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Editorial

Original Articles

Case Report

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ARE OUR HEALTHCARE PRACTITIONERS PHARMACOVIGILANT: SHOULD THIS BE AN ISSUE OF CONCERN?

Shahid Mahmood, Maria Arshad,

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Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects of medicines or vaccines or any related problem.[1] Etymologically, the word pharmacovigilance has been derived from "Pharmakon" and "vigilia" meaning "to keep watch of medicinal substance".[2]

Historically, the theme of Pharmacovigilance dates back to year 1848 when a young girl named Hannah from England died after receiving chloroform anesthesia for removal of an infected toenail; however investigation implicating chloroform as the cause of her death remained inconclusive.[3] In 1961, Dr. McBride wrote a letter to the editor of the Lancet Journal in which he suggested a connection between congenital malformation of babies and thalidomide (a drug used as hypnosis and relieving nausea symptoms in pregnancy). He observed that the incidence of congenital malformations of babies (1.5%) had increased up to 20% in women who had taken thalidomide during pregnancy.[4]The tragedy of thalidomide brought to light many problems and critical issues in healthcare system. In particular, this tragedy changed the system of Pharmacovigilance; a systematic reporting of adverse drug reaction (ADR) related to prescribed medicine initiated and a regulatory mechanism evolved.[2] In USA, during 1960s, federal food, drug and cosmetic act required practitioners to provide safety data, whereas United Kingdom introduced yellow card system to report adverse effect of prescribed medicine in 1964. World Health Organization (WHO) started a program for international drug monitoring in 1968.[4]

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In Pakistan, National Drug Policy of Pakistan in 2003 recommended to establish a drug monitoring and surveillance system. Under Drug Regulatory Authority of Pakistan (DRAP) Act in 2012, a drug regularity authority was established with a National Pharmacovigilance Centre (NPC) in federal capital in 2017 and regional pharmacovigilance centers in provincial capitals during 2018.[5,6] Pakistan became the full member of Uppsala Monitoring Centre (UMC) in 2018.[7] The main aim of pharmacovigilance is to provide data on adverse effects of drugs and vaccines after approval for its use in a country. However, it also intends to promote understanding among health care service providers through clinical training and public about safety of medicines. Adverse drug reactions (ADRs) are among the leading causes of death globally. The ADR reporting is an important part of post marketing surveillance of drugs. According to WHO, Adverse drug reaction (ADR) is a response to a drug that is noxious and unintended and occurs at doses normally used in human beings for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function.[7]

Despite all efforts from national healthcare initiatives, there is still lack of awareness among healthcare practitioners about pharmacovigilance and very few of these practitioners even practice to report adverse side effects to the regularity authority. According to a recent study conducted in a public sector tertiary care hospital, one -third of healthcare professionals were not aware of the mechanisms to report adverse drug reactions to drug regulatory authority.[8] Similarly, in another study, 83% of healthcare professionals did not know where and how to report ADR.[9] However, these professionals do realized the necessity to report ADRs. Despite poor awareness, many health professionals showed positive attitude towards reporting ADRs.[10]The main factors associated with poor reporting of ADRs are lack of time to report especially in busy hospitals in developing countries, unavailability of formal

reporting system and no monitoring by the hospital management. It has been observed that the ADR reporting practice among physicians, nurses and pharmacists in Pakistan is far below than expectations.[11] In developed countries, good practice of ADR reporting may be attributed to periodic t raining of healthcare professionals on pharmacovigilance and seminars being conducted on regular basis.[9]

To strengthen spontaneous reporting of an ADR, the Drug Regularity Authority of Pakistan (DRAP) launched an online reporting form named as "Med Vigilance" on DRAP's official website in 2018 which is available for patients, pharmaceutical companies and healthcare professionals to report any adverse drug reaction and adverse events. National Pharmacovigilance Centre (NPC) has provided 'Electronic Reporting System', 'Med Vigilance E Reporting System', 'Med Safety Mobile Application', 'Manual Reporting (Yellow Reporting Form)', and 'Reporting by Industry (E2B Reporting)'. By undertaking these measures, NPC is not only fulfilling WHO's aim of improving patient care and safety from medicine's use perspective but also contributing towards the assessment of benefits, risks and cost- effective use of medicines.[8] However, the healthcare professionals are still not aware of these forms and this has not been taught during medical training of doctors, nurses and specialists. This is need of time to propagate the existence of pharmacovigilance mechanisms in Pakistan and hospital management should ensure that healthcare professionals report ADRs using online forms of DRAP.

Physicians play a critical role in identifying, reporting and treating adverse drug reactions (ADR). Pharmacists also play a crucial role in ensuring drug safety by detecting and reporting ADRs. Pharmacists tend to have highest percentage of knowledge of pharmacovigilance than doctors and nurses.[12]

ADRs pose a serious threat to public health and need urgent attention of health authorities. With growing pharmaceutical companies and their dubious marketing strategies in our hospitals, ADRs reporting is now more important than ever as a mechanism to recognize early the health issues related to the use of new medicines being in market. Under reporting or no reporting may lead to poor drug surveillance and deficient safety measures to protect the health of our patients. There are instances where pharmacovigilance saved considerable numbers of lives. For example, a drug 'practolol' which caused blindness was withdrawn from market in 1998 after five years of approval. Similarly, another drug, 'terfenadine' was withdrawn after thirteen years in market due to adverse reaction of producing fatal cardiac arrhythmia. These examples show that if there is constant watch on ADR by the healthcare professionals, precious lives can be saved.

A holistic approach involving manufacturers, market forces, healthcare professionals and regulatory bodies in healthcare system is required to prevent ADRs. Promotion of spontaneous reporting where healthcare professionals identify and report suspected drug reaction to national drug regulatory bodies and mandatory reporting from manufacturer periodically will ensure reasonable pharmaco-vigilance in Pakistan. ADR reporting practice can also be achieved by periodic training of health professionals, repeated seminars about DRAP procedures and forms, and availability of online systems in wards will improve ADR reporting. DRAP link can be used to learn more about adverse reaction reporting system available in Pakistan: https://www.dra.gov.pk/safety-information/safety-communication/how-to-report-adrs/

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OUTCOME OF DELAYED HYSTERECTOMY FOR PLACENTA PERCRETA IN A TERTIARY CARE CENTER OF A THIRD WORLD COUNTRY— A DESCRIPTIVE STUDY

Alia Zainab Asad,[1] Humna Sajid Sial,[2] Hina Masood,[3] Filza Mukhtar,[4] Fatima Mateen,[5] Mobeen Riaz,[6] Noreen Akmal[7]

Abstract

Objective: To analyze the amount of hemorrhage, damage to the surrounding structures, need for transfusions, PPH, sepsis and mortalities arising as a result of delayed hysterectomies for Placenta Percreta.

Methods: It was a descriptive study conducted at OBGY unit 3, Sir Ganga Ram Hospital from March 2021 to March 2022. Datawastakenfrom speciallymaintainedregistersfor placentaaccretaspectrum. Patients undergoing delayed hysterectomies for inoperable placenta percretas were selected and their data regarding the mentioned outcome measures was collected and analyzed in SPSS.

Results: Thirteen (13) patients underwent delayed hysterectomy in one year. More than half of the patients had four litres or less blood loss. They showed better response to haemorrhage. No relationship of amount of bleeding with interval between the surgeries, previous surgeries or parity was noted. No ureterovesical damage. No sepsis. PPH wasnoted in 15% of patients andmildspotting in 15%.Onedeath of amorbidly obesepatient was observed. No death could be attributed to retention of placenta.

Conclusion: Encouraging results were seen where patient survival was concerned. Excellent results were noted where collateral damage to bladder and ureters was concerned. Minimum complications were noted, making this a viable option for patients with placenta Percreta, the most serious placental condition within the placenta accreta spectrum.

Keywords: Hysterectomy, placenta, percreta, placena accveta, post-partum, haemorrhage.

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Placenta Accreta spectrum is associated with high risk of morbidity and mortality. Various radical and surgical options have been proposed as management. The Percreta subset poses special surgical difficulty as the bladder walls are thinned out and incorporated in the uterine wall, resulting in hemorrhage and ureterovesical damage. In the third world countries, where arranging properly cross matched and screened blood is in itself aproblem, delayedhysterectomywith placenta in situ may be a safer option where patient outcome is concerned. Statistics can help develop confidence in this management option.

There has been a steady rise in the number of patients presenting with morbidly adherent placenta.[1] Cesarean Hysterectomy is the preferred non-conservative approach for morbidly adherent placentae especially for low resource countries, instead of conservative surgeries.[2-4] However, when placenta is percreta the patient has a high risk of the massive hemorrhage, need and complications of massive transfusion, urinary tract injuries and ischemic organ damage,[5-9] even with hysterectomy. Excessive blood loss and resultant massive transfusion has been seen as a significant contributor in maternal mortality.[10] For such patients planned delayed hysterectomy with placenta in situ may be a

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better option.

Planned delayed hysterectomy with placenta in situ is a procedure where the baby is delivered from a high uterine incision at primary surgery. Umbilical cord is tied and replaced inside the cavity and if the placental bed does not bleed, the uterine incision is closed. The abdomen is closed. Patient is scheduled for hysterectomy a few days later.[1,4] Delayed hysterectomyallows placental regression and allows dissection of bladder and parametria without torrential hemorrhage from various aberrant vasculature.[11] Planned delayed hysterectomy avoids the morbidity of severe sepsis associated with conservative approach of retaining the placenta for spontaneous expulsion.[12] However, patients may develop PPH or infections prior to scheduled date of re-surgery. Close liaison of the patient with the hospital staff and 24 hours' access to hospital services is also a very important requirement.[1]

The time of second laparotomy can be anywhere from 3 to 12 weeks postpartum as quoted by FIGO consensus guidelines[1] and other literature.[2-3] RCOG guideline number 27a considers a week to be "probably" adequate.[4] Selection method of time of second surgery is not clear.

Planneddelayed hysterectomy has shown promising results. However, there is paucity of data on secondary hysterectomy outcomes.[4,11] The largest study to date was carried out in a single center and with limited patients.[13] There is a general reluctance in adoptingthisapproachforthefear of secondaryhemorrhage and double anesthesia and surgeries.

This research is meant to see the outcome of patients who had undergone delayed planned hysterectomy in a period of one year; carried out for placenta percretapatients presenting in gynaeunit 3 of Sir Ganga Ram Hospital. Intraoperative complications of bleeding, collateral damage, and morbidity like decompensation are noted. Inter operative complications like hemorrhage, sepsis or maternal mortality due to bleedingpriortoorduringsecondsurgeryarealsoanalyzed.

METHODS

It was a descriptive study carried out in OBGY unit 3, Sir Ganga Ram Hospital from March 2021 to March 2022. Data for a period of one year was taken from pre-maintained register for placenta Accreta spectrum. Patients with placenta percreta having delayed hysterectomy with placenta in situ were included in the study. Pregnant patients with accreta or documented increta, patients with placenta percreta who have any acute illness like fever or infection just prior to first surgery and patients with any coagulopathy were excluded from the study. After ensuring the consent and taking approval from ethical review board, data were collected from Placenta Accreta Spectrum register. Patients undergoing delayed hysterectomy for placenta Percreta alongwith various outcome measures like intra operative hemorrhage, amount of blood transfusions, surgical damage to the surrounding structures and any sepsis or bleeding prior to the second laparotomy were noted, apart from the demographic details and previous surgeries of the patients (Hemorrhage is documented in the notes and register by adding blood loss from the suction bottle and gravimetric method applied on abdominal sponges used) Data analysis was done by SPSS system. Age, parity, number of previous Caesarean sections were noted and analysed. Mean blood loss and any association of the blood loss with parity, previous surgeries, interval between the two surgeries was also analysed. Collateral damage to bladder and ureters was noted. Mortalities andriskfactor of themortality was also analyzed.

RESULTS

A total of 30 patients were enrolled for delayed hysterectomy during this period but 17 of them ended up with primary hysterectomy due to bleeding at the time of Cesarean so the cohort that did have delayed hysterectomy consisted of only 13 patients. The age range was from 21 to 37 years. The mean age was 31 years (Table 1). Parity varied from Para 3 to 5, 46% of patients were P3, 38% were P5, 7.6% were P1 and same i.e. 7.6% were P4. So, majority of the patients were gravid for the 3rd time when they presented and successfully ended up in delayed hysterectomy. One of these patients (7.6%) had a previous one Cesarean

Table 1: Mean age of participants

N	Mean	Std. Deviation
13	31.38	4.556

Table 2: Parity and Previous C-Section

No	Parity	Previous Cesarean
1	3	2
2	3	2
3	3	2
4	5	4
5	4	3
6	2	1
7	5	2
8	5	4
9	5	4
10	3	2
11	3	2
12	5	4
13	3	2

section, seven of these patients (54%) were previous 2, one (7.6%) were previous 3, four (29.6%) were previous 4. Parity and previous surgery shown in table 2 Interval between the two surgeries varied from 3 to 40 days. For three of the patients the data of interval was missing. From the remaining, 40% were operated within a week (7th day inclusive), 40 % were done after a fortnight and 20 % were done in the second week after surgery. So about half of the patients had their surgery within 3 weeks due to one or other reason (Table 3). The range of blood loss was 1.8 to 7 liters.

Table 3: Haemorrhage and Transfusions Required

S. no	Haemorrhage in ltr	Transfusion bags	Interval between two procedures (days)
1	7	7	24
2	1.8	2	7
3	1	2	18
4	4	5	40
5	6	7	14
6	1	2	3
7	1.8	2	24
8	1	0	7
9	5	3	3
10	2	1	8
11	7	7	
12	4	3	
13	2.6	3	

The mean was 3.54 liters. Majority (69.2%) had less than 4 liters of blood loss while 30.7% had more than 4 liters loss. Maximum loss was of 7 liters. None of the patients required a transfusion of more than seven blood bags of various products, during the surgery (Table 4). No correlation was seen between interval between the procedures and amount of haemorrhage at hysterectomy(Table 4). There was no ureteric injury or bladder damage. There was one death in group B but that patient was morbidly obese.

DISCUSSION

Primary hysterectomy can result in excessive loss and damage to bladder and ureters when done for placenta Accreta, more than that seen in delayed hysterectomy.[14]

Hemorrhage is the number one cause of maternal mortality. Adherent placentae have a major share in causing obstetrical hemorrhage. Acquisition of blood is a problem in South Asian countries where the attendants have to arrange for donors. That is why radical procedures like Cesarean Hysterectomy with placenta in situ has been accepted as the safest procedure specially for under developed countries.[3]

However even with primary hysterectomies massive blood transfusions[15] and high morbidity and mortality is seen in placenta percreta subset. No subject in our cohort of patients required massive transfusion which compares very favorably to 42% rate seen in patients having primary hysterectomy for placenta percreta.[16] The blood loss range was from 1.4 to 7 liters. This was less than the loss encountered in our unit for patients undergoing primary hysterectomy with placenta in situ for Percreta. 9 of 13 patients had bleeding below 5 liters . Bladder and ureters are at special risk of injury and can cause long term maternal morbidity. There is no ureteric injury noted and no bladder damage in this cohort. These are very good results when compared to primary hysterectomies.[14] In our studytwopatients presentedwith history of pain lower abdomen. One had associated severe PPH but she had history of domestic abuse. Two patients presented with Per vaginal bleeding ranging from spotting

to mild bleeding and were opened on list prior to scheduled date. Outcome was very good. Risk of sepsis and PPH has placed reluctance over its use as a safe procedure. In our study the mean duration of retention was 14.8 days while the range of interval period between two surgeries was from 3 to 40 days. We did not get any septic patient. One patient presented with low grade fever and was operated upon. She remained healthy afterwards and did not develop sepsis. These results correspond to the largest study to date shows less blood loss and ureterovesical damage and less need of transfusions.[14] Two of the patients in delayed hysterectomy group had presented with APH and pain abdomen, and they had to be managed in emergency. One of the patients had history of Domestic abuse. Both survived without any further complication.

There was one maternal mortality making an incidence of 7.6% which is similar to the 7% mortality reported in delayed group by Lisa et al.[17] However, this patient was morbidly obese and that could have been a significant co-factor in her outcome.

CONCLUSION

Encouraging results were seen where patient survival was concerned. Excellent results were noted where collateral damage to bladder and ureters was concerned. Patients undergoing delayed hysterectomy have a significant reduction in the need for blood transfusion with minimum complications, making this a viable option for patients with placenta Percreta, the most serious placental condition within the placenta accreta spectrum. Our study has limitations because comparison with primary hysterectomy of elective procedures would have given better results which we has not done here as randomization in a case of placenta Percreta, surgically assessed as inoperable, wouldhave been ethically impossible. There is paucity ofdataand much literature is not available.

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RISK OF NON-HEALING IN ISCHEMIC VERSUS NEUROPATHIC DIABETIC FOOT ULCERS IN RELATION TO GRADE, STAGE OF INFECTION AND TREATMENT PROTOCOL: A FOLLOW-UP STUDY

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Abstract

Background & Objectives: Diabetic foot ulcer (DFU) is a potentially crippling consequence of diabetic foot disease. Aim of this study was to determine the risk of non-healing in ischemic as compared to neuropathic diabetic foot ulcers in relation to its grade and stage of infection.

Methods: This prospective non-interventional study was conducted from July 2019 to February 2020 in Diabetes Management Center, Services Hospital Lahore Pakistan. Patients presenting with DFU were assessed for neurological and vascular status in the lower limbs. Ulcer grading was determined by Wagner's and Texas classification. Patients were followed up to 2-6 months for healing status of the diabetic foot ulcer.

Results: Of 132 patients, 97 (73%) patients presented with neuropathic ulcer and 35 (27%) were having ischemic ulcers. Most participants were aged between 40-59 years. Based on Wagner's ulcer classification, it was observed that patient with score 2 had three times more likely to have their ulcer healed compared to those with score 1 and 3 [OR =3.09(95% CI:0.62-15.38, P=0.17)]. Kaplan-Meier survival curves showed that healing pattern among ischemic ulcer is considerably better compared to neuropathic foot ulcers. The evidence of equal survival hypothesis using Log-rank (Mantel Cox) test was statistically significant ($p<0.001$). No statistically significant difference in healing pattern through time was found across Wagner's scoring categories.

Conclusion: Peripheral neuropathy was the commonest pathology underlying DFU presenting at our tertiary level diabetes clinic. Early detection of neuropathy and timely foot care may help prevent ulceration with its often-grave consequences.

Key words: Diabetic foot ulcer, Neuropathy, Ischemia, Neuro-ischemic foot ulcer, Wound infection

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The term "diabetic foot" refers to a condition where the foot of a patient suffering from diabetes develops various levels of ulceration, infection, or damage to the deeper tissues, typically linked with peripheral vascular disease or neurological abnormalities in the lower extremity. A diabetic foot ulcer (DFU) is a full thickness dermal wound below the level of the ankle on exposed or weight-bearing parts of the foot in a patient suffering from diabetes. Diabetic foot disease begins with an infection progressing to foot ulcers, gangrene, foot deformities, and finally may result in amputations. The cost to the individual patient, his family and society, in terms of loss of mobility, low quality of

life, loss of income, and cost of treatment is huge.[1,2] Prevalence of DFU is 6.3% globally,[3] whereas lifetime incidence of foot ulcer in a diabetic person can reach up to 25%.[4] In Pakistan, diabetic foot disease prevalencerangesfrom 4% to 10%, andthe amputation rate after developing foot ulcers is between 8% and 21%.[5] The cost of care of diabetic foot syndrome (DFS) increases significantly following the appearance of foot ulcers. In the first year, it is 5.4 times higher than for diabetic patients without foot ulcers, and in the second year, it is 2.8 times higher.[6] The management of diabetic foot disease costs between 9 to 13$ billion in USA due to lost earning potential and treatment costs.[7] Although hospital stays have become shorter due to better surgical treatment and the use of improved glycemic control and multidisciplinary strategies; the number of major lower extremity amputations has not decreased.[8]

The development of a diabetic foot ulcer is the outcome of various pathological processes, including underlying diseases like peripheral vascular and neuropathy and poor glycemic control; each of which contributes to its genesis and progression. When someone has chronic high blood sugar levels, it triggers a series of metabolic pathways downstream. These pathways include excessive release of cytokines, formation of more advanced glycation end products, increased activity in the polyol pathway, activation of protein kinase C, and a higher level of oxidative stress. Over time, these derangedmetabolicprocesseslead to thedevelopment of vascular insufficiency and nerve damage.[9] Furthermore, when the blood flow to the skin is inadequate due to micro vascular insufficiency, it causes arteriesandarterioles of theskin to contract abnormally.[10]

Diabetic foot ulcers usually begin at vulnerable spots whichareabnormal plantar pressurepointsoccurring as a result of foot deformity, which is a long-term sequel of diabetic peripheral neuropathy.[11-13] Direct consequences of foot ulcers include chronic non-healing ulcers, osteomyelitis, systemic sepsis, amputation and even death. In addition, worsening of glycemic control occurs as a consequence of mobility restriction and wound infection, which in turn leads to progression of other diabetic complications.[14]

Optimum management of foot ulcer requires an accurate ulcer evaluation. This involves assessment of ulcer severity, presence of infection and the underlying patho-physiological condition.[15] Many systems forulcer severity grading have been described, but the most widely usedgrading systemsare the Wagner's classification andthe University of Texasulcer gradingsystems. The former system grades ulcer by its depth and presence of gangrene, while the latter also considers the presence of infection and underlying ischemia.[16] The presence of infection can be assessed clinically and confirmed on wound cultures. The patho-physiological categorization is based upon assessment for the presence of peripheral vascular ischemia and peripheral neuropathy. The former may be tested clinically by checking the ankle brachial pressure index or by peripheral arterial Doppler ultrasound, while the latter evaluation is usually done by peripheral sensory examination using at least a 10g monofilament and tuning fork, and more formally by biothesiometry or nerve conduction studies.[17,18] Previous studies have shown that the vast majority of diabetic foot ulcers occur in neuropathic and neuro-ischemic feet, while purely ischemic ulcers are less common.[19] Some authors have indicated that neuropathic ulcers tend to have a higher grade of ulcer severity as well as a higherrate of infectiondue to continued weight bearing on insensate feet compared to ulcers occurring in feet with intact sensations.[17] On the other hand, among ischemic ulcers, delayed ulcer healing has been observed compared to non-ischemic ulcers.[20]

Clinical characterization of diabetic foot ulcers, including assessment of ulcer severity, presence of infection and an assessment of the underlying etiology is essential for risk stratification, optimizing management, and reducing debilitating complications. This prospective study aimed to determine the risk of non-healing of diabetic foot ulcers in relation to its grade, stage of infection and treatment protocol while comparing ischemic versus neuropathic ulcers and to correlate these with ulcer severity, grading, presence of infection and short term outcomes (complete healing,

non-healing ulcers, amputation and/or death).

METHODS

This prospective, non-interventional study was conducted at a tertiary care teaching hospital of Lahore city in Pakistan. Ethical approval for this study was granted by institutional review board Services Institute of Medical Sciences (SIMS) Lahore (IRB/ 2019/562/SIMS). Participants were recruited between July 2019 and December 2020 and then followed up to June 2021. Sample size of 132 was found to be suitable to detect the effect size. This sample size was calculated using WinPEPI software, taking prevalence of diabetic foot ulcer as 5 % and at 5 % precision around the prevalence, using formula:$n=z^2pq/d^2$ (Where z = 1.96, p=5% and d=5%). Recruitment was consecutive with non-probability convenient sampling technique. Those adult patients with DFU and with serious co-morbid conditions requiring emergency treatment and those unwilling to participate were excluded. Only patients presenting in out-patient department were included in sample. After taking informed consent, patients were clinically evaluated for diabetes status, complications and their management as per departmental guidelines. Peripheral neuropathy was diagnosed based on pain in the feet, legs or hands, decreased or loss of sensation and/or degree of numbness; and confirmed by 10g mono-filament test and 128 Hz Tuning Fork test. Assessment for vascular insufficiency included palpation of arterial pulses in the popliteal, posterior tibial and dorsalis pedis arteries of both limbs, followed by measurement of Ankle brachial index (ABI) using a hand-held Doppler (Vascular Doppler HI DOP – NSL – BT-200V BISTOS (KOREA) with a frequency of 8 mHz on bothsides. ABI>0.9 was taken as normal, while ABI<0.9 was considered to indicate peripheral arterial disease (PAD). PAD was further sub classified into mild to moderate PAD, (ABI 0.4 to 0.9), and severe PAD (ABI <0.4). Ankle brachial pressure index of the patient was measured on both sides, using a handheld Doppler probe and aneroid sphygmomanometer gauge. Biochemical tests like HbA1c, complete blood count, renal function tests, fasting lipid profile were done. A sterile swab was used for wound cultures, taken to confirm infection. Stratification of wound infection was done with Wagner's grade and Taxas grading system (Table 1).[21] Patients were managed according to standard guidelines based upon the type of wound and presence of infection. Modified proforma from the Model of Care for the Diabetic foot was used.22 Considering COVID-19 restrictions, we switched our plan of regular physical follow up for measuring outcomes to interviewing participants on telephone using a structured questionnaire, and using WhatsApp to visually inspect the ulcer site. Non-healing status of neuropathic and ischemic types of ulcers during follow up follow-up time was the primary outcome. SPSS 25.0 version was used to manage data and its coding. Age of participants was examined both as a quantitative and qualitative variable. Sex, type of diabetesmellitus(DM), duration of DM, macrovascular complications, smoking status, status of wound, nephropathic stage (eGFR) were stratified and its comparison was carried out between neuropathic and ischaemic ulcers. Pathophysiological characterization and severity grading of diabetic foot ulcers were also analyzed based on Wagner's and Texas staging and grading system. Statistical significance for difference in proportions and difference in means were calculated using Pearson's Chi-Squared test and Student's t-test respectively. Fisher's Exact test was used when cell values were less than five. P-value less than 0.05 was considered statistically significant.

Logistic regression modelling was used with scores 1 andAinthe Texasstagewereused as referencecategory (OR=1). Model estimates were adjusted for age, sex, type of DM, duration of DM, Control of DM based on HBA1c, and smoking status. Kaplan-Meier survival analysis was used to estimate median healing times and a log-rank test was used to compare healing times for different levels of grade or stage. Hazard ratios with 95% Confidence intervals were estimated using Cox's proportional hazard regression model. Model estimates were adjusted for age, sex, type of DM, duration of DM, Control of DM based on HBA1c, and

smoking status. The proportional hazard assumption was examined and there was no significant violation of this assumption. Non-healing was coded 1 as our primary outcome and P value < 0.05 was considered significant.

RESULTS

The aim of this prospective study was to determinerisk of non-healing of diabetic foot ulcers in relation to itsgrade, stage of infection andtreatmentprotocol while comparing ischemic against neuropathic ulcers. Table 2 describes the baseline characteristic of participants with DFU. Of 132 participants 97(73%) patients had neuropathic ulcers and 35(27%) were diagnosed with ischemic ulcers respectively. Most participants were males with average age of those with ischemic ulcers was two years higher than those with neuropathic ulcers; with majority were between aged 40-59 years; yet no statistically significant difference was observed in these individuals. About 68% patients with neuropathic ulcers were males compared to 74% withischemiculcers.As regardssmokingstatus, no statistically significant difference was observed among those with neuropathic versus ischemic ulcers patients(p=0.66). Mostparticipantshadtype 2 Diabetes Mellitus and more than fifty percent patients had DM for ten years or less (Table 2). Regarding diabetic control of these patients, we found that more than 90% of both neuropathic and ischemic ulcer patients have poor diabetic control with HBAIc level more than 7%. Both neuropathic and ischemic ulcers patients did not give history of myocardial infarction or cardiovascular accidents, however, the difference of reporting myocardial infarction between those with neuropathic ulcer and ischemic ulcers was statistically significant (p=0.007). We found that a total of 33 patients (34%) with neuropathic ulcers and 18 patients (51.4%) with ischemic ulcers had infected wound, but this difference was not found to be statistically significant (p=0.07). Regarding the ulcer outcome in terms of healing, 82 (85%) of the patients with neuropathic ulcers and 26 (74%) patients with ischemic ulcers reported complete healing of ulcer, but there was no significant difference in healing versus non-healing found among these two types of ulcers (p=0.18).

Table 1: *Wagner's and Texas ulcer grading and staging System* [21]

Wagner's ulcer score

Score	Description
1	Superficial ulcer –not infected
2	Deep ulcer, with or without cellulitis, no abscess or bone involvement
3	Deep ulcer with bone involvement or abscess formation
4	Localized gangrene (toe, forefoot, heel)
5	Gangrene of whole foot
Texas's ulcer grading	
1	Superficial wound that does not penetrate tendon, capsule or bone
2	Wound that penetrate tendon or capsule
3	Wound that penetrate bone or joint
Texas's ulcer stage	
A	Clean wound
B	Non-Ischemic infected wound
C	Ischemic non-infected wound
D	Ischemic infected wound

Table 3 represents Pathophysiological characterization and severity/grading of diabetic foot ulcers based on Wagner and Texas classification systems. Using Wagner's ulcer score, categorizing the ulcer based on its depth and presence of gangrene, it was foundthat 55 patientswithneuropathiculcers (56.7%) where having superficial ulcers without infection (Score 1), whereas 23 patients (24%) having deep ulcer with or without infection (score 2). Likelihood of healing DFU based on Wagner ulcer score, it was observedthatpatientwithscore 2 hadthreetimesmore likely to have their ulcer healed compared to those with score 1 and 3; OR =3.09 (95% CI:0.62-15.38, P= 0.17) (Table 4). Comparatively, of 35 patients with ischemic ulcers, 13 (37%) were categorized as score-1 and 10 (28.6%) were given score 3 (deep ulcer with boneinvolvement). The likelihood of healing of ischemic ulcers of those patients with score 3 and above was higher [OR =1.09 (95% CI 0.12 -9.58, P=0.94)] compared to patients at score 1 and 2 (Table 4).

The risk of non-healing of DFU, hazard ratios comparing healing of DFU among patients with neuropathic against ischemic ulcers, in relation to Wagner

Table 2: *Baseline characteristics of participants with diabetic foot ulcers attending Diabetic Centre of Services Hospital Lahore (n=132)*

Characteristics	Patients with Neuropathic ulcers (n=97)		Patients with Ischemic ulcers (n=35)		*P**
	Numbers	Percentage	Numbers	Percentage	
Age (in groups)					
Less than 40 years	10	10.3	02	5.7	0.71
40-59 years	54	55.7	20	57.1	
60 years and above	33	34.0	13	37.1	
Sex					
Males	66	68.0	26	74.3	0.49
Females	31	32.0	09	25.7	
Smoking Status					
Smoker	20	20.6	06	17.1	0.66
Non-Smoker	77	79.4	29	82.9	
Type of Diabetes Mellitus					
Type I DM	23	23.7	08	22.9	0.91
Type II DM	74	76.3	27	77.1	
Duration of Diabetes Mellitus					
10 years or less	54	55.7	18	51.4	0.67
More than 10 years	43	44.3	17	48.6	
Diabetic Control (based on HbA1c)					
Reasonable control (HbA1c <7 %)	05	5.2	01	2.9	0.49
Poor control (HbA1c ≥7 %)	92	94.8	34	97.1	
Ever had Myocardial Infarction					
Yes	13	13.4	12	34.3	**0.007**
No	84	86.6	23	65.7	
Ever had Cardiovascular accident					
Yes	07	7.2	01	2.9	0.32
No	90	92.8	34	97.1	
Had Macrovascular complications					
Yes	14	14.4	12	34.3	**0.01**
No	83	85.6	23	65.7	
Had Intermittent Claudication					
Yes	03	3.1	07	20.0	**0.004**
No	94	96.9	28	80.0	
Have Diabetic Retinopathy					
Yes	14	14.4	04	11.4	0.45
No	83	85.6	31	88.6	
Nephropathy Stage (based on eGFR)					
eGFR 59 or less	15	15.5	06	17.1	0.87
eGFR 60-90	41	42.3	16	45.7	
eGFR>90	41	42.3	13	37.1	
Whether ulcer wound infected?					
Yes	33	34.0	18	51.4	0.07
No	64	66.0	17	48.6	
Ulcer healing outcome					
Healed	82	84.5	26	74.3	0.18
Not Healed	15	15.5	09	25.7	

ulcer scoring, we found that superficial ulcers (Score 2) had higher chance of healing compared to deep ulcers or ulcers with gangrene [HR:0.82 (95% CI: 0.47- 1.43, p=0.48].(Table 5). On the other hand, the estimates for patients with ischemic ulcers for healing pattern using Wagner's ulcer scoring were insignificant and unremarkable (p=0.68). (Table 5).

Figure 1 depicts Kaplan-Meier survival curves

Table 3: *Patho-physiological characterization and severity grading of diabetic foot ulcers based on Wagner and Texas classification, among patients attending Diabetic Centre of Services Hospital Lahore (n=132)*

	Classification system	Patients with Neuropathic ulcers (n=97)		Patients with Ischemic ulcers (n=35)	
Score		**Numbers**	**Percentage**	**Number**	**Percentage**
Wagner's ulcer score					
1	Superficial ulcer –not infected	55	56.7	13	37.1
2	Deep ulcer, with or without cellulitis, no abscess or bone involvement	23	23.7	09	25.7
3	Deep ulcer with bone involvement or abscess formation	15	15.5	10	28.6
4	Localized gangrene (toe, forefoot, heel)	04	4.1	03	8.6
5	Gangrene of whole foot	0	0	0	0
Texas's ulcer grading					
1	Superficial wound that does not penetrate tendon, capsule or bone	78	80.4	28	80.0
2	Wound that penetrate tendon or capsule	16	16.5	06	17.1
3	Wound that penetrate bone or joint	03	3.1	01	2.9
Texas's ulcer stage					
A	Clean wound	59	60.8	11	31.4
B	Non-Ischemic infected wound	28	28.9	08	22.9
C	Ischemic non-infected wound	05	5.2	06	17.1
D	Ischemic infected wound	05	5.2	10	28.6

Table 4: *Likelihood of healing of diabetic foot ulcers in relation to its stage and grades using Wagner and Texas scoring system in patients attending Diabetic Centre of Services Hospital Lahore (n=132)*

Classification system	Patients with Neuropathic ulcers (n=97)			Patients with Ischemic ulcers (n=35)		
Wegener's ulcer score*						
	Odds ratio	95% CI	*p*	**Odds Ratio**	95% CI	*p*
Score 1	**Reference**	**Reference**		**Reference**	**Reference**	
Score 2	3.09	0.62- 15.38	**0.17**	0.37	0.04 - 3.65	**0.39**
Score 3 and above	1.65	0.30 - 8.96	**0.56**	1.09	0.12-9.58	**0.94**
Texas's ulcer grading**						
Grade 1	**Reference**	**Reference**		**Reference**	**Reference**	
Grade 2 and above	5.72	1.09 - 29.87	**0.04**	0.92	0.13 -6.61	**0.93**
Texas's ulcer stage***						
Stage A	**Reference**	**Reference**		**Reference**	**Reference**	
Stage B	2.87	0.34- 24.22	**0.33**	0.41	0.05 - 3.46	**0.42**
Stage C and above	2.02	0.22 - 18.20	**0.53**	0.42	0.03 - 5.49	**0.51**

Footnotes: Logistic regression modelling was used. with score 1 & A in Texas stage were used as reference category (OR=1). Model estimates are adjusted for age, sex, type of DM, duration of DM, Control of DM based on HBA1c, smoking status

* **Wegener's ulcer Score:** Score 1: Superficial ulcer –not infected;Score 2. Deep ulcer, with or without cellulitis, no abscess or bone involvement; Score 3=Deep ulcer with bone involvement or abscess formation; score 4= Localized gangrene (toe, forefoot, heel); score 5= Gangrene of whole foot

** **Texas's ulcer Grading:** Grade 1= Superficial wound that does not penetrate tendon, capsule or bone; Grade 2= Wound that penetrate tendon or capsule; Grade 3= Wound that penetrate bone or joint.

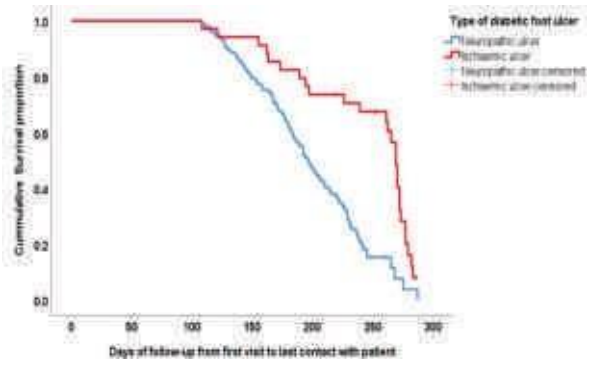
*** **Texas's ulcer stage:** Stage A= Clean wound; Stage B= Non-Ischemic infected wound; Stage C= Ischemic non-infected wound; Stage D= Ischemic infected wound

Table 5: Hazard Ratio with 95% confidence intervals comparing healing of diabetic foot ulcers (neuropathic versus ischemic) in relation to its stage and grades using Wagner and Texas scoring system in patients attending Diabetic Centre of Services Hospital Lahore (n=132)

Classification system	Patients with Neuropathic ulcers(n=97)			Patients with Ischemic ulcers(n=35)		
	Hazard Ratio	95% CI	*p*	Hazard Ratio	95% CI	*p*
Wagner's ulcer score						
Score 1	**Reference**	**Reference**		**Reference**	**Reference**	
Score 2	0.82	0.47- 1.43	0.48	1.06	0.32- 3.48	0.92
Score 3 and above	0.73	0.35- 1.51	0.39	1.22	0.45- 3.30	0.68
Texas's ulcer grading						
Grade 1	**Reference**	**Reference**		**Reference**	**Reference**	
Grade 2 and above	0.28	0.12- 0.63	0.002	1.54	0.52-4.53	0.43
Texas's ulcer stage						
Stage A	**Reference**	**Reference**		**Reference**	**Reference**	
Stage B	1.43	0.84- 2.42	0.17	0.97	0.22-4.33	0.97
Stage C and above	0.98	0.45- 2.13	0.96	0.52	0.15-1.77	0.29

Abbreviations: HR, Hazard ratio; CI, confidence interval; DM, Diabetes Mellitus
Footnotes: Cox's proportional hazard regression modelling was used. Model estimates are adjusted for age, sex, type of DM, duration of DM, Control of DM based on HBA1c, smoking status.

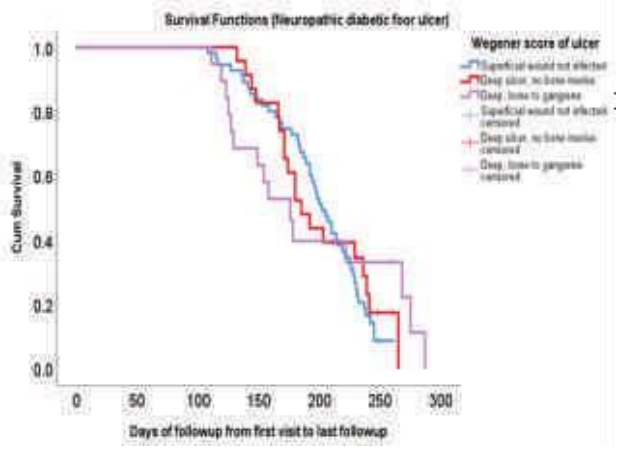
showing healing through time of neuropathic versus ischemic diabetic foot ulcers among patients. We observed that the healing pattern among ischemic ulcer is considerably better compared to neuropathic ulcers and there is strong evidence against the hypothesis of equal healing of ulcers in time (Log-rank (Mantel Cox) test= p<0.001.



Footnote: *Log-rank (Mantel Cox) p<0.001 (Rejecting null hypothesis of equal survivor)*

Figure 1: *Kaplan-Meier survival curves showing healing trend (through time) of neuropathic diabetic footversusischemicdiabeticfootulcersamongpatients attending Diabetic Centre of Services Hospital Lahore Pakistan (n=132)*

Figures 2 depicts the survival pattern (healing) of diabetic neuropathic ulcers (Mantel Cox p =0.86) and diabetic ischemic ulcers (Mantel Cox p =0.07) based on Wagner ulcer scores respectively. We found no statistically significant difference in healing pattern through time across the scoring categories. Finally, we did not find any statistically significant difference in healing through time using Texas staging and grading (data not shown).



Footnote: *Log-rank test (Mantel Cox) p=0.86 (no statistical significant difference in healing)*

Figure 2: *Kaplan-Meier survival curves showing healing trend of diabetic neuropathic ulcers based on Wegener's ulcer score, among patients attending Diabetic Centre of Services Hospital Lahore Pakistan (n=132)*

DISCUSSION

Worldwide, diabetic foot problems have become most prevalent issues which lead to severe economic crises for the patients, their families, and society.[7] The main underlying reasons of diabetic foot ulcers are diabetic peripheral sensory neuropathies, peripheral vascular diseases, and resulting deformities. Additionally, callusformation, edema, andtraumaarecommonly identified as the factors that precede the development of diabetic foot ulcers.

Ourstudyshowedthatthere arecertain risk factors that are associated with foot ulcers, including having diabetes for a longer period of time and having higher HbA1C levels. Males had a higher frequency of foot ulcers, and several studies have shown that advancing age is also a contributing factor to foot ulceration in diabetic patients.[22] We also found that the frequency of foot ulcers was particularly high among those over the age of 50 which is consistent with the findings of a previous study by Khan et al.[25]

Neuropathy plays asignificant role in the development of diabetic foot ulcers (DFU) because it causes the feet to become insensitive and lose their position sense. As a result, patients may injure their feet without realizing it andareunable to takesteps to preventfurther damage, whichimpairsthe healingprocess.[25] Adecrease in foot pulses has been linked to an increased risk of foot ulcers, and this may be a practical clinical alternative to morecomplex peripheral vascular assessments. However, the ankle/brachial pressure index has also been identified as an independent risk factor.[26]

Younis et al. found that 74% of ulcers were neuropathic, 19% were neuro-ischemic, and 7% were ischemic.[19] Our study also found that 73.48% of ulcers were neuropathic, and 26.51% were ischemic, which is similar to study by Younis et al. Other studies have reported that around 45-60% of diabetic foot ulcers are purely neuropathic, while approximately 45% have both neuropathic and ischemic components.[27] Similarly, Shahbazian et al.[28] found that 33.3% of the patients suffering from grade 1 or higher DFU had co-morbidities. In our study, we found that 57% of cases had co-morbidities, including 13.6% with retinopathy, 15.9% with an eGFR of 59 ml/min or lower, and 19.7% with macrovascular complications. These co-morbidities contribute to the development of foot ulcers probably due to factors like generalized ischemia, chronic eczema, oozing ulcers in edematous feet as well as immobility.[25]

Jia et al. Found that 37% of cases had neuropathic ulcers, 28.4% had neuro-ischemic ulcers; ischemic ulcerswerepresented in 6.2%, andtheremaining 28.4% reported having other types of ulcers. The overall infection rate of foot ulcers was 40.1% with the highest rate of 42.1% among neuropathic ulcers, 26.4% of these were ischemic ulcers, and 43.8% neuro-ischemic ulcers were infected ($p = 0.11$). Deep ulcers were found in 6.5% of neuropathic ulcers, 3.8% of ischemic ulcers, and 7.5% of neuro-ischemic ulcers ($p = 0.003\%$).[29] Furthermore, past history of amputation was reported in 28.4% of thecases. In ourstudy, we foundthat 38.6% of patients had wound infections. Neuropathic ulcers accounted for 73% of cases, while ischemic ulcers accounted for 27% of cases. On the other hand, about 34% of the neuropathic ulcers, 51.4% of the ischemic ulcers were infected ($p = 0.07$). Furthermore, 23.7% of neuropathic ulcers and 25.7% of ischemic ulcers had Wagner's grade 2 indicating a deep ulcer without bone involvement.

The most frequent reason for hospitalization relatedto diabetes is footulcerinfection, whichalsoremains a significant cause of amputation of the lower limbs. In the presence of neuropathy or peripheral arterial disease, the typical signs of local infection and the local inflammatory response are masked or reduced. Despite appropriate care, diabetic foot ulcers can progress to gravecomplicationslikeinfections, amputations, or even death. Previous studies indicate that peripheral arterial disease (PAD) is a more significant risk factor for diabetic foot ulcers compared to infection, possibly due to the participants from diverse populations. If a diabetic foot ulcer becomes infected, underlying PAD can speed up the infection's progression, leading to greater risk of hospitalization and ultimately amputation.[30] Our study shows that there was a greater infection rateamongischemictype of DFUs; Regardinghealing

pattern, it was found that comparing neuropathic diabetic foot with ischemic ulcer, healing pattern among ischemiculcer is considerablybetterwhichmaydepend upon the level of care such patients are getting over there; lack of diagnostic facilities for neuropathy at primary health care centers can also lead to a delay in diagnosis. Hence, our suggestion is for patients to receive a thorough evaluation, preferably through non-invasive testing methods such as ABI measurements. This will also create an opportunity for conducting larger-scale studies with a more extensive sample size.

Results of this study should be interpreted after considering few limitations. Participants were recruited using convenient sampling and size of sample was relatively small for precise estimates. These issues might limit the generalization of findings. Follow-up was conducted by telephone (due to COVID-19 lockdown) withimages of woundwerevirtuallyexamined. Thisindirectexaminationmightaffecttheinconsistency of grading of these wounds. We analyzed the data using both descriptive and inferential statistics especially examined the time to event analysis, which is unique for such data and highlight different aspects of exposure and outcome relationship.

CONCLUSION

Risk of non-healing DFU is significantly higher among those with ischemic diabetic ulcers compared to those with neuropathic ulcers. Infected wound at presentation is an important determinant of its subsequent healing. Early detection of neuropathy and preventive foot care may help prevent ulceration with its resultant disability. In most cases, neuropathy was the primary contributing factor to diabetic foot ulcers rather than peripheral arterial disease.

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METABOLIC SYNDROME IN PATIENTS OF CHRONIC KIDNEY DISEASE PRESENTING TO THE NEPHROLOGY DEPARTMENT OF A TERTIARY CARE HOSPITAL.

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Abstract

Background & Objective: The prevalence of metabolic syndrome (MetS) is on rise and is proven to be a known factor for cardiovascular diseases. However, its association with chronic kidney disease is also emerging which can accentuate the risk of cardiovascular events in patients of CKD. Therefore, this study was conducted to determine the frequency of metabolic syndrome and its related factors among patients with chronic kidney disease presenting to the Nephrology outdoor.

Methods: It was a cross sectional study conducted at Nephrology department Jinnah hospital Lahore. About 110 patients of CKD diagnosed for atleast 6 months, aged 18-60 and fulfilling the selection criteria were enrolled after an informed consent by non-probability consecutive sampling. Measurement of blood pressure and central obesity was done as per standard protocol and all the information was recorded in proforma. A 5 ml of blood sample was taken for triglyceride, HDL, and fasting blood sugar levels after ensuring overnight fasting. Frequency percentages were calculated for qualitative variables by using SPSS26. Chi-square test was applied to check statistical significance between metabolic syndrome and effect modifiers.

Results: The Mean age of patients was 42.46 + 5.580 with about 63(57%) being male. Majority had CKD stage-V 64(58%), and had the disease for more than 5 years i.e. 75(68%). The frequency of MetS was 39(35%) with that of high blood pressure 68(62%) being the most common among all components, followed by high fasting plasma glucose levels 52(47%), high triglyceride levels 35(32%), high HDL levels 32(29%) and central obesity 30(27%). A statistically insignificant relationship of MetS was seen on stratification for age, gender, duration, and stage of CKD.

Conclusion: It can be concluded that a considerable frequency of MetS 35% is present among patients with CKD. Thus, there is a dire need to screen all the patients with CKD for the presence of MetS as an essential component of their routine follow up. This will help in its early diagnosis and management which may halt the disease progression and decrease the morbidity and mortality associated with this lethal but manageable double burden of disease.

Keywords: chronickidneydisease(CKD), metabolicsyndrome(MetS), end-stagerenaldisease(ESRD)

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Chronic kidney disease (CKD) is increasingly recognized as a global public health problem with a prevalence of 11% to 14%.[1] Globally, the CKD mortality rate had enhanced up to 42% approximately in 2017.[2] CKD is responsible for 60% of the 58 million fatalities worldwide, with 4 out of 5 deaths occurring in low- and middle-income countries, and it is antici-pated that by 2030, chronic diseases would account for three of the four primary

causes of death, suggesting aseriousthreat to healthand health system.[3] Moreover, CKD increases the risk of death, cardiovascular events, and hospitalization leading to a greater disease burden especially in under-developing countries.[3]

Metabolic Syndrome (MetS) is characterized as having three or more of the five risk factors according the World Health Organization criteria: abdominal obesity, fasting serum triglycerides (>150 mg/dl), fasting lower high-density lipoprotein (HDL) cholesterol levels (<40 in males & <50 mg/dl in females), blood pressure > 130/85 mmHg (lying), and serum fasting glucose > 110 mg/dL, MetS have been linked to CKD in several studies.[5,7–9] Moreover, each element of MetS has been linked to the onset and development of CKD. A complicated bidirectional correlation exists between MetS and CKD. Obesity is also associated with CKD and both are on the rise in both advanced and developing worlds.[2,10,11] Lin et al. evaluated the relationship between CKD and MetS, revealed that the participants with MetS were significantly more likely to have CKD than those without MetS, and MetS is an independent risk factor for CKD. Therefore, an effective screening program for the early detection of people with MetS is required.[12]

Across-sectional studywas conductedearlier with the goal to find out the prevalence and association between MetS and CKD patients. Among the five components of MetS, waist circumference has the highest positivepredictivevaluefor CKD. Thestudyconcluded that MetSoccurs inmore thanone-third of CKDpatients which is quite alarming.[13] Hassan et al. conducted a cross-sectional study, which also showed similar results that a considerable number of patients of CKD had metabolic syndrome.[14]

The rationale of this study is to identify the frequency of MetSamongpatients with CKD. In Pakistan, the prevalence of cardiovascular complications in CKD patients is considerably large, whereas the survival rate is considerably low. MetS is a powerful predictor of CVS problems, and its occurrence in combination with CKD may have a synergistic role in the development of cardiac problems.[15,16] However, studies conducted on this has shown wide variability ranging from 28.9% to 70% of the prevalence of metabolic syndrome among patients of CKD.[11,13] Thus, this study will bridge this gap and provide information regarding the overall magnitude of the problem, helping in evidence-based decision-making regarding screening of patients with CKD for early detection. It will help to develop focus lifestyle intervention to guideindividualizedtherapeutic regimen leading to better outcomes in these patients.

METHODS

It wasa cross-sectional studyconducted in Nephrologyoutdoor, Jinnahhospital Lahore from July 2020 to December 2020. A sample size of 110 cases was calculated with a 95% confidence level, a 5% margin of error, andtaking an expectedpercentage of metabolic syndrome among patients of chronic kidney disease as 28.9%.

Patients with CKD for at least 6 months duration, aged 18 to 60 years were included in the study by non-probability consecutive sampling. Patients already suffering from hypertension, SLE, having coronary artery disease, nephrotic syndrome (Proteinuria greater than 3 g/24 hours), or nephritic syndrome (Proteinuria less than 3 g/24 hours along with hematuria on urine examination and BP>140/90 mm of Hg), dyslipidemia or those not willing to participate were excluded. An informedconsentwastakenfrom patients beforeenrolling in the study. A structured proforma was used as data collection tool and Information regarding study variables was noted in that proforma. Measurement of blood pressure and central obesity was done using standard protocol. Over-night fasting was ensured and an early morning fasting blood sample of about 5 ml was taken by venipuncture using an aseptic technique for triglyceride, HDL, and serum fasting blood sugar levels. Results were also noted in the proforma by ensuring confidentiality.

Datawereenteredandanalyzedusingthe SPSSv.26. Numerical variable i.e. age was summarized as mean and standard deviation. Qualitative variables like sex andthepresence of metabolicsyndromewerepresented

in the form of frequency and percentages. Data were stratified for the age, sex, duration, and stages of CKD to control any effect modifiers, and the chi-square test was used post-stratification taking p-value < 0.05 as significant.

RESULTS

About 110 patients with CKD presenting to the nephrology department were included in the study. Table 1 displays the frequency distribution of patients' characteristics. It can be seen that about 79(72%) patients belong age group of 40-60 years of age, majority 63(57%) were male, had CKD stage-V (58%) and 75(68%) had the disease for more than 5 years.

Figure 1 presents that the frequency of MetS among CKD patients was 39(35%) with that of high blood pressure 68(62%) being the most common among all components, followed by high fasting plasma glucose level 52(47%), hightriglycerides levels 35(32%), high cholesterol level 32(29%) and central obesity30(27%).

Table 3 displays the post-stratification data to control effect modifiers. A statistically insignificant relationship of MetS was seen on stratification for age, gender, stage, and duration of CKD with p-value as 0.996, 0.590, 0.453, 0.861 respectively.

Table 1: *Frequency distribution of patients' characteristics (n=110).*

Patient's Characteristics	Frequency	Percentage (100%)
Age Group		
18-39 years	31	28%
40-60 years	79	72%
Gender		
Male	63	57%
Female	47	43%
Stage of ckd		
Stage III	14	12%
Stage IV	32	29%
Stage V	64	58%
Duration of ckd		
Less Than 5 Years	35	32%
5 Years And More	75	68%

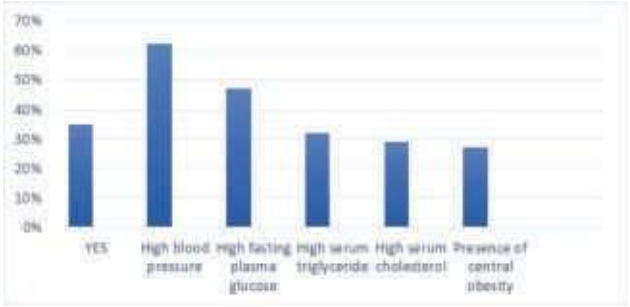

Figure 1: *frequency Distribution of metabolic syndrome and its components (n=110).*

DISCUSSION

Patients of CKD are at an increased risk of cardiovascular complications while metabolic syndrome comprises of constellation of risk factors the presence

Table 2: *Stratification of data to control effect modifiers(n=110)*

EFFECT MODIFIERS		Metabolic syndrome present		Metabolic syndrome absent		Total	p-value*
		N	%	N	%		
Age group	**18-39 years**	11	35%	20	65%	31	0.996
	40 – 60 years	28	35%	51	65%	79	
Gender	**Male**	21	33%	42	67%	63	0.590
	Female	18	38%	29	62%	47	
Stage of CKD	**Stage III**	3	27%	1	73%	14	0.453
	Stage IV	11	34%	21	66%	32	
	Stage V	25	39%	39	61%	64	
Duration of CKD	**< 5 years**	12	34%	23	66%	35	0.861
	≥ 5 years	27	36%	48	64%	75	

* p value < 0.05 taken as statistically significant

of which also increases the risk of cardiovascular diseases. The simultaneous occurrence of CKD and metabolic syndrome can be considered to accelerate the development of cardiovascular components. Therefore, timely identification of this issue and its management is the cornerstone for tertiary prevention against cardiovascular diseases. This study explored the frequency of metabolic syndrome in patients of CKD. About 110 patients of CKD were included in this study from the nephrology unit of a tertiary care hospital Lahore which caters to the health care needs of rural as well as urban population. Theresults of this studyshowed thatmajority of the patients with CKD were above 40 years of age which depicts that CKD is more prevalent in higher age groups as compared to the younger ones. These results are consistent with the findings of O Hare and colleagues who reported not only a higher incidence of CKD in the older age group but also concluded that age is an important effect modifier in the outcome of CKD. The high prevalence of CKD with advancing age, reflects the presence of a variety of different risk factors for CKD with increasing age as well as an age-associated decline in kidney function that is not explained by other known risk factors.

Similarly, the results of this study revealed that a higherproportion of males 57% presentedwithadvanced CKD stage V. This phenomenon was also pointed in earlier studies that prevalence of CKD tends to be higher in women, but the disease is moresevere in men, who also have a higher prevalence of ESRD.[15] Studies have reported that gender difference is seen in epidemiology of risk factors, evolution, and prognosis of CKD.[16]

The results of current study revealed that a considerable proportion of patients (35.5%) were having metabolic syndrome. This is much less as compared to an earlier study conducted in Pakistan reporting a much higher frequency of MetS (70%) among diabetic patients.[13] This high proportion can be attributed to thefactthat knowndiabetics are at muchhigher risk of having all the components of MetS therefore theywereexcluded in theselectioncriteria in thecurrent study. However, theresults of current studyareconsistent existing literature which reported the frequency of metabolic syndromeamong patients of CKD ranging from 28.9% to 37.5%.[11,12]

On analysis of effect modification of age, gender, stage, and duration of CKD it was seen that none of the factors was significantly related to metabolic syndrome. These findings are in contrast with previous data. It is well known that the epidemiology of renal and metabolic disease is mostly different in males and females, and gender seems to be an inevitable predictor of the initiation or progression of CKD.[14] The significant relationship of gender with metabolic syndrome was reported in another study with a female preponderance to this condition.[17] Similarly another study found that having metabolic syndrome results in a 2-fold higher chance of developing CKD compared with the general population.[18] Studies have reported that metabolic syndrome is a significant determinant of CKD progression in the early stage and exerted a 34% higher risk for progression to CKD stages 3-5 with higher number of components directly related to increase in CKD risk.[19,20] This also highlights that subjects having only two components of metabolic syndrome and not yet meeting the criteria of metabolic syndrome, maybe the potential candidate for metabolic syndrome. These patients can be labeled as 'high-risk individual' and their earlier diagnosis and prophylaxis can not only halt their progression towards metabolic syndrome but may also decelerate the progression of CKD and further deterioration in the renal function.

The limitation of this study was that it was a cross-sectional study so a temporal relationship cannot be demonstrated in such design. Further research for a better understanding of the relationship between components of metabolic syndrome, its treatment and role in progression of CKD should be conducted to identify risk of renal deterioration at an early stage, and that in turn may help us to find out more effective prevention strategies and slow down the progression of CKD.

CONCLUSIONS

This exploratory study showed that estimates of metabolic syndrome were considerable high which

is quite in concordancewithother studiesconducted in various regions of the world. This implies that special attention should be given to these patients as they may be more prone to further deterioration and progression of the disease. This calls for screening the patients of chronic kidney disease for the presence of metabolic syndrome for its early detection and management. Patients should be sensitized for its management through proper education and orientation to assess these problems at an early stage. This will lead to primaryprophylaxis toavoidthose factors as well as timely consultation with the clinicians to improve the outcome resulting in decrease mortality and morbidity, directly and indirectly, leading to an improvement in the overall health status of the population and development of the country.

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MODIFIED CHEVRON OSTEOTOMY FOR TREATMENT OF HALLUX VALGUS

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Abstract

Background & Objective: Hallux valgus is the most common forefoot deformity in adults, especially in females. Almost 150 different procedures have been described for the treatment of Hallux valgus deformity. Modified distal metatarsal Chevron osteotomy with distal soft tissue release is one of the most effective procedures for the correction of mild to moderate Hallux valgus deformity.

Methods: This is a prospective observational study conducted at Department of Orthopedic Surgery Services hospital Lahore from Jan 2018 to Jan 2019 after taking permission from the hospital ethical review board. A total number of 20 patients of age between 25-65 years were included in the study. Informed written consent was obtained from each patient. Each patient underwent X- rays in dorsoplantar and lateral views in weight-bearing position including axial sesamoid view of the foot. Hallux valgus angle (HV), inter-metatarsal angle (IMA) were measured on x rays while clinically each patient was assessed for American orthopedic foot and ankle society score (AOFAS) pre-operatively. In all these patients, we performed the Modified chevron osteotomy with lateral soft tissue release and medial eminence excision with capsular repair. Post-operative follow-up was done at two weeks, six weeks, 3 months and at one year for the radiological assessment of HV angle and IMA along with AOFAS score on clinical examination.

Results: Total no of patients enrolled in our study were 20 with 16 females and 4 males. Four patients had mild Hallux valgus while 16 patient had moderate Hallux valgus. Pre-operative mean AOFAS score was 56.50 ± 3.54. Six patients had B/L Hallux valgus deformity. Thus a total no. of 23 feet in 20 patient underwent Modified Chevron osteotomy with distal soft tissue release. Before surgery the mean HV angle was 31.52°±6.44° while mean IMA was 18°±1.10°. The AOFOS score improve from 56.50±3.54 pre-operatively to 85.95±6.15 after 06 weeks post-operatively. It further improved to 94±1.25 after 01 year at the final follow up. The mean HV angle was improved from 31.52°±6.44° pre-operatively to 6.4°±1° after 06 weeks and 6.42°±1° after 01 year post operatively. The mean IMA improved from 18±1.10 pre-operatively to 5.4±1.30 after 06 weeks post-operatively and 5.6°±1.1° at the end of 01 year. The osteotomy union time was 10-16 weeks after the surgery.

There was no recurrence of the deformity, Infection, stiffness of the joint and avascular necrosis of metatarsal head noted post-operatively at the end of one year. The mean first metatarsal shortening was 3.6±1.2mm at the final follow up. The patient satisfaction was also good (90.5%).

Conclusion: Modified chevron osteotomy with distal soft tissue release is a good procedure for correction of mild to moderate Hallux valgus. It allows a significant lateral displacement of distal fragment (4.5mm). This osteotomy improves the foot biomechanics, has got durable functional and cosmetic result.

Key words: Hallux valgus, modified chevron osteotomy, inter-metatarsal angle (IMA), Hallux valgus angle (HV).

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Halluxvalgusisonethemostdisablingandcomplex fore-foot deformity. It is not an isolated disorder but a complex pathogenesis is involved with a combinationofdeformitiesandsymptomsinthelessertoes.[1,2,3]

Hallux valgus is a progressive deformity of first metatarsal joint which causes not only the anatomical changes but also causes the biomechanical effects in foot on weight bearing. It causes a variety of problems like pain at first metatarsophalangeal joint, difficulty in wearing the shoes and tendency to fall especially in the elderly population.[4-6]

Proximal phalanx is deviated laterally while the first metatarsal is deviated medially and is adducted. Mostly it occurs in between age of 18-65 years of age in 23% of adults. The angle between first and second metatarsal is 8°-9° while Halluxvalgusangle is 15°-20°. Pronation of the great toe results when the angle of first metatarsophalangeal joint exceeds above 30°-35°. When pronation occurs, the abductor hallucis becomes more plantar ward.[7-9]

In this way the medial capsular ligament with its capsule-phalangeal portion is the only force which causesresistancetothedevelopmentofthisdeformity.[8,9,10]

Adductor Hallucis pulls the great toe further into valgus and stretch the medial capsular ligament. The capsule become attenuated and pulls the metatarsal head medially from the plantar sesamoids. The four tendonsflexor Hallucis brevis, flexor Hallucis longus, extensor Hallucis longus and adductor Hallucis further causes valgus pull at the level of metatarsophalangeal joint.[10,11,12]

As a result of these forces the sesamoid cristae becomes flattens at the plantar surface of first metatarsal. When these forces exert more pressure the fibular sesamoid is displaced either partially or completely into first inter-metatarsal space which further results in development of callosities, metatarsalgia and stress fracture in the region of lesser metatarsals on weight bearing.[11-13]

The articular surface of first metatarsal becomes further deformed resembling the scoop of ice cream with further derangement of distal metatarsal articular angle. As the deformity progresses the articular angle at the base of proximal phalanx of the great toe also become deranged (phalangeal articular angle).[14-16]

While considering the hallux valgus angle, both these angles should be taken into account specially the distal metatarsal articular angle.

Hallux valgus also causes the hammer toe deformity of second toe. There is difficulty in wearing the shoes as result of splaying the toes. It is recommended that shoes with wild toe box should be used as a shoes with narrow toe box result in dorsal bunion formation. Withfurther progression of thedeformitycornsdevelop and bursal hypertrophy occurs at the medial eminence of first metatarsal headandultimately it results in osteoarthritis of first metatarsophalangeal joint.

The exact cause of hallux valgus is unknown but other factors cancause hallux valgus. These are the genetic factors, flat foot, abnormal first metatarsal dorsiflexion, short first metatarsal, fore foot varus, abnormal foot biomechanics and gastrocnemius equinus deformity. In addition to these causes ligamentus laxity such as Ehlers-danlos syndrome, Down syndrome and Marfan syndrome are also the other contributing factors for hallux valgus. Moreover certain arthropathies like gouty arthritis, psoriatic arthritis and rheumatoidarthritisalsocancausehalluxvalgusdeformity.

The females are affected twice than the males. The individuals who wear shoes with narrow toe box or with high heels are also the most common sufferers.

The Hallux valgus is classified as mild, moderate and severe according to Mann & Coughlin classification. This classification based upon the weight bearing X Rays (dorso-plantar and lateral x rays of the foot). In mildform, HVAranges from 15°-30° and IMAfrom 9°-13°. In moderate form, HVA ranges from 30°-40° and IMA from 13°-20°. While in severe form, HVA is >40° and IMA>20°.

Many treatment options are available to treat hallux valgus. Conservative treatment is available in the form of hallux valgus splint, shoe modification i.e. using shoes with wide toe box, exercise, physiotherapy and activity modifications.

Almost 150 different surgical procedures have been devised for hallux valgus deformity correction, all having its ownmeritsanddemerits. Ideal procedure should correct the hallux valgus angle, Intermetatarsal angle should eliminate the pain and maintain the joint congruity.

One of the most commonly performed operation is Modified distal metatarsal chevron osteotomy combined with distal soft tissue release is an effective procedure for the correction of mild to moderate hallux valgus deformity.[17,18]

METHODS

After permission from hospital ethical review board, this prospective observational study was carried out at Services institute of medical sciences Lahore. A total number of 20 patient of age between 25-65 years were included in the study.

Awritten consent was obtained from each patient. Eachpatientunderwent dorsoplantarandlateral views x rays in weight bearing position including Axial Sesamoid view of the foot. On x-rays we mea-sured the Hallux valgus angle (HVA), inter-metatarsal angle (IMA) while clinically each patient was assessed for American orthopedic foot and ankle society score (AOFAS) pre-operatively.

Patients having severe or recurrent hallux valgus deformity, with marked degenerative changes at metatarsophalangealjoint, withneuropathicfootandpatients withassociated ankleandfoot deformitywereexcluded from the study.

In all these patients, we performed the Modified chevron osteotomy with lateral soft tissue release and medial eminence excision with capsular repair under regional anesthesia.

After making the longitudinal incision over the medial eminence, a long plantar and short vertical arm, 60° V –Shaped Chevron osteotomy was done with an oscillating saw, 1-1.3 Cm proximal to the articular portion of metatarsal head. After osteotomy the metatarsal head portion was displaced laterally up to 4-5mm withminimalpressureandthenitwasfixedwith Herbert's screw. The extra medial portion of the osteotomy was excised.

Post-operative follow up was done at 02 weeks, 06 weeks, 03 months and at 01 year. At each follow up these patients was assessed radiologically for HV angle and IMA.

Clinically each patient was assessed for AOFAS score.

All data were assessed by using SPSS Version 25. Demographic data, HV angle, IMA, AOFAS and operative time were assessed pre and post operatively by using student t-test. P-value of <0.05 was considered significant.

RESULTS

Total number of patients enrolled in our study were 20 with 16 females and 4 males. The mean age was 37.5 ± 5.6. Four patients had mild Hallux valgus while 16 patient had moderate Hallux valgus.

Pre-operative mean AOFAS score was 56.50 ± 3.54 with a range of 50-70. Six patients had B/LHallux valgus deformity. Thus a total of twenty three feet in 20 patient underwent Modified Chevron osteotomy with distal soft tissue release. Before surgery the mean HV angle was 31.52°±6.44° while mean IMA was 18°±1.10°.

The AOFOS score improved from 56.50±3.54 pre-operatively to 85.95±6.15 after 06 weeks post-opera-tively. It further improved to 94±1.25 after 01 year at the final follow up.

The mean HV angle was improved from 31.52°± 6.44° pre-operatively to 6.4°±1° after 06 weeks and 6.42°±1° after 01 year post operatively.

The mean IMAimproved from 18±1.10 pre-operatively to 5.4±1.30 after 06 weeks post-operatively and 5.6°±1.1° at the end of 01 year. The osteotomy uniontimewas 10-16 weeksafter the surgery.

There was no recurrence of the deformity, Infection, stiffness of the joint and avascular necrosis of metatarsal head noted post-operatively at the end of one year. First metatarsal shortening was 4-6 mm at the final follow up.

DISCUSSION

Table 1: Results of pre-operative and post-operative assessment of Hallux valgus

Parameters	Pre-Operative	Post-operative at 06 weeks	Post-operative at 01 year
. HV angle	31.42°±6.44°	6.4°±1°	6.42°±1°
. IMA	18°±1.10°	5.4°±1.30°	5.6°±1.1°
. AOFAS	56.50±3.54	85.95±6.15	94±1.25

Halluxvalgus is acomplex deformity of forefoot. Both intrinsic and extrinsic factors are responsible for it and these cause a significance impact on the fore-foot biomechanics.[7,8,9] These are flat foot, female gender, ligamentous laxity and connective tissue disorders. Modified chevron osteotomy is an excellent procedure for correction of mild to moderate hallux valgus with addition of distal soft tissue release.[19,20] It provides the improved stability, reduces the pain and correct thefootbiomechanicsultimatelyending up in improved early mobility and rehabilitation.[10,11,12]

In our study we performedthe Modified Chevron osteotomy in thirteen feet in 20 patients with mild to moderatehalluxvalgus. The HV angle, IMAandAOFAS score improved post operatively at six weeks and at the end of final follow up at one year.

Seo et al. analyzed the outcome of distal meta-tarsal chevron osteotomy in 54 patients with 77 consecutive feet withhalluxvalgus. They came to theconclusion that distal chevron osteotomy with lateral soft tissue release was a safe procedure in old patients.[1]

Giotis et al carried out the 42 cases of Modified Chevron osteotomy in 33 patients. They came to the conclusion that Modified Chevron osteotomy offers an excellent clinical outcome of HV deformity in young female athletes.[5]

Zhang et al carried his studies regarding the effect of Modified Chevron osteotomy in 20 patients with hallux valgus. They came to the conclusion that Modified Chevron osteotomy can achieve successful correction of moderate to severe hallux valgus with excellent outcomes with 4 years follow up. There was no recurrence of deformity during the post op follow up.[2]

Chen XQ et al carried out theirstudies in 26 patients with mild to moderate hallux valgus deformity. They performed the Modified Chevron osteotomy with lateral soft tissue release. They came to the conclusion that Modified Chevronosteotomy is asimpleprocedure with good exposure and provides the stable fixation with excellent recovery.[4]

Mannder et al conducted a systemic review and meta analysis on hallux valgus deformity. They performedtheminimallyinvasiveandopendistalmeta-tarsal chevron osteotomy. They came to the conclusion that both of these techniques provide equal radiological outcomes but the functional outcomes were good in open metatarsal osteotomy than in minimal invasive technique.[21]

Similarly study conducted by Kim et al. Regarding the modified chevron osteotomy with lateral soft tissue release in moderate to severe hallux valgus also reveals that modified chevronosteotomy is an excellent procedure for correction of moderate to severe hallux valgus.[3]

All these studies suggest that a significant patient satisfaction in patients who underwent Modified Chevron osteotomy for mild to moderate hallux val-gus.[13-15] It provides the stability, improve the functional andradiological status of the foot and has got excellent recovery and rehabilitation.[16-18]

CONCLUSION

Modified chevron osteotomy with distal soft tissue release is a good procedure for correction of mild to moderate Hallux valgus. It allows a significant lateral displacement of distal fragment (4-5mm). This osteotomy improves the foot biomechanics, has got durable functional and cosmetic result. The patient satisfaction was also good (90.5%).

Limitations of the Study

Number of cases in our study were small. More-over, in our study the follow up of the cases was also of short duration. It should include a study with large number of cases with follow up of longer duration.

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OUT OF POCKET AND HEALTH FACILITY CHARGES AMONG PATIENTS UNDERGOING DIALYSIS AT SERVICES HOSPITAL, LAHORE

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Abstract

Objective:- Dialysis is the process of removing waste products and excess fluid from the body. Dialysis allows the patient with kidney failure a chance to live a productive life. However, the out-of-pocket expenditure on this essential procedure can result in financial burden on these patients. The purpose of this study was to assess out of pocket expenditures and health facility charges among patients undergoing dialysis at Services Hospital, Lahore.

Methods: It was a descriptive cross-sectional study conducted in the Dialysis unit of Services Hospital. About 130 patients undergoing maintenance hemodialysis were included in the study after an informed consent. Data were collected using a pretested questionnaire regarding all the study variables and was entered in SPSS for analysis to determine the out-of-pocket expenses in these patients.

Result: Mean out of pocket expenditure (both medical and non-medical) was Rs.4950/- week while mean out of pocket charges on lab investigation were Rs.10300/- rupees during one year of dialysis. Mean monthly transport charges were Rs.1500, wheelchair charges were 150, expenditures on medicine were 2100 while charges of OPD and other treatment cost was Rs.1200. Study shows that 69.2% of the patients who had irregular treatment were suffering from co-morbidity while only 8.4% had no issue other than renal disease. There were 33 patients who reported irregularity in treatment. The reason for this irregularity was due to out-of-pocket expenditures, while 9.09% was due to other reason.

Conclusion: Our research concluded that although the health facilities provided by the dialysis unit of Services hospital to the patients is free of cost, still a considerable proportion of money is being spent in form of medical and non-medical expenses which are not being covered by the government facilities. Strategic measures should be taken to decrease these expenses as well as to relieve the financial burden of these patients.

Key words: Out of Pocket. Hemodialysis, Financial burden, Co-Morbidity.

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The incidence and burden of hemodialysis is rising dramatically with increasing burden on health care system in Pakistan. The proportionate mortality due to kidney failure rose from 2.1% in 2001 to 2.9% in the year 2010–15.[1] The life of renal patients can be saved by removing waste products and excess fluid from the patient's body thus increasing the life expectancy of renal patients. However, the services of hemodialysis can only be provided at health facilities. Government of Pakistan is providing these services through their various public sector hospitals and by special institute like Pakistan Liver and kidney Institute in Lahore. Sehat sahulat card is another facility being provided by the government of Pakistan through which services of hemodialysis can be availed free of cost

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even at private set-up which have enrolled themselves with the program. Out of pocket expenses means paid your own moneyratherthanwith money from another source.[1]

Although access to government and free medical services for the purpose of Hemodialysis has increased over a period, only a few numbers of patients are able to continue their treatment on long term basis. This is mostly because of the high out of pocket expenses. There is a widespread increase in the percentage of expenditure on long term treatment of complications like chronic kidney disease. The average annual direct costs of hospitalized patients are morethan doublethat of those not hospitalized.[2]

About 10% population worldwide is suffering from chronic renal disease and due to this millions of people die each year because they do not have access to affordable treatment.[3] Chronic kidney disease was ranked 27th in the list of causes of total number of deaths worldwide in the year 2000 which rose to 18th rank in the year 2010.[4] Most of people cannot afford the cost due to hemodialysis and the complications of chronickidneydiseasewhich in turn lead to death of more than one million people yearly due to untreated kidney failure.[5,6]

In Pakistan, the average cost of routine dialysis (twice a week) ranges between Rs.3500 to Rs.4500. A government servant earning about average rupees 12000 per month cannot afford the costly treatment. Renal dialysis is a stressful procedure with morbidity and eventually mortality. 35% of patients treated with Hemodialysis stay alive after five years.[7,8]

Only limited publishedresearch is available from Pakistan focusing on the financial hardships of these patients. This study explores different categories of expenses and its impact on their life.

METHODS

It was a Cross sectional analytical study carried out in Dialysis unit of Services Hospital, Lahore. Ethical approval was taken from the ethical review board medical education department services Institute of medical sciences and Services hospital Lahore. After getting approval, hemodialysis patients attending dialysis center for their dialysis were included in the study during study period. A sample size of 130 was calculated using WHO statistical software's size at confidence interval of 95%, anticipated population proportion of 75% and relative precision of 10%.

In study, Out of pocket means paid for with your ownmoneyratherthanwithmoneyfromanothersource (suchas company you workfor or an insurancecompany. For this study a pretested questionnaire and check list were used. The questionnaire was translated into the local language for the convenience of data collection and interviewed by research team of students of 4th year MBBS ensuring both patient's privacy and confidentiality. The questionnaire was pretested in different settings and Cronbach's alpha scale was used for its validity. Aface-to-face interview was conducted. SPSS computer software was used for data entry and analysis of the data. For qualitative variables frequency and percentage distribution table was calculated while mean and standard deviation was calculated for income and expenses. Chi square was applied to know the relationship of out-of-pocket expenses with drop out of treatment. p value of 0.05 or less was taken as significant.

RESULTS

Mean age of participant was 45±5. Out of 130 patients, 12(9.2%) were between 16-26 year age, 26(20.1%) werebetween 27-36, 39(30%) werebetween 37-46, 19(14.6%) were between 47-56 age, 24(18.5%) were between 57-66, 9(6.8%) were between 67-76 and 1(0.8%) was bet-ween 77-86 years of age.

Mean family income was 20K±7K with frequency distribution showing 68(52.2%) had incomes between 10000-25000 rupees, 52(39.9%) had their incomes between 26000-40000, 7(5.5%) had between 41000-55000, 3(2.4%) had incomes between 56000-70000 rupees. Table-1

It was also seen that 70(53.9%) were undergoing

dialysis for last 1 year while majority 60 (46.1%) were undergoing dialysis for more than 1 year. On inquiring about the frequency of hemodialysis it was seen that

Table 1: *Socio-demographic parameters of people under study*

Personal characteristics	Frequency	%	Mean ± Standard deviation
Age distribution			45 ± 5
19-40	25	19	
41-60 and above	105	81	
Sex distributing			
Male	78	60	
Female	52	40	
Monthly Family income			
10000-25000	68	52.3	20K ± 7K
26000-40000	52	40	
41000-55000	7	5.3	
56000-70000	3	2.3	

3(2.3%) were undergoing dialysis once a week, 119 (91.5%) were undergoing dialysis twice a week and only 8(6.2%) cases had their dialysis treatment more than twice a week.

The average total out of pocket expenses in a week were about PKR 4950, Mean transport charges were 1500, wheelchair charges were 150, expenditure on medicine were 2100 whilecharge of OPDand other treatment cost was 1200/-

Average out of pocket expenses required for lab investigation once in a year was 10300 in which about 3000 rupees for blood complete picture, for Serology (HIV/HBsAg/HCV) 1500/ (every three month), for Pre and post HD KFT 1500/- separately every month. Serum albumin cost 3000/- repeated on every three-month basis. (Shown in Table-2 and Table-3)

On exploring the transportation facility used to access the health care center, 67(51.1%) used public

Table 2: *Mean Indirect out of pocket expenses/ Week(n=130)*

Out pocket Cost	Mean Expenditures in NRs
Per week transport charges	1500
Wheel chair charges	150
Expenditures on medicine	2100
OPD and other treatment cost	1200
Total	4950

transport to reach the hospital, 52(40%) used personal transport to visit the hospital and 11(8.5%) used both

Table 3: *Out of pocket expenses for lab investigation during Hemodialysis (n=130)*

Out pocket Cost	Frequency of investigation	Mean Expenditures in PKRs
Blood complete pictures with hemoglobin.	Every 15 days	250
Serology (HIV/HBsAg/HCV)	Three month	3000
Pre HD KFT	One month	1500
Post HD KFT	One month	1500
Serum Calcium	One month	400
Serum Phosphorous	One month	600
Serum albumin	Three month	300
Iron Profile	six month	3000
Total		10300 (PKR)

transport facilities (public and personal) to reach the hospital. Transport expense indicates that 56(43.1%) spent up to 1000 rupees on transport and 44(33.8%) spent from 1000 to 2000 rupees and 30(23.1%) patients spent from 2000 up to 3000 rupees on transport per visit. Out of 130 patients, 42(32.3%) paid their transport charges on their own and 88(67.7%) patients paid their transport charges through financial support of their family. Inquiring about the regularity of the treatment revealed that 30(23.1%) were irregular in taking treatment due to over burden on their domestic expenditures while 3(2.3%) were irregular due to some other reason and 97(74.6%) took their treatment regularly. It was also seen that 88% were seeking treatment from the government hospitals while 12% preferred both private and government sector hospitals for dialysis. About 98.5% patients were provided with bed facility, 3% of patients avail free medicine facility, 5% patients avail the opportunity of getting food and 56.9% patients received facility of basic lab tests. Out of 130 patients, 55(42.3%) paid up to 50 rupees, 40(30.8%) paid from 50 to 100 rupees, 20(15.3%) paid from 100 up to 150 rupees and 15(11.6%) patients paid from 150 to 200 rupees for wheelchair facility per visit. Out of 130 cases, 63(48.5%) paid up to 600 rupees for treatment and further 63(48.5%) paid from 600 up to 1200 rupees, 2(1.4%) patients paid from 1200 up to 1800 rupees, 1(0.8%) patient paid about 1800 to 2400 rupees and further 1(0.8%) patient spent up to 3000 rupees on treatment per visit of 130(100%) patients, the treatment charges of 40(30.8%) were

paid by themselves and of 89(68.4%) cases were paid by their families while only 1(0.8%) patient received hospital funds to pay his treatment charges. Out of total 130 patients, 112(86.2%) were receiving medicines for health problems along with dialysis while 18(13.8%) were not taking medicines for other health problem but only dialysis. Out of 130(100%) patients undergoing dialysis, 16(12%) were taking medication for gastrointestinal disorders, 47(38%) were taking the medicines for cardiovascular disorders,10(7%) were taking medicine for respiratory diseases, 39(30%) weretakingmedicinesforendocrinal disorders especially diabetes mellitus while 18(13%) were not taking medicine for any other health problem other than dialysis. Out of 130(100%) patients, 37 (28.5%) paid their medicine charges on their own while 75(57.7%) had financial support of their families for that expenses and 18(13.8%) were such patients who were not taking medicine for health problem other than dialysis. Out of 130(100%) cases, 70(53.7%) spent up to 1000 rupees, 58(44.7%) paid from 1000 to 2000 rupees, 1(0.8%) paid from 2000 up to 3000 rupees and further 1(0.8%) patient paidabout 3000 to 4000 rupees for medicine per week. Out of 130(100%) patients, Only 70(53.8%) received dialysis treatment from private hospitals in addition to government while 60(46.2%) received the treatment from government hospitals only. The patients discontinued private treatment because it was costly.

DISCUSSION

Non medical expenditures either direct or indirect expenses affect the treatment of patients seeking hemo-dialysis. In Punjab Pakistan, Four out of ten household on Hemodialysis are spending more than forty percent of their nonfood expenses to support their medical needs, while one and half is spending eighty percent of their nonfood expenses. Government of Punjab is claiming that they are providing free medical services specially hemodialysis on priority in all district of Punjab. Even then more than 60% people bearing over-burden of their household expenditure to meet their medical requirement. For this a strong policy and com-prehensive approach is required to overcome this finan-cialburdenforthepatientsundergoingrenaldialysis.[9]

This study was designed to explore the financial hardships of people seeking renal dialysis from govern-ment and trust hospitals. The results of our study were very similar to study in India, China, south Africa, Brazil and Philippine facing rapid increase in Hemo-dialysis patients. As Pakistan is facing severe economic crisis, the cost of medicine and medical treatment is rising day by day making it difficult to facethisfinancial challenge by individual to handle their medical issues. Recent literature showed that in less than five years, a fourfold increase in patients seeking dialysis was seen which is a major concern.[9]

In recent era our policymakers, economist and medical consultants have realized and agreed that increased cost of treatment on lifelong therapy may have financial impact with loss in shape of property, assets and ultimately life of person or his employment.[10,11] In our study the mean age of participants was 45+5 years which is very similar to study conducted by Ghimire S et al. [10] Currently, Sehat Sahoolat card scheme provided by the government of Punjab is providing some relief to the patients (Netrupees Tenlac/year) for their family health issues but majority of the patients are still facing high out of pocket expenditure as only few surgical procedures are in the list of health card scheme from selected hospitals.

It is seen that the cost of medicine greatly affects the regularity in treatment as explained in the research carried In USAby Jose et al. in nephrology department in a tertiary healthcare department.[12]

Similarly a study conducted in Australia by Mateti UV et al reported that majority of the haemodialysis were receiving the treatment for more than one year which are similar to the results of this study.[13]

Further, 51.1% used public transport to reach the hospital, 40% used personal transport to visit the hospital and 8.5% used both transport facilities public and personal to reach the hospital. The results of our study are similar with study conducted by Liu ZH in China.[14] In current study the treatment charges of 30.8% were paid by themselves and 68.4% cases were paid by their families while only 0.8% patient received hospital funds to pay his treatment charges.

This is in contradiction with a prospective, observational study carried out by Suja and Saraswathy in a tertiary care hospital in India which showed that majority of the expenses were borne by the patients themselves.[15] The high burden of out of pocket expenses in our study emphasizes on the insufficiency in medical relief for long term wemodialysis care by government. The results are in accordance with the research in south India by Saravanan AK, Nancy LE, Yuvaram NV, Sara-vanan S. In most of the tertiary hospital limited medical budget influence the treatment and maintenance of renal dialysis of patients.[16] This highlights the need for more political commitment in this regard to decrease the financial burden on these patients.

CONCLUSIONS

It can be concluded from this study that there is a hefty monthly out pocket expenditures of the hemodialysis patients despite the free hemodialysis provided by government. The Health card scheme by Government must include all process of hemodialysis free of cost in maximum approachable hospital both in private as well as government hospitals.

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FETOMATERNAL OUT COME IN PLACENTA ACCRETA SPECTRUM (PAS)IN A TERTIARY CARE TEACHING HOSPITAL

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Abstract

Objective: To determine the fetomaternal outcomes in PAS-Placenta Accreta Spectrum.

Methods: This was an observational descriptive study conducted at Gynae unit 2, of FJMU/, Sir Ganga Ram hospital Lahore. Fifty patients of placenta accreta spectrum were included over one year study period. All booked and un-booked patients who had history of antepartum haemorrhage with or without per vaginal bleeding who were diagnosed of having PAS were included in study.

Results: Fifty cases of placenta accreta spectrum (PAS) were studied over one year period. 35 (70%) patients with placenta Accreta Spectrum (PAS) were un-booked. 15 (30%) were booked. In 25 (50%) of patients age group ranged between twenty six to thirty years while the gestational age ranged between 32-36 weeks. In 35 (70%) of patients having type four major degree placenta previa while type three major degree Placenta previa was noted 10 (20%) of the cases .Regarding number of caesarean sections forty five (90%) had more than one caesarean section while only five (10%) had previous one caesarean section.

Conclusion: Placenta Accreta spectrum (PAS) is associated with life threatening haemorrhage along with associatedhighfeto-maternal mortalityandmorbidity. Earlydiagnosis by Dopplerultrasoundandmultidisciplinary is necessary to improve feto maternal outcome.

Keywords: Placenta PAS -Placenta Accreta spectrum, Maternal perinatal morbidly and mortality , Previous caesarean section.

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Incidence of PAS, (Placenta Accreta Spectrum) which consists of invasive and morbidity adherent placenta varies 1:250 to1:500 of births.[1] It includes three varie-ties depending upon the range of pathology of the placenta ie when placental invasion is restricted to myometrium then it is called placenta Accreta while in place increta and percreta there is villous invasion to the myometrium and into serosa.[2,3] Placenta Accreta is most common type of of placenta Accreta Spectrum and is present in 60%of the cases of PAS while in 20% and 15%, placenta per creta and placenta increta present.[1]

All over the world there is an increase incidence of PAS-placenta Accreta spectrum and it is a fatal condition because of its association with massive postpartum hemorrhage.[4,5] There is close association of PAS with previous caesarean section as incidence of PAS increased as number of caesarean section increases in patient when there is history previous one caesarean section incidence of PAS is 3% while an incidence of 67% is reported in the patients with previous five caesarean sections while there is an incidence of 21%, 40% and 61% in a patient with previous two three and four caesarean sections respectively.[6] While history of previous uterine surgeries such as myomectomy dilation and curettage operative hysteroscopic procedure and advanced maternal age are other associated risk factors for PAS.[7,8] The clinical features of PAS are massiveobstetrichaemorrhagewhichneedstransfusion of blood, peripartumhysterectomiesanduterineartery

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embolization perinatal and maternal complications. Obstetrics ultrasound especially second tri-mester ultrasound is a primary diagnostic modality to diagnose the PAS prenatally.[9,10] Colour Doppler ultrasoundthree dimensional Doppler ultrasound is helpful in diagnosis of PAS.[11] Timely diagnosis of PAS improvedtheoutcome as bloodloss is reducedsignificantly and requirement of blood components transfusion is reduced to those cases in which diagnosis is made at the time of delivery.[12] PAS should be managed by multidisciplinary team involving expert obstetricians expert anaesthesiologist, interventioal radiologist, urologist, nursing team, and blood bank services so that fetomaternal out come can be improved.[13] Management of PAS is either non conservative ie caesarean hysterectomy or in some cases Conservative management with placenta left in situ.[14] There is an increase incidence of fetomaternal mortality and morbidity there fore the aim of this study is to determine the feto maternal out come in women who is diagnosed as a case of Placenta Accreta Spectrum (PAS). This study will be helpful to improve feto maternal out come in future by emphasizing early booking, early diagnosis of PAS and thus opting multidisciplinary approach.

METHODS

It was a descriptive study conducted at Sir Ganga Ram hospital Lahore Pakistan Gynae and Obstetrics unit 2 from December 2021 to December 2022.

This study comprises of 50 patients having Placenta Accreta Spectrum. Study included all women whether booked or un booked who presented with antepartum haemorrhage due to PAS diagnosed by Doppler ultrasound. All asymptomatic patients who have PAS diagnosed by Doppler ultrasound. Patients with gestational age from 28 weeks on wards. And all the pregnant patient having gestational age less than 28weeks having lower lying placenta. Pregnant patients who presents with antepartum haemorrhage other than Placenta previa. pregnant patients who presents with antepartum haemorrhage due to incidental causes.

Thedataofthepatientslikeherageherparitymode of delivery, number of previous caesarean sections, her socioeconomic setup, her presenting symptoms like bleeding, her Doppler ultrasound admissible investigations were recorded in a Performa. Women who were asymptomatic with diagnosis of placenta Accreta spectrum advised admission at 32 weeks of gestation.

Management included achievement of optimal health status by getting target haemoglobin between 12.5 to 13.5g/ dl. Patients were instructed in context of their condition and an increased complications including increased risk of haemorrhage, and need of blood transfusion, an increased risk of bladder and ureteral injuries. Possibilities of thromboliceventsand death are also explained. Perinatal outcome regarding prematurity need of admission to neonatal ICU and associated perinatal mortality and morbidity is also discussed.

A multidisciplinary approach involving senior obstetrician, senior surgeon, urologist anaesthesiologist, haematology and blood transfusion assistance and paediatricians were adopted. Six units of blood, freshfrozenplasmawerearranged at thetime of patients admissionbecausethere was an increased risk of unprovoked bleeding at any time. Elective delivery was prepared at 36 weeks. Classical Caesarean section was done using subumblical mid line incision. In most of the cases either total or subtotal hysterectomy was carried out. In cases where there is concern to secure fertility and when there is partial separation of placenta conservative approach with trail of haemostasis after removal of placenta completely with application of multiple uterine bilateral internal iliac artery ligation, abdominal packingwasdone. All patients were shifted to intensive care unit for immediate postoperative care. Analysis of data was done using SPSS 23 software.

RESULTS

Out of 50 patients patients 15(30%) were booked and 35(70%) patients were un booked. Out of fifty patients half of the patients have gravidity between 2 to 4 while rest of 25patients had gravidity above 4.

25(50%) patients were delivered after 34 weeks while 20(40%) delivery took placed between 32 to 34 weeks while in delivered between 28- 30 weeks. 5(10%), and 10 had previous one and previous two caesarean section and rest of 35 (70%) patients had more than two previous caesarean section. In 5(10%) patients placenta accreta was diagnosed while in 45(90%) patients placenta increta and percreta was diagnosed. In 5(10%) patients diagnosis was made preoperatively. There was association of placenta Accreta spectrum with previous caesarean section in all fifty of cases. In this study, peri partum caesarean hysterectomy was performed. 35(70%) patients having total hysterectomy'. In patients whom bleeding was not secured, further internal iliac artery ligation was carried out in 20%of the cases along with abdominal packing. In 5 (10%) cases of placenta accreta application of haemostasis sutures at the site of placental beds carried out. Bladder injury in 10% patients. While disseminated intravascular coagulation developed in 5(10%) patients, re-laparotomies were carried out in 4% of the patients while 25(50%) patients developed septicemia and admitted to ICU. Estimated bloodloss during surgery was between 2.5 to 3 litres in 45(90%) patients while 5(10%) patients this loss was above three liters. There was six maternal deaths which was due to disseminated intravascular coagulation.

Thehospitalstaysdifferedsignificantly. In 40(0%) patients it was between seven to ten days while rest of 10(20%) patients it wasmorethan ten days. Regarding neonatal out come fetal growth restriction was present

Table 1: *Clinical and Demographic characteristics of placenta Accreta spectrum.*

Sr#				
1	Patient age at presentation	20-25 years	26-30 years	30-35 years
		0	25 (50%)	25 (50%)
2	Antenatal Care	Booked 15(30%)		Un booked 35(70%)
	Gravidity	2-3 10 (20%)	4 25(50%)	>4 15(30%)
3	Gestational Age weeks	28-30	30-32	>34
		5 (10%)	15(30%)	30 (60%)
4	Previous Caesarean scars	Previous One Caesarian Section	Previous Two Caesarian Section	>Two Previous Caesarian Section
		5 (10%)	10 (20%)	35(70%)
5	Type of placental invasion	Placenta Accreta	Placenta Increta 1	Placenta Percreta 25
		15(30%)	10(20%)	(50%)
6	Management of placenta accreta spectrum (PAS)	Total abdominal Hysterectomy	Subtotal Hysterectomy	Uterine Conservation
		30(60%)	8(16%)	12(24%)
7	Additional Procedures performed.	Bilateral Internal iliac	Abdomenal packing 10(20%)	
		artery ligation 10 (20%)		
8	a) Maternal Complications	Bladder injury	Acute tubular necrosis 8	Relaparotomy 2 (4%)
		5(10%)	(16%)	
	b) Maternal Complications	DIC 4 (8%)	Septicemia and admission to ICU 20(40%)	Maternal deaths 6(12%)
9	Blood loss at the time of surgery.	Between 2.5 to-3 liters	>3 liters 15(30%)	
		35(70%)		
10	Amount of blood transfused.	4 to 6	>6	
		30(60%)	20 (40%)	
11	Hospital stay	7-10 days (40) 40(80%)	>10 days (10) 10 (20%)	
12	Fetal out come.	Fetal growth restriction. 10(20%)	Preterm birth 35(70%)	Neonatal ICU admission. 15(30%)

in 10(20/,%) cases while 35 (70%) of cases weredelivered prematurely. 15, (30%) of cases needs ICU admission.

DISCUSSION

PAS is a lethal complication of pregnancy. In this condition there is failures of separation of placenta with associated mortality and morbidity. Its incidence increased with rising number of caesarean section.

Only 15(30%) cases of our study were booked while 35(70%) of our patients are un booked. Ourstudy is not persistentwith Wasim et al[16] studywhere 86.1% of the patient are booked. This needs the early booking of patients with previous caesarean section. Most of the patients are of the age group between twenty six and thirty years age. Astudy carried out by Rabia Wajid and Aggarwal[17] which showed similar age distribution twenty six to twenty seven years .

In our study diagnosis of PAS was at 32weeks of gestation and surgery is performed at 36week. Our study is true with the most of the cases of placenta accreta spectrum (PAS)in our study were diagnosed around 32 weeks of gestation and their surgeries were planned around 36 week of gestation A study carried out by Rabia Wajid & colleagues[17]and by Aggrawal etal[18] showed similar gestation of presentationandtime of delivery.

Regarding gravidity of the patients with PAS in 90% of the patients it falls between one to five similar patternofgraviditywasseenin HassanS,etal[19]study.

There is a strong relation between placenta accreta spectrum (PAS) and number of previous caesarean sections. Our study showed that 70% of our patients had more than two caesarean section contrary to 30% and 10% of thecaseswhohadprevious twoandprevious one caesarean sections respectively. Similar association was found in s study carried out by Abas et al[20] Fifty percent,thirty percent and twenty percent of the cases had placenta percreta, Accreta and increta. However Rabia wajid and colleagues 17 showed diffe-rent percentage of Placenta Accreta spectrum ie 75.9% 21.26% and 31.5% of placenta Accreta increta and percreta.This difference is due to an increased number of caesatean sections in our study.

Patient out come is favourable when the diagnosis of placenta Accretaspectrum is madeantenatallybefore the onset of uterine contraction vaginal bleeding and disruption of placenta at level three and four maternity units.[21] Now a days two dimensional grey's scale ultrasound colour flow ultrasound and three dimensional power Doppler ultrasonography are used to diagnose placenta accreta spectrum. Almost 50% to 66% of PAS are not diagnosed antenatally which emphasized the need of prenatal PAS screening of placenta accreta spectrum and further need of appropriate management of the cases of PAS. Both feto maternal morbidly and mortality is reduced when prenatal diagnosis is made by Doppler ultrasound [21,22] In our study only thirty percent of our patients there is prior localization of placenta as most of the patients in our study were un booked how ever our study was not consistent with the study carried out by Aggrawal et al.[18] In which 70% women had placental localization before delivery.

A recent study carried out in Italy revealed that there was an improved maternal out come when PAS was diagnosed at antenatal period and patient was referred and managed in a specialized centers with multidisciplinary team involvement at a teritary care teaching hospital involving senior obstetrician, haematologist, blood transfusion experts, critical care anaesthesiateam,radiologistexpertininterventionradiology.

Fetomaternal out come is improved by the use of multidisciplinary approach.[23] In patients with placenta Accreta spectrum following complications are assessed peripartum hysterectomies blood loss and associated acute transfusion reactions renal failure DIC, injuries to bladder bowel and admission to ICU[24] Most cases of PAS ended into Hysterectomy.

Theotheralternativemeasurement isafter caesatean section leaving the placenta in situ. Uterine artery and internal illiac artery ligation application of Blynch compressions sutures.[25] conservative management is associated with infection, haemorrhage risk of hysterectomy and even mortality.[26] Among fifty patients in our study Thirty (60%) patients had total caesarean hysterectomies while subtotal hysterectomies were

carried out in 8(16%) of the patients. Bilateral Internal iliac artery ligation was carried out in 10 (20%) patients to control bleeding.

Following Postoperative complication noted. Bladder injuries (10%), acute tubular necrosis (16%) septicemia along with ICU admission 40% of cases noted.

While a study carried out by Seema Dwivedi et al[27] reported ICU admission, DIC and sepsis in 21%, 2% and 13%, of the cases respectively. In our study 40 (80%) hospital stay was between 7-10 days while 10(20%) remained admitted for more than 10 days. In our study maternal deaths reported were 6(12%) causes of these deaths were DIC due to excessive haemorrhage. Same causes of maternal deaths were reported as in a study carried out by Seems Dwivedi et Al[27] In these cases causes of maternal deaths were also haemorrhage.

Regarding the neonatal out come intrauterine growth restriction prematurity and admission to neonatal ICU detected in 10(20%), 35(70%) and 15(30%) of neonatesrespectively. In astudycarriedout by Sabreena et. al[20] 22% of the cases had Intrauterine growth restriction while premature birth was present in 66.7% of cases .31.1%admitted to neonatal ICU. This study result are consistent with our findings.

CONCLUSION

Percentage of PAS has been increasing because of an increase in number of caesarean sections.

There is an increase in fetomaternal mortality and morbidity due to this life threatening haemorrhage which can be reduced by early diagnosis by prenatal Doppler and multidisciplinary approach involving senior obstetricians hamotologist and anesthetists.

Standard management is caesarean hysterectomies with or without Internal iliac artery ligation. However in less severe cases conservative management can be practiced.

Early booking and regular antenatal care should be enforced for early detection of low lying placenta and further evaluation by Doppler ultrasound to detect PAS and further counselling the patient regarding her visits optimization of her haemoglobin admission. Counselling regarding associated feto maternal mortality morbidity and needs of blood transfusion may be done.

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OUTCOMES IN PATIENTS WITH PROXIMAL HUMERUS FRACTURES UNDERGOING OPEN REDUCTION AND INTERNAL FIXATION WITH PROXIMAL HUMERUS LOCKING PLATE

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Abstract

Background & Objective: Despite of conservative management for proximal humeral fractures, open reduction and internal fixation with proximal humeral locking plate has become the most frequent treatment for these fractures especially in elderly and osteoporotic population. Alot of complications are associated with proximal humerus internal locking system (PHILOS) plate including intra articular screw penetration, screw cut out, varus malunion, loss of reduction, nonunion and infections. Efforts have been made to improve the locking plate fixation technique and strengthen the fixation more resilient to head collapse, screws cut out, screw penetration and loss of fracture reduction.

Methods: It was an observational study conducted in the Department of orthopaedic surgery, Services Hospital Lahore. About 30 patients having isolated proximal Humerus fracture with age between 40-75 years being treated with promixal humral locking plate were included in the study after permission from ethical review board. Patient with head, spine, abdomen and chest injury or poly trauma were excluded. There were Eight with 2 – part, 15 with 3- part fractures and 7 with 4- part fractures. All these patients were followed at interval of 3 weeks, 6 weeks, 3 months, 6 months and at one year.

Results: In all our 30 patients, fracture united 3 months after the surgery. In 05 patients there were screw penetration in the shoulder joint. In these 05 patients, 03 patients developed avascular necrosis (AVN) and underwent shoulder arthroplasty. Loss of reduction was present in 04 patients in whom the revision surgery was done with addition of bone graft. Range of movements were significantly less in patients with 4- part fracture(forward elevation was 95 degree and head shaft angle was 100 degree in these patients while external rotation was 22 to 30, in rest of 35 patients it was within the normal range. Mean DASH score (Disabilities of Arm, Shoulder and Hand) after 6 weeks was 3.2 – 58.4 while after one year at the end of final follow up it was 13.3 – 48.6.

Conclusion: Our results reveal that PHILOS fixation technique is an acceptable stabilization procedure for proximal humeral fractures. One must be aware of potential hardware complications. For unstable proximal humerus fractures locking plates is a reasonable option especially in 3- part and 4- part fractures in osteoprotic bone. But at the same time it has got high complication rate like screw penetration in the joint, loss of fracture reduction and varus malunion etc.

Keywords: Proximal Humerusfracture, Proximal Humerallockingplate, screwpenetration, osteoproticbone.

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Proximal humerus fractures are amongst the most frequent fractures after femur neck and distal radiusfractures.Theseaccountfor4-6% ofallfractures.[1]

These fractures have uni modal distribution peaking as the age progresses i.e. these are common in osteo-porotic bone. As a result of high prevalence

and rise in incidence, these fractures are exerting significant healthcare burden. Complex proximal fractures with displacement occur most commonly in elderly female with comorbidities and have devastating effects on the quality of work and life.[1,2,3]

Proximal Humerus includes the head, greater tuberosity, lesser tuberosity and Humerus shaft. Fractures of anatomical neck can result in significant compromise on the vascularity with resultant avascular necrosis of head of Humerus. Anatomically greater tuberositylies on thelateral aspect whilelessertuberositylies ontheanterior borderof Humerusproximally[4,5].

Axillary nerve is the most commonly nerve injured followed by Suprascapular nerve being the second most commonnerveinjury in proximal Humerusfractures[6,7]

Bloodsupply of Humeruscomesfromtheanterior and posterior circumflex Humeral artery. Anterior circumflex humeral artery provides 30% perfusion of Humerus head while posterior circumflex humeral artery provides 64% of blood to the head of Humerus. Therefore in proximal Humerus blood perfusion is preserved even if the anterior circumflex humeral artery is damaged.[8,9]

In the elderly females the most common mechanism of injury is fall from standing height, followed by high energy trauma such as motor vehicle accident, fall from height and seizures. Pathological fractures can occur with trivial trauma. In Young patients proximal fractures caused by high energy trauma such as motor vehicle accidents or as a result of sports injury.[10,11]

A lot of classifications has been described for proximal humeral fractures includingAO classification, Kocher, Codmanand Jakoband Ganzsystem. Themost commonly used classification is Neer Classification which divides the proximal Humerus into four functional and conceptual parts i.e. greater tuberosity, lesser tuberosity, head and Humerus shaft for treatment purpose. The part should be displaced greater than 1cm or should have 45° of angulation. The greater tuberosity is an exception for this rule. It should be fixed when it is displaced more than 0.5cm.[12,13]

Fractures which are displaced, open fractures, fractures withmetaphyseal comminution, fracture dislocation, head split fractures, anatomical neck fractures and fractures with neurovascular injury should be treated surgically(as recommended by Neer).

Many different techniques regarding osteosynthesis of proximal Humerus fractures have been described. Osteosynthesis with proximal humeral locking plates are the most commonly performed procedure especially in case of osteoporotic bone. The complicationsassociatedwith PHILOSplateareheadcollapse, varus malunion, loss of fixation, pseudoarthrosis, wound infection and avascular necrosis of humeral head. Despite of the availability of intramedullary nail and PHILOS Plate, most of the surgeon agree that 3 part and 4 part fractures should be treated with Endo prosthesisandwith Reverseshoulderarthroplasty.[14,15]

All currently available techniques suggest that there is no evidence based treatment scheme for proximal Humerus fractures for implementation.[16]

METHODS

This prospective observational study was carried out at department of orthopaedic surgery services hospital Lahore from Jan 2018 to Jan 2020. After permission from Ethical Review Board, a total number of 30 patients, aged between 40-75 years, presenting to the emergency department with proximal Humerus fractures wereenrolled in thestudy. All these fracture were classified according to Neer's classification.

After admission, each patient underwent x-rays of Humerus with shoulder and elbow joints both AP & Lat views. After fitness of patient for G/A, the fracture was exposed with standard Delto pectoral approach and was fixed with PHILOS plate 1cm below the upper end of greater tuberosity. All fracture Fragment were reduced indirectly by traction sutures placed in Subscapularis or Rotator cuff tendon.

Patientswithopenfractures, pathologicalfractures and fractures older than 3 weeks were excluded from the study. Each patient was followed at interval of 03 weeks, 06 weeks, 03 months, 06 months and one year after thesurgery.At eachfollow up everypatientunder-

went x rays of shoulder joint AP and Lateral view and shoulder joint movements during these follow ups were measured.

RESULTS

The results of the study showed that 23 patients had age more 55 years (55-65 years) while 7 patients had age of less than 55 years (40-55 years). All the fractures were categorized according to the Neer's classification which showed that there were 08 with part 2 fractures, 15 with part 3 and 7 patients had 4 part fractures. All fractures united on an average within 03 months after the surgery (12-18 weeks).

Most common complication was screws penetration in the shoulder joint as the result of collapse of fracture fragment of head of Humerus in 05 (16.6%) patients. This happened after 12 weeks in 03 patients while in 02 patients this occurred after 6 weeks. Among these 05 patients, 04 patients had 4 part fractures while 01 patient had 3 part fractures. All these screws were removed. Out of these 05 patients, 03 patients developed AVN and underwent Reverse Shoulder Arthroplasty.

There was loss of reduction in 05 (16.6%) patients at 6 weeks. We performed the revision surgery in these patient with bone graft. Out of these 05 patients, 04 patients developed Varus mal union 03 months after the 2nd surgery. In these 04 patients, 02 patients had 2 part fractures. 01 patient developed implant failure after 03 months and surgery was revised in this patient (part 2 fracture).

Range of movements were significantly less in patients with 4 part fracture. Forward elevation in 05 patients with 4 part fractures was 95 degree and head shaft angle was 100 degree in these patients. The external rotation was 22-30 degree. In rest of 25 patients, the forward Elevation was 150 degree (130-170 degree) while external rotation 45 degree (35-45 degree). The head shaft angle was 120-135 degree (129 degree).

Mean DASH score after 6 weeks was 30.2-58.4 while after 3 months it was 24.2-56.5. It was 20.3-51.5 after 06 months while after 1 year at the end of final follow up it was 13.3-48.6.

DISCUSSION

Operative treatment of displaced and comminuted proximal Humerus fractures are complex and challenging for the orthopedic surgeons.[4] Proximal Humeral locking plate has demonstrated good clinical outcomes but it is frequently associated with high complications rate.[3] Main complications are AVN of head of Humerus and subacromial impingement with limited movements of shoulder joint. Another bothersome complication is screw penetration in the head of Humerus because of osteoporosis of the bone.[2]

Table 1: *Results of post-operative assessment of DASH score*

Parameter	6 weeks	3 months	6 months	1 year
DASH score	30.2-58.4	24.2-56.5	20.3-51.5	13.3-48.6

In the present study the common complications were screw penetration in the shoulder joint followed by AVN of head of Humerus with loss of reduction and limited movements of the shoulder joint.

Lot of studies are consistent with our study that although proximal Humerus locking plate provides better stability but it is associated with complications because of poor bone stock.

In a study conducted by Barlow JD et al[13,14] open reduction and internal fixation with PHILOS plate was associated with high complications rate in patients above 60 years of age because of osteoporosis. They suggested a refinement of surgical techniques for fixation of these fractures.

Kavuri V et al.[15] conducted a study regarding the fixation of proximal Humerus fractures with locking plate, reveals that growing use of proximal locking plate provides the adequate fixation of proximal Humerus fractures. At the same time it is associated with high complications rate. The common complication in their study was screw penetration followed by varus collapse, limitations of shoulder movement, AVN of humeral head, infection, non union and adhesive capsulitis.

Ali et al. concluded from his study that proximal Humerus fractures are challenging issue for surgical management of these fractures. Open reduction and internal fixation with PHILOS plate has given accept-

able result in 3 part and 4 part fractures while the prognosis for intervention is poor for 4 part fractures.

In another study conducted by Siddalingamurthy et al.[5] on 25 patients with proximal humeral fractures fixed with proximal humeral locking plate, they came to the conclusion that proximal humeral locking plate fixation has provided satisfactory result in 2 part, 3 part and 4 part fractures. The 3 part and 4 part fracture fixation has got high complication rate.

In his study regarding the functional outcomes of PHILOS plate fixation in proximal Humerus fractures in 15 patients, SK K Shashi et al[7]. came to the conclusion that PHILOS plate provides good and stable fixation in elderly osteoporotic patients.

According to study of Dhruv Pandya and Krunal Soni while analysing the functional outcome of proximal Humerus plate in proximal Humeral fractures, they came to the conclusion that Proximal humeral locking plate is a preferred technique for fixation of proximal Humerus fractures.[8] However the complications are not uncommon with this procedure.

In his study A.E Abdel Salam et al.[1] came to the conclusion that locking plates are advantageous especially in patients with osteoporotic proximal Humerus fractures. Although the reduction accomplished by PHILOS plate are preserved and has favorable outcomes. Still the complications rate especially screw perforation into joint are common.

All these studies suggest that PHIOS plate is a preferred treatment option for all proximal Humerus fractures. It provides a stable construct with divergent and convergent screw orientation with decreased chances of screw pull-out and implant failure.[6,9] Laterally it provides the buttressing effect and medially it prevents the varus displacement of the fracture. In spite of this, complications also common with PHILOS plate like screw cut-out, AVN and Varus mal-union. These can be attributed to fracture pattern specially in 3 part and 4 part fractures, poor fixation technique and improper placement of implant[10,12]. There for proper fixation technique, implant positioning and exact fracture pattern with pre-operative planning having 3D CT-Scan are essential to achieve the good functional out-comes.[11]

CONCLUSION

PHILOS plate provides good stable fixation in proximal Humerus fractures especially in 3 part and 4 part fractures in elderly population. It has got high complication rate in this age group because of osteoporosis resulting in screw pull-out, AVN of head of Humerus and varus mal-union

Study has limitations because Sample size in our study was small. Along follow up is desirable to know the functional out-comes especially in 3 part and 4 part fracture pattern of proximal Humerus.

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FREQUENCY OF ANEMIA IN THE FIRST TRIMESTER OF PREGNANCY AND COMPARISON OF PHYSIOLOGICAL SYMPTOMS OF PREGNANCY AMONG ANEMIC AND NON-ANEMIC PATIENTS IN A PRIMARY HEALTH CARE CENTER: A COMPARATIVE CROSS-SECTIONAL STUDY.

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Abstract

Background & Objective: Anemia in pregnancy accounts for one-fifth of maternal deaths worldwide and is associated with high maternal morbidity, mortality, and adverse pregnancy outcomes. Pregnancy is associated with a variety of physiological symptoms, which can be distressing and need to be managed. Hence in this study, we aim to determine the frequency of anemia and compare the physiological symptoms in the first trimester of pregnancy among anemic and non-anemic patients.

Methods: A cross-sectional comparative study was conducted on women attending a rural health center in Pakistan for their first antenatal visit from January to November 2021. A formal interview of 801 eligible participants was conducted by the investigator to determine pregnancy-related symptoms and demographic data. Hemoglobin, and urine analysis reports were obtained from the hospital's laboratory. Data were analyzed using SPSS.

Results: The mean age of participants was 27.2 ± 4.6 years and mean Hb levels were 9.82 ±0.66 g/dl. The overall frequency of anemia was 96.5%. Majority were mildly anemic (71.5%), 5.9% were moderately anemic, and 0.3% were severely anemic. It was seen that anemic females experienced more symptoms in the first trimester compared to non-anemic females i.e. 492 (63.6%) vs 12(42.8%) respectively. Nausea and vomiting were the most common symptoms reported in 190 (23.7%) females. Heartburn was reported in 117 (14.6%), urinary tract infection (UTI) in 97 (12.1%), constipation in 39 (4.9%), backache in 33 (4.1%) and 28 (3.5%) women reported pelvic pain in the first trimester.

Conclusion: There was a high prevalence of anemia among pregnant women along with higher frequency of symptoms in the first trimester which calls for awareness and education in the community. The most common symptomsfound in ourpopulationwerenauseaandvomiting, followed by heartburnandurinarytractinfection.

Keywords: Anemia of Pregnancy; Vomiting in pregnancy; First trimester; Antenatal visit

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Anemia is a serious global public health issue faced by the healthcare system worldwide. It is defined as Hemoglobin (Hb) levels less than 11g/dl. It is established that almost 1.62 billion people are blighted by anemia, which amounts to 24.8 % estimated global anemia prevalence, out of which the pregnant womenhave an estimatedanemiaprevalence of 41.8 %. In Southeast Asia, the prevalence of anemia in pregnant women is 48.2%, which is the second highest prevalence in the world. In Pakistan, anemia is a moderate public health problem with a prevalence of 39.1%.[1] Anemia has direct correlation with the increased risk of maternalmorbidityandmortality as well as lowbirth

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weight of the infants.[2] Women having moderate to severe anemia during pregnancy have a high infant mortality rate.[3] Severe anemia is associated with preterm births, resulting from both preterm labor, intra uterine growth restriction and spontaneous abortions.[4] Anemia has been found explicitly prevalent among pregnant women because of the needs of growing fetus. More than 80% of anemias diagnosed during pregnancy are iron deficiency anemias.[5] Majority of the pregnant women presenting to a healthcare facility for routine antenatalcheckupsreportthattheyexperiencecommon symptoms of pregnancy which include nausea and vomiting, heartburn, leg cramps, low back/pelvic pain, constipation, varicose veins, edema and urinary tract infections. These symptoms are due to hormonal and physiological changes during pregnancy and often are troublesome for the expecting mothers, who frequently visitthehealthcarefacilitiesinsearchforinterventions.[6]

Of all the aforementioned symptoms, mild nausea and vomiting, usually referred to as "morning sickness" is found to occur in more than 70% of pregnant women, typically during first trimester. Nausea and vomiting have a substantial effect on the lifestyle of pregnant women, often interrupting their daily activities.[7] Heartburnaffects roughly about 30-50% of pregnant women. It manifests in the first trimester of gestation and subsides soon after delivery.[8] Urinary tract infections afflict many pregnant women, causing significant morbidity and adverse outcomes, such as preterm delivery, low birth weight and anemia.[9]

The objective of this research is to determine the frequency of anemia in pregnancy during first trimester and frequency of physiological symptoms which were reported in these mothers.

METHODS

A comparative cross-sectional study was conducted at a Rural Health Center in Pakistan from January to November 2021 (11 months). Formal permission to conduct the study was obtained from the hospital's ethical review committee. Informed consent was taken and an explanation of the purpose of the study was offered to the participants. All the pregnant women in the first trimester of pregnancy, willing to participate during the study period were included. Women unwilling to participate or with some chronic disease or anemia were excluded. Data were collected using a structured questionnaire based on all study variables and females were interviewed to fill the questionnaire. A 5ml of blood sample was taken. Sahli's method was used to determine hemoglobin levels in pregnant females. These Hb levels were taken after the confirmation of pregnancy by urine preg-nancy test in thecenter. Laboratoryreports of urinalysis were used to make a diagnosis of UTI among these pregnant women in the health care facility. Pregnant women were classified into 4 categories based on severities of anemia, i.e., non-anemic, mildly anemic, moderately anemic, and severely anemic. A total of 801 first-trimester pregnant women were recruited for the study.

Non-anemic was defined as Hb levels ≥ 11g/dl or higher. Mild anemia was defined as Hb levels of 10 – 10.9 g/dl. Moderate anemia was defined as Hb levels ranging from 7.0- 9.9 g/dl and severe anemia was defined as Hb levels less than 7.0 g/dl. Data were analyzed using SPSS software.

Results

About 801 women attending the antenatal clinic (ANC) during the study period were included in the study. The minimum age was 15 years and the maximumagewas 40 years. Themeanagewas 27.2 ± 4.6 SD years. Average hemoglobin levels were 9.82 ±0.66 g/dl (Table 1). Among 801 females, only 28 (3.5%) were found to be non-anemic during the first trimester. About 711 (88.7%) pregnant women were mildly anemic, 59(7.4%) were moderately anemic and 03 (0.4%) were severely anemic (Table 2)

Frequency distribution showing symptoms experienced by anemic and non-anemic pregnant women

Table 1: *Demographic data and hemoglobin levels of pregnant females (n=801)*

	n	Min.	Max.	Mean	Standard Deviation(±)
Age (years)	801	15.00	40.00	27.1407	4.55928
Hemoglobin (g/dl)	801	6.00	13.60	9.8296	0.66503

Table 2: Age-wise stratification of severity of anemia among women in their first trimester

Age in Years	Non-anemic *f* (%)	Mild anemia *f* (%)	Moderate anemia *f* (%)	Severe anemia *f* (%)
15-25	16 (2.0)	116 (14.5)	7 (0.9)	1 (0.125)
26-35	12 (1.5)	300 (37.4)	35 (4.4)	1(0.125)
36-40	0 (0)	295 (36.8)	17 (2.1)	1(0.125)
Total	28 (3.5)	711 (88.7)	59 (7.4)	3(0.375)

are shown in Table 3. Among anemic pregnant women, Nausea and vomiting were reported in 186 women (24.1%), heartburn in 114 (14.7%), UTI was reported in 96 (12.4%), 38 women complained of constipation (4.9%), 31(4.0%) reported backache, 27(3.5%) reportedpelvicpainthusmakingatotal of 492 (63.6%) anemic women who experienced pregnancy symptoms. 281 women(36.4%) reported no symptoms duringthe first trimester (Table 3).

Non-anemic women (2.8%) in the first trimester faced the same common physiological symptoms of pregnancy as anemicwomen. Nearly 4(14.3%) reported nausea and vomiting, 3(10.7%) reported heartburn, 1(3.6%) reported UTI, 1 reported constipation (3.6%), 2 reported backaches (7.1%) and1 reported pelvic pain (3.6%), making a total 12 (42.8%) women who experienced symptoms while 16(57.2%) non-anemic women reported no symptoms during the first trimester (Table-03).

Table 3: Comparison of symptoms among anemic and non-anemic pregnant women.

Symptoms	Anemic women (n=773) *f* (%)	Non-anemic women (n=28) *f* (%)
Nausea and vomiting	186 (24.1%)	4 (14.3%)
Heart Burn	114 (14.7%)	3 (10.7%)
UTI	96 (12.4%)	1 (3.6%)
Constipation	38 (4.9%)	1 (3.6%)
Backache	31 (4.0%)	2 (7.1%)
Pelvic pain	27(3.5)	1 (3.6%)
Total	492 (63.6%)	12(42.8%)
No symptoms	281 (36.4%)	16 (57.2%)

DISCUSSION

Ourstudyshowedthatanemia is highly prevalent among pregnant women who came for their first ANC visit in their first trimester. Out of 801 women, 773 had anemia of pregnancy in varying severities. The prevalence of anemia among pregnant women was found to be 96.5%. Hameed et al (2018) found the prevalence to be 65.4%.[11] Shams et al conducted a study in Mardan and found the prevalence of anemia to be 76.7%.[12] Most of the women in our study were mildly anemic (88.7%) in their first trimester and belonged to the age group of 26 to 40 years i.e., 595 out of 711 making up 83.7% (Table 02). This prevalence of mild anemia in the first trimester of pregnancy was found to be in sharp contrast with the study conducted in Turkey by Ozturk et al (2017) whofound it to be 16.64%. The samestudy showed the anemia prevalence close to 20% in the age group of 25 to 34 years while our study showed it to be 83.7% in the same age group.[13] The WHO recommendations on ANC for a positive pregnancy experience in 2016 state thatpregnant womenshouldtake 30-60mg of elemental Iron and 0.4mg of Folic Acid once a day to prevent maternal anemia, puerperal sepsis, low birth weight, and preterm birth. In our study, anemia in the majority of these pregnant women was managed by the supplementation of ironand folic acidtabletsalong withdietarycounseling. Somewomenweregivenintravenous iron and severely anemic women were referred to tertiary care hospitals for further management.

Noronha et al (2012) found anemia is the most frequent complication in South Asian pregnant women. The common factors that increase the risk of anemia were found to be non-compliance to iron supplements, low socioeconomic status, multiparity, extremes of age, dietary deficiency, and worm infestation.[2] Although our study population is similar and it can be safely assumed that similar factors are associated with a high prevalence of anemia, the relevant data is deficient and need to be further assessed.

Many symptoms in pregnancy are related to hormonal and physiological changes during pregnancy, and it poses a challenge to identify these from pathological causes and determine when these need to be referred to specialist care for management. Antenatal visits are an important part of primary assessment for the same reason and provide a chance for early identification and appropriate management.[6]

Nausea and vomiting are found to be the commonest symptoms in early pregnancy in various studies[6,14,15] Our study showed nausea and vomiting were present in 24.1% of the females in their first trimester (Table 3). Our data is deficient in the impact of these symptomsonpatients'lifestyles, therefore further management options were not evaluated in thestudy results. Astudy conducted by Nawaz et al (2015) at LRH Peshawar and DHQ Mardan found it to be 14.5% and 8.4% respectively.[14]

Heartburnwasthesecondmostcommonprevalent finding among pregnant females i.e. nearly 14.6% of the women had heartburn while a study conducted by Lee et al (2021) showed the prevalence of heartburn as 30% in pregnancy.[15] A study conducted by Ather et al;[16] found that 22% of the women experience backpain during their pregnancy while our study showed it to be much less i.e., 4.0% of the females reported backache. Only 4.9% of the women reported constipation. These women did not have any prior history of constipation and were reported for the first time in pregnancy. A study conducted by Khalil et al, in 2019 reported it to be present among 18% of the pregnant females.[17] In our study, the prevalence of pelvic pain in the first trimester was 3.5%. Shahzad et al; in 2020 conducted a study andfound it to be nearly 5.6% in the first trimester of pregnancy.[18] Nearly 12.1% of the women had confirmed UTI on basis of urinalysis test. This prevalence was found to be less than in a study conducted by Getaneh in 2021 who found it to be 15.37% among pregnant women of Ethiopia.[19] This is an observational study that identifies the prevalence of anemia and common pregnancy-asso-ciated symptoms. Our data do not identify the risk factors associated with these. There is limited data available to ascertain the severity of the symptoms, therefore the subsequent management options cannot be explored. The researchers believe that repeating this study with a longitudinal study design, and gathering further data on risk factors will improve the results.

CONCLUSIONS

Anemia in the first trimester of pregnancy is a common finding and anemic patients have more risk of having pregnancy-associated symptoms. The findings endorse the importance of early antenatal visits, as early detection of anemia can help with appropriate referral and management of the same. The anemia may contribute in increased incidence of pregnancy associated physiological symptoms. Thus an early intervention in this regard can improve the outcomes in these patients. Females should be encouraged for regular follow-up at health care facility. This aids in the identification of not only anemia but also other common problems and their management, helping to achieve positive health in these patients for better and healthy society.

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CORRELATION OF ACTUAL TIME SINCE DEATH WITH ESTIMATED TIME OF DEATH BY MEASURING PROTEINS CONCENTRATION IN CADAVERIC CEREBROSPINAL FLUID

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Abstract

Background & Objectives: Postmortem Interval (PMI) is the time interval from death upto conducting autopsy of deceased. PMI is an overbearing perspective of medical jurisprudence used to support beholders claim, corroborate the potential in provided proof and serve as evidence for further action. The objective of this study is to estimate the time since death by measuring proteins concentration in cadaveric cerebrospinal fluid.

Methods: This cross-sectional study conducted at Forensic Medicine and Toxicology Department of Allama Iqbal Medical College, Lahore for 1 year from January 2022 to January 2023 in 50 dead bodies included through non probability consecutive sampling. After informed consent, CSF sample was taken by using lumbar puncture technique and quantitative values of proteins were obtained automatically through auto-biochemical analyzer. Data were analyzed through SPSS version 25. The relation between time of death and time estimated on CSF proteins was measured by calculating Pearson's correlation coefficient. P-value ≤0.05 was taken as statistically significant.

Results: Out of 50 bodies, 25 (50%) were male bodies and 25 (50%) were female bodies. The female to male ratio was 1: 1. Mean actual time of death was 73.46 ± 33.82 hours, while the estimated time of death on CSF protein assessment was 71.54 ± 31.92 hours. The mean CSF fluid level was observed was 170.26 ± 88.61 mm^3. A significantly strong positive correlation was observed between time estimated by using protein level in CSF fluid and actual time of death i.e. r =0.952 (p-value <0.0001).

Conclusion: CSF proteins have good correlation value for postmortem interval. It can be beneficial in estimating time of death in unknown bodies.

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To decide the time of death, the expertise of a forensic pathologist is needed to assist in investigating the death of a deceased individual. This support from a forensic expert not only helps to establish a time frame for the investigation but also helps to narrow downthepoolofpotentialsuspectsincasesofhomicide. Time since death also provides valuable information to establish timeline of proceedings leading to death.[1] It is difficult to assess time of death due to multitude of variables affecting accuratecalculation. Variousauthors have conducted research on qualitative and quantitative changes in the expression of protein in the biological samples of humans and animals over specific time periods, in post-mortem study. Nevertheless, literature on this topic is extensive and often lacks consistency, with variations in proteins, tissues, and models being

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appraised. Consequently, in practical, the application of these methods is restricted to-date.[2]

Forensic medicine faces a challenging task of accurately estimating time of death due to the imprecise nature of commonly used methods for determining thepostmortem interval. In recent decades, biochemical methods have been introduced to enhance the precision of postmortem interval estimation using postmortem samples. The focus of studies has been on the bio-chemical profiles of body fluids in close compartments as theyundergo limitedpostmortem chemical changes compared to blood. CSF has been identified as a suitable fluid for investigating these changes due to its abundance and ease of sampling.[3]

Accurately estimating the postmortem interval is essential forsuccessfulforensicinvestigation. Various methods have been employed to determine the postmortem interval, including assessment of physical changes occurring after death such as livor mortis, rigor mortis and others.[4] It is still a significant challenge to estimate the postmortem interval, and the current approaches used to determine it often result in broad postmortem intervals.[5] Postmortem changes can ominously affect and modify bio-chemical constituents of body fluids particularly blood leading to controversial results. As a result, studies have shifted their focus towards other body fluids that are present in confined compartments and are less prone to contamination immediately following death. Vitreous humor, CSF, pericardial fluidandsynovial fluidarebeingstudied now a days.[6]

CSF is an ultra-filtrate of plasmahence it hassmall percentage of proteins and small quantity of blood cells which are mainly WBC. In electrolyte concentrations, sodium ions are equal in proportion as in plasma and chloride and magnesium ions are in a bit larger concentrations.[7] Quantity of CSF is almost 150 ml in which 0.3 or 15-45 mg/dl are proteins or evenlower in case of children. Protein concentration in CSF also depends on site from where the sample has been taken. Normally protein concertation is lower in cisternal and ventricular area but a bit higher in lumbar region.[8] In a study, the coefficient between actual time of death and estimated time of death by using CSF proteins was noted as 0.1935 (correlation coefficient (r) = 0.44, p = 0.001 9.

Determining correlation among postmortem interval and estimated time of death by using CSF proteins estimation was the rationale of this study. Literature showed that CSF proteins have good correlation value for postmortem interval. It can be beneficial in estimating time of death in unknown bodies. But limited work has been done in this regard and no local study done before. Therefore, we planned this study to get evidence in local population correlating CSF protein levelswith PMI inlocal setting. Timesincedeathassessment has been requisite in investigation of forensic sciences and it needs multiple techniques and methods so that suitable methodology can be applied in any situation accordingly. Thus this study was conducted with an objective to determine the correlation between cerebrospinal protein levels in cadaveric CSF and postmortem interval.

METHODS

It was cross sectional study conducted at Forensic Medicine and Toxicology Department of, Allama Iqbal Medical College, Lahore for a period of one year i.e. 1-1-2022 to 1-1-2023. The sample size was 50 cases with 5% type I error, 10% type II error and correlation coefficient value i.e. r= 0.44 between actual time and estimated time of death on CSF protein.[9] The non-probability, consecutive sampling technique was used. Deadbodies of 5-80 years of either sex receivedwithin 1-5 days of death for autopsy with known time since death were included in the study while putrefied dead bodies, bodies with head trauma and known brain diseases were excluded.

After obtaining approval from ERB of institution, fifty dead bodies from morgue section of Forensic Medicine department were obtained after informed consent. Demographic information like age, gender, duration / time of death, cause of death were noted. CSF sample were taken by using lumbar puncture technique from space between L3-L4 and L4-L5 by using 20 gauge lumber puncture needle. Disodium molybdate, pyrogallol and succinic acid were used. The dye bin-

ding method using pyrogallol red was employed for calculation of minimum detectable concentration (0.022 g/l) of total proteins in CSF. Semi-auto biochemical analyzer was used which worked on the principle of spectrophotometry. Quantitative values of proteins were obtained automatically through auto-biochemical analyzer andthen were assessedfor CSF proteins. Findings were recorded and correlated with postmortem interval according to policerecord. Datawereanalyzed by using SPSS version 25. Pearson's correlation coefficient was calculated to measure relation between time of death and time estimated on basis of CSF proteins. P-value ≤0.05 was taken as statistically significant.

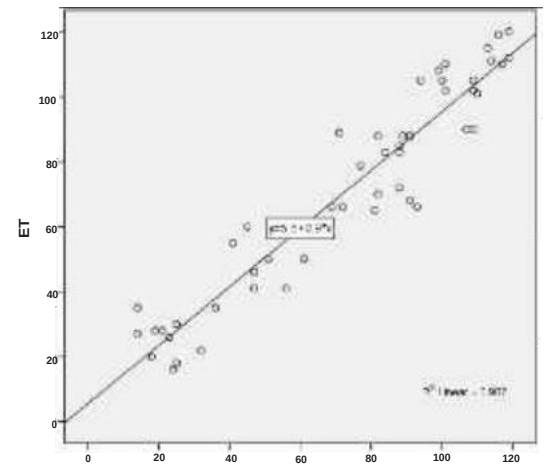
RESULTS

The mean age of dead bodies at time of death was 45.14 ± 13.25 years. There were 25 (50%) male bodies and 25 (50%) female bodies. The female to male ratio was 1: 1. Diabetes was positive among 31 (62%) cases, hypertension was reported in 39 (78%) cases, and smoking in 24(48%) cases and cardiovascular diseases were present in 32 (64%) cases. The major cause of death was natural that was observed in 31 (62%) cases, followed by accident in 12(24%), suicide in 4 (8%) and maternal mortality in 3 (6%) cases. The mean actual time of death was 73.46 ± 33.82 hours, while the estimated time of death on CSF fluid was 71.54 ± 31.92 hours. The mean CSF fluid level observed was 170.26 ± 88.61 mm3. Out of 50 autopsies, 7 (14%) bodesreceivedwithin24 hours, 8 (16%) received on 2nd day, 6 (12%) received on 3rd day, 14 (28%) on 4th day and 15 (30%) on 5th day of death. (Table I)

Table 1: *Profile of Bodies Examined (n=50)*

Feature	Mean ± SD, F (%)
Age (in years)	**45.14 ± 13.25**
Gender	
Male	25 (50%)
Female	25 (50%)
Co-Morbid conditions	
Diabetes	31 (62%)
Hypertension	39 (78%)
Smoking	24 (48%)
Cardiovascular disease	32 (64%)
Cause of death	
Suicide	4 (8%)
Natural death	31 (62%)
Accident	12 (24%)
Maternal mortality	3 (6%)
Actual time of death (hours)	**73.46 ± 33.82**
CSF protein level	**170.26 ± 88.61**
Estimated time of death (hours)	**71.54 ± 31.92**
Time interval between death and receiving of body for autopsies	
Within 24 hours	7 (14%)
After 2 days	8 (16%)
After 3 days	6 (12%)
After 4 days	14 (28%)
After 5 days	15 (30%)

A significantly strong positive correlation observed between time estimated by using protein level in CSF fluid and actual time of death i.e. r = 0.952 (p-value < 0.0001). Figure 1



Pearson's correlation coefficient = 0.952
(p-value <0.0001)

Figure 1: *Correlation between actual and estimated time of death*

DISCUSSION

Estimating the postmortem interval (PMI) in forensicpathologyposesasignificant challenge. Typically, thecalculation is carried out by comparingvarious parameters, including cadaveric rigidity, body temperature, and hypostasis.[10] Furthermore, the diagnosis is supported by analyzing metamorphic phenomena of the cadaver, postmortem ocular changes, and circumstantial information.[11] The exactitude of estimated postmortem interval (PMI) based on these parameters is

dependent on the time that has passed since death. This means that as time goes on, the calculated time range becomes less precise and more approximate.[2] Vitreous humor is the most commonly used body fluid for this purpose. The renewed literature exists on the study of inquest biochemical analysis of blood and other body fluids.

For many years, postmortem examination of cerebrospinal fluid (CSF) has been conducted. Specific markers in CSF have been studied to diagnose neurodegenerative diseases like Alzheimer's disease and suchstudies haveproveduseful. Onesuchmarker, Tau protein, is found in patients of Alzheimer's disease. It is studied in CSFalongwithothercomponentsinvolved in metabolic processes of bio-chemical interest.[12-14] PMI is accessed by various available methods but precise and reliable estimation is still fly-by-night.[15] Studieswithlargerhumansamplesizeandstandardized protocols are still required.[16] A valuable and significantparameterforestimationofPMIisCSFalbumin.[17]

In this study, we observed that there is a strong positive correlation between time estimated since death by usingproteinlevel in CSFfluidandactual time of death i.e.(r = 0.952) (p-value < 0.0001). In a study, similar findings were reported and regression coefficient of 0.991 was noted.[9] In a study, the regression coefficient between actual time of death and estimated time of death by using CSF proteins was noted as r^2 = 0.1935 (correlation coefficient (r) = 0.44, p=0.001[9].

CSF, owing to protected anatomical location suffers little change in early postmortem phase, and is arelatively stable fluid. Althoughnumerousimmunehistochemical markers used for clinical diagnostic purposes in tissue biopsy samples can now also be applied to postmortem tissues. There has been no systematic immune-cyto-chemical investigation of postmortem body fluids and for CSF in particular. Such investigations are not established at all. CSF should be examined for a more detailed categorization of the processes in CNS as it directly surrounds the brain. Comparison of traumatized tissue and CSF can provide valuable information for forensic assessment and supplement neuropathological evaluation. It can provide additional evidence for diagnosis and understanding of traumatic brain injury. This information can be crucial in forensic investigation and can aid in determining manner and cause of death.[18]

The concentration of protein in CSF changes not only with advancing age but also to smaller extent depending on the site of sampling. The protein concentration is lowest in CSF of ventricles, intermediary in cisterna magna, and highest in CSF of lumbar region. The difference in protein concentration among cisterna magna and lumbar region is approximately 0.1 g/L.[19] Tau proteins, present in CSF, are well established biomarkers of neuro-degeneration and neuronal damage. It is suggested that Tau proteins can increase in postmortem period due to death of neurons and can serve as potential biomarker of time after death.[20] The dispassion of leptomeningeal lining cells causes rise of mononuclear cells in CSF during first 24 hours of death.[19]

CONCLUSION

CSF protein levels have been found to have a strong correlation with the postmortem interval, and thus have the potential to be employed as biomarker for estimation of time since death with greater precision and accuracy than other methods. It requires fewer techniques, the process is relatively simple with no complications, and the reagents required are readily available and cost-effective. Therefore, if validated by further studies, the use of CSF protein levels as a biomarker for estimating the postmortem interval could be a significant advancement in forensic science.

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PATTERN OF SELF-POISONING AND TOXICITY IN SUICIDAL DEATHS PRESENTING FOR AUTOPSY AT THE TEACHING HOSPITAL OF THE COSMOPOLITAN CITY OF PAKISTAN.

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Abstract

Background & Objective: Suicide is a common cause of death among teenagers and young adults and day by day, an increase has been observed in this trend. In most cases, home-based materials are used for this purpose. Hence, we aim to determine the frequency of various poisonous agents used for suicide and the pattern of presentation of such suicidal death for autopsies at a teaching hospital in a cosmopolitan city of Pakistan.

Methods: This cross-sectional study was conducted at the Toxicology and Forensic Medicine Department, Allama Iqbal Medical College, Lahore over a 1-year period from January 2022 to January 2023. About 60 dead bodies of deceased committing suicide were included through non probability consecutive sampling. Poisonous material used for suicide was inquired from family or next of kin and was verified with a toxicology report. Data was then recorded in proforma and analyzed in SPSS version 25.

Results: The mean age of dead bodies at the time of death was 29.51 ± 14.92 years. There were 37 (61.7%) male bodies and 23 (38.3%) female bodies. The mean duration between death and body received for autopsy was 2.4 ± 1.7 days. Out of 60 cases, 37 (61.7%) cases had a history of depression before suicide, 6 (10.0%) were taking anti-psychiatric treatment, 2 (3.3%) had schizophrenia, 4 (6.7%) had depressive disorder, while 11(18.3%) had no depressive symptoms or relatives were unaware of that. Out of 60 cases; 12 (20.0%) committed suicide with organophosphates, 10 (16.7%) took over-the-counter drugs, 8 (13.3%) ingested household chemicals or acid, 6 (10.0%) took kala pather, 6 (10.0%) ingested wheat pills, 5 (8.3%) took cocaine in overdose, 5 (8.3%) had methamphetamines overdose, 3 (5.0%) had cannabinoids, 2 (3.3%) had methadone, 2 (3.3%) benzodiazepines and 1 (1.7%) had alcohol overdose.

Conclusion: Organophosphate (pesticide) is the most commonly used suicidal poisoning agent, followed-by household acids in cosmopolitan cities (urban areas). Stringent regulations are needed to regulate the sale of these toxic materials to avoid unnatural deaths of our youth.

Keywords: poisonous material, suicide, Organophosphates, over the counter drugs.

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Suicide is defined as "act of deliberately injuring or intoxicating own-self with the intention to cause one's own death. On the other hand, a suicide attempt is an action in which someone causes harm to themselves with the intent to die, but does not succeed in doing so.[1] From 2000 to 2021, the rate of suicide increased by approximately 36%. In 2021, suicide accounted for 48,183 deaths, which equates to approximately one deathevery 11 minutes. Suicidal ideation and attempts are more widespread than actual suicide. According

to estimates for 2021, about 12.3 million American adults seriously contemplated suicide, 3.5 million planned to suicide, and 1.7 million tried an attempted suicide.[2,3] Suicide ranked as second among leading causes of death of People aged as 10-14 and 20-34.[3,4]

Pakistan has the fifth largest population (207 million) in the world. While, predominantly, people are attached with agriculture, with about 64% of its population is residing in rural areas, according to the 2017 National Census.[5-7] Due to the absence of vital registrations, Pakistan does not have precise statistics on deaths by suicide.[8] However, compared to the international suicidal deaths rate per 100,000 people for both genders in 2017 of 9.98 , Pakistan has an estimated age-standardizedsuicidal death rate of 4.4 per 100,000 people.[9] The suicide death rates, in neighboring South Asian countries like Sri Lanka, India and Bangladesh, are 13.33, 5.73 and 7.55 per 100,000 people, respectively. Suicide is emerging as significant problem of public health as per recent data despite estimated rates of suicide are low.[10,11]

Even in advanced countries having modern and latest data collection systems of health of population, obtaining reliable information of morbidity and mortality due to poisoning is challenging. Although interpreting available data can be difficult, some general observations can be made about poisoning epidemiology. Childhood poisoning is typically accidental and is usually associated with smaller rates of morbidity and mortality.[12] There has been a concerning increase in suicide attempts through self-poisoning over time, indicating a need for greater attention to this issue. To address the risk factors that contribute to such suicide attempts, it is important to direct efforts towards prevention and intervention measures.[13]

To find the most common poisoning agent involved in suicidal deaths observed during autopsies of suicidal deaths was rationale of this study. Literature showed an increasing trend in poisoning agents that are available in homes and work places in Pakistan to be used for self-intoxication. Therefore, there is a need to find the major source of poisoning substances in our local population. Thus, this study was conducted with an objective to determine the frequency of poisoning agents used for suicide and pattern of their presentation for autopsies at teaching hospital of cosmopolitan city of Pakistan.

METHODS

This was Cross sectional study carried out at Toxicology and Forensic Medicine Section of Allama Iqbal Medical College, Lahorefor a period of one-year from January 2022 to January 2023. Sample size calculated was 60 suicidal autopsies. (with 95% confidence level, 10% margin of error and percentage of swallowing wheat pills i.e. 19.1% for suicide in Pakistani popula-tion)[14] Non-Probability, Consecutive Sampling tech-nique was used. Dead bodies of 16-65 years of both genders received within 1-5 days of suicidal deaths brought for autopsy were included. Bodies with history of prolonged use of toxic drugs or narcotics, putrefied dead bodies or burned after chemical suicide were excluded.

After obtaining approval from ERB of institution, autopsy report of sixty dead bodies brought for autopsies was studied. Informed consent was obtained from next of kin. Demographical data like age, gender, ethnicity, occupation before death, education level, stress level, dependency, smoking, history of alcoholism, duration / time of death, residence, and location of death were noted. Cause or poisonous material used for suicide was also inquired from family or next of kin and that was counter checked from toxicology report of autopsy. Proper examination of clothes with externalandinternal examination of thebodywas done. Findings wererecorded in aproforma. Datawereanalyzed through SPSS version 25. Qualitative variables were presented as percentage and frequency while numerical variables were presented as mean and standard deviation.

RESULTS

The mean age of dead bodies at the time of death was 29.51 ± 14.92 years. There were 37 (61.7%) male bodies and 23 (38.3%) female bodies. The male to female ratio was 1.6: 1. There were 28 (46.7%) cases

who belonged to Punjab ethnicity, 12(20.0%) cases belonged to Sindh ethnicity, 11(18.3%) cases belonged to KPK ethnicity and 9 (15.0%) cases were from Baluchistan. The occupation of deceased was majorly business [11(18.3%)], followed by 8 (13.3%) who were doing jobs, 15(25.0%) were students, 9(15.0%) were housewives, and 17 (28.3%) were jobless. Out of 60 cases, 23 (38.3%) were illiterate, 14(23.3%) were under matric, 9(15.0%) were under graduate, 8(13.3%) were graduate and 6 (10.0%) were post-graduate. Out of 60 cases, 12 (20.0%) were dependent on their relatives for finances, 15(25.0%) were smokers, and 7(11.7%) were alcoholics. The mean duration between death and body received for autopsy was 2.4±1.7 days. Out of 60 cases, 19(31.7%) bodies were received from rural area and 41 (68.3%) were from urban areas. Out of 60 cases, 37(61.7%) cases had history of depression before suicide, 6(10.0%) were taking anti-psychiatric treatment, 2 (3.3%) had schizophrenia, 4 (6.7%) had depressive disorder, while 11(18.3%) had no depressive symptoms or relatives were unaware of that. The most common location of death was home [26 (43.3%)], while 12 (20.0%) were found dead at work place, 14(23.3%) werefound at school, 6(10.0%) were found at unknown place and 2(3.3%) at friend's home. Table 1

Table 1: *Baseline features of patients*

Feature (n=60)	*Mean±SD: f (%)*
Age (in years)	29.51 ± 14.92
Gender	
Male	37 (61.7%)
Female	23 (38.3%)
Ethnicity	
Punjabi	28 (46.7%)
Sindhi	12 (20.0%)
KPK	11 (18.3%)
Baluchistan	9 (15.0%)
Occupation of deceased	
Business	11 (18.3%)
Job	8 (13.3%)
Student	15 (25.0%)
Housewife	9 (15.0%)
Jobless	17 (28.3%)
Education level	
Illiterate	23 (38.3%)
Under matric	14 (23.3%)
Under-graduate	9 (15.0%)
Graduate	8 (13.3%)
Post-graduate	6 (10.0%)
Dependency	12 (20.0%)
Smoking	15 (25.0%)
History of alcoholism	7 (11.7%)
Duration / time of death (days)	2.4 ± 1.7
Residence	
Rural	19 (31.7%)
Urban	41 (68.3%)
Stress level	
Depressed before suicide	37 (61.7%)
Was taking psychiatric treatment	6 (10.0%)
Schizophrenia patients	2 (3.3%)
Depressive disorder	4 (6.7%)
No depression	11 (18.3%)
Location of death	
Home	26 (43.3%)
Work place	12 (20.0%)
School	14 (23.3%)
Unknown place	6 (10.0%)
Friend's home	2 (3.3%)

Out of 60 cases; 12 (20.0%) done suicide with organophosphates, 10 (16.7%) took over the counter drugs, 8 (13.3%) took household chemical or acid, 6 (10.0%) took kala pathar, 6 (10.0%) took wheat pills, 5(8.3%) tookcocaineoverdose, 5(8.3%) tookmethamphetamines overdose, 3 (5.0%) had cannabinoids, 2 (3.3%) tookmethadone, 2 (3.3%) tookbenzodiazepines and 1 (1.7%) took alcohol. Figure 1

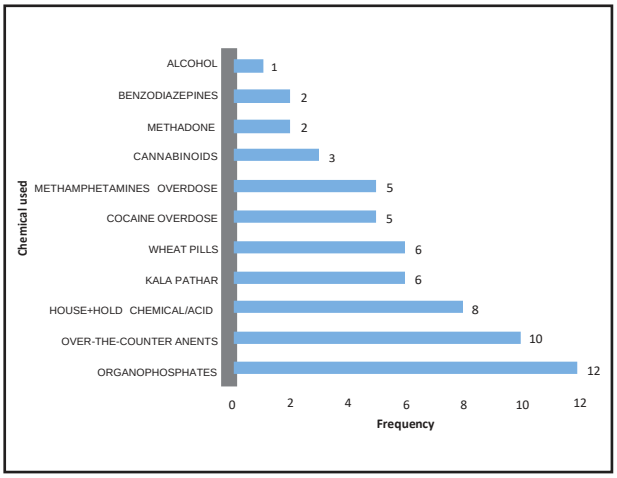

Figure 1: *Chemicalinvolved in suicide*

DISCUSSION

Forensic autopsies often require the expertise of

related scientific disciplines, in addition to forensic pathology, to diagnose crucial forensic issues. For instance, identifyingthechemicalcompounds or natural toxins involved in a case of poisoning is essential to determine the cause of death, while genetic analysis of material obtained from an unidentified autopsied body is necessary for personal identification. Forensic medicine, in a broader sense, encompasses various forensic sciences and can be categorized into three primary fields: forensic toxicology, forensic biology, and forensic pathology.[15]

Hospital populations are more likely to engage in self-poisoning, whereasself-cutting is moreprevalent in the general population. In adolescents, self-cutting may be up to twice as common as self-poisoning. The methods used for self-harm vary depending on gender and age group. Social, legal, and religious factors can inhibit reporting or result in underreporting of suicide and self-harm. Recent reports indicate that suicide and self-harm rates in the country are rapidly increasing despite these factors.[16]

Shekhani and colleagues observed that there is a stigmatization of suicidal behavior that can impede research on the subject.[17] Self-poisoning is a prevalent method of suicide, with one in five suicides in the United States involves poisoning as the primary method. Additionally, almost 70% of individuals consume a substance prior to their suicidal death.[18] The prevalence of attempted self-poisoning has increased and easier access and availability of drugs and chemicals has also replaced traditional methods of suicide. Pesticides alone are responsible for a quarter of global suicide rates.[19] Psychotropic drugs, sedative-hypnotics, analgesics, antihistamines, antidepressants and, psychoactive drugs are widely used for self-poisoning in suicidal attempts in developed countries.[20]

In our study, we observed that; 12(20.0%) done suicide with organophosphates, 10(16.7%) took over the counter drugs, 8(13.3%) took household chemical or acid, 6(10.0%) took kala pathar, 6(10.0%) took wheat pills, 5(8.3%) took cocaine overdose, 5(8.3%) took methamphetamines overdose, 3(5.0%) had cannabinoids, 2(3.3%) tookmethadone, 2(3.3%) took benzodiazepines and 1 (1.7%) tookalcohol. Tahir et al., found that toxic substance was involved in 36% cases, followed by pesticides 31%, drug overdose 11%.[21]

The higher case fatality rate of self-poisoning with pesticide ingestion is the most probable explanation for the prevalence of pesticide related suicides in developing countries. In comparison, substances commonly used for self-poisoning in the West have lower case fatality rate. In England and Wales, for instance, the case fatality rate among individuals hospitalized for self-poisoning treatment is less than 0.5%, while in rural areas of Sri Lanka, it is 7%. [22]

Typically, it involves an intended overdose of many substances. The primary drugs involved in poisoningincidentsareanxiolyticslikebenzodiazepine, tranquilizers and hypnotics, drugs used for epilepsy such as carbamazepine and valporic acid and antidepressants like TCAs and SSRI, as well as various types of neuroleptics. Drug poisoning is particularly prevalent among individuals with psychiatric conditions and drugs and alcohol addiction, as they may turn to psychotropic drugs during periods of intensified withdrawal symptoms or acute alcohol intoxication. [23]

Other psychoactive substances including over the counter available drugs capable of affecting consciousness, behavior, and emotions can be used for suicidal driveswhenconsumed in large amounts. Among these substances, opioids and their derivatives are commonly used.[24] It has been noted that since 2017, another group of brain-stimulating substances called "legal highs" havebeenpresent in thestatistics of suicidesandsuicide attempts as available with Polish police. These substances containpsychoactivecompoundssuch as N-benzylpiperazine, which is used as substitute foramphetamine, as well as synthetic cannabinoids and cathinone derivatives such as mephedrone and naphyrone. [25]

There is scarcity of the literature on comparison of regional trends of suicide and self-harm within Pakistan as well as urban and rural variation.[14] But in our study, most of the cases were from urban region 41(68.3%) with organophosphates being the most common poison used for self-poising among suicidal deaths.

Since suicidal deaths brought for autopsy were from urban areas only, many suicidal deaths from rural areas have not been taken account of, that limits our study.

CONCLUSION

Organophosphate(pesticide) is themostcommonly used poisoning agent for suicide, followed-by house hold acids in cosmopolitan city (urban area) hence stringent regulations are needed to regulate the sale of these toxic materials to avoid unnatural deaths of our youth.

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SOCIO-CULTURAL BARRIERS AND HEALTH SEEKING BEHAVIOR AMONG FEMALE PATIENTS OF TUBERCULOSIS IN SOUTHERN PUNJAB

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Abstract

Background & Objective: In Pakistan, some societies consider a woman's place is at her home, and they are discouraged to visit the outside home including health facilities. Due to these societal restrictions, many health problems remain undiagnosed and untreated. According to the latest TB trends, the female ratio in smear-positive cases is increasing each year worldwide, which is a serious threat. Hence, we aim to assess the socio-cultural barriers faced by the women and their health seeking behavior for TB.

Methods: This cross-sectional descriptive study was carried out in two District Hospitals in southern Punjab (Muzaffargarh and DG khan). About 190 females patients with tuberculosis registered at the TB clinic were selected through simple random sampling. An interview was conducted and the responses were recorded in a structured questionnaire. Data were entered and analyzed using SPSS.

Results: Out of 190 patients, a majority 161(85%) of the females claimed that their family and community are reluctant to meet them, 178 (94%) were afraid of leak of information to the community, 112 (59%) were delaying seeking treatment due to stigma, 110(58%) had health facility conveniently located from their residence, however 164 (86%) were not satisfied with the traveling costs.

Conclusion: Health-seeking behavior of the female TB patients as well as sociocultural and transport barriers influence the treatment in these patients hence mass education and dedicated health facilities along with transport facilities should be made available to these patients.

Key Word: Seeking behavior, Tuberculosis, Cultural behavior, delay services

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Tuberculosis (TB) is a worldwide prevalent infectious disease. World Health Organization (WHO) reported 32% of the world's population is suffering from Tuberculosis. Approximately eight million TB cases and two million TB deaths are being reported globally every year. 22 countries are contributing 80% of the total TB cases in the world. Pakistan is also a highly endemic country contributing 65% of all TB cases in the Eastern Mediterranean Region (EMR) of the World Health Organization. In Pakistan, Punjab is contributing the highest i.e. 50% of total TB cases reported in Pakistan.[1]

Tuberculosis is a serious public health issue in Pakistan and it had been notified as a national emergency in 2001. As a combating strategy, Directly Observed Treatment Short Course(DOTS) wasadopted because TB is completely curable through short-course chemotherapy. Pakistan stands 5th among the 22 TB highburden countries of the world, as well as 4th among 27th high Multiple Drug Resistant (MDR) countries.

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According to the National Prevalence Survey 2011[2], the reported prevalence of TB was 342, with an incidence of 275 and there were 27 deaths per 100,000 populations. The National TB Control program reported overall 384415 male and 132972 female cases in 2014 while 191885 males and 81862 females were reported from Punjabalone. It is aknownfact that one TB patient can infect 10-15 other persons in one year.[3] Therefore strategy of early diagnosis and prompt treatment with effective follow-up is very important for successful control of TB. Delayed diagnoses enhance community transmission, which increases the mortality and morbidity burden of the disease while the treatment cost increases poverty.[2]

According to the WHO report of 2004, the estimated burden of TB in Pakistan was 3,50070 cases. Out of the total registered cases, there were fewer male cases as compared to females. According to TB data, trends are changing, and the female ratio in smear-positive cases is increasing. Reportedly 500,000 women die each year of TB in the world, which is indeed a seriousthreatworldwidebecausethis is ahighernumber of deaths among women as compared to deaths associated with maternity. It has been reported in many studies that during the reproductive age period (15 -45) more women suffer from TB as compared to men. This brings a negative impact on children and families as these are economically active years of females. Female TB patients also face difficulties to get access to early diagnostic and treatment facilities due to their added childcare and earning responsibilities in addition to theirhomechoresandresponsibilities, whichultimately become the reason for deaths from TB.

Personal experience and culture influence human treatment-seeking behavior, culture is more important and therefore requires more devoutness. It is proved by many studies that without knowledge of local conduct, control measures cannot be fruitful. Urban-rural mass's behavior is significantly different, the urban female population can understand the importance to visit the doctor as soon as possible while rural females cannot even visit the doctor without the company of their husband or any senior family member, they cannot even afford the fee of a private doctor. WHO data described that males were found more positive for sputum smears positive as compared to females, one of the reasons is fewer female patients seeking health facilities for diagnosis. Hence, the diagnosis of TB in females is deferred and delayed, which increases the burden of disease in the community and also on the health system. These types of delays have been well documented in a number of studies globally.

Social stigma leads to fewer patients disclosing symptoms to others, being reluctant to seek care or a diagnosis, anddefaulting from seeking treatment from local catchment areas. In a study by Somma D, Bangladesh a female patient reported : "I do not know why Allah has given me this disease. I cannot go to any social happenings. My dignity is less because I have moved to my mother's place from my husband's home. The people from my husband's family stay away from me. My pride and dignity have been decreased a lot because of my disease".[5]

Another socio-cultural problem faced after diagnosis is that these patients quit office work because of stigma, feeling weak, and low acceptance at the workplace which adds to the economic problems of the patients, so gender bias, cultural, andpersonal experiences contribute to poor health health-seeking behavior and ultimately prognosis.

In 1983 Kroeger splits the two approaches called "the pathway model and the determinants model". The 1st was a rational-based use of health care facilities at the earliest possible and choice-based health care service. WHO (2015) chose to underpin the issues and described them differently: "Globally, more men than women fall ill with TB annually. However in some settings, such as Afghanistan, and parts of Pakistan bordering Afghanistan, and Iran, more women than men are diagnosed with TB. Social, cultural, and financial barriers can act as major obstacles for women seeking care resulting in delayed presentation and more severe illness. TB mainly affects women when they are economically and reproductively active, the impact of the disease is also strongly felt by their children and families."[6]

Rahman in 2000 testified that female patients' choice to get treatment from a specific hospital is a complex pronouncement of various actions like location, dealing of doctors, availability of facilities, and social viability of the community.[7]

Hence, we aim to assess the existence of female gender-related sociocultural barriers and health-seeking behaviors among TB patients. The identification of these barriers will help in overcoming these barriers and developing gender-sensitive TB control programs on local level as well as on national policy making level. The ultimate results will detect gaps between provider and client in the fight against TB.

METHODS

This cross-sectional study was conducted in two District Headquarters Hospitals (DHQ) of Southern Punjab (Muzaffargarh &D.G. Khan) for which we included 190, 18-50 years old female TB patients registered at DHQ Hospitals. Patients were selected randomly from a list of patients already registered at the centers. An interview was conducted and recorded on a structured questionnaire comprising 3 sections i.e. stigma related barriers, transport related barriers and health-seeking behavior of patients about tuberculosis. The accuracy and confidentiality of the data was ensured by organizing, editing, coding, and then entering in SPSS version 20 for the analysis.

RESULTS

We interviewed 190 female TB patients and data demonstrate that the majority (85%) of respondents reported that their friends, peer groups, or community members were reluctant to meet with the patient. As far as theconcernabout frequentlymeeting with colleagues at theworkplacethemajority(58%) of respondents do not meet frequently. Afraid of the treatment and consequences of information leaked surrounding the community the majority (94%) of respondents were afraid. Most (87%) of respondents think that women suffering from TB are more affected due to social stigma and community pressures, (and 59%) are delayed in seekingtreatmentdue to social stigma. Themajority (47%) of respondents' husbands or their family was thinking about divorce or reducing the chance of marriage due to social stigma. but a substantial majority (38%) of respondents feel shame to express their diseases & receiving treatment for tuberculosis due to the bad perception of the diseases in the society.

It was also seen that the majority of women who have TB faced traveling-related barriers during their visits to healthcare facilities. Data briefed that the majority 86% of respondents find it expensive to travel from their residence to thehealthcenter, 77% of respondents TB patients did not travel to the health center due to non-availability of transport, and 95% of the res-

Table 1: *Stigma and Transport Related Barriers Experienced by Female TB Patients (n=190)*

Section 1: Stigma-Related Barriers:	**Yes**		**No.**	
	f	**%**	***f***	**%**
Are your friends, peer groups, or other community members reluctant to meet you?	161	85	29	15
Are your close relatives reluctantto meet you?	85	45	105	55
Do your colleagues frequently meet you at your working place?	111	58	79	42
Are you afraid of the consequences of the leak of information to the community?	178	94	12	6
Do you think women suffering from TB are more affected due to stigma?	165	87	25	13
Are you delaying seeking treatment due to social stigma?	112	59	78	41
Is your husband or his family thinking to divorce you or ending your relationship?	89	47	101	53
Do you feel shame to express your disease & receiving treatment for it?	73	38	117	62
Section 2: Transport-related barriers:				
Is the public health facility conveniently located from your residence?	110	58	80	42
Is it expensive for you to travel from your residence to a health facility?	164	86	26	14
Do you go to a public health facility in case of non-availability of transport?	44	23	146	77
Does distance influence your choice of a health care facility?	180	95	10	5

pondents agreed that distance of health care facility plays a vital role in their health seeking behavior.

While assessing health-seeking behavior it was found that only half of the patients (51%) pay health facility visits frequently. Only 30% accept their disease when they experience the symptoms and only 25% admit giving importance and taking care of their health. 77% experienced stress regarding the disease and its treatment and 66% were afraid of consequences and death. However, 86% of respondents confess their familyandhusbands givingimportance to their health.

DISCUSSION

Many financial and political efforts have been made during the past two decades to control tuberculosis in Pakistan by creatingmassawarenessandenhancing the diagnostic and therapeutic expertise of healthcare providers. Tuberculosis is a common disease which is curable within six months of treatment. TB tests and treatment are free and available at all public health facilities in all over Pakistan. The developed world has controlled this disease by adopting good strategies and some of the developing countries have a significant dip in the number of new cases of tuberculosis and deaths. But socio–cultural barriers in our society have led to low health seeking in these patients especially women. Sudhakar M.V reported that the social, cultural, and financial burden on women due to diseases affected their health-seeking behavior because tuberculosis infections cause deaths in most females globally.[8]

Table 2: Health Seeking Behavior of Female TB patients (n=190)

Section 3: Health-seeking behavior of patients about tuberculosis	Yes		No.	
	f	%	*f*	%
Are you visiting the Health Care Facility frequently?	97	51	93	49
Do you accept the sickness, when you feel the symptoms of the disease?	58	30	132	70
Do your husband and family give importance to your health?	163	86	27	14
Do you give value to health and try to keep it safe?	48	25	142	75
Are of afraid of the treatment consequences or death from TB?	125	66	65	34
Do you have any stress about your illness and its treatment?	138	77	52	27

Gender, cultural, social, and personal experiences generally influence health seeking behavior of individuals. Lakshmi K (2014) study supported our present result that female patients face more sociocultural barriers as compared to the males. Most of the women experienced issues related to finances, low literacy, and household stigma. However, she also claimed that the socio-cultural barriers limit the access to TB care services in the context of specific gender-related differences.[9] Socio-cultural norms associated with the status and women's role, lack of family support, and women's autonomy directly affect each barrier type. Another social researcher Onifade D.Aet al supported our results and found that the health care worker overwhelmingly state that women experienced stigma and socio-cultural beliefs as a greater barrier to accessing TB treatment services.[10]

According to Eastwood S.V study, women experienced more cultural barriers in terms of travelling cost, distance from residence and behavior of health care providers.[11] Long N.H, Johansson E, Lonnroth K study indicated that longer travel time or long distance from residence to health care facility, low education and high number of family members among both sexes affected their treatment seeking.[12] The delays to diagnosis of tuberculosis among women were higher than men. Most of the women TB patients has different kinds of barriers, like, social stigma, travel cost, distances from residence, and location of health facility, organizational factors and health care providers behavior. Khan. M.S (2012) study results found that longer distance of health center from residence was a greater barrier to women than men in health seeking services.[13] The literature on preference regarding TB related health services indicate that women in several Asian setting prefer traditional healer and private practitioners over Government center due to socio-cultural and organizational factors. AStudy in Pakistan have reported that women's mobility is restricted so they prefer

the health services that are more close to their home. Accordingto Eastwood S.Vet al workerfeltthatwomen experienced more barriers then men in terms of travelling cost.[11] The results showed that demographic and cultural identifiers were very diverse and most of the respondent's knowledge about the prevention and diagnosis of tuberculosis was low. Rajeswari R, Chandrasekaran V et al and several other studies supported our study results. Family's role in treatment-seeking especially in TB treatment is very important.[14] The majority (62%) of the respondent's husbands did not go accompanied wife to health care facilities. Another study by Agboatwalla M, Qazi G.N & Shah S.K also supportedthe present studythat rural and urbanfemales were generally reluctant to visit regular health facilities alone. The rural women would not be allowed to visit the health facility unless accompanied by husbands or other close family members so nearby facilities are more likely to be visited by the females.[15,16]

One of the study by Chandrasekhar V reported that the decision of the women to visit specific health center are based on their individual needs, social & cultural factors, care providers behavior with patient and location of delivery services.[18] therefore addressing all these factors will remove all the hindrance in seeking health care for these women.

CONCLUSION

Socio-cultural barriers in health-seeking behavior have been almost a universal phenomenon all over the country. The present study found that a significant number of women having TB have different levels of socio-cultural barriers, in seeking health services, social stigma, traveling cost, longer travel time or longer distance from residence to a health care facility and inadequate location of public health facility, organizational factors like delay in treatment, insufficient staff, the behavior of health care providers, the unhealthy environment of the facility, availability of the quality medicine and social stigma.

It can be concluded that the treatment seeking behavior, organizational and transport factors, family support, and social stigma have proven to be barriers in health-seeking services of women TB Patients or "higher the socio-cultural barriers lower the health seeking behavior among women's TB Patients and vise-versa.

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PREMENOPAUSAL AND POSTMENOPAUSAL UTERINE LIPOLEIOMYOMA; A REPORT OF TWO CASES

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Abstract

Background & Objective: Uterine lipoleiomyoma are extremely rare variants of leiomyoma. Postmenopausal women frequently develop these types of tumors. but we also have a case of pre-menopausal woman. Ultrasound and CT scan findings may be nonspecific, but The use of MRI prior to surgery can be beneficial in detecting fatty tissue in the lesion. Diagnosis is usually confirmed postoperatively through histopathological examination.

Methods: Two cases were reported. A 60 years old postmenopausal woman with mass in the abdomen presented at Jinnah Hospital Lahore with differential diagnosis of Ovarian teratoma, Leiomyoma sarcoma, non-teratomatous lipomatous ovarian tumor, pelvic sarcoma, and lipomatous malignancy. Another case was reported involving a premenopausal woman who was 53 years old and presented with pelvic pain, irregular bleeding and a mass in the lower abdomen.

Result: Postoperative excision biopsy report showed a rare pathology of Lipoleiomyoma.

Conclusions: Lipoleiomyomas are clinically rare with most common occurrence in uterine corpus. They have excellent prognosis and but a long-term follow- up of patients is required to observe its potential for coexisting malignancies and metabolic disorders.

Keywords: Lipoleiomyoma, Fat cells, Premenopausal case, Postmenupausal case, MRI

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Lipoleiomyoma is a rare benign variant of leiomyoma with an incidence varying from 0.03% to 0.2%[1,2] They consist of mixture of smooth muscles, mature adipocytes and fibrous tissue.[3] In past regarded as lipomatous degeneration, adipose metaplasia, fatty metamorphosis, etc. but now regarded as Distinct True Neoplasia. Classically they are found in the uterus (subserosal, intramural, submucosal) with few case reports describing tumors in extra uterine locations such as cervix, intra-abdominal, ovary, broad ligament, retro-peritoneum and pre-peritoneal.[4,5] The clinical presentation of these tumors can vary based on their location; intra-abdominal tumors can cause symptoms due to mass effects. These tumors are typically found in postmenopausal women in their 60s and 70s, although theyhavealsobeenreported in premenopausalwomen.[6] Whiletheexactcause of fibroids is yet to be determined, there is evidence suggesting that the involvement of growth factors and estradiol is linked to their development.[7] Among the potential causes of lipoleiomyoma, the most likely one includes fatty meta-morphogenesis in smooth muscle cells of leiomyomas.[8]

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CLINICALPRESENTATIONS

Case 1

A 60-year-old woman, gravida 4 para 4 presented to gynae OPD with complaints of pain in her lower abdomen with feeling of mass and heaviness. She had back pain for 3-4 months and it got severe about 1 month ago. She menopaused at the age of 58. Under examination, there was mass in the lower abdomen on

the right side. It had firm consistency with no discharge. Ultrasound was done and it was found that the mass was in the right broad ligament with no abnormality in the uterus. The uterus was smaller than normal. The mass was also attached to the uterus (outer wall) and the ovary, but it was separately distinguished. There were no signs of inflammation outside. Laboratory tests were done and the CBC was normal. Ovarian tumor was suspected but CA-125 was done and it showed normal range. Differential diagnosis included: Ovarian teratoma, Leiomyoma sarcoma, non-teratomatous lipomatous ovarian tumor, pelvic sarcoma, and lipomatous malignancy. Taking consent from the patient, staging laprotomy was done. The uterus was removed, measuring 8 × 8 × 4cm, and the cervix measured 2 × 2 × 1cm. The mass removed consisted of 2 nodular masses with measurements of 22×20×14 cm and14×14×5 cm (Figure2). Theovary was attached to the mass but was identified separately. The operation was done successfully and the vitals were all normal. Follow up for the women was taken for 3 to 4 months, and it showed no complications.

The nodular masses were taken to the pathology department. On gross examination, it was pale yellow with firm architecture. No necrosis, hemorrhage in the cystic area was found. Under histopathology report, it showed a group of adipocytes with interlacing bundles of spindle cells and nuclei were elongated with no pleomorphism. The mitosis figures were greater than 0.3 per high power field.

Case 2

Another case described a 53-year-old premenopausal woman gravida 5 para 4 presented with pain in her lower abdomen and pelvis, irregular bleeding, feeling heaviness which gradually worsened. Under examination, there was a mass present on the lower side of the abdomen. An ultrasound was done, showing a mass in the broad ligament of the uterus which was not attached to either the ovary or the uterus wall. There was no sign of inflammation outside. Laboratory tests were done. Both CBC was normal and CA-125 were normal. The differential diagnosis were ovarian teratoma, lipomatous sarcoma, non-teratomatous lipomatous ovarian tumor, pelvic sarcoma, and lipomatous malignancy. After taking consent from the patient, the surgery was done. mass was removed, measuring 17 × 16 × 13 cm (Figure 1). The operation was done successfully. Follow-up of the patient was taken for 3 to 4 months showing no complications. The mass was taken to the pathology department. On gross examination, the mass had vas-cularity but no haemorrhage. Under histopathology examination, it showed groups of adipocytes with inter-lacing bundles of spindle cells and nuclei were elon-gated. The mitotic figures were less than 3-7 per high power field.

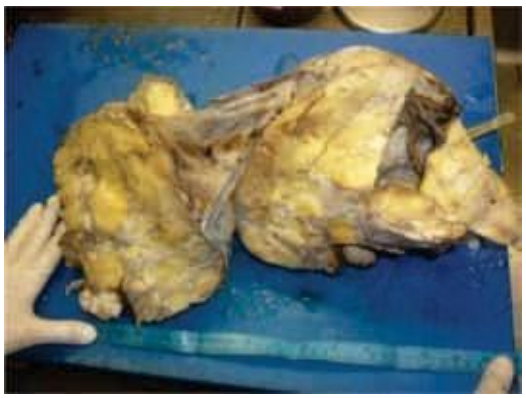

Figure 1: *Gross appearance of a lipoleiomyoma measuring 17×16× 3 cm in a 53-year-old premenopausal woman*

Figure 2: *Gross appearance of lipoleiomyoma in a 60-year-old post menopausal woman consisting of 2 nodular masses with measurements of 22×20×14 cm and 14 × 14 × 5 cm*

DISCUSSION

The lipomatous tumors of the uterus are highly uncommon entity and can be subdivided into three groups: pure lipomas made up of mature fat cells enclosed in a capsule, lipomas containing various mesodermal components (lipoleiomyomas, angiomyolipomas, and fibromyolipomas), and the rare malignant liposarcoma.[9]

Typically found in postmenopausal women who are overweight, uterine lipoleiomyoma is generally asymptomatic.[10] Similar to leiomyomas, lipoleiomyoma can cause symptoms such as an abnormal palpable mass, uterine bleeding, pelvic discomfort, urinary frequency and incontinence in patients. Imaging diagnosis is an important tool in diagnosis. In identifying the fatty nature of the lesion, magnetic resonance imaging (MRI) can be more informative than ultrasound and CT scans, which may yield nonspecific findings. While MRI is the recommended imaging technique for identifying lipoleiomyoma, the majority of cases are diagnosed by histopathology following surgery.[12] Several theories have been suggested regarding the formation of lipoleiomyoma, such as metaplasia of connective tissue or smooth muscles into fat cells, differentiation of embryonic fat cells that were misplaced, migration of pluripotent cell along the uterine vessels and nerves, and degeneration of connective tissue or infiltration of fats.

According to a study[13], the immuno-reactivity of fat cells with S-100,actin,desmin and vimentin providesevidence in favor of thehypothesisthatsmooth muscle cells can directly transform into fat cells. Cytogenetic investigations[14] of uterine lipoleiomyoma have revealed a pathogenic origin that closely resembles that of a typical leiomyoma. According to some researchers the development of uterine lipoleiomyoma may be influenced by a hyperestrogenic state resulting from metabolic disorders such as post-menopausal changes in lipid metabolism, hyperlipidemia, diabetes mellitus, hypothyroidism and toxemia during pregnancy. While lipoleiomyoma is commonly observed in older post-menopausal women[19], we report a case in a pre-meno-pausal patient. This observation could lend support to the theory that hormonal factors may contribute to the development of these rare tumors. Additional research is needed to clarify the potential contribution of hormonal factors and to improve our understanding of the pathophysiology of these uncommon tumors. Despite being a rare tumor, lipoleiomyoma is generally consideredbenignanddoesnotposearisk of localrecurrence or distant metastasis after surgical removal.[15] But, malignanttransformation is alsodemonstrated by reporting a lipoleiomyoma arising from leiomyoma.[16] Distinguishing a lipoleiomyoma from a cystic ovarian teratoma can be difficult, especially when the lipoleiomyoma is located near the ovary on the posterior wall of the uterus[18], as the latter is the most common pelvic fatty tumor in females[17].

It is crucial to accurately identify these tumors as their management can vary significantly. While isolated lipomatous tumors like lipoleiomyoma are typically benign and do not affect mortality, they may not require surgery if asymptomatic. In our patients, total hysterectomy was done in first case and myomectomy in second case and no evidence of malignancy in the female reproductive system was found. In view of complex histogenesis, consideration of malignancies and metabolic disorders in patients of uterine lipoleiomyoma, amuch larger numbers of case studies with to elucidate the histogenesis of these tumors, immunohistochemical analysis and long-term follow-up may be necessary. Therefore, it is crucial formedical professionals to be knowledgeable about this pathology since its clinical manifestation resembles that of leiomyoma, but it exhibits distinctive radiological, histological and immunohistochemical features. Physicians should keep this rare condition in mind while considering differential diagnoses.

CONCLUSION

Arare benign lipomatous tumor, lipoleiomyoma; most commonly occuring in uterine corpus. Despite the potential usefulness of MRI for preoperative diagnosis, histopathological examination remains the mainstay for diagnosing most cases of lipoleiomyoma. It

has a favorable prognosis, doesn't affect mortality and if it's not causinganysymptoms, surgery is not required. Therefore, it's crucial to keep it in mind while making a differential diagnosis. Histogenesis is controversial. A thorough clinical and pathological evaluation, as well as mandatory follow-up, are necessary in cases of lipomatous uterine tumors with coexisting metabolic disorders and gynecological malignancies. Knowledge of the tumor'scharacteristics on imaging can contribute to improvepreoperativediagnosisandmanagement.

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