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Original Research Article

Spectrum of acute kidney injury in obstetrics

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ABSTRACT

Background: Acute kidney injury (AKI) associated with pregnancy is a serious medical complication which can lead to significant maternal as well as perinatal morbidity and mortality.

Methods: Forty antenatal/postnatal /postabortal patients who fulfilled the Acute kidney injury network criteria were enrolled and followed up till 3 months of acute insult/ postpartum.

Results: Majority of the patients, 23/40(57.5%) with AKI presented in postpartum period, 14/40(35%) developed AKI in antenatal period and 3/40(7.5%) were postabortal. AKI was attributable mostly to sepsis in 11/40(27.5%) followed by hypertension and its complications which included eclampsia in 5/40(12.5%) and HELLP syndrome in 3/40(7.5%). 5/40(12.5%) patients had postpartum haemorrhage and abruptio placentae was found in 2/40(5%). Renal replacement therapy (RRT) was the treatment in majority of them 28(70%). 25/40(62.5%) had complete recovery of their renal functions whereas maternal mortality was seen in 10/40(25%) patients. Prolonged anuria was found to be highly significant in our study and served as poor prognostic factor towards maternal outcome ($p=0.034$). Out of 37 patients, 21(56.7%) had live births and 16 patients (43.2%) had still births.

Conclusions: Timely initiation of RRT in patients with AKI associated with pregnancy has a good maternal outcome in the form of complete recovery of renal functions.

Keywords: Acute kidney injury, Renal replacement therapy, Sepsis

INTRODUCTION

Acute Kidney Injury (AKI) is one of the most challenging problems faced by clinicians in the tropics owing to its fast-changing burden.

Incidence of AKI in obstetric population in developing countries is high with 4.2-15% compared with developed nations (1-2.8%).¹⁻² Obstetric AKI has a bimodal occurrence in developing countries with first peak between 8 and 16 weeks of gestation in association with septic abortions while late peak is associated with obstetric complications such as preeclampsia-eclampsia, abruptio placentae, uterine haemorrhage, and puerperal

sepsis and microangiopathies.³⁻⁵ Recovery occurs in 60% to 90% of cases. The true epidemiological picture of AKI in the tropics is not well understood due to the late presentation of patients to tertiary centres and due to absence of meta analyses it is difficult to precisely estimate its actual incidence. Due to paucity of data, this study has been conducted to know the spectrum of AKI in terms of causative factors, management/ interventions and follow up.

METHODS

This Prospective observational study was carried out in the labor ward of Obstetrics and Gynaecology department

and Dialysis unit of Nephrology department of Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh from July 2013 to June 2014 after approval by ethics committee and informed consent was obtained from all individual participants included in the study.

Antenatal/postnatal/postabortal patients who presented with oliguria (urine output <500ml/24hours) or anuria (urine output <50ml/24hours) and fulfilled Acute kidney injury network (AKIN) criteria (AKI which occurs in <48 hours and deterioration occurs in the renal function in terms of increase in serum creatinine, either absolute i.e. ≥ 0.3 mg/dl (≥ 26.4 mmol/l) or percentage rise by 50% or more and decrease in urine output <0.5ml/kg/hour for >6hours) were included.⁶ Patients with Chronic Kidney Disease (CKD) and AKI superimposed on CKD were excluded. Serial monitoring of biochemical parameters was performed.

Nephrology consultation was sought regarding the, need, frequency and timing for initiation of dialysis (electrolyte abnormalities refractory to medical treatment, volume overload with congestive heart failure and pulmonary edema refractory to standard therapy, severe metabolic acidosis, uremia or serum creatinine >5.65mg/dl). Dialytic support was initiated early in the course of illness.

Further evaluation to aid in diagnosis included renal doppler, Magnetic Resonance Angiography and renal biopsy in case of rapidly progressing renal failure, acute nephritic illness, unexplained AKI. All patients were followed up till 3 months after the acute event/ time of presentation, for recovery of renal functions.

At 3 months postpartum, final renal function assessment regarding further intervention or need for continuing dialysis was carried out.

Outcome parameters were assessed in terms of; complete recovery where serum creatinine returned to its normal levels, partial recovery when creatinine did not return to its normal value, but dialysis was not required and no recovery when creatinine did not return to its normal value and patient required further dialysis.

Data analysis was done using SPSS version 22.0. Categorical data was analysed using Chi square test and quantitative data was analysed using t- test and multiple regression analysis.

RESULTS

The patient age ranged from 19-45 years. Majority of the patients (57.5%) presented in postpartum period. 15/37 (40.5%) were preterm and 22/37 (59.4%) were at term gestation and 3/40 (7.5%) patients presented in postabortal period (Table 1). 14 (35%) patients delivered

at our institute and the rest delivered at other hospitals and were later referred to our institute.

Table 1: Demographic profile of the patients.

Parameters	Mean±range
Age (years)	25.9±4.7
Gestation at presentation (weeks)	32.6±4.4
BMI (Kg/m ²)	24.3±2.4
Booked cases	2 (5%)
Unbooked cases	38 (95%)
Parity	
Primiparous	22 (55%)
Multiparous	18 (45%)
Presentation time	
Antenatal	14 (35%)
Post-natal	23 (57.5%)
Post-abortal	3 (7.5%)
Urine output on admission:	
Oliguria	21 (52.5%)
Anuria	10 (25%)
Hemodynamic instability	7 (17.5%)

As regards mode of delivery 8(20%) had vaginal delivery, 14(35%) underwent cesarean, 14 (35%) had preterm vaginal delivery and 1(2.5%) remained undelivered as she expired due to Hepatitis E Virus (HEV) infection with Multiple Organ Dysfunction (MODS). In the present study sepsis was the commonest (11/40) etiology. Only two patients (5%) presented with sepsis in third trimester whereas six patients (15%) developed sepsis in the puerperium and three patients (7.5%) had postabortal sepsis. As regards postabortal sepsis, two of the patients who underwent surgical abortion outside had retained products of conception and needed dilatation and curettage to remove septic focus after admission in our institute.

Late pregnancy AKI was attributed to abruptio placentae in two patients (5%). Among those who presented in the puerperium, five patients (12.5%) had Postpartum Haemorrhage (PPH), three patients (7.5%) had HELLP (Haemolysis, Elevated liver enzymes, Low platelets) syndrome and eclampsia was the etiology in five patients (12.5%). Three patients (7.5%) had Acute Fatty Liver of Pregnancy (AFLP) as the cause of AKI and out of those two patients, two presented in the third trimester and other presented in the postpartum period. Patients who were diagnosed with Thrombotic Microangiopathy (TMA) presented in puerperium. No significant correlation was found between AKI etiology and maternal outcome ($p > 0.05$) (Table 2).

Renal biopsy was done in three patients who did not show improvement in renal functions after RRT for prognostication. Histopathology revealed acute tubular necrosis (ATN) and acute cortical necrosis (ACN) each in two patients of puerperal sepsis and TMA in one patient.

Table 2: Etiology of AKI.

Cause of AKI (no. of patients)		Complete recovery (%)	Partial recovery	Death (%)	No recovery	P (chi square)
Sepsis (11)	Antenatal	1 (14.3)	-	1 (33.3)	-	0.56
	Postnatal	3 (42.9)	1 (100%)	2 (66.7)	-	
	Postabortal	3 (42.9)	-	-	-	
Hemorrhage (7)	Abruption	1 (25)	-	1 (50)	-	0.64
	Postpartum hemorrhage	3 (75)	1 (100%)	1 (50)	-	
HTN disorders (8)	Eclampsia	4 (57.1)	-	1 (100)	-	0.62
	HELLP	3 (42.9)	-	-	-	
Others (14)	AFLP	-	-	1 (33.3)	1 (100%)	
	Acute gastroenteritis	1 (14.3)	-	-	-	
	Acute pyelonephritis	3 (42.9)	-	-	-	
	Thrombotic microangiopathy	-	2 (100%)	1 (33.3)	-	
	Tropical illness (malaria)	1 (14.3)	-	-	-	
	HEV +	2 (28.6)	-	1 (33.3)	-	

The mean pre-dialysis serum creatinine was 4.3 ± 3.2 mg/dl (range 1.6-13.8mg/dl) with median of 3 in the study population (Table 3).

Table 3: Laboratory parameters on admission.

Parameters	Number of cases (%)
Haematological	
Anemia (<11 gm/dl)	37 (92.5)
Thrombocytopenia (<1.5 lac)	35 (87.5)
Leucocytosis (TLC >14000)	29 (72.5)
Renal function tests	
Serum creatinine (>1mg/dl)	40 (100)
Hypokalemia	7 (17.5)
Hyperkalemia	14 (35)
Evidence of hemolysis	
Schistocytes on PBF	8 (20)
Hyperbilirubinemia (>1.1mg/dl)	24 (60)
LDH (>480 U/L)	37 (92.5)
Blood gas analysis	
Metabolic acidosis	19 (47.5)
Coagulogram	
Hypofibrinogenemia (<2g/l)	6 (15)

Dialysis was the commonest mode of treatment except in 12/40 (30%) patients who were managed conservatively (Table 4).

The indications for dialysis in the study patients included severe metabolic acidosis in 19 (47.5%), hyperkalemia in 10 (25%), none of the patients had uremic features like encephalopathy, pericarditis. Serum creatinine >5.65mg% was found in 8 (20%). Oliguria/anuria was found in 25(62.5%). Volume overload was present in only one patient. Dialysis was done in 20(50%) patients who were

refractory to medical therapy. Patients had more than one indication for dialysis.

Table 4: Treatment.

Methods	N (%)
Conservative	12 (30)
Hemodialysis	24 (60)
Peritoneal dialysis	4 (10)
Dialysis f/b Plasmapheresis	2 (5)

Two patients who received plasmapheresis had TMA and puerperal sepsis as the etiology behind AKI. Four patients received peritoneal dialysis because of hemodynamic instability- one patient underwent 40 sessions. The mean number of hemodialysis sessions required by patients were 6.5 (range 1-40).

If dialysis was given, chances of complete recovery will be there (OR=0.77) (Table 5).

So, it is not AKI per se which leads to mortality but it's the underlying cause and most of the patients who underwent dialysis early in their disease course recovered completely.

The mean difference of duration of anuria was significantly different in complete recovery and others group (Partial/no recovery/death). Mean duration of oliguria was 6.9 days. With increase in duration of anuria, chances of complete recovery are less ($p = 0.036$) (Table 6).

Multivariate analysis of present study was done as two groups: A) Complete recovery and B) Others (Partial/no recovery/death).

Table 5: Renal replacement therapy and maternal outcome.

	Complete recovery	Others (partial/ no recovery/ death)	Total	Adjusted odds ratio	p value (unadjusted)
Dialysis	17 (68%)	11 (73.3%)	28 (70%)	0.77 (0.18-3.19)	0.13
No dialysis	8 (32%)	4 (26.6%)	12 (30%)		
Total	25 (100%)	15 (100%)	40 (100%)		

Table 6: Mean difference of serum creatinine and duration of anuria with maternal outcome.

	Complete recovery	Others (partial/ no recovery/ death)	P value (by independent t- test)
Pre-dialysis serum creatinine	4.02±2.64	4.14±3.0	0.903
Duration of anuria	3.92±3.7	11.8±13.1	0.036

TABLE 7: Multivariate analysis using standard logistic regression among complete recovery and no/partial recovery/death group and selected independent variables to analyse adjusted odds ratio.

Independent factors	Beta coefficient	S.E.	p value	Adjusted odds ratio	95% CI for OR	
					Lower	Upper
Postpartum period	-0.200	0.745	.788	0.818	0.190	3.525
Duration of anuria	-2.915	1.378	.034	0.054	0.004	0.808
Predialysis S. Cr	0.423	0.669	.527	1.527	0.411	5.668

Significant correlation has been found between one variable: anuria and complete recovery. Taking normal urine output as a reference, as urine output became nil, odds of complete renal recovery decreases (OR=0.054, 95%CI 0.004-0.808, p=0.034). No correlation has been found between postpartum day and predialysis serum creatinine with maternal complete renal recovery (p>=0.05) (Table 7).

Perinatal outcome: Out of 37 patients, 21(56.7%) had live births and 16 patients (43.2%) had still births. Still births were most commonly observed in 7/37 (18.9%) patients with sepsis followed by two patients with abruption in which still birth rate was 100% in the present study.

DISCUSSION

AKI is defined as an abrupt decline in Glomerular Filtration Rate (GFR) sufficient to decrease the elimination of nitrogenous waste products (urea and creatinine) and other uremic toxins.⁷

There is approximately 40-65% increase in GFR after conception and which returns to prepregnancy values in the first 3 months postpartum.⁸⁻⁹ Renal plasma flow increases up to 85% in the second trimester.⁸ These hemodynamic changes explain a serum creatinine reduction in pregnant women to 0.4-0.5mg/dl. (Normal=0.5-1.5mg/dl)

In present study almost all patients, 39 (97.5%) were referred to our institute from other hospitals. The mean age of the study population was 25.9±4.7 years similar to the study of Aggarwal et al (26±3.8 years).¹⁰ Most of the

patients presented in various studies in the postpartum period like in present study, 26 patients (65%) were referred in the postpartum period (including postabortal patients) and only 14(35%) came antenatally.¹¹⁻¹² 6 patients (15%) had renal failure due to puerperal sepsis in present study. In the study by Aggarwal et al, 10 Godara et al and Kilari et al, AKI due to puerperal sepsis was reported in 20 (40%), 36 (63.1%), 12 (29.2%) patients respectively.^{10,11,12} Antenatal sepsis developed in two patients (5%) in present study but none of above studies reported cases of antenatal sepsis as a cause of AKI. Postabortal sepsis was the cause in 3 patients (7.5%) in present study which includes one patient in the first trimester and two in second trimester. Septic abortion accounted for majority of the cases in the study conducted in Kashmir valley by Najar et al and they reported 15 (75%) cases in first trimester and 5(25%) cases in second trimester.¹³

Antepartum and postpartum haemorrhage have been reported as major causes of AKI in pregnancy.¹⁴⁻¹⁸ In the present study abruptio placentae was found in two patients (5%) and five patients (12.5%) had PPH which led to AKI.

In severe pre-eclampsia/eclampsia, renal failure is most probably due to ATN.¹⁹ In the present study, 5 (12.5%) had eclampsia and 3 (7.5%) had HELLP.

TMA was the cause in three patients (7.5%) in present study. Silva GB et al 20 reported Thrombotic Thrombocytopenic Purpura (TTP) in 5.5% and Hemolytic Uremic Syndrome (HUS) in 9.1% cases. No other study reported cases of TMA as cause of AKI.

Aggarwal et al reported AKI in the first trimester due to prerenal cause- hyperemesis gravidarum in one patient. In index study only one patient had acute gastroenteritis in the postpartum period.¹⁰ Malaria was the etiology only in one patient in the present study whereas Godara et al reported three (5.2%) such cases.¹¹ Three patients (7.5%) developed Disseminated Intravascular Coagulopathy (DIC) in present study as was also reported by Godara et al in 8.7% of the patients.¹¹

Other etiologies behind AKI in present study were AFLP, acute pyelonephritis and Hepatitis E virus (HEV) positive in three patients (7.5%) each.

In present study 21 patients (52.5%) were oliguric, 10 patients (25%) were anuric and nine patients (22.5%) were non-oliguric. Godara et al reported oliguria and anuria in 64.9% and 21% respectively. Patients with sepsis, TMA, PPH and AFLP have prolong oliganuria of more than 10 days duration.¹¹

In present study, the interval between onset of renal failure and referral to our institute varied from one to 15 days. Whereas in the study by Godara et al interval between onset and referral was one to 30 days.¹¹ Morbidity of AKI in developing countries could be higher than developed countries due to late identification and referral of the patients. As regards need for additional investigations, CECT KUB was done in six patients and it revealed ACN in three of them secondary to TMA in two and AFLP in one patient.

One patient was diagnosed to have emphysematous pyelonephritis on CT. ACN because of puerperal sepsis led to complete maternal recovery. The other two patients who had AFLP and TMA as a cause of AKI recovered partially. One patient with TMA who expired during the course of treatment also had ACN. Godara et al reported ACN in 13 patients and ATN in 40 patients and stated it to be associated with septicemia in 28 patients.¹¹

Dialysis was the commonest mode of therapy of AKI in our institute. 24 patients (60%) received hemodialysis and four patients (10%) received peritoneal dialysis due to hemodynamic instability. Oliguria/ anuria was the most common indication for dialysis in 25 patients (62.5%) followed by being refractory to medical therapy in 20 patients (50%). Whereas in study by Pahwa et al 25 (92%) patients required hemodialysis; of these, 17 (68%) patients required more than five sessions of hemodialysis. Five patients (20%) had irreversible kidney injury and three (60%) of them were transplanted.²¹

Renal failure was previously thought to be irreversible but complete and partial recovery does occur in about 30% of these cases.²²

Complete recovery was seen in 25 patients (62.5%) in which sepsis was the most common etiology of AKI in index study compared to Godara et al where it was

52.64% (n=30).¹¹ Partial recovery was the outcome in 4(10%) in the present study and causes were sepsis, PPH and TMA in two patients (mean creatinine of 3.65mg/dl) which is same as reported by Kilari et al and anuria was present in three patients with partial recovery in present study. AFLP was the cause behind no recovery in one patient in index study.¹²

Maternal mortality occurred in 10 (25%) patients in present study population and the causes were AFLP and puerperal sepsis in two each and antenatal sepsis, PPH, eclampsia with intracranial bleed, TMA, abruption with DIC and HEV with organ failure in one each which is comparable to study by Godara et al in nine patients (15.79%) and the causes were septicemia in four patients (4.44%), preeclampsia in three patients (3.33%),

APH in one and PPH in one patient. TMA and AFLP accounted for bad maternal outcomes in present study.¹¹ But etiology of AKI was not associated to unfavorable evolution (p value= >0.05). None of studies have commented upon correlation of AKI etiology with maternal outcome.

Godara et al while analysing AKI related to various independent variables, identified significant correlation of maternal recovery with duration of anuria (p= 0.001) and significant correlation was also found in present study (p=0.034).¹¹

Dialysis initiated earlier in the disease course had better outcomes in the form of complete recovery of renal function. In present study, fetal loss was seen in 16 cases (43.2%). Still births were more common in maternal sepsis (75%) and abruption placentae (100%).

CONCLUSION

An obstetrician should have a broad knowledge about physiological alterations in the renal system in pregnancy to apply the best evidence-based strategies in treating patients with AKI considering both maternal and fetal effects of the pathology and its management.

Early diagnosis and prompt referral to tertiary care centre can avoid potentially life-threatening AKI and its sequel. Prolonged oliguria/anuria is an important poor prognostic marker for unfavourable outcome and in such cases dialysis if initiated early can improve fetal and maternal outcome.

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