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CLINICAL STUDY

Acute kidney injury in late pregnancy in developing countries

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ABSTRACT

Introduction: The data directly evaluating acute renal failure (ARF) in third trimester of pregnancy from Indian subcontinent are scanty. This study analyzes the clinical spectrum of ARF with respect to total birth in third trimester of pregnancy. Material: All pregnant women after the 28th week of pregnancy or in early postpartum period (up to 7 days) admitted to our hospital between August 2006 and August 2008 were screened for clinical evidence of ARF. Pregnant women with clinical diagnosis of ARF in third trimester were included in this study. Results: Of the 4758 pregnant women in third trimester, ARF developed in 85 cases (1 in 56 births). Preeclampsia, puerperal sepsis, and intrauterine death were responsible for ARF in 35.29, 24.7, and 16.67% of cases, respectively. Postpartum hemorrhage and antepartum hemorrhage were the causes of ARF in 10.59 and 8.29% of patients, respectively. Acute fatty liver of pregnancy was noted in one patient. Complicated preeclampsia (hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome, eclampsia, and uterine hemorrhage) was associated and higher incidence of ARF. Live birth occurred in 61.2% of patients with vaginal delivery in 70% cases. Renal cortical necrosis was diagnosed in two cases. Overall, mortality was 20%. The puerperal sepsis contributed 41% of total death. Conclusion: ARF complicated 1.78% of total delivery in third trimester of pregnancy. Preeclampsia was the most common cause of ARF followed by puerperal sepsis. In contrast to the developed countries, incidence of ARF is still very high in late pregnancy in the developing countries. Overall mortality was 20% with highest (33%) mortality in puerperal sepsis group.

Keywords: acute renal failure; pregnancy; third trimester; cortical necrosis; dialysis

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INTRODUCTION

Acute renal failure (ARF) in association with septic abortion and late obstetrical complications is well described in literature.[1,2] Although, incidence of ARF in pregnancy has decreased sharply in the past 40 years in developed countries, it is still a common problem in developing countries.[3–5] Obstetric ARF 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 hemorrhage, and puerperal sepsis.[2–4] It is useful to express the incidence of pregnancy-related ARF (PRARF) in relation to births rather than percentage of total cases of ARF.[6] The incidence of acute kidney injury requiring dialysis complicating pregnancy is approximately 1 in 20,000 births in industrialized countries. In contrast, pregnancy is still responsible for 15–20% of total ARF cases in various developing countries.[2,3,7] However, there is a shift of focus on prevention and management of obstetrical complications in late pregnancy which are associated with ARF. There is a paucity of data directly evaluating ARF in third trimester of pregnancy from the Indian subcontinent. Keeping this fact in mind, this study was undertaken with objectives to study the incidence and clinical spectrum of ARF in third trimester of pregnancy with respect to total birth.

MATERIAL AND METHODS

This prospective study was conducted from August 2006 to August 2008 at the Sir Sunderlal Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi, in the departments of nephrology and obstetrics and gynecology. Pregnant women with clinical features of ARF in third trimester of pregnancy were included in this study. All patients after 28th week of pregnancy or in early postpartum period (up to 7 days) admitted to our hospital either for safe delivery or referred for the management of obstetrical complications were screened for clinical evidence of

ARF. *Third trimester of pregnancy* was defined as the duration of pregnancy after 28 weeks and up to 42 weeks. *Acute renal failure* was defined as a syndrome characterized by a rapid (hours to weeks) decline in glomerular filtration rate and retention of nitrogenous waste products such as blood urea nitrogen and creatinine. The criteria for diagnosis of ARF were a sudden increase in serum creatinine >2 mg/dL and/or a sudden increase in serum creatinine >50% when prior renal function was normal, oligoanuria, and need for renal replacement therapy. *Oliguria* was defined as urine output less than 400 mL/24 hr. *Anuria* was defined as urine output less than 100 mL/24 hr. *Absolute anuria* was defined as no urine output or only a few drops of urine in 24hr. *Complete recovery* from ARF was declared when serum creatinine returned to normal range (below 1.2 mg/dL). *Partial recovery* was defined when renal function improved but serum creatinine did not return to normal range and patient was dialysis independent. *Cortical necrosis* was suspected in presence of anuria for >4 weeks and diagnosed with characteristic CECT scan finding of hypo-attenuating subcapsular rim of renal cortex with normal size kidneys. *Preeclampsia* was defined as the onset of hypertension and proteinuria after 20 weeks of gestation in previously normotensive and nonproteinuric pregnant women. *Eclampsia* was defined as the occurrence of new onset grand mal seizure in a patient with preeclampsia. *HELLP* syndrome was defined as laboratory evidence of hemolysis, elevation of liver enzymes, and low platelet count in preeclamptic women. *Puerperal fever* was defined as a temperature of 38.0°C (100.4°F) or higher, which occurs on any 2 of the first 10 days postpartum, exclusive of the first 24 hr, and which is taken orally by a standard technique at least four times daily. Patients with preexisting renal insufficiency, hypertension, diabetes mellitus, history of renal stone disease, small size of kidneys, and refusal to cooperate with study were not included in this study.

Detailed and meticulous history, physical examination, biochemical, coagulation, and imaging studies were carried out in all patients with ARF. Renal biopsy and CT scan were done in selected cases. Severity of ARF was assessed using urine output, duration of oligoanuria, uremic symptoms, and level of urea and creatinine at the time of admission. Dialysis support (hemodialysis or peritoneal dialysis) was given as per the standard indications of dialysis. The clinical outcome, mortality, and its causes were recorded in each patient individually. Associated comorbidities such as adult respiratory distress syndrome (ARDS), pulmonary edema, multiorgan failure, and cerebral complications were also recorded individually. Patients with ARF were followed for 3 months postpartum or until death, whichever was earlier. Renal biopsy was performed in patients with prolonged ARF (oligoanuria >4 weeks) or persistent proteinuria after 12 weeks postpartum.

RESULT

Of the 4758 deliveries that occurred from August 2006 to August 2008, ARF was diagnosed in 85 women. Thus, incidence of ARF was 1 in 56 births, that is, 1.78% of total deliveries. The age of patients with ARF in third trimester of pregnancy or early puerperium ranged between 18 and 41 years with the mean age of 27.15±4.66 years. Majority (91.7%) of the patients belonged to the peak reproductive age ranged between 20 and 35 years. Multigravida and primigravida constituted 62.6 and 37.6% of the patients, respectively. Mean parity was 2.39±1.44 in this study. Forty-three (50.6%) patients were in 37–40 weeks of gestation, 24 (28.2%) patients were in 29–32 weeks, 13 (15.3%) patients were in 33–36 weeks at the onset of ARF, and five patients had gestational age >40 weeks. The main clinical profile of patients is shown in Table 1.

Severe preeclampsia/eclampsia/HELLP syndrome was the most common cause of ARF observed in 30 (35.29%) patients. Puerperal sepsis contributed to ARF in 21 (24.70%) patients. Intrauterine death (IUD) accounted for ARF in 14 (16.67%) patients. Postpartum and antepartum hemorrhage were responsible for ARF in 9 (10.59%) and seven (8.29%) patients, respectively (Table 2). The amniotic fluid embolism, acute fatty liver of pregnancy, postpartum hemolyticuremic syndrome (HUS), and urinary tract obstruction due to gravid uterus were causative factors for ARF in one case each. The mean duration of oligoanuria was 6.91±2.77 days with a range of 1–120 days. The mean peak urea and serum creatinine concentration were 143.24±59.91 and 5.6±3.34 mg/dL, respectively. Hyperkalemia was observed in 17 patients (20%). Dialysis was carried out in 46 (54.6%) patients and 39 (45.2%) patients did not require dialysis. The mean number of dialysis procedures per patient was 2.4 ± 5.21 (range 1–42). Complete recovery of renal function was observed in 59 (69.4%) patients and partial improvement of kidney function occurred in five patients (5.88%). Renal cortical necrosis (RCN) was diagnosed in two patients (2.35%) (PPH-1; puerperal sepsis-1) and one case was dialysis dependent (Table 3).

Renal biopsy was performed in four patients (proteinuria persisting >12 weeks in two and active urinary sediment in another two after delivery). Biopsy revealed membranous nephropathy and diffuse proliferative glomerulonephritis related to lupus nephritis in

TABLE 1. Main clinical profile of patients (n = 85; study period: August 2006 to August 2008).

Parameters	n	%
Total no. of deliveries	4758	–
Multigravida	53	62.4
*Acute renal failure	85	1.78
Dialysis support	46	54.6**
Hyperkalemia	17	20**
Complete recovery of renal function	59	69.4**
Vaginal delivery	60	70**
Cesarean delivery	25	29.4**
Live birth	52	61.2**
Renal cortical necrosis	2	2.35**

Notes: *Incidence of ARF 1 in 56 births.
**Percentage indicates against the number of ARF in third trimester (n = 85).

TABLE 2. Etiology of ARF in third trimester of pregnancy (n=85).

Obstetrical complication	n	%
Preeclampsia/eclampsia/HELLP syndrome	30	35.29
Puerperal sepsis	21	24.70
Intrauterine death	14	16.67
Postpartum hemorrhage	9	10.59
Antepartum hemorrhage: placenta praevia (5), abruptio placentae (2)	7	8.29
Miscellaneous causes	4	4.70

TABLE 3. Outcome of patients with ARF (n=85).

Outcome	n	%
Complete recovery	59	69.4
Incomplete recovery but dialysis independent	5	5.88
Dialysis dependent	1	1.17
Death	17	20.0
Lost to follow-up	3	3.53
Renal cortical necrosis	2	2.35

two patients, idiopathic focal segmental glomerulosclerosis in one patient, and postpartum HUS in one patient. Seventeen patients succumbed during acute phase of illness. Acute respiratory distress syndrome, disseminated intravascular coagulation, and uremic complication were responsible for 5 (29.4%), 5 (29.4%), and 3 (17.6%) deaths, respectively. Death due to pulmonary edema (2), severe sepsis (1), and periventricular hemorrhagic infarct (1) occurred in four patients. Mortality was higher (33%) in puerperal sepsis group. Three deaths occurred each in IUD and preeclampsia/eclampsia group. The various comorbidities associated with ARF were multiorgan dysfunction syndrome in 18 (21.2%), sepsis in 16 (18.8%), disseminated intravascular coagulation (DIC) in 14 (16.5%), ARDS in 7 (8.2%), and acute hepatic failure in 3 (3.5%) patients.

DISCUSSION

The incidence of ARF in pregnancy has drastically decreased in the developed countries over the past 40 years mainly due to meticulous antenatal management. However, ARF in pregnancy, although showing a declining trend in developing countries including India, is still common in some part of the developing nation.[5,7–9] Of 4758 deliveries, ARF developed in 85 women in third trimester of pregnancy. Thus, incidence of ARF in this study was 1 in 56 births (1.78% of total delivery). In contrast to our observation, no case of ARF was observed in 12,000 and 20,000 births, respectively, in two studies reported from western countries.[10,11] Obstetrical ARF is now a very rare entity in the developed countries and current estimate of ARF requiring dialysis during pregnancy is approximately 1 in 20,000 births.[12] In our study, the possible reasons for a very high incidence of ARF in third trimester of pregnancy were poor socioeconomic status, ignorance, and unavailability of equipped hospitals for management of complicated obstetrical complication and a long time needed in traveling to reach the hospitals. ARF in pregnancy affects peak reproductive age group. Mean age of patient, parity, and gestational age in our study were 27.15±4.66 years, 2.39±1.44 and 35.32±4.31 weeks, respectively. The similar observation with respect to age of pregnant women, parity, and gestation age were reported by other workers.[13,14] Oligoanuria was the main presenting symptom seen in 73 (85.88%) patients, and mean duration of oligoanuria was 6.91±2.77 days. Twelve (14.11%) patients had nonoliguric ARF. Grunfeld et al. reported oligoanuria in 41 of 57 (71.9%) patients in their study.[1]

Ischemic acute tribularnecrosis (ATN) related to postpartum hemorrhage (PPH), abruptio placentae, preeclampsia–eclampsia, and puerperal sepsis are common causes of ARF in late pregnancy.[2,3] Preeclampsia/eclampsia was reported as the cause of PRARF in 50% of cases in the series of Grünfeld et al.[1] Similarly, in the report of Stratta et al. preeclampsia accounted for 7 of 15 cases between 1978 and 1987.[12] Hachim et al. reported preeclampsia and eclampsia in 41 of 55 (74.5%) cases as main etiology of PRARF.[15]

Similarly, preeclampsia–eclampsia replaced septic abortion as the principal cause of PRARF in South Africa, a developing country.[9] Recent study from Hyderabad, India, noted that hypertensive disorders of pregnancy were leading (43.9%) causes of PRARF.[8] We have observed preeclampsia–eclampsia as a cause of ARF in 35.29% of patients. The puerperal sepsis was reported to be the most common etiology of ARF in the Indian subcontinent in several studies.[5,13,14] We observed puerperal sepsis as the second most common cause contributing to ARF in 21 (24.70%) patients. Similar to our observation, Kumar et al. reported puerperal sepsis in 29% of patient in PRARF.[5] Ansari et al. reported puerperal sepsis in 31% of ARF during pregnancy.[14] Goplani et al. noted puerperal sepsis as the most common (61%) etiology of PRARF.[13] Uterine hemorrhage including postpartum (9/85 = 10.59%) and antepartum hemorrhage (7/85 = 8.29%) were responsible for ARF in 18.8% of patients in third trimester of pregnancy in this study. Similar to our study, Kumar et al. observed that hemorrhage of pregnancy constitutes 17% of PRARF.[15] In contrast to our observation, uterine hemorrhage was the dominant cause of PRARF in the studies by Naqvi et al. (58%), Ansari et al. (38%), and Alexopoulos et al. (38%).[7,14,16] IUD accounted for ARF in 14 (16.67%) patients in our study. This observation is similar to Ansari et al. who reported that IUD contributed 14% of PRARF.[14] However, Naqvi et al. reported that IUD contributed 25% of PRARF.[7] Amniotic fluid embolism, acute fatty liver of pregnancy, postpartum HUS, and urinary tract obstruction due to gravid uterus were causative factors for ARF in one case each in this study. This clearly shows that they are rare causes of ARF in pregnancy.

Dialysis was required in 54.6% of patients in our study. The need for dialysis was reported in 70–100% of cases in other series as well.[13,14,17] Mortality of PRARF seems to be high in developing countries. Overall, maternal mortality was 20% in our study. This is comparable to other recent studies from the Indian subcontinent.[5,7,8,13] Previously mortality was very high (55.3%) due to late referral, frequent sepsis, and high incidence of bilateral diffuse cortical necrosis.[2] Reported mortality from other studies varies from 23 to 33%.[7,14,18] We reported in our previous study that septicemia and uremic complications were the most common causes of death.[18] Sepsis and coagulation abnormalities were the main factors responsible for mortality in Naqvi et al.'s study as well.[7] Fifty-nine (69.4%) patients had complete recovery of renal function, five (5.88%) had incomplete recovery, and two (2.35%) had cortical necrosis. Similar to our observation, Goplani et al. have reported that 54.28 and 12.85% patients had complete and partial recovery of renal function, respectively.[13] In Kumar et al.'s study, complete recovery was observed in 51.22% and partial, that is, dialysis independent, in 9.76% patients.[5] Incidence of cortical necrosis was 2.35% in this study. RCN is a rare cause of ARF in developed countries, but still occurs in developing countries mainly due to the obstetrical complications of pregnancy.[2,19,20] However, incidence of cortical necrosis in PRARF has decreased significantly ($p < 0.001$) from 17% in 1982–1991 to 2.4% in the 2000s.[18] In our recent study, the overall incidence of RCN in obstetric ARF was 15.2%, and it had decreased significantly from 4.7% in 1984–1994 to 0.5% in 1999–2005 of total ARF cases.[21] Interestingly, the incidence of irreversible renal damage in Italy was quite high (7/63 = 11%) especially in preeclampsia–eclampsia (4/10 = 25%).[12]

Fetal mortality was observed in 33 (38.8%) pregnant women. Similar to this Ventura et al. reported perinatal mortality of 40% in ARF in pregnancy.[22] Perinatal mortality was 38% in ARF in severe preeclampsia requiring admission to obstetric intensive care unit.[23] Randeree et al. reported perinatal mortality in 55% of pregnant women and majority of death occurred in early gestation.[9] Thus, fetal mortality was similar to other reported studies.[9,22,23]

In summary, ARF complicated 1.78% of total deliveries (1 in 56 births) in this study. In contrast to extremely low (1 in 20,000 births) incidence of ARF in developed countries, ARF due to late obstetrical complications is still very high (1 in 56 births) in developing countries. ARF adversely affects fetal mortality (38.8%). Despite severe ARF requiring dialysis, vaginal delivery occurred in 70% of cases with live birth in 61.2% of patients. The complete recovery of renal function was observed in 70% of patients and RCN was noted in only 2.35% of cases. Patient education, early referral, and prompt treatment of late obstetrical complications are the key issues to reduce the incidence of ARF in late pregnancy.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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