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**Editorial**

# Scientists Grow 'Model Brain' from Stem Cells

**Mohsin Masud Jan**

Editor

In another milestone for regenerative medicine, Austrian scientists report they have turned stem cells into a collection of tissues that resembles the beginnings of the human brain.

The tiny organoids, as the researchers call them, grow to around 4 millimeters in size. They have many of the same specialized regions that are seen in fetal brains around nine weeks into development. Though these baby brains aren't likely to ever work as replacement parts, they are useful for understanding brain development, and where and how it can go awry. Researchers have already used the model to better understand one problem called microcephaly, a genetic condition that causes a child to be born with smaller-than-average head and brain, and results in mental disability.

The new brain-growing method may also be useful for studying other neurological disorders, such as schizophrenia and autism, and for testing new drugs, the researchers said in a news conference Tuesday. The study was published online Aug. 28 in the journal *Nature*. Previously, researchers have coaxed stem cells to grow into the beginnings of a human eye and a functioning human liver. They've also created working pituitary glands and beating hearts for mice. "But so far, the most complex of human organs, the human brain, has not been susceptible to these type of cultures," said researcher Juergen Knoblich, deputy scientific director of the Institute of Molecular Biotechnology at the Austrian Academy of Science, in Vienna.

For the new study, researchers bathed stem cells in growth factors to encourage them to divide. When the stem cells had formed tiny balls of cells and the beginnings of nerve tissue, they were implanted in droplets of a gel protein mixture that became both food and physical support. After the organoids had reached a certain size, they were transferred into flasks that were kept in constant motion to keep the cells and tissues exposed to oxygen and nutrients. After two months, the brain organoids stopped developing, probably because they lacked a blood supply to deliver oxygen and food deeper into the tissues, researchers said. By studying

the gene expression of the different tissues of the organoid, researchers were able to identify discrete brain areas including the dorsal cortex, prefrontal cortex, the forebrain and ventral forebrain, the hippocampus, choroid plexus and immature retina — the beginnings of the eye. Not all of these areas developed in every organoid, however, and they didn't look exactly like the brains of human embryos as they grow in the womb. "In a developing embryo, you have the cerebral cortex at the front, then the ventral forebrain below that, and behind that you have the mid-brain, the cerebellum and the brain stem," explained Madeline Lancaster, a postdoctoral researcher at the Institute of Molecular Biotechnology. "In ours, we don't have that spatial organization. We have those regions, but they're not spatially organized in that manner," she said. And while researchers found some evidence that the different brain regions were functioning, they don't think the organoids were fully wired and connected the way mature adult brains are, because that kind of connection is something that happens at later developmental stages.

"It's sort of like manufacturing all the transistors and resistors in a radio, but not actually wiring it all up so you can listen to the radio," said Amy Bernard, director of structured science for the Allen Institute for Brain Science in Seattle. "But certainly getting those building blocks set in is the first step." However, "it's very impressive to see the level of differentiation that's achieved in this model," added Bernard, who was not involved with the study. To further prove the value of watching early brain development this way, the researchers took stem cells from an individual with microcephaly, a developmental problem that affects about 25,000 of the roughly 4 million children born in the United States each year. They treated the stem cells with chemicals to return them to an embryonic state and then watched them as they began to grow into an early brain. Compared to the way previous organoids had grown, the stem cells from the individual with microcephaly stopped dividing earlier, so they had fewer total stem cells with which to build a brain, resulting in a smaller overall brain size.

# Traumatic Brain Injury: Experience at Divisional Headquarter Teaching Hospital, Mirpur, AJK

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## ABSTRACT

**Objective:** Traumatic brain injury is one of the leading causes of morbidity, mortality and severe economic loss; especially in the patients who are in productive years of life. The objective of our study was to find out the etiological pattern and distribution of traumatic brain injury at Mirpur, Azad Kashmir.

**Study Design:** Prospective study.

**Place and Duration of Study:** This study was carried out at surgical wards at DHQ hospital, Mirpur from Nov 2012 to April 2013.

**Materials and Methods:** In this study epidemiological and clinical data of all the patients with traumatic brain injury admitted in surgical wards at DHQ hospital, Mirpur were included.

**Results:** A total of 309 patients with traumatic brain injury were admitted. The age range was between 3 years to 80 years. The mean age was 23.8 years. The most commonly affected age group was between 25-30 years (89.3%). Males were predominant (81.9%). Students involved constituted 44.7% of patients. Commonest mode of trauma was pedestrians hit by motorized vehicles (70 %) followed by physical assaults (15.9%). Majority of the patients (88.3 %) were from local district and 70.2 % reached the hospital within two hours of trauma. 46.6 % of the patients had a GCS of 13-15 on arrival. 3.9% had subdural hematoma while 1% of patients had skull fractures and intracerebral bleeds. Overall mortality was 5.8%.

**Conclusion:** Road traffic accidents are the leading cause of traumatic brain injury affecting the young population at Mirpur and led to 5.9% mortality and 9.5 % total dependency in the affected population. Better traffic control system and awareness can reduce the incidence of traumatic brain injuries.

**Key Words:** Head injury, Traumatic brain injury.

## INTRODUCTION

Traumatic brain injuries (TBI) are the major cause of morbidity and mortality especially in the young age group in the second to fourth decade of life<sup>1</sup>. The urbanization of developing countries leading to rapid motorization has resulted in increased incidence of motor vehicle accidents<sup>2</sup>.

It is estimated to cause an annual loss of \$30 billion in developed countries<sup>3</sup>. It is also estimated that more than 1.7 million head injuries are encountered in the US alone<sup>4</sup>.

The incidence of TBI has been estimated as more than 600 per 100,000 cases by WHO<sup>5</sup>, leading to about 90 per 100,000 admissions in US hospitals. The annual incidence of head injury in Pakistan has been estimated at 50/100,000 population based on data from public sector hospitals<sup>6</sup>.

After injuries the major challenge encountered is to protect the patient from secondary damage following trauma which includes proper pre hospital care, transportation to the hospital by trained ambulance personals and rapid and rational management in the hospital. Unfortunately in our country due to poor traffic control, there is a high incidence of road traffic accidents. Lack of pre hospital care and poor

transportation by untrained personals leads to increased morbidity and mortality. There is need for public awareness, campaigning, and enforcement of traffic rules to reduce the incidence of road traffic accidents. The present study is aimed to highlight the pattern and distribution of traumatic brain injuries in order to improve treatment strategies and prevention.

## MATERIALS AND METHODS

In this prospective study of all the patients with traumatic brain injury admitted in the surgical wards of DHQ hospital Mirpur from Nov 2012 to April 2013 were included. The patients who were discharged from emergency department were excluded. A total of 309 patients were included in the study. All the patients were managed according to ATLS protocol. After initial resuscitation and stabilization patients were subjected to neuroimaging along with the imaging of other relevant systems. Canadian CT head rules were followed for imaging of the patients with GCS 7-13-15<sup>7</sup>.

Head injury was classified as mild when GCS at presentation was 13 – 15, moderate, when GCS was 9-12 and severe with GCS less than 8. The data collected were about age, sex, residence of patient, mode of trauma, time since trauma and hospital arrival, Glasgow



Coma Scale, concurrent injuries and length of hospital stay. CT scan findings, type of management and outcome were also noted. At the time of discharge, outcome was graded according to Glasgow outcome scale.

Data were analyzed using SPSS version 17

## RESULTS

A total of 309 patients with traumatic brain injury were admitted. The age range was between 3 years to 80 years. The mean age was 23.8 years. The most commonly affected age group was between 25-30 years (n 135, 43.7%), followed by 13-24 years (n 114, 36.9%) while 10% of patients were between 31-60 years (Table 1). There were 253 male (81.9%) and 56 female (18.1%) (Table 2).

**Table No. 1: Age Groups**

Age	Group	Frequency	Percent
	3-12	27	8.7
	13-24	114	36.9
	25-30	135	43.7
	31-60	31	10.0
	>60	2	.6
	Total	309	100.0

**Table No.2: Sex**

Sex	Frequency	Percent
Female	56	18.1
Male	253	81.9
Total	309	100.0

**Table No.3: Occupation**

Occupation	Frequency	Percent
Student	138	44.7
Unemployed	87	28.2
Office /Mental worker	15	4.9
Laborers	40	12.9
House wife	24	7.8
Retired	5	1.6
Total	309	100.0

Students were the most common victims (n 138, 44.7%) followed by unemployed community (n 87, 28.2%). Laborers were involved 12.9%. Mental/office workers were 4.9% and retired personals were 1.6%. (Table 3) Majority of the patients (N 273, 88.3%) belonged to local district followed by other districts (n 24 7.8%) about 3 hours drive from Mirpur.

Commonest mode of trauma was pedestrians hit by car/four wheel vehicle (n 138 44.7%) followed by hit by motor bike (n 79 25.6%). Forty nine patients

(15.9%) were injured in physical assaults. Thirty (9.7%) patients had a fall. Twelve patients (3.9%) were injured in a motorbike crash. One patient (0.3%) had firearm injury. (Table 4)

**Table No.4: Mode of Trauma**

	Frequency	Percent
Motor bike driver	12	3.9
Hit by motor bike	79	25.6
Hit by four wheel vehicle	138	44.7
Fall	30	9.7
Physical assault	49	15.9
Firearm	1	.3
Total	309	100.0

**Table No.5: GCS**

GCS	Frequency	Percent
3-8	24	7.8
9-12	141	45.6
13-15	144	46.6
Total	309	100.0

**Table No.: Outcome**

		Frequency	Percent
Valid	Good recovery	241	78.0
	Moderate disability	21	6.8
	Severe disability	29	9.4
	Expired	18	5.8
Total		309	100.0

Majority of the patients (n 217, 70.2%) reached in hospital within two hours of trauma. 76 patients (24.6%) presented between 2-6 hours. Only 16 patients (5.2%) presented after 6 hours.

Fifteen patients 5% had compromised airway on arrival. 46 patients (15%) were hypotensive. 24 patients (7.8%) had breathing difficulties due to chest trauma.

Majority of the patients (n 144 46%) had minor head trauma with GCS 13-15. There were 141 patients (45.6%) with a GCS between 9-12. Twenty four patients (7.8%) had severe head trauma with a GCS of 8 or below. (Table 5)

Majority of patients (n 203 65.7%) had closed head injury, 85 patients (27.5%) had scalp laceration, skull was exposed in 18 (5.8%) whereas brain was exposed in 3 (1%) patients. Forty two patients (13.6%) had ear bleeding, 9 patients (2.9%) had CSF otorrhoea. Thirty

six patients (11.7 %) had nasal bleed. Twenty two patients (7.1%) had associated abdominal injuries. Associated limb injuries were found in 135 patients (43.7 %). Fracture pelvis was present in ten patients (3.2%).

CT scan brain was performed in 237 (76%) patients. It was normal in 207 patients. Twelve patients (3.9 %) had traumatic subdural hematoma and subarachnoid hemorrhage while 3 patients (1%) had intracerebral bleeds.

Three patients had neurosurgical intervention with craniotomy and evacuation of subdural hematoma. Rest of the patients had conservative management from neurosurgery point of view.

Majority of the patients (n 241, 78%) had good recovery and were back to their routine work. 21 patients had moderate disability and were able to look after themselves. Twenty nine patients (9.4%) had severe disability while 5.8 % expired. (Table 6)

## DISCUSSION

Rapid industrialization and urbanization has resulted in a silent epidemic of head injury<sup>8</sup>.

Conventionally head injuries are classified as mild (GCS 13-15), moderate (GCS 9-12) and severe (GCS less than 8). In our study 82% of patients were males. Male gender is an independent risk factor for traumatic brain injuries<sup>9</sup> but Bazarian JJ et al., found poorer outcome after mild TBI in females<sup>10</sup>.

Eighty percent of our patients were between 13-30 years. The age incidence of traumatic brain injury is bimodal with one peak at 15-24 years and another after 65 years<sup>11</sup>. Raja et al., and Jooma et al., in two separate studies estimated second and fourth decade respectively as the most vulnerable age group from the same region<sup>12, 13</sup>.

In another local study carried out by Umerani et al., most of the patients were in third decade of life<sup>14</sup>. The shift of the age group to lower side in our study is apparently due to more involvement of teenagers in driving.

Most of the patients reached hospital within 2 hours of trauma. There are no first aid services at the site of scene and almost all of the patients are brought in private transport. Five percent of patients had compromised airway and 15% were hypotensive. It is need of time to improve ambulance services with trained paramedics for safe rapid transfer of critically ill patients to hospital to reduce morbidity and mortality.

The commonest cause of head injury in our study was road traffic accidents. There were about 70% pedestrian hit by vehicle. This can be attributed to lack of traffic rules awareness, and neglect of safety measures. In two other studies carried out in Pakistan by Hyder et al.,<sup>15</sup> and Umerani et al.,<sup>14</sup> demonstrated proportional increase in RTA associated death with increasing motorization in Pakistan. Moreover, wearing helmets

and seat belts are not compulsory and certain cars are even made without seatbelts<sup>12</sup>.

Fall from height is a common cause of TBI especially in children and females in Pakistan<sup>12,13</sup>. This is principally attributed to flaw in designing with fenceless roofs. Thirty patients (9.7%) in our study had fallen from heights. Children are especially prone to fall from stairs due to negligence of family. They may also fall while climbing trees and fences. Additionally fall from poles is an occupational hazard in the absence of adequate safety precautions.

Helmets have proven efficacy in preventing TBI for two-wheel riders (16). Twelve (3.9%) of our patients were injured in motor bike crash. None of our patient was wearing helmet whereas in other two local studies less than 1% of patients were wearing helmet<sup>14</sup>. In another local publication helmet usage has been estimated less than 3 % (17). In a study by Rastogi et al., two wheeler related accidents were the most common (40.3%) cause of head trauma<sup>18</sup>. Head injuries due to assault are very common in our area due to illiteracy and poverty. Commonly used weapons are rods, axe or even firearms. In our study 49 patients (14.9%) were injured in physical assaults. Blunt trauma usually results in depressed skull fractures<sup>14</sup>. Penetrating brain injuries (PBI) are commonly caused by firearms and carry a worse prognosis<sup>19, 20</sup>. They carry high mortality if they are suicidal or there is bi-spheric involvement or intraventricular extension.

During the first 24 hours following Traumatic brain injury CT scan is the imaging modality of choice<sup>21, 22</sup>. In a study Umerani et al., CT scan was performed in 756 (84.65%) patients, out of which only 75 (9.92%) had positive CT findings (14). The incidence of subdural hematoma has been reported at about 5%<sup>23</sup> and the mortality as high as 1 out of 5 cases<sup>24</sup>. The mortality reported is 6.4% in study by Agrawal et al.,<sup>2</sup>. In a study carried out on autopsy basis death was due to injury to the head in 386 (66.4%) victims<sup>25</sup>.

Outcome of the patients with traumatic brain injuries and length of stay in ICU and hospital has been found significantly less in the patients who were properly transported to hospital from the scene of accident<sup>26</sup>.

## CONCLUSION

1: Road traffic accidents are the leading cause of traumatic brain injury affecting the young population at Mirpur and led to 5.9% mortality and 9.5 % total dependency in the affected population.

2: Pedestrians hit by motor vehicles is the major etiology of traumatic brain injury in our study

3: Better traffic control system and awareness can reduce the incidence of traumatic brain injuries.

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# Aetiology of Epistaxis: A Retrospective Study of 87 cases at Bolan Medical Complex Hospital, Quetta

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## ABSTRACT

**Objective:** To objective of this study was to describe the aetiology of epistaxis.

**Study Design:** Retrospective, descriptive study.

**Place and Duration of Study:** This study was carried out at the Department of Otorhinolaryngology and Head & Neck Surgery, Bolan Medical Complex Hospital, Quetta from December 2011 to December 2013.

**Materials and Methods:** This study included 87 patients of epistaxis of the afore-said period. Medical records of patients were reviewed retrospectively and results were analyzed.

**Results:** The mean age of the patients was  $26.70 \pm 18.10$  (SD) years and male to female ratio was 2:1. Trauma (32.18%) was the commonest cause of epistaxis, followed by idiopathic group (22.99%) and hypertension (14.94%). Other causes were nasal and nasopharyngeal tumours (10.34%), inflammatory diseases of nose and sinuses (8.05%), blood dyscrasias (6.90%) and miscellaneous causes (4.60%) which included one case of aspirin induced epistaxis, one case of hereditary hemorrhagic telangiectasia, one patient of typhoid fever and one case of liver cirrhosis.

**Conclusion:** Nasal trauma is the most common cause of epistaxis. Idiopathic group is the second in which exact cause of epistaxis is not known, followed by hypertension, while other causes are rare.

**Key Words:** Epistaxis, Aetiology, Trauma, Idiopathic, Hypertension

## INTRODUCTION

Epistaxis is the most common otolaryngologic emergency, reported to occur in up to 60% of the general population.<sup>1,2</sup> It has a bimodal age presentation with incidence peaks in below 25 years and above 50 years of age and affects males twice more than females.<sup>3</sup> The cause of epistaxis is multifactorial and it results from the interaction of a series of factors that affects the nasal mucosa and the blood vessels, these include environmental, local and systemic factors.<sup>4</sup> Humidity and temperature are environmental factors. Cold, dry air increases cases of epistaxis.<sup>5</sup> Local factors include trauma, anatomic abnormalities, inflammation, allergies and tumours.

Systemic factors like hypertension, platelet and coagulation abnormalities, renal failure and alcohol abuse may cause epistaxis. Medications affecting clotting like anticoagulants and nonsteroidal anti-inflammatory drugs can also lead to epistaxis. Hereditary haemorrhagic telangiectasia (Osler-Weber-Rendu disease) is an unusual cause of severe, recurrent anterior epistaxis.<sup>6</sup>

Post traumatic pseudoaneurysm of internal carotid artery is an uncommon but potentially fatal cause of epistaxis.<sup>7</sup> Trauma is the commonest cause of epistaxis, while, idiopathic causes and hypertension are other common causes of epistaxis.<sup>8</sup>

## MATERIALS AND METHODS

Eighty seven patients of both genders with epistaxis were included in this study. Medical records of these

patients were reviewed retrospectively from December 2011 to December 2013 for aetiology of epistaxis and results were analyzed statistically.

## RESULTS

There were 87 patients of age 3 to 70 years with a mean age of  $26.70 \pm 18.10$  (SD) years. There were 58 male patients and 29 female patients and male to female ratio was 2:1. In seventy nine patients (90.81%) There was anterior epistaxis, while 8 patients (9.19%) suffered from posterior epistaxis. Trauma (32.18%) was the most common cause of epistaxis, followed by idiopathic (22.99%) and hypertension (14.94%). Other causes were nasal and nasopharyngeal tumours (10.34%), inflammatory diseases of nose and paranasal sinuses (8.05%), blood dyscrasias (6.90%) and miscellaneous causes (4.60%) as shown in Table 1. There were 28 patients (32.18%) who suffered from nasal and maxillofacial trauma. Causes of trauma in epistaxis patients were road traffic accidents, physical assaults, nose picking, sports injury, foreign bodies of nose and iatrogenic trauma as depicted in figure 1.

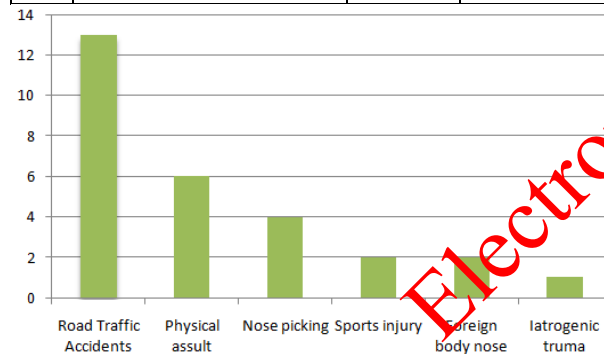
Tumours that caused epistaxis were juvenile nasopharyngeal angiofibroma, nasopharyngeal carcinoma, bleeding polypus of nasal septum, and squamous cell carcinoma of nose. Juvenile nasopharyngeal angiofibroma was found in 4 patients (4.60%), nasopharyngeal carcinoma in 2 patients (2.29%), bleeding polypus of nasal septum (haemangioma) in 2 patients (2.29%), and squamous

cell carcinoma of nose in one patient (1.15%). Blood dyscrasias caused epistaxis in 6 patients (6.89%). In three patients (3.45%) there was idiopathic thrombocytopenia, in 2

There were 4 patients (4.60%) in miscellaneous group, which included one case of aspirin induced epistaxis, one case of hereditary haemorrhagic telangiectasia (Osler-Weber-Rendu disease), one case of Typhoid fever and one case liver cirrhosis.

**Table No.1: Causes of epistaxis (n=87).**

S. No	Causes	No. of patients	Percentage
1.	Trauma	28	32.18%
2.	Idiopathic	20	22.99%
3.	Hypertension	13	14.94%
4	Tumours	09	10.34%
5.	Inflammatory diseases	07	8.05%
6.	Blood dyscrasias	06.	6.90%
7.	Miscellaneous	04	4.60%
	a) Aspirin induced epistaxis.		
	b) Hereditary Haemorrhagic Telangiectasia.		
	c) Typhoid fever		
	d) Liver cirrhosis		



**Figure No..1: Causes of trauma in epistaxis (n=28).**

## DISCUSSION

Many studies showing, local trauma as the main cause of epistaxis.<sup>9, 10</sup> Gilyoma JM et al. reported that the most common cause of epistaxis is trauma followed by idiopathic and hypertension.<sup>11</sup> Trauma resulting from road traffic crush is the most common etiological factor for epistaxis. Hanif M et al. in their study on 205 patients concluded that Hypertension (48%) in old age, trauma (37%) and upper respiratory tract infection (14%) in young adults and children are the common causes of epistaxis.<sup>12</sup> Mahmood T et al. in a study of 640 cases of epistaxis reported that accidental trauma is the commonest (28%) cause of nose bleeding, followed by inflammatory causes (17%) and idiopathic (14.5%).<sup>13</sup> Iseh KR et al. found that the commonest cause of epistaxis is idiopathic (29.2%), followed by

trauma (27.8%) and hypertension (18%) in a study of 72 cases.<sup>14</sup>

In our study trauma was the commonest cause of epistaxis followed by idiopathic group and hypertension. However, several studies have shown no relationship between hypertension and epistaxis.<sup>15, 16</sup>

Many national and international studies have shown hypertension as a common cause of epistaxis.<sup>8, 11, 12, 14</sup> Hypertension is frequently associated with posterior epistaxis.<sup>9</sup> It may be more responsible for prolonging bleeding than for initiating it.<sup>17</sup> The elevated pressure, which disrupts thrombus formation, and the diminished constrictive ability of atherosclerotic vessels compromise the hemostasis.

In 9 patients (10.34%) cause of epistaxis was nasal and nasopharyngeal tumours. The most common tumour which presents with recurrent epistaxis is juvenile nasopharyngeal angiofibroma.<sup>5</sup> In juvenile nasopharyngeal angiofibroma the patient presents with recurrent epistaxis and nasal blockage with intranasal mass.<sup>18</sup>

Inflammatory diseases of nose and paranasal sinuses caused epistaxis in 7 patients (8.05%). Many studies have documented inflammatory diseases of nose and paranasal sinuses as a common cause of epistaxis.<sup>13, 14</sup>

Blood dyscrasias, particularly platelet disorders, von Willebrand disease and haemophilia can cause epistaxis.<sup>19</sup> In our study 6 patients suffered from blood dyscrasias. In this study other causes of epistaxis were aspirin induced epistaxis, hereditary haemorrhagic telangiectasia (Osler-Weber-Rendu disease), Typhoid fever and Liver cirrhosis. It is thought that the link between the of nonsteroidal anti-inflammatory drugs and the occurrence of epistaxis may be due to alteration of platelet function.<sup>20</sup> The diagnosis of hereditary haemorrhagic telangiectasia (Osler-Weber-Rendu disease) include epistaxis, telangiectasia, visceral lesions and an appropriate family history.<sup>21</sup> Chronic liver disease (cirrhosis) may cause epistaxis. Kodiya AM et al, in a study of 101 patients with epistaxis, have shown that chronic liver disease caused epistaxis in 3 patients (2.97%).<sup>22</sup>

## CONCLUSION

Trauma resulting from road traffic accidents is the most common cause of epistaxis, followed by idiopathic causes and hypertension. Other causes of epistaxis are tumours of nose and nasopharynx, inflammatory diseases of nose and paranasal sinuses and blood dyscrasias. Drug induced epistaxis, hereditary haemorrhagic telangiectasia typhoid fever and chronic liver disease are rare causes of epistaxis.

**Recommendation:** Since in this study road traffic accident is the commonest cause of epistaxis in our setup, therefore, the management of traumatic epistaxis should focused and follow the guide lines.

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# Response Rate of Standard Interferon Therapy in Chronic Hepatitis C

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## ABSTRACT

**Objectives:** Interferon combination therapy is used to eradicate the Hepatitis C Virus from infected individuals. HCV (hepatitis C virus) infections respond to standard conventional interferon (INF) therapy along with ribavirin (RBA). The aim of study was to look for response of chronic HCV infections to standard conventional combination interferon therapy and ribavirin.

**Study Design:** Interventional non randomized trial

**Place and duration of Study:** This study was carried out at Azad Kashmir Combined Military Hospital (AK CMH)/Sheik Khalifa Bin Ziyad (SKBZ) Muzaffarabad (MZD) from June 2009 to July 2012.

**Materials and Method:** A total of 210 patients were selected for interferon combination therapy. After confirmation of active HCV infection by PCR-RNA, conventional interferon alpha 2a with ribavirin (RBA) was given to patients for 6 months. After end of treatment (ETR), the efficacy was defined as sustained virological response (SVR) if HCV-RNA remained undetected 6 months after stoppage of combination interferon therapy.

**Results:** Out of total 210 patients, 144 (68.6%) showed SVR and 66 (31.4%) did not show SVR. Hence out of 68.6 % were negative and 31.4% were positive for HCV RNA after 6 months of therapy. The non parametric chi squared showed age ( $p < 0.001$ ), (age category  $p < 0.001$ ), gender ( $p < 0.006$ ), and HCV PCR response ( $p < 0.001$ ) had statistical significant association.

**Conclusion:** Conventional Interferon and ribavirin combination therapy (INF-RBA) remains effective in chronic hepatitis naïve patients. HCV-RNA qualitative PCR test at 6 months of ETR is important predictor of SVR. The response of antiviral therapy against HCV infection in chronic HCV patients is 68.6 %. The high response rate may be due to the prevalence of IFN-responsive HCV genotypes type 3 in our country.

**Key Words:** Sustained virological response; Conventional Interferon; Ribavirin; Chronic Hepatitis C

## INTRODUCTION

The hepatitis C virus (HCV) is a global health problem and the leading cause of chronic liver disease in world. The HCV genome is single-stranded RNA. HCV infection effect annually more than one million people in world.<sup>1-3</sup> the effective therapy and prevention of HCV infection is our ultimate goal. It is major economic and life threatening infection in underdeveloped and developed countries. In our country patients have financial problems for its treatment.

The primitive goal of hepatitis C treatment is eradication of the virus. The sustained virological response (SVR) is defined as absence of HCV RNA in serum after 6 months of treatment which is confirmed by absence of hepatitis C virus by Polymerase Chain Reaction (PCR).<sup>2, 4-5</sup> Hepatitis C therapy is started with ribavirin (RBA) and recombination interferon therapy.<sup>6</sup> Interferon is very active against HCV. It decreases the level of serum alanin aminotransferase (ALT) as well HCV RNA level. These effects led to a sustained absence of virus in a proportion of patients.<sup>7-8</sup> Ribavirin is nucleoside analogues has activity against several flaviviruses and lowers ALT level and improves histological abnormality of the liver. Ribavirin had little

effects on serum HCV RNA levels. The combination therapy of ribavirin with interferon has been observed with increased SVR.<sup>9</sup> Interferon and ribavirin in combination has SVR of 40-50% and has been used as treatment in chronic HCV infection.<sup>10</sup> It has less good response as compared to Pegylated interferon with Ribavirin.<sup>11</sup> Combination interferon and ribavirin therapy has been recommended due to economic reasons, genotype 3 prevalence in our county<sup>12</sup> and provision of free of cost therapy by our AJK Government.

## MATERIALS AND METHODS

This study included 210 consecutive Hepatitis C Virus (HCV) patients of either sex, 20 to 69 years referred to (CMH) /SKBZ Muzaffarabad. The patients who were HCV positive by ELISA (enzyme-linked immunosorbent assay) the PCR (polymerase chain reaction) qualitative test HCV- RNA assays (Amplicor HCV test, version 2.0 Roche Diagnostics) was performed to confirm HCV positive RNA cases. An analysis of response of combinational interferon alpha 2a with ribavirin therapy against HCV PCR positive was conducted. Among the confirmed HCV patients, 210 naïve patients with PCR –RNA positive, were selected for interferon therapy keeping in mind the

exclusion criteria. HCV-PCR positive patients were given standard interferon combination therapy, interferon alpha 2a (3 MIU, S/C thrice weekly) plus Ribavirin (1000-1200 mg/day) continuously for 6 months with repeated monitoring of Blood CP, ALT level and coagulation profiles. HCV-RNA PCR testing was done at the end and after 6 months of interferon therapy to look for ETR and SVR respectively.

The data entry and analyses were done on software statistical package SPSS 20. Chi square nonparametric test done to show statistical significance of response to therapy.

**RESULTS**

After completion of the 6 months interferon therapy, the result of SVR was observed. Out of total 210

patients, 144 (68.4%) were negatives for HCV- RNA PCR and showing SVR while 66 (31.4%) were positive for HCV- RNA PCR and did not show SVR. Demographics and therapeutic response to conventional combination interferon therapy (Tables 1, 2 and 3).

**Table No.I: Response rate of Interferon Therapy in Chronic HCV infections according to SVR**

No.	Age group	Gender		SVR+ (%)	SVR- (%)
		Male (%)	Female (%)		
210	20-65	125 (59.5)	85 (40.5)	144 (68.6)	66 (31.4)

**Table No.2: Descriptive Statistics demographics**

	N	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
Age	210	20	69	39.73	.814	11.800
Age category	210	1	6	3.56	.085	1.237
Gender	210	1	2	1.40	.034	.492
HCV PCR AFTER THERAPY RESPONSE	210	-1	1	36	.064	.934
Valid N ( listwise )	210					

**Table No.3: Nonparametric Test Statistics according demographics & HCV PCR response**

	Age	Age category	Gender	HCV PCR after therapy response
Chi-Square	83.752 <sup>a</sup>	76.571 <sup>b</sup>	7.619 <sup>c</sup>	27.505 <sup>c</sup>
df	43	5	1	1
Asymp. Sig.	.000	.000	.006	.000

- a. 44 cells (100.0%) have expected frequencies less than 5. The minimum expected cell frequency is 4.8.
- b. 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 35.0.
- c. 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 105.0.

**DISCUSSION**

Hepatitis C Virus infection is global health problem and HCV prevalence is nearly 200 million people worldwide.<sup>13</sup> The seroprevalence of Hepatitis C virus in different parts of Pakistan has been reported from 2.2%-13.5%. The highest seroprevalence of hepatitis C has been reported from Lahore (13.5%) as compared to other part of cities.<sup>14-16</sup>

Pakistan has low literacy rate and the people have lack of information of virus transmission. The parenteral

routes are common mode of spread .Hence HCV infection has become an economic burden in our country. SVR defined as the absence of HCV- RNA after 6 months of IFN therapy in chronic HCV patients. The average response rate of combination of conventional INF therapy with ribavirin in chronic HCV patients in our study was 68.6% [Table]. The HCV response rate p=<0.001) was statistical significant in our study comparable to other studies conducted locally<sup>17-19</sup> and internationally<sup>20-21</sup>. In HCV RNA infection six genotypes subtypes have been recognized. These genotyping are important predictors for duration of interferon and SVR<sup>22</sup>.Genotype 1 is the commonest in North, South America, Europe and Japan. In China genotype 4 and genotype 3 is predominant in Pakistan and is involved in 67% to 87% cases.<sup>23-26</sup> Due to high cost, genotyping was not performed in most ours cases and presumed the prevalence of genotype 3 as evidence based on from many studies of our county.

The different responses to INF in our country may be due to prevalence of different strain of genotypes of HCV RNA viruses. Besides this lower response rate in our country could be attributed to the prevalence of resistant HCV genotypes, non compliance to treatment, poor maintenance of colds chain, poor type and quality of therapy .The immigration of people from HCV resistant region like Central Asian Countries to this



region and their virus transmission can result poor response of viruses resistance to conventional combination INF RBA therapy.<sup>27-30</sup> This study has obvious limitations as HCV 'genotyping was not done because of overall poverty of many patients..

## CONCLUSION

This study shows that combination antiviral therapy of conventional interferon alpha along with ribavirin is effective against chronic HCV infective patients. The high response rate may be due to prevalence of IFN-responsive HCV genotypes in our district..

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# Income Status and Medical History of Older Persons in Rawalpindi: Anthropology of Ageing

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## ABSTRACT

**Objective:** The aim of study is to highlight the hidden ageing population and its problems. The specific purpose of the study was to explore the interrelationship of ageing with income as well as the medical history among the older persons of Rawalpindi city.

**Study Design:** Cross Sectional

**Place and Duration of Study:** This study was commissioned to the research team on behalf of Help Age Pakistan. The data collection was done in various union councils of Rawalpindi city. The study duration was three months of 2013.

**Materials and Methods:** Structured questionnaire was developed to collect information on Older Persons' health, economic and psychological status. In this regard, an extensive questionnaire was designed and pre-tested vigorously. Number of researchers from PMAS-Arid Agriculture University was engaged to collect data.

**Results:** There is a strong relationship between the income statuses of OPs with their health physical conditions. The lack of permanent source of income leads to the high tendency of contracting various health problems among OPs. Similarly the inactive status of OPs also affects their health wellness which later on leads to create a multiplier effect regarding various health problems like heart problems, hypertension, diabetes, arthritis, asthma, etc.

**Conclusion:** There is a strong relation of income stability with the various psycho-somatic problems. The sense of being actively involved in familial functions especially economic chores provide a sense of independence and psychological sense of control over life results in better health among OPs.

**Key Words:** Ageing, Older Persons (OPs), Income, Health Issues, Diseases, Heart Problems, Hypertension, Arthritis, Asthma

## INTRODUCTION

Ageing though an important stage of human's life but yet unexplored in Pakistan has several implications regarding its productivity and contributions in the overall development of Pakistani society. Getting older in South Asian social environment is associated with a sense of getting senile as well as disappearing into a state of oblivion.

Anthropology is the scientific study of humankind's origin, biology, and culture. It encompasses a vast and some might say untidy-body of knowledge that has rarely been organized<sup>1</sup>.

Anthropology is the only human science that explores the humanity in a systematic way while connecting the remote and recent past and connects it with the current scenario of man while explaining the change over various epochs of history. The life cycle of man includes conception, birth, adolescence, adulthood and ageing.

Biological anthropologists have contributed to the study of aging in numerous areas, with an emphasis on chronic disease, bone biology, reproductive biology, and body composition. Since aging and the processes of senescence clearly involve complex interactions among

biological, environmental, and cultural domains, anthropologists with a bio-cultural and evolutionary perspective are well equipped to study variation in aging and senescence. Despite this advantage, relatively few biological anthropologists have focused on aging<sup>2</sup>.

Income security during retirement is a primary social achievement of the 20th century. As individuals retired from work at younger ages and life spans increased, the period between the formal end of work and death became one of the most significant stages of life. This enormous accomplishment, however, was accompanied by fundamental public policy challenges associated with the risks posed by population aging. The two most basic challenges were (1) that individuals would have sufficient income security during their retirement years so that retirement did not necessarily imply a substantial decline in living standards and (2) that individuals would have protection against the increasing risks of falling into poor health. During the last century, industrialized nations responded to the problem of having sufficient income to achieve a decent standard of living during retirement by developing the now-familiar three-tiered system: the primary role of the public tier is to guarantee through governmental transfers at least a minimum income standard during

retirement; the second tier is based on employer-provided pensions; and the third tier consists of wealth accumulation through private household savings (National Academy of Sciences, 2001).

Health, although it is a factor of importance for both individuals and society as a whole, is a difficult entity to define. Culyer (1981) distinguishes between four main approaches to the definition of health: health as the absence of disease (a medical model approach); health as the absence of illness (a sociological perspective); health as an ideal state (the World Health Organization model); and health as a pragmatically defined entity<sup>3</sup>.

The medical model of health focuses upon the identification, diagnosis and treatment of disease. The term disease is usually used to describe the medical concept of a defect or abnormality in function or structure of any part, process or a system of the body. This is the province of physicians and specialists in the treatment of older people. In this conceptualization individuals (or groups or entire societies) are healthy if they are characterized by the absence of disease. Hence health is defined by what it is not, i.e. health is not having a disease. If you are not 'sick' then you are 'healthy'. This is a rather limited conceptual framework for the study of ageing; the medical model offers only limited insights into the complex phenomena of health for three major reasons. First, this approach is highly reductionist. Explanation for the presence or absence of disease in individuals is sought in terms of physiological and biological functions without reference to the social or psychological context within which individuals' live<sup>4</sup>.

Indeed Estes and Binney (1989) suggest that 'ageing' has also been medicalised with the result that older people and old age are pathologised and ageing is constructed as a medical problem with a consequent emphasis upon medical research and medically based 'solutions' to the problem of ageing. Emphasis is placed upon identifying the 'abnormal' rather than the 'normal' in the experience of ageing<sup>5</sup>.

Many aspects of the experience of ageing, therefore, are 'problematised' and become the domain of experts and problem solvers rather than being seen as part of a normal transition or changes that characterize the post-mature individual<sup>6</sup>.

Talcott Parsons (1951) argued that those who are ill are not required to perform their normal social roles but adopt the 'sick role' that is characterized by the adoption of a dependent rather than an independent status. This transition may be very distressing for the individual concerned given the heavy emphasis placed in our society upon remaining independent and autonomous. The sick role is not expected to be of long duration. The long-term sick, or those with particular illnesses such as epilepsy or various mental disorders, can come to acquire a highly stigmatized status because

of the extensive duration of their illness. A similar stigmatizing status may be ascribed to older people because of the perceived widespread prevalence of chronic illness and its extensive and debilitating nature that can compromise independence and autonomy<sup>7</sup>.

Illness behavior is a complex aspect of social interaction that involves the individual in monitoring their body, interpreting symptoms, taking curative action and seeking help from the health care system or other appropriate agencies. Even in Britain, which has a national health care service which provides care free of charge, the vast majority of illness is not presented for consideration by the health care services. Only an estimated quarter to one-third of all illness episodes result in a medical consultation<sup>8</sup>. The decision to seek medical aid is only one illness behavior strategy out of a whole range of possible options, which includes self-care, folk remedies, consultation with friends or relatives or use of 'alternative' or complementary over-the-counter therapies.

Sociologists interested in illness behavior have largely focused upon the younger members of the population. Ford (1985) has attempted to review illness behavior in later life and its variation from that characteristic of younger age groups. One of the enduring stereotypes about old age is that treatable illnesses are mis-ascribed by older people to the process of ageing rather than being the manifestation of 'disease'<sup>8</sup>. Consequently, it is argued, older people do not seek appropriate treatment. In support of this view; a variety of studies have demonstrated that there are a large number of previously unidentified medical conditions to be found among older people living at home<sup>9</sup>.

Regardless of the age of individuals, attitudes towards health beliefs are complex and often, apparently, contradictory. Views of, and definitions of, health are culturally and historically rooted and related to the values and expectations of particular groups. Furthermore health related beliefs and attitudes almost certainly vary with regard to class, gender, age, and ethnicity<sup>10</sup> and, taking this complexity one stage further, a single individual may hold apparently conflicting, and mutually exclusive, beliefs at the same time<sup>11</sup>.

Evandrou (2000) reports that rates of acute illness are elevated among elders from Bangladeshi/Pakistani backgrounds but that there are also gender variations within this overall pattern<sup>12</sup>.

Chronic health problems are, by definition, long term and not usually characterized by a cure. Implicit within the term is also the notion of inevitable decline or deterioration. Medical intervention may (or may not) alleviate some, or all, of the associated symptoms and may halt (or slow down) the rate of decline. Examples of such long-term health problems are multiple sclerosis, dementia and arthritis. It is this type of health problem that is specifically identified by both the

general public and many professional health workers alike as an integral, inevitable, natural and universal feature of old age<sup>4</sup>.

Christina R. Victor (2005) describes Ageism, it is argued, is not experienced equally by men and women for older women experience both ageism and sexism. They are discriminated against, or viewed negatively, because they are both old and female<sup>4</sup>. This double disadvantage is reflected in what has been termed the double standard of ageing. The notion that men and women differentially experience old age is not a new one: indeed it has a long historical pedigree. Hippocrates considered that old age started for men between the ages of 55 and 60 while for women old age started a decade earlier. In a similar vein Plato saw the prime of life as 30 years for man and 20 years for a woman. According to this widespread social view, old age for women starts earlier than for men and lasts for many more years. However, this discrepancy in the perceived onset of old age has no biological basis: life expectancy for a male is several years shorter than that of a female. Rather, this difference in the perceived onset of old age is socially defined, constructed, maintained and legitimized.

Cardiovascular disease (defined for these purposes as history of myocardial infarction, angina pectoris, coronary insufficiency, intermittent claudication, or congestive heart failure) and diabetes mellitus are among the leading causes of death in the elderly, while the other CVRFs also are strongly associated with mortality<sup>13</sup>.

As reviewed by Hayward (1995), several older studies found associations between depression and cardiovascular disease, hypertension, or hypercholesterolemia. However, interpretation of most of these studies must be tempered by methodological issues, including retrospective design, samples from long-term psychiatric institutions, or depression assessments using solely self-report scales or non-standardized diagnostic schemes<sup>14</sup>.

Despite this, there is substantial evidence that disability is associated with depression as well as with CVRFs<sup>15-17</sup>. Psychological models can be invoked to explain how external disability may lead to the changes in mental experiences that are part of depression. For example, disability may be viewed as representing a breakdown in primary control processes<sup>18</sup>.

Disability was independently associated with depressive symptoms and syndromes in primary care elderly<sup>19</sup>.

Older depressives, as compared to both younger depressives and age-matched non-depressed controls, demonstrate both a breadth and severity of neuropsychological abnormalities that may reflect underlying brain dysfunction<sup>20,21</sup>.

A review of the current literature on the relationship between aging and depression consistently implicates a

third variable, functional disability; persons with more disability tend to be more depressed, and functional disability tends to increase with age<sup>22,23</sup>.

## MATERIALS AND METHODS

To collect the data of Older Persons' of Rawalpindi a Structured questionnaire was developed including their health, economic and psychological status. To gather the data in this regards, an extensive questionnaire was designed and pre-tested to improve the quality of the tool.

Questionnaire consisted on the areas of bio-informatics including demographic information of clients and the second area covered base-line information, third area contained information on economic status, fourth area was about the medical histories of the older persons, fifth section comprised information on Social and Psychological profile of OPs, and the last & sixth part consisted information about legal and social protection issues of OPs.

Questionnaires were administered through a research team that comprised the graduates of department of Anthropology of PMAS-Arid Agriculture University along with professionals of Regional Development Network (RDN) as well as field staff of Pakistan National Center on Ageing (PNCA).

## RESULTS

Below chart co-relates the source of income with disease status. The table proves that OPs who did not have any permanent source of income had the tendency to catch more diseases as compared to the OPs with somewhat defined source of incomes.

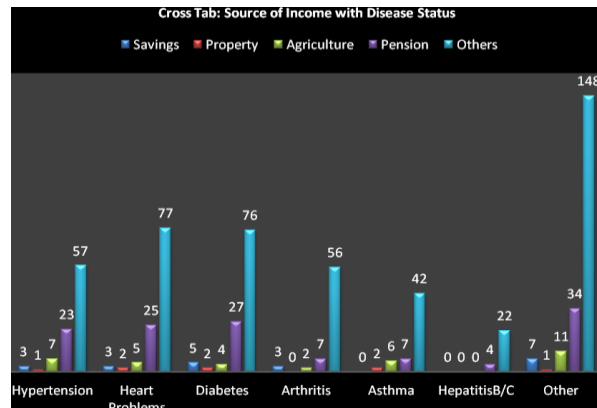


Chart: Source of Income with Disease Status

The current table clearly establishes the co-relation of older persons' economic status and the diseases contracted by them. It strongly proves that economically inactive OPs possess highest tendency to catch health problems as compared with the ones who are still economically active and earning their living.

**Table No. 1: Comparison of OPs economically active status with Disease Status**

Still Economically Act	Disease Status								Total
	Hypertension	Heart Problems	Diabetes	Arthritis	Asthma	Hepatitis B/C	Other	NA/ No disease	
Yes	34	44	49	24	19	9	91	173	443
No	62	75	67	47	40	18	114	134	557
Total	96	119	116	71	59	27	205	307	1000

## DISCUSSION

The older persons' study and the intensive interviewing revealed that the economic turmoil of the down trodden segments of the society has negatively affected them. The rising tide of employment in the national scenario is creating a multiplier effect that directly results in the socio-economic instabilities of the families. The low income of families leaves them in compromising to extreme compromising situation in which the health is the domain that is usually ignored or thrown in adjournment due to the non-negotiating status of the families that are poverty stricken. The poor economic situation further affects the health of OPs who usually sacrifice or are expected to sacrifice their health wellness as the cost of other family members especially the earning hands. This finding fully reinforces the argument presented by Ford who says 'even in Britain, which has a national health care service which provides care free of charge, the vast majority of illness is not presented for consideration by the health care services. Only an estimated quarter to one-third of all illness episodes result in a medical consultation'<sup>8</sup>.

It was observed that the OPs of Rawalpindi city preferred to work even beyond the call of duty just to make sure that they earn something for the family which indirectly wins social approval and protects them from social exclusion in various matters of family concern. It was also noted down that the OPs generally wished to keep themselves busy in order to avoid certain tensions and mental stresses that directly bears upon their health. The sample of the study presented important statistics regarding the health wellness and its relation with the income earned by the family and especially the OPs.

The respondents with savings, property, agricultural land, pensions and other alternate sources of livelihood scored better on their health status. On the contrary the OPs with no such options suffered from heart related complications, arthritis, asthma, and hypertensions. This observance confirms the contention advocated by Talcott Parsons who adds that sickness is a kind of social behavior is a behavior that is 'not expected to be of long duration.

It is important to understand that the 'long-term sick, or those with particular illnesses such as epilepsy or various mental disorders, can come to acquire a highly stigmatized status because of the extensive duration of their illness.

The lack of appropriate knowledge regarding health well-being among older persons is rightly stated by the scholar Ford who says that various medical complications are simply interpreted in terms of ageing process instead of seeking proper medical advice on it. Similarly, Williamson et al. (1964) seemed true that 'there are a large number of previously unidentified medical conditions to be found among older people living at home'<sup>9</sup>.

The important observations made during the study emphasize that the overall poor health performance of the older persons is directly related to the instable and irregular income of the families. The situation goes more worth noticing that among OPs the older females scored very low and alarmingly poor within the respondent group. Though medically, socially and religiously the older persons are graded at a high level but the miserable material conditions make it inevitable for them to keep economically active. This trend on the contrary seemed positively responsive in relation to the healthy status of OPs. The review of literature contends that various psychoneurosis issues are also related to the psychosomatic problems. As in case of findings presented by Broadhead, Blazer, George, & Tse, (1990); Kennedy, Kelman, & Thomas (1990); as well as with CVRFs (Bush et al., 1990); Schulz, Heckhausen, & O'Brien (1994) and Lyness et al. (1998).<sup>15-19</sup>

The Pakistan Economic Survey 2012-13 though surveys the main health related interventions planned on behalf of the government but unfortunately lacks any mentionable interventions aimed at the welfare of the Older Persons. The health insurance sector in Pakistan is still in its infancy and does not at all guarantees its universal coverage to all Pakistanis irrespective of their age, area or any other special requirements. Similarly, the health targeted programs like Individual Financial Assistance (IFA), Child Support Programs (CSP) and Special Friends of Pakistan Bait-ul-Maal (PBM) severely lack any quantitative or qualitative data to ensure the transparency of the initiatives and its universal access. Even during the phases of data collection, the respondents revealed that Benazir Income Support Program (BISP) is highly politicized and accused of political nepotism. Even the monetary support provided to the so-called poor does not make any plausible and arguable difference in the lives of beneficiaries' families<sup>24</sup>.

Pakistan being a third world country is entangled with numerous developmental challenges ranging from

political instability, poor economic performance, serious violations of human rights, low regional and continental as well as international performance on health, education and gender indicators. Ageing is relatively a new topic for the development intelligentsia, development champions, legislators, policy makers, development and human rights agencies and media. There is a need to mainstream ageing into the so-called development agenda of the Pakistan especially in an international scenario where the world has recently adopted the Global Age Index in recent October 2013 to evaluate the countries' performance on Global Age Index.

## CONCLUSION

The income or the material assets of a person or a family is a social guarantee of material gratifications. The older persons are usually the victims of adverse economic clutch that is directly responsible for their poor health status. There is direct interrelationship between the income and the health indicators. Similarly, the OPs still economically operational report less health issues but the sub-indicators of lack of awareness and health sensitization also play its role in health issues faced by OPs.

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# Familial Predisposition and Gender Discrimination in Patients with Facial Clefts in Local Population

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## ABSTRACT

**Objective:** To objective of this study was to know Familial Predisposition and Gender Discrimination in Patients with Facial Clefts in Local Population.

**Study Design:** Retrospective observational study.

**Place and Duration of Study:** This study was carried on the data was retrieved from the documented files of patients presenting for plastic surgery at Shalimar Hospital and Children's Hospital and Arif Memorial Hospital from September 2009 to September 2012.

**Methods and Material:** The current study was conducted to cross link the occurrence of facial clefts with family history and gender. The profile of 126 patients was collected which were under treatment at various hospitals and was analyzed and evaluated.

**Results:** Results of the study demonstrated clear gender discrimination; with the incidence of bilateral cleft lip and palate more in males, and unilateral cleft lip and palate had a female predominance. A close association of patients with a positive family history was also seen in the study, 50% of patients with unilateral cleft lip and 50% of patients with bilateral cleft lip exhibited a positive history. 75% of patients with unilateral cleft lip and palate and 25% of the patients with bilateral cleft lip and palate had positive family history. All patients with unilateral cleft palate had a positive family history. A close association demonstrated between the gender, positive family history and facial clefts led us to postulate that a probability of a genetic predisposition cannot be overlooked.

**Conclusion:** The call of the day is that the future researches pertaining to facial clefts should aim their energies in isolation and localization of the Genetic and/or environmental factors responsible for the congenital malformation. The cleft per se could disappear from the Earth in a near future owing to the gene therapy and prenatal or, perhaps pre-conception screening, which will be able to eliminate the menace before it can disfigure the face of humanity.

**Key Words:** Facial Clefts, Cleft palate, Cleft lip

## INTRODUCTION

Surveillance studies have shown that cleft lip and cleft palate is one of the commonest Cranio-facial anomalies occurring in approximately 1 in 500 live births<sup>1</sup>. They accounts for 65% of all head and neck anomalies<sup>2</sup>. These clefts are conspicuous as they result in abnormal facial appearance and defective speech<sup>3</sup>. Palatal clefts have also been associated previously with a progressive hearing loss<sup>4</sup>.

Clinical and epidemiological studies on the incidence of cleft lip and palate were carried out in Pakistan in 2004 which showed that it was 1.91 per 1000 live births. Cleft lip alone was 42% and cleft palate 24% and combined cleft lip and palate was 34%<sup>5</sup>.

The development of head and neck begins in the 4<sup>th</sup> week of intrauterine life, even before a woman is aware that she is pregnant. The initiation of face development is by the appearance of five facial primordia around the stomodeum. These include one frontonasal prominence, and paired maxillary and mandibular prominences. A major contribution is also provided by an ectodermal placode formed at the inferior part of fronto-nasal prominence, termed Nasal placode. The nasal placode proliferates to form the medial and lateral nasal

prominences which contribute in the development of nose, upper lip and primary palate by formation of the inter-maxillary segment<sup>3</sup>.

Facial clefts, that is, of lip and palate occur whenever there is a failure of union of these facial primordia with each other or with the nasal prominences. A unilateral cleft lip is produced from failure of maxillary prominence on affected side to unite with medial nasal prominence. A bilateral cleft lip results from failure of both maxillary prominences to meet and unite with merged medial nasal prominences<sup>2</sup>. A median cleft lip is rare and is produced due to incomplete merging of two medial nasal prominences in midline. Cleft palate results from lack of fusion of palatine shelves<sup>6</sup>.

The incidence of facial clefts has been also associated with a magnitude of factors including alcohol abuse, smoking, malnutrition, retinoic acid and positive family history<sup>7, 2</sup>. A close association between occurrence of facial clefts and congenital heart disease has also been reported<sup>8</sup>.

Clinical and epidemiologic studies of defined geographic populations can serve as a means of establishing data important for the diagnosis, treatment, and counseling of patients with cleft lip and cleft palate. Several descriptive epidemiologic studies have been



carried out in many countries worldwide; however, no such study in Pakistan has correlated the occurrence of facial clefts with gender predisposition and family history. The purpose of this study is to document the frequency with which the clefts appear in males and females and the association of facial clefts with family history.

**MATERIALS AND METHODS**

This is retrospective observational study. The study group consisted of all children with cleft lip alone and cleft palate alone and cleft palate with or without cleft lip. Data was retrieved from the documented files of patients presenting for plastic surgery at Shalimar Hospital and Children’s Hospital and Arif Memorial Hospital. Firstly all patients with cleft lip and palate were recognized and categorized. Those who were born with cleft on their lip were called CL patients. Those who were born with cleft on their palate were called CP patients and those who have clefts on their lips extending to their palate were called as CL+CP patients<sup>9</sup>.

**RESULTS**

Total number of patients with facial cleft was 126. patients with cleft lip were 31, cleft lip and palate were 43, cleft palate were 35, cleft lip and nasal deformity were 2, median cleft lip were 2 and with cleft lip, palate and nasal deformity were 3.

Following variants of facial clefts were analyzed.  
**Gender:** Total number of patients was 126 with 64 males and 62 females.

**A) Cleft lip:**

Out of 31 patients with cleft lip, 25 patients have unilateral cleft lip, among which 48% were males and 52% were females.

3 patients were suffering from bilateral cleft lip, out of which 66.67% were females and 33.33% were males (Table 1).

3 patients were diagnosed to have median cleft lip. 66.67% of them were males and 33.33% were females (Table 1).

**B) Cleft lip and palate:**

Unilateral cleft lip and palate was found in 32 patients. 43.75% of these patients were males and 56.25% were females.

Bilateral cleft lip and palate was present in 10 cases. 70% of them were males and 30% were females (Table 1).

**C) Cleft palate:**

There were 35 cases of cleft palate. 16 patients of cleft palate were males and 19 of them were females. 50% of the male patients had cleft of both soft and hard palate and 50% had cleft of soft palate alone. Cleft of hard palate alone was found in none of them.

47.37% of female patients had cleft of soft palate and 52.63% had cleft of both soft and hard palate. Cleft of hard palate alone was not found in any female patients (Table 1).

**D) Cleft lip and nasal deformity:**

There were 2 patients with cleft lip and nasal deformity. 50% of them were males and 50% were females (Table 1).

**E) Cleft lip, palate and nasal deformity:**

There were 3 patients with cleft lip, palate and nasal deformity. 33.33% of which were males and 66.67% were females (Table 1).

**Table No.1: Sexual distribution of facial clefts**

	Diagnosis	Males	Females
1.	Cleft lip		
2.	Unilateral	48%	52%
3.	Bilateral	66.67%	33.33%
4.	Median	66.67%	33.33%
5.	Cleft lip and palate		
6.	Unilateral	43.75%	56.25%
7.	Bilateral	70%	30%
8.	Cleft palate		
9.	Soft palate	50%	47.37%
10.	Soft and hard palate	50%	52.63%
11.	Cleft lip and nasal deformity	50%	50%
12.	Cleft lip, plate and nasal deformity	33.33%	66.67%

**Table No.2: The frequency of positive family history of facial clefts.**

	Diagnosis	Positive family history of facial clefts
1.	Cleft lip	
	Unilateral	50%
	Bilateral	50%
2.	Cleft lip and palate	
	Unilateral	75%
	Bilateral	25%
3.	Cleft palate	
	Unilateral	100%

**Positive family history of facial clefts:**

Out of 126 patients 9 had positive family history of facial clefts and 117 had negative family history. 5 Patients with positive family history of facial clefts were males and 4 were females.

**A) Cleft lip:**

2 patients with positive family history were suffering from cleft lip. 50% of them were unilateral and 50% had bilateral cleft lip.

**B) Cleft lip and palate**

Positive family history was present in 4 patients with cleft lip and palate. 75% of them had unilateral cleft lip and palate and 25% was suffering from bilateral cleft lip and palate (table 2).

**C) Cleft palate:**

3 out of 9 patients with positive family history of facial clefts had cleft palate and all of them had unilateral cleft palate (table 2)

**DISCUSSION**

Genetic, environmental and drug abuse have previously been associated with the occurrence of facial clefts.

A study conducted in Poland in 2007 by Kot et al concluded that 17% of patients with cleft lip and/or palate had a positive family history which is in accordance with our study in which familial predisposition was seen in 7% of patients. The study also reported that the type of cleft in a child depends not only on the type of cleft in parent but there is greater risk of clefts in sons of mothers with cleft lip (CL) or cleft lip and palate (CL+P) or fathers with cleft lip (CL) and in daughters of mothers or fathers with cleft palate (CP)<sup>10</sup>.

A close association between children born of a consanguineous marriage and the incidence facial clefts was also reported by Shafi et al in 2003, this study, however, also reported that facial clefts observed in patients born of a consanguineous marriage had associated malformations particularly heart disease. The co-occurrence of facial clefts with heart defects can be owed to a fact that neural crest cells make a major contributor in the development of both, any malformation in migration or differentiation of neural crest cells can lead to the two defects to co-exist<sup>8</sup>. Gender discrimination was also evident in the study, a higher incidence of unilateral cleft lip (CL) and cleft lip and palate (CL+CP) was exhibited in females as compared to a high frequency of bilateral cleft lip in males. Clefts of soft palate alone were more frequent in males; however clefts of both soft and hard palate were more frequent in females (Table 1). These results are in accordance with results of study done in country of Stockholm between 1991 and 1995 which reports high incidence of bilateral clefts lip (CL), cleft palate (CP) and cleft lip and palate (CL+P) in males than in females<sup>11</sup>. Kim S. et al reported in 2002 that the male: female ratio was 2.1:1 in cleft lip (CL) group, 2.5:1 in cleft palate (CP) group and 0.95:1 in cleft lip and palate (CL+P) group<sup>12</sup>. J Womersley and DH Stone reported in 1987 that males predominated for cleft lip, females for cleft palate.

Peterka M. et al. in 1996 documented that among children of mother with cleft lip, 68% were boys and 32% were girls with cleft lip or cleft lip and palate. If the mother had cleft lip and palate, the same cleft was

found in 64% of boys and 15% of girls. If the mother had cleft palate, the same type was present in 37% of boys and 51% of girls. Similar results were found for affected fathers and their children with only exception among children of fathers with cleft lip and palate, the percentage of boys and girls with cleft lip was 43% and 40%, respectively<sup>9</sup>.

The gender predisposition observed in the studies can be postulated to be caused by a gene, as previously suggested by Mladina et al in 2009. According to them the probability and possibility of presence of a gene responsible for the onset of facial clefts is great<sup>1</sup>. Specific environmental factors are known to contribute to facial clefts, these include infectious agents, x-ray radiations, drugs, hormones and nutritional deficiencies. Hox family of homeobox genes expressed in rhombomeres is important in head and neck development<sup>14</sup>. Retinoic acid regulates Hox complex which in turn regulates head and neck development<sup>6</sup>.

**CONCLUSION**

The call of the day is that the future researches pertaining to facial clefts should aim their energies in isolation and localization of the Genetic and/or environmental factors responsible for the congenital malformation. The cleft per se could disappear from the Earth in a near future owing to the gene therapy and prenatal or, perhaps pre-conception screening, which will be able to eliminate the menace before it can disfigure the face of humanity.

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# Frequency of Thyroid Cancer at King Fahad Hospital, Madinah

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## ABSTRACT

**Objective:** To assess the frequency of common thyroid cancer at King Fahad Hospital, Madinah.

**Study Design:** Retrospective study.

**Place and Duration of Study:** This study was carried out on all the patients treated for Cancer of Thyroid Gland, at King Fahad Hospital (KFH)-Madinah between Jan 2009 to February 2012.

**Patients and Methods:** Ninety-one patients diagnosed with Cancer of Thyroid of various Age, Sex & Races were registered with King Fahad Hospital Madinah.

**Results:** 75% patients were Saudi nationals, 10 % patients were from other Arab countries and the remaining 15 % were non-Arabs. There were 72% females and 28% Males. The Ages ranged from 14 years to 94 years. 34% of these patients were less than 30 years of Age at the time of the diagnosis. Over 90 % of the cases presented with Swelling Anterior Neck while in other 10% of the cases Dysphagia or Dyspnoea with Rt. or Lt. supraclavicular mass/swelling was the major complaint. 71% patients under went various surgical procedures for the Neck swelling. The Total Thyroidectomy was done in 48% patients. The Histology revealed 52 % of pure Papillary Carcinoma and 23 % were of Follicular origin. Majority of the diagnosed patients of Ca. Thyroid were referred to King Faisal Specialist Hospital Riyadh for Radioactive Iodine Ablation Therapy. The follow-up was poor as patients were from highly mobile population and belonged to Nine different countries.

**Conclusion:** The study reveals that the presentation of Ca. Thyroid in our series is essentially similar to what has been reported from other parts of the world.

**Key Words:** Radioactive Iodine (RAI) Ablation Therapy, Thyroidectomy, Thyroglobulin, Goiter, Malignancy, Thyroid.

## INTRODUCTION

Thyroid cancer is a relatively rare and comprises a heterogeneous group of malignant neoplasms that show differences in biological behavior, but the prognosis as well<sup>1-2</sup>. Follicular cancer tends to metastasize to the lungs and bones, while the papillary carcinoma commonly spreads to the lymph nodes. Metastases to the cervical lymph nodes are located in the 15% -50% of papillary carcinoma when time of diagnosis<sup>3</sup>. Thyroid cancer is the most common of all cancers of the endocrine glands, which represents 87% of all cancers of the endocrine glands. Thyroid cancer, although relatively rare, is the second most common cancer among women in Saudi Arabia<sup>4-7</sup>.

Over the past two decades, there has been significant improvement in the survival of the cancer patients in general and those suffering from Cancer of thyroid. This is largely attributed to the multicentre prospective studies conducted by various Centers in the United States, Europe and other internationally recognized institutes<sup>8,9</sup>. However this may not be the case in the developing countries where social as well as the regional factors contributes to the outcome of the disease. The study of epidemiology and pattern of cancer is of the utmost importance for the establishment of the both preventive and therapeutic measures. This

calls for the setting up of a Multicentre National Cancer Registry in the Kingdom of the Saudi Arabia for Ca. Thyroid patients.

## PATIENTS AND METHODS

The King Fahad Hospital (KFH)-Madinah is a tertiary care referral hospital in the Kingdom of Saudi Arabia. A retrospective study was done of all the patients treated for Cancer of Thyroid Gland at the hospital between Jan 2009 to February 2012. Between this period 91 patients were treated at the hospital for the various types of thyroid malignancies. The Medical Records of these patients of Ca. Thyroid were reviewed for the Age at diagnosis, Sex & Mode of presentation. An attempt is also made to analyze the Ethnic distribution, Initial diagnosis before registration with KFH, Clinical Extent of the disease at Initial Presentation, the Commonest type of Malignancy and the type of treatment given in these patients.

## RESULTS

Ninety-one (91) patients diagnosed with Cancer of Thyroid of different Age, Sex and races were registered at KFH between the study period. Of these, 68 patients were Saudi nationals, 09 patients were from other Arab countries and remaining 14 patients were

non-Arabs Chart No-1. There were 66 Females and 25 Males. The Female to male ratio was 5:2. The Ages ranged from 14 years to 94 years. 31 of these patients were less than 30 years of Age at the time of the diagnosis. Over 90 percent of the cases presented with Swelling Anterior Neck while in other 8 to 10 percent cases Dysphagia & Dyspnoea with Rt. or Lt. supraclavicular mass/swelling was the major complaint. Their mode of presentation is given in Table-1. Of these 91 patients , one patient was diagnosed having Sub-Sternal mass, one patient came with the complaints of Scrotal swelling who was diagnosed coincidentally as a case of Ca. Thyroid and the one patient came with the diagnosis of Lipoma Thyroid. Majority of the patients 63 (69%) were referred from various local or territory hospitals around Madinah with the provisional diagnosis of Goiter while 07(8 %) patients were referred with the diagnosis of Ca. Thyroid.

**Clinical Extent:** Well Differentiated Papillary Ca. tends to metastasize to local neck nodes while Follicular lesions tends to hematogenously metastasize mostly to Lungs and Skeleton<sup>3,9,10,11</sup>. In our series the disease was diagnosed at early stage as in 73 ( 80 %) patients the disease was localized while wide spread Metastasis ( Lungs Bone etc.) was noted in 13 ( 14 %) patients. Five (5.5 %) patients came with the Recurrence of the disease.

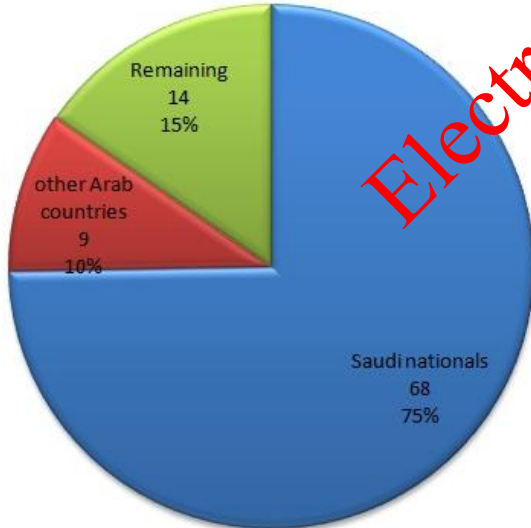


Chart No.1: Nationality

**Predominant Histology & Treatment:** Primary treatment offered at KFH was Surgery which was followed by the Radioactive Iodine 131 Ablation Therapy at King Faisal Specialist Hospital (KFSH)-Riyadh. The surgical procedures were chosen according to the Clinical Status and the Extent (staging) of the disease. 65 ( 71% ) patients under went various surgical procedures for the Neck Swelling. The Total Thyroidectomy was done in 31 ( 48 % ) patients, Near

Total Thyroidecomy in 8 (12 %) patients, Sub-Total Thyroidectomy in 12 cases (18%) while the Partial Thyroidectomy was carried out in 14(21 %) patients Table No. 2. Due to poor general condition or other accompanying systemic diseases the surgery was not possible in 10 (11 % ) patients and these patients were given only symptomatic treatment. Due to extensive disease 11 (12 %) patients were Inoperable , these patients were refereed to KFSH Riyadh for further management while in other 5 patients the details of the surgery was not available.

Majority of the diagnosed patients of Ca. Thyroid from KFH-Medina were referred to King Faisal Specialist Hospital - Riyadh for Radio-active I-131 Ablation Therapy.

Table No.1: Presenting symptoms

Symptoms	No. of Patients	Percentage
Neck mass	91	100%
Dysphagia	17	18.68%
Pain	10	10.98%
Dyspnea	8	8.79%
Hoarseness	6	6.59%
Thyrotoxicosis	3	3.29%
Weight loss	2	2.19%

Table No.2: Surgical Procedures (n=65)

Symptoms	No. of Patients	Percentage
Total	31	48%
Thyroidectomy		
Near Total	8	12%
Sub-Total	12	18%
Partial	14	21

**DISCUSSION**

The incidence of thyroid cancer is increasing much faster than any other cancer in the United States (including liver cancer), almost tripled from 1980 to 2006. Improved diagnosis has been proposed as the main reason for this change by some, while others argue that other factors are responsible for the increase<sup>10,11</sup>. Cancer of thyroid is more common in women than men<sup>12</sup>. In our set up, majority of the female patients attending out patient clinics are Muslims , covering their faces and neck and hesitate to uncover. Without proper physical examination of the neck, small or deeply cited thyroid nodule may remain obscure or undiagnosed . This indicates the importance of the physical examination of the neck even if the presenting complaint is only dysphagia or dyspnoea. The female patients may be explained the importance of the physical exam to overcome this problem.

It is interesting to note that patients with the complaint

of Neck swelling attended the hospital after considerable laps of time. 10 % of these patients came with the history of Neck swelling for a period more than 10 years while 22 % patients with Neck swelling for a duration between 5 to 10 years. Despite of other complications, in the long-standing cases there is high probability of cancerous changes in thyroid nodules. Awareness in the general population regarding Thyroid related diseases and its outcome in long-standing cases may be an ultimate remedy.

Although most thyroid nodules are not cancerous, thyroid cancer is diagnosed in about 10,000 people each year in United States<sup>13</sup>. The Fine Needle Aspiration Cytology (FNAC) of palpable nodules in the thyroid gland may also greatly contribute in the early detection of the disease. The thyroid scan may differentiate between Hot and Cold nodules. As reported in many international journals the cold nodules are more prone to be cancerous than Hot nodules<sup>14</sup>. This may increase the sensitivity of FNAC and help in selecting patients for the procedure. The thyroid scintigraphy and FNAC is routinely carried out in our hospital and majority of our patients had thyroid scanning and FNAC in this series.

Total or near Total thyroidectomy is preferable to a more limited excision, specially in persons with primary lesions that are larger than 2.5 cm, multiple or locally invasive<sup>15,16</sup>. In our series 39 patients (60 %) out of selected 65 patients for thyroid surgery had Total or near Total Thyroidectomy.

The use of Radioactive Iodine 131 in the treatment of cancer of thyroid has a sound theoretical basis<sup>17</sup>. Iodine organification is a thyroid specific function and <sup>131</sup>I is an effective agent for delivering radiation to the thyroid tissue with low radiation dose to other portions of the body. Despite the theoretical suitability it is not clear whether such therapy prolongs life. Various series report either no effect or an effect only in a subset of patients. However this modality is commonly employed because of paucity of long-term complications and acute adverse effects at least in the adult. Due to some limitations, this treatment was not possible at KFH Medina. With the provision of a consultant Endocrinologist and active Nuclear Medicine department, this treatment will soon be started at this hospital.

The Human Thyroglobulin (Tg) is secreted only by thyroid gland and can be elevated in benign thyroid conditions (goiter, benign nodules). It is also secreted by most differentiated thyroid cancer<sup>18</sup>. Post thyroidectomy and ablation therapy, the thyroglobulin measurement does appears to be highly sensitive and specific in the follow up. Sensitivity range 83-100 % and specificity 83-97%. We noticed that very few patients were screened for this important diagnostic modality in our series. This may be due to the reason as the patients were treated in "Split Manner" between

KFH-Medina and King Faisal Specialist Hospital Riyadh and the follow up record of majority of the patients was maintained by KFSH Riyadh.

It was difficult to define the long-term survival rate of these patient as the patients were from a highly mobile population and patients over 9 countries were included in this study. The follow up of the patients was also very poor as most the patients were attending KFSH-Riyadh for their follow-up visits after Radioactive Iodine 131 Therapy.

## CONCLUSION

We have attempted to document those aspects of the management of Thyroid cancer which we believe to be important. We are concerned that patients managed outside the King Fahad Hospital-Medina following surgery, face considerable inconvenience of traveling for their treatment & also for the follow up visits post Radioactive Iodine 131 therapy. Moreover the documentation at re-referral is usually inadequate, which make logical decision making with regard to further therapy at our hospital difficult. Often, it is necessary to make empirical decision based on little data provided. This situation is clearly not ideal for the patients. We hope that the provision of Radioactive Iodine 131 therapy at this hospital will bring an improvement in patients care and management. We also purpose to undertake a quantitative analysis of the problems we have pointed out in this paper.

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# Effect of Relining Methods on Dimensional Accuracy and Stability of Conventional Complete Dentures - A Literature Review

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## ABSTRACT

**Objective:** To review the literature in order to evaluate the effect of relining methods on dimension accuracy and stability of conventional complete denture.

**Study Design:** Review of literature.

**Materials and Methods:** The literature search was mainly performed through internet. Abstracts and full text of articles published in journals indexed by index Medicus were searched Pubmed. A Google search was also performed to obtain material available at websites of different dental associations. The comparison was made among original research studies, cross sectional surveys, meta analysis, review articles and guidelines in context to the purpose of study.

**Results:** The laboratory reline method has relatively good dimensional stability and strength, but presents a major drawback i.e patient has to be without denture for a certain period of time, on the other hand chairside reline method seems to be convenient and easy and require short working time. Autopolymerising acrylic resins have the potential of causing chemical or thermal burns of the oral mucosa. Autopolymerising direct chairside relining materials have been used widely in clinical setting.

**Conclusion:** The Direct chairside method is advisable as it presents the least gap at posterior palatal seal area. However chairside relines are technique sensitive and require experience.

**Key Words:** Relining, Complete Denture, Stability, Retention

## INTRODUCTION

The likelihood of tooth loss increases with age as a result of the cumulative effects of caries, periodontal diseases, trauma and dental treatment<sup>1</sup>. The total number of patients requiring complete dentures is increasing worldwide<sup>2</sup>. Complete dentures are the most common prescription offered to the edentulous patients worldwide<sup>3</sup>. The loss of natural teeth is associated largely with low socioeconomic status<sup>4</sup>.

The recognition, understanding and incorporation of certain mechanical, biologic and physical factors are necessary to ensure optimal complete denture treatment<sup>5</sup>. These factors are the determinants that promote the properties of retention, stability and support in complete dentures<sup>6</sup>. Patient requirement of complete denture are to restore the normal contour, function, comfort and speech. Most of these goals are accomplished through achieving retention<sup>7,8</sup>.

Alveolar ridge inevitably undergoes resorption with advancing age, irrespective of individual uses denture or not. Means available to deal with loss of denture fit are fabricating new dentures or relining<sup>9</sup>.

Relining is a procedure to resurface the tissue surface of denture with new base material to make the denture fit more accurately<sup>10,11</sup>. Relining can reduce the frequency of patients visit and expenses as compared to fabricating new dentures. There are two methods of

relining; direct (Chairside method) or indirect (laboratory method)<sup>12</sup>. In direct method cold cured acrylic or tissue conditioners are used but are not very durable and it's the only short term solution<sup>13</sup>. In indirect method the fitting surface is cleaned. The undercuts are removed and the flanges are shortened. Minor defects and extensions can be corrected with self cure acrylic<sup>14</sup>. The indirect method has advantage over the direct method in that an appropriate thickness can be ensured more easily and adhesion is stronger due to lack of exposure to saliva<sup>15</sup>.

## MATERIALS AND METHODS

The literature search was mainly performed through internet. Abstracts and full text (if available) of articles published in journals indexed by Index Medicus were searched PubMed. A Google search was also performed to obtain material available at the websites of different dental associations. Print material and textbooks were also accessed from different libraries of Liaquat University of Medical & Health Sciences, Jamshoro, including postgraduate section of main library and library at Institute of Dentistry. Some material was also obtained on request from the libraries of College of Physicians & Surgeons Pakistan, Karachi and Jinnah Postgraduate Medical Institute, Karachi.

The material was classified and relevant material was extensively reviewed. The comparison was made



among Original research studies, Cross sectional Surveys, Meta Analysis, Review Articles, and guidelines, in context to the purpose of study i.e to clarify that whether there is any significant role of posterior palatal seal in maxillary complete denture.

## RESULTS

The laboratory relined method has relatively good dimensional stability and strength, but presents a major drawback i.e patient has to be without denture for a certain period of time, on the other hand chairside relined method seems to be convenient and easy and require short working time. Although the materials employed constantly improve, but problems still exist. Autopolymerising acrylic resins have the potential of causing chemical or thermal burns of the oral mucosa. Other disadvantages include poor color stability, porosity, and a foul odor. In addition they are difficult to position correctly, are technique sensitive, and can be toxic due to residual monomer. Autopolymerising direct chairside relining materials have been used widely in clinical setting. It should be mentioned, however, that these materials present problems such as odor, poor color stability, porosity, poor physical and mechanical properties, and irritation of the oral mucosa. The oral tissue irritation is caused by methyl methacrylate, the major constituent of the liquid.

## DISCUSSION

In this study the available literature was reviewed to find out that the effects of relining methods on dimensional accuracy and stability of conventional complete dentures.

Kim Y and associates conducted an *in vitro* study to evaluate the dimensional accuracy of different denture relining methods. In their study they used a stainless steel cast to construct 50 identical average sized human definitive casts, which were used to evaluate the dimensional accuracy and stability of different relining methods<sup>16</sup>. They found that the casts relined by direct (chairside) method showed the best dimensional accuracy and stability, which were significantly different ( $p < 0.0001$ ) from those cases that were relined by indirect (laboratory heat polymerizing) method.

Results of another study showed that dentures relined by direct (chairside) method were more accurate when compared to the dentures relined by indirect (laboratory heat polymerizing) method<sup>17</sup>. As the temperature increases in mold is low, and there is a narrow cooling range, the shrinkage that occurs is largely an indication of the polymerizing shrinkage<sup>18</sup>. Results of the study conducted by Smith and coworkers showed that relines that employ autopolymerizing resins have significantly less ( $p < 0.0001$ ) changes than those with the heat polymerizing resins<sup>19</sup>.

Assery MK and Al-Shamrani SM also advocated chairside relining of conventional complete dentures in

their study<sup>20</sup>. Yoshinobu M and associates recommended direct relining method due to its simplicity and better accuracy<sup>21</sup>.

Pow and coworkers conducted a study to evaluate the linear dimensional changes after relining the complete dentures<sup>22</sup>. They reported that in direct chairside method the shrinkage of polymerized base was clinically undetectable and insignificant, thus did not cause clinically significant dimensional changes to complete dentures.

## CONCLUSION

The direct chairside method is advisable for cases in which:

- The denture cannot be deposited
- Stimulation of the mucosa overlying the residual ridge is unlikely to occur
- A certain thickness can be ensured
- The occlusal vertical dimension is unlikely to be changed

Direct chairside relines present the least gap at the posterior palatal seal area. However chairside relines are technique sensitive and require experience.

**Recommendations:** Further large studies are recommended to evaluate the physical and the mechanical properties, as well as of the dimensional stability of the relined dentures after a period of time that may help to draw definite conclusion.

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# Clinical Presentation of Dry Socket at Teaching Hospital of Hyderabad City

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## ABSTRACT

**Objective:** To find out frequency and clinical presentation of dry socket in Department of Oral and Maxillofacial Surgery Liaquat University of Medical & Health Sciences, Jamshoro.

**Study Design:** Observational study.

**Place and Duration of Study:** This study was carried out at Department of Oral & Maxillofacial Surgery, Liaquat University of Medical & Health Sciences, Jamshoro from Jan 2011 to June 2012.

**Materials and Methods:** Age from 11 to 70 years with both gender groups was included in the study. They were observed for the presence of dry socket. Patients with previous history of two or more days of extraction, pain, sensitivity on gentle probing of the extraction socket and empty/ partially empty socket were included in the study. Data was analyzed using SPSS version-13.

**Results:** Total 2300 extractions were included in study; dry socket was recorded in 66 (3.3%) routine dental extraction except 3rd molars and 598 (26%) surgical& non-surgical extraction of 3rd molar respectively. Majority of the patients belong to 3<sup>rd</sup> decade of life

**Conclusion:** In oral Surgery practice dry socket is unavoidable, but oral surgeons must identify additional risk factors in patients with particular medical conditions and include this information as a part of the informed consent.

**Key Words:** Dry socket, Prevalence, Halitosis, Prevention.

## INTRODUCTION

Dry socket (Alveolar osteitis) defined as frequently experienced postoperative complication characterized by inflammation inside and surrounding areas of socket with stressful severe throbbing pain which aggravates in extracted socket between the first and third post extraction day, accompanied by completely or partially devoid of the intraalveolar blood clot and with or without halitosis.<sup>1,2</sup> The term Dry Socket was recognized by an American dentist James Young Crawford in 1896, who used it to define a socket absence of blood clot and always associated with severe pain.<sup>3</sup> Several other terms have been suggested for this condition such as alveolar osteitis, localized osteitis, necrotic alveolitis, and fibrinolytic alveolitis, and alveolalgia.<sup>4</sup> Although, the term dry socket is still the most common term used for this disorder.<sup>5</sup>

Even though the etiology of dry socket is argued, it is may be multifactorial and its exact pathogenesis not universally recognized but usually supposed that postoperative clot fibrinolysis following by bacterial invasion is most common cause of dry socket.<sup>4</sup>

Many other factors as well stimulate to the incidence of dry socket for instance in experienced operator, surgical trauma, preoperative infection, gender, site of extraction, use of oral contraceptives, smoking, and use of local anesthetics with vasoconstrictor.<sup>6</sup>

Women are more susceptible to evolving alveolar osteitis due to the use of contraceptives and usually Individuals above age 30 also show a higher ratio.<sup>7</sup> The frequency of dry fluctuant from 1% to 4% of all

extractions<sup>8</sup> but it is generally supposed that dry socket is maximum seen as a result of the removal of impacted third molars, with an frequency of 20-30%.<sup>2</sup>

The occurrence is greater in the mandible as compared with maxillary molars with the ratio of 10:1.<sup>9</sup>

An increased incidence of dry socket ensues in the presence of pericoronitis, periodontitis, gingivitis, Periapical infection, and in Patients with poor oral hygiene.<sup>6,7</sup>

To prevent the of prevalence dry socket numerous techniques are stated such as the use of antibiotics, antifibrinolytic agents, Chlorohexidine mouthwashes, application of medicated packing into the extraction sockets, steroids and intra-alveolar ointments.<sup>10</sup>

The rationale of this study was to conclude the incidence of dry socket following extraction of permanent teeth and its clinical presentation after extraction.

## MATERIALS AND METHODS

The setting of study was carried at Oral & Maxillofacial Surgery Department of Liaquat University of Medical & Health Sciences, during the year January 2011 to June 2012. The study was undertaken with two thousand patients of both genders. Individuals from 11-70 years age had go through one or multiple extractions were observed for the incidence of dry socket. The analytic measures for dry socket were centered on history of dental soreness after extraction, clinical examination for sensitivity of socket, trismus and halitosis.

Pain was measured by visual analogues scale. Pain subjectively from out of three i.e. mild pains as ranged

from 1-4, moderate pain ranged from 5-7 and severe pain as ranged from 8-10. Sensitivity test was taken by gentle probing of the extraction socket. Halitosis and trismus were assessed. Patients had inter-incisal space less than 30 were considered as having trismus. This space was measured with ruler. Socket was considered as partial or fullempty. Data was calculated using SPSS version-13. Graphic figures were used for age, gender, pain, sensitivity, halitosis, trismus, site and number of extracted tooth, and oral hygiene.

**RESULTS**

Total 2300 extractions were observed in a one and half year.

Out of the 2000 patients, dry socket was recorded in 66(3.3%) routine dental extraction except 3<sup>rd</sup> molars and 598 (26%) surgical & non-surgical extraction of 3<sup>rd</sup> molar respectively.

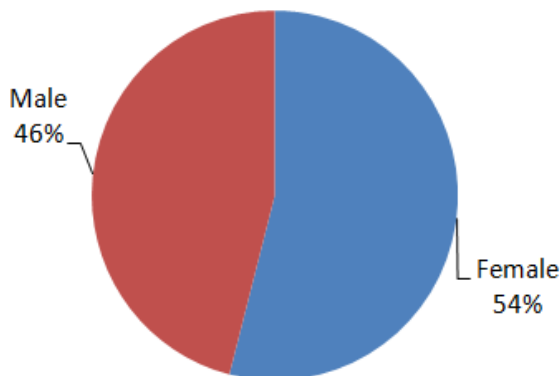
Out of this dry socket developed with high incidence of mandibular third molar extraction 425(71.07%) followed by maxillary 3<sup>rd</sup> molar impaction 173 (28.87%).

The age of patients were ranged from 11 to 70 years. The maximum incidence was seen in 21 to 30 year age group followed by 31 to 40 years. In our study youngest patient was 17 years and oldest patient was 70 years old.

This study was evaluating the overall frequency of dry socket; teeth were assembled according to anatomical sites for purpose of analyzing dry socket frequency that was approximately 3.3% for all routine extractions and become over 26% for surgical & non-surgical extractions of 3<sup>rd</sup> molar impactions.

**Table No.1: Distribution of Extractions & Dry Socket**

Tooth Type	Maxilla	Mandible
Canine	2 (2.2%)	7(8.0%)
Premolar	3(3.4%)	9(10.3%)
1 <sup>st</sup> Molar	9(10.3%)	22(25.28%)
2 <sup>nd</sup> Molar	2(2.2%)	11(19.5%)
3 <sup>rd</sup> Molar	173(28.7%)	425(71.7%)



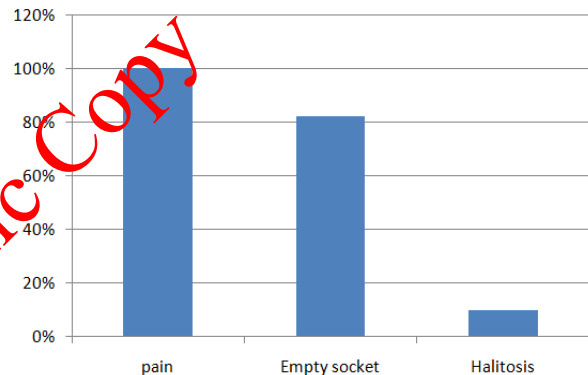
**Graph No.1: Gender distribution of patients**

**Table No.2: Distribution of patients according to Age Group (N=2000)**

Age groups	Routine Extraction	3rd molars Extraction
11-20	09	08
21-30	34	337
31-40	26	239
41-50	11	14
51-60	5	-
61-70	2	-
total	66	598

**Table No.3: Showing Patients Presents With Pain**

Post-operative pain	No of patients	percentage
immediatly	18	3.01%
In 24 hours	42	7.02%
In 48 hours	138	23.07%
In 72 hours	292	48.82%
After 72 hours	108	18.06%
total	598	100%



**Graph No. 2 Showing Clinical Features**

**DISCUSSION**

Dry socket is an annoying distressing complication of tooth extraction and as suggest in many theories, the accurate etiology of the disorder is unidentified, though many influencing factors have been discussed, however generally thought that partial or total premature loss of the blood clot that forms in the interior of the alveolus after extraction.<sup>13</sup>

Throughout this research study, the over-all proportion of dry socket was 66 (3.3%) in total 2300 extractions out of two thousand patients. overall of 598 (26%) 3<sup>rd</sup> molar extractions were complicated by dry socket including 425(71.07%) in mandible followed by maxilla 173 (28.87%).

The prevalence of dry socket in this study was considerably higher in the mandible (71.07%) than in the maxilla (28.9%). The outcome of this study concerning about mandible to maxilla correlation equals other studies for instance the findings of Upadhyaya C<sup>16</sup> also equivalent to this study according

to them maximum number of the dry socket were happened in mandibular teeth (68.93%) than maxilla (31.06%).

Oganni FO<sup>15</sup> and khitab U et al<sup>4</sup> also has been found that the mandibular third molar had the upper most occurrence of dry socket. The potential description of raised risk in the mandible than maxilla may be due to increased bone density, decreased vascularity, and a reduced capacity of producing granulation tissue.<sup>14</sup>

This Study shows females (54%) were more than males in dry socket with female male ratio 1:0.85, these findings were comparable with the results of Fahimuddin<sup>11</sup>, but challenge with the results of Abu Younis M<sup>6</sup> where males were more susceptible than females. The reason for the high percentages of female may be due to; probably use of oral contraceptive.<sup>4</sup> similarly higher female to male ratio was reported by Upadhyaya C<sup>16</sup>, according to them, occurrence of dry socket was higher in female patients.

The age of patients were from 11 to 70 years, the outcomes in this study in relation to age discovered that the maximum frequency was in the third and fourth decades, with a highest prevalence in the 21-30 year age group, followed by 4<sup>th</sup> decay.

The cause for this age involving is still scientifically unclear.<sup>4</sup> Qadus A et al<sup>3</sup> shown almost same results about the age gender frequency, site distribution of teeth. According to him females were 2.37 times more disposed to dry socket as compared to males. However, dry socket was established 2.94 times more common in mandibular extractions as compared to maxillary.

Postoperatively throbbing pain, empty socket followed by halitosis were the most common clinical feature. In our study tenderness and gentle probing was present in all patients. Pain with empty socket present in 492(82%) individuals. Halitosis was present 61(%). Similar results were shown in the study by Fahimuddin<sup>11</sup>, Upadhyaya C<sup>16</sup> and Nusair<sup>17</sup> Pain was ordered individually as severe accordingly visual analogue scale. According to Fahimuddin<sup>11</sup> he stated that Dry socket soreness is due to nerve endings exposure in the bone of the socket to air, diet, liquids and release kinins from traumatized tissue which liberates pain mediators. In this study resulting removal of the tooth, 9 (3%) patients immediately report an early upgrade in pain followed by 42(7%) in 24 hours, 138 (23%) in 48 hours, 294 (49%) in 72 hours and 114(19%) patients next to 72 hours develop severe, unbearable, continuous pain.

Regarding treatment modality for dry socket our focus is to relieve the patients from severe pain and associated clinical features so that it improves the patient's quality of life. Various treatment options are available for dry socket like; Topical application of eugenol, Iodoform and Butylpara-minobenzoate<sup>18,19</sup> or mixture of above have been used. According to Ikram et al application of honey to empty socket has also been found effective<sup>20</sup>.

## CONCLUSION

In oral Surgery practice dry socket is unavoidable, but Oral Surgeons must identify additional risk factors in patients with particular medical conditions and include this information as a part of the informed consent.

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# Treatment and Incidence of Recurrence of Varicose Veins of Lower Limbs

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## ABSTRACT

**Objective:** To study the presentation of varicose veins of lower limbs, treatment in our patients; and to see the causes of recurrent varicose veins at Islam Medical College, Sialkot, Pakistan.

**Study Design:** Observational and descriptive study.

**Place and Duration of Study:** This study was carried out at the Department of Surgery, Combined Military Hospital, Sialkot; from June 2007 to August 2010. Department of Surgery, & Islam Teaching Hospital, Sialkot from September 2010 to September 2013.

**Materials and Methods:** Adult patients referred by general practitioners with varicose veins of lower limb were included in the study. Data of sixty seven patients with varicose veins of lower limb was collected from June 2007 to September 2013. Patients were distributed in four groups depending upon the surgical procedures carried out. Full detailed history, examination, and investigations were done. Results of treatment were assessed by regular follow up. Data of only those patients was included who could complete follow up for at least 6 months.

**Results:** Out of 67 patients included in our study, 25 cases were having recurrence; 8(32%) was recurrent cases from pervious surgeries from somewhere else and 17(68%) cases were diagnosed with recurrence after surgery at our hospitals. So, the incidence of recurrence in our cases exclusive remained to be 29%.

Failure or recurrence in "Ligation" only was 38.5%, in ligation and reverse stripping was 30.7%, stab avulsions was 44.44% and in patients who underwent ligation, reverse stripping and stab avulsions was 12.5% after follow up of minimum 6 months. The patients are still on followup and the percentages are likely to increase with time as varicosities could be obvious.

The anomalous double great saphenous veins, neovascularisation or missed tributaries of great saphenous vein during surgery and deep venous thrombosis before and after surgery were the most observed finding of recurrence. The recurrence of varicose veins was more in leg only as compared to both leg and thigh.

**Conclusion:** Saphenofemoral ligation with below knee stripping and stab avulsions combined has the least frequency of recurrence, while Trendlenberg operation alone has the highest.

**Key Words:** Causes, Patterns, Recurrence, Varicose veins, stab avulsions and stripping

## INTRODUCTION

Varicose veins are not only a cosmetic problem: they can lead to complications that result in lost time from work and lost wages. Treatment has improved with the use of minimally invasive techniques that reduce recovery time and complications, considering that the problem affects 10% to 20% of adult men and 25% to 33% of adult women<sup>6</sup>.

Saphenofemoral junction was the most common site of reflux in the varicose veins. As colour duplex scan is non-invasive, repeatable, and readily accepted by the patients, it should be the investigation of choice for patients presenting with varicose veins.

Treatment is based on different indications: etiological, clinical and diagnostic. The treatments include: conservative therapy, sclerotherapy, phlebectomy, endovenous laser therapy, radiofrequency ablation, and surgery involving saphenous ligation and stripping<sup>7</sup>.

Short-term advantages appeared to be associated with sclerotherapy and endovenous treatments, and long-term effectiveness was more evident after surgical intervention. Evidence suggests conservative therapy is

less effective than sclerotherapy and surgery for the treatment of varicose veins. Ligation with stripping plus phlebectomy is generally regarded as the "gold standard" for treating primary long saphenous veins<sup>8</sup>. Surgery is a reasonably definitive therapy of primary varices, but secondary varices usually require rest, elevation and elastic support<sup>9</sup>.

Sclerotherapy has been shown to be an effective and increasingly popular therapeutic strategy for the treatment of varicose veins. However, recent reports of serious side effects, including cerebrovascular accidents (CVA) and transient ischemic attacks (TIA), as well as speech and visual disturbances, have caused serious concern regarding its use<sup>10</sup>. Superficial venous insufficiency is a common problem associated with varicose veins. Endovenous laser ablation (EVLA) and concomitant ultrasound (US)-guided foam sclerotherapy are recent treatment methods alternative to surgery in the treatment of superficial venous insufficiency<sup>11,12</sup>.

Varicose vein surgery is characterized by high recurrence rate of 60% after 5 years of follow-up observation, and this is a disappointing finding, both for

the patient and surgeon. A prospective study was conducted to evaluate and determine the effectiveness of different modalities of treatment of varicose veins of lower limb and to establish the cause of recurrence<sup>13,14,15</sup>.

## MATERIALS AND METHODS

After approval of hospital ethical committee, this prospective observational study was carried out in the Department of surgery, Islam Teaching Hospital, affiliated to Islam Medical College, Pasrur road, Sialkot. All the cases operated in Department of Surgery, Combined Military Hospital, Sialkot; from June 2007 to August 2010. Department of Surgery, & Islam Teaching Hospital, affiliated to Islam Medical College, Pasrur road, Sialkot, Pakistan; from September 2010 to September 2013 were included. In the study, sixty seven patients undergoing treatment for varied indications in general as well as regional anesthesia were serially included. The patient's age group was between 23-58 years and belonged to American Society of Anaesthesiologists' (ASA) physical status class 1-3 patients. All the patients were examined clinically and venous Doppler study was a must for checking and marking of incompetent perforators, incompetence of saphenofemoral junction and to rule out deep venous thrombosis.

Ligation of saphenofemoral junction mostly "flush ligation" and a few high ligation in obese patients was carried in patients who had proven incompetent SFJ but had not much prominent varicosities in legs and thighs. Thirteen patients under went this treatment.

Ligation of SFJ and reverse stripping of the great saphenous vein and stab avulsions combined was the most commonly performed procedure i.e. 52 patients. These patients had proven incompetent SFJ along with prominent varicosities in the legs and thigh as well.

The patients were distributed in four groups. In group – I, "Ligation" thirteen were operated and only the saphenofemoral junction was ligated. In group – II, "ligation and reverse stripping" thirteen patients were included, the saphenofemoral junction was ligated as well as reverse stripping of great saphenous vein was performed. In group – III, "stab avulsion" of prominent varicose veins was carried and nine patients were included. In group – IV, the patients with definite saphenofemoral junction incompetence and prominent varicose veins as well as incompetent perforators were treated by saphenofemoral junction ligation, reverse stripping and stab avulsions; in this group thirty two patients were included. The standard preoperative assessment was done in all the patients. The regional and general anaesthesia was also done under standard protocols. The surgical aseptic technique including antibiotic prophylaxis remained same for all the patients. The post-operative course was similar; all the patients were admitted for at least 3 days and dressings

changed on 3<sup>rd</sup> post-operative day before being discharged from the hospital. The follow-up in outpatient was done on 8-10<sup>th</sup> day including assessment for removal of stitches. Minimum follow-up of 6 months was made mandatory for inclusion in the study and complications were recorded. In recurrent varicose veins, Doppler studies and venography were conducted to establish the cause of recurrence. Patients with cardiovascular diseases and ASA-IV were excluded from the study. Patients with recurrent varicose veins operated elsewhere and not clear about the method of treatment already done were also not included.

Data was compared and analyzed by SPSS version 17. Mean  $\pm$  S.D was calculated for quantitative variables, age etc. Frequencies and percentages were presented for qualitative variables e.g. gender and other variables used in the study.

## RESULTS

Patients having varicose veins of the lower limb were included serially presenting to surgical outpatients department. Patients with cardiovascular diseases and ASA-IV were excluded from the study. Generally, the patients were between 30 to 45 years age group with a range of 23-58 years (median of 34.45 years). Table I show the overall data of all the cases. The overall data shows the co morbid conditions as well as the surgical procedures carried out.

**Table No.1: General data all cases. n=67**

Age	23-58 (34.45)
Sex	M : F 39:28 (58.2:41.8%)
Smoking	21 (31.3%)
Obesity	19 (28.4%)
Blood transfusion	2 (3%)
Anaemia	11 (16.4%)
Diabetes	18 (26.9%)
Hepatitis B status	13 (19.4%)
Hepatitis C status	16 (23.9%)

**Table No.2: Presentation of varicose veins of lower limb**

Cosmetic concerns	14 (20.8%)
Aches and pains	31 (46.3%)
Discolouration of skin	8 (11.9%)
Leg ulcers	4 (6%)
Recurrent varicose veins after previous surgery	8 (12%)
Haemorrhage	1 (1.5%)
Phlebitis	0 (0%)
Eczema	1 (1.5%)
Calcification	0 (0%)
Periostitis	0 (0%)



Patients presentations were not much different and usual complaints of pain and discomfort and cosmetic reasons and discolouration of skin around ankles especially in ladies were the leading presenting reasons. Recurrent varicose veins after previous surgery and nonhealing ulcers were the commonest complaints. Haemorrhage from the varicosities and eczema was also encountered. Table II show its detail.

**Table No.3: Complications (n=67)**

Bleeding	2 (3%)
Wound infection	3 (6%)
Reccurence	17 (25.37%)
Seroma formation	3 (4.5%)
Deep venous thrombosis	1 (1.5%)
Reoperation	9 (13.43%)
Mortality	0 (%)

**Table No.4: Outcome of treatment**

Procedure	no	satisfactory	Failure/ recurrence
Group I – Ligation	13 (19.4%)	8(61.5%)	5(38.4%)
Group II – ligation and reverse stripping	13 (19.4%)	9(69.2%)	4(30.7%)
Group III- stab avulsions	9 (13.4%)	5(55.55%)	4(44.44%)
Group IV- ligation, reverse stripping and stab avulsions	32 (47.7%)	28(87.5%)	4(12.5%)
Total	67 (100%)	50(74.6%)	17(25.37%)

**Table No.5: Recurrent cases**

	no	Accessory great saphenous veins	Missed tributaries in high ligation of SFJ	Post operative Deep venous thrombosis
Recurrent varicose veins after previous surgery (n= 8)	8 (32%)	5 (62.5%)	2(25%)	1(12.5%)
Reccurence in our patients(n=59)	17 (68%)	12 (70.58%)	4(23.5%)	1(5.8%)
Total	25	17 (68%)	6(24%)	2(8%)

Overall out of 67 patients included in our study, 25 cases were having recurrence; 8(32%) was recurrent cases from previos surgeries from somewhere else and 17(68%) cases were diagnosed with recurrence after

surgery at our hospitals. So, the incidence of recurrence in our cases exclusive remained to be 29%.

Failure or recurrence in “Ligation” only was 38.5%, in ligation and reverse stripping was 30.7%, stab avulsions was 44.44% and in patients who underwent ligation, reverse stripping and stab avulsions was 12.5% after follow up of minimum 6 months. The patients are still on follow up and the percentages are likely to increase with time as varicosities could be obvious.

## DISCUSSION

In patients who presented with recurrent varicose veins and unsatisfied with the previous surgeries; Doppler study of the veins were carried. Six of them showed accessory great saphenous veins which then stripped off. Rest the patients were managed by stab avulsions.

Maximum indication of surgery came out to be aches and pains explained by the patients. Most of them claimed to be cured while 3 patients still are on the follow up for no improvement.

Four patients with leg ulcers presented with long history of treatment from general practitioners and skin specialists. These had Ulceration i.e. Marjolin’s ulcer. All these patients were having ulcers on medial aspect of legs just above the medial malleoli. These patients having associated varicose veins were investigated and after correction of varicose veins had excellent healing in three to four weeks time.

The patients presenting with pigmentation of legs i.e. 8 and one with proven infection i.e eczema ; presented due to cosmetic concerns . These were all female patients and had history of treatment from different physicians. They were all cured of their symptoms after the treatment of underlying varicose veins.

Overall recurrence was encountered in seventeen of our cases i.e. 29% which is comparable to the study of Gad MA<sup>16</sup> having a recurrence rate of 32.6% after saphenofemoral disconnection i.e. Trendelenberg operation, 23.9% had recurrence after Saphenofemoral disconnection, with stripping below knee , 30.4% had recurrence after saphenofemoral disconnection with stripping above knee and 13.1% had recurrence after Sapheno-popliteal disconnection with stripping. This rate is likely to increase as the time passes and more follow up is done.

In the study by Corrales NE<sup>17</sup>, there was evidence of duplication of the LSV ( long saphenous vein) in 50 (49 per cent) of the 103 saphenograms; we encountered duplication of great saphenous vein in 17 i.e. 68% of cases in which recurrence was found. On follow up duplex scan and venography showed presence of accessory great saphenous vein in 12 and residual tributaries in 4 patients while deep venous thrombosis encountered in one patient. Nine patients with recurrence have to be re-operated to achieve cure; while

8 patients with recurrence after completing a follow up of 9 - 12 months were offered surgery but they opted further treatment elsewhere. The cases who had presented with recurrence after surgery from other hospitals; were investigated and revealed presence of accessory great saphenous veins in 5 patients, 2 had missed tributaries of great saphenous vein and 1 had deep venous thrombosis.

We encountered haemorrhage in two patients and on follow up it was revealed that one had smaller arteriovenous malformation associated with the perforators in the leg. The second patient in which haemorrhage was encountered had history of hepatitis and in spite of normal liver profile including prothrombin time, the bleeding was profuse and required transfusion of fresh blood as well as fresh frozen plasma.

Wound infection at the site of groin surgical site was noticed in 2 patients in ladies with more than average weight i.e obesity; one patient who was emaciated and chronic smoker had superficial infection at the site of stab avulsions.

Seroma formation occurred in 3 patients and was managed conservatively. We had no case of postoperative deep venous thrombosis or mortality. Two cases of recurrence after saphenofemoral junction ligation were investigated and postoperative Doppler study showed that one who had high ligation had a duplication of great saphenous vein and had to be re-operated. One patient with recurrence and had reverse stripping and prominent residual tributaries and was redone.

## CONCLUSION

The indications for surgery in varicose veins of lower limb are in evolution. The recurrence after surgery is due to missed tributaries and presence of accessory great saphenous which can be missed during high ligation and reverse stripping respectively. It is very important to use a duplex scan before the treatment and venography especially in recurrent cases to establish the cause. Recurrence is encountered even in patients undergoing ligation, reverse stripping and stab avulsions as combined surgery.

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# Risk Factors of Hypoglycemia in Diabetics

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## ABSTRACT

**Objective:** To find the frequency of risk factors of hypoglycemia in diabetics in our setup.

**Study Design:** Prospective observational study

**Place and Duration of Study:** This study was conducted at Emergency and Medical Wards Nishtar Hospital Multan from January 2010 to December 2013.

**Patients and Methods:** One hundred and eighteen patients presented with hypoglycemia to Nishtar Hospital Multan. One hundred and eighteen diabetic patients above the age of 16 years admitted with hypoglycemia were included in the study. Written informed consent was taken from the patients or the attendants in case of patients with altered state of consciousness. Approval was taken from hospital ethical committee.

**Results:** Mean age of patients was  $60.46 \pm 14.20$ . Forty two patients (35.6%) were males and 76 (64.4%) were females. Mean duration of diabetes was  $6.4 \pm 6.04$  years. Mean blood glucose level at the time of presentation was  $36.25 \pm 12.49$  mg/dl. Thirty four (28.8%) patients had only neuroglycopenic symptoms without autonomic symptoms while 4 (3.4%) had autonomic symptoms alone. Eighty (67.8%) presented with both adrenergic and neuroglycopenic symptoms. Regarding risk factors, 77 (65.25%) had renal failure, 66 (55.93%) had missed meal, 37 (31.35%) had vomiting, 23 (19.49%) had recent increased dose of hypoglycemic agents, 19 (16.10%) had delayed meal, 16 (13.55%) had diarrhea, 14 (11.86%) had liver dysfunction and 2 (1.69%) had excessive physical activity.

**Conclusion:** Hypoglycemia is common in old patients with long history of diabetes. Patients usually present late when they develop neuroglycopenic symptoms. Renal failure and missed meal are most common risk factors followed by vomiting and increased dosage of hypoglycemic agents. Patients need education about early symptoms of hypoglycemia, common risk factors and remedial steps to avoid this serious complication.

**Key Words:** Diabetes mellitus, Hypoglycemia, Risk Factors

## INTRODUCTION

Diabetes mellitus is very common and hypoglycemia is its serious complication as a result of strict glycemic control. It can lead to neuronal damage and even sudden death. There are number of risk factors which can be identified to avoid this dreadful complication.

Diabetes mellitus is very common all over the world as well as in Pakistan. It has affected 240 million people worldwide and the number could increase upto 380 million by 2025.<sup>1</sup> According to a survey done by Shera AS et al, the prevalence of Diabetes in Pakistan in the urban versus the rural areas was 6.0% in men and 3.5% in women against 6.9% in men and 2.5% in women respectively.<sup>2</sup>

Diabetes causes microvascular complications which can be prevented by strict glycemic control. Hypoglycemia is a well-recognized complication of treatment of diabetes mellitus and also a barrier in its management.<sup>3</sup> Attempts made at intensive glycemic control is associated with increase in the risk of hypoglycemia. It is defined as reduction in blood glucose to a level that induces symptoms and signs. Glucose level at which an individual becomes symptomatic is highly variable, threshold generally is less than 70mg/dl.<sup>4</sup> The clinical syndrome is documented by Whipple's triad: symptoms consistent

with hypoglycemia, a low plasma glucose concentration, and relief of those symptoms when plasma glucose is raised.<sup>5</sup>

Patients present with autonomic symptoms like palpitations, tremors, sweating and neuroglycopenic symptoms like confusion, fits and loss of consciousness. Normally autonomic symptoms precede neuroglycopenic symptoms and allow early warning and self-treatment. Failure to recognize autonomic symptoms of hypoglycemia is called hypoglycemia unawareness. It occurs due to impairment of counter regulatory system.<sup>6</sup> It is seen in patients with frequent hypoglycemic episodes. It can lead to severe hypoglycemia which is defined as hypoglycemia requiring medical treatment.

Severe hypoglycemia can cause neural damage, impaired cognitive function or even death.<sup>7</sup> Severe hypoglycemia is also strongly associated with cardiovascular disease. Hypoglycemia can lead to a prothrombotic state which can predispose to cardiac ischemia. Alterations in ventricular repolarization can be the cause of sudden death.<sup>8,9</sup>

Various risk factors have been identified like old age, long duration of diabetes mellitus, hypoglycemia unawareness, renal insufficiency, alcoholism, missed meal and poly pharmacy in different studies.<sup>11-15, 20-25</sup>

## MATERIALS AND METHODS

This study was carried out at emergency and medical wards of Nishtar Hospital Multan from January 2010 to December 2013. One hundred and eighteen diabetic patients above the age of 16 years admitted with hypoglycemia were included in the study.

Written informed consent was taken from the patients or the attendants in case of patients with altered state of consciousness. Approval was taken from hospital ethical committee.

Detailed history was taken regarding symptoms, duration of diabetes, family history of diabetes mellitus, medications with doses, meal timings or any excessive physical activity. Detailed examination was done including blood pressure and pulse at presentation and

after hypoglycemia was corrected. Blood samples for blood glucose, renal parameters and liver function tests were sent to central lab Nishtar Hospital. All details were filled in a Proforma.

## RESULTS

The age of patients ranged from 20 to 96 years with a mean age of  $60.46 \pm 14.20$ . Forty two patients (35.6%) were males and 76 (64.4%) were females. Duration of DM ranged from one day to 35 years with a mean duration of  $6.4 \pm 6.04$  years. Family history of diabetes mellitus was present in 29 (24.57%) patients. (Table I) Blood glucose levels at the time of presentation ranged from 10 to 60mg/dl with a mean of  $36.25 \pm 12.49$ mg/dl.

**Table No.I:-Demography**

	Oral Drugs (N=78)	Insulin (N=25)	Oral Drugs + Insulin (N=15)	Total(N=118)
Age (Mean)	$62.51 \pm 12.39$	$55.40 \pm 18.76$	$58.20 \pm 12.75$	$60.46 \pm 14.20$
<50	07(8.97%)	08 (32%)	03 (20%)	18 (15.3%)
≥50	71(91.03%)	17 (68%)	12 (80%)	100 (84.7%)
Sex				
Male	23 (29.48%)	10 (40%)	09 (60%)	42 (35.6%)
Female	55 (70.51%)	15 (60%)	06 (40%)	76 (64.4%)
Duration of DM (Mean)	$5.77 \pm 5.40$	$8.35 \pm 7.61$	$6.75 \pm 6.00$	$6.4 \pm 6.04$
<5yrs	42(53.84%)	12 (48%)	08 (53.33%)	62 (52.5%)
≥5yrs	36(46.15%)	13 (52%)	07 (46.66%)	56 (47.5%)
Family history	20(25.64%)	08 (32%)	01 (6.66%)	29 (24.57%)

DM=Diabetes Mellitus

Values are presented as mean  $\pm$  standard deviation or number(% of total number)

**Table No.2: Clinical presentation of patients of hypoglycemia**

		Oral Drugs (N=78)	Insulin (N=25)	Oral Drugs + Insulin (N=15)	Total (N=118)
<b>Neuroglycopenic symptoms</b>	Unconsciousness	68 (87.17%)	15 (60%)	09 (60%)	92 (77.96%)
	Confusion	42 (53.84%)	12 (48%)	07 (46.66%)	61 (51.69%)
	Seizures	06 (7.69%)	09 (36%)	05 (33.33%)	20 (16.94%)
<b>Adrenergic symptoms</b>	Sweating	41 (52.56%)	18 (72%)	10 (66.66%)	69 (58.47%)
	Tremor	22 (28.20%)	09 (36%)	02 (13.33%)	33 (27.96%)
	Palpitations	17 (21.79%)	06 (24%)	02 (13.33%)	25 (21.18%)
	Paresthesia	03 (3.84%)	01 (4%)	0 (0%)	04 (3.38%)
	Hunger	02 (2.56%)	01 (4%)	01 (6.66%)	04 (3.38%)
<b>Signs</b>	Tachycardia	60 (76.92%)	16 (64%)	13 (86.66%)	89 (75.42%)
	Pallor	56 (71.79%)	17 (68%)	09 (60%)	82 (69.49%)
	Sweating on exam	40 (51.28%)	18 (72%)	10 (66.66%)	68 (57.62%)

Regarding clinical presentation, 92 (77.96%) patients were unconscious, 69 (58.47%) had sweating, 61 (51.69%) presented with confusion, 33 (27.96%) had tremors, 25 (21.18%) had palpitations, 20 (16.94%) had seizures, 4 (3.38%) had hunger and 4 (3.38%) had paresthesia. On examination, 89 (75.42%) patients had

tachycardia, 82 (69.49%) had pallor, clinical evidence of sweating was present in 68 (57.62%). (Table 2)

Over all 114 (96.6%) patients presented with neuroglycopenic symptoms and 84 (71.2%) presented with adrenergic symptoms. Eighty patients (67.8%) presented with both adrenergic and neuroglycopenic symptoms. Thirty four (28.8%) patients had only

neuroglycopenic symptoms without adrenergic symptoms while 4(3.4%) had adrenergic symptoms alone without neuroglycopenic symptoms. (Table 3) Regarding risk factors evaluation, 77(65.25%) patients had renal failure, 66(55.93%) had missed meal, 37(31.35%) had vomiting, 23(19.49%) had increased dose of hypoglycemic agent, 19(16.10%) had delayed meal, 16(13.35%) had diarrhea, 14 (11.86%) had liver dysfunction and 2(1.69%) had excessive physical activity. (Table 4)

We divided the patients into three groups according to the treatment being taken: 78 (66.10%) patients were taking oral hypoglycemic drugs, 25 (21.18%) were on insulin and 15 (12.71%) patients were taking a combination of oral drug and insulin.

Demography, clinical presentation, comparison of neuroglycopenic and adrenergic symptoms and frequency of risk factors in these three groups is as shown in Table 1 to 4.

**Table No.3: Comparison of Neuroglycopenic and Adrenergic symptoms**

	Oral Drugs (N=78)	Insulin (N=25)	Oral Drugs + Insulin(N=15)	Total (N=118)
Neuroglycopenic symptoms	77(98.71%)	23(92%)	14(93.33%)	114 (96.6%)
Adrenergic symptoms	51(65.38%)	21(84%)	12(80%)	84 (71.2%)
Adrenergic + Neuroglycopenic symptoms	50(64.10%)	19(76%)	11((73.33%)	80 (67.8%)
Neuroglycopenic symptoms without Adrenergic symptoms	27(34.61%)	4(16%)	3(20%)	34(28.8%)
Adrenergic symptoms without Neuroglycopenic symptoms	01(1.28%)	2(8%)	1(6.66%)	4 (3.4%)
Without Adrenergic or Neuroglycopenic symptoms	0 (0%)	0 (0%)	0 (0%)	0 (0%)

**Table No.4: Frequency of risk factors of hypoglycemia**

Risk factors	Oral drugs (N=78)	Insulin(N=25)	Oral Drugs + Insulin (N=15)	Total (N=118)
Renal failure	53 (67.94%)	15 (60%)	09 (60%)	77 (65.25%)
Missed meal	46 (58.97%)	18 (40%)	10 (66.66%)	66 (55.93%)
Vomiting	24 (30.76%)	07 (28%)	06 (40%)	37 (31.35%)
Increased dose	09 (11.53%)	06 (24%)	08 (53.33%)	23 (19.49%)
Delayed meal	14 (17.94%)	03 (12%)	02(13.33%)	19 (16.10%)
Diarrhea	14 (17.94%)	02 (8%)	0 (0%)	16 (13.55%)
Hepatic dysfunction	07 (8.97%)	02 (8%)	05 (33.33%)	14 (11.86%)
Excessive physical activity	02 (2.56%)	0 (0%)	0 (0%)	02 (1.69%)

## DISCUSSION

According to UK Prospective Diabetes Study and Diabetes Control and Complication Trial, strict blood glycaemic control is necessary for management of diabetes to prevent its micro and macro vascular complications. However this can increase the risk of hypoglycemic events which is the most undesirable side effect of anti-diabetic drugs. This serious iatrogenic complication can be sometimes fatal.<sup>10</sup>

Identification of risk factors of hypoglycemia is necessary to predict and reduce its frequency. Many studies have been done to find these risk factors. Purpose of our study was to identify the common risk factors of hypoglycemia in diabetics in our setup so that we can educate our patients about their prevention.

In our study we found that hypoglycemia is more common in old age as mean age of patients was 60.46±14.20 years. Linn YY et al found mean age of 74.1± 9.8years.<sup>11</sup>Burderer et al observed that mean age of patients was 61.7 ± 13.0 years.<sup>12</sup>Shorr et al also

found that advanced age is a risk factor for hypoglycemia.<sup>13</sup>

In our study 64.4% patients were females. Allen et al observed that 60.5% patients were females.<sup>14</sup> Heller et al found that 70% patients were males.<sup>15</sup>So hypoglycemia can occur in both females and males. Although the prevalence of diabetes is higher in men than in women.<sup>2,16</sup>

In our study mean duration of diabetes was 6.44 ± 6.04 years which is much shorter than that reported by Heller et al who observed that mean duration of diabetes was 29.8 years in type 2 diabetics.<sup>15</sup> Allen et al also found that hypoglycemia is associated with longer duration of diabetes.<sup>14</sup>So patients with long duration of diabetes should be well educated about risk factors of hypoglycemia and their prevention.

Out of 118 patients, 66.10% were taking oral drugs, 21.18% were on Insulin and 12.71% were taking both oral drugs and insulin. These results are comparable with a study done by Ha et al (65.9% were on oral drugs, 29% on insulin and 5% on both insulin and oral drugs).<sup>17</sup> But we cannot conclude that hypoglycemia is

more common with oral drugs without knowing the percentage of diabetic patients taking oral drugs. Perhaps we have more type 2 diabetic patients taking oral drugs in our population. Although oral hypoglycemic drugs are known to cause severe hypoglycemia requiring hospital admission in patients with chronic kidney disease.<sup>18</sup>

Regarding clinical presentation we observed that 28.8% patients presented with neuroglycopenic symptoms alone without preceding adrenergic symptoms indicating hypoglycemia unawareness. Similar to our study Burge et al found hypoglycemia unawareness in 25% cases.<sup>19</sup> In a study done by Leese et al, 36% patients presented with coma.<sup>20</sup> Feher et al observed fits and coma in 49% patients.<sup>21</sup> While in some other studies frequencies observed were much less (5% and 8% by Muhlhauser et al<sup>22</sup> and Henderson et al<sup>23</sup> respectively). Patients with impaired awareness of hypoglycemia could have a high risk of severe hypoglycemia.

This indicates that very few patients present early and our patients have very little education about these warning symptoms of hypoglycemia. They are brought to the hospital when they develop altered consciousness.

In our study only 3.4% patients presented with adrenergic symptoms alone. Over all 67.8% patients presented with both neuroglycopenic and adrenergic symptoms. Our study indicated that majority of our patients present late. Either our patients are not aware of early symptoms of hypoglycemia or even if they are aware, they don't react to manage them. Or perhaps patients with these early symptoms are treated by local doctors and don't present to tertiary care hospitals. All clinicians must educate their diabetic patients about these warning symptoms and advise them to take some sweet food which otherwise is restricted in their diets.<sup>24</sup>

Regarding risk factors of hypoglycemia in our study the most common was renal impairment found in 65.25% patients. Similarly many other studies done by Lin YY et al, Krinsley et al and Koster et al also showed that renal insufficiency was a risk factor for hypoglycemia.<sup>11,25,26</sup> This is due to longer half-life of medicines that need renal excretion. As well as decreased renal gluconeogenesis in patients who are also anorexic. All clinicians must monitor serum creatinine levels in diabetics. A serum creatinine level of more than 2mg/dl is a contraindication for most oral drugs; these should be replaced by safer drugs or insulin.<sup>27</sup> Targets of glycemic control should also be relaxed in renal dysfunction.

A common risk factor of hypoglycemia in diabetics is delayed or missed meal as observed in some other studies.<sup>11,28</sup> In our study 55.93% gave history of missed meal while 16.10% delayed their meals. Burge et al found that 80% cases of hypoglycemia were due to missed meal.<sup>19</sup> In our study 31.35% patients took their meals but they vomited either due to renal failure or due to gastropathy also common in diabetics. For prevention of hypoglycemia all patients must know the

importance of taking their meal within 30 minutes of injection of insulin or intake of oral anti-diabetics. Similarly, if patient has diarrhea and/or vomiting hypoglycemia can occur. In this situation blood glucose should be monitored and patient should immediately contact nearby hospital for parenteral nutrition.<sup>24</sup>

Excessive dosage of anti-diabetics is also a cause of hypoglycemia. In our study 19.49% gave history of recent increase in their doses of anti-diabetic drugs either by their doctors or by themselves. Feher et al observed increased dose of insulin as a predisposing factor in 17% hypoglycemic patients.<sup>21</sup> Ha et al observed change in the dose of current medication in 12.5% cases of hypoglycemia.<sup>17</sup> Burge et al also observed that drug over dosage is a risk factor for hypoglycemia.<sup>19</sup> Patients should never attempt to increase the doses of anti-diabetic drugs without advice of their physician.

Coexistence of chronic liver disease in a diabetic patient is also a risk factor for hypoglycemia.<sup>29</sup> In our study 11.86% patients had abnormal liver function tests. Burge et al also observed liver disease as a risk factor of hypoglycemia.<sup>19</sup> Liver has important role in glucose homeostasis. Some anti-diabetic drugs are contraindicated or their doses need to be reduced in liver dysfunction. Targets of glycemic control should also be relaxed in hepatic dysfunction.<sup>30</sup>

Unaccustomed physical activity is another risk factor which should be avoided or extra meal should be taken before such activity. Although in our study we found that only 1.69% patients gave history of unaccustomed exercise. Burge et al also observed that strenuous exercise can cause hypoglycemia.<sup>19</sup> Feher et al observed exercise as a predisposing in 12% cases<sup>18</sup> while Ha et al observed it in 9% cases.<sup>21</sup> Lesser frequency of exercise as a risk factor in our study could be due to sedentary life style of our patients. Diabetic children, athletes and players should take extra meal before starting the play. Patients should carry a fast acting carbohydrate when they exercise.<sup>24</sup>

## CONCLUSION

Hypoglycemia is common in old patients with long history of diabetes. Patients usually present late when they develop neuroglycopenic symptoms. Renal failure and missed meal are important risk factors of hypoglycemia in our patients followed by vomiting, increased dosage of hypoglycemic agents, delayed meal, diarrhea, liver dysfunction and excessive physical activity. Patients need education about early symptoms of hypoglycemia as well as about common risk factors to avoid this serious complication. Important preventive measures include monitoring renal parameters and adjustment of treatment accordingly, emphasis in the instruction about regularity of meals, monitoring blood glucose levels in case of diarrhea, vomiting and liver dysfunction and avoiding unaccustomed exercise or taking an extra meal prior to it.

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# An Analysis of Caesarean Birth in A Private Teaching Hospital

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## ABSTRACT

**Objective:** The objective of this study was to analysis the Caesarean Birth in Private Teaching Hospital.

**Study Design:** Retrospective study

**Place and Duration of Study:** This study was carried out at the Department of Gynae /Obst Alkhidmat Teaching Mansoorah Hospital, Lahore affiliated with University College of Medicine and Dentistry, Lahore over a period of 1 year from April 2012 to March 2013.

**Materials and Methods:** The study was carried out to analysis the indications and to assess the maternal mortality and mortality as well as fetal outcome after C/S. The frequency of caesarean section during the study period was about 46%. Indications included, repeat caesarean (38.21%), failed inductions (19.9%), fetal distress (15.6%), Cephaloplevic disproportions (7.6%) breech presentation (6.36%), APH and PIH (4.7%), Twins and mal presentations (3.82%) and other (3.66%).

**Results:** Out of 628 patients (79.62%) were booked patients while (51.6%) patients had elective cesarean section. Anaemia, UTI, PPH and wound sepsis were common maternal complications. Two patients 0.31% died due to complications of surgery or anaesthesia. (97.29%) babies were born alive, (1.43%) were IUD either fresh or macerated while only (1.27%) babies died in the early neonatal period. Although caesarean section rate i.e. 46.38% is quite high in our hospital but this is not a true caesarean section rate for a specific population. Majority of the patients who underwent C/s were booked, belonging to educated middle class families having awareness of the complications that may occur during trial of labour.

**Conclusion:** Provision of adequate antenatal health services timely identification of high risk cases use of electronic fetal monitoring; involvement of senior, skilled and experienced personnel in the management of obstetrical emergencies are responsible for the apparently higher rate of caesarean section. In order to reduce C/S rate frequency of trial of labor must be increased with the goal of vaginal delivery but without compromising maternal and fetal health.

**Key Words:** Caesarean Section, Caesarean Section rate, mortality, morbidity APH, PIH and C/S.

## INTRODUCTION

Caesarean section is a major obstetrical operation. Caesarean section rate was initially very low i.e. about 5% in 1965 which rose to 20-25% in 1985 in developed countries<sup>1</sup>. In a recent study in USA, more than 30% birth occur by caesarean delivery<sup>2</sup>. The rate of caesarean section increased 7% from 2001 to 2002 upto 26.1% of all US births and rising further to 29% in 2004, an increase of approximately 40% since 1996<sup>3</sup>. Another study by Hamilton, et al, in US documented 32.2% rate of C/S in 2010-2011<sup>4</sup>. Similar situation arose in developing countries in the last two decades, where there is tremendous increase in the rate of caesarean section. In a study from Nigeria 34.6% and Italy 32.9% rates are documented<sup>3</sup>. In a study from Multan 51.43% rate is observed, while in a study from Quetta 46.38% and Karachi 28% CSR is documented<sup>5-7</sup>.

Major obstetrical medication of the caesarean section include, previous LSCS, failed inductions, Fetal distress, CPD, breech presentation and APH, PIH. Specific literate population, increasing awareness regarding health related problems, provisions of

adequate antenatal health services, timely identification of high risk cases use of electronic fetal monitoring and above all involvement of skilled and experienced personnel in the management of obstetrical emergencies are responsible for apparently high rate of caesarean section.

The patients with previous scar are difficult to manage during pregnancy and labor. However, women of low socio economic status with poverty and illiteracy with previous caesarean section try to avoid the hospital in subsequent pregnancy and prefer to stay at home at the disposal of untrained and unskilled traditional birth attendants. But the patients coming to this hospital belong to educated middle class families were aware of the complications thus majority of them were booked. In USA 20-40% of the women undergo repeat LSCS due to previous caesarean<sup>2</sup>. Another study suggested that out of 9 of 10 women with previous C/S are having repeat C/S in the United States<sup>8</sup>. If the high rate of caesarean section is to be lowered the no of elective procedure must be reduced by increasing the frequency of trial of labor with the goal of vaginal delivery<sup>9</sup>. The trial of labor is a reasonable option for many pregnant women with prior one LS,CS<sup>10</sup>.

## MATERIALS AND METHODS

The study was carried out to find out the frequency, indications, to assess maternal mortality and morbidity as well as fetal morbidity and mortality over a period of one year from April 2012 to March 2013 at the department of obstetrics and Gynecology Alkhidmat teaching Mansoorah hospital Lahore affiliated with university college of medicine and dentistry, Lahore. This Hospital receives patient from the city as well as from the neighboring rural areas. Total no of deliveries during the study period were 1354 out of which 628 patients underwent caesarean section.

This was a retrospective study the source of information was the record of labor room, operation theater, antenatal and post natal wards. This record provided the information that whether the procedure was elective or emergency, patient was booked or non booked, what was the indication of caesarean section, fetal outcome as well as maternal mortality and morbidity.

## RESULTS

Total no of deliveries during 1 yr. study period i.e. from April 2012 to March 2013 were 1354 at Alkhidmat Teaching Mansoorah Hospital Lahore. Out of 1354 patients 628 (46.38%) underwent caesarean section. The results are shown in the tables.

**Table No.1: Elective caesarean versus emergency caesarean section. No=628**

Sr. No.	Type of C/S	No of cases	Percentage
1	No of Electives c/s	324	51.60%
2	No of emergency c/s	304	48.40%
	Total:	628	100%

Out of 628 patients 324 (51.6%) had elective C/S while 304 (48.40%) had emergency C/S out of 628 patients 500 (79.62%) had regular antenatal checkup.

**Table No.2: Indications of caesarean section n=:628**

S.No	Indications	Numbers	Percentage
1	Previous LSCS	240	38.2%
2	Failed induction	125	19.9%
3	Fetal Distress	98	15.6%
4	Cephalo pelvic disproportion	48	7.6%
5	Breech Presentation	40	6.36%
6	APH+PIH	30	4.7%
7	Mal presentation & Twins	24	3.82%
8	Others	23	3.66%

Repeat caesarean section, failed induction Fetal distress & CPD, were the common indications for Caesarean delivery.

**Table No.3: Age of the patient n=:628**

Maternal Age (Years)	No of patients	Percentage
Below 20 Years	81	9.72%
20-25 yrs	250	41.4%
26-30 yrs	280	32.6%
31-35 yrs	60	10.35%
Above 35	37	5.89%

Age of the women in the study population ranged from 18 years to 40 years. Maximum no of patients 280(32.6%) were between 26-30 years of age.

**Table No.4: Parity of the patients n=628**

Parity	No of Patients	Percentage
Primigravida	232	36.95%
1-2	264	42.03%
3-4	113	17.99%
5-6	14	2.23%
Above 6	5	0.80%

Parity of study population ranged from nullipara to para 8, highest number of the patients who underwent caesarean section had 1-2 children.

The perinatal mortality during the study period was 27/1000 births i.e. 611(97.29%) babies were born alive. Only 8 babies (1.27%) were born alive and died afterwards either because of prematurity or some congenital abnormality.

Out of 628 patients 1 patient (0.15%) had caesarean hysterectomy because of placenta accreta. 2 Patients (0.31%) died due to complications of surgery and / or anaesthesia. Other maternal complications were anaemia 23 (3.6%) wound sepsis 15(2.38%) UTI 15(2.38%) and PPH 5(0.79%)

## DISCUSSION

In our study the frequency of Caesarean section was 46.38% it is quite consistent with another study done in tertiary care hospital, Multan i.e. 51.43%<sup>5</sup> In England and Wales the figure is about 22%(11). Maximum No of patients the fell in 26-30 years age group. But majority of patients who underwent Caesarean section had 1-2 children. Most of our patients belonged to literate middle class families and they used to come for regular antenatal visits. In a study from South Korea it is stated that higher Caesarean section are prevalent in patients where there is higher maternal education and residence in big cities<sup>12</sup>. In another study<sup>13,14</sup> it was stated that 5-40 % higher CSR in upper social class and 20%Caesarean section rates among educated women were observed.

The ratio between elective 51.6% and emergency (48.40%) operations are almost similar to a study from UK<sup>15</sup> which quoted 52% elective Vs 48% emergency but differ markedly from other studies conducted at

tertiary care teaching hospital which stated elective 17% and emergency 85% in a study conducted at tertiary care hospital. Quetta<sup>6</sup>. The difference in the studies of private teaching hospital and tertiary care Government hospital is because of the fact that women who land in Government teaching care hospitals usually belong to low socio economic class mostly illiterate. More than 80% deliveries are conducted by untrained or trained TBA's. Thus most of the time complicated pregnancies are brought to the hospital. In those situations both mother and baby are in a moribund condition. Thus rates of emergency Caesarean section are high in Govt. set up<sup>16</sup>. All complications of Caesarean section are more likely and more severe if it is done as an emergency after a failed attempt at vaginal delivery rather than as a planned operation<sup>17</sup>. Repeat C/S was the commonest indication i.e. 38.3% of caesarean section. If rate of C/s is to be reduced, both 1<sup>st</sup> C/S as well as repeat C/S must be reduced. According to American pregnancy association 90% of the women who have undergone caesarean deliveries are candidate for vaginal birth after caesarean<sup>17</sup>. According to a Wikipedia<sup>18</sup> trial of labor is a reasonable option for many pregnant women with one prior low transverse incision<sup>10</sup>. There is emerging evidence of serious harms relating to multiple cesarean<sup>14</sup>. American college of obstetrician and Gynecologist ACOG suggests attempting a vaginal birth after Caesarean (VBAC) is a safe and appropriate choice for most women who have had a prior Caesarean delivery<sup>19</sup>. About 0.15% patients had Caesarean hysterectomy because of placenta accrete, 2 patients (0.31%) died due to complications of surgery and /or anaesthesia. In our study perinatal mortality during one year period was 27/1000 births i.e. 611(97.29%) babies were born alive. Only 8 babies (1.27%) were born alive and died afterwards either because of prematurity or some congenital abnormality. Generally Caesarean section is considered a relatively safe option for the fetus<sup>19,14</sup>. However, perinatal mortality depends upon the indications for C/S & gestational age of the fetus.

## CONCLUSION

Significant reduction in the CSR can be achieved by adapting the policy of trial of labour after previous one caesarean section, active management of labour, adapting the policy of external cephalic version in selected cases and selective vaginal breech delivery. Proper counseling of the patients at the time of 1<sup>st</sup> caesarean regarding the contraception, significance of proper antenatal checkups during next pregnancy and briefly explaining the complications that can occur in the subsequent pregnancy and labour because of the presence of previous uterine scar.

Improvement of facilities at primary and secondary health care level, efficient referral chain, last but not the least increasing the awareness of the illiterate general population of Pakistan may decrease the current high CSR and reduce the maternal and fetal morbidity & mortality, by early seeking of the health care facility.

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# Awareness Regarding Early Initiation of Insulin in Type 2 Diabetes Mellitus in Family Physicians

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## ABSTRACT

**Objective:** (1) To assess the perception of early initiation of insulin in type 2 diabetic mellitus in family physicians of Karachi. (2) To develop a plan to motivate the family physicians to give preference for insulin in type 2 diabetic patients.

**Study Design:** Cross sectional study.

**Place and Duration of Study:** This study was conducted on Family Physicians of Karachi which was divided in 18 towns from April 2010 to December 2010.

**Materials and Methods:** 10 family physicians were included from each town from hospitals and clinics through non probability purposive sampling technique. The data was collected through pre tested structured questionnaire have questions regarding their perception and preferences of use of insulin in type 2 diabetic patients as first treatment as compared to oral hypoglycemic therapy.

**Results:** over all 180 family physicians were contacted out of which 133 were provide full information (response rate was 74%). Out of these 93(69.1%) were male and 40(30.1%) were female family physicians. Overall perception (63.9%) was not in favor of early initiation of insulin as monotherapy or as combined therapy. The rest (36.1%) who were of the opinion that insulin is better than oral hypoglycemic therapy, none of them were apply it clinically.

**Conclusion:** Majority of the family physicians suggest combination of life style changes with nutritional advice and oral hypoglycemic therapy. No one suggested insulin. Only few were had the knowledge about early insulin initiation as treatment in type 2 diabetics' mellitus. However all of them show their willingness for preferences to use insulin as first therapy in type 2 diabetes mellitus

**Key Words:** early initiation of insulin, Diabetic mellitus Type 2, Insulin as first resort, family physicians perceptions.

## INTRODUCTION

Diabetes mellitus is a syndrome characterized by hypoglycemia due to absolute or relative deficiency of insulin.<sup>1</sup> According to the etiological classification of diabetic mellitus; adult onset type 2 is most common. The factors known to be associated with it are insulin resistance, pancreatic islet cells destruction, genetic predisposition and environment. It can be treated by dietary modification, oral hypoglycemic agents and occasionally required insulin therapy.<sup>2</sup> the clinical complications incidences was reported strongly associated with glycemia.<sup>3</sup> According to the WHO 2009 report, it is estimated that there are more than 200 million people worldwide who have diabetics. The mortality associated with diabetes is expected to be double between 2005-2030 with much of it in developing countries. The major disease burden of it is due to it's long term complications and more than 80% diabetic deaths occurring in low and middle income countries.<sup>4</sup> Hyperglycemia is the single most independent predictor for the development of both micro vascular and macro vascular complications. Cardiovascular disease is the major cause of morbidity and mortality in patients with diabetes. In experimental

models, prolonged exposure to hyperglycemia has been shown to result in glucotoxicity<sup>(7)</sup> and oxidative stress<sup>(8-9)</sup>, culminating in cell destruction<sup>(10)</sup> and microvascular and macrovascular complications<sup>(11-12)</sup>. The recent ADOPT study showed that by using insulin sensitizers, the rate of rise in HbA1c could be markedly reduced from 2.4% per year with sulphonyurea to 1.2% per year with metformin and 0.7% per year with rosiglitazone<sup>(13)</sup>. However, zero deterioration in the long run has not yet been achieved up till now. Therefore, one can expect that almost every diabetes patient will need insulin if they survive long enough. This has been well demonstrated in the UKPDS study, in which multiple therapies including insulin were needed as disease progressed<sup>(14-15)</sup>. The recent IDMPs study, which was a clinic based survey of diabetes patients, showed that 31% of Type 2 diabetes patients were on insulin treatment<sup>(40)</sup>. Due to delayed presentation, a significant proportion of Type 2 diabetes patients have rather severe hyperglycaemia at the time of presentation. These patients are usually characterized by poor beta cell function and are in fact at a later stage of the disease<sup>(16)</sup>.

The awareness programmes regarding diabetics may help in the control of it as well as reduction in

complications through all the physicians, medical students, NGO's, media etc.<sup>5</sup> it is also important that the physicians should select the right choice of insulin regimens for better result of the patients.<sup>6</sup> Therefore this study was developed to assess the physician's perception regarding use of insulin in type 2 diabetes mellitus.

## MATERIALS AND METHODS

This descriptive cross sectional study was done on family physicians of Karachi irrespective of gender, age and experience over a period of 9 months from April 2010 to December 2010. Karachi has been divided into 18 towns and we have selected 10 family physicians on non-probability purposive sampling method from each town. But due to different reasons 47 family physicians either not respond or provide very little information. So finally 133 family physicians were included in this study. A pre tested questionnaire was use to collect the data. Those family physicians who were working for a particular specialist were excluded. A written consent was taken by each participant. The questionnaire has the questions regarding age, sex, experience, number of diabetic patients seen per day, research experience, knowledge about insulin use in type II diabetic patients and their way of treatment and finally their perception regarding use of insulin as first therapy in type II diabetic mellitus cases. The data thus collected was analyzed through SPSS version 16.0.

## RESULTS

Over all 133 respondents agreed to fill the questionnaire. Out of these 70 (52.6%) were at hospital place where as remaining 63 (47.4%) were at their clinics. The gender of the respondents was 59.9% male and 30.1 % were females. 59.4% of the respondents were only MBBs where as 40.6% were post graduate. Most of them (44.4%) have <5 year experience. Majority (60.9%) have no experience of research. Most (46.6%) of the respondent doctors deals more than 5 diabetic patient per day and they suggest treatment to them. In majority (63.9%) cases, their suggestion is combined therapy of life style changes with nutritional advice and drugs. the drugs they suggested in oral tablets where as only in 12% cases of type II diabetics they give insulin therapy. The physician's opinion regarding role of insulin therapy in the patients with diabetes type II were also recorded. They were of the opinion that it maintain strict blood glucose level (35.3%), prevents organs complications (27.0%), effective when Oral Hypoglycemic Agents fails (18.0%) and have fewer side effects (3.0%). Majority of them (75.2%) have the knowledge that insulin keeps HBA1C with in normal range as compare to Oral Hypoglycemic Agents. similarly majority (59.4%) have the knowledge that insulin is better than Oral Hypoglycemic Agents

because latter have more devastating side effects. However majority (51.1%) think that Oral Hypoglycemic Agents are better treatment in diabetic mellitus type II. Knowledge of the physicians regarding way of prevention of organ complication, majority think that tight control of blood sugar level is the best way. However 31.6% were of the opinion that early initiation of insulin can prevent the organ complications. Response of majority of physicians (60.2%) was negative regarding use of insulin as first resort in diabetic mellitus type II.

## DISCUSSION

This study is for the first time with no available data to compare with but only these results can be supported by related studies on strict glucose control and long term complications both micro vascular and macro vascular. In past as by Krolewski., James., Lawrence., Ronald., 1987 proposed that type 2 diabetes can be treated by dietary modification, oral hypoglycemic agents and occasionally requires insulin therapy, but now there are evidence that early initiation of insulin prevent pancreatic exhaustion and it is review under article "Early and Aggressive Initiation of Insulin Therapy for Type 2 Diabetes". Which also emphasis on the fear of doctors and patients regarding the hypoglycemia and weight gain and suggests that by using new insulin analogues this problem can be prevented. In studies<sup>7, 8</sup> it also prove that early start of insulin therapy in patients with type 2 diabetics is better. In other study, it was reported significant results of use on insulin in type 2 diabetics.<sup>9,10</sup> Though in UKPDS it was said that there is no difference regarding prevention of complication by intensive glyceemic control with either of oral hypoglycemic drugs or insulin it's the intensive glyceemic control which is important which in contrast to a china study which says insulin is better therefore there is need to do further research regarding early use of insulin in diabetic mellitus type II. So the purpose of this study was to know knowledge of physicians of Karachi regarding this matter and further more to highlight this problem for further research.

## CONCLUSION

As most of the family physicians have no experience of research therefore they have not come to understand the change in the therapy to start insulin early in type ii diabetic patients. Their perception is still the old one to use oral hypoglycemic therapy alone or in combination with other oral hypoglycaemic drugs.

**Recommendations:** Family and general physicians should be educated from time to time by conducting workshops and other discuss at different forums on new research and disease management strategies.

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# Comparative Efficacy of H<sub>1</sub> blocker, H<sub>2</sub> blocker, and Corticosteroid Individually and in Combination in Resolution of Sign and Symptoms of Acute Urticaria

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## ABSTRACT

**Objective:** To compare the efficacy of H<sub>1</sub> blocker, H<sub>2</sub> blocker, corticosteroid in combination or individually in resolution of the sign and symptoms of acute urticaria.

**Study Design:** Randomized control trial

**Place and Duration of Study:** This study was carried out at Medical Department, Naseer Teaching Hospital, Peshawar, Khyber Pakhtunkhwa (KPK) for the period of six months (July 2012 through December 2012).

**Materials and Methods:** In this study 140 adult patients of both gender with acute urticaria were treated with either H<sub>1</sub> blocker (group A), H<sub>2</sub> blocker (group B) or in combinations of H<sub>1</sub> blocker + H<sub>2</sub> blocker (group C), H<sub>1</sub> blocker + H<sub>2</sub> blocker + dexamethasone (group D), H<sub>1</sub> blocker + dexamethasone (Group E), H<sub>2</sub> blocker + dexamethasone (Group F) or Dexamethasone (group G) alone. The end points were resolution of sign and symptoms in each group of patients (minimum 3 hours after treatment). Pregnant females, anemic and Patients with cardiac disease were excluded.

**Results:** H<sub>1</sub>+ H<sub>2</sub> blockers + dexamethasone found to be most effective therapeutic combination (95% of patients) in resolution of sign and symptoms of acute urticaria, followed by H<sub>1</sub> blocker + dexamethasone (90%) and H<sub>1</sub>+ H<sub>2</sub> blockers (85%).

**Conclusion:** This study concludes that the combination of H<sub>1</sub>+H<sub>2</sub> blockers + dexamethasone is more effective in relieving the patient from the sign and symptom of acute urticaria as compared to H<sub>1</sub> blocker or H<sub>2</sub> blocker or dexamethasone given alone or in combination of any two.

**Key Words:** Urticaria, H<sub>1</sub> blocker, H<sub>2</sub> blocker, dexamethasone

## INTRODUCTION

Urticaria is commonly referred to as hives, is the most frequent dermatologic disorder seen in the Emergency Department (ED). It appears as raised, well-circumscribed areas of erythema and edema involving the dermis and epidermis that are very pruritic<sup>1-2</sup>. It is characterized by typical lesion or wheal formation which is often erythematous, usually pruritic papule or plaque that appears and disappears over relatively short periods of time<sup>3</sup>. They are caused by vasoactive mediators, predominantly histamine, released from mast cells. In the vast majority of cases the wheal is transient, lasting for only a few hours in any one place, but with new wheal appearing in other places<sup>4</sup>.

Urticaria is one of the most common dermatologic problems and 20-30% of individuals have at least one attack of urticaria in their lifetime<sup>5-6</sup>. Both children and adults may develop urticaria with the peak age of onset in adults being between 20 and 40 years of age<sup>4</sup>. Urticaria may be acute when the duration is less than 6 weeks<sup>7</sup> or chronic when it lasts for more than 6 weeks<sup>5,8</sup>. Acute urticaria usually develops more severe

clinical and life-threatening symptoms compared with chronic urticaria<sup>9-10</sup>. Common causes of urticaria are drugs, infections, parasites, food and food colours, systemic disease, psychogenic factors, autoimmune disease, endocrine disease and malignancy<sup>3</sup>. Acute urticaria is more common and is characterized with more severe symptoms at onset, which may be life threatening. Clinical symptoms of chronic urticaria are often less severe but much more troublesome than those of acute urticaria, chronic urticaria may have highly variable etiological factors and duration<sup>11</sup>. Large variety of urticaria variants exist, including acute immunoglobulin-E (IgE) mediated urticaria, chemical-induced urticaria, autoimmune urticaria, delayed pressure urticaria, cholinergic urticaria, cold urticaria, solar urticaria, aquagenic urticaria, physical urticaria and many others<sup>1-2</sup>.

Urticaria may be often confused with a variety of other dermatologic diseases that are similar in appearance and are pruritic including maculopapular drug eruption, atopic dermatitis (eczema), contact dermatitis, erythema multiform, insect bites, pityriasis rosea and others.



Usually, the experienced clinician is able to distinguish these from urticaria because of its distinctive appearance, the fact that it is intensely pruritic, and because it blanches completely with pressure<sup>12</sup>.

A number of studies showed the effectiveness of antihistamines treatment either with H<sub>1</sub> blocker<sup>13-15</sup> or with H<sub>2</sub> blocker<sup>16</sup> or their combination in treatment of acute urticaria<sup>17</sup> but these remained ineffective in the treatment or prevention of most forms of urticaria. In addition corticosteroid therapy involving a multitude of formulation is widely used in nearly all fields of medicine<sup>18</sup>. Although the combination of H<sub>1</sub> blocker and H<sub>2</sub> blocker has been reported to improve certain cutaneous outcomes in patients with acute allergic syndromes<sup>16</sup>, data is scanty on combination therapy of acute urticaria. However to the best of our knowledge the data on combination of H<sub>1</sub> blocker + H<sub>2</sub> blocker with dexamethasone is lacking.

## MATERIALS AND METHODS

A total of 140 patients with urticaria were treated with mentioned drugs alone or in combination who presented at out-patient department of Medical Department, Naseer Teaching Hospital, Peshawar during six months (from July 2012- December 2012). Patients between ages 20-60 years of both gender were included in this study who visited the hospital with urticaria developed due to any reason e.g. history of drug intake, history of disease, history of food intake and any allergic reaction which induced urticaria. Approval of hospital ethical committee and informed written consent were taken from the subject. Pregnant ladies and patients with anemia, heart diseases or any other illness were excluded.

Proper history was taken from all the patients. Diagnosis was made on basis of clinical presentation, physical examination and pathological findings. Patients were divided in seven equal groups; A (treated with 22.7mg H<sub>1</sub> blocker), B (treated with 50mg H<sub>2</sub> blocker), C (treated with 22.7mg H<sub>1</sub> blocker + 50mg H<sub>2</sub> blocker), D (treated with 22.7mg H<sub>1</sub> blocker + 50mg H<sub>2</sub> blocker + 4mg Dexamethasone), E (treated with 22.7mg H<sub>1</sub> blocker + 4mg Dexamethasone), F (treated with 50mg H<sub>2</sub> blocker + 4mg Dexamethasone) and G (treated with 4mg dexamethasone). Each group comprises of 20 patients. Patients were observed for minimum of three hours after treatment to evaluate and compare the efficacy of drugs in each group. Duration of the effectiveness was also measured to see the interval of effective drug. All the data collected in pre designed proforma and recorded on SPSS 10.

## RESULTS

As depicted in table-1 males were 78 (56%) with 62 (44%) female. Known etiological findings of acute urticaria in clinical history taking revealed six patients (4%) with positive history of either respiratory tract

infection, gastrointestinal infection, whereas fifteen patients (11%) had positive history of drug intake i.e. ciprofloxacin, metronidazole, non-steroidal anti-inflammatory drugs. Four patients (3%) had positive history of food induced acute urticaria i.e. fish, nuts and mushroom as shown in table 2.

**Table No.1: Frequency and percentage with relation to different ages.**

	Frequency (s)	Percentage
Age		
20-30 years	51	36%
30-40 years	53	38%
40-50 years	27	20%
50-60 years	09	06%
Male	78	56%
Female	62	44%
Total	140	

**Table No.2: History of finding of subjects.**

History findings	Response	Frequency (s)	Percentage
History of Disease	Yes	6	4%
	No	134	96%
History of drug intake	Yes	15	11%
	No	125	89%
History of food intake	Yes	4	3%
	No	136	97%
Total		140	

**Table No.3: Efficacy of drugs in different groups of subjects.**

Groups	Effectiveness	Efficacy Frequency (n)	Percentage	Total
H <sub>1</sub> Blocker	Effective	14	70%	20 cases
	Not Effective	6	30%	
H <sub>2</sub> Blocker	Effective	5	25%	20 cases
	Not Effective	15	75%	
H <sub>1</sub> +H <sub>2</sub>	Effective	17		
	Not Effective	3		
H <sub>1</sub> +H <sub>2</sub> + dexamata- sone	Effective	19	85%	20 cases
	Not Effective	1	15%	
H <sub>1</sub> + dexamata- sone	Effective	18	90%	20 cases
	Not Effective	2	10%	
H <sub>2</sub> + dexamata- sone	Effective	11	55%	20 cases
	Not Effective	9	45%	
dexamata- sone	Effective	8	40%	20 cases
	Not Effective	12	60%	

Table-3 depicted the most effective treatment in the resolution of sign and symptoms. H<sub>1</sub> blocker + H<sub>2</sub> blocker with dexamethasone were effective in 95% whereas rest of the combination of treatment or individual treatment showed less therapeutic efficacy. Table-4 showed effectiveness of the treatment i.e. how quickly drug resolves the symptoms of urticaria after

drug treatment (minimum 3 hours). Fastest resolution of symptoms occurs in group of patients treated with H<sub>1</sub> blocker + H<sub>2</sub> blocker with dexamethasone (between 15-40 minutes). Whereas longest duration was observed in patients treated with H<sub>2</sub> blocker (3-6 hours).

**Table No.4: Duration of effectiveness of drugs in subjects**

Groups	Duration of Effectiveness
H <sub>1</sub> Blocker	2-4 hours
H <sub>2</sub> Blocker	3-6 hours
H <sub>1</sub> +H <sub>2</sub>	1-2 hours
H <sub>1</sub> +H <sub>2</sub> + dexamatasone	15-40 minutes
H <sub>1</sub> + dexamatasone	1 hour
H <sub>2</sub> + dexamatasone	2 hours
dexamatasone	2 ½ hours

## DISCUSSION

Antihistamines are widely used group of drugs for the treatment of acute urticaria. A number of studies showed the effectiveness of antihistamines treatment either with H<sub>1</sub> blocker<sup>13-15</sup> or with H<sub>2</sub> blocker<sup>16</sup> or their combination in treatment of acute urticaria<sup>17</sup>. Linet *al* showed pretreatment effect for H<sub>2</sub> blocker in allergic reaction. Their study demonstrates the benefit of adding H<sub>2</sub> blocker to H<sub>1</sub> blocker antihistamine in treatment of ongoing allergic reactions<sup>16</sup>. Although few studies described the effects of both H<sub>1</sub> and H<sub>2</sub> blockers in treatment of acute urticaria<sup>16</sup>, our study has the value of evaluating different combinations of H<sub>1</sub> blocker, H<sub>2</sub> blocker and corticosteroid. The maximum efficacy in our study was observed in patients received the combination of H<sub>1</sub> blocker + H<sub>2</sub> blocker with dexamethasone (95%) followed by the combination of H<sub>1</sub> blocker + dexamethasone which was effective in 90% cases and the combination of H<sub>1</sub> blocker + H<sub>2</sub> blocker was effective in 85% cases. On the other hand effectiveness of H<sub>1</sub> blocker was found in 70%, H<sub>2</sub> blocker was found in 25% while dexamethasone was found in 40% cases as shown in table-3. Similar observation has been reported by Zuberbier *et al* had mentioned that combination therapy with H<sub>1</sub> and H<sub>2</sub> histamine blockers can benefit patients with acute allergic syndromes<sup>19</sup>. Similar observations were also recorded by Lin *et al* that most cases of simple acute urticaria can be treated with H<sub>1</sub> antihistamine agents. In cases of severe or persistent urticaria, H<sub>2</sub> antihistamines may be added and are probably additive to the effect of H<sub>1</sub> antihistamines if simultaneously given intravenously<sup>16</sup>.

Some patients with urticaria had only cutaneous symptoms whereas some patients had systemic symptoms such as headache, joint pain and gastrointestinal complaints as well<sup>9-10</sup>. Results of the present study showed that the number of patients was more with the history of drug induced urticaria 11% as

compared to the history of food intake induced urticaria patients which were 3% and history of disease induced urticaria patients which were 4%. In this study, most commonly reported drugs which induced urticaria were ciprofloxacin, metronidazole, aspirin, and non-steroidal anti-inflammatory drugs. Urticaria induced by food was due to intake of fish, nuts and mushroom. Diseases which cause urticaria include respiratory tract infections<sup>20</sup>. Similarly, it was observed that 4% urticaria patients in this study had a history of these diseases.

Another merit of our study is the assessment of degree of effectiveness of the drug in all groups in terms of duration of time in which drug showed its effect to clearly resolve the symptoms of urticaria. The patients were observed for a minimum of 3 hour in the current study. Results of the present study showed that combination of H<sub>1</sub> + H<sub>2</sub> blockers and dexamethasone took lesser time in effectiveness as compared to H<sub>1</sub> or H<sub>2</sub> blockers and dexamethasone alone. The results also revealed that the duration of effectiveness of H<sub>1</sub> blocker + H<sub>2</sub> blocker + dexamethasone was observed between 15-40 minutes followed by H<sub>1</sub> blocker + H<sub>2</sub> blocker in which the duration of effectiveness was 1-2 hours and duration of effectiveness of H<sub>1</sub> + dexamethasone was only one hour. On the other hand duration of effectiveness of H<sub>1</sub> blocker was 2-4 hours, H<sub>2</sub> blocker was 3-6 hours and dexamethasone effectiveness was found to be 2 ½ hours as shown in table-4. An improved outcome over the course of one or two hours was seen with combined H<sub>1</sub> blocker and H<sub>2</sub> blocker in patients who were presented with urticaria and angioedema<sup>16</sup>. However, in this study no such significant difference of H<sub>1</sub> blocker, H<sub>2</sub> blocker and dexamethasone was found in different age group and in gender distribution.

No patients developed any severity to intubate or resuscitate them. Parenteral route of administration was used for the patients in all age groups of the present study. No trials of treating the patients orally were done in this study, the medication and treatment resulted in rapid improvement in signs and symptoms of urticaria. However, further studies and trials are needed to ascertain whether similar results are observed if the drugs are administered orally in different age groups of patients suffering from urticaria. The small number of sample size in each group may be the limitation of this study.

## CONCLUSION

Patients presented with acute urticaria in all groups did not have any specific difference regarding gender and age. The statistical difference is noted in improvement of urticaria with different drugs treatment and duration of resolution of signs and symptoms. The presentation of patients was almost same but was treated with different drugs and different strategies. The poorest response was noted with H<sub>2</sub> blocker alone and while

treatment with H<sub>1</sub>blocker + H<sub>2</sub>blocker + dexamethasone gave excellent response in acute urticaria as compared to H<sub>1</sub>blocker alone, H<sub>1</sub> + H<sub>2</sub>blockers and dexamethasone alone.

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# The Relationship between Developmental Dysplasia of Hip and Mode of Delivery in Term-breech-neonate

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## ABSTRACT

**Objective:** To investigate the relationship between developmental dysplasia of the hip and mode of delivery in term breech neonates.

**Study Design:** Prospective Cohort Study

**Place and Duration of Study:** This study was conducted in Khyber Teaching Hospital Peshawar from May 2012 to April 2013.

**Materials and Methods:** Over the study period all neonates delivered at term as singleton breech in the Obstetrics & Gynecology department of Khyber Teaching Hospital were included in the study. Period of gestation, parity, and mode of delivery, fetal gender and birth weight of each neonate was recorded. All neonates were assessed for DDH both clinically and through ultrasound. Severity of dysplasia was graded using modified Graf's static morphological method. Correlation was made between DDH and mode of delivery. Mode of delivery was categorized as vaginal delivery, emergency cesarean section and elective cesarean section.

**Results:** There were a total of 283 breech deliveries during the study period, out of which 16 had DDH. Incidence was more in primigravidae. Majority were females. DDH was more common in vaginally delivered breech babies, in majority of whom DDH was more severe (Graf type III & IV, as opposed to babies delivered through elective cesarean section).

**Conclusion:** Vaginally delivered breech babies constitute a high risk group for DDH. Clinical examination followed by ultrasound examination of both hip joints should be undertaken in all babies delivered as breech so as to institute management in time to prevent avascular necrosis of femoral head.

**Key Words:** Dysplasia of Hip, Breech Neonates, Vaginal Delivery, Cesarean section.

## INTRODUCTION

Developmental dysplasia of the hip (DDH) formerly known as congenital dislocation of the hip, comprises a spectrum of abnormalities that include abnormal acetabular shape (dysplasia) and malposition of the femoral head, ranging from dislocatable hip and mild subluxation to fixed dislocation.<sup>1,2</sup> It is difficult to assess the true incidence of DDH, as the definition varies and there is no gold-standard test. Incidence varies from 1.5 to 20 in 1,000 births.<sup>3</sup>

Diagnosis of DDH at birth includes clinical evaluation and imaging such as radiography and ultrasound examination.<sup>4,5</sup> Findings suggesting DDH include asymmetric skin folds in the proximal thigh and shortening of the thigh on the dislocated side.<sup>2,4,6</sup> Confirmatory findings include a positive Ortolani test or a positive Barlow test.<sup>4,7</sup> Radiographs are readily available and relatively low in cost. The main limitations are radiation exposure and radiography's inability to demonstrate the cartilaginous femoral head.<sup>8,9</sup> Radiographs are of limited value during an infant's first 3 months of life, when the femoral heads are composed entirely of cartilage, but they become more reliable for use in infants 4–6 months of age, with the appearance of femoral head ossification.<sup>8,9</sup>

Ultrasound evaluation of the hip is performed using a high-frequency linear array transducer. Two methods have emerged: a static acetabular morphology method proposed by Graf<sup>10</sup> and a dynamic stress technique proposed by Harcke.<sup>11</sup> Graf method is based on a single coronal image. Graf developed a morphologic and geometric hip classification scheme (types I-IV) using an alpha angle, which measures the osseous acetabular roof angle, and a beta angle, which defines the position of the echogenic fibrocartilaginous acetabular labrum. Harcke developed the dynamic or real-time method, using ultrasound to attempt visualize the Barlow and Ortolani maneuvers. This technique is performed in both the coronal and transverse planes, with and without stress.

Breech presentation is an important risk factor for developmental dysplasia of the hip (DDH).<sup>12</sup> Other risk factors being female gender, positive family history and oligohydramnios.<sup>13,14,15</sup> The obstetric management of term singleton breech deliveries has been greatly influenced by the results of the Term Breech Trial in 2000.<sup>16</sup> This study concluded that reduced perinatal morbidity is associated with term singleton breech births undertaken by elective Caesarean section. In 2001, the Royal College of Obstetrics and Gynaecology<sup>17</sup> published guidelines supporting this conclusion. This study was carried out to find out

whether this change in delivery policy has any effect on reducing the incidence of DDH in breech deliveries. The study examined whether the mode of delivery plays a role in DDH in term singleton infants presenting by the breech.

## MATERIALS AND METHODS

All singleton term neonates delivered as breech ( $\geq 37$  weeks gestation) between January 2012 and January 2013 over a one year period at the Obstetrics and Gynecology department of Khyber Teaching Hospital were included. For each neonate the maternal parity, birth weight, gender and breech type (extended or flexed) were recorded. For each breech birth, the mode of delivery was categorized as vaginal, emergency caesarean section in labour or elective pre-labour caesarean section. Each breech infant was examined by the author to identify those with DDH and correlate them with mode of delivery. Ortolani and Barlow tests were done to assess each neonate. To classify the neonates according to hip instability, we used the Tonnis system<sup>18</sup>: grade 1, slight capsular instability with no snapping sign; grade 2, subluxatable hip (Ortolani's snapping); grade 3, dislocatable and reducible hip (dislocation sign); grade 4, fully dislocated, irreducible hip. All neonates were subjected to ultrasound examination to grade the severity of DDH. To reduce inter-observer variation ultrasound was performed by a single expert ultrasonologist. Severity of dysplasia was graded using modified Graf's static morphological method.

## RESULTS

During the 12 month period a total of 9,438 babies were born in the Khyber Teaching Hospital Peshawar, of whom 283 fulfilled our inclusion criteria. There were 210 deliveries by caesarean section and 73 vaginal births. Of the 283 neonates, 10 had clinical evidence of DDH however ultrasound examination detected 6 extra cases making a total of 16 cases of DDH. There were 4 bilateral dysplasias, 3 right hips only and 9 left hips only. The breech classification comprised 8 extended, 4 flexed and 4 unspecified. There were 11 females and 5 males. Among the mothers, 10 were primiparous and 6 multiparous. The mean birth weights for the infants with DDH according to delivery category were: 3.3 kg (2.43 to 4.0) vaginal, 3.4 kg (2.8 to 4.0) emergency caesarean, 3.7 kg (2.8 to 4.5) elective caesarean. The DDH incidence among vaginal breech births was 6 of 73 breech births (8.21%), compared with 7 of 120 (5.83%) for emergency caesarean sections and 3 of 90 (3.33%) for elective prelabour caesarean sections. The incidence of DDH was significantly different between breech infants delivered vaginally and those delivered by elective caesarean section (8.21% vs 3.33%;  $p < 0.02$ ).

**Table No.1: Characteristics of neonates with DDH**

Gender	Female =11	Male=5
Maternal Parity	Primiparas = 10	Multiparas=6
Mode of delivery	Vaginal = 73 Emergency caesarean =120 Elective caesarean= 90	
Birth weight (Mean)	Vaginal= 3.3kg Emergency caesarean=3.4kg Elective caesarean= 3.7kg	
Type of breech	Extended= 8 Flexed = 4 Unspecified = 4	
Laterality of DDH	Bilateral= 4 Left hip= 9 Right hip=3	

**Table No.2: Relationship between the mode of delivery and the incidence of developmental dysplasia of the hip (DDH) in term breech infants**

Mode of delivery	Number of neonates	Number of DDH (%)
Vaginal	73	6 (8.21%)
Emergency caesarean	120	7 (5.83%)
Elective caesarean	90	3 (3.33%)
Total	283	16 (5.65%)

Taking all grades of hip dysplasia into account (Graf types II, III and IV), there was no statistical difference in the incidence of dysplasia between the groups (elective section 8.2%, emergency section 7.9% and vaginal delivery 6.8%). However, when cases with Graf type II dysplasia, which may represent physiological immaturity, were excluded, the rate of type III and IV hips, which we consider to be clinically relevant, increased in the vaginally delivered group (4.8%) compared with the elective section group (1.2%), with a relative risk of approximately 1:4 (95% confidence interval 1.03 to 15.91). No difference was observed between the emergency and elective section groups, or between the emergency section and vaginally delivered groups.

## DISCUSSION

Our findings indicate that the mode of delivery influences the incidence of DDH in infants in breech presentation. Those delivered vaginally had an incidence more than double that of breech infants delivered by pre-labour elective Caesarean. This correlates with the study done by Chan et al<sup>13</sup> who conducted a multicentre analysis of perinatal risk factors for hip dysplasia, and noted higher rates among infants delivered vaginally. Clausen et al<sup>12</sup> reported the same findings.

We suggest the force of labour on the fetal hip contributes to DDH. The resting intrauterine pressure is 4 to 5 mmHg but during the active phase of labour this

can increase to as much as 100 mmHg, which possibly contributes to the increased rates of hip dislocation in the vaginally-delivered group. Pressure may cause a hip, already susceptible to dislocation by virtue of ligamentous laxity to dislocate. This also explains the relatively increased risk of dysplasia in the emergency cesarean section group where there are increased compression forces on the neonate as compared to pre-labour elective cesarean section where the neonate is not exposed to the stress of labour. However, pressure alone does not explain the acetabular dysplasia associated with dislocation in some infants. In our study the incidence of DDH was more in primigravida with breech as opposed to multigravida mothers. This is similar to the observation of Wilkinson et al<sup>15</sup>. This finding is again due to the fact that the fetus is subjected to less pressure effects in the multigravidae with lax uterus and relatively compliant birth canal.

We confirmed a higher rate of dislocation among girls, which is long recognized<sup>13,15</sup> and possibly related to increased joint laxity in response to maternal hormones such as relaxin. When considering the birth weights of breech infants with DDH, we found DDH to be more common in neonates with average birth weight as opposed to high birth weight. This is contrary to previous studies<sup>13,15</sup> which showed that the incidence of DDH was greater among larger babies. However it was so because the heavier infants were in the group with the lowest incidence of DDH (elective Caesarean section).

In our study we did ultrasound examination of hips in all neonates. Several studies<sup>5,19,20,21</sup> have compared clinical examination and ultrasound as methods of screening infants for DDH. Marks et al<sup>19</sup> reported that ultrasound screening for DDH can detect cases of instability not diagnosed at birth by routine clinical examination and in infants who have no risk factors for DDH. Tonnis et al<sup>18</sup> and Rosenberg et al<sup>5</sup> reported respectively that 52.2% and 50% of the ultrasonographically pathological hips in their studies had no clinical sign of instability. Omeroglu and Koparal<sup>6</sup> found that ultrasonography can detect acetabular dysplasia in patients whose clinical examination findings are normal. Our findings are similar to these where ultrasonography detected an extra 6 cases with no evidence of DDH on clinical examination. It is therefore recommended that high risk neonates like breech deliveries should be subjected to ultrasound examination.

Taking into account the Graf classification the incidence of Type III and IV hips which constitutes abnormal hips with frank subluxation was more in the vaginally delivered neonates. Incidence of Type II hips which do not require active management was not statistically different between the two groups. Same was observed by Clausen et al.<sup>12</sup>

We calculate that for every 1000 term singleton breech presentations there would be 81 cases of hip dislocation if all were delivered vaginally compared with 37 if all were delivered by elective caesarean section. This represents a 54% reduction in DDH. This not only represents a major financial benefit but also indicates the magnitude of the mechanical effects of labour on the hip joint in term breech cases.

## CONCLUSION

Our study indicates that the mode of delivery has a significant influence on the incidence of DDH. It is more common in vaginally delivered breech neonates as compared to neonates born through planned pre-labour elective cesarean section. However the incidence is not decreased much when the cesarean section is done in emergency where the mother is already in labour. This implies that it is not only the actual phase of delivery but also the stress of uterine contractions which predispose the breech baby to DDH.

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## ACKNOWLEDGMENTS

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

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