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Original Article

Obstetrics and Gynaecology Section

Acute Renal Failure in Pregnancy: A Prospective Cohort Study

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ABSTRACT

Introduction: Pregnancy related acute renal failure is a common occurrence and is associated with substantial maternal morbidity and mortality in developing countries. It may comprise up to 25% of the referrals to dialysis centres in developing countries. Acute kidney injury in pregnancy bears a high risk of bilateral renal cortical necrosis and resultant chronic renal failure. Acute renal failure in pregnancy follows bimodal relation to period of gestation. First peak is seen in early pregnancy between 7-16 weeks of gestation and second peak occurs in later part of pregnancy and puerperium. The incidence and aetiology are changing over time. Socio-economic and environmental factors are accountable for a regional difference in incidence, aetiology and outcome also.

Aim: To analyse the current aetiological factors, clinical spectrum of presentation of Acute Renal Failure (ARF) in pregnancy and to assess its maternal and foetal outcome.

Materials and Methods: It was a prospective cohort study of 100 patients presenting with acute renal failure during pregnancy and puerperium which was done at SCB Medical College, Odisha, India. Inclusion criteria were previously healthy pregnant females with sudden oliguria anuria, sudden increase in serum creatinine to more than 1.5 mg/dL or increase in serum creatinine of more than 0.5 mg/dL per day from base line if haemodialysis was indicated. Maternal outcomes were recovery with conservative treatment, dialysis, Intensive Care Unit (ICU) admission and maternal death. Foetal outcomes were gestational age at delivery, birth weight, stillbirth or perinatal death. All these were recorded.

Results: During the first trimester of gestation acute renal failure developed most often due to septic abortion (3%). Preeclampsia was the most common cause of acute renal failure (50%) in late third trimester and postpartum periods followed by puerperal sepsis (9%), abruptio placentae (3%), and Postpartum Haemorrhage (PPH) (5%). Oedema and oliguria were the most common presentation in 81% and 30% of cases. A 87% with i.v. fluids and diuretics (conservative management), 13% required dialysis, 23% required blood and Fresh Frozen Plasma (FFP), 30% needed ICU admission and 11% died during treatment. Foetal outcome were measured in terms of foetal growth restriction (24%), preterm delivery (14%), foetal distress (13%), Special Newborn Care Units (SNCU) admission (23%) and stillbirth (5%).

Conclusion: This study concludes that pregnancy related acute renal failure is associated with serious prognosis both for the mother and child. Even though, good obstetric care can reduce morbidity and mortality associated with it, these patients require special and intensive care management facility which can bring them better survival rates.

Keywords: Abruptio placentae, Acute kidney injury, Co-morbidity, Preeclampsia

INTRODUCTION

Acute renal failure is a syndrome characterised by a rapid decline in the glomerular filtration rate and retention of nitrogenous waste products such as blood urea nitrogen and creatinine. Pregnancy related acute renal failure, although a preventable condition is a challenging problem both to the obstetrician and the nephrologist. There is an overall marked decline in the prevalence of pregnancy related acute renal failure over the past 50 years in the developed countries as a result of improved antenatal care and obstetric practices [1]. However, the incidence has increased almost three times in the recent decade in the United States, from 0.04% in 2006 to 0.12% in 2015 among hospitalised patients, because of older maternal age with more co-morbidities, higher detection rates of Acute Kidney Injury (AKI), increase in the incidence of hypertensive disorders of pregnancy, and increase in obesity rates [2]. In contrast, it is still relatively common in the developing countries, though the overall incidence has fallen from 15% in the 1980s to 1.5% in the 2010s among hospitalised women [2].

The important causes of obstetrical acute renal failure are divided into those in early pregnancy, usually between 8 and 16 weeks of gestation in association with septic abortion, in late pregnancy and immediate puerperium, namely eclampsia, preeclampsia, antepartum haemorrhage (abruptio placentae), Haemolysis, Elevated Liver enzymes and Low Platelets (HEELP) syndrome, Postpartum Haemorrhage (PPH), puerperal sepsis and Haemolytic Uraemic Syndrome (HUS). Socioeconomic and environmental factors are accountable for huge difference in the incidence, causes and outcome of Pregnancy Related Acute Kidney Injury (PRAKI) in developed countries compared with the developing countries. Incidence and aetiology is also changing over time. Therefore, present study was conducted with an aim to determine the present epidemiology of PRAKI in our region.

MATERIALS AND METHODS

It was a prospective cohort study of 100 patients with acute renal failure who were followed-up to discharge from hospital or death in hospital. IEC approval was obtained (328). The study was done over two years from September 2018 to September 2020. All pregnant women who were admitted in emergency unit of SCB Medical College, Cuttack, Odisha, India, with acute renal failure, or developed acute renal failure after admission, after fulfilling the inclusion criteria were enrolled in the study.

Sample size calculation: Sample size was calculated by the formula $n=z^2pq/d^2$ (z=1.96, p=4.5% and d=5%) 'P' was taken from a previous study [3]. $n=z^2pq/d^2=(1.96)^2*0.045*0.955/(0.05)^2=66$.

Inclusion and exclusion criteria: Inclusion criteria were previously healthy pregnant females with sudden oliguria (urine output <300 mL over 24 hours), or anuria with sudden increase in serum creatinine to

more than 1.5 mg/dL or increase in serum creatinine of more than 0.5 mg/dL per day from base line. Exclusion criteria were evidence of renal disease prior to pregnancy, history of hypertension or diabetes before gestation, history of renal stone disease, renal scarring on ultrasonography, small size of the kidneys, elevated serum creatinine prior to gestation.

Study Procedure

After written consent was obtained from patients, data regarding demographic characteristics, detailed history, clinical presentation and laboratory investigations i.e., renal function tests, serum electrolytes, liver function tests when required, complete blood count, complete obstetric examination, mode of delivery, need for blood transfusion and surgical intervention were collected. Outcome was considered favourable if patient made a complete recovery, if patient required no dialysis, had good urine output and normal renal function. Patients with improved, but abnormal renal function who did not require dialysis were considered to have partial recovery. Progression to either chronic kidney disease or mortality was considered as an unfavourable outcome.

STATISTICAL ANALYSIS

All the data were entered in the Microsoft Excel 2007 software and analysed in Statistical Package of Social Sciences (SPSS) software version 24 (IBM Inc. Chicago). The categorical variables were expressed in terms of number and percentages. All the continuous variables were expressed in terms of mean and standard deviation.

RESULTS

Mean age of the study participants was 25.83±4.27 years with a minimum age of 18 years to a maximum age of 42 years. Mean gestational age of the study participants was 36±4.03 weeks with a minimum of 14 weeks to a maximum of 40 weeks.

Out of the total study population 81% belonged to 21-30 years of age. Only 2% are of more than 35 years of age [Table/Fig-1].

Most of the study population (61%) were primipara and 14% had history of abortion [Table/Fig-2].

Age distribution of patients with AKI (in years)	Frequency (n=100)	Percentage (%)
15-20	10	10.0
21-25	40	40.0
26-30	41	41.0
31-35	7	7.0
36-40	1	1.0
41-45	1	1.0

[Table/Fig-1]: Age distribution among patients.

Obstetric history	Frequency (n)	Percentages (%)
Gravida		
Primigravida	31	31.0
Multigravida	69	69.0
Parity		
Primipara	61	61.0
Multipara	39	39.0
Livebirths (n=60)		
Single livebirth	31	31.0
More than one	29	29.0
Abortion history		
Present	14	14.0
Absent	86	86.0

[Table/Fig-2]: Obstetric profile of study participants.

Majority of the participants had antepartum eclampsia (50%). Among those with antepartum eclampsia, 29% had antepartum eclampsia in latent labour, 9% had antepartum haemorrhage eclampsia in prelabour and 2% had antepartum eclampsia in preterm labour and rest (10%) were not in labour or prelabour [Table/Fig-3].

Age group	Frequency (n)	Percentages (%)
Abruption placenta	3	3.0
Antepartum eclampsia	50	50.0
HELLP syndrome	10	10.0
Postpartum eclampsia	4	4.0
Primary PPH	5	5.0
Puerperal sepsis	9	9.0
Septic abortion	3	3.0
Preeclampsia	16	16.0

[Table/Fig-3]: Diagnosis among the study participants (N=100).

Clinical features among the study participants revealed that oliguria was seen in 30% of the patients while anuria was seen in 11% [Table/Fig-4]. Mean systolic blood pressure was 156.18±28.60 mm of Hg with a minimum of 70 to a maximum of 200 mmHg. Similarly, mean diastolic blood pressure was 100.36±18.92 mmHg with a minimum of 50 to a maximum of 130 mmHg.

Clinical feature	Frequency (n)	Percentages (%)
Urination		
Oliguria	30	30.0
Anuria	11	11.0
No urinary abnormality	59	59
Oedema		
Present	81	81.0
Absent	19	19.0
Convulsion		
Present	54	54.0
Absent	46	46.0
Fever		
Present	14	14.0
Absent	86	86.0
Bleeding per vaginum		
Present	12	12.0
Absent	88	88.0
Jaundice		
Present	10	10.0
Absent	90	90.0
Foul smelling discharge per vaginum		
Present	11	11.0
Absent	89	89.0
Pain abdomen		
Present	67	67.0
Absent	33	33.0
Consciousness		
Unconscious	20	20.0
Conscious	80	80.0

[Table/Fig-4]: Clinical features at diagnosis.

Mean haemoglobin level was low at 8.52±1.63 gm/dL. Serum urea and creatinine at the time of admission and the peak values were higher [Table/Fig-5].

Out of those in whom conservative management (IV fluids with input output monitoring, diuretics and treatment of the cause) was done, 82 (94.2%) were discharged after recovery. However, 5 (5.74%) died after conservative management. Main management was fluid restriction with strict input and output monitoring and diuretics. Abnormality in serum electrolytes was corrected. Moderate to severe anemia

Laboratory parameter	Minimum	Maximum	Mean	SD
Haemoglobin (gm/dL)	3.00	10.00	8.52	1.63
TLC* (cells/mm^3)	4100.00	26000.00	9246.00	5216.55
TPC† (cells/mm^3)	0.50	3.40	2.18	0.52
Serum urea at admission (mg/dL)	46.00	228.00	102.98	41.48
Serum creatinine at admission (mg/dL)	2.00	9.60	3.60	1.58
Peak serum urea (mg/dL)	50.00	268.00	109.06	44.91
Peak serum creatinine (mg/dL)	2.10	9.60	3.76	1.79
Serum uric acid (mg/dL)	2.80	9.30	5.51	1.32
Direct bilirubin (mg/dL)	0.10	98.00	2.12	9.78
Indirect bilirubin (mg/dL)	0.10	6.40	0.59	0.98
Serum AST‡ (U/L)	32.00	380.00	68.84	55.08
Serum ALT§ (IU/L)	38.00	468.00	79.08	63.01
Serum ALP‖ (U/L)	123.00	560.00	216.40	97.44
Serum sodium (mmol/L)	122.00	147.00	136.61	4.58
Serum potassium (mmol/L)	2.60	6.40	4.54	0.73
Serum albumin (g/L)	2.10	3.60	2.89	0.33
PT** (seconds)	11.70	24.00	15.60	3.71
aPPT†† (seconds)	20.50	70.00	31.97	13.96
INR‡‡	1.00	1.80	1.26	0.25
FDP§§ (µg/mL)	148.0	410.0	238.24	77.97

[Table/Fig-5]: Laboratory parameters.
*TLC: Total leucocyte count; †TPC: Total platelet count; ‡AST: Aspartate transaminase; §ALT: Alanine transaminase; ‖ALP: Alkaline phosphatase; **PT: Prothrombin time; ††aPTT: Activated partial thromboplastin time; ‡‡INR: International normalised ratio; §§FDP: Fibrin degradation product

correction was done by blood transfusion. Those with hypertension were given antihypertensives. In cases of deranged coagulation profile, Fresh Frozen Plasma (FFP) was given. Daily serum renal function tests were sent for evaluation of progress. Patients that had anuria or oliguria benefitted from fluid management.

Renal replacement therapy was required in 13% cases. All required intensive care management. The patients selected for renal replacement therapy, based on consultation with the nephrologist, were those in whom serum urea and creatinine increased despite conservative management. Of those taken up for renal replacement therapy, 7 (53.84%) recovered successfully and were discharged. However, a significant number of patients, 6 (46.16%) died during the course of treatment [Table/Fig-6].

Maternal outcome	Frequency (n)	Percentage (%)
Conservative treatment	87	87.0
Renal replacement therapy (Dialysis)	13	13.0
Blood/Fresh frozen plasma requirement	23	23.0
Intensive care requirement	30	30.0
Maternal death	11	11.0

[Table/Fig-6]: Maternal outcomes among the study participants.

Preterm birth seen in 14% of the newborns was iatrogenic. Foetal distress was noticed in 13% of the newborns, 23% required SNCU admission and 62% had an Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) score of more than 7. Mean weight of the newborn was 2.51±0.83 kg with a minimum of 0.1 kg to a maximum of 3.8 kg [Table/Fig-7].

Outcome	Frequency (n)	Percentages (%)
FGR*	24	24.0
Preterm birth	14	14.0
Foetal distress	13	13.0
SNCU† admission	23	23.0
Stillbirth	5	5.0

[Table/Fig-7]: Foetal outcomes among the study participants.
*FGR: Foetal growth restriction; †SNCU: Special newborn care unit

DISCUSSION

The minimum age in the present study was 18 years, with the maximum of 42 years, which is comparable to the studies of Lufullah A et al., Goplani KR et al., and Prakash J et al., [4-6]. The comparison between mean age of participants in the present study with several other studies is shown in [Table/Fig-8] [5,6].

Mean age of participants in current study	Mean age in the study by Goplani KR et al., [5]	Mean age in the study by Prakash J et. al., [6]
25.83±4.27 years	26.6 years	27.15 years

[Table/Fig-8]: Mean age of participants compared in several studies [5,6].

Regarding the parity in the present series, it was found that 31% of the cases were primigravida and 69% cases are multiparous [Table/Fig-9] [6,7].

Parity	Present study	As per study by Chaudhri N et al., [7]	As per Prakash J et al., [6]
Primigravida	31%	11.7%	37.6%
Multigravida	69%	88.2%	62.6%

[Table/Fig-9]: Parity comparison in several studies [6,7].

In this present study, mean gestational age of the study participants was 36±4.03 weeks with a minimum of 14 weeks, to a maximum of 40 weeks, which is in contrast to that reported by Goplani KR et al., where 14 (20%) patients were in early pregnancy, 5 (7.14%) were in late pregnancy and 72.85% were in the puerperium [5]. The discrepancy is possibly due to eclampsia and preeclampsia being the main causative factor in the present study in contrast to the study of Goplani KR et al., where puerperal sepsis was the main cause [5].

In the present study, preeclampsia and eclampsia was detected to be the leading cause of pregnancy related acute renal failure. Majority of the participants had antepartum eclampsia (50%), followed by preeclampsia seen in 16% of the participants. This finding is similar to the study by Prakash J et al., which reported preeclampsia and eclampsia to be the most common cause of pregnancy related acute renal failure, contributing to 35.29% of the cases [6].

In the present study, 3% cases had septic abortion as an aetiological factor, which is in contrast to the reports by Goplani KR et al., who found it to be one of the major causes of AKI in 20% of the patients and Chaudhri N et al., in 5.8% cases [5,7]. The cause for this discrepancy may be due to the increasing adoption of family planning services and use of safer abortion measures. In the present study, puerperal sepsis accounted for only 9% of the cases of pregnancy related acute renal failure, whereas Goplani KR et al., and Kumar KS et al., reported puerperal sepsis as the most common aetiological factor (39% and 61%, respectively) leading to acute renal failure in pregnancy [5,8]. Ansari MR et al., reported antepartum and PPH as the leading causes, in 50% and 38% cases, respectively; whereas in the present study, ante partum haemorrhage and PPH was present in 3% and 5% of cases only [1]. Thus, it is obvious from the present study that the trend of pregnancy related acute renal failure is shifting from first trimester towards the third trimester and third trimester complications such as preeclampsia and eclampsia have replaced sepsis and haemorrhage as the leading cause.

In this present study, the presenting clinical feature generalised oedema was found in 81% cases, hypertension in 76% cases, pain abdomen in 67% cases, convulsion in 54% cases, oliguria in 30% cases, fever in 14% cases, unconsciousness in 20% cases, bleeding per vaginum in 12% cases, foul smelling vaginal discharge in 11% cases, anuria in 11% cases and jaundice was seen in 10% cases at the time of presentation. All these clinical features were present in different combinations. The mean serum creatinine and the mean serum urea level at the time of admission in the present study were 3.60 mg/dL with SD 1.58 and 102.98 mg/dL with SD 41.48, respectively. The peak serum urea during the course of treatment

was 109.06 mg/dL and peak serum creatinine was 3.76 mg/dL, which was lower than the finding of Prakash J et al., [6].

The treatment modalities were conservative management in 87% cases and dialysis was required in 13% cases. This is in contrast to the study of Prakash J et al., in which haemodialysis was required in 54.6% and conservative treatment was given in 45.2% and Goplani KR et al., in which haemodialysis was required in 97.14% cases [5,6]. Around one-third (30%) of the patients required intensive care admission. Maternal death was seen in 11% of the patients. The recovery rate and survival in the present study was 89%, which is greater in comparison to the report of Ansari MR et al., where 26% developed irreversible renal failure and complete recovery was observed in 55% patients only [1]. Similar report was given by Prakash J et al., who gave a recovery rate of 69.7% [6]. The most severe form of acute renal failure was found to develop in the following conditions: equally attributed to severe preeclampsia and eclampsia leading to 27.2% mortality, puerperal sepsis (27.2%) and HELLP syndrome (27.2%), followed by primary PPH (18.1%).

Foetal mortality was observed in 5% cases, which is in contrast to observations given by Randeree IG et al., who reported foetal mortality in 55% and majority of deaths occurred in early gestation [9]. A recent review in 2017 showed that there were 123 stillbirth/perinatal deaths of the 412 pregnancies with acute renal failure (29.8%) [10,11].

Limitation(s)

We took non probability sampling and bias could not be avoidable.

CONCLUSION(S)

This study concludes that pregnancy related acute renal failure is still a significant occurrence. It is associated with serious prognosis for the mother and the child. The number of cases of acute renal failure due to septic abortion, antepartum haemorrhage and PPH in this study is relatively less, probably reflecting safe abortion procedures and better blood transfusion facility. The alarming increase in the prevalence of severe preeclampsia and eclampsia as a cause of acute renal failure during pregnancy, calls for early recognition of high risk groups, prevention of the severity of hypertension, and effective management. Even though, good obstetric care can reduce the morbidity and mortality associated with acute renal failure, intensive care management facility is needed.

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