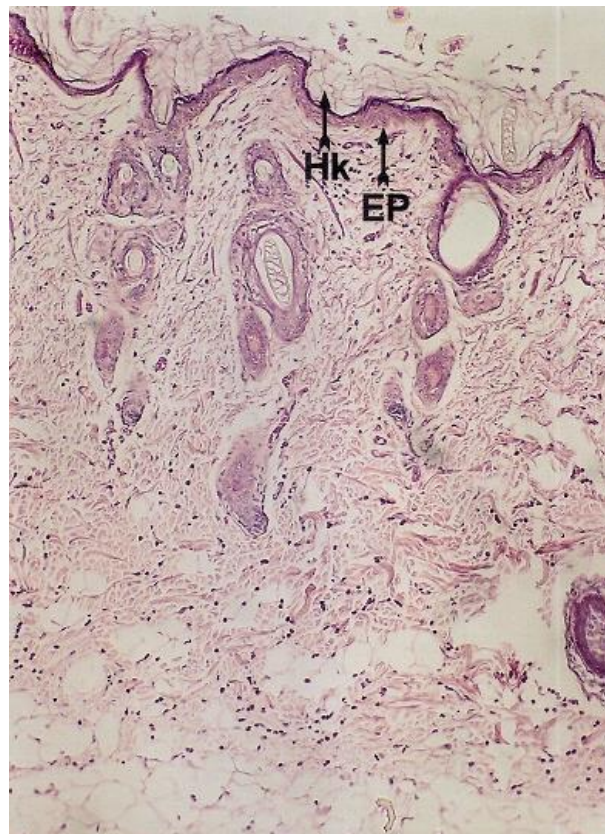


**Figure No.5:** H&E stained 5µm thick longitudinal section of abdomen skin showing increase in thickness of epidermis (Ep) due to hyperkeratinization (Hk) 15 days after treatment with x-radiation in Guinea pig. Photomicrograph X 100.

The Group C1 animals were ill looking, skin appeared thin and dehydrated showing patches of alopecia and hyperemia, number of cell layers were reduced to half and there was desquamation of surface epithelium. Mean thickness of epidermis was  $21.00 \pm 0.27$ ,  $29.68 \pm 0.42$  and  $38.04 \pm 0.52$  in face, abdomen and back respectively. When thickness of face and abdomen was compared to the control group the results are highly significant ( $P < 0.001$ ) and, insignificant ( $P > 0.05$ ) when compared with subgroup B1 but in case of thickness of epidermis of the back the results are highly significant when compared to control and subgroup B1. In gross examination of skin of Group C2 animals appeared thin and dry and hairs were very sparse. And epidermis showed increased number of cells layer near to control. Mean thickness of epidermis in face was  $40.00 \pm 0.64$ ,  $48.86 \pm 0.84$  and  $57.00 \pm 0.32$ . When compared to control Group and B2 insignificant ( $P > 0.05$ ) results were found. In gross examination of the skin of Group C3 animals at three sites was found thicker and dry with diminished hyperemia. Number of cell layers was increased near to control. The mean thickness of epidermis was  $39.88 \pm 0.66$ ,  $49.60 \pm 0.51$  and  $58.20 \pm 0.80$  in face, abdomen and back respectively. When



compared with control Group and B3 insignificant ( $P>0.05$ ) results were found.



**Figure No.6: H&E stained 5µm thick longitudinal section of back skin showing increase in thickness of epidermis (Ep) due to hyperkeratinization (Hk) 15 days after treatment with x-radiation in Guinea pig. Photomicrograph X 100.**

## DISCUSSION

The ever increasing use of radioactive substances both in industry and medicine has made the study of radiation damages of great practical importance. On human body its effects vary from local tissue necrosis to genetic damage, cancer and death (Walter and Talbot, 1996). X-ray irradiation (XRI) can affect both normal and neoplastic cell especially the rapidly growing one such as epidermal cells (Hussein et al., 2005).

Ascorbic acid is one of the important water soluble vitamin and natural anti-oxidant compound. It is expected to help in restricting the propagation of chain reaction initiated by free radicals which are produced either naturally or as a result of environmental factors (Shamberger et al., 1979). The previous studies are based on morphological x-rays induced skin changes. The present study was designed to observe the morphometric changes in skin of different locations induced by x-rays with role of vitamin-C in Guinea pigs.

In the present study, in gross examination in all the treated animals of groups-B and C, hair loss was seen in all three sites. The above findings were in agreement with Hopewell (1990) and Malkinson and Prasad (1995). They observed that loss of hair occurs after treatment with relatively low doses of radiation, indicating the hair follicles are highly sensitive to ionizing radiation.

Animals of groups-B1 and C1 with dose of 5 Gy radiation the thickness of epidermis in face, abdomen and back was reduced to half as compared with the control. This finding was in agreement with observation of Hussein et al (2005) who observe in their study that in x-ray irradiated skin the stratification of epidermis was reduced to one layer each of basal, spinous, and granular as well as few layer of corneocytes.

Increase in thickness of epidermis in face, abdomen and back of C2 and C3 was in agreement with the observation of Shamber (1979) who explained that vitamin-C, a natural anti-oxidant compound being anti-oxidant, it is expected to help in restricting the propagation of chain reaction initiated by free radicals.

## CONCLUSION

The study concludes that X-radiation produces damaging effects on the epidermis of skin and vitamin-C treatment has beneficial effects on irradiated epidermis of skin.

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