Factors Predicting the Outcome of Acute Renal Failure in Pregnancy

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ABSTRACT

Objective: To determine the factors predicting renal outcome in patients developing acute renal failure in pregnancy.

Study Design: Descriptive cohort study.

Place and Duration of Study: Study was conducted at Nephrology Unit of Sindh Institute of Urology and Transplantation, Karachi, from October 2006 to March 2007.

Methodology: Patients with acute renal failure due to complications of pregnancy, with normal size of both the kidneys on ultrasound were enrolled, and followed for a period of 60 days or until recovery of renal function. Patient's age and parity, presence of antenatal care, type of complication of pregnancy, foetal outcome and duration of oliguria were compared between patients who remained dialysis dependent and those who recovered renal function. Chi-square/Fisher's exact test and student's t-test, were used for determining the association of categorical and continuous variables with dialysis dependency.

Results: The mean age was 29±6 years. Most patients came from rural areas of interior Sindh. Sixty eight percent did not have antenatal checkups. Antepartum haemorrhage (p=0.002) and prolonged duration of oliguria (35±15.7 days, p= < 0.001) were associated with dialysis dependency, which was observed in 50% of the study group.

Conclusion: Ante-partum haemorrhage and prolonged oliguria were strong predictors of irreversible renal failure. This highlights the need for early recognition and referral, and the importance of trained birth attendants and antenatal care.

Key words: Acute renal failure.   Pregnancy.   Renal cortical necrosis.   Dialysis.   Antepartum haemorrhage.   Oliguria.

INTRODUCTION

In the developed world, the incidence of acute renal failure (ARF) during pregnancy and childbirth is decreasing, mainly as a result of improved prenatal care and decreased postabortal sepsis.[1] However, this problem remains an important cause of hospital admission, mortality and morbidity in the developing countries.[1] The causes of ARF in this setting include spontaneous and induced abortion, pre-eclampsia, eclampsia, HELLP (hemolysis, elevated liver enzymes, low platelet syndrome), ante-partum haemorrhage (APH), post partum haemorrhage (PPH), combined APH and PPH, and DIC (disseminated intravascular coagulopathy).[2,3]

In developing countries, most of the deliveries in rural areas are conducted at home due to the limited or non-availability and inaccessibility of obstetric healthcare and antenatal care. Poor management of ARF at its early stage can lead to cortical necrosis and dialysis dependency. Optimal management, however, generally leads to the return to a normal renal function after 3 or 4 haemodialysis treatments.[4]

This study was conducted to identify factors which predict the poor renal outcome as defined by persistent haemodialysis dependency, in order that high risk mothers may be identified and managed optimally.

METHODOLOGY

This was a descriptive study of a convenience cohort, carried out at Nephrology Unit of Sindh Institute of Urology and Transplantation (SIUT), Karachi, from October 2006 till March 2007. Approval by the Institutional Ethics Committee was obtained for the study. Eligible patients included women admitted during the study period to CCU, ICU, and the Nephrology Ward through SIUT Emergency room with the diagnosis of ARF due to complications of pregnancy. Those with ARF due to other causes, chronic renal failure, acute on chronic renal failure, and end stage renal failure on maintenance haemodialysis were excluded. Detailed history was taken; complete physical examination and investigations were done and data were entered in a pre-designed proforma at admission and during follow-up. Patients were followed-up during their hospital stay and after discharge until renal function returned to normal, or day 60 post-discharge, whichever was earlier.

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Patients were divided into two groups: those who had complete or partial recovery of renal function such that they remained dialysis-independent, and those who had no recovery and remained dialysis-dependent. Frequency of categorical variables was reported as percentage and compared using the chi-square/Fisher-exact test, whereas continuous variables were compared using student's t-test. SPSS10.0 was used for the data analysis. A p-value of < 0.05 was considered as statistically significant.

The independent variables tested as predictors in the study included; maternal age in years, maternal parity, presence of antenatal care, live birth, cause of ARF related pregnancy or childbirth (abortion, antepartum haemorrhage, postpartum haemorrhage, sepsis) and duration of oliguria in days.

RESULTS

Fifty female patients met the inclusion criteria and were enrolled in the study. Their ages ranged from 18-42 years, with a mean of 29 ± 6 years. There was no significant difference between age of the patients in dialysis dependent group and those who recovered (p=0.1). Fifteen (7.5%) patients were primiparous and the remaining 35 (17.5%) patients were multiparous (Table I).

Table I: Clinical characteristics of patients and relation with renal outcome.

	Dialysis dependent (n=25)	Recovered (n=25)	p-value
Age (years)	30.2±6.5	27.8±5.3	0.1
Primipara	6 (24%)	9 (36%)	0.35
Multi (≥ 2)	19 (76%)	16 (64%)	
Still birth and abortion	16 (64%)	18 (72%)	0.54
Live birth	9 (36%)	7 (28%)	

The cause of ARF was antepartum haemorrhage (APH) in 20 patients, postpartum haemorrhage (PPH) in 16, eclampsia/pre-eclampsia/HELLP syndrome in 14, puerperal sepsis in 16, and lower segment caesarean section (LSCS), obstructed labour, twin pregnancy, and abortion in 21 patients, either alone or in combination (Table II).

Table II: Nature of insult and its impact on the renal outcome.

Nature of insult	Dialysis dependent	Recovered	CR*	IR**	p-value
APH (antepartum haemorrhage)	14 (56%)	6 (24%)	2	4	0.002
PPH (postpartum haemorrhage)	6 (24%)	10 (24%)	5	5	0.7
Puerperal sepsis	9 (36%)	7 (28%)	3	4	0.5
Eclampsia, pre-eclampsia	7 (28%)	7 (28%)	5	2	1
HELLP syndrome (haemolysis, elevated liver enzymes, and low platelets)	2 (8%)	1 (4%)	2	0	0.8
others (LSCS, obstructed labour, abortion)	11 (44%)	10 (45%)			0.7

*CR=Complete remission;   **IR=Incomplete remission.

Overall, 25 (50%) patients remained dialysis dependent at the end of 60 days. Among those who were dialysis independent, there was complete renal recovery in 14

(7%) and incomplete recovery in 11 (5.5%) all with serum creatinine of > 2 mg/dl after 60 days follow-up.

In terms of predictors of renal outcome, only 16 (32%) patients had one or more antenatal checkup during pregnancy, and this had no effect upon renal outcome. Six (40%) of the primiparous women remained dialysis dependent at 60 days follow-up, whereas 19 (54%) multiparous women remained dialysis dependent (p=0.35). Four (1.4%) multiparaous mothers succumbed to their illness during follow-up, and all of these were dialysis dependent at the time of their death. The duration of oliguria in patients remaining dialysis dependent ranged from 21 to 60 days, with a mean of 35±15.7 days. The corresponding duration in those who recovered was 13.7±10.2 days, averaging 6.64 days in those with complete renal recovery and 16 days in those with incomplete recovery. Duration of oliguria was found to be significant predictor of renal outcome (p < 0.001).

Amongst 50 deliveries, foetal outcome was intrauterine death in 34 (68%) and live birth in the remaining 16 (32%). Of women who had foetal loss, 16 remained dialysis dependent. Of those who delivered a live baby, 9 were dialysis dependent (p=0.54).

DISCUSSION

While acute renal failure due to obstetric causes has become a rarer entity in developed countries, it continues to be common in developing countries.[5,6] The reported incidence of acute renal failure in critically ill patients varies widely between 1-25%.[7,8]

There is not much change in the demographic profile of patients. The mean age in this study was 29 ± 6 years which was similar to the observation made by other workers.[2,5,9-11] Mjahed et al. observed that the mean age of the patients who developed ARF was higher in comparison to those who did not, 28 years and 26 years respectively though not significant statistically.[4]

Thirty-two, 70% of the patients came from the rural areas of interior Sindh, and did not have antenatal checkups in as many as 34 patients. Ahmad et al. observed that in their study all the pregnancy related ARF were brought from the peripheral areas.[15] Though statistically not significant in influencing the outcome in this study, its significance has been highlighted by Naqvi et al.[9] and Ahmad et al. in their studies.[15] Antenatal checkup helps in creating awareness among the pregnant mothers and thus seek help from trained birth attendants and not the untrained one whenever they are in need.

The total number of primipara and multiparous were similar, 9 primi-had recovered renal functions while 6 remained dialysis dependent and 16 multiparous recovered leaving nineteen in the dialysis dependent group, however, 74% patients in a study, conducted by

Ramzan *et al*. were multipara and 67% of their patients did not have antenatal checkup.[16] Similarly, 55% were multipara, 45% were grand multipara in the study conducted by Ali *et al*.[2] In a series of 442 pregnancies complicated by HELLP syndrome, 33 patients developed ARF, of whom 15 patients (47%) were primiparous and rest of them were multiparous.[10] Celik *et al*. found that 70% of their patients were multipara and its difference with the incidence of primigravida was not significant in ARF developing and non-developing group.[11] However, primigravida predominated in the study conducted by Prakash *et al*. who were looking into the hypertension in pregnancy.[17] Similarly primigravida predominated in Mjahed *et al*. observation, though not significant statistically 52% of the primigravidas developed ARF.[4] This shows that when acute renal failure is generally looked upon in pregnant mothers it is more frequent among the multiparous, however, when pregnancy induced hypertension is considered as well it mostly affects the primigravida.

Nine in those who remained dialysis dependent and 7 of those who recovered, gave birth to alive baby and the remaining 34 patients had foetal loss, 17 in each group. In a study conducted by Ali *et al*. there were 45% foetal loss including 20% still birth, and 40% live birth.[2] Sixty-two percent had live birth and 31% had still birth in the study conducted by Prakash *et al*.[12] Perinatal mortality in the cases with ARF was observed in the cases of oliguric ARF and had creatinine levels above 2 mg/dl. It was higher in those who had HELLP syndrome and ARF and the difference was statistically significant in the observation made by Gul *et al*.[1] Celik *et al*. reported that 19% patients had intrauterine dead fetuses.[11]

The unusually high rate of foetal death in our patients was perhaps a reflection of severity and number of insults occurring during pregnancy which not only caused foetal death but also caused severe renal failure requiring dialysis.

This is corroborated by the observation made by Gul *et al*. perinatal mortality rate of the cases subsequently developing ARF was 20% while in those without ARF was 9%. Further analysis pointed out that all perinatal mortality were observed in the cases of oliguric ARF and had creatinine levels above 2 mg/dl. It was higher in those who had HELLP syndrome and ARF and the difference was statistically significant.[1]

Intravascular volume depletion due to severe blood loss is an important cause of ARF. Haemorrhage has been reported as the leading cause of pre-renal azotemia in 15 of their patients and included traumatic, operative and obstetrical haemorrhage.[18] Similar had been the observation of Iqbal *et al*.[19] They found hypovolaemia as the major cause of intrinsic ARF in 15 of their patients and 9 out of them were due to obstetrical reasons.

ARF is much more common with antepartum haemorrhage than following postpartum haemorrhage, and yet the blood pressure remains unchanged or rises in the former while tends to fall in later. Possibly the compensating renal vasoconstriction which accompanies the reduction in circulating blood volume following postpartum haemorrhage is not so great or so prolonged as in antepartum haemorrhage. Disseminated intravascular coagulation which often complicates antepartum haemorrhage may be an additional contributing factor.[20] Antepartum haemorrhage in this study emerged as the only significant insult adversely associated with non-recovery of renal function. This is in contradiction to the study conducted by Khan RN, where postpartum haemorrhage and eclampsia were the two conditions associated with ARF due to obstetrical complications.[21]

Thirty-eight (76%) patients in this study required blood transfusions at the referring centre. In a study done by Ali *et al*. 50% patients had required blood transfusions.[2]

Six patients had radiological evidence of acute cortical necrosis on admission. Only 2 of the patients in this study had undergone renal biopsy as the cause of renal failure was debatable and both showed histological features of acute cortical necrosis. Later during the follow-up, an additional 4 patients developed cortical necrosis, all 10 patients who had radiological and histological evidence of renal cortical necrosis (RCN) remained dialysis dependent and were undergoing evaluation for renal transplantation.

Similar work was done in this region, by Prakash *et al*. where 210 cases of obstetric ARF were included, 32 patients had developed renal cortical necrosis, while 25 patients who ARF of non-obstetric origin had renal cortical necrosis, making it a less frequent cause of RCN. However, the incidence of RCN has declined over last ten years in developing countries.[18] Naqvi *et al*. in 1996 had shown that in 9 of their 43 patients who had obstetric ARF acute cortical necrosis was present.[9] Turney *et al*. reported that 70% cases of ACN occurred with APH, fourteen had evidence of abruption of which 21% of the patients developed ACN.[13] However, Sibai *et al*. observed that only one out of 33 patients who developed ARF due to HELLP syndrome developed ACN that too in association with abruptio-placentae.[14,22] Kazi *et al*. looked into the pathological lesions underlying ARF and found that together with acute cortical necrosis (ACN), ATN accounts for a vast preponderance of ARF cases 60% whereas ACN was the pathological lesion in 22% of the renal biopsies. Obstetric ARF was the etiological factor in 21% cases, in their series of 97 patients.[23]

The patients who remained dialysis dependent were oliguric for a highly significant longer period than those who recovered. Furthermore those who had complete

recovery were oliguric for around a week while those who had incomplete recovery were oliguric for sixteen days. Similarly acute cortical necrosis resulted in prolonged oliguria and consequently more haemo-dialysis in the study done by Turney *et al.* 52 of their patients had normal renal function from 1-31 years after recovery from the episode of ARF. Chronic renal failure only developed after complete or partial ACN, majority of whom died during the initial illness or from end stage renal failure within a short period. They proposed that disappearance of illegal abortions, improvement in ANC with effective management of complicated pregnancies, the facility for safe early elective delivery when indicated, the improvement in resuscitation of obstetric haemorrhage and increased proportion of hospital births; had all contributed to the prevention of this devastating complication of pregnancy.[13] Ali *et al.* managed 21% of their patients conservatively, 49% of the patients required dialysis for one week only and 15% required it for 5-6 weeks period. Ten percent of their patients ended in chronic renal failure at one year follow- up.[2] Out of 1150 patients only 12 patients developed renal failure, ten of them had complete recovery and two required renal transplant as reported by Noorani *et al.* Ramzan *et al.* had enrolled 31 patients of established pregnancy related ARF and observed complete recovery of renal functions in 19 patients, 6 did not require dialysis support and remaining 4 had irreversible renal dysfunction.[13] In the series of 442 pregnancies complicated by HELLP syndrome, there were 4 immediate maternal deaths; 22 patients had normal renal functions on follow-up at 4 years. One patient was dialysis dependent with cortical necrosis, one required dialysis after 7 years and one patient had serum creatinine of 1.7 mg/dl.[10] The reason of larger number of patients remaining dialysis dependent in this study is because of the fact that the study is the longer tertiary referral centre in Sindh and receives the patients in later stages of their illness who have established renal failure. In as much as 25% patients' haemodialysis had already been started by the referring unit. Furthermore the lack of resuscitation and safe elective delivery facilities makes the scenario worse. Still a large number of women deliver at home and the deliveries are not handled by trained birth attendants. All these factors were responsible for the larger number of intrauterine foetal deaths, prolonged duration of oliguria resulting in irreversible renal dysfunction.

CONCLUSION

ARF due to the obstetric complications remains an important problem. The proportion of patients requiring dialysis remains high. Prolonged duration of oliguria and antepartum haemorrhage were strong predictors of poor renal outcome and irreversible renal failure.

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