

Etiology and Outcome of Acute Renal Failure in Pregnancy

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ABSTRACT

Objective: To determine the etiology and outcome of Acute Renal Failure (ARF) in pregnancy.

Study Design: A case series.

Place and Duration of Study: Nephrology Department of the Jinnah Postgraduate Medical Centre, Karachi, from August 2007 to July 2008.

Methodology: Pregnant women who were healthy previously and had developed ARF, diagnosed on oliguria (urine output <400 ml/day) and mounting azotemia (serum creatinine > 2 mg%) were included in the study. Percutaneous renal biopsy was performed for delayed recovery, i.e. after three weeks. Patients were followed up for a period of 6 months. Percentages were calculated for qualitative variables i.e. causes of ARF, mortality, morbidity and outcome in form of complete recovery, partial recovery, demise and non-recovery.

Results: A total of 43 patients with pregnancy-related ARF were included in the study. The puerperal group comprised 36 patients (83.7%). Haemorrhage was the etiology for ARF in 25 (58.1%), antepartum haemorrhage APH in 8 (18.6%) and postpartum haemorrhage PPH in 16 (37.2%) of patients. In 12 (27.9%), puerperal sepsis was the etiological factor, while 4 (9.3%) patients had DIC on presentation. Pre-eclampsia, eclampsia and HELLP syndrome accounted for 5 (11.6%). While 1 (2.3%) was diagnosed with hemolytic uremic syndrome and another one was diagnosed as ARF secondary to hypotension produced by hyperemesis gravidarum. Renal biopsy was performed in 31 patients showing that 10 had acute cortical necrosis and 21 had acute tubular necrosis. Maternal mortality was 16.2% (n=7). Of the 36 (83.7%) surviving patients, 18 (41.4%) had complete recovery of renal function; 12 (27.9%) had partial recovery; and 6 (13.9%) required chronic dialysis.

Conclusion: Pregnancy-related ARF was associated with poor outcome. Antepartum and postpartum haemorrhage were the most common cause of ARF in pregnancy.

Key words: Pregnancy. Acute renal failure. Antepartum haemorrhage. Postpartum haemorrhage.

INTRODUCTION

There are profound changes in renal function in normal pregnancy, which lead to marked alterations from the non pregnant physiologic norms.^{1,2} Pregnancy-related Acute Renal Failure (ARF) may comprise upto 25% of the referrals to dialysis centres in developing countries and is associated with substantial maternal and fetal mortality.³

In recent years, there has been a marked decline in the incidence of ARF associated with pregnancy; currently, cases that are severe enough to require dialysis occur in fewer than 1 in 20,000 pregnancies although complications with transient mild to moderate Glomerular Filtration Rate (GFR) decrease, occur in approximately 1 in 8000 deliveries. The rate of septic abortion as the reason of ARF was 33.3% in 1980-85 and has decreased to 6.3% in 1989-97.⁴ ARF in pregnancy is associated with a high risk for maternal mortality

(9-55%).⁵ All factors that can cause ARF in a non-pregnant woman can theoretically cause renal failure in a pregnant woman, including volume depletion, bleeding and sepsis.⁶

Several general categories of pregnancy-specific ARF can be delineated: hypovolemic, thrombotic microangiopathic, infectious and obstructive.⁷ In pregnancy, the most common cause of volume depletion of this magnitude is obstetrical haemorrhage, which can occur at any gestational age. In rare cases, severe hypovolemia can result in pre-renal ischaemia and ARF.⁶⁻⁸ Unskilled and septic abortions can also be associated with consumptive coagulopathy, or disseminated intravascular coagulation, which can cause direct intrarenal damage.^{9,10} In advanced gestation, ARF is most commonly associated with pre-eclampsia or abruptio placentae. An important and difficult differential diagnosis is that of acute renal failure in late pregnancy in association with microangiopathic hemolytic anemia and thrombocytopenia. There are two main entities that must be considered: Thrombotic Thrombocytopenic Purpura-Hemolytic Uremic Syndrome (TTP-HUS) and severe pre-eclampsia, usually with the HELLP syndrome (hemolysis with a microangiopathic blood smear, elevated liver enzymes, and a low platelet count). Postpartum renal failure is a specific entity and

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may be considered as a form of hemolytic-uremic syndrome occurring in the postpartum period.^{6,11}

ARF in pregnancy bears a high risk of bilateral renal cortical necrosis and consequently of chronic renal failure. Renal cortical necrosis is an uncommon entity and accounts for only 2% of all the cases of ARF. Obstetric complications are the most common (50-70%) cause of renal cortical necrosis; abruptio placentae, septic abortion, pre-eclampsia, postpartum haemorrhage and puerperal sepsis are the conditions associated with pregnancy, and are responsible for renal cortical necrosis.^{6,9,10} Many patients require dialysis, but 20 to 40 percent have partial recovery with a creatinine clearance that stabilizes between 15 and 50mL/min.^{9,10} Pyelonephritis is the most common infectious complication of pregnancy.¹²

The gravid uterus can cause significant compression of the genitourinary system, particularly in settings of uterine over distention such as polyhydramnios, multiple gestation, or uterine fibroids. There have been several case reports of PR-ARF in these scenarios.¹⁰ Blood should be replaced early in all the obstetrical haemorrhages.¹³

The objective of this study was to determine the cause and outcome of pregnancy-related ARF.

METHODOLOGY

Between August 2007 and July 2008, 130 patients with ARF were admitted at the Nephrology ward 22 of Jinnah Post graduate Medical Centre Karachi.

A total of 48 patients with ARF were pregnant. Of these, 5 patients had evidence of renal disease prior to pregnancy and were excluded; hence, 43 patients with pregnancy-related ARF were studied.

Inclusion criteria were the following: pregnant women who were healthy previously and had developed ARF were diagnosed in oliguria (Urine output < 400 ml/d) and for mounting azotemia (Serum creatinine > 2 mg%).

Exclusion criteria were the following: Those pregnant women who had any evidence of renal insufficiency like glomerulonephritis, raised serum creatinine, history of hypertension and diabetes before pregnancy and any history or any current evidence of stone diseases were excluded from this study.

Once enrolled for the study, a complete history including the obstetrical history, detailing the particulars of the ante natal period was taken, a detailed clinical examination was performed in all the patients and the relevant investigations were done. Obstetrical examination with any obstetrical intervention as and when needed was done in a few patients. Renal biopsy was performed in those patients who remained oliguric or whose renal function did not improve even at the end of the third week.

Patients who needed renal replacement therapy were subjected to either peritoneal or hemodialysis as per indication. Follow up included all the patients and those who became dependent on renal replacement therapy were registered.

Descriptive statistics were used in this study and percentages were calculated for qualitative variables like, causes of ARF and outcome in form of complete recovery, partial recovery, demise and non-recovery. Mean ± standard deviation were calculated for age. SPSS Version 10 is used for all statistical analysis.

RESULTS

A total of 130 ARF patients were admitted at the Nephrology Department of the Jinnah Postgraduate Medical Centre, between August 2007 and July 2008. Of these 48 had pregnancy-related ARF; from 5 these were excluded because of the evidence of renal disease before pregnancy.

Therefore a total of 43 patients were studied. The mean age of the patients with pregnancy-related ARF was 25 ± 6.1 years. The youngest patient was 18 years old and the eldest was 40 years old. Forty (93%) were multigravida and 3 (6.9%) patient were primigravida.

The major group was the puerperal group comprising 36 patients (83.7%). Four patients (9.3%) presented in early pregnancy and 3 (6.9%) in late pregnancy, 27 (62.7%) had not received antenatal care and 16 (37.2%) had received antenatal care.

A total of 25 patients (58.1%) delivered at home, while 18 (41.8%) had delivered at hospitals. Of the former, 4 died due to septicemia and Disseminated Intravascular Coagulation (DIC), 33 (76.7%) patients presented with oliguria, 8 patients (18.6%) presented with anuria and 2 (4.6%) patients had non-oliguric renal failure. Other presenting features were edema in 36 (83.7%), dyspnea in 34 (79%), fever in 25 (58.1%), and vaginal bleeding in 23 (53.4%).

Haemorrhage as the etiology of ARF was found in 25 (58.1%) as APH in 8 (18.6%) and PPH in 16 (37.2%) of patients. Twelve (27.9%) had puerperal sepsis and 4 (9.3%) of the patients had DIC. Pre-eclampsia, eclampsia and HELLP syndrome accounted for 5 (11.6%) cases. One (2.3%) each was diagnosed with HUS and ARF secondary to hypotension produced by hyperemesis gravidarum (Table I).

Table I: Etiology of ARF.

Etiological factors	Number of patients	Percentages
Puerperal sepsis	12	27.9%
PPH	16	37.2%
APH	8	18.6%
EC.PRE.EC./HELLP	5	11.6%
DIC	4	9.3%

PPH = Postpartum haemorrhage

APH = Antepartum haemorrhage

EC.PREEC. = Eclampsia pre-eclampsia;

HELLP = Haemolysis elevated liver enzymes low platelets

DIC = Disseminated intravascular coagulation

A majority of the patients (n=41 95.3%) required hemodialysis, while two died without dialysis; none of the patients received peritoneal dialysis. Evacuation of the products of conception was required in 2 patients (4.6%) and obstetric hysterectomy was required in 1 (2.3%) case. Maternal mortality was 16.2% (n=7). Sepsis accounted for 4 (9.3%) cases, pulmonary edema for 1 (2.3%) who died after 2 days of admission, and severe metabolic acidosis was the cause in two of those patients.

Of the 36 (83.7%) surviving patients, 18 (41.4%) had complete recovery of renal function; 12 (27.9%) had partial recovery; and 6 (13.9%) required chronic dialysis. In the present study, renal biopsy was performed in 31 patients, of which 10 (23.2%) had Renal Cortical Necrosis (RCN) and 21 had Acute Tubular Necrosis (ATN). In the remaining 10 patients, biopsy could not be performed due to various factors such as early recovery, early demise, and refusal by the patient or the attendant.

Factors affecting patient mortality were sepsis, thrombocytopenia, DIC and liver involvement whereas the duration of dialysis and anuria on presentation were found in cases with poor renal survival. Pre-eclampsia/eclampsia/HELLP was associated with ARF in 5 (11.6%) of the patients. Their mean age was 25 years, and 60% of the patients were multipara. The expired group of the study included those 7 patients who were clinically diagnosed as having RCN or ATN, but they expired before renal biopsy could be performed.

DISCUSSION

The incidence of pregnancy-related ARF in developed countries is 1-2.8%. In developing countries, the incidence still remains at 9-25%, mostly due to late referral of pregnancy-related complications.^{6,14} In the present study, the frequency was 33%, which is almost equal to the other studies done in Pakistan where it was found to be 36%.¹⁵

Haemorrhage was the most common etiology for ARF including both the APH and PPH, while other had puerperal sepsis, DIC, pre-eclampsia, eclampsia and HELLP syndrome HUS and ARF secondary to hypotension caused by hyperemesis gravidarum.

The data reported in various local studies showed high mortality (18-23%) and morbidity (13-26%) related to pregnancy-related ARF.^{16,17} Situation in some of the developing countries like India, South Africa and Turkey has shown improvement. The reason for the lower incidence in developed countries is the prevention of pregnancy-related complications through improvised antenatal care and early and more effective treatment of pre-eclampsia. There were very few patients in this study who had received any antenatal care; hence, their eclampsia and other complications remained un-

diagnosed. The absolute risk of ESRD (end of stage renal disease) in women who have had pre-eclampsia is low; pre-eclampsia is a marker for an increased risk of subsequent ESRD.¹⁶ Septic abortion is not observed any more in developed countries.¹⁵

In this study, the incidence of cortical necrosis was 23.2%. In another study conducted at Hyderabad Pakistan, it was 9.5% and renal biopsy was done only in 4 patients).¹⁵ It was 23.8% in another study previously conducted in India.⁶ However, this rate is still higher than other causes of ARF which are < 5%.⁶

In this study, maternal mortality was 16.2%. Sepsis accounted for 9.3% cases, while in a previous study conducted in Pakistan, it was as approximately 26%.¹¹ This decrease in maternal mortality appears to be the result of aseptic delivery practices and early management of antepartum and postpartum haemorrhages.

Data from Pakistan on pregnancy-related ARF is very sparse although this is a very serious health issue. In 1996, Naqvi *et al.* reported 18 obstetrical ARF from Karachi city with 23% mortality and 26% morbidity.¹⁷ Karachi has the maximum healthcare facilities as compared to the rest of the country so the plight in other less preveliged areas need attention.¹⁷ In this study, the root cause of the problem seems to be either lack of facilities or lack of access to the available healthcare facilities. In this study, the major group involved was in the puerperal stage comprising 83.7%. and 62.7% had no antenatal care.

In Northern areas obstetrical ARF was reported to be 7-10% of total ARF cases with 18% mortality.¹⁸ No such data is available from Balochistan, where it is expected to be much higher than the rest of the country because of multiple factors, like social trends of Dai assisted home deliveries, poverty, remote, under-manned and under-equipped district headquarter hospitals, the high parity, because of religious believes of not following the family planning parctices.

The overall incidence of acute renal failure in pregnancy has decreased. Despite this decline there has been little change in overall mortality and long-term morbidity.¹⁹

CONCLUSION

Peripartum hemorrhage was found to be the most common etiological factor causing pregnancy related acute renal failure. This included both biopsy proven acute tubular necrosis and renal cortical necrosis. But renal cortical necrosis was seen more commonly in those patients who had associated sepsis as well. Duration of anuria and renal replacement therapy were the predictors of a long term poor outcome. Sepsis, thrombocytopenia disseminated intra vascular coagulation and raised live enzymes were the predictors of maternal mortality.

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