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CATARACT AWARENESS AMONG PEOPLE ATTENDING OUTDOOR PATIENT DEPARTMENT OF OPHTHALMOLOGY OF ALLAMA IQBAL MEMORIAL TEACHING HOSPITAL SIALKOT, PUNJAB

Isma Munir Rana , Hafiza Anam Saleem Khan, Bilal Umar

Abstract

Background: Cataract is the major cause of blindness in Worldwide. This study was undertaken to determine the awareness of cataract among subjects residing in Sialkot, Punjab. Study was conducted in Allama Iqbal Memorial Teaching Hospital Sialkot. The department of ophthalmology of Allama Iqbal memorial teaching hospital Sialkot provides outdoor patient services as a tertiary eye unit.

Methods: Subjects of different age groups were selected. we conducted a cross-sectional survey during two weeks OPD session of AIMTH in Sialkot. Sialkot is a city in Punjab. During survey, 100 subjects underwent a structured interview regarding awareness (heard of) and knowledge (understanding of the disease) of cataract. We made necessary modifications and clarifications of terms based on pretest procedure. Questions were close-ended

Results: A total of 100 subjects were interviewed during one week study period. 61% of them had some understanding about cataract. The remaining 39% participants were not aware of cataract. 32 participants responded that cataract was blurred eye vision. The source of knowledge about cataract in 20 respondents was information from family members. 31 participant mentioned that one could have cataract without having any symptoms and 36 participant believed that vision loss due to cataract was not reversible. 32 participants believed that old age was a risk factor for developing cataract .32 participants believed that there is risk of developing glaucoma in cataract.

Conclusion: We documented that awareness of cataract is good among people attending ophthalmic outdoor patient department of Allama Iqbal memorial teaching hospital Sialkot. but the level of knowledge among those reporting to be aware of cataract was poor. One can suspect that the level of cataract knowledge will be similarly low in the general population.

Cataract is the leading cause of blindness worldwide. It is estimated that 50% of all global blindness is caused by cataract. Globally it cause moderate to severe disability in 53.8 million, 50 million of whom are in middle and low income countries. In the eastern Mediterranean region, cataract is responsible for over 51% of blindness.

Although cataract can be surgically removed, in many countries barriers exist such as cost, lack of information and transportation problems that prevent patient to access surgery. Not only can education and preventive eye care save needless sufferings, it can also reduce the economic burden of the disease. Subgroups of the population who are having insufficient knowledge about it need to be identified and targeted in order to most effectively used resources for public education.

The department of ophthalmology of allama iqbal memorial teaching hospital Sialkot provides outdoor patient services as a tertiary eye unit. The activities include general eye health evaluation, refraction and the anterior and posterior segment eye surgeries. A wide range of individuals from different socioeconomic and educational background present in outdoor patient department of ophthalmology for eye evaluation.

METHODS

We conducted a cross-sectional survey during two weeks OPD session of AIMTH in Sialkot. Sialkot is a city in Punjab, Pakistan. Sialkot is one of

thirty six district of Punjab, and is part of north-east Punjab – one of Pakistan's most highly industrialized region. Based on figures published by the Pakistan bureau of statistics in 2017,population of Sialkot was 3,893,672, of whom 1,921,643 are males, 1,971,746 are females and 282 transgender persons .

There are ninety basic health units (BHU), eight rural health centers (RHC),two tehsil headquarters (THQ) and one district headquarter that is AIMTH where the study has been conducted. There are consultants and residents of ophthalmology with the nursing staff in DHQ Sialkot.

A total 300 people of different ages presented for eye evaluation during one week session, out of which 100 people, randomly, constituted the study population .Data on demographics and awareness of cataract were collected by trained doctors through face to face interview using a structured questionnaire. The questionnaire was prepared in English but the interview was conducted in the language each participant understood best.

We made necessary modifications and clarifications of terms based on pretest procedure. The questionnaire was designed to be brief and easily understandable. Questions were close-ended. Respondents were not prompted to possible responses.

Questions regarding awareness of cataract were asked after collecting demographic information. Respondents were first asked whether or not they heard about cataract and what their source of information was. They was inquired to describe what they understood by cataract and their responses were recorded according to the options.

A participant was classified as being aware of cataract if s/he said 'YES' to the question have you heard about cataract?, and gave such answers as' cataract is opacity of lens 'and ' blurred vision ' or similar answers when they asked 'what do you understand by cataract'. Those who were aware of cataract were then asked whether they knew about risk factors for cataract. And whether someone can have cataract without having any symptoms.

RESULTS:

A total of 100 subjects were interviewed during one week study period. Majority of them were females (60%) and married (83%). About 26% were illiterates and 44% were housewives.

61% of them had some understanding about cataract. The remaining 39% participants were not aware of cataract.

Socieodemographic Data of Participants at Ophthalmic out Patient of AIMTH,Sialkot.	Total=100
Age	
20-39	50%
40-59	36%
60-79	14%
Gender	
Male	40%
Famale	60%
Marital status	
Married	83%
Unmarried	17%
Education	
Illiterate	26%
Read and write only	1%
1-4 grade	7%
5-8 grade	21%
9-12 grade	27%
College education	10%
University education	8%
Occupation	
Farmer	2%
Housewife	44%
Govt./Non-Govt. Employee	22%
Merchant	1%
Daily Labourer	17%
None/Dependent on family	8%
others	6%

Awareness of catarct in relation to socio-demographic characteristics of respondents at an ophthalmic out door patient department of AIMTH, Sialkot.

The responses of those study participants who were aware of cataract are presented in Table ---- . 32 participants responded that cataract was blurred eye

Characteristics [N = 100]	Aware [n =61]	Not aware [n = 39]
Gender		
Male	24	16
Female	37	23
Age		
40-49	4	0
50-59	4	101
60-69	0	76
70-79	0	32
80+	0	7
Marital status		
Married	49	34
Non-married	12	5
Education		
Illiterate	13	13
Read & write only	1	0
1-4 grade completed	4	3
5-8 grade completed	12	9
9-12 grade completed	15	12
Collage education	8	2
University education	8	0
Occupation		
Farmer	1	127
Housewife	1	73
Employee	6	62
Merchant	0	32
Daily laborer	0	13
Others	0	25

Response	no (%) [N = 61]
Meaning of cataract	
Blurred vision	32
blindness	5
Pearl like opacity	19
Rainbow halos	1
Raised eye pressure	1
Unmatched answer	1
do not know	2
Source of information	
family members	20
Hospital	5
doctor	10
Friends/neigbour	7
Radio/newspaper	3
Others	14
Do not know	2
Can someone have catarct without any symptoms?	
Yes	31
No	20
Not sure	10
Are symptoms due to cataract reversible?	
Yes	19
No	36
Not sure	6
Factors identified as risk for cataract	
Family history	6
Old age	32
Not sure	8
Do not know	15
Is there any risk of developing glaucome in catract?	
High	32
None	8
Not sure	21

vision. The source of knowledge about cataract in 20 respondents who were aware of cataract was information from acquaintance who had history of cataract. 31 participant mentioned that one could have cataract without having any symptoms and 36 participant believed that vision loss due to cataract was not reversible. 32 participants believed that old age was a risk factor for developing cataract and another 6 identified family history as a risk factor. 32 participants believed that there is risk of developing glaucoma in cataract.

Answers responded to various questions by those participants who were aware of glaucoma at out patient department of AIMTH ,Sialkot.

DISCUSSION

Cataract is the leading cause of blindness worldwide. Most common risk factor for this disease is Age Factor of the patient. Most of the time people comes with the complaints of decreased visual acuity, blurring of vision, can't read and write properly, difficulty while inserting a thread inside the hole of needle. In Early stages of the disease they can see objects placed at far distance and feel difficulty only for near things but afterwards they are unable to appreciate the objects which are placed at a far distance, ultimately they decided to get operated and be able to see clear again.

While conducting a survey in Allama Iqbal memorial teaching hospital , District Sialkot related

to Awareness of Cataract. We label a person as aware who responded "YES" to the question are you aware of cataract?. The awareness about cataract was good due to high prevalence of cataract in Sialkot district. 32 people called it blurring of vision and 19 people mentioned it as pearl like opacity rest of them said about the other options who don't know about the disease at all. Since it's a prevalent disease most of people who are aware about it, came to know about catract by some family member. Other source of information was from doctors and very few from hospital management/ information desk. There is no association found between gender and awareness of cataract as 60% males and 61% females had awareness about cataract. Also the relationship between age and awareness was not significant. Marital status showed no significant association.

The only socieodemographic factor associated with awareness of cataract in our study was education. Participants who had university level education showed 100% awareness.

We asked them whether the symptoms are reversible or not. Majority (59%) of them nodded negatively. Reasons behind this fact it that people might have noticed that even after being treated patient still complaint of blurring of vision again and are bound to wear glasses, so they concluded that the disease is not cured fully. But an ophthalmologist knows about posterior capsular opacification (PCO) after surgery and loss of accommodation because in pseudophakic eye flexibility of lens is lost and ciliary muscle can't accommodate for far vision. So this needs to be addressed before surgery of the patient.

Still majority of people know that it's an age related disease and about 52% of people are also aware of the fact that if left untreated then it will be higher risk of developing glaucoma.

CONCLUSION:

We documented that awareness of cataract is good among people attending ophthalmic outdoor patient department of Allama Iqbal memorial teaching hospital Sialkot. but the level of knowledge among those reporting to be aware of cataract was poor. One can suspect that the level of cataract knowledge will be similarly low in the general population. An efficient information, education and communication strategy needs to be designed. Educational programmes to enhance public awareness about cataract are needed to improve the effectiveness of health awareness especially eye health. This will also prevent unnecessary blindness.

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GLAUCOMA AWARENESS AMONG PEOPLE ATTENDING OUT DOOR PATIENTS DEPARTMENT OF OPHTHALMOLOGY AT ALLAMA IQBAL TEACHING HOSPITAL SIALKOT , PUNJAB .

Hafiza Anam Saleem Khan, Maryam Umar, Bilal Umar

Abstract

Background: Glaucoma is the second leading cause of blindness worldwide. Up to 50% of glaucoma patients are already blind in one eye at presentation. This study was undertaken to determine the awareness of glaucoma among subjects residing in Sialkot, Punjab. Study was conducted in Allama Iqbal Memorial Teaching Hospital Sialkot. The department of ophthalmology of Allama Iqbal memorial teaching hospital Sialkot provides outdoor patient services as a tertiary eye unit.

Methods: Subjects of different age groups were selected. we conducted a cross-sectional survey during two weeks OPD session of AIMTH in Sialkot. Sialkot is a city in Punjab. During survey, 100 subjects underwent a structured interview regarding awareness (heard of) and knowledge (understanding of the disease) of glaucoma. We made necessary modifications and clarifications of terms based on pretest procedure. Questions were close-ended

Results: A total of 100 subjects were interviewed during one week study period. 37% of them had some understanding about glaucoma. The remaining 63% participants were not aware of glaucoma. 10 participants responded that glaucoma was blurred eye vision. The source of knowledge about glaucoma in 14 respondents was information from family members. 16 participant mentioned that one could have glaucoma without having any symptoms and 27 participant believed that vision loss due to glaucoma was not reversible. 10 participants believed that old age was a risk factor for developing glaucoma .

Conclusion: We documented that awareness of glaucoma is average among people attending ophthalmic outdoor patient department of Allama Iqbal memorial teaching hospital Sialkot. And the level of knowledge among those reporting to be aware of glaucoma was poor. One can suspect that the level of glaucoma t knowledge will be similarly low in the general population.

Glaucoma is the second leading cause of blindness worldwide. Up to 50% of glaucoma patients are already blind in one eye at presentation. Eye health education that influences people to participate in regular ophthalmologic care may be an important step to detect glaucoma early, thereby preventing needless blindness. Not only can education and preventive eye care save needless suffering, it can also reduce the economic burden of the disease. Subgroups of the population who are at highest risk both for developing the disease and having insufficient knowledge about it need to be identified and targeted in order to most effectively use resources for public education.

The Department of Ophthalmology of Allama Iqbal memorial teaching hospital, sialkot provides outreach ophthalmic activities in addition to regular services at its tertiary eye unit. This includes general eye health evaluation, refraction and surgery. A wide range of individuals from different socioeconomic and educational background present for eye evaluation .

METHODS

We conducted a cross-sectional survey during two weeks OPD session of AIMTH in Sialkot. Sialkot is a city in Punjab, Pakistan. Sialkot is one of thirty six district of Punjab, and is part of north-east Punjab – one of Pakistan's most highly industrialized region. Based on figures published by the

Pakistan bureau of statistics in 2017,population of Sialkot was 3,893,672, of whom 1,921,643 are males, 1,971,746 are females and 282 transgender persons .

There are ninety basic health units (BHU), eight rural health centers (RHC), two tehsil headquarters (THQ) and one district headquarter that is AIMTH where the study has been conducted. There are consultants and residents of ophthalmology with the nursing staff in DHQ Sialkot.

A total 500 people of different ages presented for eye evaluation during one week session, out of which 100 people, randomly, constituted the study population .Data on demographics and awareness of glaucoma were collected by trained doctors through face to face interview using a structured questionnaire. The questionnaire was prepared in English but the interview was conducted in the language each participant understood best that is Urdu and Punjabi.

Questions regarding awareness of glaucoma were asked after collecting demographic information including occupation of respondants. Respondents were first asked whether or not they heard about glaucoma and what their source of information was. They was inquired to describe what they understood by glaucoma and their responses were recorded according to the options provided in questionnaire.

A participant was classified as being aware of cataract if s/he said 'YES' to the question have you heard about glaucoma ?

RESULTS

100 respondents were asked about glaucoma out of which 37% were aware of the glaucoma rest of 63% were not even understand the word glaucoma. Most of the participant were females 61% and married 78% and house wives 42.

Most of the participants were 31-60years of age. 27 participant were illiterate out of which 7 have some understanding about glaucoma. The relation of awareness with university education was 86%.

Table 1: *Sociodemographic Data of Participants at Ophthalmic Out Patient of AIMTH*

Characteristics	Total=100
Age	
10-30	37%
31-60	52%
61-90	11%
Gender	
Male	39%
Female	61%
Marital status	
Married	78%
Unmarried	22%
Education	
Illiterate	27%
Read and write only	3%
1-4 grade	2%
5-8 grade	23%
9-12 grade	29%
College education	9%
University education	7%
Occupation	
Housewife	42%
Govt./Non-Govt. Employee	24%
Merchant	1%
Daily Labourer	15%
None/Dependent on family	14%
others	4%

Awareness status related to demographics is given in table.

The responses of those study participants who were aware of cataract are presented in Table ---- . 10 participants responded that glaucoma was blurred eye vision. The source of knowledge about glaucoma in 14 respondents who were aware of cataract was information from acquaintance who had history of cataract. 16 participant mentioned that one could have glaucoma without having any symptoms and 27 participant believed that vision loss due to glaucoma was not reversible. 10 participants believed that old age was a risk factor for developing glaucoma and another 5 identified family history as a risk factor.

Table 2: *Awareness of Glaucoma in Relation to Sociodemographic Characteristics Of Respondents at An Ophthalmic Out Door Patient Department of Aimth, Sialkot.*

Characteristics [N = 100]	Aware [n =37]	Not aware [n = 63]
Gender		
Male	15 (38.5%)	24
Female	22 (36%)	39
Age		
10-30	11	26
31-60	21	31
60+	5	6
Marital status		
Married	31	47
Non-married	6	16
Education		
Illiterate	7	20
Read & write only	1	2
1-4 grade completed	1	1
5-8 grade completed	10	13
9-12 grade completed	8	21
Collage education	4	5
University education	6	1
Occupation		
Housewife	16	26
Employee	10	14
Merchant	0	1
Daily laborer	6	9
dependant on family	3	11
Others	2	2

Table 3: *Answers Responded to Various Questions by Those Participants Who Were Aware of Glaucoma at Out Patient Department of AIMTH ,Sialkot.*

Response	no (%) [N = 37]
Meaning of cataract	
Blurred vision	10
Blindness	13
Pearl like opacity	1
Rainbow halos	1
Raised eye pressure	10
Unmatched answer	1
do not know	1
Source of information	
family members	14
Hospital	2
Doctor	5
Friends/neigbour	5
Radio/newspaper	0
Others	11
Do not know	0
Can someone have glaucoma without any symptoms?	
Yes	16
No	12
Not sure	9
Is blindness due to glaucoma reversible?	
Yes	10
No	27
Not sure	0
Factors identified as risk for glaucoma?	
Family history	5
Old age	10
Not sure	15
Do not know	7

DISCUSSION

Patient of Glaucomatous eye ultimately presents with visual field defect of left untreated. Because raised intraocular pressure will damage optic nerve fibers permanently and once nerve is damaged it's irreparable. An ophthalmologist can only prevent further damage but unable to revert the damage already occurred.

In Pakistan Glaucoma is notorious with a term i.e "Kala motiya" as they know that this disease will leave a person in the darkest corner of life, so we decided to ask about the disease in the language of people during our survey in Allama Iqbal memorial Teaching hospital District Sialkot.

We asked them whether they know about Kala motiya or not, those who answered yes we asked them further what do they know about the disease? The awareness about glaucoma was average despite high prevalence of glaucoma in Sialkot district. We gave them few options from which 35% of them defined it as blindness, 27% as raised eye pressure and 27% as blurred vision. As people might have observed people with same disease but different type of severity/complaints. Then further we asked them about their source of information , 38% of them came to know it from family member who suffered from this disease. There is no association found between gender and awareness of glaucoma as 38.5% males and 36% females had awareness about glaucoma. Also the relationship between age and awareness was not significant. Marital status showed no significant association.

The only socieodemographic factor associated with awareness of glaucoma in our study was education. Participants who had university level education showed 86% awareness. Afterwards we inquired that can someone have glaucoma without any symptoms? 43% of people said yes, 32% nodded negatively, 24% were not sure about it. It means people have started searching about this disease as in early stages of disease if Intraocular Pressure is controlled by medications or sugical techniques it

will not show symptoms or less severe. When we asked them about risk factor of the disease, majority of them are not sure about it, while 27% opt for old age , 19% totally unaware and 14% said that it might be hereditary. It means they don't know about the fact that most of the time glaucoma is hereditary and spread by consanguineous marriages.

CONCLUSION

We documented that awareness of glaucoma is average among people attending ophthalmic out-door patient department of Allama Iqbal memorial teaching hospital Sialkot. And the level of knowledge among those reporting to be aware of glaucoma was poor. One can suspect that the level of glaucoma knowledge will be similarly low in the general population. An efficient information, education and communication strategy needs to be designed. The data suggest the need for community-based health education programs to increase the level of awareness and knowledge about glaucoma. These programs will help in reducing vision related problems.

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AGREEMENT BETWEEN T2 WEIGHTED AND STIR SEQUENCES IN THE DIAGNOSIS OF BONE BRUISES ASSOCIATED WITH ACUTELY INJURED ANTERIOR CRUCIATE LIGAMENT

Naeem Ahmad Khan[1], Beenish Javed[2], Fatima Iqbal[3], Aamer Nadeem Chaudhary[4]

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Abstract

Objective: Bone bruise is post-traumatic bone marrow change, which is seen frequently after injury to anterior cruciate ligament (ACL). T2W and STIR sequences of MRI are used to detect the bone bruises. The objective of the study is to determine the degree of agreement between conventional T2W sequences and STIR sequences of MRI in the diagnosis of bone bruises in acutely injured ACL.

Design: Descriptive cross-sectional study.

Place of study: Department of Radiology Jinnah Hospital / Allama Iqbal Medical College, Lahore.

Duration of study: 6 months (from July 2017 to December 2017)

Patients & Methods: Total 150 patients with acute knee injury were included in study. All the patients had MRI done with T2W sequences, followed by STIR sequences for detection of bone bruise. Agreement was labeled in true positive and true negative patients.

Results: T2W sequences could detect the bone bruise in 111(74%) patients, while STIR sequences in 123(82%) patients. Agreement was detected in 138 (92%) patients. Kappa statistics showed substantial agreement (kappa = 0.681

Conclusions: Although the frequency of detection of bone bruise high with both T2W and STIR sequences, STIR sequences should be preferred to determine the bone bruise among patients with ACL injury

Key Words: STIR sequence (short Tau Inversion Recovery), T2W sequence, bone bruise; anterior cruciate ligament injury

The anterior cruciate ligament (ACL) is the most commonly injured of the major knee ligaments. These injuries plague both athletes and non-athletes. The ACL is a vital ligamentous stabilizer of the knee that resists anterior translation and secondarily resists varus and valgus forces. The ACL also functions as a mechanoreceptor that relays information about knee tension to the central nervous system.[1]

Injury to the ACL is potentially functionally debilitating and often requires surgical intervention followed by an extensive course of rehabilitation. Approximately 200 000 ACL injuries occur annually in the United States, leading to nearly 100 000 ACL reconstruction surgeries, one of the most common orthopaedic surgeries, which has expectations of excellent outcome.[2]

The overall incidence of ACL tear is between 29-30 per 100,000 people.[3] Approximately, 70% of ACL injuries occur during a sporting activity, especially those involving cutting or twisting, such as skiing, soccer, basketball, or football.[4] A study in the USA analyzed National Collegiate Athletic Association (NCAA) soccer players and found an ACL injury incidence of 14 per 100,000 athletic exposures per year between 1989 and 2004.[25]

Anterior cruciate ligament injury has been shown to cause an immediate reduction in function and increase the risk for long-term joint degene-

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ration.[5] ACL injury is more common in females than in males due to valgus alignment of the knee, Q angle, and the thickness of the ACL, joint laxity, hormonal influences and training techniques in females.[6]

Bone bruise is a common finding in acutely injured knee found on a magnetic resonance imaging (MRI).[3] Bone bruise is post-traumatic bone marrow change, which is caused by the combination of hemorrhage, edema and microtrabecular fracture without disruption of adjacent cortex.[7] Bone bruises are classified as either reticular or geographic based on the pattern of osseous injury.[8] Killian ML et al.[9] and Viskontas DG et al.[10] found that 83% of patients with ACL rupture had a bone bruise in the lateral compartment i.e. lateral femoral condyle and lateral tibial plateau. The overall prevalence of bone bruise in acute ACL injury is from 20-50%.[3,7,11] In a recent review, it was reported that 0-39% of patients following isolated ACL injury and 40-90% patients with combined ACL and meniscus injury will develop knee osteoarthritis within 10 to 15 years.[11]

Since the introduction of magnetic resonance imaging in early 1980s, it has proven to be an excellent technique for evaluating patients with knee problems including acute or chronic trauma cases. Magnetic resonance imaging has a high soft tissue contrast. It provides direct visualization of soft tissue structures, including ligaments, tendons, joint capsules, menisci, and joint cartilages – structures that are impossible to see on plain radiographs and often not clearly distinguishable by CT.[12] Studies have shown it to be highly sensitive, specific and accurate non-invasive method for diagnosing internal derangement of knee involving menisci, ligaments, patellofemoral joints and other soft tissues and osseous structures in the knee.[13]

Magnetic resonance imaging (MRI) is the imaging modality of choice for detecting bone bruises in ACL injury, which usually cannot be seen using other radiological methods.[14] Bone bruise on MRI is seen as focal abnormal signal of the bone marrow of the femoral condyles or tibial plateau. It is seen as increased signal in T2W sequence and hyperintensity of the signal in STIR (short Tau inversion recovery) sequence, which described the best appearance of bone bruise.[15] This change in signal intensity is caused by posttraumatic edema which is one of the major histopathological feature of bone bruise.[16] Sensitivity of MR imaging for detecting bone bruise of the knee is 83-96% and specificity is 86-96%.[7,11,17] STIR is the preferred sequence for diagnosis of bone bruises as compared to T2W sequence with diagnostic accuracy reaching upto 100%.[18] A study done by Hou-you Li et al.[18] showed presence of bone bruises in 26 cases out of 31 on T2W sequence and in all 31 cases on STIR sequences giving us an agreement of 83.8%.

This study will help us to determine the degree of agreement between conventional T2W sequences and STIR sequences in detecting bone bruise in acutely injured ACL. Due to its clinical significance, definitive diagnosis of bone bruise will helps the clinicians to formulate a management plan with appropriate rehabilitation protocol and keep follow up for prevention of reported late complications of traumatic bone bruises such as knee osteoarthritis. Since the previous studies were done with inadequate sample sizes (35 to 46) we took larger sample (150) to find the agreement between T2W and STIR sequences in diagnosing bone bruises in acutely injured ACL.

METHODS

STUDY DESIGN

Descriptive cross-sectional study

SETTING

This study was conducted at Department of Radiology, Jinnah Hospital / Allama Iqbal Medical College Lahore.

DURATION OF STUDY: Six months.

SAMPLING TECHNIQUE

Non probability purposive sampling

SAMPLE SIZE

Sample size of 150 cases calculated with 95% confidence level, 8% margin of error and taking

expected percentage of agreement that is 83.8% between T2W sequences and STIR sequences of MRI in the diagnosis of bone bruises in acutely injured ACL.

SAMPLE SELECTION

Inclusion criteria

a. All patients with acutely injured knee (within one month of trauma).
b. Patients of age 15-65 years of either sex.

Exclusion criteria

a. Patient's in which bone marrow edema is due to other causes i.e. ischemia, infection, migratory osteoporosis and neoplasm which will be determined before by history, clinical symptoms and signs.
b. Patients having osteoarthritis.
c. Patients with h/o previous knee surgery.
d. Not willing to participate in the study.
e. Patients with injuries other than ACL injury like meniscal injury or collateral ligament injury etc.
f. Patients with contraindications to MRI like cardiac pace-maker, metallic implants etc.

DATA COLLECTION:

According to sample size, 150 patients who presented in outdoor departments of Jinnah Hospital, Lahore and are referred by clinician to the radiology department fulfilling the inclusion/ exclusion criteria were selected. After taking informed consent and relevant history including history of trauma i.e. type and duration, magnetic resonance imaging (MRI) of injured knee was performed in every patient by using 1.5 Tesla MR with T1W, T2W and STIR images. Each MRI was reviewed by a radiologist, blinded to patient identification, for presence of ACL tear and associated bone bruises. Bone bruise was seen as low signal intensity on T1-weighted, high signal intensity on both T2W and STIR sequences. All data was recorded on a specially designed proforma which contained two parts, Part 1 included the patient's bio-data while part 2 contained the study variables i.e. ACL tear and bone bruises with findings on T2W sequences and STIR sequences recorded separately.

DATA ANALYSIS

Collected data was analyzed through computer software SPSS 16.0. Mean and standard deviation were calculated for quantitative variables i.e. age. Frequency and percentage was calculated for qualitative variables i.e. gender, ACL and bone bruises on T2W sequences and STIR sequences and their agreement. Effect modifiers like age (≤ 30 years, >30 years), gender (male, female) and type of trauma (sports, motor vehicle accident, domestic) were controlled through stratifications. Kappa statistics was used to see the strength of association between T2W and STIR sequences in the diagnosis of bone bruise in acutely injured ACL.

RESULTS

One hundred and fifty patients were included in the study.

Distribution of patients by age:

The mean age of the patients was 31.43 + 12.09 years. [Range 15 – 48 years]. There were 32 (21.3%) patients in the age range of 15 – 20 years, 69 (46%) patients of age range of 21 – 30 years, 30 (20%) patients of age range of 31 – 40 years, 19 (12.7%) patients of age range of 41 – 50 years and none of the patients was of age > 50 years.

Distribution of patients by sex:

There were 97 (64.7%) male patients and 53 (35.3%) female patients. The female to male ratio in this group was 1:1.83

Distribution of patients by type of tear:

Complete tear was present in 40 (26.7%) patients, while partial tear was seen among 110 (73.3%) patients.

Distribution of patients by mode of injury:

The knee injury results by motor vehicle accident in 105 (70%) patients, sports injury in 7 (4.7%) patients, and by domestic injury in 38 (25.3%) patients

Distribution of patients by presence of bone

bruise on T1W, T2W sequences:

On T1, TW2 sequence, bone bruises were present in 111 (74%) patients, while 39 (26%) did not have bone bruise.

Distribution of patients by presence of bone bruise on STIR sequences:

On STIR sequence, bone bruises were present in 123 (82%) patients, while 27 (18%) did not have bone bruise.

Distribution of patients by presence of agreement of T1W, T2W sequences and STIR sequences:

Agreement was labeled as yes in 138 (92%) patients, while as no in 12 (8%) patients.

Kappa calculations of agreement between the conventional T1W, T2W and STIR sequences:

There were 111 (74%) cases that were found to be true positive and 27 (18%) cases that were found to be true negative. So, the analysis using the Kappa statistic was performed to determine an agreement between the two techniques. The results were K = 0.681, and p <0.05. There was found a substantial agreement (kapp = 0.61 – 0.80).

Distribution of patients by location of bone bruises:

There were 123 patients who were labeled as yes with bone bruises. Among those, there were 66 (53.4%) patients in whom bone bruise were present lateral femoral condyle, and in 38 (30.1%) patients on lateral tibial plateu. Collectively, bone bruises were present in 104 (84.6%) patients on lateral aspect of knee joint. There were 11 (8.9%) patients in whom bone bruise were present on medial femoral condyle. In medial tibial plateu, bone bruise were seen in 8 (6.5%) patients. Collectively, bone bruises were present in 19 (15.4%) patients on medial aspect of knee joint.

Stratification of Effect modifiers with presence of bone bruise:

With respect to age, there were 101 patients of age < 30 years. Among these, there 93 (92.1%) patients had bone bruise, while in 49 patients of age group >30 years, 30 (61.2%) had bone bruise. Statistically, there was no significant difference between the two groups (P>0.05).

Among 97 males, bone bruise was seen in 75 (77.3%) patients and in 53 female patients, bone bruise was seen among 48 (90.6%) female population. Statistically, there was no significant difference between the two groups (p >0.05).

Upon mode of injury, of the 5 patients with sports injury, 5 (71.4%) patients had bone bruises, of 107 patients with RTA, 90 (84.1%) patients had bone bruises. Of 38 patients with domestic trauma, bone bruises were seen among 28 (73.7%) patients. Statistically, there was no significant difference between the two groups (p >0.05).

DISCUSSION

Bone bruise, is a unique entity on MRI. Conventional radiological techniques like X-rays are rather limited in showing bone marrow. Because of that, analysis of bone marrow characteristics especially bone bruises, is based on MR imaging. Bone bruise on MR is presented as focal abnormal signal of the bone marrow of the femoral condyles or tibial plateaus. This study was a comparison of two different sequences of MRI i.e. T2 weighted sequences versus STIR sequences among a population of 150 patients. The results of this study showed that STIR sequence could detect bone bruise in higher frequency as compared to T2W sequences (i.e. 82% versus 74%) and the agreement between the two sequences was also found to be high (92%).

The mean age of the patients in our study was 31.43 + 12.09 years. The majority of patients were included in age group < 30 years, i.e. 67.3% patients. The male patients dominated over female population (64.7% patients were male). When compared to another study, by Jelic D, et al,[7] the mean age of the patients was 31 years, 73% patients were male and 27% patients were female.

In our study, road traffic accident was the most common etiology found in 71.3% patients, followed by domestic injuries in 25.3% and then sport injuries in 4.7%. Studies by Tervonen et al.[19] and Bealle et

al.[20] represent the limited data available in the literature regarding patient activity at the time of knee trauma. Tervonen et al,[19] limited their analysis to 27 patients diagnosed with a bruise and reported 78%, 11%, and 11% of bruises were associated with trauma in sporting activities, domestic activities, and motor vehicle accidents, respectively. When a similar analysis is made of the 538 bruised patients in the study by Atkinson et al,[8] 45%, 52%, and 3% were involved in sporting activities, domestic activities, and motor vehicle accidents, respectively. The different frequencies represented in the 2 studies could be due to sample size differences.

In our study, T2W sequences could detect bone bruise in 74% cases, while STIR sequences could detect in 82% cases. Thus STIR sequences showed a higher sensitivity of detecting bone bruise. While there was an agreement of 92% between the two sequences. The analysis using the Kappa statistic was performed to determine an agreement between the two techniques which showed substantial agreement. The results were K =0.681, and p <0.05.

In our study, the bone bruises were located more frequently on lateral side of knee i.e. 84.6%. There were 53.7% bruises present on lateral femoral condyles, and 30.1% bruises were on lateral tibial plateu. Bruises on medial side constituted only 15.4% population, 8.9% on medical femoral condyle and 6.5% on medial tibial plateu. In Spindler's series, 86% and 67% of contusions involved the lateral femoral condyle (LFC) and lateral tibial plateau (LTP) respectively and bruising of both occurred in 56%. Lesions in the medial femoral condyle (7%) and tibial plateau (21%) were less common.[21]

There have not been too many studies which analyze the frequency of bone bruises following knee injury. Some of them show the incidence of 20%[23] and some up to 27%.[22] The frequency of bone bruise with injury of ACL was seen 69% of the patients detected on T2W images.[7] In another study based on T2W sequences, reported by Davies et al, the frequency of bone bruise was 67%.[24] Hou-you Li et al.[18] performed a similar study like ours. They showed presence of bone bruises in 83.8% on T2W sequence of MRI. Among those patients, they also found that bone bruise could be detected in all 100% patients. They detected an agreement of 83.8% between the two techniques. In our study, the agreement was detected in 92% cases because, as per operational definition, we included all the true positive cases (74%) and true negative cases (18%), total sum of 92%. While in study by Hou-you Li et al, the agreement was based on the finding of only true positive cases.

The effect modifiers like age, sex and mode of injury were also stratified with frequency of bone bruise. With respect to age, 92.1% patients had bone bruise among 101 patients of age group < 30 years, while in 49 patients of age group >30 years, 61.2% had bone bruise. So, majority of the patients in younger age group contributed a higher frequency of bone bruises (P>0.05). Among 97 males, bone bruise was seen in 77.3% patients and in 53 female patients, bone bruise was seen among 90.6% female population (p >0.05). Approximately 71.4% patients of sports injury, 84.1% patients of road traffic accident and 73.7% patients of domestic injuries had bone bruises (p>0.05).

This study had certain limitations. This was a single center study, with a limited population size. All the sequences were reported by a single expert operator, who had at least 5 years of experience of interpreting the MRI reports.

CONCLUSION

The frequency of bone bruise among patients with anterior cruciate ligament injury was very high. Comparatively, a higher frequency of bone bruises was detected on STIR sequences as compared to T2W sequences. Statistically, a substantial agreement found between the two. Although, T2W sequences can detect bone bruises in large number of patients, STIR sequences should be preferred for detection of bone bruise in ACL injury for not to miss the diagnosis.

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FREQUENCY OF ABNORMAL THYROID FUNCTION TESTS IN CHRONIC KIDNEY DISEASE PATIENTS

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Abstract

Background: Thyroid dysfunction is commonly seen endocrine abnormality among chronic kidney disease (CKD) patients. CKD has been known to affect the hypothalamus-pituitary-thyroid axis and peripheral metabolism of thyroid hormones. The kidney normally plays an important role in the metabolism, degradation, and excretion of several thyroid hormones (THs). It is not surprising therefore that impairment in kidney function leads to disturbed thyroid physiology.

AIM: To determine the frequency of abnormal thyroid function tests in Chronic kidney disease patients.

METHOD: This cross sectional study was conducted at Pathology Department, Allama Iqbal Medical College, Lahore, from 1st September 2017 to 28th February 2018. Thirty three samples were collected from known CKD patients from urology/nephrology department of Jinnah hospital LHR, and thirty three were collected from healthy control subjects. Serum fT3, fT4 and TSH were performed on patient and control groups and were compared.

RESULTS: Among 33 CKD patients 17/33(51.5%) were euthyroid, 4/33(12.1%) patients were having subclinical hypothyroidism, 5/33(15.2%) patients were hypothyroid, 6/33(18.2%) patients were having subclinical hyperthyroidism and 1/33(3.0%) patient was hyperthyroid. Among 33 controls all (100%) were euthyroid having normal thyroid function levels.

CONCLUSION: The chances of thyroid hormones alterations are increased in patients with CKD, this aspect merits attention both from the diagnostic and therapeutic perspective for the better management of patients. We conclude that screening for thyroid disease among patients with CKD should be routinely performed.

Key words: chronic kidney disease, hypothyroid, hyperthyroid, euthyroid, thyroid hormones.

The thyroid gland located in the base of the neck plays pivotal role in our body, influencing the function of many of the body's most important organs, including the heart, brain, liver, kidneys and skin. It regulates majority of the body's physiological actions. The thyroid gland produces hormones (T3andT4) that have many actions including metabolism, development, protein synthesis, and the regulation of many other important hormones. Any dysfunction in the thyroid gland can affect the production of thyroid hormones (T3 and T4) which can be linked to various pathologies throughout the body. Disorders in renal function have been associated with altered levels of thyroid hormones.[1]

Chronic kidney disease is a worldwide public health problem and also associated with cardiovascular problems. Chronic kidney disease (CKD) is the progressive loss in renal function over a period of months or years.[2] Thyroid hormones are necessary for growth and development of kidney and for maintenance of water and electrolyte homeostasis. Chronic kidney disease affects both hypothalamus-pituitary-thyroid axis and thyroid hormone peripheral metabolism.[3,4]

Moreover, the decline of kidney function is followed by changes in the synthesis, secretion, metabolism and elimination of thyroid hormones.[5] Such changes explain higher frequency of hypothyroidism in patients with chronic kidney disease. So, Thyroid dysfunction is a commonly seen endocrine

abnormality among CKD patients.[6,7]

This aspect merits attention both from the diagnostic and therapeutic perspective for the better management of patients. We conclude that screening for thyroid disease among patients with CKD should be routinely performed. Very few studies have been conducted in our settings so this study will help us in the management of chronic renal disease.

METHODS

Study Design:

Cross-sectional/ purposive study

Duration of Study:

1st September 2017 to 28th February 2018

Study Setting:

This study was carried out in the Pathology department, Allama Iqbal Medical College Lahore, Pakistan.

Study Population:

Patients admitted in Urology and Nephrology wards with a diagnosis of Chronic Kidney Disease of Jinnah hospital, Lahore and full filling the inclusion and exclusion criteria.

Sample Size:

A total of 66 samples were collected among them 33 were cases with Chronic Kidney disease and 33 were normal healthy controls.

Sampling Technique:

Non probability purposive sampling

METHODOLOGY

Detailed clinical history and examination were carried out and recorded in a Performa. 5cc venous blood samples were collected in a vial without any anticoagulant. The blood samples were allowed to clot and then serum was separated out in a serum cup.

Then serum was subjected to determination of fT3 by Competitive ELISA , fT4 by Competitive ELISA , TSH by Sandwich ELISA (Roche Diagnostics).

Serum Creatinine was estimated by Jaffe's method , Serum urea was performed by Berthelot method and serum uric acid was performed by URICASE/PAP method on Microlab300.

OPERATIONAL DEFINITIONS:

CHRONIC KIDNEY DISEASE:

CKD is defined as urea>50mg/dl , creatinine >1.4mg/dl ,present for >3 months.

HYPOTHYROIDISM:

Hypothyroidism defined as fT4<0.8 ng/dl , fT3 < 1.4 pg/ml , TSH > 6.2 mIU/l.

HYPERTHYROIDISM:

Hyperthyroidism defined as fT4> 2.0 ng/dl, fT3 > 4.2 pg/ml , TSH < 0.3 mIU/l.

SUBCLINICAL HYPOTHYROIDISM:

Thyroid hormone levels are in normal reference range i.e fT3=1.4-4.2 pg/ml and fT4=0.8-2.0 ng/dl but elevated TSH i.e > 6.2 mIU/l.

SUBCLINICAL HYPERTHYROIDISM:

Thyroid hormone levels are in normal reference range i.e fT3=1.4-4.2 pg/ml and fT4=0.8-2.0 ng/dl but low TSH i.e < 0.3 mIU/l.

EUTHYROIDISM:

Thyroid hormone levels are in normal reference range fT3=1.4-4.2 pg/ml, fT4=0.8-2.0 ng/dl and TSH=0.3-6.2 mIU/l.

RESULTS

The age varied from 15-80 years. These 66 subjects were divided into two groups. First group was from 15-40 years of age and the other group was with age > 40 years. 9/33(27.3%) patients were in age group of 15-40 years whereas 24/33 (72.7%) patients were in age group of >40 years. However,

Table 1: **Age Destribution**

Showing Age Distribution of Cases and Control

Group	Age Group		Total
	15-40 Years	> 40 Years	
Cases	9(27.3%)	24(72.7%)	33(100%)
Controls	22(66.7%)	11(33.3%)	33(100%)
Total	31(47.0%)	35(53.0%)	66(100%)
Mean age cases =50.1 ±15.6 SD, Mean age control = 32.9 ±13.9 SD			

22/33(66.7%) control subjects were in age group of 15-40 years and 11/33(33.3%) control subjects were in age group > 40 years. The mean age in cases was 50.1 ±15.6 SD and in controls was 32.9 ±13.9 SD. (Table No. 1)

Gender wise distribution of 66 subjects was as 16 (48.5%) males and 17 (51.5%) females in case group and 17 (51.5%) male and 16 (48.5%) female in control group.(Figure No.1)

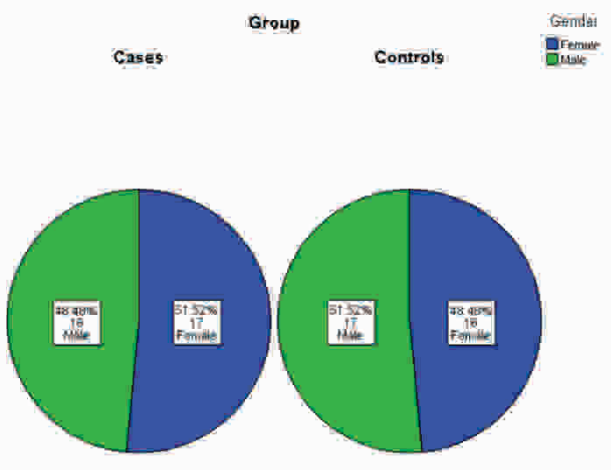

Figure No. 1. *Gender wise Distribution.*

The mean ± SD value of serum urea, creatinine and uric acid in CKD patients were 145± 94.5 mg/dl, 7.1±5.7 mg/dl and 8.8±3.7 mg/dl respectively. The mean± SD value of serum urea, creatinine and uric acid in healthy controls were 27±10.1 mg/dl, 0.91±0.22 mg/dl and 4.7±0.86 mg/dl respectively. These values were significant higher in patients with CKD. This shows statistically significant difference between cases and controls with p-value < 0.05. (Table No. 2)

Distribution of thyroid function condition

Among 33 CKD patients 17/33(51.5%) were euthyroid, 4/33(12.1%) patients were having sub-clinical hypothyroidism, 5/33(15.2%) patients were hypothyroid, 6/33(18.2%) patients were having subclinical hyperthyroidism and 1/33(3.0%) patient was hyperthyroid.

Group Statistics

Total(N)=66,Cases=33,Controls=33

Table 2: *Descriptive Statistics of Lab Parameters.*

Parameter	Group	Mean	Std. Deviation	P value
Urea	Cases	145.45	94.525	.000
	Controls	27.36	10.182	
Creatinine	Cases	7.179	5.7756	.000
	Controls	0.918	0.2297	
Uric Acid	Cases	8.809	3.7696	.000
	Controls	4.745	0.8664	
fT3	Cases	2.509	1.2130	0.068
	Controls	2.952	0.6150	
fT4	Cases	1.048	0.4751	0.119
	Controls	1.191	0.1974	
TSH	Cases	6.3667	12.11178	0.082
	Controls	2.5667	0.95219	

Among 33 controls all (100%) were euthyroid having normal T3, T4 and TSH levels. The p value obtained was 0.000 which was less than 0.05 which shows that results are highly significant. There was significant alterations of serum T3 level, T4 level and TSH level in cases (CKD patients) as compared to controls (normal healthy patients).

DISCUSSION

In our study 66 samples were included among them 33 were CKD patients and 33 were normal healthy controls with 16 (48.5%) males and 17 (51.5 %) females in case group and 17(51.5%) male and 16(48.5%) female in control group. The mean ± SD

Table 3: *Showing Distribution of Thyroid Function Condition*

Group	euthyroid	Hypothyroidism	Hyperthyroidism	subclinical hypothyroidism	subclinical hyperthyroidism	Total	P value
Cases	17	5	1	4	6	33	
	51.5%	15.2%	3.0%	12.1%	18.2%	100.0%	
Controls	33	0	0	0	0	33	
	100.0%	0.0%	0.0%	0.0%	0.0%	100.0%	0.000
Total	50	5	1	4	6	66	
	75.8%	7.6%	1.5%	6.1%	9.1%	100.0%	

value of serum urea, creatinine and uric acid in CKD patients were 145± 94.5 mg/dl, 7.1±5.7 mg/dl and 8.8 ±3.7 mg/dl respectively. The mean± SD value of serum urea, creatinine and uric acid in healthy controls were 27±10.1 mg/dl, 0.91±0.22 mg/dl and 4.7±0.86 mg/dl respectively. The values were significant higher in patients with CKD. Out of total 33 cases 17(51.5%) patients were euthyroid, 4/33 (12.1 %) patients were subclinical hypothyroid, 5/33 (15.2 %) patients were hypothyroid, 6/33(18.2%) patients were having subclinical hyperthyroidism and 1/33 (3.0%) patient was hyperthyroid. Among 33 controls all (100%) were euthyroid. Significant alterations in TFTs has been observed in cases as compared to controls.

A study was conducted by Pakhle K, et al in 2017 in India including 50 patients of CKD. There were 26 (52%) patients diagnosed with euthyroid. Similarly, there were 16 (32%) and 8 (16%) patients diagnosed with subclinical hypothyroidism and overt hypothyroid respectively. In this study, patients with hypothyroidism and subclinical hypothyroidism; were found and no cases of hyperthyroidism were found.[8] The results of this study are in accordance with our study.

In another study of 461,607 patients with CKD in US who underwent serum TSH testing from 2004–6 (84% of the cohort), 23% had hypothyroidism. But in our study 5(15.2%) patients were hypothyroid from 33 patients of CKD. The result is slightly less in our study which may be due to difference in sample size.[9]

Another study carried by Chonchol M. et al in 2008 in Italy, included 3089 adult outpatients. Among 3089 adult participants, 293(9.5%) had subclinical primary hypothyroidism. The prevalence of subclinical primary hypothyroidism increased with severity of disease from 7% to 17.9%.[10] Our study have 4/33(12.1%) patients with subclinical hypothyroid nearly in accordance to above study.

CONCLUSION

The present study finds thyroid dysfunction to be very common in CKD patients and reveals the significant association between CKD progression and thyroid dysfunction. Thyroid dysfunction is mostly an ignored aspect in CKD. Altered thyroid function is a risk factor for cardiovascular diseases which can also lead to further worsening of kidney function. So routine thyroid function screening programme should be instituted to avoid morbidity in CKD patients.

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CLINICAL EVALUATION AND OUTCOME OF VULVAR CARCINOMA

Nudrat Sohail, Nargis Iqbal, Alia Asad, Naureen Huma,Fazeela shehzad

ABSTRACT

Introduction: Vulvar cancer is an infrequent malignancy of women, commonly affecting elderly1. HPV associated vulval cancer incidence is rising among young females for the last few decades. Most common histological type of this cancer is squamous cell carcinoma. There is no universal screening method for this malignancy. Common presentation is vulval pruritus, an ulcer or lump involving vulva. Histopathological diagnosis is required for confirmation of diagnosis.

Objective of the study: To determine the clinical outcome of vulval carcinoma in women presenting in gynae unit 3 at Jinnah hospital Lahore.

Material & methods: A descriptive study, with convenient sampling, conducted from August 2009 to June 2015 in unit III of OBGY in a tertiary level hospital of Lahore. A total of 17 patients presented with suspicion of vulval carcinoma, all had biopsy, and only 4 had confirmed diagnosis of squamous cell carcinoma of vulva.

Results: The age of the patients ranged from 57- 67 years. Out of 4 patients with confirmed histological diagnosis of vulval cancer, two presented with an ulcer and others with itching and growth. Two patients had stage 1 cancer and one in stage 2 and 3 each. Stage 1 and 2 patients underwent radical vulvectomy along with removal of inguinal and femoral lymph nodes. One patient with stage 3 malignancy had extensive urethral spread and was referred for radiotherapy.

Conclusion: The first line treatment for early stage disease remains radical vulval surgery, while radiotherapy is primary modality for advanced stage vulvar cancer.

Key words: vulval carcinoma, treatment and outcome.

Vulval cancer is a rare cancer and it accounts for approximately 4 % of all gynecological tumours.[2] This is said to be the twentieth common cancer in women. It is a disease of the elderly women rarely occurring before the age of 50 years.[2] The mortality rate associated with this cancer is 0.6 / 100,000 women.[3] In the last three decades there is a rise in the incidence of this malignancy in women aged 40 to 49 years attributed to human papilloma virus infection.[4,5,6]Vulval carcinoma has many histological types, among them squamous cell carcinoma is the most common histological type (95%), other types include melanoma, sarcoma, basalioma.[7,8]

There is as yet no screening available to predict its presence. There is no recommendation as such by any screening program to predict vulval carcinoma.[2] The usual presentation is after the lesion is visible or the inguinal lymph nodes become palpable. The lesion is ulcerative or in the form of a lump.[2] Any ulcerative lesion or a lump or fungating growth must always be biopsied and never delayed as the chances of carcinoma are very high with this presentation. The premalignant lesions may present along with benign lesions with itching and white discoloration of vulval skin. Diagnosis is always biopsy based and occasionally multiple biopsies may be needed to confirm or refute the diagnosis of vulval carcinoma.[2] The biopsy must be adequate to make the diagnosis and hence must be carried out by experienced surgeon and should not be left to be performed by inexperienced.[9] Similarly the histopathology diagnosis must be conducted by senior pathologist. Chief modality of treatment for early stage cancer of vulva remains extensive surgery comprising of wide local excision with inguino-femoral lymph node removal, and radiotherapy can be a follow up treatment.[9-11]

This approach promises gives good prognosis but is associated with short and long term complica-

tions primarily because of groin surgery.[9,12] Prognosis of vulvar cancer is linked to site and stage of tumour, involvement of inguinal lymph nodes and distance of tumour free margin.[13,14] Vulvar cancer patients that undergo SLN dissection have similar groin recurrence rates to superficial inguinal lymph node dissection. SLN dissection in vulvar cancer is associated with few groin complications.[15] In recurrent vulvar cancer an inguino femoral lymphadenectomy is recommended. Evidence supports that treatment for recurrent vulvar cancer must be customized according to individual case.[16] The repeat Sentinel Lymph Node (SLN) procedure is technically demanding. Repeat SLN procedure is feasible, but not yet a safe alternative.[17,18]

This study was carried out to look into the presentation, management and follow up of women presenting with vulval lesions diagnosed as vulval carcinoma.

METHODOLOGY:

All patients who presented with vulval lesions to Gynae unit 3 were included in the study. A total of 17 patients were recruited with the suspicion of vulval carcinoma. Detailed history, family history and clinical examination were carried out. All patients underwent biopsy to confirm the diagnosis. Out of these 4 patients had confirmed vulval carcinoma. These patients underwent management according to the stage of the disease. The complications and recovery were noted. The patients were followed with their histopathology and clinical recovery.

A total of 17 patients were included with suspicion of vulval carcinoma. The age of the patients ranged from 57 years to 67 years. Only 4 had carcinoma on biopsy. Out of these 4 patients, 2 patients presented with an ulcer and one each with itching and growth. 2 patients presented in stage 1 of the disease and one in stage 2 and stage 3 each.

RESULTS

The patients who had confirmatory diagnosis of vulval carcinoma on biopsy were 4 in number .The rest of the patients were not included in the study. The age of the patients ranged from 57 years to 67 years. The presentation to the hospital was itching, presence of ulcerative lesion and presence of a growth in the vulval area. The clinical staging carried out at the time of biopsy showed that two patients were in stage 1, and one each in stage 2 and 3 of the disease. Three patients, included in stage 1 and 2, were managed with radical vulvectomy with three separate incisions, one for vulval and one each for inguinal region to remove inguinal and femoral lymph nodes. The patient with stage 3 malignancy had extensive involvement of urethra was referred for radiotherapy. The histopathology of all the four patients came out to be squamous cell carcinoma. The follow up of these patients were carried out to look into their well being and recurrence if any of the tumor. Among the patients, who underwent radical vulvectomy only one patient developed infection of the skin wound which settled with oral antibiotic and local application of antibiotics. The patient who presented with stage 3 disease and referred for radiotherapy did not opt to follow at Jinnah hospital. Out of the rest of the patients, two patients regularly followed for two years and one patient followed for three years post operatively and was disease free and in acceptable good health.

Table 1: *Distribution of Cases by Symptoms*

Symptoms	Patients	Percentage
Itching	1	25
Ulcer	2	50
Growth	1	25

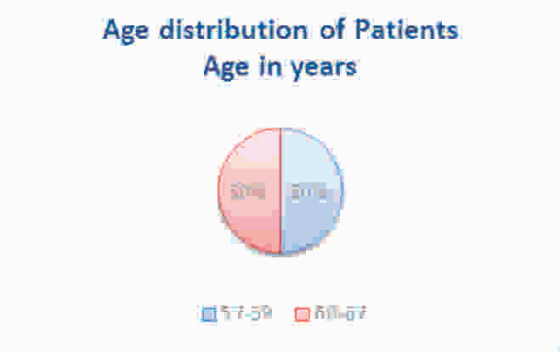

Figure *Distribution Of Cases By Age*

Table 2: Comorbidities in the Patient

Comorbidities	Patients	Percentage
Hypertension	2	50
Diabetes melletus	1	25
Any other	0	

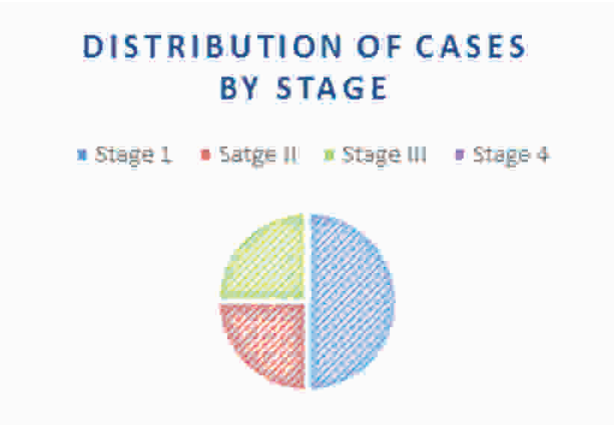

Table 3: Management Performed

Management	Stage of disease	Patients	Percentage
Radical vulvectomy	1&2	3	75
Radiotherapy	3	1	25

Table 4: Complications of Treatment

Management	Complication	Patients	Percentage
Radical vulvectomy	Wound infection	1	25
Radiotherapy	Vaginal stenosis	1	25

Table 5: Follow up After Treatment

Years after management	First year	Second year	Third year	Fourth year
Patient 1	Yes	Yes	Yes	No
Patient 2	Yes	Yes	No	No
Patient 3	Yes	Yes	No	No
Patient 4	Yes	No	No	

Figure *Distributions of Cases by Stage*

DISCUSSION

There are no recommendations available for screening vulval malignancy. The only suggested way is self examination. Self examination is not a recommendation. As self examination remains difficult and unreliable, therefore presentation of cancer for treatment remains late. In this study all patients presented to the hospital after developing a persistent complaint like itching, growth or ulcer. Patients with itching had spent time trying to get cured of their itching either with their own home remedies or local steroid application as prescribed by local physicians. This practice indicates a very important mind set of our population in not seeking help from healthcare providers and also lack of knowledge of the clinicians not to refer elderly women with vulval itching to the gynecologist for proper evaluation.

Vulval cancer predominantly affects elderly women when the morbidities like hypertension and diabetes may also be present, thus posing challenges to plan its management. Sometimes the co morbidities like hypertension and diabetes delay the plan of the management especially like extensive surgery of vulvectomy and lymph node removal. Co morbidities also demand that the anesthesia must be given by experienced anesthesiologist and presence of intensive care facilities for the patient. Patients must be operated in tertiary care facilities equipped with all possible resources to monitor the wellness of the patient. In this study two women were hypertensive and one diabetic whose fitness and control of the hypertension and diabetes was sought prior to surgery so that smooth intra operative and post operative recovery was possible.

Radical vulvectomy was performed in 3 of the patients with removal of inguinal and femoral lymph nodes in all the three patients. The surgery of the primary tumor must be adequate to remove the tumor with adequate margins. This has been shown to be at least 15 mm margins which should be disease free along with the tumor in a freshly excised specimen. This ensures reduction in the recurrence of the tumor. Lymph node dissection demands patience and good tissue recognition. Dissection of lymph nodes is relatively easier if they are enlarged otherwise the expertise of the surgeon has to be there to adequately remove the lymph nodes. Evidence also suggests that good care of groin is essential in

invasive vulvar cancer[19]. In this study lymph node dissection did not pose any difficulty. The concept of sentinel lymph node removal although very reliable but had never been used by us therefore we opted to remove all the lymph nodes. The patient who presented in stage 3 had involvement of the urethra and dissection was not possible without sacrificing the whole urethra therefore the patient was sent for radiotherapy.

All patients were given three separate incisions for vulvectomy as this prevents tension on the skin wound. Classically the radical vulvectomy made use of butterfly incision involving the vulval area along with skin over the groin area on both sides. This incision resulted in a greater rate of wound dehiscence and subsequent infection adding to post operative morbidity of the patients. In our study despite using separate incisions one patient developed wound infection. The infection was treated with oral antibiotic and keeping the wound clean. Literature supports that radical vulvectomy and triple incision technique are safe treatment choices for early stage vulvar carcinoma.[20]

The follow up of the patients was difficult despite adequate explanation of the condition. This is a common observation that patients do not comply with the follow up advice. Up to one third of the vulval cancer will recur even after satisfactory primary treatment thus making the follow up important. The common practice for a three monthly follow up for one year, then six monthly in the second year and then one yearly is followed by many centers is not evidence based. Elderly patient find self examination difficult, adding to the delay in presenting the recurrence.

CONCLUSION

The first line treatment for early stage disease remains radical vulval surgery, while radiotherapy is treatment modality for advanced stage vulvar cancer. Inguinal lymph node dissection necessitates good tissue identification and surgical expertise. Radical vulvectomy was related to post-operative morbidity particularly increased rate of wound dehiscence.

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ACCEPTABILITY, COMPLICATIONS AND REASONS FOR REMOVAL OF IMPLANON AS A CONTRACEPTIVE

Nudrat Sohail, Fazeela Shahzad, Alia Zainab, Shazia Ashraf

Abstract

Pakistan has a high birth rate[1]. According to the latest demographic survey the overall contraceptive rate is 34%[2-4]. Different contraceptive methods have been used in an attempt to provide suitable contraceptive to couples desiring family planning. To achieve an acceptable birth rate, long acting reversible contraceptive are required[5-6]. One of these is implanon. It is a single rod implant containing 68 mg of etonogestrel (a Progestogen). It is placed sub dermally and it offers contraception for 3 years[7]. Implants have been in use for more than 20 years[8]. It was approved by the world food and drug authority for use in 2006[9]. Although it is freely available all over the world, its use in developing countries remains low due to its price and restricted availability[10]. The use of implanon in Pakistan depends on its availability as it has to be procured from outside Pakistan. Moreover the availability of implanon remains unreliable and most of the times it is not a free available choice to the women.

Aims & objectives: To study frequency of choosing implanon as a contraception and to assess complications and adverse effects associated with use of implanon as a contraceptive.

Material & methods: This study was planned to study the frequency of choosing implanon as a method of contraception when it was freely available for the women appearing at district headquarter hospital Gujranwala. The implanon were provided free of cost by an NGO, along with other contraceptives including oral contraceptive pills, injectable contraceptives and intrauterine contraceptive device. Trained health care providers counseled the patients to make their decision to select their method of contraception. The women were followed regularly and any complications, adverse effects and request for its removal were recorded. It was a descriptive study.

Results: A total of 186 patients chose implanon as a contraceptive. Out of these 146 patients were inserted implanon. Three patients were lost to follow up so data of 143 patients available for analysis. The youngest patient was 18 years and oldest was 36 years enrolled in the study. The patients were followed every 3 months for a year. Complications at the site of insertion like redness, irritation and bruising was reported in 23 patients. Pain at the site was reported by 128 patients, which was mild in 120 and moderate to severe in 8 patients. Out of these 12 presented with complaint of irregular spotting vaginally and only one requested for removal within 6 months of insertion. No pregnancy was reported in any patients.

Conclusion: The acceptance of women for implanon as a contraception is high with minimal complications and request for its removal is low.

Key words: acceptability, complications, removal, implanon, contraceptive

The knowledge about insertion and removal of implanon requires training. Similarly the knowledge about indications and contraindications for insertion, removal and side effects is also mandatory.[9,11] Implanon acts by suppressing ovulation.[12] Acceptance for insertion for implanon will depend on counseling and the contraceptive needs of the women desiring family planning.[9,13] The fore most knowledge is evaluating that the woman is within the eligibility criteria as suggested by the WHO[13]. Next is counseling for insertion and informing the client about its mechanism of action, possible side effects or complications and finally reasons for its removal. Involvement of male partner can add advantage in counseling. All this information is provided by health care personnel trained to do so.[14-15]

The implanon is a single rod implant having length of 4 cm and 2 mm diameter and has a solid

core of ethylene vinyl acetate imbued with 68 mg of etonogestrel.[16-17] The insertion of implanon requires learning the correct technique. It is placed typically in the non- dominant arm approximately 6 centimeters above the elbow on the anterior surface. After insertion proper palpation must be carried out to ensure the position of the rod. The entire procedure can usually be completed in 2 minutes by a trained health care provider.[18-19]

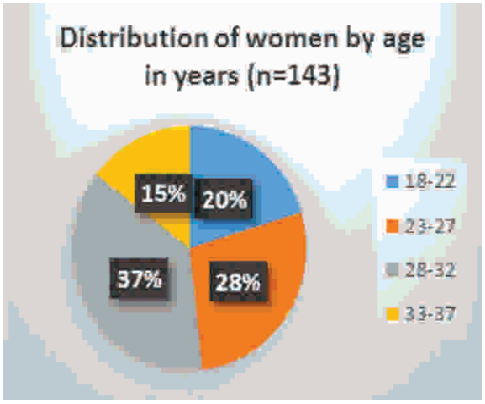
MATERIALS AND METHODS

A project was designed with a nongovernmental organization to provide implanon contraception to suitable patients presenting at district headquarter hospital Gujranwala. In the first phase the consultants working at hospital were trained for counseling, indications, contraindications, insertion and removal through a series of hands on training workshops by the master trainer. A skills lab was established within the hospital containing models, mannequins and all necessary training material. The consultants were certified once they were aptly trained. In the next phase an ample free supply of implanon was provided to the hospital. A room in the outdoor department was set up for reception, counseling and registering the selected patients suitable for implanon insertion. Implanon insertions were carried out by the trained staff. The selection criteria for inserting implanon was the WHO eligibility criteria. Pregnancy was excluded in all the patients with the best possible method through history and investigations. Patients on anti-tuberculous drugs and antiepileptic drugs were excluded from the study. Patients with undiagnosed vaginal bleeding and those who were not sure to follow in case of complications were also excluded from the study The patients were reassured that the device would be removed if they were not satisfied with it or due to any complication A record of all the patients was kept in a register with their contact numbers and address. The study started in November 2016 and was completed in August 2018.

The main objectives of the study were to assess the frequency of acceptance for implanon, study the complications associated with it and to look into the reasons for request of its removal.

RESULTS

A total of 186 patients chose implanon as a contraceptive method. Out of these 146 patients were inserted implanon. Three patients were lost to follow up so data of 143 patients available for analysis. The youngest patient was 18 years and oldest was 36 years enrolled in the study. The patients were followed every 3 months for a year. Complications at the site of insertion like redness, irritation and bruising was reported in 23 patients. Pain at the site of insertion was reported by 128 patients, which was mild in 120 and moderate to severe in 8 patients. Out of these 12 presented with complaint of irregular spotting vaginally and only one requested for removal within 6 months of insertion. No pregnancy was reported in any patients.



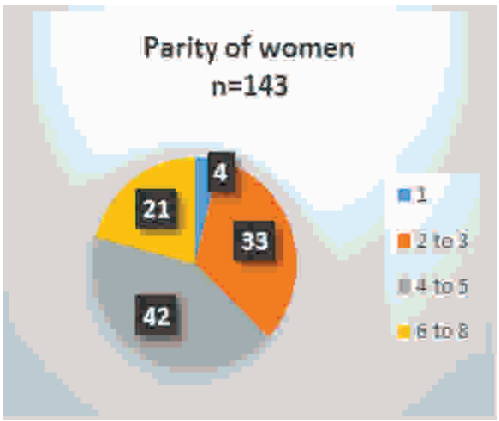


Figure 1 & 2: *Demographic & Reproductive Characteristics of Women in Study*

Table 1: *Total Number of Patients*

	No. of patients
Total number of patients who accepted implanon as contraceptive choice	186
Total number of patients who fulfilled the criteria for implanon insertion	146
Total number of patients lost to follow up	03
Total number of patients for follow up	143

Table 2: *Frequency of Various Complications & Adverse Effects Among Implanon Users (n= 143)*

Sr. No	Complications	No.	Percentage
a.	pain at site of insertion		
	Mild	120	83.91
	Severe	08	5.59
b.	Redness	22	15.38
c.	Bruising	5	3.49
d.	Irritation	2	1.39
e.	acne	1	0.69
f.	Infection/haematoma at injection site	0	0
g.	Menstrual disorders:		
	Irregular spotting	12	8.39
	Heavy bleeding	1	0.69
	Prolonged bleeding	3	2.09
	Amenorrhea	1	0.69
h.	Breast pain	0	0
i.	Reduced libido	0	0
j.	Weight gain(more than 2 kg)	3	2.09
k.	pregnancy	0	0
	ADVERSE SIDE EFFECTS		
i.	Headache	0	0
ii.	Raised blood pressure	0	0
iii.	Transient ischemic attack	0	0
iv.	Developing ovarian cyst	0	0

DISCUSSION

This was the first organized study carried out on using implanon as a contraceptive in the district of Gujranwala. The provision of training for implanon insertion and availability of implanon was entirely provided free of cost by a nongovernmental organization. In the first three months a skills lab was set up and training with certification was provided to all the consultants involved in healthcare provision. In the second three months outdoor services were started to provide information about implanon to the women desiring contraception. This again was conducted by a full time trained councilor accompanied by hospital staff that was later on to be trained to carry on the program. All the data of the patients was recorded.

A minimum of 20 minutes were spent on each woman in providing information and helping chose implanon for them. Selection of patient was according to the WHO eligibility criteria. Almost 43 patients did not fit in the eligibility criteria. The reasons were as grave having epilepsy or undiagnosed bleeding to as simple as not being able to return for follow up. The women who were not sure if they would continue implanon even for 6 months were not included. The youngest patient was 18 years while the eldest patient was 37 years selected for implanon. A few women had information about implanon as a contraceptive but none of them had seen it before. This indicates lack of available information to the end users those who had heard about implanon were either from the family planning center or from women who were using it. This brings us to the point to think about methods to disseminate awareness about relevant information to the end users.

The acceptability for implanon can be said to be at a mid-level between good and bad. While the women who opted for it wanted to try it for absence of possible side effects or complications rather than for usefulness of the method itself. The acceptability can also be attributed to the fact that the device was available to them free of cost but at the same time oral contraceptive pills or intrauterine contraceptive The women found it very useful that the device was palpable and could be removed easily whenever required, this was especially true in cases where they had heard about displacement of intrauterine device and its subsequent retrieval through surgery.

The largest number of women seeking contraception was in the age range of 22 years to 32 years with more than 2 children up to 5 children. Marriage at early age is still prevalent leading to motherhood at early age. In this study, the women having 4 to 5

children seek contraception; this is in alignment with the fact that 3 to 4 children is still the acceptable norm for married couples in Pakistan.

The most notable side effect was pain at the injection site. All patients complained of at least some degree of pain at the insertion site of implanon despite use of local anesthesia. Usually no analgesia was provided to the clients post insertion, however 8 patients complained of severe pain so they were given oral Paracetamol.

Redness at the site of insertion was also noted in 22 patients. The patients were not worried for redness and they were asked to report back if it did not disappear. No infection or hematomas at insertion site were observed. In 2 patients few drops of blood continued to trickle for a while which was stopped with minimal pressure for up to 5 minutes. Five patients developed bruising at insertion site, but it was not extensive or painful and the patients were satisfied as the bruising was minimally painful and did disappear in a week's time.

The most serious side effect observed in this study was heavy bleeding. One patient developed heavy bleeding within a month of insertion. Her evaluation was done to rule out any other cause of her bleeding besides implanon. She was prescribed mefanemic acid and Tranexemic acid. The bleeding did not settle with these measures and the patient requested for removal of implanon. Her implanon was removed. Gezgincl et al, reported much higher incidence of irregular heavy bleeding (17.5%) and amenorrhea (41.25%) in his study[20].

The adverse side effects like persistent headache, rise in blood pressure, transient ischemic attack, developing a fibroid or ovarian cyst were also looked into, and however no patient developed any of these complications. No patient in this study using implanon became pregnant. This can be attributed to the small number of participants in the study and also to the strict evaluation to rule out pregnancy prior to insertion of implanon.

CONCLUSION

This study concludes that acceptability of women for implanon as a contraceptive is high in most instances. It offers promising results in preventing unintended pregnancies as effective long acting reversible contraception (LARC). Lowering the commodity cost of implants can be a way to increase its use in low resource countries. Proper selection of women using WHO eligibility criteria for its insertion leads to minimal side effects and negligible removal rates. Procurement of implants for availability in immediate postpartum period could enhance its usage.

CONFLICT OF INTEREST: None

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EMERGENCE OF DRUG RESISTANCE PSEUDOMONAS AERUGINOSA, A TERTIARY CARE EXPERIENCE

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Abstract

Objective: The aim of the study was to provide antibiogram patterns of pseudomonas aeroguinosa,for future guidance in urgent empirical therapy, in suspected cases.

Material and Methods: This cross-sectional study was conducted at Microbiology Department of AllamaIqbal medical college during the period of six months 1stjune 25thnovember 2016. Identification criteria include Colonial morphology, Gram stain, oxidase positive, pyocyanin production. API 20NE was put up for species differentiation. A standard Panel of Antimicrobial disks, there concentrations and Zone sizes were followed interpreted according to CLSI 2016 Guidelines.

Results: Of total 675 samples, 370 were gram negative of which P. aureginosa isolation rate was 37.8% (n=140) Lactamase + beta-lactamase inhibitor combination (Piperacillin + Tazobactam) showed very low 14% resistance, against P. aureginosa, while Cefoperazone + sulbactam being similar combination showed 44% resistant similar resistant rate 43% was also observed in Fluoroquinolone 2nd generation (ciprofloxacin). Monobactam (Aztreonam), Cephalosporin (Ceftazidime), were resistant to 90%, 65% isolates respectively, among aminoglycosides Amikacin showed 67% resistance, while gentamycin showed low resistance 40% as compared to other groups and similar to Carbapenem (Meropenem, Imipenem) 22%, 22% respectively.

Conclusion: Drug resistance among Pseudomonas Aeruginosa, is on the rising the rising stat

Emergence of drug resistance is one of the alarming issues around the globe. (Martin, Williams, & Tanksley, 1991) There are multiple factors responsible to the emergence of resistance such as, misuse and overuse of antibiotics inappropriate prescriptions by the physicians, self medications especially young adults, use of broad spectrum antibiotics and synergistic combinations, un necessary promotions by pharmaceutical industry, untrained staff in microbiological testing laboratories, lack of awareness with the new guidelines recommended for antimicrobial testing etc. (Trivedi, Patil, Shettigar, Gangwar, & Jana, 2015)

Pseudomonas aeruginosais one of the major cause of hospital acquired infections especially patients admitted in ICU (Intensive Care Unit). Data presented by the Center for Disease Control and Prevention (CDC), Nosocomial Infection Surveillance System, in the USA, (F. Z. Khan, Khan, & Kazmi, 2014) P.aeruginosacause diverse variety of infections and was found to be the second most common cause of nosocomial pneumonia, the third most common cause of nosocomial urinary tract infections, and the eighth most common cause of nosocomial bacteraemia.(Brigham, Woolverton, Blake, & Staub, 1974) Majority of the infections caused by P. aeruginosaare often severe, life threatening and are un treatable because of the higher resistance to antimicrobial agents and lack of new drugs development. Over all, resistance rates keep on increasing and differ according to epidemiology of different geographical locations.(Fadeyi, Akanbi 2nd, Nwabuisi, & Onile, 2005)

Pseudomonas aeruginosa belongs to a vast genus of obligate aerobic, non-fermenting, saprophytic, Gram-negative bacilli widespread in nature, particularly in moist environments. (Kovacs, 1956) Most of the cases infected with Pseudomonas com-

prise of immuno compromised patients including those with burns, cancer or on mechanical ventilation. It can usually be isolated from tap water in clinical settings as well. However these isolates are more resistant to conventional antibiotics as compared to their environmental counterparts. The organism is pathogenic when introduced into areas devoid of normal defences and infections are both invasive and toxigenic. (McCABE & JACKSON, 1962)

Pseudomonas has been incriminated in cases of meningitis, septicaemia, pneumonia, ocular and burn infections, hot tubs and whirlpool-associated folliculitis, osteomyelitis, cystic fibrosis-related lung infection, (Oliver, Cantón, Campo, Baquero, & Blázquez, 2000) malignant external otitis and urinary tract infections with colonized patients being an important reservoir.(Tang et al., 1996) Cross-transmission from patient to patient may occur via the hands of the health care staff or through contaminated materials and reagents .however person to person spread is considered to be rare. Despite recent advances in therapy, P. aeruginosa bacteremia remains fatal in more than 20% of cases. Over 50% of deaths occur within a few days . Therefore, prompt administration of adequate anti-pseudomonas treatment is essential

Therefore, this study was performed using antibiogram as epidemiological marker to show general sensitivity patterns of Psuedomonasaeroguinosa to commonly used antibiotics at a tertiary care hospital in lahore.

METHODS

This cross-sectional study was conducted at Microbiology Department of Allama Iqbal medical college & Jinnah hospital Lahore (AIMC & JHL) during the period of six months 1st june 25th november 2016.

Every specimen was processed for bacterial culture for the isolation and identification. Blood agar, chocolate agar, and MacConkey's agar were used. Inoculation was done by four flame streak method. Only single organism p. aureginosa from every specimen was included in the project and processed for further testing. Identification criteria include Colonial morphology, Gram stain, oxidase positive, pyocyanin production. API 20NE was put up for species differentiation

Antimicrobial Susceptibility testing:

A suspension of P. aureginosa equal to 0.5 McFarland turbidity standards was prepared, by inoculating in nutrient broth. Loning was done by sterile culture swab stick on Mueller– Hinton agar plates according to standard guidelines. A standard Panel of Antimicrobial disks were applied and there Zone sizes were recorded according to CLSI 2016 Guidelines.

RESULTS:

Of total 675 samples,370were gram negative of which P. aureginosa isolation rate was 37.8% (n= 140), Figure:1

Figure isolation rate of pseudomonas aureginosa

Table:1 showed department wise distribution of

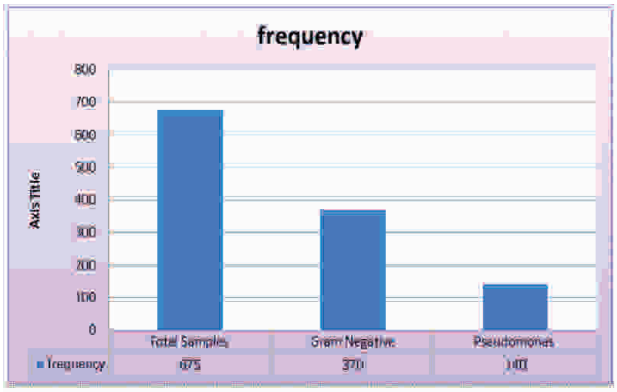

Table 1: Department Wise Distribution of Total Samples and P. Aureginosa Isolates

Location	Samples	Percentage	Isolates	Percentage
ICU	195	28.8	45	32.1
Surgical unit	210	31.1	50	35.7
Medical unit	110	16.2	23	16.4
Gynae	85	12.5	12	8.5
OPD	75	11.1	10	7.1
Total	675	100	140	100

samples & pseudomonas isolates during study period, maximum number of specimens were received from surgical unit 31.1% (n=210/675) followed by ICU28.8% (n=1950675),Medical unit16.2% (n=110/675), 12.5% (n=85/675) from Gynae ward ,Maximum rate of P. aureginosa was noticed from surgical unit 31.1% (n=50/140) ,Table:1

Among 675 specimens, maximum number of samples were blood 215 and wound swabs 160 and least amount of bronchial alveolar lavage 35 were received, Table:2 Frequency of pseudomonas isolates obtained were as followed, Among 675 samples P. aureginosa was grown in 140 samples, over all maximum number of P.aureginosaisolates were in wound swab 34%, followed by urine 26% sputum 21% least rate found in blood 3%. Table:2

Table 2: Sample Wise Distribution of P. Aureginosa

Sample Type	Total samples	Pseudomonas Percentage
Wound Swab	160	34%
Tracheal aspirate	85	9%
Urine	150	26%
BAL	35	5%
Blood	215	3%
Sputum	30	21%`

Lactamase + beta-lactamase inhibitor combination (Piperacillin+ Tazobactam) showed very low 14% resistance, against P. aureginosa, while Cefoperazone + sulbactam being similar combination showed 44% resistant similar resistant rate 43% was also observed in Fluoroquinolone 2nd generation (ciprofloxacin). Monobactam (Aztreonam), Cephalosporin (Ceftazidime), were resistant to 90%, 65% isolates respectively, among aminoglycosides Amikacin showed 67% resistance, while gentamycin showed low resistance 40% as compared to other groups and similar to Carbapenem (Meropenem, Imipenem) 22%, 22% respectively. Table:3

Table 3: Resistant Pattern of Pseudomonas Isolates

Drugs	Resistant
Gentamycin	40%
Meropenem	22%
Imipenem	22%
Cefoperazone+ Sulbactam	44%
Piperacillin +Tazobactum	14%
Ciprofloxacin	43%
Aztreonam	90%
Ceftazidime	65%
Amikacin	67%

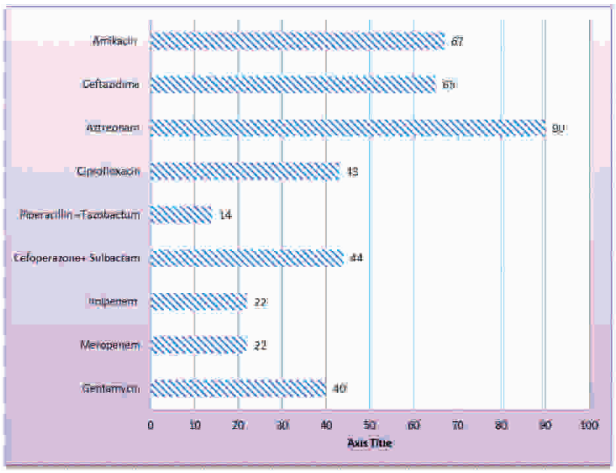

Figure 2: *Resistant Pattern of Pseudomonas Isolates*

DISCUSSION

Infections caused by P. aeruginosaare often severe, life-threatening and are hard to treat because of partial susceptibility to antimicrobial agents and great frequency of emergence of antibiotic resistance through therapy.[5] The antibiotic resistance mechanisms include the acquirement of extended-spectrum-lactamases (ESBL), carbapenemases, aminoglycoside-modifying enzymes and 16S ribosomal ribonucleic acid methylases.

Mutational changes causing the up-regulation of multidrug effluxpumps, derepression of ampC, modification of antimicrobial targets and changes in the outer membrane permeability barrier are also described. Moreover, the propensity of P. aeruginosato exist in vivo and in the environment as slow-growing organism embedded in its extracellular matrix adds to its resistance mechanisms. Thus, emergence of MDR P. aeruginosais of clinical concern and the pandrug-resistant (PDR) isolates, treatable only with colistin, are on the rise.

Shah et al (Shah, Wasim, & Abdullah, 2015) P. aeruginosawas isolated in 5.4% cultures. The most resistant drugs included 100% Ceclorand Cefzox followed by 99.6% Amoxil/Ampicillin Ceflixime 99.6% Doxycycline 99.6% Cefuroxime 99.2% Cephradine 99.2% Cotrimoxazole 99.2% Nalidixic acid 98.8%, Pipemidic acid 98.6% andAugmentin 97.6%. Dash et al (Dash, Padhi, Narasimham, & Pattnaik, 2014) out of 6280 clinical samples 53.8%

yielded significant growth and 9.7% samples were positive for P. aeruginosa out of which 6.8% were nosocomial and 2.9% community-acquired infections. Maximum 67.6% isolates were obtained from pus/swab, followed by urine 15% and blood 4.9%. Elderly, in-patients and invasive procedures were found to be significant risk factors in the setup investigated ($P < 0.05$). Out of 327 isolates, 84.7% isolates were multidrug-resistant, 35.7%, isolates were extensively drug-resistant. No pandrug-resistant isolate was obtained.

Garba et al (Garba et al., 2012) reported the isolation rate 55(55%) were Gram-negative organisms and 44 (44%) were Gram-positive. Pseudomonas aeruginosaaccounted for 25% of the Gram negative organisms. For pseudomonas isolates the highest sensitivity of ofloxacin, and moderate susceptibility of ampicillin, cefuroxime and ceftriazone was observed. very strong resistance to cotrimoxazole, amoxicillin tetracycline and augmentin was observed .

Similarly Khan et al (M. A. Khan & Faizb, 2016) reported The overall drug resistance among 121 strains of P aeruginosa. Very low resistance was observed for piperacillintazobactam (4.9%; P<.05). Meropenem showed significantly high resistance (30.6%; P<.05) as comparedticarcillin (22.3%) and imipenem (19%), cefepime (8.3%), amikacin (7.4%) and piperacillin-tazobactam,which showed lowest resistance (4.9%). Although, data varied between hospitals, meropenem and ticarcillin had the highest drug resistance in all hospitals. Multidrug resistance was 10.7%.

Ali et al (Ali, Mumtaz, Naz, Jabeen, & Shafique, 2015) Of the 204 pseudomonas isolates, 39% were obtained from ICU. Overall, 66% were from men, and 17.2% belonged to 10-15 year age group. The overallpattern showed high resistanceto Ofloxacin 61.3%, Cefepime57.3%, Ceftazidime 53.9%, Amikacin53%. Of all the isolates, 63.2% were considered MDR. The most active antibiotics wereColistin, Polymyxin B and Meropenem.

Pathmanathan et al (Pathmanathan, Samat, & Mohamed, 2009)Piperacillin-tazobactam was the most effective drugs with 91.8%susceptibility, followed by the aminoglycosides amikacin, 86.6% and gentamicin, 84.5%, the quinolone ciprofloxacin, 83.5%and the beta-lactams cefepime, 80.4%, ceftazidime, 80.4%, imipenem, 79.4% and meropenem, 77.3% with 19.6% MDR isolates

Rostamzadeh et al (Rostamzadeh, Mohammadian, & Rostamzade, 2016) showed extreme antibiotic resistance (99.5%) of P. aeruginosa against Trimetoprime Solfametoxasole and Ciprofloxacin 55.3%, Amikacin 61%, Imipenem 33%.

Khan et al (F. Z. Khan et al., 2014) reported The frequency of MDR 30% P. aeruginosaisolated from different clinical specimens. Amikacin was found to be the most effective antibioticfollowed by Cotrimaxazole and Quinolones.

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SAFETY, EFFICACY AND ACCEPTABILITY OF SUB DERMAL CONTRACEPTIVE IMPLANT EXPERIENCE AT JINNAH HOSPITAL LAHORE

Zareen Amjad, Amtullah Zarreen, Sara Saeed, Naila

Abstract: Progestin-only contraceptive implants are a highly effective reversible contraceptives Acceptability and continuation by clients is growing high. Menstrual irregularities are most common symptoms that can be well managed by pre insertion counseling. Headache, weight gain , acne and breast tenderness are other adverse effects.

Objective; To study Safety, efficacy and acceptability of Progesterone containing sub dermal contraceptive implants among women at Jinnah Hospital Lahore.

Material and method; A study conducted at Gynae unit 1 in collaboration with Family planning centre at Jinnah Hospital Lahore from June 2015-June 2018. Implanon was available from June 2015- Dec 2016 and 312 insertions were done. Jadelle was available from Jan 2017 onwards. 300 women had jadelle insertion from Jan 2017-June 2018. Follow up with implanon was completed and women with Jadelle insertion are still in follow ups.

Results: 612 women participated in study. 312 had implanon while 300 had jadelle insertion.67% 0f women were using contraception previously. None of them had previous exposure to contraceptive implant. Irregular vaginal bleeding was commonest side effect faced by 27% of women with implanon. 40% of women having Jadelle had prolonged heavy vaginal bleeding. Menstrual irregularities were present in 100% of women with Jadelle while 67% with Implanon. There was no difference in both implants regarding other adverse effects like headache, weight gain, breast tenderness and acne. Acceptability and satisfaction was found to be high with implanon.

Due to their high efficacy and safety contraceptive implants have been licensed in over 60 countries in the world and used by millions of women for over four decades. Other then above mentioned benefits of the implants , they are user friendly, have long duration of action, non problematic during intercourse, client is unaware of implant presence, and fertility returns immediately after removal.[1] Norplant was first sub dermal contraceptive implant containing levonorgestril, introduced in market in 1983 and withdrawn globally in 2008 due to its difficult insertion ,removal and complications. Researchers centered on to facilitate insertion and removal easy and reducing side effect profiles. Another Levonorgestril containing implant Jadelle was launched in the United States in 1996.Shortly after this in 1999 Implanon, a new implant containing Etonogestril was introduced .In 2010 Implanon NXT was introduced and now being widely used in many countries worldwide.[2] **JADELLE** is a set of two flexible cylindrical implants, each containing 75 mg of the progestin levonorgestrel. The total administered (implanted) dose is 150 mg. Dail release rate of levonorgestrel provided by the implants is about 100 µg/day at END OF Ist Month, followed by a decline to about 40 µg/day at 12 months and to about 30 µg/day at 24 months and beyond.[3] Implanon is single rod containing 68 mg of etonogestrel (progestogen). Plasma levels of ENG(etonogestrel) sufficient to inhibit ovulation (>90 pg/mL) are achieved within 8 hours of insertion. Ovulation returns within 3 weeks of implant removal in more than 90% of women[4]. These sub dermal contraceptive implants act by inhibiting ovulation and increasing viscosity of cervical mucus.[5] Irregular periods, weight gain, acne, headache and breast tenderness are commonly experienced side effects.[6]

METHODS

A study was conducted in Jinnah hospital Lahore in Gynae unit 1 From June 2015- June 2018 to assess safety, efficacy and acceptance of sub dermal contraceptive implants by users at Jinnah hospital Lahore. Study conducted in 2 parts depending upon the availability of subdermal implants. Implanon available from Jan 2015- December 2016. 312 insertions done. From 2017 only Jadelle available and 300 insertions done from Jan-2017-june 2018. Total number of clients was 612 in 36 months.

Informed consent was taken. Adequate information about Implants was revealed to the women regarding type of contraception, mechanism of action and insertion and removal. Pre designed proforma filled regarding patient's information in terms of age, parity, mode of delivery, previous contraception. In addition to this bleeding complications, other adverse effects, satisfaction rate of patients and reasons for removal of implant also noted.

Table 1: *Patients Demographics*

Age(years)	N=612	%
Less than 20	101	16.4
20-30 years	370	60.5
More than 40	141	23

Table 2: *Parity of Patients*

Parity	N=612	%
P1-2	176	28.8
P3-4	357	58.3
P5 or more	79	12.8

Table 3: *Mode of Delivery*

Mode of delivery	N=612	%
Cesarean section	367	60
Vaginal delivery	245	40

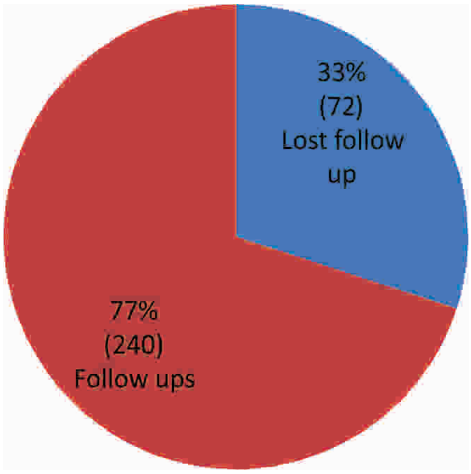

Figure 1: Follow up with Implanon

Table 5: *Menstrual Irregularities with Implanon*

Complications	N=240	%
Irregular vaginal bleeding	65	27
Amenorrhea	36	15
Prolonged heavy bleeding	48	20
Prolonged spotting	43	18
Normal menstruation	28	20

Table 6: *Adverse Effects of Implanon other than Menstruation*

Adverse effects	N=240	%
Headache	81	34
Weight gain	48	20
Mood swings	19	8
Mastalgia	22	9
No Symptoms	70	29

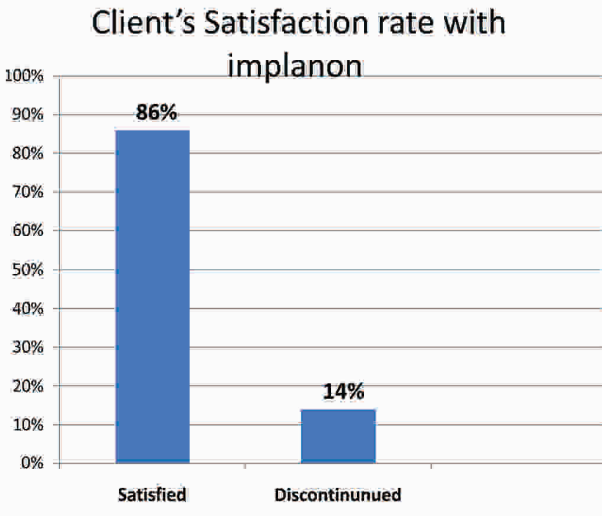

Figure 2:

Table 7: Removal of Implanon

Total insertions	Removal	
312	84	72 completed tenure 12 removed due to complications

Table 8: Insertion of Jadelle (Available since 2017 in Jinnah hospital lahore)

Total insertion	300
Follow ups	260
Removal	Nil

Table 9: Menstrual irregularities with jadelle

Complications	N=240	%
Irregular vaginal bleeding	62	24
Amenorrhea	42	16
Prolonged heavy bleeding	104	40
Prolonged spotting	52	20

Table 10: Adverse effects other than menstruation with jadelle

Adverse effects	N=240	%
Headache	94	36
Weight gain	57	22
Mood swings	26	10
Mastalgia	23	9
No Symptoms	60	23

Women Acceptability of Jedelle

Comparison of Implanon and Jedelle regarding side effects profile

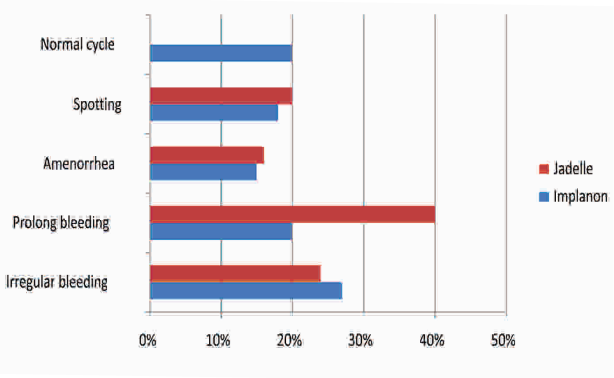

Figure 3: *Menstrual Irregularities*

Other adverse effects

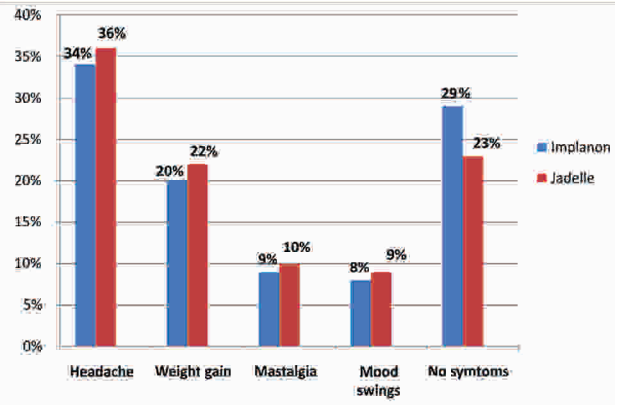

Figure 4

DISCUSSION

Millions of implants having been inserted around the world but the prevasiveness of use remains low. Contemplating that even the surgical method of female sterilization has a prevalence of use of 18% worldwide, and even as high as 36% in India,6 implants have been slow to take off [7]. For example, in France, only 2.6% of women younger than 30 years were using an implant in 2010.[7] In Great Britain, in 2008, 1%–2% of women of child-bearing age were using the implant[8]. Short-term and permanent methods are the most common contraceptive methods used in Pakistan, while the use of long-acting and reversible methods like IUDs and implants is only 2.3% and 0.1%, respectively.[9]

Current population of Pakistan is 201million and will be 310 million by year 2050. By Population Pakistan rank 6th country in world, 4th among Asian countries and 2nd in Muslim countries. [10]

Family planning services first started in 1953 in private sector then introduced to public hospitals in 1960. Contraception prevalence rate in Pakistan estimated to be 35% now on decline. According to FPP 2020 (Global partnership for family planning) Pakistan aimed at to increase contraception rate up to 50%. [11]

The present study was conducted to evaluate sub dermal contraceptive implants for their acceptability, efficacy and safety in Jinnah hospital Lahore. Implanon insertions done in Jan 2015-Dec2016 were 312.

50(16%) women were younger than 20years. More than half of participants 190(60.8%) belonged to age group between 20-30 years and 72(23%) patients were more than 40 years. 176(28.8%) clients were P1-2. 357participants were having 3-4 kids making 58.3% of total and only 79(12%) had kids 5 or above. 60%of women opting for Implanon had cesarean section and 40% had vaginal delivery.

Approximately 67% of women were already practicing contraception. Condom use observed in 169 (27.6%) of users, 96(15.7%) were IUD users, 84 (13.7%) had injections and 61(10%) were pill users. 33% of them not practicing any contraception. A study carried out at Nigeria by V.C.Pam and J.A. Karishma showed 80% of patients were practicing contraception previously. 50% of Nigerian women had used injectable contraception and 10-20% of them had used sub dermal implant previously. While only 10% of our women were using injectable contraceptives and none of them had exposure to sub dermal implant previously.[12]

Women with implanon were followed for 3 years. Initial follow ups done at 1st, 6th and 12th week of insertion then at 6th and 12th month or according to their complaints. 72 (23%) lost Follow up and 240(77%) women followed till end of study. Irregular cycles were most common and experienced by 65(27%) of women, followed by prolonged heavy bleeding in 48(20%) and prolonged vaginal spotting in 43(18%). 36(15%) women had amenorrhea while 48(20%) had no complaint regarding cycle. Gazginck et al reported less incidence of irregular bleeding(17.5%) but amenorrhea was common upto 41.5% with implanon.[13] According to a local study carried out by Abid S and Iqbal N amenorrhea was most common complaint 44%, followed by irregular periods 28%. Prolonged heavy periods and normal cycle experienced by 13.5% and 13.3% respectively.[14] Results of 11 clinical trial done on Implanon insertion in 923 patients showed that regarding bleeding problems irregular bleeding was most common 33.6%, followed by amenorrhea 22.3% and prolonged heavy cycles in 17.7%.[15]

Most common adverse effect observed in our study was headache, reported in 81(34%) of patients. Weight gain upto 5 kg at end of 12 months seen in 48(20%) of patients. Breast tenderness was present in 22 (9%) and mood swings affected 19(8%). However 70(29%) women were symptom free. Brache et al reported incidence of headache upto 30% in implanon users and weight gain up to 1.5 kg /year in 22% which is comparable to our study[16]. Local study carried out at SIMS reported weight gain in only 7.8% and Mood changes in 9.8% of implant user which is comparable to our study.[17] Breast pain reported in 22% by Iqbal N.[14]

Implanon was found highly acceptable by users. 86% of users continued it. Only 12(14%) requested removal due to complications. Out of 12 removals which were done due to side effect, most common were bleeding problems accounting for more than half removal i.e up to 6 removals. Second most common reason for removal was intractable headache and 4 removals were done due to this. 2 were removed due to persistent raised B.P. Pushpa B had shown removal in 37% cases. All of these were due to menstrual problem. No removal was done for adverse effects other then menstruation.[18]

No insertion or removal complications occurred in our study. Injury to ante brachial cutaneous nerve during removal and to ulnar nerve during insertion has been reported by Wechselberger et al and Osman et al respectively.[19,20] Spontaneous snapping of Implanon in two halves in situ at 33 months has been reported by Agarwal and Robinson.[21]

Implanon was not available after 2016 in our hospital .Since 2017 we are using Jedelle at our setup so long term experience with jedelle is not available at Jinnah hospital Lahore. Total 300 insertions had been done during 18 months. 260 patients are in follow up. 40% of patients reported prolonged heavy cycles after insertion of Jadelle. 24% had irregular cycle. 20% were having prolonged spotting. In comparison to implanon bleeding complications were more with jadelle. Almost all patients were having menstrual abnormalities and prolonged heavy bleeding was worrisome for patients while only 20% of patients were having this problem with implanon. However no removal is done due to this. There were no differences in adverse effects other then menstruation like headache, weight gain, breast pain, mood swings by both implants. They were almost same. Contrary to our study, research carried out on use of Jadelle in Thai and Nigerian women showed that commonest menstrual problem was amenorrhea reported 44% and 41% respectively.[22]

Satisfying the unmet need for modern contraception in developing countries would further prevent 54 million unintended pregnancies, including 21 million unplanned births, 26 million abortions (of which 16 million would be unsafe), and 7 million miscarriages; this would also help to prevent 1.1 million infant deaths. Globally, 56% of women use a modern method of contraception. However, the worldwide implant-prevalence rate is extremely low, at 0.3%.[23] If only 4% of current oral contraceptive users (100,000 women) in Pakistan switched to IUDs or implants, it is estimated that more than 25,000 unintended pregnancies could be averted over 5 years.[24]

CONCLUSION:

In our setup patient's satisfaction rate was found to be less with jadelle. 60% patients accepted

bleeding problems but 40% found them difficult to complete the tenure of 5 years. Rendering to its easy insertion and removal and fewer side effects Implanon found to be most effective and acceptable contraceptive method among women attending family planning clinic at Jinnah hospital Lahor. Proper pre insertion counseling can help to reduce the anxiety related with adverse effects and increase the acceptance by users. It is needed to follow women with jedelle insertion further to see its impact in our users. It would be more suitable for patients requiring long term effective contraception like patients with recurrent cesarean sections, hysterotomies , ruptured uterus with maternal morbidity for whom permanent methods for contraception are not suitable due to bad obstetric history.

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TRENDS IN IN-HOSPITAL MORTALITY AMONG PATIENTS WITH FIRST STROKE IN PAKISTAN

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Abstract

Background: The incidence and burden of stroke in Pakistan is increasing rapidly. However, there is scarce data about mortality trends during stroke hospitalization in Pakistan.

Objectives: To evaluate trends in in-hospital mortality among patients presented with first ever stroke using clinical and lab indicators (either ischemic or hemorrhagic stroke).

Subjects and methods:

Study design: Cross-sectional study.

Study setting and duration: Medical unit Jinnah Hospital Lahore. 1st April 2017 to December 2017.

Inclusion Criteria: Patients admitted in medical ward with 1st attack of stroke confirmed on CT scan or MRI.

Exclusion Criteria: Patients with history of recent head trauma, intra cranial tumor and sub-arachnoid bleed on CT.

Data collection and analysis: 100 acute stroke patients with first attack of stroke confirmed on CT scan or MRI admitted to medical unit were included in this study through a Non probability / consecutive sampling. Data was entered and analyzed in SPSS version 21.0. Factors such as demographic characteristics, clinical characteristics, co-morbidities and outcomes in terms of discharge or mortality trends were assessed. Data was presented as frequency and percentages for nominal variables and mean and standard deviation for numerical variables.

Results: 100 subjects included in our study, 61% were between age of 35-64 years, 39% were between age of 65-95 years, 62% were males and 38% were females. Total length of stay was less than 5 days in 75% of patients while 6-10 days for 14% of patients. 33% have no co-morbidity. 27% were hypertensive and only 7% were diabetics. 3% were having heart disease and 4% were having atrial fibrillation. 22% were having multiple co-morbidities. 58% had severe stroke according to NIHSS scoring with 27% had moderate and only 15% had mild stroke. 84% had ischemic stroke and 16% had hemorrhagic stroke. 22% patients died and 69% were discharged, 9% left against medical advice.

CONCLUSION: Nearly one fourth of patients died after 1st stroke. Ischemic stroke is more common than Hemorrhagic stroke. Proportion of stroke was higher between ages of 35-64 years.

Key words: Ischemia, stroke, hemorrhagic strokes NIHSS

Stroke is one of most important causes of death and disability worldwide. It is responsible for 4.4 million (9%) of the total 50.5 million deaths each year. The in hospital mortality rates were (6-9%) for ischemic stroke and (22-45%) for hemorrhagic stroke patients.[1] However, these studies were conducted before the conduction of stroke units were optimized and by the use of recombinant tissue plasminogen activator (rt-pa) was approved for use of acute stroke patients. Even with recent advancements in stroke management, the mortality of stroke patients during hospitalization remains between 18-30%.[2] Recent information about in-hospital mortality trends after stroke hospitalization is lacked in Pakistan.

The risk of stroke death varies greatly across

stroke type with higher mortality from intra-cerebral hemorrhage and sub arachnoid hemorrhage compared with ischemic stroke (IS) . In recent year there have been important advancements in management of stroke patients such as availability of specialized stroke units, thrombolytic therapy, endovascular therapy performed for stroke patients who are compatible with fibrinolytic therapy. The predictors of in-hospital mortality are age, stroke severity, increased intra cranial pressure and aspiration pneumonia.

Knowing of in-hospital deaths after stroke may be helpful for knowing the "real world" and interfere of challenges in optimizing overall pre morbid health status, stroke prevention, acute stroke treatment and acute general medical care at the individual, hospital and health system levels.[3,4] Stress upon needs for establishment of separate stroke units in tertiary care hospitals.

Objective: The objective of this study was to assess trends of in-hospital mortality in patients presenting with first ever stroke at a tertiary care hospital in Pakistan

SUBJECTS AND METHODS:

This cross-sectional study was conducted at medical unit Jinnah Hospital Lahore, from 1st April 2017 to December 2017. All patients admitted in medical ward with 1st attack of stroke confirmed on CT or MRI, were enrolled after taking written informed consent. All patients were provided standard of care according to their type of stroke and followed up till discharge or death. Confidentiality was maintained. Data was collected, entered and analyzed in SPSS version 21.0. Factors such as demographic characteristics, clinical characteristics, co-morbidities and outcomes in terms of discharge or mortality were assessed in frequency and percentages. Chi-square test was used to evaluate outcome and demographic variables like age, gender and type and severity of stroke with p <.05 as statistical significance.

RESULTS

100 subjects included in our study, 61% were between age of 35-64 years, 39% were between age of 65-95 years, 62% were males and 38% were females. Total length of stay was less than 5 days in

Table 1: Socio-Demographic Characteristics of Subjects

Variables n= 180	Frequency	Percent
Age		
35- 64 years	61	61.0
65 - 95 years	39	39.0
Gender		
Male	62	62.0
Female	38	38.0
Occupation		
Housewife	32	32.0
Blue collar (Farmer, Laborer)	26	26.0
Businessman	11	11.0
White collar (employee)	15	15.0
Retired / not working	16	16.0
Length of Stay (days)		
< 5 days	79	79.0
6 - 10 days	14	14.0
11 - 15 days	6	6.0
16 - 20 days	1	1.0

Table 2: Clinical Profile and Outcome of Subjects

Variables n=100	Frequency	Percent
Co-morbodities		
Diabetes Mellitus	7	7.0
Hypertension	27	27.0
Heart Disease	3	3.0
Fibrillation	4	4.0
DM, HTN	4	4.0
DM, HD, HTN, FIB	22	22.0
No Comorbidities	33	33.0
Smoking		
Yes	20	20.0
No	80	80.0
Stroke Severity (NIHSS)		
Mild	15	15.0
Moderate	27	27.0
Severe	58	58.0
Subtype		
Ischemic	84	84.0
Hemorrhagic	16	16.0
Outcome		
Discharged	69	69.0
Death	22	22.0
LAMA	9	9.0

Table 3: *Stoke Severity, Type, Age, Gender and Outcome Crosstabulaiton*

		Outcome			Total	
		Discharged	Death	LAMA		
Stroke Severity (NIHSS)	Mild	13	1	1	15	X^2=18.037 P=.001
		18.8%	4.5%	11.1%	15.0%	
	Moderate	25	0	2	27	
		36.2%	0.0%	22.2%	27.0%	
	Severe	31	21	6	58	
		44.9%	95.5%	66.7%	58.0%	
Type of stroke	Ischemic	62	13	9	84	X^2=13.631 P=.001
		89.9%	59.1%	100.0%	84.0%	
	Hemorrhagic	7	9	0	16	
		10.1%	40.9%	0.0%	16.0%	
Age	35 - 64 years	44	14	3	61	X^2=3.182 P=.204
		63.8%	63.6%	33.3%	61.0%	
	65 - 95 years	25	8	6	39	
		36.2%	36.4%	66.7%	39.0%	
Gender	Male	44	13	5	62	X^2=.329 P=.848
		63.8%	59.1%	55.6%	62.0%	
	Female	25	9	4	38	
		36.2%	40.9%	44.4%	38.0%	

79% of patients while 6-10 days for 14% of patients, 6% and 1% stayed for 11-15 and 16-20 days respectively. 33% had no co-morbidity. 27% were hypertensive and only 7% were diabetics. 3% were having heart disease and 4% were having atrial fibrillation. 22% were having multiple co-morbidities. Out of 100 20% percent were smokers and 80% non-smokers. 58% had severe stroke according to NIHSS scoring with 27% had moderate and only 15% had mild stroke. 84% had ischemic stroke and 16% had hemorrhagic stroke. 22% patients died and 69% were discharged, 9% left against medical advice.

Mortality was 95.5% in patients with severe type of stroke as compare to 4.5% in patients with mild variety of stroke. No death was observed in patients with moderate stroke. Mortality was more in patients with Hemorrhagic stroke (56%) than ischemic one (15.47%).Death was more prevalent in age group with 35-64 years with 63% than with 36% in age group of 65-95 years. Males had high mortality rate 59.1% than 40.9 % in females.

DISCUSSION

This analysis of proportions of in-hospital mortality after stroke from April 2017 to December 2017 in our hospital showed that deaths during stroke hospitalization are less than 25%, probably mainly reflecting improvements in hospital care or early admission after occurrence of a stroke. This decrease in the percentage of stroke hospitalizations resulting in death is consistent with the observational study from the Sino-MONICA-Beijing study.[10]

In my study Ischemic stroke subtype were the largest, followed by hemorrhagic. This data is generally in accordance with the incidence of stroke in the survey based on community population and other Stroke Registry data in Asia.[12–15] The male proportion was higher than female in both type of strokes, which was also similar with other studies.[7,12,15] 61.0% of our poplation age was < 64 years and 63.6 % died in hospital, age difference among subtypes also appeared in some community population.[13] In Our study the hospital mortality was less during this specified period and the decrease trend is comparable to other studies in developed countries like United States e.g. death from hemorrhagic stroke was from 26.90% in 1997–1998 to 23.80% in 2005–2006, ICH: from 30.47% to 28.23%, IS: from 9.76% to 8.78%)[7] and in Germany (from 11.9% in 2005 to 9.5% in 2010).[17] The in-hospital mortality in this study was nearly equal to study of trends in In-hospital mortality among stroke patients in china by

Qian He et al.[4] There can be some explanation., the age of patients in this study was younger as compared to other studies (in our study was less than 64 with increased in patient mortality as compared to study done in Germany were median age was 73 years old. Also patients were earlier transferred to smaller regional hospitals or home. The decreasing of mortality in the United States was likely driven by revascularization strategies among ischemic strokes and better acute stroke care in addition to prevention of stroke.[7] The severity and type of stroke among our patients and outcome was significant associated (P < .05) and mortality was high among NIHSS with higher score (p=<.05) but outcome compared among age groups and gender was not that significant in our study. Our study concluded that some health reform strategy and mass approaches on decreasing mortality should be included in stroke prevention, various unconventional local therapeutic traditions, and several national guidelines on stroke prevention and treatment.[11,19,20]

CONCLUSION

Nearly one fourth of patients died after 1st stroke. Ischemic stroke is more common than Hemorrhagic stroke. Proportion of stroke was higher between ages of 35-64 years.

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OUTCOMES IN PATIENTS OF INCOMPLETE ABORTION WITH AND WITHOUT PARACERVICAL BLOCK

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Abstract

Background: Incomplete abortion is one of the main causes of maternal mortality and morbidity in the developing world. Infection and hemorrhage are the main complications in incomplete abortion. Role of the paracervical block is less clear.

Objective: To compare the outcomes in patients of incomplete abortion with and without paracervical block.

Study Design: Randomized Controlled Trial.

Setting: Department of Obstetrics & Gynecology, Services Hospital Lahore.

Duration of Study: 10th July 2016 to 10th January 2017.

Subjects and Methods: A total of 620 (310 in each group) pregnant women with gestational age < 12 weeks of any parity with incomplete abortion were included in the study. Group A patients received paracervical block. Group B was treated with MVA without paracervical block. Manual vacuum aspiration was performed with IPAS double valve syringe and no 5 to 8 plastic cannula as required. Intraoperative pain in both groups was recorded.

Results: Mean age of 28.919±2.60 years in group A while 29.525±2.34 years in group B, mean gestational age was 7.745±1.63 weeks in group A and 8.525±1.36 weeks in group B, Intraoperative pain was seen in 245(79%) patients in MVA with paracervical block group or group A as compare to 214(69%) patients in MVA without paracervical block group or group B (P 0.004).

Conclusion: paracervical block technique used in this study do not provided sufficient pain control. It is recommended that randomized comparative studies be designed to determine the effectiveness of other paracervical block techniques and the efficacy of the use of analgesics in patients suffering from incomplete abortion treated with manual vacuum aspiration.

Keywords: incomplete abortion, manual vacuum aspiration, paracervical block

Incomplete abortion is one of the main causes of maternal mortality and morbidity in the developing world. Infection and hemorrhage are the main complications in incomplete abortion.[1] Approximately 11–15% of pregnancies end in spontaneous first-trimester miscarriage.[2] Standard post-abortion care has involved surgical intervention, such as dilatation and curettage or vacuum aspiration (manual or electric), to complete uterine evacuation and prevent infection.[3]

Evacuation of the uterus with manual vacuum aspiration or suction evacuation is usually performed procedure for the first trimester termination of pregnancy, in which uterine size is less than 12 weeks.[4] A variety of factors are related to the variations in controlling pain, including institutional norms, the availability of medications, geographical location, provider preference and training for pain management, and the surgical technique used to evacuate the uterus.[5] In addition, guidelines for appropriate pain management during treatment for incomplete abortion are few and usually not very

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clear.[6]

The use of sharp curette has been described as being associated with pain in patients undergoing dilation and curettage[7]; however, in managing incomplete abortion, curettage has been associated with a greater level of pain than manual vacuum aspiration.[1] However, there is little information about how useful local anesthesia is in term of pain management when manual vacuum aspiration is used for treating incomplete abortion.

Available studies have evaluated the efficacy of local anesthesia in patients with abortions with a closed cervix, and as such, the evidence cannot be directly extrapolated to the treatment of incomplete abortion, in which the cervix is usually open.[8] When the cervix is closed, it is necessary to dilate the cervix through mechanical procedures; this is the most painful part of the procedure.[9] In an incomplete abortion, the cervix is usually open, requiring no dilation for evacuation. Thus, the role of the paracervical block is less clear.[10] It has been reported that the control of pain through the use of pharmacological agents is not necessary when manual vacuum aspiration is being used and that only 10% of patients require medication to lessen their pain.[11]

Ansari R and her associates has found in a study that manual vacuum aspiration with paracervical block procedure showed efficacy of 97.7% with hemorrhage rate of 0.8%.[12]

Go´ mez P, and his associates has found in a study that frequency of intraoperative pain 6++ (VAS > 4) was 76.6% in patients of manual vacuum aspiration treatment with paracervical block as compare to 67.6% in patients of manual vacuum aspiration treatment with no paracervical block in incomplete abortion.[13]

Manual vacuum aspiration treatment with paracervical block has been widely used to manage pain in USA, Asian and European countries; but its use in Pakistan has been limited. So far there is no local data available on the treatment with paracervical block for pain management in our population. Moreover most studies have been done only in efficacy of MVA in our local literature. So I have decided to do this study to determine the outcome of manual vacuum aspiration with paracervical block as a pain management in incomplete abortion in our general population.

OBJECTIVE:

To compare the outcomes in patients of incomplete abortion with and without paracervical block.

A total of 620 (310 in each group) pregnant women with gestational age < 12 weeks of any parity with incomplete abortion were included in the study.

Subjects and Methods: A Randomized Controlled Trial was conducted at Department of Obstetrics & Gynecology, Services Hospital Lahore from 10th July 2016 to 10th January 2017. A sample size of 620 cases (310 in each group) was calculated with 80% power of test, 5%level of significance and taking expected percentage of moderate to severe pain (i.e VAS≥ 4) in both groups i.e. 76.6%13 in MVA with paracervical block versus 67.6%13 in MVA without paracervical block in patients with incomplete abortion through a non-probability consecutive sampling.

Women of Age 20-35 years with gestational Age < 12 weeks by LMP of any Parity were included in the study. Pregnant women with live fetus on ultrasound, history of allergies to lidocaine or pelvic mass on ultrasound were excluded. Group A patients received paracervical block. Group B was treated with MVA without paracervical block. Manual vacuum aspiration was performed with IPAS double valve syringe and no 5 to 8 plastic cannula as required. Intraoperative pain in both groups were recorded. Incomplete abortion: It was defined as positive urine pregnancy test with gestational amenorrhea <12 weeks presented with per vaginal bleeding and ultrasound reveal presence of vascularity within the echogenic material and the endometrial thickness >10 mm. Outcome was determined as in term of intraoperative pain during the procedure evaluated by the VAS score (on a 0–10 scale). 0 score

was no pain and score 10 was described as worst pain. Intraoperative pain was labeled if patient reports a pain score ≥ 4. Data was analyzed with statistical analysis program (SPSS version 20). Analysis was done to compare proportion of group A and group B. Frequency and percentage was computed for qualitative variables like age groups, parity and intraoperative pain. Mean ±SD was presented for quantitative variables like age, gestational age, duration of procedure and BMI. Chi-square test was applied to compare intraoperative pain in both groups taken p ≤0.05 as significant.

RESULTS

Age range in this study was from 20 to 35 years with mean age of 28.919±2.60 years in group A while 29.525±2.34 years in group B, mean gestational age was 7.745±1.63 weeks in group A and 8.525±1.36 weeks in group B, mean BMI was 26.932±1.47 Kg/m2 in group A and 27.029±1.34 Kg/m^2 in group B and mean duration of procedure was 7.596±1.28 minutes in group A and 7.148±1.23 in group B as shown in Table-I. Majority of the patients were of 28-35 years of age in both groups as shown in Table-II. Majority of patients were of 0-3 parity in both groups as shown in Table-III. Intraoperative pain was seen in 245(79%) patients in MVA with paracervical block group or group A as compare to 214(69%) patients in MVA without paracervical block group or group B (P 0.004) as shown in Table-IV.Stratification of Intraoperative pain with respect to age, gestational age, parity, BMI and duration of procedure in group A and group B are shown in Table-III

DISCUSSION:

The treatment of incomplete abortion always requires removal of retained products of conception (POC) from the uterus. Dilatation and Curettage (D&C), the traditional method of removing tissues from the uterus is accompanied by scraping the uterus walls with a metal curette. Vacuum aspiration uses suction to remove uterine tissue through a cannula with minimum scraping of the uterine walls.

Table 1: *Central Tendency for Age, Gestational Age, BMI and Duration of Procedure*

	Group A Mean ± SD (n=310)	Group B Mean ± SD (n=310)
Age (years)	28.919±2.60	29.525±2.34
Gestational age(weeks)	7.745±1.63	8.525±1.36
BMI (Kg/m2)	26.932±1.47	27.029±1.34
Duration of Procedure (mins)	7.596±1.28	7.148±1.23

Table 2: *Baseline Characteristics Among Groups*

Variables	Group A Frequency (%age) (n=310)	Group B Frequency (%age) (n=310)
Age Groups (years)		
20-27	70 (22.6%)	70 (22.6%)
28-35	240 (77.4%)	240 (77.4%)
Parity		
0-3	230 (74.2%)	222 (71.6%)
>3	80 (25.8%)	88 (28.4%)
Intraoperative pain		
Yes	245(79%)	214(69%)
No	65(21%)	96(31%)

Table 3: *Stratification of Intraoperative Pain with Respect to Age, Gestational Age, Parity BMI and Duration of Paint Among Groups.*

Groups		Intraoperative pain Yes	Intraoperative pain No	P value
Age 20-27 years	Group A	61(87.1%)	9(12.9%)	0.008
	Group B	48(68.6%)	22(31.4%)	
Age 28-35 years	Group A	184(76.7%)	56(23.3%)	0.064
	Group B	166(69.2%)	74(30.8%)	
G.A ≤ 5 weeks	Group A	29(76.3%)	9(23.7%)	0.508
	Group B	20(83.3%)	4(16.7%)	
G.A ≤ 5 weeks	Group A	216(79.4%)	56(20.6%)	0.002
	Group B	194(67.8%)	92(32.2%)	
For Parity 0-3	Group A	184(80%)	46(20%)	0.001
	Group B	148(66.7%)	74(33.3%)	
For Parity >3	Group A	61(76.2%)	19(23.8%)	0.850
	Group B	66(75%)	22(25%)	
For BMI ≤ 25 Kg/m^2	Group A	44(75.9%)	14(24.1%)	0.001
	Group B	35(72.9%)	13(27.1%)	
For BMI > 25 Kg/m^2	Group A	201(79.8%)	51(20.2%)	0.003
	Group B	179(68.3%)	83(31.7%)	
For ≤ 8 minutes	Group A	180(78.6%)	49(21.4%)	0.014
	Group B	181(68.8%)	82(31.2%)	
For > 8 minutes	Group A	65 (80.2%)	16(19.8%)	0.196
	Group B	33(76.2%)	14(29.8%)	

World Health Organization has listed Manual Vacuum Evacuation as an effective and safe method of uterine evacuation and hence the technique is being employed increasingly in the developing world under minimal anaesthesia or sedation in the management of incomplete abortions. However, pain control is an important and relevant issue in managing incomplete miscarriages using manual vacuum aspiration (MVA).

The purpose of pain control therefore is to ensure that the woman suffers the minimum of anxiety and discomfort as well as the least risk to her health. The majority of pain carrying fibres from the uterus and cervix pass through the paracervical tissue. Thus paracervical block with lignocaine will relieve pain during the manipulation.

In my study Intraoperative pain was seen in 245(79%) patients in MVA with paracervical block group as compare to 214(69%) patients in MVA without paracervical block group (P 0.004).

My study results are comparable with a study by Go´ mez P, and his associates who that frequency of intraoperative pain was 76.6% in patients of manual vacuum aspiration treatment with paracervical block as compare to 67.6% in patients of manual vacuum aspiration treatment with no paracervical block in incomplete abortion.[13]

When pain levels are compared with those in previously published studies that evaluated pain exclusively associated with endouterine evacuation, it can be seen that the level of pain ranged from 5.1 to 7.9. This value varies with the use of analgesics in premedication, use (or no use) of local anesthetic, the type of drug used, and the moment when the pain was measured.

Donati et al85 evaluated pain by categories, finding 40% of those who had received paracervical block in the moderate-to-severe pain category. Fuentes Vela´squez (cited in Memories of the Global Conference on advances and challenges in operational research into post abortion attention), mentioned that approximately 40% of the patients reported severe pain during manual vacuum aspiration.[14,19.20]

It is well known that pain is a bio psychosocial experience, where previous experiences and the socio cultural perception of pain mark great differences in the development, severity, and control of pain[15,16]. Studies suggest that woman are likely to consider the rates and severity of pain during uterine interventions when performed awake to be unacceptable in the absence of neuraxial blockade, which are unaltered by paracervical block.[17,18] Thus, measuring the degree of pain becomes a difficult task. This makes it difficult to generalize observations among different populations.

CONCLUSION

This study concluded that paracervical block technique used in this study do not provided sufficient pain control. It is recommended that randomized comparative studies be designed to determine the effectiveness of other paracervical block techniques and the efficacy of the use of analgesics in patients suffering from incomplete abortion treated with manual vacuum aspiration.

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OUTCOME OF INTRAMEDULLARY SCREW FIXATION WITH COMBINATION OF TENSION BAND WIRING IN OLECRANON FRACTURES OF ADULTS.

Muhammad Zafar Iqbal, Sajid Mumtaz Khan, Tayyab Mahmood Khan

Abstract

Background: Olecranon fractures are one of the most common orthopedic emergency. Theses fractures account for10 % of all upper limb fractures. Intramedullary screw fixation, with or without tension band wiring is the most secure treatment option in displaced olecranon fractures with better outcome than other treatments.

Objectives: To evaluate outcome of intramedullary screw fixation with combination of tension band wiring in olecranon fractures in adults.

Subjects and methods:

Study Design: Descriptive case series.

Study Duration: One year duration from march10, 2016 to march9, 2017

Setting: Department of Orthopedics, Allama Iqbal Medical College, Jinnah Hospital, Lahore.

Data collection and Analysis: 120 patients with olecranon fractures of mayo's type IIA non comminuted fractures with displacement of proximal segment without elbow instability occurred within a week after the injury between age 18 – 65 years of either gender were included in study through a non-probability / consecutive sampling technique were included in study. Patients with associated fractures of ipsilateral limb, patients with open olecranon fractures, patients already treated for fracture of olecranon and patients having any superficial or deep skin infections were excluded. Data was entered and analyzed in SPSS Ver: 21.0. Data was entered and analyzed in SPSS Ver: 21.0. Mean and SD was calculated for age. Outcome was assessed according to mayo's criteria consisting of assessed pain intensity (45 points), motion (20 points), stability (10 points) and function (25 points) of elbow joints and was categorized as excellent, good and fair.

Results: Mean age of subjects was 44.32 + 12.34 with minimum age of 16 years and maximum age of 75 years. 66.3% were males and 33.7% were females. Results were excellent in 60% good in 25% fair in 15% there was no patient with poor results

Conclusion: Intramedullary screw fixation with combination of tension band wiring in olecranon fractures is simple and effective technique and based upon the Bio-mechanical principles of tension band wiring.

Key Words: olecranon fracture, tension band wiring technique, AO cancellous screw, intramedullary screw fixation

Olecranon fracture is one of the common fractures of upper limb occurring approximately 7 to 10 % of all upper limb fractures in adults and 38% of all elbow fractures.[1&2] The fracture results from direct or an indirect trauma of elbow. Falling on 90 degrees flexed elbow and forced hypertension of the elbow joint are the common causes of this fracture.[3] It is an intra-articular injury. The extension mechanism of the elbow joint is frequently lost. There are various classification systems for olecranon fractures.[4] Commonly used classification systems are Mayo's classification and Schatzker classification. The Mayo classification of olecranon fractures is based on fracture displacement, communition, and ulno-humeral instability.

The treatment of an olecranon fracture can be conservative or surgical.[5] Surgery is indicated in significant displacement (>2mm) or communution,[12] Joint reconstitution. stability and full range of motion are the main aims.[6] Tension band wiring,[7,13]

intramedullary devices[8&11] and plate & screw fixation are the various surgical options.[9] Intramedu-llary screw fixation, with or without tension band wiring is the most secure treatment option in displaced olecranon fractures.[10] Use of a single large-diameter cancellous screw in olecranon fractures repair has been in discussion for a long time. The intramedullary screw should be properly placed along the ulnar shaft long axis. However it should accommodate the ulnar bow and anatomical reduction of the fracture. When it is used alone, it does not provide a stable fixation as compared to tension band wiring. However the combination of intramedullary screw and tension band wiring gives a very stable fixation.[8] Intramedullary screw plus tension band wiring is excellent according to Mayo's criteria in 73.3% and good in 26.7% patients operated for olecranon fractures. The rationale of this study was to evaluate outcome of intramedullary screw with tension band wiring for olecranon fractures is excellent technique and the elbow joint motion and stability after the procedure is good.

Objectives: To evaluate efficacy intramedullary screw combined with tension band wiring in olecranon fractures of adults in terms of union, pain control, joint motion and functional outcome.

METHODS

A descriptive case series was carried out from March, 2016 to March 2017 at Department of Orthopedics, Allama Iqbal Medical College, Jinnah Hospital, Lahore. 120 patients with olecranon fractures of mayo's type IIA non comminuted fractures with displacement of proximal segment without elbow instability occurred within a week after the injury between age 18 – 65 years of either gender were included in study through a non-probability / consecutive sampling technique were included in study. Patients with associated fractures of ipsilateral limb, patients with open olecranon fractures, patients already treated for fracture of olecranon and patients having any superficial or deep skin infections were excluded. All patients presented in emergency within 24 hours after the olecranon fracture. X-rays of elbow joint AP & lateral views were done. Back-slab was given. Each patient was counseled regarding the patient and written consent was taken. These patients were operated on 3rd day after the injury (average 2nd – 9th day). A written permission was obtained from the hospital ethical committee. All fractures were classified according to Mayo's classification on the basis of X-rays of elbow joint AP and lateral views. Among these olecranon fractures of Mayo's type IIA were fixed with tension band wiring combined with 6.5mm cancellous screw. Patients were discharged on the 3rd post-operative day (on an average). After surgery the accuracy of reduction and joint movements were checked. Post-operative analgesia and antibiotics were given and the effected limb was elevated. Hand and finger movements were started on the same day of surgery while the elbow movements were started as the patient permitted (on an average the 3rd post-operative day). All patients were followed on1st, 2nd,4th, 6th and 12th week and each patient was assessed according to Mayo's functional index. At the end of 1st week back-slab was removed and protected range of movements was started, while in the subsequent visits in every patient. Data was entered and analyzed in SPSS Ver: 21.0. Mean and SD was calculated for age. Outcome was assessed according to mayo's criteria consisting of assessed pain intensity (45 points), motion (20 points), stability (10 points) and function (25 points) of elbow joints and was categorized as excellent, good and fair. (Table no: 2).

RESULTS

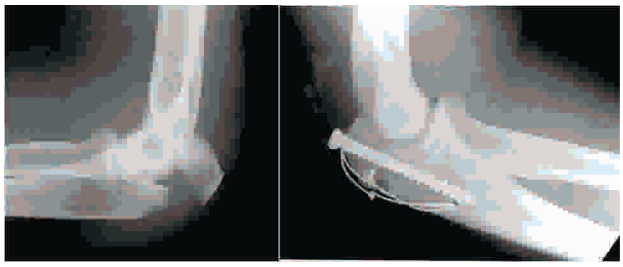
Mean age of subjects was 44.32 + 12.34 with minimum age of 16 years and maximum age of 75 years. 66.3% were males and 33.7% were females. Results were excellent in 60% good in 25% fair in 15% there was no patient with poor results.(Table no:1)

Table 1: *Demographic and Clinical Outcome of Subjects:*

Age: Mean = 44.32 SD ± 12.34 Min= 16 Max 75		
16 – 45		
46 – 75		
Male	80	66.7
Female	40	33.3
Mechanism of injury		
Road traffic accident	90	75
Fall from height	25	21
Direct blow	05	4
Outcome		
Excellent	72	60.0
Good	30	25.0
Fair	18	15.0

Table 2: *Mayo's Criteria for Evaluation of Outcome*

Results	Pain	Motion	Stability	Function	Total
Excellent	42	18	08	22	90
Good	38	15	07	20	80
Fair	30	12	06	18	66



DISCUSSION:

Fractures of olecranon process of ulna occur most commonly as a result of Motor vehicle accidents, or fall, or as a result of assault.[12] The main aim behind treatment of intrarticular fractures is not achieving union but also achieving the optimal function of the adjacent joint and soft tissue. Fixation must be stable enough for early mobility of elbow to prevent the fracture disease.[3]

The ultimate goals for olecranon fractures is restoration and stability of the joint and to gain full range of muscle strength without pain.[4] This can only be achieved by Open Reduction and Precision Osteosynthesis to prevent complications like post-traumatic arthritis and joint stiffness. Moreover the implementation of early joint motion also prevent the chances of post-traumatic arthrofibrosis[5].

In our study we used 6.5 mm cancellous AO screw with washle on guide wire under image intensifier with combination of tension band wires. This could convert the tensile forces into compressive forces with additional resistance to displacement of fracture fragments because of its lag mechanism. Our experience with this technique has favorable results compared to other studies. The clinical outcomes and the end results were analyzed and comparison was done with other similar studies[7]. Most of the studies showed excellent results in around 60% of the cases8.

In study of Ahmed AR et al shows that I/M screw fixation with TBW for displaced Transverse and Oblique fractures give better results in terms of fracture union and has got much less re-operative rate8. In another study conducted by Raju and Rashmi the results were comparable to our original study.[14]

Similarly Murphy et al also got 60% excellent results with cancellous screws combined with TBW for olecranon fracture.[15] Study conducted by Jiang Xie Yuan and Chang also showed excellent (53.3%) and good results.[16,17] There were no poor results with regards of fracture union and preservation of joint movements. Study by Haddad showed s minimal tissue dissection and operating time is decreased and there is minimal risk of metalwork prominence as screws obtain good purchase in the anterior cortex of ulna. Good interfragmentary compression is achieved as screws are perpendicular to the fracture line and two screws provide good rotational stability.[18]

Our study is consistent with the above mentioned studies in terms of fracture union, stability of implant to resist the tensile forces and recording the fracture displacement. Moreover the re-operation rate was almost negligible.

This technique is simple, cost effective and based on the sound bio-mechanical principles of fracture fixation.

CONCLUSION

From the present study it is concluded that ORIF with 6.5 mm AO cancellous screw combined with TBW is one of the most simple and effective technique for treating olecranon fractures. It not only provides rigid fixation but also resist fracture displacement. So, early, active and functional movements are achieved to prevent joint stiffness. Considering all these aspects, this mode of fixation where 6.5mm AO cancellous screw in combination with TBW is method of choice for olecranon fractures

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EFFECT OF TECHNOLOGY ON THE SLEEP PATTERNS OF MEDICAL STUDENTS OF AIMC

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Abstract

Objectives: The main objective of our study is to determine the effects of technology devices like laptops, mobile phones, computer on sleep patterns of medical students. The changing sleep patterns not only affect the health but also the study of medical students

Methods: The study was designed as a cross sectional survey and non-probability convenient sampling was used to select 300 students. Respondents completed a self-administered questionnaire in which their use of technology and its effect on sleep was accessed. Data was entered and analyzed in SPSS ver: 21.0. Frequency and percentages were calculated and cross tabulation was done for effect on sleep and use of technology Chi-square test was used to assess any statistical significance with $p < .05$ as statistical significant.

Results: 95% of subjects in our study used mobile phones and laptop/computer. 63.7 % of students had prolonged sleep onset latency and 69.7% had the issue of daytime drowsiness. 47% of students showed irritability at daytime and 63.3 % students reported difficulty in concentrating during morning lecture

Conclusion: Our study concludes the extravagant use of technology by medical students and it has a negative relation on their sleep quality and psychological health

Key word: sleep disturbance, technology, mobile, computer use.

Sleep is a naturally recurring state of mind characterized by altered consciousness, relatively inhibited sensory activity, inhibition of nearly all voluntary muscles, and reduced interactions with surroundings[1] Centers for Disease Control 2012 described that average teenager needs 8.5 to 9.25 hours of sleep in 24hours of a day.[2]

The 2011 Sleep America Poll found that adults of age 19-29 are major users of modern day technology; 67% use cellphones, 43% music devices and 18% video games and the majority complaint of not having profound sleep.[3]

Sleep deprivation is having improper or inadequate sleep and its consequence is sleepiness which is defined as problems in alertness during the wake hours of the day leading to un intended lapses into drowsiness.[3]

It is scientifically proven that screen devices transmit artificial short wavelength light exposure which disrupt circadian rhythms, sleep and neurobehavioral operations in evening.[2] Increased sleep latency due to suppression of melatonin is also its effect.[4]

Technology has greatly prevailed our lives especially mobile phone use. A study from Malaysia showed. Out of total of 1340 students' majority 91.9% used their mobile phones for calling, text messages 89.4% and receiving phone calls 80%.[5]

Evening TV use was associated with increase in Sleep Problem Score of 0.743[6] Social media, especially Facebook addiction has disturbed students routine and sleep patterns[7] same goes for computer use. A study showed that 31.2% students use computers during week and 53.6% during weekends ended up in sleep deprivation.[8] Students,specially Medical students due to their academic commitment have decreased nocturnal sleep time, increased daytime sleepiness and hence poor acade-mic performance[9] Increment of social phobia and poor school performance are result of pathological gaming.[10]

Sleep deprivation effects prefrontal cortex functioning, causes sleep apnea and decline in neurocognitive functions.[11] The intensive mobile use

among girls in their adolescent period can cause psychological and social distortion.[12]

The main objective of our study is to determine the effects of technology devices like laptops, mobile phones, computer on sleep patterns of medical students. The changing sleep patterns not only affect the health but also the study of medical students.

METHODS

This cross sectional study was conducted at Allama Iqbal Medical College, Lahore affiliated with Jinnah Hospital Lahore, Pakistan from April to May 2016, 300 students were selected by stratified random sampling technique.

SAMPLE SELECTION

Inclusion criteria

- Medical students of AIMC
- Both Gender
- Both Boarders and Day Scholars

Exclusion criteria:

Students who already have some medical issue like stress which is changing his sleep pattern.

Variables

- Independent variables:
- technology, age , gender
- Dependent variables
- sleep latency
- sleep duration
- sleep onset
- Day time sleep

DATA COLLECTION PROCEDURE

- We collected the data from 300 medical students fulfilling our inclusion criteria. All the data will be collected through a structured questionnaire.

DATA ANALYSIS PROCEDURE

- Data analyzed by SPSS version 17.0. Mean and standard deviation calculated for numerical variables like age, duration of use of technology (mobile, laptop, and computer). Frequency tabulation and percentages will be generated for nominal variables.

RESULTS

A cross sectional study was conducted amongst the medical students of ALLAMA IQBAL MEDICAL COLLEGE (AIMC) Lahore. The number of students participated in our study was 300 (81.67% females and 18.33% males). Among 300 students 163 (54.3%) were of age 17-21 and 137 (45.7%) of 22-26. This is shown in table no. 1 and graph. no 1 .

The major technology device used by the students was mobile phone (65.3%) while (30.67%) of students reported of using both mobile phones and laptops/computers (graph.no.2). They used these devices for surfing social networking sites (34%), listening to music (6.67%), watching movies (44.33 %), gaming (4.67%) , while the majority of students (50.33%) reported of doing all above mentioned activities on their technology devices. (graph no. 2)

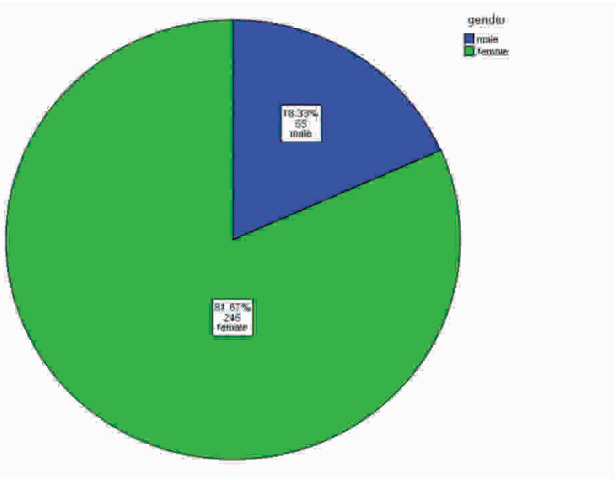
The extravagant use of technology has greatly disturbed the sleep quality of medical students. Our study showed different parameters of sleep quality like sleep latency, sleep duration, day time drowsiness etc. The prolong sleep onset latency, reduced sleep duration and daytime drowsiness was reported by 58%, 58%, 71.3%of students respectively (table no. 3).

This clearly explains the negative relation of over use of technology and sleep quality. In addition, 67% medical students reported difficulty in concentrating morning lectures most likely owing to the poor sleep hygiene. In addition, 41.7 % students say that technology has affected their academic performance. Our study also relates the poor sleep quality and its psychological effect on the students like anxiety, depression, irritability etc. 47.1% of students reported psychological disturbance when the use these devices excessively.

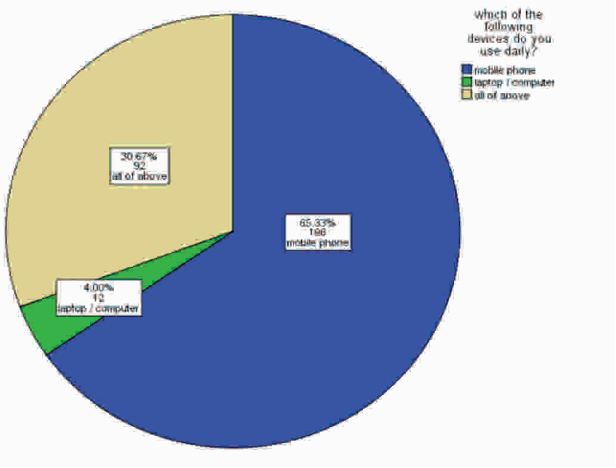
DATA ANALYSIS

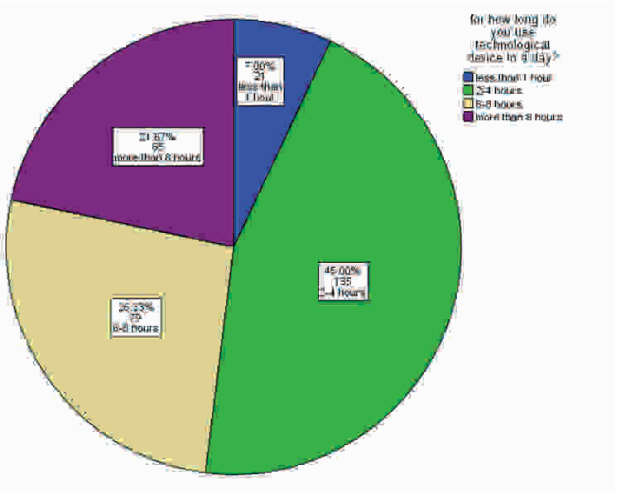
Table 1: *Age of Respondents*

Age	Frequency	Percent
17-21	163	54.3
22-26	137	45.7
Total	300	100.0

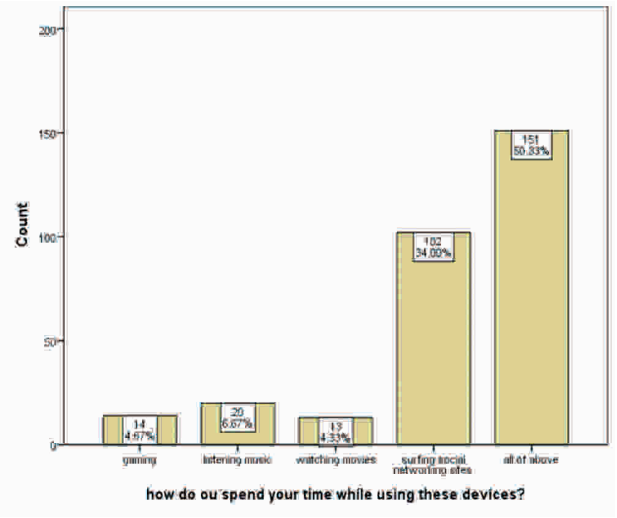


Graph .1 : *Gender Distribution*





Graph 3 : *how long do you use technology device in a day?*



Graph. 4 *How do you Spend time while using these Devices?*

Graph.2

Table 2:

Sleep Disturbance Frequencies			
	Responses		Percent of Cases
	N	Percent	
Does it take longer to fall asleep when you use these devices at night?	174	12.7%	60.2%
Does it affect the duration of your sleep at night?	174	12.7%	60.2%
Do you have to use any drugs at night to help you fall asleep?	13	0.9%	4.5%
Do you feel any difficulty in waking up in the morning?	185	13.5%	64.0%
Do you feel drowsiness in daytime?	214	15.6%	74.0%
Do you feel any irritability in daytime?	148	10.8%	51.2%
Do you feel difficulty in concentrating during morning lectures?	201	14.7%	69.6%
Does it affect your academic performance?	125	9.1%	43.3%
Do you feel psychological disturbed after excessive use of these devices?	136	9.9%	47.1%
Total	1370	100.0%	474.0%

Table 3: *Sleep Disturbance*Gender Cross Tabulation*

	Gender		Total	P value
	male	**female**		
Does it take longer to fall asleep when you use these devices at night?	43	131	174	.001
	78.2%	56.0%		
Does it affect the duration of your sleep at night?	40	134	174	.014
	72.7%	57.3%		
Do you have to use any drugs at night to help you fall asleep?	3	10	13	.651
	5.5%	4.3%		
Do you feel any difficulty in waking up in the morning?	36	149	185	.523
	65.5%	63.7%		
Do you feel drowsiness in daytime?	39	175	214	.939
	70.9%	74.8%		
Do you feel any irritability in daytime?	24	124	148	.350
	43.6%	53.0%		
Do you feel difficulty in concentrating during morning lectures?	41	160	201	.188
	74.5%	68.4%		
Does it affect your academic performance?	31	94	125	.014
	56.4%	40.2%		
Do you feel psychological disturbed after excessive use of these devices?	17	119	136	.012
	30.9%	50.9%		
Total	55	234	289	

Table 4: *Sleep Disturbance* Use technological device in a day Cross tabulation*

	For how long do you use technological device in a day?				Total	P value
	less than 1 hour	2-4 hours	6-8 hours	more than 8 hours		
Does it take longer to fall asleep when you use these devices at night?	14	75	43	42	174	.416
	70.0%	57.3%	58.9%	64.6%		
Does it affect the duration of your sleep at night?	12	78	44	40	174	.965
	60.0%	59.5%	60.3%	61.5%		
Do you have to use any drugs at night to help you fall asleep?	2	2	6	3	13	.109
	10.0%	1.5%	8.2%	4.6%		
Do you feel any difficulty in waking up in the morning?	12	84	47	42	185	.897
	60.0%	64.1%	64.4%	64.6%		
Do you feel drowsiness in daytime?	18	88	57	51	214	.100
	90.0%	67.2%	78.1%	78.5%		
Do you feel any irritability in daytime?	14	55	44	35	148	.040
	70.0%	42.0%	60.3%	53.8%		
Do you feel difficulty in concentrating during morning lectures?	14	90	50	47	201	.723
	70.0%	68.7%	68.5%	72.3%		
Does it affect your academic performance?	10	58	29	28	125	.741
	50.0%	44.3%	39.7%	43.1%		
Do you feel psychological disturbed after excessive use of these devices? Total	8	66	40	22	136	.739
	40.0%	50.4%	54.8%	33.8%		
	20	131	73	65	289	

DISCUSSION

Our study explored the association of excessive use of technology (cell phones, laptop/computers) with the sleep patterns of medical students. It describes that a large number of medical students of AIMC are using the technology excessively and it has produced negative impact on their sleep quality. The most used technology device was the cell phone 65.33% subjects used mobile phones while 30.67 percent used both mobile phones and laptop/

computer. Interestingly this finding is quite consistent with earlier studies. [5]

Data from the study suggested that students mostly use technology for surfing social networking sites like Facebook etc. (34%) this finding was also indicated by a previous study[7]. Not only social networking sites but also the use of technology for games (4.67%) music (6.67%) movies (4.33%) was reported by students. This was also seen in the previous studies. [8][5]

Data from our study demonstrated that over use of technology has positive association with prolonged sleep onset latency (SOL), day time drowsiness and decreased duration of sleep. 58.0% of subjects reported prolonged sleep onset latency while day time drowsiness and decreased sleep duration was found in 71.3% and 58.0% of students respectively. These findings also concurs with the other studies[3][5]. This exaggerated use of technology was also associated with irritability (49.3%) and psychological (45.3%) disturbance during day time .the similar observation was noticed in the previous studies.[12]

CONCLUSION

According to our study the use of technology has been hugely accepted by the medical students of AIMC. Data obtained from this study clearly shows that there is negative impact of technology use on sleep quality. In addition the intense use of technology is also associated with psychological symptoms.

Our study has got some limitations a) the number of students involved in our study was only 300 so we cannot generalize the results to the whole community b) some of the students might not be filling the questionnaire seriously so the results may not be reliable c) the duration of our study was short so that may have affected our results.

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COMPARISON BETWEEN SOKAL AND HASFORD SCORING SYSTEM IN UNTREATED PATIENTS OF CHRONIC MYELOID LEUKEMIA

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Abstract

Chronic myeloid leukemia is a myeloproliferative neoplasm. In clinical practice, Sokal, Hasford and European Treatment Outcome Study (EUTOS) prognostic scoring systems are used for CML risk stratification.. The aim of present study is to compare Sokal and Hasford scoring system in CML patients to suggest which one is more useful in determining the prognosis.

Material and Methods: Descriptive cross sectional study conducted at department of AIMC. Fifty five patients of all age groups, both genders and all the three clinical phases were included. In every patient about 5ml EDTA blood sample was collected. Complete blood counts were performed on haematology analyzer (Sysmex KX-21) Peripheral blood smears were prepared and stained using Giemsa stain. Differential count was performed. Bone marrow aspiration was done. The diagnosis of CML was made by complete blood count, examination of peripheral blood smear and bone marrow findings. Sokal and Hasford scoring was applied at time of presentation for risk stratification.

Result: The mean age at time of diagnosis was 38.1±11.5 SD years (range 17-66). The patients were divided into three age groups and majority of patients, 29(52.7%) were between 20-40years age group. Out of 55, 21(38.2%) were male and 34 (61.8%) were females. According to Sokal score, majority of the patients were in high risk (47.3%) and intermediate (43.6%) prognostic group. Whereas according to Hasford score only 4(7.3%) were grouped under high risk, 18(32.7%) were in intermediate risk group and 33(60%) of patients were placed in low risk group.

Conclusion: Many scoring systems have been developed for CML risk stratification .It can be concluded from our study that Hasford score is a better predictor of prognosis of CML patients than Sokal index.

Chronic Myeloid Leukemia (CML) is a clonal myeloproliferative neoplasm resulting from reciprocal translocation of ABL gene on chromosome 9 to BCR gene region on chromosome 22 t(9:22).[1,2] This translocation leads to the formation of the BCR–ABL fusion gene which encodes an aberrant chimeric protein (BCR–ABL p210) with constitutively activated tyrosine kinase activity that promotes growth and replication through downstream pathways which influence leukemogenesis by creating a cytokine-independent cell cycle with aberrant apoptotic signals in response to cytokine withdrawal.[3,11]

CML is the commonest type of chronic leukemia in Pakistan, and accounts for about 15 percent of leukemias in adults. The median age at presentation is 45 to 55 years whereas 12-30% of patients are 60 years of age or older.[4,7]

CML usually runs a biphasic or triphasic course.[4] This process includes an initial chronic

phase and a terminal blastic phase, which is preceded by an accelerated phase in 60% - 80% of patients.[4,5,14] Many patients, especially if they present with delay, may have accelerated or even blast stage at the onset. Splenomegaly is documented in 30-70% of cases. The liver is enlarged in 10-40% of cases.[4,6]

Many prognostic scoring systems have been developed for CML risk stratification. First was proposed by Tura et al in 1981. Carvantes and Rozman designed the prognostic score in 1982. Kantarjian et al in 1990 introduced the so called simple synthetic prognostic staging system.[4,8] In 1984, Sokal risk score was developed and achieved widespread usage as a prognostic discriminator for survival in patients treated with chemotherapy (mainly busulfan and hydroxyurea).[4,9] This scoring system was based on four variables: age, percentage of blast cells, spleen size and platelet count at the time of diagnosis and patients were stratified into various prognostic groups as shown below;

Low risk (good prognosis) group with score <0.8

Intermediate risk (moderate prognosis) group with score of 0.8 -1.2

High risk (poor prognosis) group with score >1.2

The Hasford CML score also called the Euro score, uses age, spleen size (measured from the left costal margin), blast cell count, platelet count, and eosinophil and basophils. All variables are measured at the time of diagnosis. According to Hasford the patients were stratified into various groups as follows:

Low risk group <780

Intermediate risk group 780 -1480

High risk group >1480

The aim of study to compare Sokal and Hasford scoring system in newly diagnosed untreated cases of CML and to suggest which one is more useful in determining the prognosis of CML.

MATERIAL AND METHODS

Descriptive cross sectional study conducted during period from 1st July 2017 to 31st December 2017 at department of AIMC. A total of 55 consecutive patients with suspicion of chronic myeloid leukemia referring from oncology department to hematology department of AIMC belonging to all age groups, both genders and all the three clinical phases were included.

In every patient about 5ml EDTA blood sample was collected. Complete blood counts were performed on a fully automated hematology analyzer (Sysmex KX-21). Peripheral blood smears were freshly prepared and stained using Giemsa stain. The slides were examined under a microscope and differential count was performed. Bone marrow aspiration was performed; multiple smears were made. The smears were examined and at least five hundred cells were counted. The diagnosis of CML was made by complete blood count, examination of peripheral blood smear and bone marrow findings. The disease was classified into chronic, accelerated or blast phases by using WHO criteria. Cytogenetics and molecular studies could not be done due to lack of these facilities at AIMC.

Patients who had received cytotoxic treatment previously were excluded from the study. Sokal scoring was applied for risk stratification on all cases by using following formula:

Exp [0.116 (age- 43.4)] +0.0345 (spleen size-7.51) +0.188[(platelets/700)2-0.563] +0.0887 (blast %-2.10).

The patients were stratified into three prognostic groups (low risk , intermediate risk, and high risk)

Hasford score was also performed on all cases using the formula:

0.6666 *x* age [0 when age <50 years; 1, otherwise]+0.0420 x spleen size[cm below costal margin] + 0.0584 x blasts[%]+0.0413 x Eosinophils [%] +0.2039 x Basophils[0 when basophils < 3%; 1. otherwise] + 1.0956 x Platelet count [0 when platelets < 1,500 x 109/L; 1, Otherwise] x 1,000.

Based on the score obtained, the patients were stratified into various groups as follows:

Low risk group, Intermediate risk group , High risk group.

The results were statistically analyzed using the statistical programme SPSS version 23.

RESULTS

A total of 55 patients were diagnosed as chronic myeloid leukemia, over a period of six months. The mean age at time of diagnosis was 38.1±11.5 SD years (range 17- 66). The age was divided into three groups and majority of patients, 29(52.7%) were between 20-40 years age group (Table No.1)

Out of 55, 21(38.2%) were male and 34 (61.8%) were females with male to female ratio0.6:1 (figure No.1)

Table 1: Age Groups in Chronic Myeloid Leukemia.

AGE GROUPS	Frequency	Percent
<20YEARS	4	7.3
20-40 YEARS	29	52.7
>40 YEARS	22	40.0
Total	55	100.0

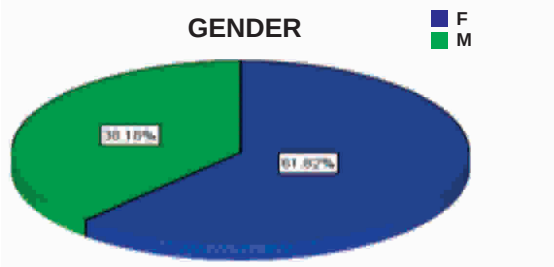

Figure No. 1: *Shows Gender Distrubution*

At time of diagnosis, chronic phase was seen in 49 patients (89.1%), 5(9.1%) had accelerated phase and 1(1.8%) was in blast crisis of chronic myeloid leukemia, according to WHO criteria for phases of disease.(Table No.2)

At the time of presentation, patients were also classified into prognostic groups, using the Sokal formula and Hasford formula. According to Sokal score, majority of the patients were in high risk (47.3%) and intermediate (43.6%) prognostic group. Whereas according to Hasford score 33(60%) of patients were placed in low risk group; 18(32.7%) were in intermediate risk group and 4(7.3%) were grouped under high risk group. (Table No. 3)

Table 2: Showing Phases of CML According to WHO Criteria

CML PHASES	Frequency	Percent
CHRONIC PHASE	49	89.1
ACCELRATED PHASE	5	9.1
BLAST PHASE	1	1.8
Total	55	100.0

SOKAL SCORE HASFORD CML SCORE Cross tabulation

Sokal shows 26 patients in high risk group which are categorized as 11 in low risk group, 11 in intermediate group and only 4 patients are placed in high risk group by Hasford.

Table 3: Prognostic Stratification of CML Cases

Prognostic groups	Sokal score	Hasford score
Low risk	5(9.1%)	33(60%)
Intermediate risk	24(43.6%)	18(32.7%)
High risk	26(47.3%)	4(7.3%)

Table 4: Showing Comparison of Sokal and Hasford Groups

		HASFORD CML SCORE			Total
		Low risk gp	Intermediate risk gp	High risk gp	
Sokal Score	Low risk	5 15.2%	0 0.0%	0 0.0%	5 9.1%
	Intermediate risk	17 51.5%	7 38.9%	0 0.0%	24 43.6%
	High risk	11 33.3%	11 61.1%	4 100.0%	26 47.3%
	Total	33 100.0%	18 100.0%	4 100.0%	55 100.0%

Similarly intermediate Sokal score have 24 patients which are catagorized as 17 in low risk group, 7 in intermediate group according to hasford. According to sokal which fell in low risk group also belongs to low risk group by Hasford. (Table No. 4) P value is <0.05 which is statistically significant. This highlights that Hasford is better prognostic scoring system.

DISCUSSION

Considering the importance of prognostic factors and their impact on various treatment

modalities. Many attempts have been made in the last 20 years to predict survival for patients with CML[4,13]. The Sokal and Hasford (Euro) scores were developed in the chemotherapy and interferon eras and are widely used as prognostic indicators in patients with chronic myeloid leukemia (CML)[10].

In the present study we evaluated freshly diagnosed cases of CML for Sokal and Hasford score and graded them accordingly. According to Sokal score 5/55(9.1%) patients were placed in low risk group, 24/55(43.6%) in intermediate risk group and 26/55(47.3%) in high risk group. According to Hasford score 33/55(60%) were grouped under low risk group, 18/55 (32.7%) in intermediate risk group and only 4/55 (7.3%) in high risk group. Thus, Hasford score has placed 50% more patients in low risk group than Sokal score.

Similar observation were made by Khalil R et al[4] according to which Hasford score 15 (25.5%) of patients were grouped under low risk, 26 (44%) of patients were placed in intermediate risk group; and 18(30.5 %) were in high risk group. Whereas according to Sokal Score, majority of the patients were in intermediate (50.8%) and (44.1%) high risk groups; only 5.1% cases were observed to be in low risk group. In this study Hasford score has also placed more patients in low risk group than Sokal score as in our study. The results of our study also corroborate with the results of the study made by Thomas et al[13] (high risk group according to Hasford system was (7% vs. 7.3% in our study), intermediate group (39% vs. 32.7% in our study) and low risk group (55% vs. 33%in our study), which say that Sokal index is no longer the best method of reliably predicting length of survival of CML patients[20]. Similar observations were made by Italian co-operative study group on CML[12].

In CML survival varies from few months to years from diagnosis and an accurate prediction of duration of survival could help patients and clinicians make decisions about many treatment options. We have analyzed prognostic stratification of patients using both Hasford and Sokal scores. Although Sokal score is still widely used, studies suggest that it is no more the best method of reliability[4].

In a study done by Thomas et al looking at survival of these groups (grouped both by Sokal and Hasford criteria) it was found that 5 years survival was better in low risk groups[13]. They also suggested that Sokal was less informative. They recommended that Hasford is a better scoring system and is highly predictive of survival particularly in patients <60 years age[4].

The variables used in Hasford scoring system are routinely measured in clinical practice and their measurement is highly reliable4.

CONCLUSION

It can be concluded from the study that Hasford score is a better predictor of prognosis of CML patients than Sokal index. So Hasford score may help CML patients and their physicians in making better informed decisions about the adoption of alternative higher risk treatment options and may help in the analysis of outcome in studies of newer, experimental drug regimens.

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DERMATOMYOSITIS-CREST OVERLAP SYNDROME

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Abstract

Dermatomyositis is an autoimmune disorder characterized by proximal muscle weakness along with characteristic skin lesions. The disease is more common in females with female to male ratio 2.5 : 1. Auto-antibodies are formed that get deposited in skeletal muscle perifascicular vasculature leading to skeletal muscle fiber vacuolization and damage. Here a case of 45 years old lady presented to us with symmetrical both upper and lower limb weakness, predominantly involving the proximal muscle groups, along with the skin lesions. In addition to that, there were features of limited scleroderma (CREST-syndrome) like dysphagia and thickening of skin over the fingers. Later on the clinical, biochemical and immunological parameters confirmed the diagnosis of Dermatomyositis-CREST overlap syndrome.

Dermatomyositis is an autoimmune disease. It usually affects the females in their 40s and 50s with male to female ratio 2.5:1.[1] It usually affects the skeletal muscles (very rarely the smooth muscles). Pathologically autoantibodies are formed against the blood vessels in skeletal muscles and skin. These antibodies get deposited in perifascicular vasculature with vacuolization within the skeletal muscles fibers, leading to muscle fiber damage and necrosis[2]. Clinically the diseased is characterized by limb weakness predominantly in proximal muscle groups, dysphagia and skin lesions. skin lesions are in the form periocular redness called helitropic rash, thickening and purple discoloration of knuckles called gottron papules and periungual capillary dilation, skin erosions and redness called mechanic hands[3]. Among investigations, serum creatine phosphokinase is markedly elevated (usually in thousands) along with raised ALT and AST (AST>ALT) coming from muscle breakdown. Other inflammatory markers like ESR may be elevated.[4] Among the immunological markers, anti-jo (anti-histidyl tRNA antibodies) antibodies, Anti-Mi-2 antibodies and anti –SRP (signal recognition particle) antibodies are usually positive.[5,6,7] In 30 % of the cases , disease is linked to underlying malignancy.[8] The malignancies with which it is most commonly linked are ovarian, lung, pancreatic, and stomach carcinoma.[9] The diagnosis is made using Bohan and Peter diagnostic criterion based on clinical, biochemical and histopathological parameters and supportive immunological markers.[8] EMG shows myopathic picture.[10] MRI shows skeletal muscle inflammation along with the edema.[11] Biopsy is helpful and can be performed if the diagnosis is unclear .

Case presentation

A case of 45 years old lady presented to us with complaints of limb weakness affecting proximal muscle groups more predominantly then the distal ones (the patient was unable to go upstairs or combing her hair along with the dysphagia to both solids and liquids). The patient had these symptoms for the last 1 & 1/2 months. There were no other systemic complaints. On general physical examination, there was periungual swelling with redness and skin excoriation (mechanic hands) but also the thickening of skin over the fingers (later not a feature of DM), on face there was erythema over the cheeks and shawl like rash over the neck and upper torso. There were no gottron papules or helitropic rash. On central nervous examination, the patient was well oriented and cooperative. Patient had some difficulty in swallowing on repeated commands, otherwise the cranial examination was unremarkable. Among the motor examination the bulk and tone were normal in all the four limbs, the power was 4/5 in distal muscle groups and 3/5 in proximal muscle groups. Reflexes were intact and planter were bilateral down-going. There were no sensory abnormality and cerebellar sign were absent though gait

was not tested due to limited patient mobility. A clinical diagnosis of dermatomyositis was made. However, there was thickening of skin over the fingers and dysphagia that are the characteristics of localized systemic sclerosis (CREST-syndrome). So an overlap of these condition was considered. Among the investigations serum creatine phosphokinase was 18474 u/l. ESR was raised (95). Among the liver function tests, ALT & AST were raised (ALT=338 and AST=683) while the rest of liver markers were normal along with AST >ALT indicating skeletal muscles as source of these raised enzymes not the liver. Among the immunological markers anti Mi-2 antibodies were considerably raised specifying the diagnosis of Dermatomyositis along with the raised anti CENP A-B (anti-centromere) antibodies strengthening the overlap of dermatomyositis with limited systemic sclerosis. Steroid pulse therapy was started and patient condition improved. A search for underlying malignancy was carried out. CXR was normal. CT-Abdomen showed a simple ovarian cyst. CA-125 level was sent and was within normal range.

DISCUSSION

Dermatomyositis is an autoimmune disorder which affects the adults in their 40s & 50s. The disease is more common in females as compared to males with female to male ratio 2.5:1. In dermatomyositis the history is sub-acute with duration of symptoms for weeks to months. The patient usually presents with painless limb weakness affecting the proximal muscle groups more predominantly than distal ones along with the skin lesions. The patient is unable to stand from sitting position or performing the tasks above the head. The skin lesions are in the form of periungual capillary dilation with the redness and erosion of skin called mechanic hands, thickness and redness of skin over the knuckles called gottron papules, redness in periocular region called helitropic rash and the redness over the front of the chest, neck and proximal portion of upper limbs called shawl sign. But all the cutaneous findings need not to be present as in dermatomyositis sine dermatitis there are little skin findings. The neurological examination is un-remarkable except for the objective findings of weakness in limbs affecting proximal muscle groups more prominently than distal ones. In our case patient was a female with age 45 years at the time of presentation with the painless proximal muscle weakness in both upper and lower limbs and dysphagia. Among the skin findings, the patient had the mechanic hands and redness over the cheeks and shawl like rash over the neck and upper torso but none of the other typical cutaneous findings like gottron papules or helitropic rash. The neurological examination showed weakness in the limbs involving proximal muscle groups more than distal ones. Among the investigations in dermatomyositis, serum level of creatine phosphokinase is raised in thousands indicating the muscle damage. The ALT and AST are also raised (AST> ALT) with the normal rest of the LFTs indicating that source of these enzymes is skeletal muscles and not the liver. ESR may or may not be raised. Among immunological markers, anti-jo (anti-histidyl tRNA antibodies) antibodies, Anti-Mi-2 antibodies and anti –SRP (signal recognition particle) antibodies are usually positive. In our case, ESR was raised (95), serum creatine phosphokinase was high (18474) along with the raised ALT (338) and AST (683) with AST>ALT. Among immunological markers, anti-Mi-2 antibody was positive, specific to dermatomyositis. EMG showed myopathic picture indicating the muscle damage. The diagnosis of dermatomyositis is made by following Bohan and Peter diagnostic criterion .

1…. progressive symmetric both upper and lower limb girdle weakness.

2…EMG with myopathic features indicating the muscle damage.

3…muscle biopsy findings indicating myositis.

4…elevated muscle enzymes (50 folds or greater than the normal values.)

5…Characteristic skin findings.

5 plus 3 out of remaining 4 findings …... definitive DM

5 plus 2 out of remaining 4 findings…… probable DM

5 plus 1 out of remaining 4 findings…… possible DM

There is an increasing evidence that immunological markers may also prove as an important evidence and may be considered in near future in diagnostic criteria but above mentioned criteria is still sufficient to diagnose the condition quite confidently. In our case, skin findings along with the 3 out of remaining 4 findings sufficiently fulfilled the criterion for the diagnosis of dermatomyositis. But there was more than that. The patient had thickening of skin over the fingers along with the dysphagia, the former one not a typical finding of DM. Also the thickening of skin of fingers and dysphagia are the features of CREST-syndrome. So an overlap of CREST– syndrome with DM was considered. Immunological markers like ANA and anti CENP A-B (anti-centromere) antibodies, later the specific one for CREST-syndrome, were positive . So a definitive diagnosis of dermatomyositis CREST-overlap syndrome was made .

As DM is associated with malignancy in 30% of the cases, a work up was carried out to trace any underlying malignancy. CT-abdomen and pelvis showed a simple benign right ovarian cyst. Serum CA-125 level was found within normal range.

RESULT

An overlap syndrome of dermatomyositis and limited scleroderma (CREST-syndrome) was made in our case with enough clinical, biochemical and immunological evidence.

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EFFICACY OF A SINGLE LOCAL PLATELET RICH PLASMA INJECTION IN PATIENTS WITH PAINFUL MEDIAL EPICONDYLITIS UNRESPONSIVE TO CONSERVATIVE TREATMENT

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Abstract

Objective: To determine the efficacy of a single local platelet rich plasma injection in patients with painful Medial epicondylitis unresponsive to conservative treatment

Study Design: Descriptive Case Series. Setting and Duration of Study: The study was conducted at Orthopaedic Department, Jinnah Hospital, Lahore from June 14, 2017 to December 14, 2017.

Methodology: 100 subjects fulfilling the inclusion criteria were be included in the study. Patients with complaint of painful medial epicondylitis having ages between 30-50 years and either gender were included in this study. The painful area was identified with palpation and the target area was marked. A local anesthetic (1% xylocaine without epinephrine) was used to numb the subcutaneous tissue before platelet-rich plasma injection. Patients were cautioned to refrain from any repetitive activities that reproduced the elbow pain for the next 4 weeks. Pain assessment on VAS was done at 6 month period.

Results: In this study, 100 patients with complaint of painful medial epicondylitis were enrolled. Among these patients, 72(72%) were males, while 28(28%) were females. Among 100 patients, 63(63%) had efficacy (in terms of ≥25 % reduction on VAS).

Conclusion: A single platelet-rich plasma injection (PRP) could be pain reliever, as a result could be avoided from surgery.

Key Words: Platelet Rich Plasma, Medial Epicondylitis, Visual Analogue Scale.

Medial Epicondylitis also known as Golfer Elbow is a condition where the inner part of the elbow becomes sore and tender.[1] The cause of Medial epicondylitis is unknown. It is thought that lesions occur in the common origin of the wrist and finger flexors on the medial epicondyle because of a combination of mechanical overloading and abnormal microvascular responses.[2]

Historically, typical conservative treatment strategies focused on reducing inflammation with rest, non-steroidal anti-inflammatory drugs (NSAIDs), bracing and physical therapy.[3]

Newer treatment modalities have been tried, such as extracorporeal shock wave treatment, iontophoresis and injection of botulism toxin. If conservative treatment fails, the last resort is surgery with the primary objective of relieving pain.[4]

One novel treatment strategy is the use of local injection of platelet-rich plasma. These activated platelets then secrete a variety of growth factors and other signaling molecules, including leukocyte derived catabolic cytokines and fibrinogen, which collectively influence the tissue healing processess.[5] Hechtman et al[6] injected platelet-rich plasma in patients with epicondylitis and showed that it was effective (in terms of ≥ 25 % reduction in worst pain at 1-year follow up) in 90% patients.

Peerbooms et al[7] determined the effectiveness (in terms of ≥25 % reduction in VAS at 1-year follow up) of PRP compared with corticosteroid injections in patients with chronic lateral epicondylitis and showed that PRP was effective in 75% of patients at one year follow up.

Since our follow up will be for 6 months so we

assume that efficacy (in terms of >25% reduction on VAS can be achieved in 60% of patients.

As previous studies are showing variable results of platelet rich plasma, so that is why this study was conducted to study the effectiveness of PRP in epicondylitis so that better technique could be substitute conventional corticosteroids injection to reduce morbidity in patients with epicondylitis.

OBJECTIVE

To determine the efficacy of a single local platelet rich plasma injection in patients with painful Medial epicondylitis unresponsive to conserative treatment

METHODOLOGY

After approval from department and informed written consent about the study procedure, 100 subjects fulfilling the inclusion criteria were included in the study from the Othopaedic Department, Jinnah Hospital, Lahore. Patients with complaint of painful medial epicondylitis having ages between 30-50 years and either gender were included in this study.

Presence of infection at the site, diagnosed at examination, Steroid injections within 2 months of enrolment, Pregnant patients, Patients with severe vascular or neurological disease (diagnosed patients of Diabetes having fasting blood sugar >126, patients with peripheral vascular disease diagnose on color Doppler, Severe degenerative bone disease (diagnosed patients of osteoarthritis, Rheumatoid arthritis) and patients history of carpal tunnel syndrome were excluded from study.

The study design was Descriptive Case Series. Non-Probability Consecutive Sampling technique was used to collect to patients. Sample size of 100 cases was calculated with 95% confidence level, 10% margin of error and taking expected percentage of efficacy (in terms of ≥25 % reduction on VAS) i.e. 60% after 6 months follow up of a single local PRP injection in patients with painful medial epicondylitis.

Patients taking NSAIDs were asked to stop taking the medication for 2 weeks prior to platelet-rich plasma injection. Patients remained in a supine position. Medial epicondylar tendinopathy patients had their affected arm rest at their side with their elbow flexed to 45° and their hand pronated.

The painful area was identified with palpation and the target area was marked. The area was prepped with alcohol. A local anesthetic (1% xylocaine without epinephrine) was used to numb the subcutaneous tissue before platelet-rich plasma injection. The 3ml of platelet-rich plasma was injected with an 18-gauge needle into the common flexor tendon as well as the insertions into bone, using a peppering technique. This technique involved a single skin portal followed by 9 penetrations of the tendon.

This delivered platelets plasma on contact with tendon tissue. Patients were instructed to limit extensive use of their am for the next 24 hours Patients were permitted to continue with activities of daily living immediately. However, they were cautioned to refrain from any repetitive activities that reproduced the elbow pain for the next 4 weeks. Pain assessment on VAS was done at 6 month period. All data were entered into SPSS v23.0. Mean and standard deviation was calculated for quantitative data such as age, mean pre and post injection VAS score while frequency and percentage was calculated for gender and efficacy. Data were stratified for age and gender to deal with effect modifiers. Post-stratification, Chi-square test was applied. A p-value ≤0.05 was considered significant.

RESULTS

After approval from department and informed written consent about the study procedure, 100 subjects fulfilling the inclusion criteria will be included in the study from the Othopaedic Department, Jinnah Hospital, Lahore.

In this study, 100 patients with complaint of painful medial epicondylitis were enrolled. Among

these patients, 72(72%) were males, while 28(28%) were females.

Age range in this study was from 30 to 50 years with mean age of 39.6±6.1 years. Majority of the patients 58(58%) were <40 years of age group. While 42(42%) were >40 years of age group.

Among 100 patients, 63(63%) had efficacy (in terms of ≥25 % reduction on VAS).

There is a significant difference between efficacy and gender (p>0.002). There is no significant difference between efficacy and age (p>0.518).

Table 1: Frequency Distribution of Gender

Gender	Frequency	Percent
Male	72	72.0
Female	28	28.0
Total	100	100.0

Table 2: Frequency Distribution of Age Groups

Age groups	Frequency	Percent
<40 years	58	58.0
≥40 years	42	42.0
Total	100	100.0

Table 3: Frequency Distribution of Efficacy

Efficacy	Frequency	Percent
Yes	63	63.0
No	37	37.0
Total	100	100.0

Table 4: Stratification of Efficacy with Respect to Gender

Efficacy	Gender		Total	p-value
	Male	Female		
Yes	52	11	63	0.002
	72.2%	39.3%	63.0%	
No	20	17	37	
	27.8%	60.7%	37.0%	
Total	72	28	100	
	100.0%	100.0%	100.0%	

Table 5: Stratification of Efficacy with Respect to Age

Efficacy	Age groups		Total	p-value
	<40 years	≥40 years		
Yes	35	28	63	0.518
	60.3%	66.7%	63.0%	
No	23	14	37	
	39.7%	33.3%	37.0%	
Total	58	42	100	
	100.0%	100.0%	100.0%	

DISCUSSION

Visual analogue scales (VAS) for assessing pain are the most commonly used method for measuring painful conditions because they are quickly and easily applied.[8] Several mechanisms of action for PRP have been described in the literature.

In principle, these explain the clinical improvement, the local hemostatic action of the substance during the postoperative period, along with its influence on osteogenesis and soft-tissue healing, especially muscle healing.[9]

There is also the hypothesis that autologous blood injections have a direct influence on the cascade of inflammation and cause an early start to recovery of the degenerated tissue.[10]

Local infiltration of corticosteroids, which is considered by many surgeons to be the best option for treating lateral epicondylitis of the elbow, has been questioned. Some authors have suggested that the improvement observed in these patients only has partial and temporary efficacy.[11]

The results of this study suggest that a single platelet-rich plasma injection can relieve pain and improve function in patients with long-term medial epicondylitis. Among 100 patients, 63% elbows met the criterion of successful treatment: a 25% reduction in worst pain score for at least 1 follow-up visit with no further intervention at 6 months.

It is estimated that 5% to 10% of patients with epicondylitis will seek operative treatment.[12] Surgical repair of epicondylitis is generally associated with high success rates.[12] However, the surgical morbidity and costs of surgery argue against the surgical option if other options are available.

The time course of change in VAS pain scores in the platelet-rich plasma-treated patients in our study was similar to what was observed by Peerbooms et al.[7]

In a study, a successful treatment was defined as ≥ 25% reduction in the VAS for pain without re-

intervention after 1 year. Results showed that 73% of patients receiving PRP had relief of pain at 1 year.[7]

Hechtman et al[6] injected platelet-rich plasma in patients with epicondylitis and showed that it was effective (in terms of ≥25 % reduction in worst pain at 1-year follow up) in 90% patients.

Other studies have evaluated the effect of platelet-rich plasma in various orthopedic conditions.[9,11] Unfortunately, results have varied, and few randomized controlled studies have been performed.

CONCLUSION

A single platelet-rich plasma injection (PRP) could be pain reliever, as a result could be avoided from surgery.

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AMELIORATION OF HYPERGLYCEMIA BY AJWA DATE SEED AND FLESH IN ALLOXAN INDUCED DIABETIC RATS

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Abstract

Background: Defect in insulin secretion or insulin action & oxidative stress produced by prolonged hyperglycemia leads to diabetes mellitus. Adverse effects of drugs for treatment of this disorder lead to use of medicinal plants. Ajwa is conventionally used for treatment of diseases caused by oxidative stress. It is packed with flavonoids and rich antioxidants.

Objective: The objective of this study is to investigate the antihyperglycemic potential of Ajwa date seed and flesh separately on diabetic rats where diabetes is induced by a chemical alloxan monohydrate.

Methodology: Rats were divided into 4 groups. Group one was treated as normal control. Group 2, 3 and 4 were injected alloxan monohydrate to induce diabetes mellitus. Date seed powder and flesh was given to groups 3 & 4 separately for a period of 4 weeks after establishment of diabetes. Fasting blood sugar levels & body weight were recorded weekly till 4 weeks. Glucometer was used to measure the fasting blood sugar levels.

Results: Significant change in mean fasting blood glucose levels is seen between groups 3& 4 from second week. Treatment with seed powder for four weeks resulted in significant low FBG levels & improved the body weight ($p<0.01$) when compared to diabetic group. Treatment with ajwa flesh did not show ameliorative effect on FBG and it also did not improve body weight.

Conclusion: Ajwa date seed has antihyperglycemic action and seeds are more helpful than flesh in lowering blood sugar levels in diabetes mellitus.

Key words: Antihyperglycemic; Diabetes Mellitus; Oxidative stress; Date seed.

Diabetes mellitus is one of the major chronic metabolic diseases and is presented with prolonged hyperglycemia which occurs either due to insulin deficiency or resistance. Different complications can occur with this persistent hyperglycemia including neuropathy, nephropathy and retinopathy[1].

The rate of developing diabetes in younger people is higher in low income countries[2]. In Pakistan, there will be 13.8 million diabetic persons in 2030[3]. Many of the emergent studies revealed that oxidative stress is the primary factor in the progression of diabetes. The continual hyperglycemia generates injurious free radicals which result in protein and lipid peroxidative damage to cellular membranes.

Oxidative stress is noticeable in investigational model of alloxan induced diabetes. Alloxan induces diabetes through diverse means together with oxidative damage in pancreatic tissue of rats and at last hyperglycemia occurs

Phoenix dactylifera (date) seeds and flesh has been reported to contain vast array of antioxidants. Both seed and flesh contain phenolics and flavonoids which fight against oxidative injuries in the body through free radical scavenging properties[4]. Rutin, quercitin, gallic acid and many other easily

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absorbable polyphenols are said to be present in seed of phoenix dactylifera.[5]

Since many years dates have been used in traditional medicine for treatment of diabetes. P. dactylifera seeds & flesh have shown their protective effects in liver diseases6, renal damage,[7] cancer and their potential in dealing with oxidative stress.[8]

Hayani[9] & Sukkari[10] date varieties have demonstrated their antihyperglycemic effects in few recent studies. But antihyperglycemic effect of Ajwa date has not ruled out yet. This study aimed at demonstrating the potential effect of Ajwa date in ameliorating hyperglycemia induced by alloxan monohydrate.

METHODS

It was an experimental study conducted in Post Graduate Medical Institute Lahore after getting approval from Ethical Review Committee, Post Graduate Medical Institute, Lahore.

Ajwa date was purchased from Madina-tul-Munnawara and identified by the Botany Department, Government College University Lahore. After grinding the seeds and mashing the flesh, both were mixed to rat chow. Pallets were prepared and stored.

24 healthy male rats, weighing 120-150 g were weighed and placed into four groups. All animals were kept in experimental research laboratory at controlled room temperature (22-24°C) and humidity (45-65%). The animals were kept under 12 h light and dark cycle and were given standard rat chow and water ad libitum. Rats from group 2 (diabetic control), 3 (seed diet group) and 4 (flesh diet group) were given intraperitoneal injection of alloxan monohydrate and Group 1 (control group) was injected with normal saline.

Only the animals having fasting blood glucose level of ≥300 mg/dl on 3rd day after alloxan injection were included in the study. Mashed flesh (7g) and seed powder (1.5 g) were added to 100 gram rat chow separately for animals of groups 3 and 4 respectively. This diet was started after establishment of diabetes and was continued till 4 weeks.

A portable Accucheck performa Glucometer (Roche) was used to measure the blood glucose level of animals. The blood glucose level of each rat was measured in mg/dl after 12 hour fasting by tapping dorsal tail vein.[11] Diabetes was established at 3rd day of injection. FBG and body weight was measured weekly till 4 weeks.

One way Anova and Post hoc tuckey's test were used to determine difference amongst groups using SPSS.[16] Presentation of data was done by mean ± standard deviation. P value of ≤ 0.05 was considered as statistically significant.

RESULTS

The diabetic group showed sharp increase in fasting blood glucose level compared with the control group (p 0.001) as demonstrated in table 1. Treatment with ajwa seed diet lowered the blood glucose level compared with the diabetic group (p≤ 0.001) while ajwa flesh did not decrease hyperglycemia. However, the ajwa seed diet did not restore FBG levels to the normal levels (p 0.01 compared with control group).

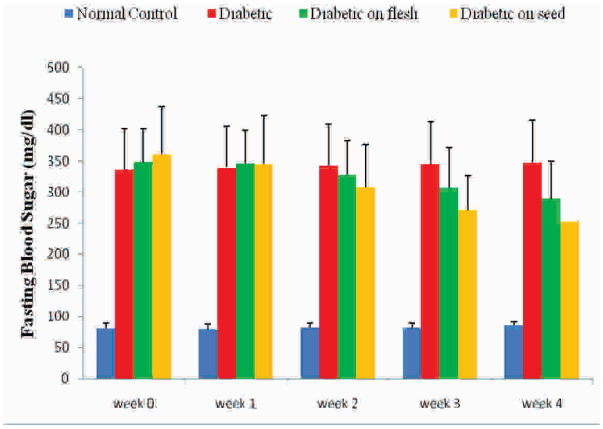

Figure 1: *Showing Effect of Ajwa Date Treatment on Fasting Blood Sugar Level (mean±SD) of Experimental Groups*

**p-value≤0.05, **p-value ≤0.01, ***p-value ≤0.001 Vs diabetic rats*

Table 1: *Comparison of the Fasting Blood Glucose Levels in Different Experimental Groups of Rat*

Weeks	Healthy Control	Diabetic Control Gp	Diabetic on flesh	Diabetic on seed
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Week 0	81±7.9	335.8±66.3	348.5±53.5	360.1±76.8
Week 1	78.9±9.5	339.1±66.4	345.5±53.5	345.3±77.5
Week 2	81.8±7.6	342.1±67.2	327.5±54.4	307.6±61.2
Week 3	81.3±7.6	345.1±67.3	307±64.1	270.8±55.2
Week 4	85.8±6.3	347.6±67.2	289.9±64.1	252.6±60.6

The alloxan induced diabetes caused significant growth retardation compared with the control rats ($p \leq 0.001$). Oral administration of ajwa seed diet powder improved the growth significantly compared with the diabetic group (p value ≤ 0.01). Body weight of rats taking flesh diet increased very less and remained insignificant from diabetic control. (Table 2, Fig 2).

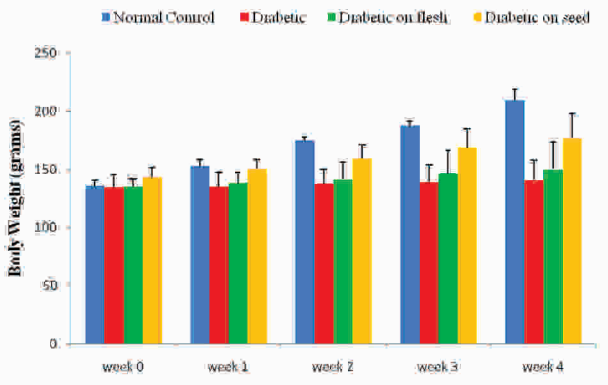

Figure 2: *Showing Effect of Ajwa Date Treatment on Body Weight (Mean±SD) of Experimental Groups *p-value≤0.05, **p-value ≤0.01 Vs Diabetic GP*

Discussion

Although P. dactylifera seeds have been used in folk medicine to manage diabetes for many years, very few studies have investigated their antidiabetic effect. This study was conducted to investigate the effect of oral administration of date variety "Ajwa" date seed powder and flesh on severe hyperglycemia in alloxan induced diabetic rats.

Table 2: *Comparison of Body Weights in Different Experimental Groups of Rat*

Weeks	Healthy control gp	Diabetic control gp	Diabetic on flesh	Diabetic on seed
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Week 0	136.2±4.8	134.8±10.9	135.4±6.6	143±8.8
Week 1	152.8±5.7	135.5±12	138.4±8.8	150.5±8.1
Week 2	174.9±2.8	137.6±12.7	141.4±14.7	159.6±11.8
Week 3	188.1±3.6	139.2±14.8	146.7±19.8	169.1±16.1
Week 4	209.5±9.4	140.6±17.3	149.9±23.8	176.4±22

Results of fasting blood sugar level described that alloxan monohydrate significantly increased FBG levels in all groups (P value ≤ 0.001) except normal control. Fasting blood glucose levels in diabetic control group remained significantly high throughout the study as compared to all other groups. Comparing group taking seed diet to group on flesh diet, no significant change could be observed between them in the mean blood glucose levels at the beginning of experiment till week 1. However the change became significant between the two groups beginning from week 2 onwards. Comparison between mean fasting blood glucose levels of rats of group taking seed powder at every week showed significant decrease until week 4.

Comparison of fasting blood glucose levels in Ajwa seed powder group showed highly significant decrease (p value ≤ 0.01) but it was significantly high from normal control group (P value <0.001) and at the same time, group treated with Ajwa flesh did not improve hyperglycemia (P value ≤ 0.168). The difference between both groups was significant from each other at this time.

These results are in accordance with a previous study 10 which demonstrated that aqueous seed extract of "Sukkary" date variety significantly decreased blood sugar levels in diabetic rats in combination of insulin as compared to insulin alone when given for a period of 4 weeks and this effect may be attributed to induction of insulin secretion. In his study the hypoglycemic effect of date seed extract started showing after two weeks which is in exact correspondence with our study. Our results are also similar to a study in which Phoenix dactylifera "Hayani" variety seed powder suspension ameliorated the fasting bloood sugar levels in diabetic rats (P value ≤ 0.01).[9]

In the present study significant weight loss and

attenuated growth were observed in alloxan induced diabetic group after 4 weeks with respect to control group. Results of body weight described that after 4 weeks, significant decrease in body weight of diabetic group (p value ≤ 0.001) was observed when compared to group NC. These results are in accordance with previous reports which demonstrated that muscle wasting and loss of proteins are charecters of uncontrolled diabetes and also in line with Manna et al 1 who reported that hyperglycemia is the main reason for weight loss .

Administration of Ajwa seed powder restored body weight (P value ≤0.01) when compared to diabetic gp. Our results are similar to a study in which Phoenix dactylifera (Hayani variety) seed powder suspension restored the body weight of rats in streptozotocin induced nephrotoxicity in a 4weeks duration with p value of ≤0.05 when compared to diabetic group 9. There is another study in which plant extract of Merremia emarginata along with glibenclamide (sulphonylurea- drug used to treat hyperglycemia in type 2 diabetic patients) restored body weight (p value ≤0.05)[12]. Daily oral administration of extract of tuber Icacina trichanta and glibenclamide[13] showed valuable effects on body weight (p value ≤0.01) as compared to alloxan treated rats. In all of the above mentioned studies, body weight was less than normoglycemic, non treatment group and the current study also supports this result.

Concerning the potential mechanism of date seed powder, it might be recommended that seed powder stimulate undifferentiated cells in islets of pancreas and formed new β cells. The time period which this process takes that is diffenciation and insulin secretion might match the gap period between treatment with Ajwa seed powder and acquiring a response.

Second potential mechanism for decreasing hyperglycemia is reversal of oxidative damage through polyphenols, minerals and favonoids. Minerals like selenium and zinc along with Vit C & E are present in flesh[14] and seeds [15], have antioxidant potential.

Rutin is major flavonoid present in Ajwa seed 5 and its hypoglycemic effects have already been documented. In another study, Quercetin has also shown improvement in hyperglycemia when given alone and along with insulin in diabetic rats [16].

The current study would propose additional studies to explore the effect of dosage and time variation of Ajwa date seed powder and flesh on fasting blood glucose levels of diabetic rats and to see histopathological changes in β cells of islets of langerhans for knowing the exact hypoglycemic mechanism. It also proposes to investigate the effects of Ajwa date seed powder and flesh on complications of diabetes. Also research of possible adverse effects of seed and flesh by studying hepatic and renal biochemical markers and histological alteration would be suggested in diabetic rats

Such studies would be preliminary step for testing its efficacy in humans. Finally the results would also encourage the use of complementary and alternative medical therapy in Pakistan for treatment of diabetes mellitus.

RESULTS

Results of this study indicate that Ajwa date seed has antihyperglycemic effect. Ajwa date seeds are more effective than flesh in lowering blood sugar levels Ajwa date seed may be used for prevention of diabetes mellitus.

Conflict of Interest

The author declares no conflict of interest

Acknowledgement

We are thankful to the Research Laboratory and Animal House Pharmacology Department, Post Graduate Medical Institute, Lahore for continuous support.

CONCLUSION

Current study displays that seed of Phoenix dactylifera (Ajwa variety) possesses highly significant antihyperglycemic activity in rat model of alloxan induced diabetes, validating its traditional use in oxidative stress induced diseases. The data

displayed that Ajwa seed powder significantly improved body weight of diabetic rats. Further studies are required for the identification and isolation of active compounds responsible for antihyperglycemic action.

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FREQUENCY AND PREDICTORS OF LEG LENGTH DISCREPANCY (LLD) IN PATIENTS MANAGED FOR TIBIAL NON-UNION

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Abstract

Objective: To determine the frequency of leg length discrepancy and their predictors in patients managed for tibial non-union in a tertiary care hospital, Lahore, Pakistan.

Methodology: This was a retrospective cohort analysis, in which leg length discrepancy (LLD), gender, Young adulthood age groups, coexisting systemic disease, side of the fracture, anatomic location of tibial lesion, coexisting skin trauma, mode of reduction of fracture, and bone grafting were the qualitative variables, while age of the patients was the only quantitative variable. SPSS version 25 was used, where frequencies and percentages were computed for qualitative variables and mean and standard deviation for quantitative variable. While applying chi-square test, a p-value of < 0.05 was considered significant. Odds ratios with 95% confidence interval for predictors of LLD were also calculated.

Results: Out of total of 144 patients, 69 (47.9%) suffered shortening of their affected leg (LLD). Amongst patients with LLD, 66 (95.7%) were male and 3 (4.3%) were female, with their mean age 30.22 + 16.11 years. The mean age of the patient who did not suffered LLD was 39.52 + 18.38 years. 75 (52.1%) patients had no LLD, 42 (29.2%) patients had LLD upto 1cm, 24 (16.7%) patients had LLD upto 2cm, and 3 (2.1%) patients had LLD more than 2cm. LLD has a statistically significant association with gender, side involved in fracture, and anatomic location of tibial lesion with their p-values of 0.005, 0.038, 0.032 respectively. However, it has no statistically significant association with coexisting systemic disease, oexisting skin trauma, mode of reduction of fracture, and bone grafting. The p-values of the correlations were 0.307, 0.412, 0.468, 0.831 respectively.

Conclusion: LLD was a common complication in patients managed for non-union tibia. Younger age was relatively more affected. LLD occurred significantly in male gender, left leg fracture, and proximal location of tibial lesion. However, coexisting systemic diseases, coexisting skin lesion, mode of reduction of fracture, and bone grafting had no statistically significant association with occurrence of LLD.

Keywords: Tibial fracture, Non-union, leg length discrepancy, predictors, SPSS

Tibial fractures are the most common long bone fractures, with an incidence of more than 75,000 per year in the USA.[1] Fracture nonunion is a common complication of tibial fracture.[2] It is defined as a fracture that has not united without additional intervention within 6-9 months.[3] Its incidence ranges between 8-13%[3,4,5] and its treatment failure rate have been reported upto 20%.[6] Leg Length Discrepancy (LLD)[7] is a common complication seen after healing of tibial nonunion. Clinical measurements of leg length can be obtained with a tape measure and comparison of the two sides provides LLD.[8] Antero-superior iliac spine (ASIS) to the tip of medial malleolus (MM) is measured to obtain actual LLD. The gold standard for measurement is radiographic LLD assessment.[9] Orthoroentgenograms, teleoro-entgenograms, and computed tomographic scout films are common types of radiographic assess-ment.[10] In general, LLD greater than 2 cm can deteriorate trunk balance and load asymmetrical stress to lower limb joints and pelvic girdle, increasing the likelihood of early degenerative

changes.[11] International as well as national data on predictors of LLD is scarce. Our study will provide the frequency of LLD among patients managed for the non-union of the tibia fracture in our population. In addition, many predictors of LLD will also be evaluated.

METHODOLOGY

This retrospective cohort[12] study was conducted in the Department of Orthopedics, Mayo hospital, Lahore on the data of the patients from July 2002 till June 2012. All the patients suffering tibial non-union of all age groups were included in this study. Non-union was defined by non-healing at 9 months of management of the fracture.[3] The shortening of the affected leg after healing i.e. LLD was noted in centimeters. The age of the patients was categorized into childhood if < 13 years, adolescence if 13-18 years, young adults if 19-44 years, middle aged adults if 45-65 years, and older adults if >65 years.[13,14] The age was further categorized into 2 groups; young adulthood and age group other than young adulthood. Gender of the patients, coexisting systemic disease, side of fracture, anatomic location of tibial lesion, coexisting skin trauma, mode of reduction of fracture, and bone grafting were also noted.

Statistical analysis was completed using the Statistical Package for Social Science (SPSS), version 25. Age of the patients was the only quantitative variable, while LLD, gender, Young adulthood age groups, coexisting systemic disease, side of the fracture, anatomic location of tibial lesion, coexisting skin trauma, mode of reduction of fracture, and bone grafting were the qualitative variables. Frequencies and percentages were computed for qualitative variables, while mean and standard deviation was calculated for quantitative variable. The chi-square test[15] was applied on the data and p-values were considered as statistically significant if < 0.05. Odds ratios16 with 95% confidence interval for predictors of LLD were also calculated.

RESULTS

Out of total of 144 patients managed for tibial non-union, 69 (47.9%) suffered shortening of their affected leg (LLD). Amongst patients with LLD, 66 (95.7%) were male and 3 (4.3%) were female, with their mean age 30.22 + 16.11 years (Picture 1). 75 (52.1%) patients had no LLD, 42 (29.2%) patients had LLD upto 1cm, 24 (16.7%) patients had LLD upto 2cm, and 3 (2.1%) patients had LLD more than 2cm (Picture 2).

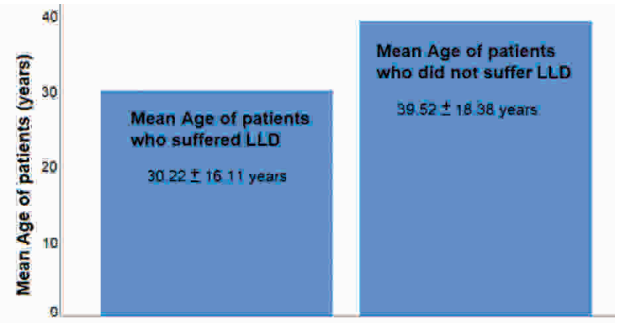

Fig.1: *Comparison of mean ages of patients managed for tibial non-union with or without leg length discrepancy (n=144)*

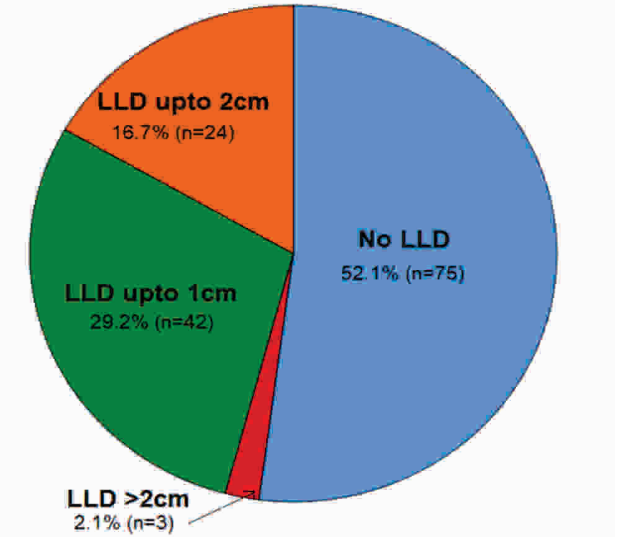

Fig.2: *Leg length discrepancy (LLD) in patients managed for tibial nonunion (n=69/144)*

Amongst non-union tibia patients managed with external fixation, 42.4% (66 out of 126) males & 16.7% (3 out of 18) females suffered LLD. The association between gender and LLD was statistically significant (p = 0.005). While considering different age groups, amongst young adult age group

53.6% (45 out of 84) patients suffered LLD while amongst age groups other than young adults, 40% (24 out of 60) patients suffered LLD. The association between age groups and LLD was statistically insignificant (p = 0.075). 42.1% (24 out of 57) patients with co-existing systemic disease & 51.7% (45 out of 87) patients without co-existing systemic disease suffered LLD. The association between co-existing systemic disease and LLD was statistically insignificant (p = 0.307). While considering that whether tibia fracture was of right or left limb, 60% (27 out of 45) patients with left tibia fracture and 42.4% (42 out of 99) patients with right tibia fracture suffered LLD. The association between side involved in fracture and LLD was statistically significant (p = 0.038). LLD was observed 3.194 times more in proximal tibial lesion as compared to middle or distal tibial lesion. 71.4% (15 out of 21) patients with proximal tibial fracture & 43.9% (54 out of 123) patients middle or distal tibial fracture suffered LLD. The association between anatomic location of tibial lesion and LLD was statistically significant (p = 0.032). Amongst the patients with coexisting skin trauma, 50% (57 out of 114) patients and amongst the patients without coexisting skin trauma, 40% (12 out of 30) patients suffered LLD. The association between coexisting skin trauma and LLD was statistically insignificant (p = 0.412). While considering mode of reduction of tibia fracture, 50% (51 out of 102) of patients with open reduction & 42.9% (18 out of 42) of patients with closed reduction suffered LLD. The association between mode of reduction and LLD was statistically insignificant (p = 0.468). Similarly, LLD occurred in 44.4% (12 out of 27) non-union tibia fracture patients in which bone grafting was performed. LLD also occurred in 48.7% (57 out of 117) fracture patients in which bone grafting was not performed. The association between bone grafting and LLD was statistically insignificant (p = 0.831). (Table 1)

Table 1: *Statistical Correlation between Predictors and Leg Length Discrepancy in Patients Suffering Tibial Non-Union Managed using External Fixator (n = 144)*

Predictors / Factors	Leg length discrepancy		Total	p-value	Odd ratio with 95% Confidence interval
	Yes	No			
Gender:					
Male	66 (42.4%)	60 (47.6%)	126	0.005	5.5 (1.517-19.939)
Female	3 (16.7%)	15 (83.3%)	18		
Young Adulthood (Age group):					
Yes	45 (53.6%)	39 (46.4%)	84	0.075	
No	24 (40.0%)	36 (60.0%)	60		1.731 (0.346 - 3.387)
Side of lesion:					
Right	42 (42.4%)	57 (57.6%)	99	0.038	0.491 (0.240 – 1.006)
Left	27 (60.0%)	18 (40.0%)	45		
Anatomic location of tibial lesion:					
Proximal	15 (71.4%)	6 (28.6%)	21	0.032	3.194 (1.162 – 8.784)
Middle or distal	54 (43.9%)	69 (56.1%)	123		
Co-existing skin lesion:					
Yes	57 (50.0%)	57 (50%)	114	0.412	1.500 (0.662 – 3.397)
No	12 (40.0%)	18 (60.0%)	30		
Co-existing systemic disease:					
Yes	24 (42.1%)	33 (57.9%)	57	0.307	0.679 (0.346 - 1.331)
No	45 (61.7%)	42 (48.3%)	87		
Mode of reduction:					
Open	51 (50.0%)	51 (50.0%)	102	0.468	1.333 (0.646 – 2.750)
Closed	18 (42.9%)	24 (57.1%)	42		
Bone grafting:					
Yes	12 (44.4%)	15 (55.6%)	27	0.831	0.842 (0.363 – 1.953)
No	57 (48.7%)	60 (51.3%)	117		

DISCUSSION

LLD frequently occurs on healing of tibial non-union. It was seen in 47.9% of our patients. LLD less than 2cm often has no clinical importance and more than 2cm can aggravate osteoarthrosis of Hip, sciatica and knee joint disease.[11] Thanks God, only 2.1% (n=3) of patients had LLD > 2cm. It means majority LLD in our patients was clinically harmless and requires adjustment for cosmetic reason only. Our data also suggested that LLD is relatively more common at younger age (30.22 + 16.11 years versus 39.52 + 18.32 years). In literature, no data was found that would address this correlation; however, studies with larger data are required to validate our findings. While studying LLD in gender, Guichet et al[7] found its male to female ratio of 1.95:1, suggesting its male predominance. Similarly, our study found that LLD significantly occurs in male gender (p=0.005). Multiple studies[17,18,19] suggest that proximal tibial fractures are more prone to LLD because they angulate more than mid-shaft fractures. Our study also found that LLD occurs statistically significantly if anatomic location of tibial lesion is proximal shaft as compared to middle or distal lesion (p=0.032). LLD was observed 3.194 times more in proximal tibial lesion as compared to middle or distal tibial lesion. Hence, our findings are in concordance with already available findings. Our data also found that tibial lesion involving left leg are significantly prone to LLD as compared to right leg (p=0.038), while LLD has no statistically significant correlation with coexisting systemic disease, coexisting skin trauma, mode of reduction of fracture, and history of bone grafting. There are multiple valuable findings in our research work; however, further prospective studies with larger sample size are required to validate all these findings.

CONCLUSION

LLD was a common complication in patients managed for tibial non-union. Younger age was relatively more affected. LLD occurred significantly in male gender, left leg fracture, and proximal location of tibial lesion. However, coexisting systemic diseases, coexisting skin lesion, mode of reduction of fracture, and bone grafting had no statistically significant association with occurrence of LLD.

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FREQUENCY OF APLASTIC ANAEMIA IN PAEDIATRIC AND ADULT AGE GROUPS IN A TERTIARY CARE UNIT

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Abstract

Background: Aplastic anaemia (AA) is a rare hematological disease with considerable morbidity and mortality at a younger age.

Objective: This study was carried out in order to determine the frequency of aplastic anaemia in tertiary care unit of Lahore.

Methods: This retrospective cross-sectional study was conducted at hematology department of Allama Iqbal Medical College/Jinnah hospital. Medical records of Patients referred for the bone marrow biopsy were reviewed from Jan 2016 to May 2017.

Results: Out of 882 bone marrow aspirations/biopsies performed 63(7.1%) were diagnosed to have AA. Out of these 73% of the patients were male. Their ages ranged from 1.5 to 80 years. Mean age of the participants were 34 ± 17 years. The peak incidence (45.8%) was in 11-20 years age group.

Conclusion: According to our study, in 1.5 year of period 882 patients were reffered for bone marrow examination. Out of these only 63 (7.1%) were diagnosed to have AA. The mean age was 34 ± 17 years, 46 (73%) patients were male 17 (27 %) patients were female. 29 (46%) of the patients was below 30 years and 10 (12.6 %) were above 50 years of age. Male to female ratio observed was 2.7 :1

Key words: aplastic anaemia, Hematology, Bone marrow examination, autoimmune disease

Aplastic anaemia (AA) is a rare hematological disease with considerable morbidity and mortality at a younger age.[1] It is characterized by the decreased production of all the cell lines i.e. red blood cells (R.B.C.), leukocytes (W.B.C) and platelets due to the irreversible damage of hematological cell lines residing in the bone marrow.[2,3] The term Aplastic refers to the inability of the stem cells to produce mature blood cells.[4]

A world famous case of AA struck the Fleay Family, in Perth, Western Australia. On April 19, 1946, William Arnold Fleay died after receiving a total of 192 pints of blood on a regular basis, in order to keep him alive. Although, thought a rare disease its incidence ranges from 2-6 per million per year in different regions of the world.[5] The incidence of aplastic anaemia in the West is 2 per million with a recently reported 2.34 per million per year in Barcelona. It is about 2–3 fold higher in Asia.[6] AA most commonly presents between 15 years and 25 years, but there is second smaller peak in incidence after 60 years in West and USA.[7] The Barcelona study reported severe and very severe aplastic anaemia to be the commonest stage of presentation.[8] Aplastic anaemis is not a genetic disorder. It is thought to occur due to certain environmental factors such as exposure to certain chemicals (benzene), drugs (chloramphenicol, carbamazepine, felbamate, phenytoin, quinine, and phenylbutazone), radiation, infection (parvovirus), auto immune diseases; in about fifty percent of cases, yet a definitive cause is unknown.[4,12] Aplastic anemia is present in up to 2% of patients with acute viral hepatitis.[9] Age of presentation of aplastic anaemia vary from region to region. Patients usually present with progressive pallor, fever, hemorrhagic manifestations like bruising and petechiae[1]. The diagnosis of AA is confirmed on bone marrow biopsy/aspiration.[9] Treating immune-mediated aplastic anemia involves suppression of the immune system, an effect achieved by daily

medicine intake, or, in more severe cases, a bone marrow transplant, a potential cure.[10]

OBJECTIVE

To determine the frequency of aplastic anaemia in tertiary care center of Lahore.

MATERIALS AND METHOD:

This retrospective cross-sectional study was conducted at hematology department of Allama Iqbal Medial College/ Jinnah hospital Lahore. Medical records of patients referred with work up of pancytopenia between January 2016 and May 2017 were reviewed. Inclusion criteria were: at least two depressed blood cell lineages (hemoglobin less than or equal to 10 g/100 mL and reticulocytes less than or equal to 50 × 10(9)/L, granulocytes less than or equal to 1.5 × 10(9)/L, platelets less than or equal to 100 × 10(9)/L) and a bone marrow biopsy compatible with the disease. The diagnosis of AA was established on the basis of cellularity observed on bone marrow-trephine biopsy. Trephine biopsy cellularity of < 30 % is considered as hypocellular.

Data Analysis: Data was entered and analyzed in SPSS version 22. Mean with standard deviation was calculated for quantitative variable like age while frequency and percentage was calculated for categorical variable like gender.

RESULTS:

In this 1.5 year of period 882 patients were referred for bone marrow examination. Out of these only 63(7.1%) were diagnosed to have aplastic anaemia. Their ages ranged from 1.5 to 80 years. Mean age of the participants were 34.70±17.73. Above 70% of the patients were male (Table 1).The peak incidence was in 15-20 years age group. A second peak occurred in 31-40 years of age group representing a typical bimodal distribution seen in European studies.

Table 1: *Distribution of Aplastic Anaemia According to Gender*

GENDER	Frequency	Percentage
MALE	46	73.0%
FEMALE	17	27.0%
TOTAL	63	100%

Table 2: *Distribution of Aplastic Anaemia According to Age*

AGE IN YEARS	NO. OF PATIENTS
1-10	2
11-20	14
21-30	13
31-40	15
41-50	2
51-60	7
Above 60	1

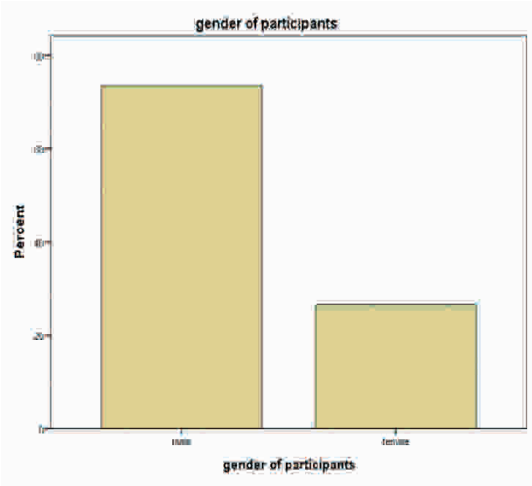

Fig 1: *Bar chart Showing the Gender of Participants*

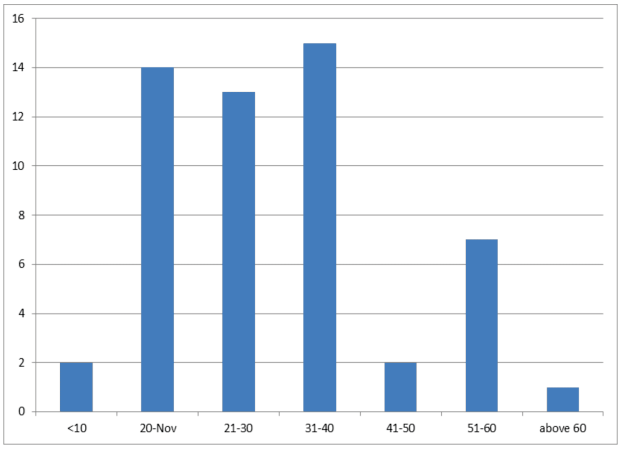

Fig 2: *Bar Chart Showing the Peak Age Group of Diseased Patient*

DISCUSSION

Our study was a first ever attempt to determine the frequency of aplastic anaemia in Allama Iqbal Medical College/ Jinnah hospital Lahore. According to our study 63 (7.1%) of patients had AA. The mean age was 34±17 years. Out of these 46 (73%) patients were male. 29 (46%) of the patients was below 30 years and 10 (12.6%) were above 50 years of age. Male to female ratio was observed 2.7:1. These findings are in consistent with a study done at Agha Khan Hospital Karachi by Adil et al and also a small study from Northern Pakistan. Study done in northern Pakistan by Anwar et alsuggested a higher frequency of AA in young adults. Similarly, the study done at Agha Khan Hospital Karachi by Adil et al showed the peak incidence (45.8%) was in 11-20 years age group. Male to female ratio observed was 2.8:1.[11]. However, this study failed to show typical bimodal peak. In contrast to Agha khan study our study showed a second peak in 31-40 years of age group representing a typical bimodal distribution seen in Malaysia and many European studies. According to a study done in Malaysiathe highest incidence is in those aged 15 to 24 (7.9 per million) and those aged 25 to 39 (6.2 per million)15. A study done in France showed bimodal distribution of age first peak below 30 years and the second after 60 years[14]. This can be explained on the basis of geographical factors operating in the epidemiological determination of aplastic anemia. Male to female ratio in our study was 2.7:1, in accordance with the study done at Agha khan but at variance with the study done in Nepal where this ratio was 1.23:1[16].

Limitation of Study:

This study was conducted on a small sample size. Alarge multi-center study is recommended.

Conclusion

Aplastic anaemia is more prevalent in our population than in western population and in younger age group. Males are more affected by aplastic anaemia than females. Bimodal peak of aplastic anaemia is appreciated in our population as well.

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16- S P Sah,GA RajP Karki.clinic hematological and management profile of aplastic anaemia- a first series of 18 cases from Nepal.

FREQUENCY OF MULTIDRUG RESISTANT TUBERCULOSIS IN NEWLY DIAGNOSED PULMONARY TUBERCULOSIS PATIENTS BY USING GENE XPERT.

Muhammad Younus, Afshan Qureshi, Saba Akram, Sabah Usman, Yasir Nasir, Abdul Basit

Abstract

Background: Tuberculosis (TB) is one of the most common infectious disease in developing countries which is associated with high risk of morbidity and mortality. Early diagnosis is very important to control its spread. Multidrug resistant TB (MDR-TB)is the new threat for developing countries. GeneXpert system using the Xpert MTB/RIF assay, has recently been established and tested for the quick diagnosis of MDR-TB.

Objective: To determine the frequency of MDR TB by using GeneXpert MTB/RIF assay in newly diagnosed smear positive cases of pulmonary tuberculosis

Methodology: This cross sectional descriptive study was conducted at Department of Pulmonology, Gujranwala Medical College, Gujranwala. A total of 120 cases were included through Non-Probability, PurposiveSampling technique.Sputum sample of all patients were obtained and sent for ZN staining. Patient having AFB smear positive were included in the study and sent for GeneXpert MTB/RIF Assay. The collected data was analysed statistically by using SPSS version 22.

Results: The mean age of patients was 41.39±09.01years. There were 59 (49.16%) males while 61 (50.83%) females. Out of 120 newly diagnosed cases of pulmonary TB, rifampicin was sensitive in 115 (95.83%) cases while resistant in 5 (4.16%) cases. Out of 120newly diagnosed cases of pulmonary TB, MDR TB was positive in 5 (4.16%) cases while negative in 115 (95.83%) cases.

Conclusion: Early diagnosis of TB & MDR are of great importance. Diagnosis of drug resistant TB using a GeneXpert may be helpful to decrease mortality and morbidity in primary MDR TB patients.

Key words: Tuberculosis, multidrug-resistant strains, GeneXpert system, rifampicin

Tuberculosis (TB) is caused by Mycobacterium tuberculosis that most often affect the lungs. Tuberculosis is curable and preventable. In a study conducted in 2016 by World Health Organization, 10.4million people have TB, and 1.7million died due to TB. Over 95% of TB deaths occur in low- and middle-income countries.[1]

Tuberculosis is one of the most important health problem in developing countries and is associated with high morbidity and mortality. Mycobacterium tuberculosis is a serious issue for global TB control, further presence of drug resistant TB is life threatening.[2] Seven countries including Indian, Indonesia, China, Philippines, Pakistan, Nigeria, and South Africa, 64% in total had TB and India is leading country.[1]

Drug resistance, however, has remained a challenge. Drug resistance is well established as an inevitable outcome of antibiotic us and compliance to medications led to poor outcomes. The global efforts against tuberculosis have always been mediated by both biologic and social determinants, and the reasons for the divergence in the rates of tuberculosis and drug resistance between rich and poor countries are biosocial.[3,4]

Multidrug-resistant TB (MDR-TB) remains a public health crisis and a health security threat. WHO estimated that there were 600,000 new cases with resistance to rifampicin, of which 490,000 had MDR-TB. Globally, TB incidence is falling at about 2% per year. This needs to accelerate to a 4–5% annual decline to reach the 2020 milestones of the end TB Strategy.[1]

National guidelines on TB management in 2014, have reported that MDR prediction rate was 1.8% in new cases compared to 6.7% for the initial

cases of TB. The number of young patients with MDR-TB is expected to be 8,000.5In one study, the incidence of MDR was 3.8% (12/313) in new cases.[6]

For the extent of intervention, important information is available from time to time in connection with the resistant TB and active drugs for MDR-TB. In general, Acid Fast Bacilli (AFBs) are used as the first line diagnostic method, because it is time saving, cheaper and require minimum lab standards. Although it has less sensitivity (45-80% positive culture), the process is efficient , with the exception that most AFB transmissions (17%) are due to already diseased lung and immunosuppression.[7]

Culture on Lowenstein Jenson Medium for MTB, is a gold standard method for diagnosis of TB, however, due to slow growing bacilli, it usually needs 4 to 8 weeks for isolation and detection.[2,8]

Center For Dosage Control (CDC) have recently introduced various diagnostic methods and tools including molecular techniques for early and fast detection of MDR-TB strains, some of which apply to undeveloped countries. Once diagnosed, successful treatment of MDR-TB requires a series of effective anti-tuberculosis therapy or medications.[9,10] In recent years, direct detection methods, many of which are based on nucleic acid amplification tests, are considered to be a potentially beneficial and convenient tool for rapid and quick detection of TB. Guidelines for the use of these methods have recently been established, upgraded and updated.[11]

A definitive diagnosis of tuberculosis can only be made by culturing Mycobacterium tuberculosis organisms from a specimen taken from the patient (most often sputum, but may also include pus, CSF, biopsied tissue, etc.). A diagnosis made other than by culture may only be classified as "probable" or "presumed" .[12]

Sputum smears and cultures should be done for acid-fast bacilli if the patient is producing sputum. The preferred method for this is fluorescence microscopy (auramine-rhodamine staining), which is more sensitive than conventional Ziehl-Neelsen staining.[12,13]

For the nucleic acid amplification tests and the first sample in liquid culture (BACTEC 460), a crop concrete (Lowenstein-Jensen [LJ]] and selective 7H11 and AFB fluorescent coatings and (Business General-Investigating Mycobacterium Direct Test Signals TB) each Three samples were obtained for the patient. In 797 patients, 81(10.2%) TB was diagnosed. Nucleic acid amplification tests (NAAT), BACTEC, LJ, 7H11S were the first sensitivity and speckle samples, 90%, 85%, 67%, 53% and 58%, while the sensitivity of three sample groups were 90%, 95% and 74%, 74% , 70% Positive predictive value for all tests were 100% and 79% for AFB coatings. Detection of TB is another diagnostic sensitivity of 75% of NAAT time, liquid culture for 21 days, less than 75% for 4 days. In the two weeks about the diagnosis and testing of each of the clinical samples before NAAT, the overall business of diagnosis of laboratory TB starts decreasing.[2]

GeneXpert MTB/RIF Assay (Cepheid, Sunnyvale, CA) (GX)) has been built and tested by the GeneXpert system real-time automation integration system (called GX). In GX, DNA is extracted and amplified (heminested PCR), cartridge was measured in a semi-quantitative and rifampicin, MTC (Mycobacterium Tuberculosis Complex) report antibody.[14-16]

This study will help to determine the prevalence of TB and frequency of new MDR-TB cases using GeneXpert MTB/RIF. It is known that the GeneXpert MTB/RIF is the gold standard used for detecting MDR in patients who had received pretreatment or were re-processed. Traditionally, MDR-TB LJ is based on culture / DST diagnosis and requires a minimum of 12 weeks for diagnosis. The primary objective of MDR-TB initiation is the timely diagnosis of effective second line therapy, and coverage of these patients to prevent transmission. This study will help us to apply GeneXpert MTB / RIF to newly diagnose smear positive TB cases in contrast to current recommendations.

MATERIAL AND METHODS

This Cross sectional study was conducted at

Department of Pulmonology, Gujranwala Medical College, Gujranwala. Sample size of 120 cases is calculated with 90% confidence level, 3% margin of error and taking expected percentage of MDR i.e. 3.8% among newly diagnosed cases of PTB by using GeneXpert MTB/RIF assay[3] by using following formula:

$$n = \frac{z^2_{1-\alpha/2} P(1-P)}{d^2}$$

Sampling Technique was Non-Probability, Purposive Sampling. Patients of 16 and above years of age, both gender and newly diagnosed with smear positive PTB on ZN staining were included. Patients already diagnosis with PTB and taking ATT more than four weeks (on medical record), Patients having extra-pulmonary TB (on medical record) and Patients on re-treatment were excluded from the study.

After taking written informed consent, patients who fulfilled the inclusion and exclusion criteria were enrolled from indoor and OPD of Department of Pulmonology, Gujranwala Medical College, Gujranwala. Sputum samples of all patients were obtained and were sent for ZN staining. Patient having AFB smear positive on sputum test were included in the study. All samples were sent for GeneXpert MTB/RIF assay. Demographic information (name, age, sex, address and contact) was also noted. All this information was recorded through pre-designed proforma. The collected data was analysed statistically by using SPSS version 22. Quantitative variables like age was calculated as mean and standard deviation. Qualitative variables like gender and Multidrug resistance was calculated as frequency and percentage.

RESULTS:

Descriptive statistics of age of patients

The mean age of patients was 41.39±09.01. Minimum age was 16years while maximum age was 85years.

Table 1: *Descriptive Statistics of Age of Patients*

Age (years)	**n**	120
	Mean	41.39
	SD	09.01
	Minimum	16
	Maximum	85

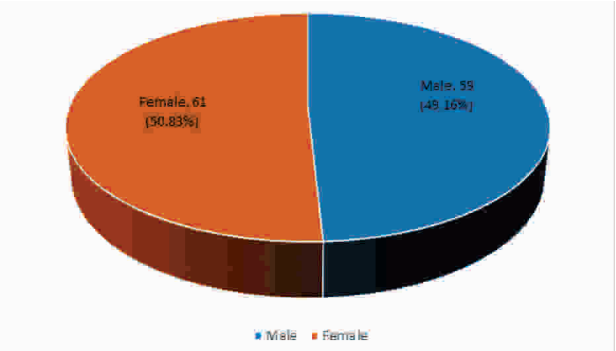

Fig 1: *Distribution of Gender of Patients*

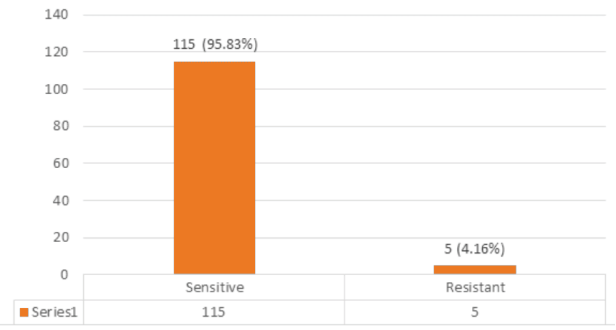

Fig 2: *Distribution of Sensitivity of Rifampicin*

There were 59 (49.16%) males while 61 (50.83%) females.

Out of 120 newly diagnosed cases of pulmonary TB, rifampicin was sensitive in 115 (95.83%) cases while resistant in 5 (4.16%) cases.

Table 2: *Distribution of MDR TB*

		Frequency	Percent
MDR TB	**Yes**	5	4.16
	No	115	95.83
	Total	120	100.0

Out of 120newly diagnosed cases of pulmonary TB, MDR TB was positive in 5 (4.16%) cases while negative in 115 (95.83%) cases.

DISCUSSION

After the initial infection with mycobacterium tuberculosis, in the first 18 months, the risk of active disease is about 5% and in the rest of life the risk of activation is also about 5%.[17] Worldwide two billion peoples have latent tuberculosis and they are at risk of reactivation in the later life when immunity weakens.[18]

In 2004 for the very first time concept of Gene Xpert was introduced. Gene Xpert system based on the Gene Xpert platform was launched in 2008.[19,20] First clinical test was performed in 2009. After that mega studies were conducted in South Africa, India and different other countries to assess the effectiveness and uses on routine basis.[21]

World Health Organization recommended this new test called Xpert MTB/RIF (commonly referred as GeneXpert) for routine use in 2010.[22] In controlled studies Gene Xpert can detect tuberculosis and multidrug resist tuberculosis with very high sensitivity and specificity. It detects Rifampicin resistance at the same time and gives very rapid results within two hours. It is especially useful in patients with HIV and tuberculosis. The overall sensitivity was 86.8% and Specificity was 93.1%.[23]

This is the reason that we conducted this study to find out the number of patients found to be positive for drug resistant TB by using GeneXpert MTB / RIF Assay. The average age of the patients was 41.39±09.01 years in the present study. There were59 (49.16%) males while 61 (50.83%) females. The male-to-female ratio in our study was 1: 1.03. Akhtar et al., also conducted a study to find the prevalence and drug resistance pattern of MDR TB in recurrent TB patients and reported that the mean age of patients was 32±13.5years and there were 664(53%) were males while remaining 47% were females.24Rehman et al., reported the mean age of patients as 42.17±21.1years and there were 54% males and 46% females.[25] Which are comparable with our study.

Of the new 120 TB patients, 115 patients (95.83 %) were sensitive to rifampicin and 5 (4.16%) were resistant to rifampicin in present study. A study conducted by Atashi et al., in 2017 in Iran, the reported prevalence of MDR-TB as 3.1% using GeneXpert in newly diagnosed TB patients.[26] These results correlate with results of our study.

A study also showed that 6 out of 52 (15.7%) cases were detected for MDR-TB by using line probe assay, however, previous history of anti-TB treatment were not determined.[27] In another study, from same settings reported the incidence of MDR TB was 16.58%. Primary MDR-TB was detected in 12.83% and acquired in 24.18% cases. Mono resistance against Isoniazid, Rifampicin, Ethambutol and streptomycin was found in 6.12%, 6.81%, 2.6% and 2.15% respectively.[28] However, the results of both studies are not comparable with present study.

Masenga et al., also reported that mono-resistance with rifampicin was found in 5.9%.[29] This is in favor of our study results. MDR-TB was more common in age 16-50 years belong to this age group. In present study, out of 5 MDR-TB cases, 3 MDR-TB cases belong to age 15-50 years. This is in agreement with study conducted by Akhtar et al. They also reported that MDR-TB was more prevalent in the most productive age group 15-45 years (57%).[24] This phenomena also reflects that the most infected people lie in the best productive age of 15-45 years reflecting the socioeconomic loss at country level.

The results of the present study are comparable with the global report 2017 of WHO that revealed 4.1% rifampicin resistance among new cases. For Pakistan, WHO reported the prevalence of MDR-TB as 4.2% (95% CI: 3.2–5.3%) with notified tested for rifampicin resistance as 3%.[18] Later on, National TB Program in 2017 reported the prevalence of MDR-TB as 4.2% in newly diagnosed cases of TB.[30] So, results of our study are compatible with WHO global report and with results of National TB Program report.

CONCLUSION

The frequency of MDR TB on GeneXpert is

although low in newly diagnosed smear positive cases of PTB. Thus we have got the local evidence. Prompt diagnosis of TB & MDR are of great importance. Now we are able to recommend GeneXpert MTB/RIF for detection of MDR-TB in < 2hours. Now in future, we can use GeneXpert for early detection of MDR-TB in new TB cases and early effective treatment can be initiated.

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COMPARISON OF LINEZOLID WITH CO-AMOXICLAV IN THE TREATMENT OF DIABETIC FOOT DISEASE

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Abstract

Background: Conventionally Diabetic foot disease (DFD) is treated with Co-Amoxiclav (a penicillin group antibiotic) but a lot of patients don't respond well and end up in surgical debridement/amputation leading to disability. Organisms infecting diabetic foot are now resistant to Co-Amoxiclav so newer drugs like Linezolid need to be evaluated. Objective of this study is to prove that Linezolid is more effective than Co-Amoxiclav in the treatment of DFDs.

Material and Method: This randomized controlled study was open label and multicentre trial carried out in 2 hospitals i.e. Noor hospital (Kot Radha Kishan) and Bhatti International Teaching hospital (Kasur) from 04-09-17 to 21-09-18. 164 patients were randomized into 2 groups by using simple random method. Group A patients received Linezolid while group B patients received Co-Amoxiclav. 4 parameters of DFDs were studied i.e. cellulitis, nail bed infection, superficial ulcers and deep soft tissue infections. Successful result was considered if redness, swelling or discharge subsided and wound started to granulate.

Results: Total 88% of patients with cellulitis were successfully treated with Linezolid while only 67% of patients had successful treatment with Co-Amoxiclav. Nail bed infections success rate i.e. 100% in Linezolid while 80% in Co-Amoxiclav group. Superficial ulcers had 83% success rate with Linezolid while it was only 60% in Co-Amoxiclav group. Deep soft tissue infections success rates were 64% and 8% in Linezolid group and Co-Amoxiclav group respectively. Overall 84% of patients treated with Linezolid had successful recovery while only 56% of patients were successfully treated with Co-Amoxiclav (2-sided sig. 0.012).

Conclusion: Linezolid is more effective in superficial as well as deep diabetic wounds then Co-Amoxiclav. In deep seated infections both drugs have relatively lower effectiveness and surgical intervention is mandatory.

Key words: Linezolid, Co-Amoxiclav, Diabetic foot

Diabetes mellitus is one of the most common metabolic disorders affecting our population. The morbidity and mortality related to diabetes is an alarming threat second to cardiovascular problems.[1] Diabetes has become an epidemic in the world now and it is estimated that by year 2030 the prevalence of this disease would reach up to 500 million.[2] Diabetes is associated with a lot of complications, of which diabetic foot is a major one. Diabetic foot is characterized by peripheral neuropathy, vasculopathy and hyperglycemia. About 70% of diabetic foot patients develop diabetic foot infection/disease in their lifetime.[3] Diabetic foot disease (DFD) increases the overall duration of the hospitalization, which results in a massive financial burden.[4] Even after good antibiotic treatment and surgical debridements a lot of patients of DFDs end up with amputations of lower limbs causing disability.[5,6]

DFD is caused by multiple microbes including aerobic gram positive & gram negative bacteria as well as anaerobes.[7] Staphylococcus aureus (SA) is the most common organism isolated from the

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wounds of DFD.[7] Combination of Amoxicillin (a penicillin group antibiotic) and clavulanic acid (a beta lactamase inhibitor) also called Co-Amoxiclav is most commonly used to contain the microbes in DFD. With the progressive development of antibiotic resistance and more prevalence of MRSA (methicillin-resistant Staphylococcus aureus) in DFDs, Co-Amoxiclav is deemed less effective in controlling infection. In a study antibiotic resistance was checked for various organisms in DFDs and co-amoxiclav was found to have 48% resistance against SA.[8]

Infection of DFD if treated early with antibiotics results in lesser complications and lesser chances of amputations and consequently lesser disability. As Co-Amoxiclav is becoming more and more resistant,[8] it's time to switch to newer drugs which have less resistance like Linezolid, Imipenem, Vancomycin and Moxifloxacin.[9] Linezolid is under study now a days and is being prescribed by the clinicians for DFDs but it's clear cut role in DFDs is not yet established. Linezolid is an oxazolidinone group antibiotic and is effective against gram-positive bacteria, including Methicillin and Vancomycin resistant SA.[10,11]

The purpose of this study is to compare the efficacy of Linezolid with that of traditional antibiotic (i.e. Co-Amoxiclav) for the treatment of patients with diabetic foot disease.

METHOD

This was a randomized, open label and multi-centre trial which was carried out in 2 main hospitals of periphery of Punjab i.e. Noor hospital (Kot Radha Kishan) and Bhatti International Teaching hospital (Kasur). Data collection was done from 04-09-17 to 21-09-18. Patients were randomized into 2 groups by using simple random method. Hospital ethical committee approved the research as there was no ethical issue and no conflict of interest. Consenting diabetic patients of adult age group and both sex having foot infections were enrolled from the OPD. Foot Infections which were included for this antibiotic trial were cellulitis, nail bed infection, superficial ulcers and deep soft tissue infections.

Foot infections which required surgical intervention, in the form of debridement or amputation, like abscess, necrotizing fasciitis or osteomyelitis were excluded from the trial. All those patients who were already taking antibiotics for DFD or for any other infection were also excluded from this trial. Patients allergic to any one of the two drugs as well as lactating or pregnant females were also excluded from the trial.

All the enrolled patients were admitted in the ward. Complete history and detailed wound examination done and base line investigations carried out in the ward. Blood sugar levels were checked three times a day and they were controlled using regular insulin given three times a day. X-ray and ultrasonography of foot is done as well as duplex scan of the limb to look for any complications. Cultures were taken before the start of antibiotics. Topical antibiotics and antibiotic impregnated dressings were not allowed, however simple dressing of the wound was done daily in the ward. Both the antibiotics were given either in oral or intravenous form according to discretion of treating clinician. The antibiotics were given for 2 weeks and in the mean time wounds assessed daily. If condition of wound worsened then debridement was done.

Successful result was considered if redness, swelling or discharge subsided and wound started to granulate. The result was considered a failure if the condition of the wound worsened i.e. increased swelling, increased tenderness, persistence of purulent discharge or the development of gangrene.

Sample size of 164 patients was calculated (82 in each group) with 95% confidence interval and 90% power of study. For quantitative variables, mean + SD was calculated. Frequencies and percentages were given for categorical variables. Pearson Chi-Square and Fischer Exact test was applied to observe association between qualitative variables. All the collected data was entered and analyzed using SPSS version 20.

RESULTS

164 patients were evenly distributed (1:1) between the 2 groups i.e. 82 patients in each group. The age and sex of patients were statistically similar in both the groups. Mean age of patients in Linezolid group was 56+10 years while it was 54+11 years in Co-Amoxiclav group. 73.2% of patients from Linezolid Group were male while 26.8% were female patients. On the other hand, 61.0% patients were male and 39.0% were female in Co-Amoxiclav group. (Table 1)

7 patients from Linezolid group and 10 patients from Co-Amoxiclav group didn't complete the treatment and left against medical advice. 4 types of infections were studied, which included Cellulitis, Nail bed infection, superficial ulcers and deep infections. Types of infection in both the groups were also almost similar with more patients with cellulitis and superficial ulcers. Success rate of treatment was more in favour of Linezolid group which was statistically significant.

Table 1: *Demographic Data*

	Linezolid Group (n=82)		Co-Amoxiclav group (n=82)	
Gender	N	%	N	%
Male	60	73.2	50	61.0
Female	22	26.8	32	39.0
Mean Age	56±10		54±11	

Of patients who presented with cellulitis, 88% were successfully treated with Linezolid while only 67% of patients had successful treatment with Co-Amoxiclav. Nail bed infections had good results in both the groups i.e. 100% in Linezolid while 80% in Co-Amoxiclav group. Superficial ulcers also responded well with Linezolid (83% success rate) while it was only 60% in Co-Amoxiclav group. Deep soft tissue infections in DFDs didn't go well and most of them had treatment failure resulting in surgical interventions. Success rate was 64% and 8% in Linezolid group and Co-Amoxiclav group respectively.

Overall 84% of patients of DFDs treated with Linezolid had successful recovery while only 56% of patients were successfully treated with Co-Amoxiclav (2-sided sig. 0.012). (Table 2)

Table 2: *Treatment Results*

	Linezolid Group (n=75)		Co-Amoxiclav group (n=72)		Chi-square (2-sided sig.)
Type of infection	**N**	**Successful**	**N**	**Successful**	
Cellulitis	26	23(88%)	30	20(67%)	0.017
Nail bed infection	8	8(100%)	5	4(80%)	0.52
Superficial ulcers	30	25(83%)	25	15(60%)	0.005
Deep infections	11	7(64%)	12	1(8%)	0.001
Total	75	63(84%)	72	40(56%)	0.012

DISCUSSION

In diabetic patients, due to long standing hyperglycemia, the immune system of the body becomes week. Moreover, elevated sugar levels in the wound exudates make an ideal environment for the proliferation of bacteria which results in diabetic foot Disease (DFD).[12] Once a wound forms in DFDs, it is very hard to heal because of extensive soft tissue damage, neuropathy, peripheral vascular disease and antibiotic resistance, resulting in bad prognosis.[13,14] DFD is more prevalent in elderly diabetic patients because of co-morbidities and low immunity.[15] Almost 85% of the amputations, which are not traumatic, are the result of DFDs.[16] Diabetic foot disease is poly microbial in nature having mostly gram positive, gram negative and anaerobic organisms.[17] Staph. aureus is the most common pathogen involved in DFDs and causes suppurative inflammation.[18] There is now development of increased resistance against these organisms especially MRSA making traditional drugs (Co-Amoxiclav) ineffective.[19] Newer drugs (Linezolid and Moxifloxacin) are not only effective against MRSA but have good bioavailability even in oral preparations making them an easy-to-use initial drug.

In the past a lot of work has been done on diabetic foot disease including various antibiotic trials. Older antibiotic trials on DFDs have differed

in their antibiotic groups, study designs, treatment end results and type of infections which make these trials difficult to interpret and compare.[20-23] Moreover results with different antibiotics were observed to be similar, with no single drug or combination of drugs being superior.[20,22] This randomized controlled trial used simple parameters and compared a traditional drug with a newer one making it easy to interpret and establish guidelines for future treatment of DFDs. This trial used a large sample size (164 patients) and only a few patients left the study (17 patients) making results more reliable. We admitted all the patients and no patient was treated on OPD basis, in this way all the progress was in front of our eyes and documented. Surgical debridement was done in case of treatment failure in any specific group.

Results of our study showed that superficial and simple infections responded very well with both the drugs (>90% & >65%) while deep infections didn't go well with either of the drugs (64% & 8%). The probable reason might be less penetration of antibiotic in deep necrotic soft tissue. Similar results were seen in other studies which showed that deep infections like necrotizing fasciitis, osteomylitis, abscess and gangrene do not respond well with antibiotics and they always need surgical intervention.[24-25] Overall cure rates in our study were markedly better in Linezolid group as compared to Co-Amoxiclav group (84% v 56%) and the results were statistically significant (Chi-square 2-sided sig.=0.012). Older antibiotic trials showed equivocal results with no one antibiotic superior to other in DFDs.[26] The reason of this difference is because of development of resistance, over the years, against conventional drugs (like Co-Amoxiclav).

There were certain limitations in our study. Osteomyelitis and necrotizing fasciitis were not studied as they required debridement. These two problems are common complications of DFDs and results of antibiotics after debridement needed to be evaluated. Newer drugs like Imipenem and Moxifloxacin need to be compared with Linezolid and combination drugs need to be evaluated so that better drug regimen is evolved for treatment of DFDs.

CONCLUSION

Linezolid is more effective in superficial as well as deep diabetic wounds then Co-Amoxiclav. In deep seated infections both drugs have relatively lower effectiveness and surgical intervention is mandatory.

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INTEREST OF SENIOR REGISTRAR IN RESEARCH: A PROSPECTIVE CROSS SECTIONAL STUDY:

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Abstract

Background: Globally there is decline in the number of graduates from medical schoolwho choose carrier academics of perform research, consummation of new knowledge is also hammered by the reduction for research oriented doctors, clinical experience with patients provides an essential step to the evidence based research engagement among doctors; we have conducted the follow-up survey of investigate the progress in of research interest among clinical doctors

Objectives: Toevaluate the status of research interest among senior registrars in public tertiary come hospitals.

Materials & Methods:

Study Design: Cross sectional study

Setting and duration: Department of Surgical 2 June 2018 to Aug 2018

Data Collection and analysis: 260 senior registrars working in different specialties were included in the study. After an informed consent, a questionnaire was administered regarding interest in research, previous publications and reasons not to indulge in it. Data was entered and analysis in SPSSver: 21.0 Frequency and percentages was calculated demographic variables and research activities. Data was cross tabulated for previous publications and demographic variables chi- square test was used to assess statistical significance at $P< 0.05$

Results: Among260 senior registrars 59.2% respondents were of 30 – 35 years 53.1% were males. 59.2% were doing private practice. 66.9% had no publication after fellowship. 68.3% (149) had ongoing research projects. The main reason for doing research was to get higher portfolio 48.1 % . SR with more than 5 publications, 50.0% were of older age 41 – 45 years, (p =.000) 87.5% were doing private practice(p =.001) and 50.0% had fellowship of more than 5 years. (p =.000).Conclusion:The conclusion of study is majority of senior registrars have low interst in research, and no publications or intent to do research. Age, private practice and years of fellow ship have significant association with post fellowship publication.

Key words: Research, senior registrar, medical research.

In recent decades, there has been a reduction in the number of graduates from medical schools who choose to pursue a career in academics and perform research. That has an impact on the profile of graduates, since medical education depends on understanding the formation of scientific evidence.[1] The construction of new knowledge is also hampered by the reduction of research oriented doctors, whose clinical experience with patients provides an essential step towards evidence based medicine. Although interest in research is clearly present among the doctors especially working in tertiary care hospital, this is still an under explored are studied in developing countries. The incorporation of research in the learning process depends on stimulus and guidance until it becomes culturally consolidated as an essential element of the medical training. The proportion of doctors undertaking doctoral studies is decreasing. Early recruitment of internees could counteract this trend.[2,3]

Studies from the developed countries like United states on research activity by medical students report that the number of US medical graduates interested in research has decreased, as has the percentage of US medical doctors among those receiving National Institute of Health (NIH) government grants [4, 5]. The number of US physicians with research as their main professional activity is also decreasing[6]. In Sweden, the proportion of physicians among PhDs, and PhD students at Swedish medical faculties, has declined progressively since the beginning of the last decade. Moreover, the median age for Swedish physicians to finish their doctoral studies is currently 41 years, as compared with 34 years for other doctoral degrees.[1,4]

Physicians trained in the scientific disciplines and the field of clinical medicine is essential for bringing patient-oriented research questions into focus, and bridging the gap between basic and clinical sciences.[7,8] A shortage of physicians in research could in the future have negative consequences for academia, clinical research and health care,[1] undermining the translation of basic research into patient care.[8,9] To counteract this trend, early recruitment of medical students has been suggested, and medical students engaged in research during medical studies conduct more postgraduate research compared with their peers in the US[10,11,12] and the Netherlands.[13] Research conducted by medical students has been shown to be productive in terms of publications, as reported from Norway[14] and Germany.[15]

As in our country as compared to developed countries the medical education spans 5.5 years but for example in Sweden half a year at the end of the medical programme is dedicated to writing a research Master's thesis mandatory for all students as part of the curriculum. An additional 1.5 years of internship is required to obtain a licence to practise medicine. With the PhD education in Sweden currently lasting 4 years, this adds up to a total of 11 years to become a licensed physician holding a PhD. One of six medical schools in Sweden is located in Gothenburg at the Sahlgrenska Academy. For extracurricular research, a part of the students are involved in the 'Research assistant programme' which was initiated in 2009 to stimulate research among medical students. Currently the programme offers ten positions per year.[16] Students are accepted for a 3-year period with scheduled research activities, such as lectures and presentations, and financial compensation for part-time research in parallel with their medical studies. Similar research stimulating projects can be found at other Swedish universities, in the forms of summer research programmes and research preparatory courses.

In light of this and other efforts made to stimulate research engagement among medical students in Gothenburg, we have conducted a follow-up survey to investigate the progression of research interest and extracurricular research activity among medical students.

METHODS

A questionnaire composed of both open and closed questions was administered 260 seniors registrars working in tertiary care hospitals in Lahore during the June 2018 – August 2018. The questionnaire was based on socio-demographic variables, years of experience, pre and post-graduation research publications and interest in research. Research was defined as participating in a medical research project on scholarship, during registrar ship in hospital.. Answers were required for all questions except for the open response questions. Data was entered and analyzed in SPSS ver: 21.0. Frequency and percentages were calculated and cross tabulation was done for research publications and socio-demographic variables. Chi-square test was used to assess statistical significance at $p < .05$.

RESULTS

260 senior registrars were interviewed. 59.2% respondents were of 30 – 35 years and 30.8% were between 36 – 40 years. 53.1% were males, 78.1% were married and 42.7% were from middle class. 59.2% were doing private practice. 53.8% (140)

were from surgery and allied and 46.2% (120) were from medical and allied. (Table 1). 54.6% (142) had done fellow ship between 1 – 5 years. 66.9% had no publication after fellowship. 68.3% (149) had ongoing research projects. (Table 2). The main reason for doing research was to get higher portfolio 48.1 %. 23.1% were doing research to synthesize new knowledge. (Graph 1). 85.0% had intention for future research were in academics. (Graph 2). Cross tabulation was done for post fellowship publication. SR with more than 5 publications 50.0% were of older age 41 – 45 years, (p =.000) 62.5% were females(p =.633),, 87.5% were married (p =.733), 87.5% were doing private practice(p =.001) and 50.0% had fellowship of more than 5 years. (p =.000) (Table 3).

Table 1:

Variables n= 260	Frequency	Percent
Age		
30 - 35 years	154	59.2
36 - 40 years	80	30.8
41 - 45 years	26	10.0
Gender		
Male	138	53.1
Female	122	46.9
Marital status		
Married	203	78.1
Single	57	21.9
Socio economic status		
High	34	13.1
Middle	111	42.7
Low	115	44.2

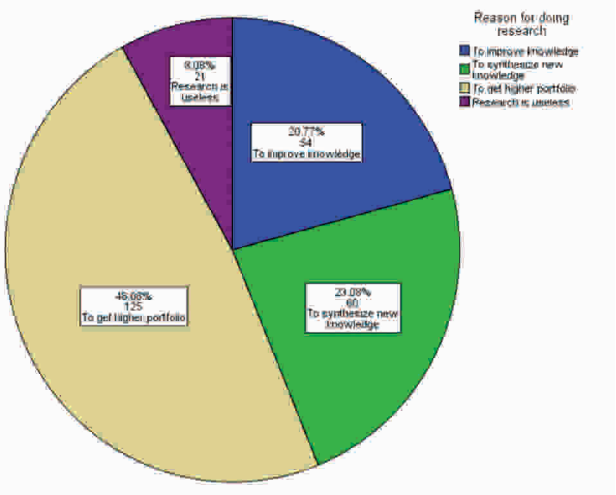
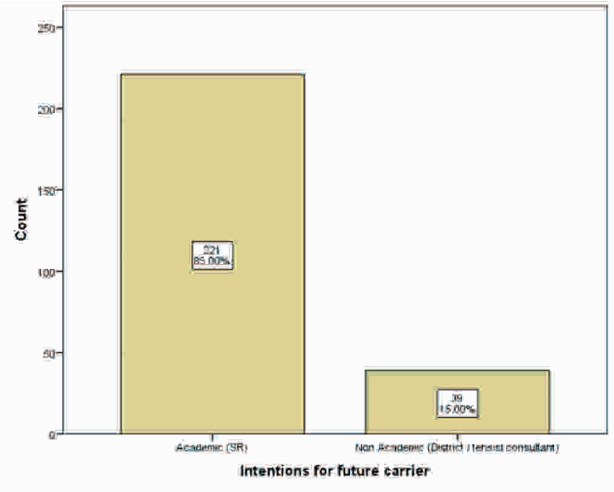


Table 2:

Variables n= 260	Frequency	Percent
Private practice		
Yes	154	59.2
No	106	40.8
Specialty		
Surgery & Allied	140	53.8
Medicine & Allied	120	46.2
Years of Fellowship Mean =3.20 SD= 2.70 Min =.00 Max =14.00		
< 1 year	75	28.8
1 - 5 years	142	54.6
> 5 years	43	16.5
Pre Fellowship Publication Mean.=31 SD=.645 Min =.00, Max=4.00		
None	245	94.2
< 2	11	4.2
> 2	4	1.5
Post Fellowship publication Mean =1.21, SD= 1.60 Min=.00, Max=9.00		
None	174	66.9
1 - 5	78	30.0
5 - 10	8	3.1
Any ongoing research projects		
None	111	42.7
< 2	137	52.7
Ø 2	12	15.6

Table 3: *Post Fellowship Publication and Socio-Demographic Cross Tabulation*

Variables		Post Fellowship publication			P value
		None	1 - 5	5 - 10	
		Percen -tage	Percen-tage	Percen-tage	
Age	30 - 35 years	71.3%	37.2%	12.5%	.000
	36 - 40 years	24.1%	44.9%	37.5%	
	41 - 45 years	4.6%	17.9%	50.0%	
Gender	Male	52.9%	55.1%	37.5%	.633
	Female	47.1%	44.9%	62.5%	
Specialty	Surgery & Allied	55.2%	51.3%	50.0%	.828
	Medicine & Allied	44.8%	48.7%	50.0%	
Marital status	Married	77.0%	79.5%	87.5%	.733
	Single	23.0%	20.5%	12.5%	
Socio economic status	High	13.8%	12.8%	0.0%	.372
	Middle	40.2%	44.9%	75.0%	
	Low	46.0%	42.3%	25.0%	
Private practice	Yes	51.1%	74.4%	87.5%	.001
	No	48.9%	25.6%	12.5%	
Years of Fellowship	< 1 year	40.8%	5.1%	0.0%	.000
	1 - 5 years	52.9%	59.0%	50.0%	
	> 5 years	6.3%	35.9%	50.0%	



DISCUSSION

Research is a fundamental tool in health sciences for the development of new therapies prevention and improvement of health issues among patients. Most of the participants in our study were reluctant towards doing research because of lack of right concepts and skills regarding research, incompetency in doing data analysis as seen in previous studies conducted.[16] Extra research related work needs time involvement, commitment, and concentration. Majority of the doctors at senior registrar level were involved in private practices and are overworked, in our study 59.2% (154) of participants were doing private practices, similar results were seen in the research conducted in Faisalabad by Aslam and others.[17] Issues in approaches, non-supportive behaviour of Hospital administration, noncompliance on the part of participants were other reasons for showing disinterest towards research.

We found that lack of reward in the form of failure to publish, lack of acknowledgement was another factor of discouragement for the doctors towards involvement in conduction of researches as was seen in other studies done.[18,19] Pre fellowship publications were only 5%, people were only forced to indulge, to get a higher portfolio, a major reason, driving force towards research, 48.08% (125). Identical thoughts with other participants in the research done in Germany.[19]

We found that doctors complained of lack of opportunities, both in the medical colleges as well in other governmental institutions same was observed in the study conducted in Army medical college in Rawalpindi.[20] A research discipline should be started in medical colleges at least for facilitation.

CONCLUSION

The conclusion of study is that majority of senior registrars have low interst in research, and no publications or intention to do research. Age, private practice and years of fellow ship have significant association with post fellowship publication.

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FREQUENCY OF PREDIABETES IN PATIENTS INFECTED WITH HEPATITIS C VIRUS

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Abstract

Introduction: Prediabetes as a proxy for insulin resistance is a predictor for success of interferon in treatment for chronic hepatitis C. Burden of prediabetes in patients with hepatitis C virus infection may help in tailoring therapy on an individual basis.

Objective: To determine the frequency of prediabetes in patients with hepatitis C virus infection.

Study Design: Cross Sectional survey

Study Setting: The study was conducted in medical outpatient department, Services Hospital, Lahore.

Duration Of Study: Six months from 9th May 2014 to 8th November 2014.

Methods: 181 patients with Hepatitis C virus infection without any sign of decompensation were included in the study. Patients were screened for prediabetes and checked for glucose intolerance. Body mass index was measured and BMI > 24.9kg/m2 was used as an effect modifier.

Results: Mean age of patients was 40.4 ± 2.7 years. 54.1% were below 40 years of age. 83 patients (45.9%) were male and 28.7% were female. 12 (6.6%) had BMI >24.9kg/m2 while rest (93.4%) were not obese. 28 (15.5%) had prediabetes. Prediabetes was significantly associated with female gender and obesity.

Conclusion: It is concluded that prediabetes in chronic hepatitis C patients was found in 28 (15.5%) individuals among the sampled population in the study.

Keywords: Prediabetes, Insulin resistance, Interferon therapy, Chronic Hepatitis C.

Globally 150 million people are suffering from hepatitis C Viral (HCV) infection and 350,000 people die from HCV related complications every year[1]. HCV infection is nowadays recognized as a disease of global importance and available data suggest that the prevalence of HCV infection is approximately 2.2–3.0% worldwide with the highest prevalence in the African and the Eastern Mediterranean region where Pakistan1 and Egypt share the major chunk.[1-3] Diabetes is also very common globally[4] showing prevalence about 16.68% in males and 19.37% in females in Pakistan[5] quite different from world which was projected to be 7.7% by 2030.[4]

Prediabetes and HCV coexist with different age and gender distribution in different geographical areas.[6] This double burden of disease is a new phenomenon seen in developing countries now days. Same holds true for simultaneous presence of prediabetes in patients with chronic hepatitis C virus infection.[7] In a Japanese study the prevalence of prediabetes in chronic hepatitis C patients came out about 13.6% showing almost double the rate present in non HCV healthy population.[8]

HCV is able to induce insulin resistance directly and has consistently been found to be closely linked to fibrosis in HCV infection.[9] Severe fibrosis is more likely in diabetic patients than those with no diabetes.[6] Insulin resistance may promote hepatic fibrosis in chronic hepatitis C and has emerged as a cofactor in failure to achieve sustained viral response (SVR). [10]

There is scarce local data available showing the coexistence of prediabetes and hepatitis C Virus (HCV) infection in our population. It is not our routine practice to screen every patient with HCV for prediabetes. As outcome of treatment depends highly on co existing prediabetes or diabetes,[7] local

prevalence of prediabetes in HCV patients is essential to be known. Our population differs from others in circulating genotype[6] and sedentary lifestyle[3]. The rationale of my current study is that it will help devise some screening guidelines for all patients presenting to our hospitals as early detection of prediabetes in Hepatitis C can lead to early intervention with significant positive impact on two main things. Firstly, early detection of prediabetes in HCV patients may help us to control diabetes before its complication. Secondly it will help us to predict the success of antiviral therapy to attain sustained viral response.

METHODS

SETTING: Medical outpatient department, Services Hospital, Lahore

DURATION: Study was completed in six months from 9th May 2014 to 8th November 2014.

STUDY DESIGN: Cross Sectional survey

SAMPLESIZE: Taking frequency of prediabetes among chronic hepatitis C 13.6% 7 and acceptable difference of 5%, required sample size is 181.

SAMPLING TECHNIQUE: Non-probability purposive sampling.

INCLUSION CRITERIA

- Age: 18-60 years
- Either sex
- Patients with Hepatitis C virus defined as patients with positive qualitative polymerase chain reaction for HCV RNA
- Never diagnosed as diabetic or glucose intolerant determined by history
- No sign of decompensation i.e. history of hematemesis, ascites and splenomegaly (by ultrasonography) and hypoalbuminemia by chemical auto analyzer

EXCLUSION CRITERIA

- Body mass index (BMI) more than 35 kg/m^2
- Relapse of HCV infection due to failed interferon treatment determined by history
- History of chronic kidney disease determined by serum creatinine and BUN
- Any other connective tissue disorder like rheumatoid arthritis and SLE determined by history.

DATA COLLECTION PROCEDURE

After approval of synopsis and informed consent, 181 patients according to selection criterion were included in the study from medical OPD of Services Hospital Lahore. All participants were explained the purpose of study. All variables of interest like age, sex, BMI and fasting & post glucose level were recorded on a standard questionnaire. Prediabetes was determined as per operational definition (if 8 hours fasting blood sugar levels were impaired i.e. between 100 to 126 mg/dl on two separate occasions 24 hours apart and was confirmed if blood sugar level came 140 to 200 mg/dl two hours after administration of 75g oral glucose solution) after administration of 75g glucose in solution form by standardized calorimetric method. Under aseptic conditions 3ml venous blood was drawn by phlebotomy and sent immediately to laboratory. Body mass index was measured and BMI > 24.9kg/m^2 was used as effect modifier i.e. data was stratified for obese and non-obese.

DATA ANALYSIS

Data collected was entered and analyzed in the SPSS version 17. Mean with standard deviation was calculated for quantitative variables like age, weight, body mass index and blood glucose level and frequency and percentages in case of categorical variables like gender and prediabetes. Data was stratified by age, gender and BMI to determine the effect modification. Post stratification chi square test was applied. A p value < 0.05 was considered significant.

RESULTS

Mean age was 40.4 ± 2.7 years ranging from 35-45. (Table I) 54.1% were below 40 years of age while rest were above 40 years. (Table II). 181 patients according to inclusion criteria were included in the study 83 (45.9%) were male while rest (54.1%) were

female. (Table III). 12 patients (6.6%) had BMI > 24.9kg/m^2 while rest (93.4%) were not obese. (Table IV). 28(15.5%) had prediabetes according to operational definition while rest (84.5%) were free from prediabetes. (Table IV).

When we cross tabulated the age groups with prediabetes, we found a non-significant difference (p= 0.632, Table VI). When we cross tabulated the sex of respondents with prediabetes, we found a significant difference (p= 0.04, Table VII). 20.4% were female with prediabetes as compared to 9.6% male.

When we cross tabulated the obesity (Body mass index >24.9kg/m^2) with prediabetes, we found a highly significant difference (p=0.001, Table VIII).

Table 1: *Age Distribution of Sampled Population*

	N	Minimum	Maximum	Mean	Std. Deviation
Age	181	35	45	40.45	2.725

Table 2: *Frequency Distribution of Sampled Population by Age Groups*

	Frequency	Percent	Valid Percent	Cumulative Percent
Below 40 Years	98	54.1	54.1	54.1
40 Years & above	83	45.9	45.9	100.0
Total	181	100.0	100.0	

Table 3: *Frequency Distribution of Sampled Population by Sex*

	Frequency	Percent	Valid Percent	Cumulative
Male	83	45.9	45.9	45.9
Female	98	54.1	54.1	100.0
Total	181	100.0	100.0	

Table 4: *Frequency Distribution of Sampled Population by Prediabetes*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	153	84.5	84.5	84.5
	Yes	28	15.5	15.5	100.0
	Total	181	100.0	100.0	

Table 5: *Frequency Distribution of Sampled Population by Body Mass Index >24.9kg/m^2*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	No	169	93.4	93.4	93.4
	Yes	12	6.6	6.6	100.0
	Total	181	100.0	100.0	

Table 6: *Crosstab between Age Groups & Prediabetes*

Age groups		Prediabetes		Total
		No	Yes	
40 Years & above	Count	69	14	83
	% within Age groups	83.1%	16.9%	100.0%
Below 40 Years	Count	84	14	98
	% within Age groups	85.7%	14.3%	100.0%
Using chi square test, p value =.632 (Non-significant)				

Table 7: *Crosstab between Sex & Prediabetes*

Sex		Prediabetes		Total
		No	Yes	
Female	Count	78	20	98
	% within Age groups	79.6%	20.4%	100.0%
Male	Count	75	8	83
	% within Age groups	90.4%	9.6%	100.0%
Using chi square test, p value =.04 (significant)				

Table 8: *Crosstab between Body Mass Index >24.9kg/m^2 & Prediabetes*

Body mass index >24.9kg/m^2		Prediabetes		Total
		No	Yes	
Yes	Count	0	12	12
	% within Age groups	0.0%	100.0%	100.0%
No	Count	153	16	169
	% within Age groups	90.5%	9.5%	100.0%
Using chi square test, p value < 0.001 (significant)				

DISCUSSION

Hepatitis C virus (HCV) infection is associated with insulin resistance (IR) and subsequent poor response to antiviral therapy.[2] The clinical relevance of prediabetes in Hepatitis C virus arises from its ability to promote hepatic inflammation and fibrosis and to impair response to antiviral therapy. Several studies are focused on the relationship of insulin resistance and chronic hepatitis C (CHC). Different lines of evidence have found that IR is a common feature in patients with CHC.[3-5]

In our study, 28 patients (15.5%) had prediabetes according to operational definition while rest (84.5%) were free from prediabetes. This is quite high prevalence showing the need to screen all patients with Hepatitis C virus infection to undergo screening for glucose intolerance and prediabetes. We may tailor antiviral therapy according to needs of individual patients.

Our results are comparable with previous studies. In a Japanese study the prevalence of prediabetes in chronic hepatitis C patients came out about 13.6% showing almost double the rate present in non HCV healthy population. [8]

Although Diabetes is very common globally showing a stage of global pandemic.[4] Excess prevalence i.e. almost double the projected (7.7% by 2030) shows association of Hepatitis C virus infection with development of prediabetes.[4]

Among included 181 patients, 83 (45.9%) were male while rest (54.1%) were female. It implies that female were more in our sampled population showing that it may be due to health seeking behavior or change in pattern for seeking advice in our sampled population but on the other hand they are more at the risk of contracting this disease by obstetric surgeries, by infected blood transfusion etc.[5,8]

The patients without prediabetes are more likely to achieve early viral response patients and subsequently sustained viral response at 6 months.[9]

When we cross tabulated the age groups with prediabetes, we found a non-significant difference (p= 0.632). The age of a patient is a common risk factor for developing prediabetes. Non-significant association may be due to younger population in our study sample. Mean age was 40.4 ± 2.7 years ranging from 35-45 years. 54.1% were below 40 Years of age while rest were above 40 Years.

Then we stratified the patients for gender and when cross tabulated the gender with prediabetes we found that there is a difference in prevalence of prediabetes among male and female patients. (p= 0.04, Table VII).

20.4% were female with prediabetes as compared to 9.6% male. The reason may be obesity, poor and sedentary life style along with malnutrition.

To determine the effect of obesity among patients with Hepatitis C virus infection, we stratified data for Body mass index >24.9kg/m^2. When we cross tabulated the obesity (Body mass index >24.9kg/m^2) with prediabetes, we found a highly significant difference (p= 0.001). All obese patients had prediabetes. A preventive program may help reduce the double burden of disease i.e. prediabetes and Hepatitis C virus infection.

CONCLUSION

It is concluded that prediabetes in chronic hepatitis C patients was found in 28 (15.5%) individuals among the sampled population in the study. Prediabetes was found associated with female gender and obesity (Body mass index >24.9kg/m^2). Further studies should be encouraged in this regard.

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TREATMENT OUTCOME OF INTERLOCKING INTRAMEDULLARY NAIL AND NARROW DYNAMIC COMPRESSION PLATE OF DIAPHYSEAL FRACTURE OF TIBIA IN ADULTS

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Abstract

Objective: To compare the treatment outcome of intra-medullary interlocking and narrow dynamic compression plate for the closed diaphyseal tibial fracture in adults.

Methods: This randomized controlled trial was conducted using probability simple random technique at the Department of Akhtar Saeed Trust Teaching Hospital, Lahore from July 2017 to September 2018. Our sample size was 38 patients either gender, age between 16- 70 year with closed fracture shaft of tibia diagnosed on history, clinical examination and radiograph. We excluded patients with decompensated liver disease, chronic kidney disease, pathological fracture and cardiac failure diagnosed on history, clinical examination, baseline and radiographs.

Results: Out of total 38 patients there were 21 (55.3%) male and 17 (44.7%) were female. In group-A, there were 11 (57.9%) male and 08 (42.1%) were female. In group-B, there were 10 (52.7%) male and 09 (47.3%) were female. The mean age in group-A was 34.7±7.814 while in group-B it was 33.6±9.214.Primary union in group-A was in 18 (94.7%) patients and secondary union was present in 01 (5.3%) patient. While in group-B primary union was present in 17 (89.4%) patients and secondary union in 02 (10.6%) patients.

Conclusion: There more male population in our study. the treatment outcomes in term of union was better in patients treated with intra-medullary interlocking nail with little implant failure and deep infection.

Key words: Diaphyseal tibial fracture, dynamic compression plate, union, intramedullary interlocking nail.

Tibial fractures are the highest reported fractures in long bones. They account for 26 per 100, 000 in an average population.[1,2] Pakistan is a populated country and motorbike is mostly used mode of transportation in young population. Tibia is the most vulnerable bone due to its sub-cutaneous course.[3] In recent years, closed reduction and internal fixation with intra-medullary interlocking nail is widely accepted in orthopedic surgeons.[4] It provides better mechanical stability in long bones and maintains proper biological environment with preserved extra-medullary blood supply.[5]

Dynamic compression plates are used in treating tibia with fracture line extending into the metaphyseal area of the bone. They have disadvantages over interlocking nail due to open reduction. There are chances of deep infection, implant failure, soft tissue injury and blood loss while intra-medullary nail of tibia required image intensifier. The facility isn't commonly available in developing country like Pakistan. The duration of the surgery also varies with technically demanding locking of the nail without distraction at fracture site and knee pain.[6]

There is no clear answer to the question for the treatment of diaphyseal fracture of the tibia in our population. The current study assesses the problems and complications in both procedure during opera-

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tive treatment of diaphyseal fractures of tibia.

METHODOLOGY

This randomized controlled trial was conducted using probability simple random technique at the Department of Akhtar Saeed Trust Teaching Hospital, Lahore from July 2017 to September 2018. Our sample size was 38 patients either gender, age between 16- 70 year with closed fracture shaft of tibia diagnosed on history, clinical examination and radiograph. We excluded patients with decompensated liver disease, chronic kidney disease, pathological fracture and cardiac failure diagnosed on history, clinical examination, baseline and radiographs.

All patients were presented in the out-patient department were admitted in the ward. They were applied back-slab above knee for skeletal stabilization. After taking informed written consent from the patients we included patients in the study. They were randomized by lottery method into group-A and group-B. All patients in group A were treated with closed reduction internal fixation with intramedullary interlocking nail (CRIF IM IL nail) under image intensifier and in group-B all patients were treated with open reduction inter fixation with 4.5mm narrow dynamic plate (ORIF DCP). Data was collected on a questionnaire. Pre-operatively all patients were given intra-venous ceftriaxone half an hour before the surgery in the recovery room. All patients were given spinal anesthesia. Post-operatively injection ceftriaxone 2gm was given 24hourly for three days.

All patients were discharged between 4-6th post-operative day on oral antibiotics for another five days. Later they were followed in the out-patient department. They followed on 14th day, one month, 3rd month, 6th month, 8th and 10th month. Our primary outcome of interest was union and secondary outcome were duration of the surgery, superficial and deep infection, non-union, mal-union and implant failure. All patients were encouraged with stretching exercises on 2nd post-operative day and walk non-weight bearing with the help of walker on 3rd post-operative day. The partial weight bearing was started on 3rd month in group-A and in 4th month in group-B. Union was assess using Hammer et al criteria.[7]

Data was entered and analyzed using SPSS version 21.0. Quantitative variables like age and union time was presented as mean±SD. Qualitative variables like gender, side of the limb, superficial and deep infection were presented as frequencies and percentages. Paired T-test was applied to see the statistical significance in two groups for union and p-value <0.05 was regarded to be significant.

RESULTS

Out of total 38 patients there were 21 (55.3%) male and 17 (44.7%) were female. In group-A, there were 11 (57.9%) male and 08 (42.1%) were female. In group-B, there were 10 (52.7%) male and 09 (47.3%) were female. The mean age in group-A was 34.7±7.814 while in group-B it was 33.6±9.214. The mode of injury in group-A was road traffic injury on two wheels in13 (68.5%%), four wheels in 05 (26.3%) patients and fall from height in 01 (5.3%) while in group-B it was motorbike in 12 (63.1%), car in 05 (26.4%) and fall from height in 02 (10.65) patients (Table 01).

Primary union in group-A was in 18 (94.7%) patients and secondary union was present in 01 (5.3%) patient. While in group-B primary union was present in 17 (89.4%) patients and secondary union in 02 (10.6%) patients. The secondary union was due to the implant failure in both groups. There was no malunion reported in both groups. There were 22 (57.9%) right sided and 16 (42.1%) were left side tibial fracture (p-value <0.05). The mean duration of surgery in group-A was 72.62 (45-124) minutes while in group-B, it was 67.60 (31-128) minutes (p-value 0.317). The mean duration of union in group-A was13.57±6.014weeks and in group-B the mean duration of union was 24.68±5.278weeks (p-value 0.46) (Table 02).

DISCUSSION

The treatment of diaphyseal fracture of the tibia is challenging for the Orthopedic surgeon. In literature there are conflicting reports about the superiority of one treatment method, type of implant for diaphyseal tibia fracture[8]. The treatment has its own merits and demerits. OR IF with DCP provide rigid fixation and has risk of periosteal stripping, hematoma loss, and high risk of infection. In contrast closed nailing provides biological way of treatment diaphyseal fracture of tibia.

Table 1: Demographic Data of Age, Gender, Mode of Injury and Side of Involved Limb

Variables	Group A n=19 (%)	Group B n=19 (%)	n=38 (%) P value
Sex of the Patient			
· Male	11 (57.9%)	10 (52.7%)	21 (55.3%)
· Female	08 (42.1%)	09 (47.3%)	17 (44.7%)
Mean Age in Years	34.7±7.814	33.6±9.214	
Mode of Injury			
· Motorbike	13 (68.5%%),	12 (63.1%)	25 (73.33%)
· Car	05 (26.3%)	05 (13.34%)	10 (16.67%)
· Fall from Height	01 (5.3%)	02 (10.6%)	03 (10%)
Union			
· Primary union	18 (94.7%)	17 (89.4%)	35 (92.1%)
· Secondary union	01 (5.3%)	02 (10.6%)	03 (7.9%)

Table 2: Independent T-Test for Superficial and Deep Infection, Duration of the Surgery, and Union Time in both Groups.

Variables	Group-A	Group-B	p-value
Infection			
· Superficial infection	02 (10.6%)	03 (18.5%)	0.05
· Deep infection	01 (5.3%)	02 (10.6%)	
Duration of Surgery minutes (Range)	72.62 (45-124)	67.60(31-128)	0.318
Mean duration of union weeks	13.57±6.014	24.68±5.278	0.46

Motorbike injury was the most common mode in our study which was present in 25(65.8%) patients. It is quite alarming. With the passage of the time, there needs to address the tibial fracture association with motorbike injuries. Im et al.[9] reported that ORIF with DCP provides better alignment than IM IL nail tibia. Kwok et al.[10] reported in his study that plate fixation has reduced chances of mal-alignment compared to interlocking nail with no-difference in union and complication rate in both groups. In our study primary union in group-A was in 18(94.7%) patients and secondary union was present in 01(5.3%) patient. While in group-B primary union was present in 17(89.4%) patients and secondary union in 02(10.6%) patients. There was no malunion reported in both groups. Our findings of the study are consistent with the findings of Kwok et al. Our findings of the study are also similar to the Hung et al[11]. He conducted a randomized controlled trail. He reported that there is no statistical difference of union in two groups.

The mean duration of union in with intra-medullary interlocking nail was 13.57±6.014 weeks and in dynamic compression plate the mean duration of union was 24.68±5.278(p-value 0.46). Saied A et al.[5], conducted randomized controlled trail reported union time 4.30±1.48 months in plating and mean union time 4.34±1.45 months in patients treated with interlocking nail, with dynamization being required in four (12%) of the patients, while one case of non-union persisted even after that. Vallier HA et al.[13] had union at 4.7months in his study. The findings are consistent with this study. Although both groups have union till last follow up in our study, but the infection rate was high in ORIF with DCP. The deep infection was treated according with removal of implant (DCP), debridement, application of external fixator with antibiotics according to culture and sensitivity. All patients had union till last follow up.

Anterior knee pain was the additional reported in our patients who were treated with interlocking nail. We didn't recorded this variable during the early follow-up till 3rd months while there was no reported data in patients treated with ORIF with DCP. The knee pain was present in 03 (15.8%) patients. Katsoulis E et al.[11] reported anterior knee pain in 10% patients treated with interlocking nail. They were treated with non-steroidal anti inflammatory oral and topical drugs and physiotherapy. Shrestha et al[14] had 30% patients required implant

removal due to prominence. In our study, the secondary union was due to the implant failure in both groups.

Our study has small sample size with addition of other complication like calf muscle atrophy, knee function in both groups should be recorded. Multi-centric study can be done to confirm the findings of our study.

CONCLUSION

We concluded that union in patients treated with interlocking nail was good that narrow dynamic compression plate in adult diaphyseal tibial fracture. The deep infection, implant failure was also low in patients treated with interlocking nail. Union in both groups were achieved in both groups but patient with nail were able to bear weight early.

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ROLE OF ANTICHOLINERGIC OR ALPHA BLOCKER ALONE AND IN COMBINATION, IN TREATMENT OF DOUBLE J STENT RELATED SYMPTOMS

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Abstract

Objectives: To evaluate the efficacy of anticholinergic or alpha blocker alone and in combination, in treatment of double J stent related symptoms.

Subjects and Methods: Patients with indwelling double j stent either symptomatic or asymptomatic were asked to fulfill the proforma. Follow up was done on weekly basis till DJ was removed. Ninety symptomatic patients with double j stent were allocated in three groups; group A, B & C, each group of 30 subjects. Group A, patients were given 0.4 mg tamsulosin one daily Group B, patients were given 2 mg tolterodine twice daily. Group C were given combination of 0.4 mg tamsulosin & 2mg tolterodine. Patients in all groups were kept on follow up on weekly basis for relief of their symptoms. Responders in all groups took their responding drugs till the DJ stent were removed. Meanwhile the non-responders of all groups were labeled as failure of therapy and they were managed accordingly. Stent removal was done after the desired objective of DJ stent insertion was obtained. Effectiveness among three therapy i.e alpha-blocker, anti-cholinergic alone and in combination was assessed by comparing the relief of symptoms in all the groups.

Results: The average age of all included ninety patients was 28.14 years SD 7.57, with minimum age of 16 years & maximum age of 40 years. Mean IPSS score at baseline in Group A was 16.10 SD 5.73, In Group B mean score was 18.60 SD 4.42, and in Group C mean was 17.433 SD 4.530.(P>.05). Mean IPSS score at 14 days in Group A was 11.033 SD 3.96, In Group B mean score was 7.033 SD 3.37, and in Group C mean score was 3.433 SD 2.812.(P<.000). Mean IPSS final score in Group A was 8.300 SD 3.38, In Group B mean score was 4.833 SD 3.33, and in Group C mean score was 1.533 SD 2.515.(P<.000).In Group A 13.6% responded to treatment, in group B 39.0% responded to treatment and in Group C 47.5% responded to treatment. Chi-square test were applied for the assessment of statistical significance (X = 31.985, P < .000)

Conclusion: Combination of tamsulosin and tolterodine was superior in relieving obstructive subscore, irritative subscore and VAP score than the montherapy. Hence, combination of tamsulosin and tolterodine must be prescribed in the patients with DJ stent related symptoms.

Key Words: Urethral stent/DJ Stent, Anticholinergic, Alpha blockers.

Stent are now extensively used as a basic tool in routine endourological surgery. They are generally placed in anticipation to prevent ureteric obstruction postoperatively from mucosal edema, mucosal erosion/damage following uretrorenoscopy for ureteric stone or other upper tract interventions. The history of DJ stenting is too old, Gustav Simon in 1800s performed first DJ stenting following open cystostomy. Following his success, Zimskind et al in 1967 placed DJ stent endoscopically. With the passage of time, multiple changes were made in features & structure of DJ stent to ensure a good urinary drainage with lesser complications. In modern age of urology the uses of DJ stent have been expanded.

Ureteric stents are now used in treatment of various diseases related to urinary tract. For example, following uretrorenoscopy for ureteric stone or other upper tract interventions, following ballon dilatation of ureteric stricture, following endopyelotomy / pyeloplasty, to relive obstruction in pelvic malignancy etc. (Chew et al., 2010). Though the use of DJ stent has been increasing day by day, its use is not free of symptoms & complications. There are relatively less side effects reported in early researches but later researches shows that these ureteric stents can cause

hematuria, dysuria, pain suprapubic region, frequency, urgency etc. Moreover DJ stent may get broken, migrate or can have encrustation over it. The problem of stent migration was resolved by Finny in 1978 by introducing double coiled stent i.e JJ stent or DJ stent. (Finny et al., 1978).

About 83% of patient with DJ in stent are symptomatic. (Manoj et al., 2009). (Joshi et al., 2003). In order to resolve these stent related symptoms many studies have been done and different new ideas were brought in practise.

A variety of medicines were used in relieving symptoms related to DJ stent. Selective alpha blockers / antimuscarinic are used in alleviating such symptoms.

Symptoms due to DJ Stent and the symptoms of overactive bladder (like urinary urgency, frequency & painful urination) are alike. As bladder contraction is mediated by activation of muscarinic receptor leading to contraction of bladder musculature (Park et al., 2009).

This study is designed to evaluate the efficacy of anticholinergic or alpha blocker alone and in combination, in treatment of double J stent related symptoms at the Urology & Renal Transplantation Department, JHL / AIMC, Lahore.

OBJECTIVE

- To see the role of α-blockers (tamsulosin) or anticholinergics (tolterodine) alone and in combination, in the management of DJ related symptoms.

METHODS

Research design

Randomized control trial

Setting

Department of Urology, Jinnah Hospital / AIMC, Lahore

Research duration

One year

Sampling technique

Non-probability: purposive sampling technique.

Sample size

Win-pepi-ver: 11.5 to estimate a proportion

SAMPLE SELECTION:

INCLUSION CRITERIA

- Both Male & female cases with average age 16-40 years
- Patients with DJ stent surgery (endoscopic & open surgery) for any indication.

EXCLUSION CRITERIA

- Coagulopathy
- Current Pelvic trauma/fracture
- Urogenital carcinomas
- Prostatic enlargement or Chronic prostatitis
- Bladder neuropathy
- Stone in bladder
- DJ in reimplantated ureters
- Untreated UTI
- Pregnant females
- Diagnosed retroperitoneal fibrosis
- Patients with residual stone after surgery
- Patients with contraindications for using alpha-blocker or anticholinergics Female diagnosed as stress/urge incontinence
- Patients already on drugs like; alpha blocker, anticholinergic, painkiller or psychiatric drugs.

DATA COLLECTION

This study was conducted at the Department of Urology & Renal transplantation department JHL/ AIMC, lahore. Patients were selected from outpatient urology department who fulfilled inclusion criteria. Informed consent about the study was taken from all patients. Demographic data/information including the indication for double j stent placement was documented. Serum profile (CBC, Renal function test), urine microscopy, urine culture & sensitivity, ultrasonography KUB was done before surgery. All Patients were given prophylactic inj. ciprofloxacin 200mg I/V 2 hours prior to surgery and

24 hrs after surgery. Operations were conducted under general anesthesia /spinal anesthesia and stent position was verified by scout film of X-ray KUB. A coiled double-j stent with 6 F diameter, 28 cm in length made of polyurethane with side-holes were used for all the cases. Postoperative problems and complications were documented in proforma A if any. On discharge patients were prescribed tablet Ciprofloxacin 500 mg Bid and tablet Diclofenac Sodium 50 mg Bid for one week.

All patients with DJ stent in situ were followed on weekly basis in outpatient department. A total of ninty patients, who develop symptoms during their course of follow up were separated in three groups, group A, B & C, each comprising of 30 patients. Group A, patients received 0.4 mg tamsulosin daily. Group B, received 2mg tolterodine twice daily. Group C, received 0.4 mg tamsulosin daily & 2mg tolterodine twice daily. All patients received analgesics on demand. Patients in all groups were kept on follow up on weekly basis for the relief of symptoms. Additionally, if the number of patients group A , B & C remains below 30, more patients were incorporated in study to complete the requisite number Responders in all groups will keep on to take their responding medicine and was followed till completion of study. During the course of follow up if any patient develops symptoms related to infection (like fever, hematuria) urine complete examination and urine culture sensitivity were done and he were excluded from study and accordingly managed. Double J stent were removed after the objective of stent placement were obtained. For all the symptomatic patients, weekly relief of symptoms were defined in terms of; no response (no/minimal relief of symptoms, patient unhappy), partial response (moderate relief of symptoms, patients satisfied) and complete response (more than 90% relief of symptoms, patient happy).The LUTs were classified with irritative (urgency, frequency, nocturia) and obstructive symptoms(weak stream, intermittency, straining, incomplete voiding) and were scored as IPSS score, irritative subscore s& obstructive subscore. The intensity of painful micturition/flank pain were scored with visual analogue pain score (VAPS).

IPSS and VAPS score were compared within and in between groups at enrollment, during each follow up weeks and at the completion of study. The result will a be compared between Group A, B (monotherapy) and group C (combination therapy).

DATA ANALYSIS

Data were entered and analyzed in SPSS ver: 21.0. Mean and SD was calculated for numerical variable like age and IPSS score. Frequency and percentages were calculated for nominal variable like gender, relief of symptoms. Anova test compared the mean variation inbetween the groups. A $P<0.05$ was taken as statistical Significant

OUTCOME & UTILIZATION

This study compared the efficacy of α-blockers or anticholinergics alone and in combination, in management of DJ stent related symptoms. Based upon this study, recommendations were made to choose appropriate drug in management of symptoms due to DJ stent.

RESULTS

Table 1: *Age of Subjects*

Group	N	Mean age	Standard Deviation	Min. age	Max. age
Group A (Tamsulosin 0.4 Mg H.S)	30	27.7667	8.20716	16.00	40.00
Group B (Tolterodine 2mg Bid)	30	29.1333	7.42658	16.00	40.00
Group C (Combination Therapy)	30	27.5333	7.20983	16.00	40.00
Total	90	28.1444	7.57370	16.00	40.00

Male patients	Female patients	Total patients
49 (54.4%)	41 (45.6%)	90 (100%)

Table 2: *IPSS Irritable Subscore Comparison at Baseline, 14 Week and Final.*

Group		IPSSIB	IPSSI14	IPSSIF
Group A (Tamsulosin 0.4 Mg H.S)	Mean	10.0667	8.5667	7.2333
	N	30	30	30
	Std. Deviation	3.03921	2.66113	3.12590
	Minimum	3.00	3.00	.00
	Maximum	15.00	14.00	12.00
Group B (Tolterodine 2mg Bid)	Mean	10.9333	2.4000	1.1333
	N	30	30	30
	Std. Deviation	2.74092	2.76181	2.09652
	Minimum	3.00	.00	.00
	Maximum	15.00	10.00	6.00
Group C (Combination Therapy)	Mean	9.9667	1.4000	.6667
	N	30	30	30
	Std. Deviation	3.48873	1.75381	1.47001
	Minimum	.00	.00	.00
	Maximum	15.00	5.00	5.00
Total	Mean	10.3222	4.1222	3.0111
	N	90	90	90
	Std. Deviation	3.10066	3.99389	3.79087
	Minimum	.00	.00	.00
	Maximum	15.00	14.00	12.00
F test between groups		**.879**	**76.234**	**74.000**
P value		**.419**	**.000**	**.000**

Table 3: *IPSS Obstructive Subscore Comparison at Baseline, 14 Week and Final.*

Group		IPSSOB	IPSSO14	IPSSOF
Group A (Tamsulosin 0.4 Mg H.S)	Mean	6.0333	2.4333	1.1000
	N	30	30	30
	Std. Deviation	3.91710	2.28463	1.51658
	Minimum	.00	.00	.00
	Maximum	12.00	8.00	5.00
Group B (Tolterodine 2mg Bid)	Mean	7.6667	4.6333	3.5667
	N	30	30	30
	Std. Deviation	3.11097	1.80962	2.29968
	Minimum	.00	.00	.00
	Maximum	16.00	8.00	7.00
Group C (Combination Therapy)	Mean	7.5000	2.0333	.8667
	N	30	30	30
	Std. Deviation	3.00287	1.97368	1.50249
	Minimum	.00	.00	.00
	Maximum	13.00	6.00	5.00
Total	Mean	7.0667	3.0333	1.8444
	N	90	90	90
	Std. Deviation	3.41115	2.31483	2.17189
	Minimum	.00	.00	.00
	Maximum	16.00	8.00	7.00
F test between groups		**2.136**	**14.238**	**20.458**
P value		**.124**	**.000**	**.000**

Table 4: *Response Among Group Crosstabulation*

Group	RESPONSE		Total	Chi-Square P value
	No Response	Response		
Group A (Tamsulosin 0.4 MG H.S)	22	8	30	X2=31.985 P= .000
	71.0%	13.6%	33.3%	
Group B (Tolterodine 2MG BID)	7	23	30	
	22.6%	39.0%	33.3%	
Group C (Combination Therapy)	2	28	30	
	6.5%	47.5%	33.3%	

Table 5: *Response Among Group and Gender Cross Tabulation*

Gender	Group	RESPONSE		Total	Chi-Square P value
		No Response	Response		
Male	Group A (Tamsulosin 0.4 MG H.S)	13	4	17	X2 = 21.786 P= .000
		76.5%	12.5%	34.7%	
	Group B (Tolterodine 2MG BID)	4	14	18	
		23.5%	43.8%	36.7%	
	Group C (Combination Therapy)	0	14	14	
		0.0%	43.8%	28.6%	
Female	Group A (Tamsulosin 0.4 MG H.S)	9	4	13	X 2 = 10.897 P= .000
		64.3%	14.8%	31.7%	
	Group B (Tolterodine 2MG BID)	3	9	12	
		21.4%	33.3%	29.3%	
	Group C (Combination Therapy)	2	14	16	
		14.3%	51.9%	39.0%	
		6.5%	47.5%	33.3%	

Total 90 patients were included in this study and these patients were randomly allocated to three groups (30 each). Group A (Cap.TAMSULOSIN 0.4 MG H.S), Group B (TOLTERODINE 2MG BID) and Group C (COMBINATION THERAPY). The average age was 28.14 yearsSD 7.57, with minimum age of 16 years & maximum age of 40 years. Mean age in Group A was 27.76 SD 8.20, In Group B mean age was 20.133 SD 7.42, and in Group C mean age was 27.533 SD 7.20 and there was no noteworthy difference inbetween the groups (Table no 1). In Group A had 43.3 % females and 56.7% males. In Group B, had 40.0 % females and 60.0% males. In

Group C had 53.3% females and 46.7% males (Graph 1).

IPSS baseline, 14 day and final score were compared among three groups. Mean IPSS score at baseline in Group A was 16.10 SD 5.73, In Group B mean score was 18.60 SD 4.42, and in Group C mean was 17.433 SD 4.530.(P>.05). Mean IPSS score at 14 days in Group A was 11.033 SD 3.96, In Group B mean score was 7.033 SD 3.37, and in Group C mean score was 3.433 SD 2.812.(P<.000). Mean IPSS final score in Group A was 8.300 SD 3.38, In Group B mean score was 4.833 SD 3.33, and in Group C mean score was 1.533 SD 2.515.(P<.000).

Irritative and obstructive subscore was calaculated for each groups. On group A iritative subscore was Mean 10.06 SD 3.03, obstructive subscore Mean 6.03 was SD 3.91. group B irritative subscore was Mean 10.933 SD 2.74, obstructive subscore was mean 7,66 SD 3.11 and group C irritative subscore was Mean 9.96 SD 3.48, obstructive subscore was Mean 7.50 SD 3.00. On 14th days group A iritative subscore was Mean8.56 SD 2.66, obstructive subscore was Mean 2.43 SD 2.28. group B irritative subscore was Mean 2.40 SD 2.76, obstructive subscore was Mean 4.631.80 and group C irritative subscore was Mean 1.491.75, obstructive subscore was Mean 2.03 SD 1.97. On final day group A irritative subscore was mean7.23 SD 3.12, obstructive subscore was Mean 1.10 SD 1.51. group B irritative subscore was Mean 1.13 SD 2.09, obstructive subscore was Mean 3.56 SD2.29 and group C irritative subscore was Mean 0.66 SD1.47, obstructive subscore was Mean 0.86 SD 1.50. (Table no.3). VAPS baseline, 14 day and final score were compared among three groups. Mean VAPS score at baseline in Group A was 5.86 SD 4.43, In Group B mean score was 6.30 SD 5.28, and in Group C mean score was 4.200 SD 4.94.(P>.05). Mean VAPS score at 14 days in Group A was 1.233 SD 2.34, In Group B mean score was 2.333 SD 3.14, and in Group C mean score was 4.200 SD 4.912.(P>.05). Mean VAPS final score in Group A was 1.167 SD 2.29, In Group B mean score was 1.666 SD 2.39, and in Group C mean score was .633 SD 1.449.(P>.05). (Table no: 3) IPSS and VAPSB baseline, and final score were compared among three groups using paired sample t test. Mean IPSS baseline and final was 12.48 SD 6.33. (p <.000) and Mean VAPS baseline and final was 4.300 SD 4.45. (p <.000). (Table no:2 ,3).

On the basis of response to treatment, and improvement in IPSS score patients were categorized into responders and non-responders. In Group A 13.6% responded to treatment, in group B 39.0% responded to treatment and in Group C 47.5% responded to treatment. Chi-square test was used to assess statistical significance (X = 31.985, P < .000) (Table no 4,5).

Response was stratified for age and gender among three groups. In group A< 30 years only 6.1%, In Group B 36.4% and In Group C 57.6% responded to treatment. (X = 26.596, P < .000). In group A> 30 years only 23.1%, In Group B 42.3% and In Group C 34.6% responded to treatment. (X = 7.922, P < .000) (Table no 6). In group A among males only 12.5%, In Group B 43.8% and In Group C 43.8% responded to treatment. (X = 21.7866, P < .000). In group A among females 31.7%, In Group B 29.3% and In Group C 39.0% responded to treatment. (X = 7.922, P < .000) (Table no 4,5)

DISCUSSION

DJ stents are widely used in endourology. For example, in anticipation to prevent obstruction of ureters, to avoid damage to the kidney because of obstruction. Chew et al., 2004).Ureterals stents are mostly used after ureteroscopy, especially after ureterorenoscopy / lithotripsy (Haleblian et al., 2008).DJ stent helps a lot in management of renal tract pathology, but patients with DJ stents have been identified to complain of a series of stent associated symptoms. These symptoms are transitory and patients get symptomless after stent removal. The exact pathophysiology of stent related symptoms is mysterious. Thomas et al postulated that in patients with indwelling DJ stent there is increased intrarenal pressure(upper coil) and

irritation of trigone (lower coil) during urination which is the cause of stent related symptoms (Thomas et al., 1993). Joshi & his co-worker in their study mentioned that because of DJ stent related symptoms, 80% of patient have a decreased quality of life. (Joshi et al., 2003). Zimskind et al tried to change the material of stent in order to reduce symptoms (Zimskind et al., 1967). Beiko et al tried to modify the distal end of DJ stent, tapering the distal end and coating with silicone & hydrophilic material (Beiko et al., 2003). Injection of botulinum toxin type A following DJ stent insertion in subtrigonal region has been shown to reduce pain and sedative requirement (Gupta et al., 2010).

Botulinum toxin treatment have many methodological difficulties as well as it is expensive. It is therefore necessary to find a safe & cost effective way of management to resolve DJ stent related symptoms and pharmacological therapy is one ways

Lee et al studied tamsulosin and tolterodine in treatment of DJ symptoms with a placebo group (Lee et al., 2010). No significant differences were showed by each group in the IPSS or VAPS. In their report it was found that stent position/ location was more important in development of DJ symptoms. IPSS score had remarkable change in the combination therapy group & VAP score was unremarkable. Following are the limitations of Lee et al study. On the preoperative day, few patients did not full filled the questionnaire. As a result, we could not make use of this questionnaire. Due to small groups study, entirely valuable information couldn't be gathered. Hence, large scale, randomized, prospective study is required to get more precise information.

There are few data about pharmaceutical management of treatment related to DJ stent symptoms. Among the pharmaceutical drugs, alpha-1 antagonists have been the most valuable used for the relief of DJ associated problems along with improving quality life of these patients. The mechanism of alpha-1 adrenergic receptor antagonist involves the reduction of ureter and trigone smooth muscle activity. And the mechanism of the anticholinergic drug involves relief of involuntary bladder contraction that is mediated with muscarinic receptors.

Meta analysis were executed to evaluate the positive effect of alpha blockers in management of patient among DJ problems, however the quantity of studies were small (lamba et al., 2011), hence we collected available prospective RCT research plus meta analysis to see the effects of alpha blocker, antimuscranic as monotherapy and combination therapy in patient among DJ related symptoms.

In total 13 RCT study with 1408 patients included, the individuality of the patient were displayed in table.1 seven RCT enrolled patients went DJ stenting following Ureteroscpic removal of stone, one RCT enrolled patients who went DJ stenting to manage hydronephrosis, five following open surgery including URS (ureteroscopy), PCNL (percutaneous nephrolithotomy) and reimplantation of ureter. All were published in English. Assessment of symptoms score was done in 1st and 6th week.

Seven RCT studies together with 696 patients have been published to evaluate the role of an alpha blocker on DJ stent including symptoms with USSQ. Alfuzosin was assessed in four studies, tamsulosin is now in two studies, along with combination of two drugs was done in one study. By joining the result of these studies, alpha blockers positively reduced urinary symptoms score (−6.37 [−9.63 to −3.10]; P=0.0001) and pain score (−7.30 [−11.14 to −2.91]; P<0.00001) when relatable with control.

Among seven studies, the total score were obtained at 1st and 4thweek. To evaluate the drugs activity over stent related symptoms, subgroup analysis were also done. It was establish that in any matter if patients received alfuzosin or tamsulosin for 1week or 4week there was considerable variation in symptoms index score among alpha blocker category and control category In 1st week Alfuzosin treated group had the low frequency 3.17;tamsulosin treated group had 9.01. on 4th week alfuzosin treated group had 5.59 and tamsulosin treated group had 4.36, when compaired to control group. (Completing fig.2, enhancing data are present online at the

website…

Some studies adopted IPSS to assess the DJ stent related symptoms. Some studies were conducted that used IPSS, QoL & VAPS as a measuring tool. Among these studies few studies assessed tamsulosin and one terazosin. Alpha blockers are helpful in improving the total IPSS (mean difference [MD]: −4.16; 95% confidential interval [CI], −6.55 to −1.77; P=0.0006), VAPS (MD: −2.48; 95% CI, −2.84 to −2.12; P<0.00001), and QoL of IPSS (MD: −1.42; 95% CI, −2.26 to −0.58; P=0.0009).Two studies were conducted evaluating antimuscarinics singly over control for quantitative analysis, which assessed efficacy of tolterodine and solifenacin. The result demonstrated antimuscarinics lower the total IPSS (MD: −3.76; 95% CI, −5.08 to −2.43; P< 0.00001). QoL (MD: −0.82; 95% CI, −1.31 to −0.32; P=0.001). VAPS was the only study to be proven (P<0.00001).

Randomized control trial study with the combined therapy of alpha blockers and antimuscarinics with alpha blockers monotherapy. Those Patients who were treated with combined therapy showed statistically significant score in total IPSS score (MD: −3.74; 95% CI, −4.94 to −2.54; P<0.00001), VAPS (MD: −0.50; 95% CI, −0.89 to −0.11; P=0.01) and QoL (MD: −0.93; 95% CI, −1.30 to −0.55; P<0.00001)

Lamb & Yakoubi and colleagues summarized the adverse effect of alpha blocker and anitimuscarinics. They reported that adverse effect of alpha blockers were minimal compared to antimuscarinics. Three studies proved that those patients taking alpha blockers didnt discontinued their drug because of side effect. (lamba et al.,2011) (Yakoubi et al 2011). However Tehranchi & colleagues in their study found 3 patients taking antimuscarinic as monotherapy suffered orthostatic hypotension & mouth dryness (Beiko et al., 2003); 11 patients with combined therapy faced orthostatic hypotension, headache dizziness & mouth dryness. Lee & coworkers diagnosed that only one patient had the experience of dry mouth with combined therapy group (Lee et al.,2010).

The sympathetic nervous system modulate involuntary ureteric contraction and relaxation of alpha receptors in the human ureters in response to ureteric stone to flush out stone. Davenport & associates studied that alpha blockers decreases the peak contraction pressure of ureters (Davenport et al., 2006) Therefore, alpha blockers reduce spasm of ureteric muscle & decreased reflux of urine to the renal pelvis which ultimately reduces lumbar pain. similarly urinary frequency, urgency improved by blocking the alpha receptors at trigone. Alpha blocker significantly decreased total IPSS score, VAP score, and Quality of life, in comparision to other control groups.

Regarding DJ stent, the DJ distal coil in bladder is cause of local trigone irritation which results in urgency, frequency. Acetylcholine release induces local contractions of detrusor muscle,which lead to involuntary bladder contraction/ spasm (Anderson et al., 2007) (Tehranchi et al.,2013) (Park et al.,2009). Antimuscarinics blocks muscarinic receptors and lessen contraction of detrusor (Yamaguchi et al.,2013). Antimuscarinic used at recommended doses, have slight effect on contractions during voiding phase.

Combined therapy of alpha blocker with antimuscarinic has been confirmed to be much better than alpha blocker to treat symptoms (Norris et al.,2008) (Hao et al.,2014). Lim and colleagues (Lim et al.,2011) also reported that combination of solifenacin & tamsulosin considerably improved DJ symptoms than single use of drug. However, Lee & his workers (Lee et al., 2010) in their research of 20 patients found no difference in tamsulosin and tolterodine combination & tamsulosin monotherapy.

An additional cause may be due to DJ stent itself which reduce or augment subclinical cases of bladder overactivity leading spontaneous bladder contraction, which may possibly be ground against use of antimuscarinic agents to improve DJ symptoms (Agarwal et al., 2006 Lim et al., 2011) (Deliveliotis et al., 2006). The urgency & urge

incontinence might be due to movement of DJ stent in prostatic urethra that interfers normal sphincter mechanism.(Joshi et al., 2002).

The success of many therapeutic protocols with objective to treat DJ associated symptoms is still under survey. The role of alpha blockers in treating DJ related symptoms was already reported. (Wang et al., 2009) Many research reported that other alpha-blocker alfuzosin superior in relieving DJ related symptoms/ general health and less painkiller demand than placebo group (Deliveliotis et al., 2006) (Beddingfield et al., 2009). Lee et al. (Lee et al., 2010) found that solifenacin was valuable & had less side effect in management of DJ related symptoms, pain. Moradi et al in 2017 in his study over patients with indwelling DJ stent. All patients had same stent placement technique to minimize trial variability. Combination therapy of tamsulosin and tolderodine made drastic reduction in symptoms in a chronological manner from the first week to the fourth week. All the patients in three groups had fewer pain scores in the fourth week than the first week. These effects in drug groups were more significant than placebo. Patients had better general health in the fourth week of Tolterodine consumption. No other group made a significant difference even by time passage. Tamsulosin group had a worse quality of work in the first week than the two other groups. Although, only three patients reported significant side effects of Tamsulosin (Moradii et al., 2017). Asthenia is a known side effect of tamsulosin and can be responsible for the impairment of "rest", job efficacy and regular hours of work. Although this can be interpreted as a placebo effect, drug groups had really greater improvement compared to placebo. Neither drugs nor placebo resulted in any difference in QoL. Overall, positive effects of Tolterodine were remarkable in the fourth week, and indeed, time passage itself had positive effect in some symptoms. In the subgroup who had pain, they had some noteworthy difference between drug groups & placebo. Tolterodine was more effective in controlling pain index score. (Moradii et al., 2017). This study showed that anticholinergic and alpha blockers are effective in improving DJ stent related symptoms and pain also, these drugs, especially Tolterodine, are very effective in control of irritative symptoms incomparision to alpha blocker. The limitations of this study was small sample size specially for pain score index, and the 90 patients reduction in comparison to primary estimated sample size because of mentioned reasons in its 'Results' section maybe is a big bias, and it might be better to assess the effect of Tamsulosin and Tolterodine as combination so as to evaluate the prosperity of prescription.

CONCLUSION

- Combination of tamsulosin and tolterodine was superior in relieving obstructive subscore, irritative subscore and VAP score than the montherapy.
- Among monotherapy, tolterodine and tamsulosin groups, tolterodine was better in relieving total IPSS and VAP score.
- Hence, combination of tamsulosin and tolterodine must be prescribed in the patients with DJ related symptoms.

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DEMOGRAPHIC PROFILE OF UROTHELIAL MALIGNANCIES

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Abstract

Objectives: Bladder cancer, its precursor lesions, the field effect with multiple synchronous lesions, papillary and flat types, all continue to pose biologic and clinical challenges for the urologists. Bladder cancer itself remains the most common lesion treated by urologists. About 95% of the bladder tumors are of epithelial origin, the remainder being mesenchymal in origin.

Objectives of the present study were to establish the demographic profile of urinary bladder tumors

Subjects and Methods: The study was performed in the department of Pathology, Allama Iqbal Medical College, Lahore in collaboration with the department of Urology, Jinnah Hospital, Lahore. Sixty patients of both sexes above 45 years of age with the complaint of painless hematuria, imaging evidence of urinary bladder lesion or recurrent tumor were included in the present study. Biopsy specimen was taken to determine the histological pattern of tumors.

Results: Age of the patients in the present study ranged from 50 to 81 years. The male to female ratio was 4:1 for the study population. Smoking being strongly implicated as a risk factor for bladder cancer was also enquired about regarding its duration and frequency. Painless, off and on macroscopic haematuria was the presenting complaint in all our patients in the study group.

Conclusion: Urothelial cancer is more common in males than females and is more prevalent in older age group. Smoking and the occupational risk factors play a major role in carcinogenesis of Urothelial cancers. Painless hematuria is the most common mode of presentation.

Key Words:

Bladder cancer, its precursor lesions, the field effect with multiple synchronous lesions, exophytic and papillary types, all continue to pose biologic and clinical challenges for the urologist. Bladder cancer itself remains the most common lesion treated by clinicians. Despite significant inroads into their origins and improved methods of diagnosis and treatment, they continue to impose a high toll in morbidity and mortality. Bladder cancer is among the top eight most frequent cancers (1). Despite improvements in detection and management of these neoplasms, the death toll remains at about 12,000 cases annually because the increased prevalence offsets any gains as have been made (2). Many of these deaths could be prevented with early detection of new tumors and vigilant surveillance for recurrence. Hence the need for prompt diagnosis and accurate staging of the bladder cancer cannot be overemphasized.

About 95% of bladder tumors are of epithelial origin, the remainder being mesenchymal in origin. The majority of epithelial tumors is composed of urothelial (transitional) type cells and is thus interchangeably called urothelial or transitional cell tumors. However squamous and glandular carcinomas also occur infrequently (2). Since decades cystoscopy has been the gold standard for the diagnosis of primary and recurrent urothelial cancers. Yet even with the flexible instruments, the process remains invasive and bothersome to the patient. Its diagnostic power is also far from being perfect. Whence the exophytic tumors are reliably diagnosed but flat urothelial cancers; particularly carcinoma in situ continues to be an endoscopic dilemma (3).

Aschnes (1931) was the first to propose classification of bladder cancer into papillary versus a solid configuration and he also categorised it into invasive and non invasive forms (4). Jewett and Strong in 1944 examined autopsy material from 107 patients

and analyzed the depth of penetration (stage) to the incidence of local recurrence and metastases (4). In 1950 the Union International Contra le Cancer (UICC) appointed a committee on tumor nomenclature and statistics to develop a classification system that took into account the status of primary tumor, lymph nodes and metastasis. In 1952 Jewett arbitrarily divided bladder cancer into superficial and deep. Marshall staged the patient clinically on the basis of a bimanual examination and biopsy (4). However this classification system got only a modest support from the Urologists (5). The continued effort of UICC and AJCC resulted in further reinforcements and development of a classification system with sufficient clarity and simplicity (AJCC, 1992) (6).

In 1940's Jewett formulated his staging scheme, in which carcinoma-in-situ was not appreciated as a clinical entity. He characterized all papillary, mucosal confined tumors as "stage 0", subsequently combining all superficial tumors in the category of "stage A". A revolution in the diagnostic aspects of bladder cancer occurred when in 1947 Papanicolaou popularized the use of urinary cytology for the diagnosis of transitional cell carcinoma. This was the first non invasive method for the investigation of bladder cancer. He investigated urinary sediment and did show that exfoliated cells from transitional cell tumor could be detected in the urine (7). Ever since then it has become one of the test protocol for the diagnosis and follow up of the patients with transitional cell carcinoma of the bladder. In 1952 Carcinoma-in-situ was described by Melicow who noted the anaplastic intraepithelial neoplasia at sites remote from visible tumor (8). Mostofi in 1954 clearly established the potentialities of bladder urothelium i.e. its transformation capability into squamous epithelium and glandular epithelium (9). In 1970's intra vesical chemotherapy was started with encouraging results. Radiotherapy was introduced in the treatment of bladder cancer in mid 1970's (10).

Urothelial tumors can arise at any location in the bladder. The various distribution patterns are reported as lateral wall 37%, ,posterior wall 18%, , trigone 12%, , neck 11%,, ureteric orifices 10%, ,dome 8% and anterior wall 4% (11). They have also been reported within diverticula and even arising from regenerated urothelium over a lyophilized dura patch or within the gastric remnant following gastrocystoplasty (12). The pattern of growth may be exophytic, endophytic or combination of both. Approximately 70% of the bladder tumors are papillary, 10% are nodular and 20% show a mixed pattern (13). When exophytic the tumor may adopt a papillary configuration or a solid nodular appearance. When growing endophytically, it may result in clusters of tumor cells in lamina propria, referred to as nested variant.

In 1998, the World Health Organization and International Society of Urologic Pathologists (WHO/ISUP) established a new classification system for urothelial neoplasms (14). The World Health Organization / International Society of Urological Pathology (WHO/ISUP) consensus classification of urothelial neoplasms of the urinary bladder was developed in an attempt to both improve upon prior classification systems as well as to adopt a classification system that would have widespread acceptance (15). Prior to this classification system, numerous diverse grading schemes for bladder cancer existed whereby the same lesion seen by different pathologists would result in very different diagnoses solely based on definitional differences of the various lesions. Another strength of the consensus classification system is that it provides detailed histological criteria for the papillary urothelial lesions [15].

WHO / ISUP CONSENSES CLASSIFICATION OF UROTHELIAL NEOPLASMS

This classification system categorizes bladder urothelial lesions into two broad categories of PAPILLARY and FLAT with several subcategories.

PAPILLARY UROTHELIAL LESIONS include Papillary Hyperplasia, Papilloma, Papillary urothelial neoplasm of low malignant potential, Low grade papillary urothelial carcinoma and High grade papillary urothelial carcinoma

FLAT UROTHELIAL LESIONS include Flat urothelial hyperplasia, Reactive urothelial atypia, Urothelial atypia of unknown significance, Urothelial dysplasia, Carcinoma-in- situ and Invasive urothelial carcinoma.

The development of a staging system for bladder cancer has been based on observations of prognostic differences between various forms of tumor as represented either by the extent to which they may have penetrated the bladder wall or by their histological grade.

The American Joint Committee on Cancer – Union International Centre Le Cancer (AJCC – UICC) system is currently most commonly used staging system. This system encompasses both clinical and pathologic staging.

EPIDEMIOLOGY OF BLADDER CANCER

INCIDENCE

Bladder cancer is the second most common cancer of

genitourinary tract (16,17). It is the fifth most common cause of cancer death in men (18). Incidence of bladder cancer in different countries varies considerably with higher rates in Great Britian and United States of America than Japan and Finland (19,20).

AGE

Bladder cancer can occur at any age but it is generally a disease of the middle aged and elderly. The median age at the diagnosis of urothelial carcinoma varies in different studies. It is 69 years for male and 71 years for females (17,18,21).

GENDER

This disease has strong male predominance with male to female ratio of 2.7:1.7 (22). In other studies a much higher male predominance is reported with a ratio of 5:1 (23).

OCCUPATIONAL EXPOSURE

Aniline dyes, introduced in the late 1800's to color fabrics, have been strongly implicated as urothelial carcinogens. Occupational exposure accounts for 15-35% of cases in men and 1-6% in women respectively in United States (24). Workers in the chemical dye, rubber, petroleum, leather printing industries are at increased risk. The specific chemical carcinogens encountered in these occupations are benzidine, beta-naphthylamine and 4-amino biphenyl (16). Populations exposed to high arsenic levels in their water supply have reported elevated bladder cancer mortality and incidence rates (25).

CIGARETTE SMOKING

Cigarette smokers have up to a fourfold higher incidence of bladder cancer than non smokers (19). It accounts for 50% and 31% of cases in men and women, respectively (24). The etiological chemical agents are thought to be alpha and beta naphthylamine, which are secreted in the urine of smokers (4). Interestingly there is no increase in risk for bladder cancer with coffee and tea drinking (4).

ANALGESIC ABUSE:

Consumption of large quantities (5-15 kg over a 10 year period) of phenacitin is associated with an increased risk for transitional cell carcinoma of the renal pelvis and of the bladder (4,26).

CHRONIC CYSTITIS AND OTHER INFECTIONS

Chronic cystitis n the presence of indewelling catheters or calculi is associated with an increased risk for squamous cell carcinoma of the bladder (27).

Schistosoma hematobium cystitis is causally related to the development of bladder cancer, often squamous cell carcinoma (20). In Egypt where schistosomiasis is endemic among males, squamous cell carcinoma of the bladder (Bilharzial bladder cancer) is the most common malignancy however the mechanism of carcinogenesis is not known yet (17). It is presumed that formation of nitrite and N-nitoso compounds from parasitic or microbial metabolism in the urine is responsible. However in most of the cases squamous metaplsia of the transitional epithelium is the preceding change.

Other causes which may be associated with increased risk for bladder cancer are pelvic irradiation, cyclophosphamide therapy and tryptophan metabolites (4).

STATUS IN PAKISTAN

In Pakistan the incidence is almost similar to global incidence. A multicenter study reported on the epidemiology of cancer in Pakistan conducted by Pakistan Medical Research Council (PMRC) ranked the bladder cancer among the first ten cancers in male and is on the top of the list of urological malignancies (28,29).

Another multicenter study on frequencies of malignant tumors in Pakistan for the period 1977-1980 showed the percentage of carcinoma of urinary bladder among all cancers as 4.1, 3.7, and 2.5 at Lahore, Peshawar, Karachi and Hyderabad centers respectively (30).

In the study carried out in Karachi by Hashmi and coworkers (1995) male preponderance was reported with male to female ratio of 4.3:1 with a peak age group between 51-60 years (31). Same study also established that etiologically occupational factors were involved in 13.6% of cases of bladder cancer. The occupations at risk identified in their study were petrol pump workers, tailoring, leather work and hair dressing. The history of smoking was present in 68% of the patients with variable duration (32).

MATERIALS AND METHODS

STUDY DESIGN

This is a validation study of a series of sixty cases suspected cases of bladder malignancy or known cases of bladder tumors who presented as recurrent growths.

SETTING

This study was conducted in the Department of Pathology, Allama Iqbal Medical College, Lahore, in collaboration with the Department of Urology, Jinnah Hospital, Lahore.

DURATION

The study was completed in six months after the approval of the synopsis.

SAMPLE SIZE

Sixty clinically and radiologically suspected cases of

urothelial malignancy were included in the present study.

SAMPLING TECHNIQUE

Non probability, purposive sampling technique was used in this study.

SAMPLE SELECTION

INCLUSION CRITERIA:

1. Patients above 45 years of age
2. Both sexes.
3. Patients having macroscopic hematuria.
4. Patients having imaging evidence of urinary bladder lesion.
5. Patients with recurrent tumor.

EXCLUSION CRITERIA:

1. Patients with long term indwelling urinary catheter.
2. Patients with history of urolithiasis.
3. Patients with clinical / laboratory confirmed urinary tract infection.

SAMPLE COLLECTION :

Sixty clinically and radiologically suspected cases of bladder cancer were selected from the outpatient and indoor department of Urology, Jinnah Hospital, Lahore. The demographic profiles including the age, sex, occupation, socioeconomic status, address and contact numbers were recorded on the performa. Relevant history regarding the intensity and duration of the symptoms were recorded on the performa. History of previous surgery for bladder tumor, ultrasonographic and computed tomographic findings were also recorded. After admission of the patient to Urology ward, his/her fresh voided urine sample and bladder washing samples were collected, followed by cystoscopic biopsy.

RESULTS:

The present study was conducted at the department of Pathology in collaboration with the Urology department, Jinnah Hospital, Lahore. A total of 60 patients with suspected bladder carcinoma were selected through urology outpatient department. Clinical parameters were recorded. Patients underwent radiologic studies. Ultrasonography was performed in all the patients. Fresh voided urine and bladder washings were collected and cytological examination performed. Following that the patients were subjected to cystoscopy and biopsy was taken from the suspected area for histopathological examination. Variables have been placed in the same order as in the SPSS spread sheet.

AGE INCIDENCE:

Age of the patients in the present study ranged from 50 to 81 years. The mean age was 61 years. The minimum age was 50 and maximum was of 81 years (Figure 1).

SEX DISTRIBUTION:

There were 55 males (91.7%) and 5 females (8.3%) amongst the total of 60 patients included in the present study (Figure 1). The male to female ratio was 4:1 for the study population.

ENVIRONMENTAL / OCCUPATIONAL RISK FACTORS:

We tried to evaluate our cohort of patients for any association of carcinoma bladder with the known environmental or occupational risk factors. Twenty one (35.0%) of the patients were labourers, 9 (15%) were shopkeepers and 8 (13.3%) were farmers by profession in our study group. Taking into account the known occupational risk factors for bladder cancer, 3 (5.0%) patients were leather factory workers, one (1.7%) was working in a paint factory and one (1.7%) in a shoe making factory (Figure 2). Interestingly all the female patients were house wives with no occupational exposure to known chemical carcinogens for bladder cancer. Smoking being strongly implicated as a risk factor for bladder cancer was also enquired about regarding its duration and frequency. Fifty two (86.7%) patients gave history of smoking cigarettes with a mean of 16 cigarettes per day. The range of cigarettes smoked per day was from 10 to 40 in number (Figure 3). Eight (13.3%) patients also gave history of hukka smoking in addition to the habbit of smoking cigarettes. One (1.7%) female was a pan chewer and 3 (5.0%) males were used to niswar cheweing.

Figure 2: Pie Chart Showing the Occupational Status of Patients in the Study.

Figure 3: Bar Chart Showing Number of Cigarette SmMODE OF PRESENTATION:

Painless, off and on macroscopic haematuria was the presenting complaint in all our patients in the study group. Duration of the symptoms was told in months by the patient which was converted to number of days with the range of 7 to 120 days in this study group (Figure 4). The mean duration of hematuria was 68.11 days. Sixteen (26.7%) patients presented in the outdoor 60 days after initiation of the symptoms. The haematuria was graded as mild, moderate and severe with 43 (71.6%) 8 (13.3%) and 9 (15%) patients presenting with mild, moderate and severe grades respectively.oked per Day (n=52).

Figure 4: Bar chart showing duration of Hematuria (n=60)

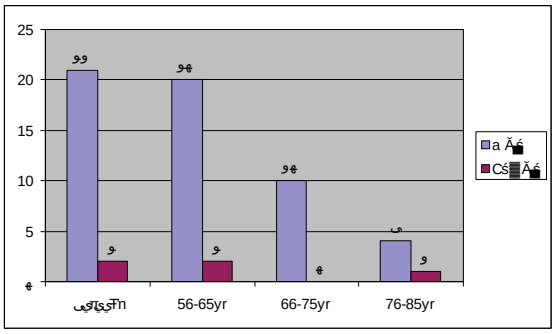
Some additional presenting features were also recorded in the study population. Fever was also observed as one of the presenting features. Thirteen

(21.7%) patients out of 60 had fever with 7 (11.7%) having high grade and 6 (10.5 %) presented with low grade fever. The minimum duration of the fever was 5 days and maximum was 60 days.

Painful micturation was seen in 3 (5.0%) of the patients. None of the patients complained of burning micturation or any uretheral discharge. All the patients in the study group had a history of weight loss associated with the symptoms. None of the patients had history of renal or urinary bladder stones. Six (10.0%) patients out of 60 had under gone surgery for the urinary bladder tumor in the past and had presented now with the recurrent tumor. The duration of the previous surgery was less than 2 years in all the 6 patients. One of the patients also had the history of the previous intravesical chemotherapy.

RADIOLOGIC INVESTIGATIONS;

All the patients in the study group underwent ultrasonograhy of the abdomen and pelvis. Lesions were identified and the site and the size of the lesions were reported by the radiologist. Seventeen (30.0%) of the lesions were on the posterior wall and 17 (30.0%) were on the left lateral wall of the urinary bladder, followed by 12 (18.3%) on the right lateral wall, 4 on the base, 4 on the anterior wall and 3 at the trigone (Figure 5). Three of the cases had focal wall thickening. No definite growth was seen in these patients. The maximum size of the cystoscopically visible lesion was revealed as 12x9x4cm whereas the minimum size was 1x1x1cm. Nine of the lesions

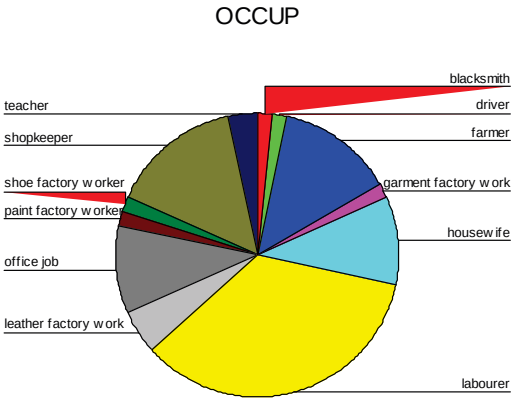


were 4x3x2cm while in the size category of 2x2x1cm again 9 lesions were present. The remaining cases were scattered in between the range. CT scan was performed in only 16 (26.7%) of the patients which confirmed the ultrasonographicaly detected lesion. We did not analyse CT scan findings in the present study further since the numbers of patients were small.

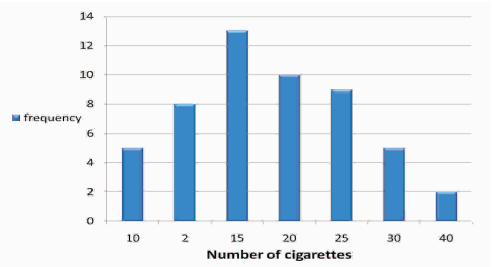
Figure 5: Pie chart showing site of lesion in urinary bladder on ultrasonography.

DISCUSSION

Bladder tumors, the second most common genitourinary malignancy, represent a heterogeneous group of neoplasias. The natural history of these cancers is that of recurrence of disease and progression to higher grade and a higher stage disease. Furthermore, recurrence and progression rates of superficial bladder cancer vary according to several tumor characteristics, mainly tumor grade and the stage (33). The early diagnosis of bladder cancer allows for effective local treatment; transuretheral resection of bladder tumor (TURBT) and intravesical BCG, and optimizes the success of surgical therapy. When detected early, both primary and recurrent bladder tumors can be treated without the need for more aggressive surgical therapies. Presently the diagnostic modalities available are urine and bladder washing cytology, cystoscopy and certain marker studies like Lewis X, NMP22,



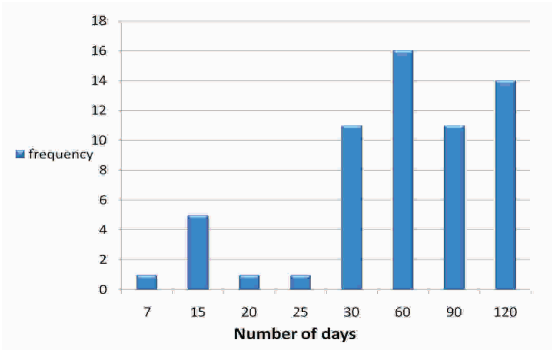
microsatellite analysis (MA), CYFRA 21.1. cytokeratin 20 and the UroVysion fluorescence in situ hybridization (FISH) test (34). Cytological



examination of urinary specimens is increasingly recognized as an essential component of detection and monitoring for patients with bladder neoplasms. Among the available techniques, urinary cytology is

reported as the most useful diagnostic modality (35,36).

Bladder urothelial carcinoma is typically a disease of older individuals and rarely occurs below the age of 40 years (21). Age range of the patients in the present study was 50 to 81 years with a mean age of 61 years. Interestingly one fifth of our total cohorts of patients were at the lower end of the age range (50 years). Weiner et al and Pode et al (1999) in their series reported an age range of 14 years to 102 years and the mean age had been reported between 65-66 years (3, 37). Hashmi et al in their study had similar observations with their patients falling in the age range of 14 to 81 years with peak age between 51-60

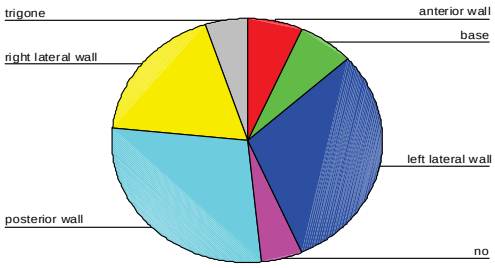


yaers (30). Javed et al (2002) in their study from southern Pakistan reported the same peak age range. The mean age of 61 years in our study group is slightly higher than some of the local reports but is lower than the western studies. The reason could be lower life expectancy in our population as compared to the west.

There is a debate and uncertainty in the literature regarding the clinicopathologic characteristics of bladder urothelail neoplasms in younger patients compared with older patients, although no consistent age criteria have been used to define "younger" age group category. Similar to older patients, bladder urothelail neoplasms in patients 40 years or younger occur more commonly in male patients, present mainly with gross painless hematuria and are more commonly located at bladder trigone / uretheral orifices. In contrast however, these tumors have a greater chance for unifocality (21). Delay in diagnosis of bladder urothelial neoplasms seems not to be uncommon in younger patients probably because of its relative rarity and the predominance of benign causes of hematuria in this age group with resultant hesitancy for an aggressive work-up (21). Lowest age reported in literature is of two cases of well differentiated non invasive transitional cell carcinomas in children aged 8 and 9 years. They underwent complete resection and follow up with urine cytology, vesical ultrasound and check cystoscopy for a period of 4 years. They showed no evidence of recurrence on followup (38).

Studies on the demographic pattern of the bladder tumor report a male predominance with the male female ratio of 4:1 or 3:1 (20, 31, 39). In our study population there were 55 males and 5 females making the ratio 4:1. Hashmi and colleagues in their series reported almost same observation with male to female ratio of 4.3:1 (30). Concurrent with these some of the western studies also reported the ratio between 2.5-4.5:1 (37, 16). The studies from Karachi and Quetta in our country reported the male to female ratio as 4:1 and 4.5:1 respectively (31,39). Javed et al in their study on cystoscopic biopsies reported a male to female ratio of 5.3:1 for bladder cancer (40). The reason for the higher incidence in male is not well understood. However it has been attributed to higher exposure to occupational and non-occupational risk factors in males compared to females (30).

In our study we also analyzed the putative risk factors for bladder cancer. Cigarette smoking is taken as a high risk factor for bladder cancer. Smokers are reported to have up to fourfold higher incidence of bladder cancer than non smokers, attributed to the presence of nitrosamine in tobacco (19). Fifty two of



our patients (86.7%) in the present study were smokers with a range of 10 – 40 cigarettes per day and a mean of 16 cigarettes per day. All these patients were males. One of the females was a pan chewer and 3 male patients were niswar chewers. Eight of the male patients were also hukka smokers along with the cigarette smoking. Concurrently in a study from Quetta a considerable number of patients with bladder cancer were using various preparations of tobacco (Cigarette Smoking: 6%, Hubble Bubble: 50% and Niswar: 12%) (31). Hashmi and his coworkers (1995) reported the incidence of smoking

as 69% in their cohort of patients with bladder cancer (30). This figure is lower than our study which can be attributed to patient selection bias. Several studies in the past have addressed the issue of risk of bladder cancer development in smokers. Howe et al reported a population based case control study of 480 males and 152 females. The relative risk for development of bladder cancer for ever used verses never used cigarettes was 3.9 for males and 2.4 for females, with a dose response relationship in both sexes (41). Randomised case control studies are needed however in our country which can compare the prevalence of cigarette smoking in bladder cancer patients with that in general population.

Bladder cancer being a common malignancy has been well investigated regarding its etiology (42). Multiple chemical agents have been suggested as urinary bladder carcinogens (43). Arsenic is one of these and a high incidence for bladder cancer has been reported in population exposed to high arsenic levels in their water supply (25). The occupational risk factors for bladder cancer are also well established. An increased risk has been reported for workers in the chemical, rubber, photographic, petroleum, medical and food processing industries (41). In the present study 8.4% of our bladder cancer patients were exposed to known occupational risks factors. Hashmi et al (1995) reported a figure of 13% in their study from Pakistan which is higher than our study (30). The discrepancy can be attributed to patient selection in our limited study population. In USA it has been estimated that occupational exposures account for roughly 20% of bladder cancer (41).The higher percentage in western studies may be explained by higher proportion of exposure to industrial and other occupational risk factors in the western population. In our study population the occupational risks encountered were leather, shoe and paint factories, eight patients were farmers and exposure to pesticides could explain the development of urothelial cancer in these cases. All the females in our study group were housewives however.

Bladder cancer is a heterogenous and frequently multifocal disease with a variable clinical course (44). It is suspected on the basis of clinical features. Painless hematuria , a frequent presentation , when encountered in patients over 50 years of age is highly suspicious of bladder cancer unless proven otherwise (16). Haematuria may be gross or microscopic but is usually painless and intermittent. Weiner et al (1998) reported that 70% of patients first presented with hematuria, which was supported by the series of Pode et al (1999) and Ramkumar et al (1999) who reported 80.6% and 68% of their patients presenting with hematuria respectively (3, 37, 45) . In the present study macroscopic hematuria was the presenting feature in all of our patients. Minimum duration of painless hematuria was 7 days whereas the maximum duration was 120 days. The hematuria was graded as mild, moderate or severe with 43 patients presenting with mild hematuria for duration of more than a month in the present study. Late presentation in the course of disease accounts for the high prevalence of gross hameturia since presentation to the urologist by the patient at the stage of microscopic hemeturia is rare.

Only 3 of our patients presented with painful micturation. We did not encounter any case of irritative voiding symptoms alone in our study. Western studies suggest that an irritative voiding symptom is second most common mode of presentation which is usually associated with carcinoma in situ (47,48). It was again emphasized by later series of Ramkumar et al (1999) (45). They reported 10-30% patients of bladder cancer presenting with irritative symptoms. However the single case in our study diagnosed on biopsy as having carcinoma in situ, presented with mild painless gross hematuria without any irritative symptoms. The prevalence rate of bladder cancer in male patients with Lower Urinary Tract Symptoms (LUTS) is reported to be low (48). Similarly Wu JM et al observed in their cohort of female patients with irritative voiding symptoms that microscopic hematuria was not predictive for bladder cancer (32).

CONCLUSION

We conclude that:

1. Urothelial cancer is more common in males than females and is more prevalent in older age group.
2. Smoking and the occupational risk factors play a major role in carcinogenesis of Urothelial cancers.
3. Painless hematuria is the most common mode of presentation.

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INCIDENCE OF HYPOTHYROIDISM IN HYPERPROLACTINEMIC PRIMARY INFERTILE FEMALES

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Abstract

OBJECTIVE: The objective of this study was to see incidence of hypothyroidism in hyperprolactinemic primary infertile females.

METHODOLOGY: This study was conducted at department of Gynecology unit II Jinnah hospital Lahore and was completed in 6 months, February 2016 to July 2016. It was cross sectional study. DATA was collected using non-probability purposive sampling. 312 cases of diagnosed hyperprolactinaemic infertile subjects were taken from outpatient department of Gynae unit II Jinnah hospital Lahore. Age and other parameters was noted after inform consent form those who meet inclusion criteria. All patients with hyperprolactinemic (as per operational definition) with primary infertility were then enrolled in this study to see their hypothyroidism. From all subjects blood sample was drawn and sent to hospital laboratory for their clinical evaluation regarding hypothyroidism. Then thyroid dysfunction of each patient was measured and noted through TSH and FT4 levels as per operational definition. All data was collected in an attached proforma. RESULTS: The mean age of patients in this study was 31.87 ± 4.80 years. According to duration of marriage 91(29.2%) patients had 2-5 years duration of marriage and 221(70.8%) patients had > 5 years duration of marriage. There were 58(18.6%) patients were obese and 254(81.4%) were non-obese. According to operational definition, 126(40.4%) patients were diagnosed of hypothyroidism. When we stratified data over age, duration of marriage and obesity, we found no association between age, duration of marriage and obesity, p-value > 0.05. CONCLUSION In current study we found high prevalence of hypothyroidism 126(40.4%) patients was diagnosed of hypothyroidism. We found no association between hypothyroidism and age, obesity and duration of marriage. Hence, assessment of serum TSH levels should be mandatory in the work up of all infertile women, especially those presenting with Hyperprolactinemia.

Keywords: primary infertile females, hyperprolactinemic, hypothyroidism, TSH, FT4

Infertility is the inability to conceive after one year of intercourse without contraception. The main causes of infertility are: Male factor in 20 to 30% of cases, anovulation in 10 to 30%, tubal factor in 15%, cervical factor in 5%, endometriosis in 5 to 25% and unexplained causes of infertility in 15 to 30%.[1] However, the causes of infertility may be different in different geographic parts.[2] Since approximately 85% of couples may be expected to achieve pregnancy within that interval without medical assistance, evaluation may be indicated for as many as 15% of couples.[3] Although Pakistan is among the currently most populous countries of the world, and has a population growth rate of around 2%, it also has high rate of infertility (21.9%); 3.5% primary and 18.4% secondary This signifies that more than one fifth of the country's married population is directly associated with this problem.[4] Another study reported the prevalence of infertility reported by Shaheen R, et al in 2010 was 7%. [5]

Hyperprolactinemia is usually associated with menstrual and ovulatory disorders like amenorrhea, oligomenorrhea, anovulation, ovulatory cycles with short or inadequate luteal phase, and galactorrhea.[6] approximately two thirds of women having both galactorrhea and amenorrhea will have hyperprolactinemia. Of that group, approximately one third will have a pituitary adenoma.[7] Estimation of serum prolactin levels is recommended in women with unexplained infertility, any menstrual irregularity

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with or without hirsutism, galactorrhea with or without amenorrea, luteal phase defects, anovulation, anovulatory bleeding, and delayed puberty. Apart from these groups of women, infertile women with regular menses also may have hyperproplactinemia. With the determination of serum prolactin levels, greater attention is now been directed to the clinical and laboratory evaluation of hyperprolactinemic women. Some of the women with galactorrhea and hyperperolactinemia might have primary hypothyroidism. This disease is characterized by low serum level of thyroxine (T4) and decreased negative feedback on the hypothalamopituitory axis. The resulting increased secretion of thyrotropin releasing hormone (TRH) stimulates thyrotrophs and lactotrophs, thereby increasing the levels of both thyroid stimulating hormone (TSH) and prolactin

Hyperprolactinaemia, the presence of abnormally high levels of prolactin in the blood is the most common endocrine disorder of the hypothalamic-pituitary axis.[8] Hypothyroidism and hyperprolactinaemia are found to be closely interrelated. Some of the women with high prolactin levels have been diagnosed with hypothyroidism, which is characterized by high levels of serum TSH.[8] Hyperprolactinaemia present in as high as 9 to 17% in women with reproductive disorders.[9]

Verma I et al reported that hypothyroidism is present in 2-4% in women and Hypothyroidism can affect fertility due to anovulatory cycles, luteal phase defects, hyperprolactinemia, and sex hormone imbalance.[10] Some of the women with high prolactin levels have been diagnosed with hypothyroidism characterized by high levels of serum TSH and low T3 and T4.[11] A local study reported that hypothyroidism in hyperprolactinaemic subjects was observed to be 22.7% (but they took both primary and secondary infertility)[11]. Another study from Sharma N, reported the incidence of hypothyroidism in hyperprolactinemic was 28.26%. [12]

We planned this study to find the frequency of hypothyroidism in hyperprolactinemic primary infertile women. International data support this concept but we need more specified study for our population to investigate frequency of hypothyroidism in hyperprolactinemic primary infertile women.[11] Although a local study was done but they took both primary and secondary infertile women[11] So we will take only primary infertility with female factors, if we find high thyroid dysfunction in hyperprolactinemic primary infertile women it will help to set guidelines to manage the patients of primary infertility by evaluating and managing thyroid dysfunction along with the primary treatment for primary infertile women.

Hyperprolactinemia (HP) is the presence of abnormally-high prolactin levels in the blood. Values lesser than 580 mIU/L are considered normal for women. Prolactin is produced by the anterior pituitary gland and is primarily associated with breast development during pregnancy and induces lactation. However, prolactin also binds to specific receptors in the gonads, lymphoid cells, and liver.[13] Hyperprolactinaemia may occur primarily as a result of normal physiological changes during pregnancy, breastfeeding, mental stress, hypothyroidism, or sleep. Pathologically, it may be due to diseases affecting the hypothalamus and pituitary gland or secondary to disease of other organs such as the liver, kidneys, ovaries and thyroid. Also, it may be as a result of disruption of the normal body regulations of prolactin levels by drugs, medicinal herbs and heavy metals.[14] Hyperprolactinemia causes infertility by increasing the release of dopamine from the hypothalamus which inhibit gonadotrophin- releasing hormone (GnRH) and thus gonadal steroidogenesis and eventual infertility.[15]

Thyroid disease had been shown to be associated with increased risk of prematurity or stillbirth[16]. The prevalence of hypothyroidism in women of reproductive age (20-40 years) varies between 2% to 4%. In primary hypothyroidism the serum thyroxine (T4) level is low and there is decreased negative feedback on the hypothalamopituitary axis. The resulting increased secretion of thyrotropin relea-

sing hormone (TRH) stimulates the thyrotrophs and lactotrophs, thereby increasing the levels of both thyroid stimulating hormone (TSH) and prolactin and thus ovulatory dysfunction due to hyperprolactinemia. Prolactin production can also be stimulated by vasoactive intestinal peptide (VIP), epidermal growth factor and dopamine receptor agonists.

OBJECTIVE

The objective of this study was to see incidence of hypothyroidism in hyperprolactinemic primary infertile females.

OPERATIONAL DEFINITION

Primary infertility: It is the inability to conceive for one year with regular unprotected intercourse in the absence of known reproductive pathology (i.e. PCOS, Tubal blockage and pathology on USG) Hypothyroidism: It was labeled if serum TSH was >4.7mIU/L

Hyperprolactinaemia: It is the presence of abnormally high levels of prolactin in the blood, i.e. Prolactin > 500 mIU/L [20 ng/mL or ug/L].

METHODS

This study was conducted at department of Gynecology unit II of Jinnah hospital Lahore and was completed in 6 months, February 2016 to July 2016. It was cross sectional study. Sample of 312 cases with hyperprolactinemic and primary infertility is calculated using expected frequency of hypothyroidism in hyperprolactinaemic subjects is 28.26%.10 Sample is calculated using 95% confidence level, 5% absolute precision using WHO formula. Non-probability purposive sampling technique was used.

Inclusion Criteria:

1- All females with the diagnosis of primary infertility having hyperprolactinemia (as per operational definition), with age between 18-40 years

2- Subjects must have duration of marriage of more than one year

Exclusion Criteria: The patients with following conditions was excluded

- Male factor infertility (was assessed on past medical history)
- Any congenital anomaly of the urogenital tract, or any obvious organic lesion (was assessed on pelvic ultrasound).
- Females with tubal factors (was assessed performing hysterosalpanpingography)
- Patients on treatment for hyperprolactinemia. Any history of thyroid disease or previous thyroid surgery or being on thyroid medications. (Was assessed on past medical history)

DATA COLLECTION METHODS: 312 cases of diagnosed hyperprolactinaemic infertile subjects were taken from outpatient department of Gynae unit II Jinnah hospital Lahore. Age and other parameters was noted after inform consent from those who meet inclusion criteria. All patients with hyperprolactinemic (as per operational definition) with primary infertility were then enrolled in this study to see their hypothyroidism. From all subjects blood sample was drawn and sent to hospital laboratory for their clinical evaluation regarding hypothyroidism. Then thyroid dysfunction of each patient was measured and noted through TSH and FT4 levels as per operational definition. All data was collected by an attached proforma.

DATA ANALYSIS: Data was entered and analyzed through SPSS version 18. Mean ± standard deviation was calculated for all quantitative variables like age, TSH and FT4. Frequency and percentages was calculated for all qualitative variables like hypothyroidism (yes or no). Data was stratified for age, BMI (obesity) and duration of infertility. Chi-square test was applied post stratification with p-value ≤ 0.05 considered as significant.

RESULTS:

The mean age of patients in this study was 31.87 ± 4.80 with minimum and maximum age 18 and 40 years. Table-1

- A total of 88(28.2%) patients were 18-29 years

old and rest of 224(71.8%) were 30-40 years of age. Table-2

- According to duration of marriage 91(29.2%) patients had 2-5 years duration of marriage and 221(70.8%) patients had > 5 years duration of marriage. Table-3
- There were 58(18.6%) patients were obese and 254(81.4%) were non-obese. Table-4
- The mean TSH was 4.70 ± 2.37 with minimum and maximum value of 1.10 and 17.60. Table-5
- According to operational definition, 126 (40.4%) patients were diagnosed of hypothyroidism. Table-6
- When we stratified data over age, duration of marriage and obesity, we found no association between age, duration of marriage and obesity, p-value > 0.05. Table-7,8,9

Table 1: *Descriptive Statistics of Age (Years)*

AGE (years)	Mean	31.87
	Std. Deviation	4.80
	Range	22.00
	Minimum	18.00
	Maximum	40.00

Table 2: *Frequency Distribution of Age Groups (Years)*

		Frequency	Percent
Age groups	18-29	88	28.2
	30-40	224	71.8
	Total	312	100.0

Table 3: *Frequency Distribution of Duration of Marriage*

		Frequency	Percent
Duration of marriage (years)	2-5	91	29.2
	> 5	221	70.8
	Total	312	100.0

Table 4: *Frequency Distribution of Obesity*

		Frequency	Percent
BMI	Obese	58	18.6
	Non-obese	254	81.4
	Total	312	100.0

Table 5: *Descriptive Statistics of TSH*

	TSH
Mean	4.70
Std. Deviation	2.37
Range	16.50
Minimum	1.10
Maximum	17.60

Table 6: *Frequency Distribution of Hypothyroidism*

		Frequency	Percent
Hypothyroidism	Yes	126	40.4
	No	186	59.6
	Total	312	100.0

Table 7: *Comparison of Hypothyroidism in different Age Groups*

		Hypothyroidism		Total
		Yes	No	
Age Group (years)	**18-29**	32	56	88
		25.4%	30.1%	28.2%
	30-40	94	130	224
		74.6%	69.9%	71.8%
Total		126	186	312
		100.0%	100.0%	100.0%

p-value=0.364

Table 8: *Comparison of Hypothyroidism with Respect to Duration of Marriage*

		Hypothyroidism		Total
		Yes	No	
Duration of marriage	**2-5 years**	33	58	91
		26.2%	31.2%	29.2%
	>5 years	93	128	221
		73.8%	68.8%	70.8%
Total		126	186	312
		100.0%	100.0%	100.0%

p-value=0.341

Table 9: *Comparison of Hypothyroidism in different Age Groups*

		Hypothyroidism		Total
		Yes	No	
BMI	**Obese**	27	31	58
		21.4%	16.7%	18.6%
	Non-obese	99	155	254
		78.6%	83.3%	81.4%
Total		126	186	312
		100.0%	100.0%	100.0%

p-value=0.289

DISCUSSION

A study reported, most of the women were in the age group of 24-28 years in both the groups.[17] One more study reported maximum of 106 (53%) cases were in the age group of 26 - 30 years, with the mean age as 27.50±3.76years.[5] We in this study found mean age of patients in this study was 31.87 ± 4.80 with minimum and maximum age 18 and 40 years. A total of 88(28.2%) patients were 18-29 years old and rest of 224(71.8%) were 30-40 years of age. In this study mean age was comparable to both cited studies. [9,17]

A study reported the mean duration of infertility in the patients with primary infertility was 4.58 years and in those with secondary infertility 3.39 years.[17] we found duration of marriage 91(29.2%) patients had 2-5 years duration of marriage and 221(70.8%) patients had > 5 years duration of marriage. There were 58(18.6%) patients were obese and 254(81.4 %) were non-obese in present study. Similarly, in literature the serum TSH in the infertile group was 9.05±2.64 that higher to our study.18 we also found mean TSH was 4.70 ± 2.37 with minimum and maximum value of 1.10 and 17.60.

A study reported the incidence of hypothyroidism in hyperprolactinemia was 25.5% but they took cases of primary and secondary infertility.[17] Singh et al in hypothyroidism was diagnosed in 57% of the women.[19] One more study reported frequency of hypothyroidism was diagnosed in 22% in Hyperprolactinemic infertile women.[20] A study in 2009 reported hypothyroidism was seen in 8% of the infertile subjects whereas in the control group it was found to be 5%.[21] Agarwal et al reported that 21.73% cases of hyperprolactinemia had hypothyroidism.[5] In current study 126(40.4%) patients were diagnosed of hypothyroidism that is comparable (is high) to few reported studies[9,17,20] and lower to that's study of Singh.[19] When we stratified data over age, duration of marriage and obesity, we found no association between age, duration of marriage and obesity, p-value > 0.05

So the increased prevalence of upper normal limit of TSH and raised anti-thyroperoxidase antibody titer indicate, relatively more frequent occurrence of compensated thyroid function in infertile women. This finding necessitates considering such cases for a thorough investigation of pituitary-thyroid axis. In addition, as some patients may exhibit the clinical picture of hypothyroidism despite normal TSH and free thyroxin (FT4) concentrations, so investigation of hypothyroidism in these females should be considered in routine lab investigation.[21]

CONCLUSION

In current study we found high prevalence of hypothyroidism. 126(40.4%) patients was diagnosed of hypothyroidism. We found no association between hypothyroidism and age, obesity and duration of marriage. Hence, assessment of serum TSH levels should be mandatory in the work up of all infertile women, especially those presenting with Hyperprolactinemia.

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FREQUENCY OF HISTOPATHOLOGICAL FINDINGS IN HYSTERECTOMY SPECIMEN OF PATIENTS WITH ABNORMAL UTERINE BLEEDING IN PERIMENOPAUSAL AGE GROUP

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Abstract

OBJECTIVE: To determine the frequency of common histopathological findings/diagnosis in hysterectomy specimens of patients with abnormal uterine bleeding in perimenopausal age group.

METHODS: The study was conducted at the Department of Histopathology, Services Institute of Medical Sciences, Lahore. All patients fulfilling the inclusion criteria were taken from Gynae Outpatient Department of Obstetrics &Gynecology, Services Hospital Lahore. After assessment of patients, the history, clinical examination and investigations by gynecologist, hysterectomy was performed and specimens were sent for histopathology in 10% formalin. The formalin fixed samples were routinely processed and 4-5µ thick sections were cut from paraffin blocks. The sections were stained by routine haematoxylin and eosin stains and additional special stains if required. After microscopic examination by consultant along with researcher, diagnosis was made.

RESULTS: There were 31.4% patients in age group between 40-43 years and 41.9% patients in age group 44-47 years and 26.7% patients in age group 48-51 years with mean age 45.19±3.14 years. According to histopathological findings, 5.2% patients had endometrial polyps, 25.2% had adenomyosis, 32.8% had leiomyoma, 18% had endometrial hyperplasia, 13.3% had chronic endometritis and 5.2% had endometrial carcinoma.

CONCLUSIONS: Histopathological examination of endometrial biopsy is a major diagnostic tool in evaluation of abnormal uterine bleeding and a specific diagnosis could help the gynecologists to plan therapy for successful management of abnormal uterine bleeding.

Keywords: Frequency, Histopathological findings, Abnormal uterine bleeding, Perimenopausal.

Abnormal uterine bleeding is diagnosis of exclusion in which there is abnormal bleeding (i.e. quantity, frequency, duration, regularity) from the uterus not caused by pelvic disease, uterine fibroids, ovarian cysts, endometrial polyps, coagulation disorders, malignancy, inflammation, medical illness or pregnancy. In the general population, abnormal uterine bleeding is estimated to affect 11% to 13% of reproductive age women at any given time; this prevalence increases with age, reaching 24% in those ages 36 to 40 years.1,2

The International Federation of Gynecology and Obstetrics (FIGO) Classification recommends a structured history followed by uterine evaluation of patients presenting with abnormal uterine bleeding (AUB).4 The FIGO classification includes nine categories of abnormal bleeding arranged according to the acronym PALM-COEIN.4,5 Four have objective visual criteria detected by imaging, biopsy or pathology (i.e.; PALM: polyps; adenomyosis; leiomyoma and malignancy and hyperplasia) while another five are not directly related to structural abnormalities (i.e.; COEIN: coagulopathy; ovulatory dysfunction; endometrial; iatrogenic and not yet classified).

Abnormal uterine bleeding occurs most commonly

at beginning and end of

repro reproductive years.6 Peri-menopause is the period 2-8 years preceding

menopause and 1 year after the final menses (WHO).

To diagnose the true pathology, endometrial sampling is important. Endometrial tissue can be obtained through various techniques like Pipelle and Vebra. Among these methods, uterine curettage or biopsy remains a preferred sampling procedure. Since the early 20th century, hysterectomy has been a definite treatment of pelvic pathologies including abnormal uterine bleeding. It is one of the most common surgical procedures with a rate of 6.1-8.6/1000 in all the age groups. The ultimate diagnosis can be made only by histopathology and so every hysterectomy specimen should be subjected to a histopathological examination.7

In one local study, the most common histopathological finding was endometrial hyperplasia (30%), followed by chronic endometritis (13%), endometrial polyps (12%) and leiomyomas (7%). While frequency of malignancy was low (5%).8In another local study, PALM-COEIN categorization was done which showed 3% polyps, 15% adenomyosis, 25% leiomyoma, 6.6% malignancy and hyperplasia.9

In contrast, fibroid uterus was responsible for abnormal uterine bleeding in 54% followed by adenomyosis 29.4% in another study.10According to a study in India, adenomyosis was the commonest pathology (46.34%) followed by leiomyoma (41.46%) in perimenopausal age.11

The rational of this study is to provide the local magnitude of the problem because local data is very much conflicting and also differs from international data and most of the literature is focused on post-menopausal bleeding while the present study will give the assessment of architectural evaluation of endometrium in peri-menopausal age group so that comparison can be done with international data and new suggestions and recommendations can be planned for routine management principles of women with abnormal uterine bleeding.

Methods:

This was a descriptive cross-sectional study, conducted in Department of histopathology SIMS in collaboration with Gynae department of Services hospital Lahore. Study was completed in one year (January2013 to February 2014).After taking approval from hospital ethical committee, patient's demographics and clinical data was recorded. . After assessment (i.e.; history, clinical examination and investigations) by gynecologist, hysterectomy was performed and specimens were sent for histopathology in 10% formal saline. The formalin fixed samples were routinely processed and 4-5µ thick sections were cut from paraffin blocks. The sections were stained by routine haemotoxylin and eosin stains and additional special stains if required. After microscopic examination by consultant along with researcher, diagnosis was made. All the data was entered in the attached proforma to record different outcome variables like polyps, adenomyosis, leiomyoma, hyperplasia, endometritis or malignancy.

Data was analyzed using SPSS (Statistical Package for Social Sciences) version 17. Quantitative variable like age was presented by means ± SD (Standard Deviation), while qualitative variables like histopathological findings including polyps, adenomyosis, leiomyomas, endometritis, hyperplasia or others by calculating frequency and percentages.

Results:

From January 2013 to February 2014,210 women with complaints of abnormal uterine bleeding were included in this study.

There were 66 patients (31.4%) in age group between 40-43 years, 88 patients (41.9%) in age group 44-47 years and 56 patients (26.7%) in age group 48-51 years. The mean±SD of age was 45.19±3.14 years (Table 1).

According to histopathological findings, 11 women (5.2%) had endometrial polyps, 53 women (25.2%)

had adenomyosis, 69 women (32.8%) had leiomyoma, 38 women (18%) had endometrial hyperplasia, 28 women (13.3%) had chronic endometritis and 11 women (5.2%) had endometrial carcinoma (Table 2).

Table-1: *Frequency and Percentage of Age*

Age (years)	Frequency	Percentage
40 – 43	66	31.4
44 – 47	88	41.9
48 – 52	56	26.7
Mean±SD	45.19±3.14	

Table-2: *Frequency and Percentage of Histopathological Findings*

Histopathological finding	Yes		No	
	No.	%	No.	%
Endometrial polyps	11	5.2	199	94.8
Adenomyosis	53	25.2	157	74.8
Leiomyoma	69	32.8	141	67.1
Endometrial hyperplasia	38	18.0	172	82.0
Chronic endometritis	28	13.3	182	86.7
Others (Endometrial CA)	11	5.2	199	94.8

Figure-1:*Endometrial Polyp*

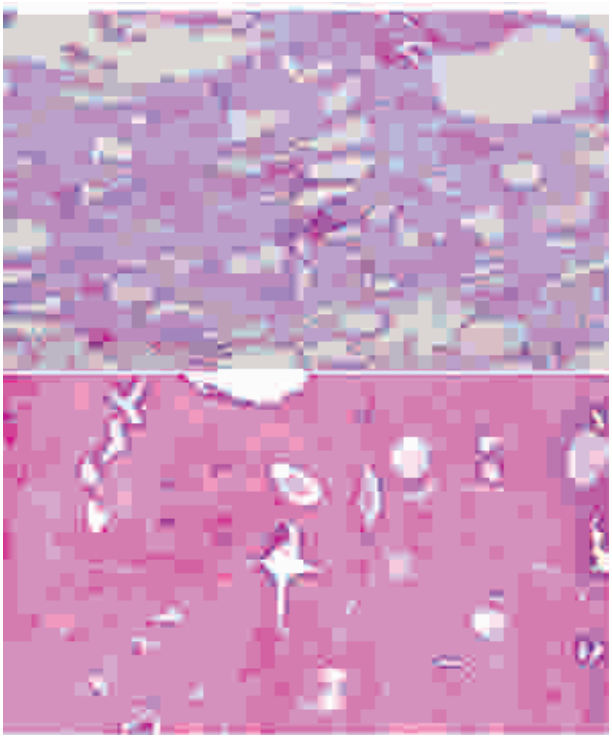

Figure 2&3:*Simple Hyperplasia &Atrophic Endometrium*

DISCUSSION

Abnormal uterine bleeding is the main reason women are referred to gynecologists and accounts for two thirds of all hysterectomies.91 Evaluation of patients with abnormal uterine bleeding and identifying those with dysfunctional uterine bleeding is achieved with a combination of the following: history, physical examination, ultrasound and histopathological evaluation. Abnormal uterine bleeding in perimenopausal women is associated with endometrial carcinoma in 10% patients91, so evaluation of women's risk factors for endometrial hyperplasia or carcinoma is recommended.

Saadia et al95 reported the age of the patients presenting abnormal uterine bleeding ranged from 20 to 65 years with a mean age 42.5 years in their study. Vaidya et al96 also reported the age of such patients from 18 to 70 years with a mean age of 43 years. Whereas in the present study the age range was 40-52 years with mean age of abnormal uterine bleeding of the patients is 45.19 years (Table 1). The results are consistent with the local and international studies.

Abnormal uterine bleeding can be a significant symptom of underlying malignant lesions affecting

female genital tract. Abnormal bleeding is observed in 80 to 90% of pre and post-menopausal woman with endometrial cancer. A careful diagnostic approach is necessary in perimenopausal woman with abnormal uterine bleeding because of potential malignant condition. Uterine curettage or endometrial sampling is usually performed to demonstrate the underlying causes of abnormal bleeding. Histopathological diagnosis established in endometrial biopsy was evaluated in the present study, 5.2% patients had endometrial carcinoma, while 94.8% patients had no endometrial carcinoma (Table 2). These results are in accordance with the study conducted by Ozdemiret al97 in Italy who found 5.5% incidence of endometrial carcinoma. Our results are consistent with the international literature.

Conclusion:

As incidence of endometrial carcinoma (5.2%) is very high in our area, so all patients having dysfunctional uterine bleeding during late reproductive age should be screened for any endometrial pathology especially to detect endometrial carcinoma at very early stage. These results clearly show that histopathological study is mandatory for all cases of abnormal uterine bleeding so as to rule out the process of developing or fully developed malignant lesions. This study of endometrial biopsy itself can be of a great help to the gynecologists to plan therapy of a patient, by a close follow up.

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