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DEPRESSION;

PREVALENCE AND SEVERITY OF DEPRESSION AMONG PATIENTS WITH PREGNANCY RELATED ACUTE KIDNEY INJURY PRESENTING TO A TERTIARY CARE HOSPITAL OF A DEVELOPING COUNTRY

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ABSTRACT… Background: Acute kidney injury (AKI) in pregnant women is commonly seen in developing countries. It is associated with significant morbidity, social and personal implications. We conducted a study to assess the prevalence and severity of depression in patients with pregnancy related AKI (PRAKI) in a tertiary care center. **Methodology:** Patients with PRAKI admitted from 1-16 to 6-16 under Nephrology service, Jinnah Hospital, Lahore were included in this cross-sectional study. The Hamilton Rating scale for depression (HAM-D) version translated and adapted in Urdu, was used to assess the study population. These patients were interviewed with the HAM-D questionnaire on their first encounter with Nephrology department. Previous history of psychiatric illness was excluded. The diagnosis of AKI was based on the classification of the Acute Kidney Injury Network group. **Results:** The mean age of the patients was 24±5 years. Seventeen (57%) patients were multipara and 13(43%) patients were primigravida. Of the 30 patients with AKI, 8 (27%) presented before 28 weeks and 22 (63%) presented after 28 weeks of gestation. The causes of AKI included postpartum hemorrhage in 9 (30%), sepsis in 8 (27%), preeclampsia/eclampsia in 6(20%), shock in 4 (13%) and coagulopathy in 3 (10%) patients. Alive and healthy fetus was found in only 15 (50%) patients. Twenty-one (70%) patients received average of 5-8 hemodialysis sessions during their hospital stay. Twenty-three (76%) had no depression (0-7 score), 2 (7%) had mild (8-13 score), 3 (10%) had moderate (14-18 score) and 2 (7%) had severe (19-22 score) depression according to HAM-D score. **Conclusions:** Our study depicted considerable depression of varying degrees in women with PRAKI, increased awareness and effective monitoring for depression should be integrated into regular maternal care to decrease morbidity associated with it.

Key words: Acute Renal Failure, Hemodialysis, Depression.

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INTRODUCTION

Acute kidney injury (AKI) is one of the most perilous and unusual complications of pregnancy in developed countries but frequently seen in developing countries. Obstetric AKI is the acute kidney injury occurring during pregnancy, delivery and labour and/or postpartum period. Its incidence being reported as 1-2.8% in developed countries and 9-25% in developing countries.[1] Prior studies have reported the increased incidence of pregnancy related acute kidney injury (PRAKI) at the time of delivery.[2] PRAKI can wreak havoc in a woman's life physically and emotionally. It bears a high risk of development of bilateral acute tubular or cortical necrosis and, consequently of, chronic renal failure. The diagnosis of acute kidney injury in pregnancy is based on serum creatinine increase. Serum creatinine 1.0mg/dl and BUN 13mg/dL would be considered normal in a non-pregnant individual, but reflect renal impairment in a pregnant female. In a pregnant female the renal disorders can be attributed to those occurring in early pregnancy and those occurring in late pregnancy categorized as pre-renal, intra-renal and post-renal etiologies (Table-I).

CAUSES
Pre renal: Renal hypoperfusion
Hyperemesis gravidarum
Sepsis
Obstetrical hemorrhage
Placental abruption
Postpartum hemorrhage
Intra renal:
Acute tubular injury, including acute cortical necrosis
Severe hypovolemia or hemorrhage
Sepsis-associated
Pyelonephritis
Septic abortion
Thrombotic microangiopathy
Acute fatty liver of pregnancy
Preeclampsia/HELLP syndrome
Thrombotic thrombocytopenic purpura (TTP)
Post renal: Ureteral obstruction (rare)
Nephrolithiasis
Bilateral ureteral obstruction due to distended gravid uterus

Table-I. Etiology of obstetric acute kidney injury

In the first trimester of gestation, acute kidney injury develops most often due to hyperemesis gravidarum or septic abortion. Other disorders arising in early pregnancy are acute tubular necrosis, prerenal azotemia, renal cortical necrosis, pyelonephritis and thrombotic thrombocytopenic pupura. In the third trimester, the renal pathologies due to pregnancy become more challenging and devastating, which are preeclampsia/HELLP syndrome, acute fatty liver of pregnancy and thrombotic microangiopathies. According to several studies, preexisting hypertension remains one of the largest risk factor for PRAKI.[3] In rare cases, obstructive uropathy and nephrolithiasis may impair renal function as well but these usually resolve with delivery. Though the incidence rates have seen a favourable trend over the past 50 years due to improved ante-natal care and a decrease in infections[3], maternal and perinatal morbidity, mortality and fetal loss remain significant challenges.

Another dark aspect of PRAKI is yet to be explored which is psychological morbidity associated with obstetric AKI. The paucity of data on specific psychological impact of PRAKI has led to the need of conducting this very research. Among victims and survivors of AKI, there are higher chances of continued adverse impact on quality of life. Comorbid mood, depression and anxiety disorders predict a poorer outcome and a lower chance of remission in the general population. A brief discussion on psychiatric disorders associated with kidney disease is presented below.

NEUROPSYCHIATRIC DISORDERS ASSOCIATED WITH KIDNEY DISEASE

Major depressive disorder

Depressive disorders have the highest frequency of association with renal diseases. There are recent estimates of 20-30% prevalence of depressive disorders in kidney disease patients especially the hemodialysis population.[4] The prognosis of kidney disease is adversely affected by the presence of depression symptoms. The repercussions include reduced compliance to treatment, nutritional status worsening, impaired immune system, debilitated recovery and higher death rates. Despite its high prevalence and associated adverse outcome, most cases remain undiagnosed and untreated. One possible explanation for the lack of study and clinical and interventional trials is the confusion in defining and recognizing depression in patients with renal disorders. This can be attributed to the strong overlap of uremic and depressive symptoms which makes identification of psychiatric issues difficult against the backdrop of medical illness.[5]

Anxiety disorder

When describing depression and anxiety disorder and their symptoms Wenzel says: the core diagnostic feature of generalized anxiety disorder is the report of excessive and uncontrollable worry that is present more often than not.[6] Such anxiety disorders are found very frequently in patients of acute and chronic diseases but very scarce literature is available on its role and management in this population.

Cognitive alterations

Patients with kidney disease are susceptible to cognitive deficits in any stage of the disease but they are difficult to identify as mild cognitive alterations and dementia are also correlated with

mental function deterioration. The major factor in causing these changes, besides uremic toxins, seems to be brain ischemia which elucidates the involvement of brain in kidney disorders. Another serious complication suffered by patients on dialysis is 'dialysis dementia' which seems to have a very poor prognosis if preventive measures, such as discontinuation of aluminum salts in dialysis fluid, are not taken into consideration.

Delirium

Delirium is a clinical syndrome marked by an acute confusional state, fluctuating course, attentional deficits and severe disorganization of behavior caused by any medical disease outside the brain. In a patient with kidney disorder the triggering factors for these cognitive function alterations are metabolic disorders, hospitalization and changes in drug metabolism (opioids, psychotropic drugs, antibiotics, antiviral medication).

Dialysis and cognition

Although it is observed that hemodialysis may improve cognition in patients with end stage kidney failure, some studies reveal that in patients receiving hemodialysis symptoms of depression and anxiety are common, with 45.7% of subjects falling in the category of anxiety disorders and 23.7% in significant depressive disorders. [7] The process of dialysis may cause cognitive impairment by directly inducing brain ischemia. The reason being the rapid decrease in intravascular volumes and fluid exchanges during dialysis sessions which cause reduced cerebral perfusion and cerebral edema. It has been documented that patients with acute kidney injury are more prone to cerebral hypoperfusion during dialysis sessions than patients with end stage renal disease.[8]

PREGNANCY AND DEPRESSION

Depression is frequently seen in pregnant females, both during and after pregnancy, and has unfavourable effects not only on the female herself but the fetuses, infants and the families. More often than not this kind of depression is strongly attached to socioenvironmental factors such as financial problems, inadequate social support, limited access to antenatal care, substance abuse and a prior history of depressive episodes. Depression is also associated with the risk factors for untoward pregnancy outcomes such as smoking, hypertension, pre eclampsia and gestational diabetes.[9] Women with depression during pregnancy are at increased risk of pre-term birth, low birth weight and intrauterine growth retardation which makes its screening, diagnosis and management indispensable. Talking about postpartum depression, it is more commonly found in women who have experienced prenatal depression, however antenatal depression seems to be more common than post natal depression.[10]

METHODS

We conducted a single-center cross sectional study from Jan'2016 to June'2016 during which 30 patients with pregnancy induced acute kidney injury were admitted under Nephrology service, Jinnah Hospital Lahore. The study was approved by the institutional review board. The patients with evidence of renal disease prior to pregnancy, history of hypertension and diabetes before pregnancy, history of renal calculi and previous history of psychiatric illness were excluded. A pre designed proforma was used to obtain basic demographic data and detailed clinical history of patients regarding number and outcome of pregnancies, preexisting hypertension, diabetes, cardiovascular or renal disease. Each patient also underwent complete obstetric examination. Determinants of renal failure in pregnancy including age of mother, parity, gestational age, mode of delivery, edema and proteinuria, sepsis, other puerperal infections, placenta previa, placental abruption, uterine rupture and antepartum hemorrhage were also inquired.

Measures of renal disease outcomes

We employed AKIN (Acute Kidney Injury Network) Criteria for diagnosis of acute kidney injury in the aforementioned pregnant females. The criteria proposed by AKIN i.e. abrupt (within 48hrs) reduction in kidney function defined as an absolute increase in serum creatinine of 0.3mg/dL or more **or** a 50% increase in serum creatinine or more ($\geq$26.4μmol/L) **or** a reduction in urine

output (oliguria of <0.5ml/kg/h for >6h), was followed.[11] Furthermore data about number of blood transfusions and operative procedures, time from onset of azotemia and/or oliguria to initiation of hemodialysis, number and outcome of hemodialysis, hematologic parameters, liver function tests and urine analysis were recorded.

Assessment of depressive symptoms

Depressive symptoms were evaluated by using the Hamilton Depression Rating Scale (HAM-D) adapted and translated in Urdu. The structured questionnaire was presented to all the patients with PRAKI at the Nephrology Department of Jinnah Hospital, Lahore. According to Strik et al. the sensitivity of this scale is 86.4% and specificity is 92.2%.[12] It uses a list of 21 items to assess the psychiatric health of a person but the score is based on the sum of the first 17 items only.

RESULTS

The mean age of the patients with PRAKI was 24±5 years. Out of these 30 patients, 17(57%) were multiparous and 13(43%) were primigravida. Eight (27%) of the females presented to the hospital in their first or second trimesters (before 28 weeks of gestation) and 22 (63%) presented in their last trimester. Alive and healthy fetuses were found in only 15 (50%) of patients and the rest of the 50% females met with adverse pregnancy outcomes. Among these 30 patients, 21 (70%) females received 5-8 sessions of hemodialysis in the hospital and the remaining 9 (30%) of patients were treated conservatively. [Table-II]

General Characteristics	Mean ± Average
AGE	24 ± 5 years
PARITY • Multiparous • Primigravida	 17(57%) 13(43%)
FIRST AND SECOND TRIMESTER	8(27%)
LAST TRIMESTER	22(63%)
MANAGEMENT • Hemodialysis • Conservative	 21(70%) 9(30%)
OUTCOME • Alive and Healthy Fetus	 15(50%)

Table-II. General Characteristics of the Participants

The patients with acute kidney injury due to post-partum hemorrhage were 9(30%) in number making it the most common cause of PRAKI in our study. Sepsis was the second leading cause of PRAKI and affected 8(27%) of the patients. Other causative factors were preeclampsia/eclampsia in 6(20%) patients, shock in 4(13%) patients and coagulopathies in 3(10%). No association of live birth with depression in these patients was noted. Table-III summarizes the etiological factors of acute kidney injury in pregnancy.

Etiological Factors	Patients	Percentage
Post-Partum Hemorrhage	9	30
Sepsis	8	27
Pre Eclampsia/Eclampsia	6	20
Shock	4	13
Coagulopathy	3	10

Table-III. Etiological Factors of Pregnancy Induced Acute Kidney Injury

According to the HAM-D Criteria used for depression assessment, 23 (76%) patients had no depression (0-7 score), 2 (7%) had mild depression (8-13 score), 3(10%) had moderate depression (14-18 score) and 2 (7%) had severe depression (19-22 score). [Figure-1]

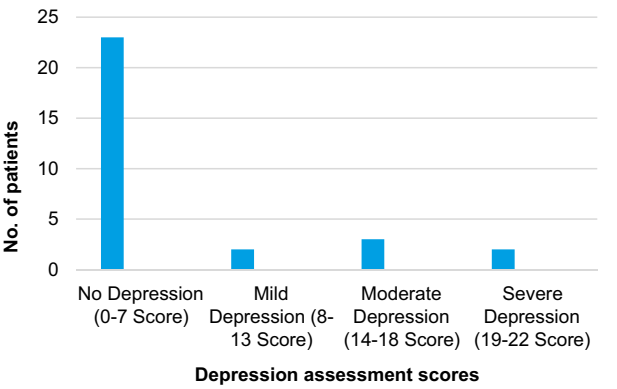

Figure-1. Assessment of Depression in PRAKI using HAM-D Scale

DISCUSSION

Obstetrical AKI remains one of the main causes of AKI in developing countries in contrast to the declining incidence in developed countries,[13] in part due to irregular antenatal consultation.

Before we go on to extract conclusions from our results, it is high time to revise that the physiologic and hemodynamic changes occurring during pregnancy cause an increase in plasma volume, increase in GFR together with proteinuria. Together all these changes in renal blood flow system are enough to mask mild kidney pathology. Therefore, it is safe to say that even in severe cases of preeclampsia, renal failure is not imminent, unless there is marked bleeding with hemodynamic instability or disseminated intravascular coagulation (DIC) or HELLP syndrome,[14] as blood loss secondary to these conditions sets up the stage for injury at a micro level. The results of our study prove to be in accordance to this theory, as the leading cause of PRAKI in our setup was post-partum hemorrhage (PPH) with 30% of our patients suffering from it. In some developed countries, the contribution of PPH and ante-partum hemorrhage remains fairly low i.e. 10.59% and 8.29% respectively, according to one study.[15]

The 2nd most common cause of PRAKI in our study is sepsis which was seen in 27% of the patients. In comparison, the study of Aurora et al outlined the leading causes of PRAKI, in their study of 57 cases, to be sepsis (33.3%), hemorrhage (28.1%) and hypertensive disorders (26.3%).[15] The results of our study follow a similar pattern with PPH in 30% of cases, sepsis in 27%, preeclampsia/eclampsia in 20%, shock in 13% and coagulopathies in 10%.

Obstetric AKI tends to follow a bimodal occurrence in developing countries where the first peak falls between 8-16weeks of gestation associated with septic abortions and the last peak is mostly linked to obstetric complications like preeclampsia/eclampsia, placental abruption, uterine hemorrhage and perinatal sepsis. Out of the 30 patients in our scenario, 8 (27%) presented in their first and second trimesters whereas 22 (64%) presented in the last trimester which is comparable to the study of Sivakumar et al[16] where maximum patients developed PRAKI in their post-partum period and the third trimester i.e. 74.57% and 16.94% respectively, 6.77% in their 2nd trimester and 1.69% in their first trimesters. Thus, demonstrating that PRAKI is more common in the last trimester of gestation worldwide. Nevertheless the major cause of PRAKI in their study was puerperal sepsis.

The mean age of pregnant females suffering from PRAKI in our study came out to be 24±5 years which is lower than studies conducted by Grunfeld et al[17] and Chug et al[18] in which the mean age was 28.4 and 29.5 years respectively. This is due to the practice of early marriages in our society. Multiparous females in our study were affected more with PRAKI i.e. 57% of the patients were multiparous and 43% were primigravida. This finding is in accordance with studies carried out by Goplani KR et al[19] and Patel ML[20] in which there were 68.57% and 46.7% multiparty.

Our study depicts a higher rate of fetal loss in patients with PRAKI. Only 50% of the pregnancies ended with alive and healthy fetuses which is in contrast to a study conducted in Casablanca where the fetal death was reported in only 5.5% of patients and maternal mortality in only 9.1% patients.[21] The negative effects on neonatal outcomes are not only due to the underlying kidney damage, but also due to the detrimental effects of mother's psychological instability which comes with PRAKI. Maternal mortality rates due to PRAKI are still high all over world ranging from 12.5% to 24.39%.[20]

In our study, 70% of the patients were dependent on hemodialysis for treatment which is similar to the dialysis dependence in a study by Ansari et al.[22] In contrast, studies from developed countries depict a lower proportion of patients requiring dialysis which is 8.4% to 14.5% because of better initial resuscitation facilities and time to dialysis.[20] Timely treatment and proper care can ensure complete renal recovery in all such patients. It is seen that the added burden of dialysis and renal replacement therapies increase the prevalence and severity of depression, anxiety and stress in this group of patients. This has been proposed by a recent meta-analysis as well that higher rates of depression and prolonged hospitalization

are found in patients undergoing dialysis than individuals getting conservative treatment and post-transplant patients.[23] According to another study conducted in Brazil, out of 244 patients on hemodialysis 5.3% were reported to have social phobia and anxiety disorder.[24]

This study was set out to test our hypothesis that depression is prevalent among patients of PRAKI and has unfavorable effects on the quality of life of the patient. After viewing the results, we found a considerable association of depression in such patients as 7 out of 30 females in our study group confirmed of having varying degrees of depressive symptoms which was evaluated using the HAM-D score. Two (7%) patients had mild degree of depression (0-7 score), 3 (10%) suffered from moderate depression (8-13 score) and 2 (7%) were found to be struggling with severe depression (14-18 score) in our study. The rates of prevalence of depression in our study were proportionate to other studies in kidney disease and other medically ill populations.[4] These findings depict that the presence of raised depressive symptoms is linked with AKI independent of uremia, ischemic heart disease, cardiovascular risk factors and other health behaviors. Thus the link of depression in PRAKI is not due to underlying medical ailments and comorbidities, rather the delay in seeking health care, polypharmacy and hospitalization play important role in affecting brain along with kidneys in pregnant females. These pathways are yet hypothetical and need further research. The depressive symptoms are further found to cause decline in kidney function in patients of AKI. However certain specific cognitive alterations are found to be more associated with chronic kidney disease than AKI like Alzheimer's disease and vascular dementia in particular.[25]

Maternal illness coupled with psychological symptoms during pregnancy result in physiological consequences for the fetus. Thus, without accurate diagnosis and proper treatment a woman's mental instability is bound to affect her unborn infant's wellbeing. Untreated depression in PRAKI may lead to obstetric complications such as spontaneous abortion, neonatal growth retardation, preterm deliveries along with mother's own social withdrawal and excessive concern regarding their future ability to parent. It is a well-established fact that maternal morbidity and mortality is strongly associated with untreated medical conditions. A negative relationship between depression in pregnancy and quality of life has been demonstrated by other studies as well.[7] These studies have incorporated social, physical and psychological parameters in assessing the impact of AKI on quality of life.

LIMITATIONS

Despite fulfilling the purpose, our study lacked a substantial size of sample to determine prevalence accurately. Such small sized samples are common to all psychiatric studies in pregnant women. However, if we look at data of patients presenting with peripartum AKI, our sample size was quite reasonable. Furthermore, due to financial and social constraints, renal biopsy could not be performed, here in our setup, to identify the extent of kidney damage. Long term follow up of these patients to see the progression of disease, association of depression with possible CKD (chronic kidney disease) in peripartum patients and its complications was also beyond the scope of this study.

CONCLUSION

The ignorance of the community about detrimental effects of AKI on body and mind of a pregnant female are the reason of its delayed diagnosis and under treatment. Prevalence of depression and its severity should not be underestimated in PRAKI and multidisciplinary care should be offered immediately. Hence, AKI in pregnancy is treatable and only timely, aggressive measures can save mother's physiologic and psychological health and reduce obstetric complications.

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PREVIOUS RELATED STUDY

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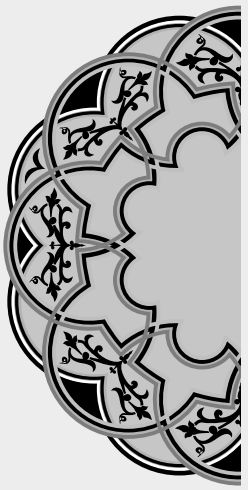

"Confidence is silent.
Insecurities are loud."

The God Father

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