Original Article

Spectrum and Short Term Outcome of Pregnancy related Acute Renal Failure among Women Admitted in Nephrology Ward; Pakistan Institute of Medical Sciences

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Objective: To determine the clinical spectrum of pregnancy related acute renal failure (PR-ARF) and its outcome in terms of maternal and fetal morbidity and mortality.

Study Design: Case series

Place and duration: Department of Nephrology, Pakistan Institute of Medical Sciences, Islamabad from May 2009- April 2010.

Materials and Methods:
PR-ARF was diagnosed with sudden onset oligoanuria or serum creatinine elevated to above 1.5 mg% on two consecutive occasions . Patients with underlying CKD were excluded from the study.

Results: 346 patients with acute renal failure were admitted in one year. 51 women fulfilled the criteria of PR-ARF. Frequency of PR-ARF was 51/346(14.7%). The clinical spectrum included 20/51(39.2%) cases of PIH/ PET / eclampsia with or without sepsis/DIC. 7/51(13.7%) had Acute tubular Necrosis (ATN), 10/51 (19.6%) had puerperal sepsis. 12/51(23.5%) had sepsis along with ATN, out of these 3 had septic abortion. RPGN 1/51 (1.9 %) and acute cortical necrosis 1/51 (1.9%) respectively. Pregnancy related ARF was seen mostly in third trimester/post partum in 46/51(90.2 %). It followed vaginal delivery in 32/51 (62.7%) patients and in 15/51 (29.4%) cases after cesarean section, and 3/51 (5.8%) patients after septic abortion with Dai handling. Dai (traditional birth attendant) handling was found in 17/51 (33.3 %).Antenatal care was not available to 39/51(76.4 %). Maternal outcome showed that 17/51 (33.3%) patients died 25/51 (49.0%) showed complete recovery, 2/51 (3.9%) had partial recovery, whereas irreversible renal failure in 4/51 (7.8 %). Outcome was unknown in 3/51(5.8 %).

Conclusion Most common cause of pregnancy related acute renal failure is PIH associated with other risk factors like abruption, IUD, DIC and RPOC. Sepsis is the main contributory factor in PR-ARF. No antenatal care and Dai handling was seen in most of patients. Pregnancy related acute renal failure has a very high maternal mortality and morbidity.

Key Words: Acute renal failure, Pregnancy related Acute Renal failure, Clinical spectrum.

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Introduction

Acute renal failure (ARF) in pregnancy is a rare medical complication that has a high mortality and morbidity.[1,2,3,4] It has a potential high risk of bilateral renal cortical necrosis.[2-4] Acute renal failure in pregnancy can be induced by any of the disorders leading to ARF in the general population; however complications characteristic of each trimester can also result in acute renal failure.[2] Frequency distribution of

pregnancy related ARF is bimodal in relation to the period of gestation. The first peak is in early pregnancy between 7 to 16 weeks and the second peak is seen later between 34 to 36 weeks.[1,3] Majority of pregnancy related ARF cases are seen in late pregnancy or puerpeium.[4-7] In early pregnancy it is mostly prerenal azotemia due to hyperemesis gravidarum and ATN due to septic miscarriage. [1,3,7] In later pregnancy many different disorders can lead to ARF, of which blood loss causing APH and PPH is the most common.[1] Others causes are puerperal sepsis and thrombotic microangiopathies (HELLP, HUS/TTP). [2, 7] Acute fatty liver of Pregnancy is an uncommon cause of pregnancy related ARF [3] and still rarely urinary tract obstruction[2]

Over the past few decades, the overall incidence of pregnancy related ARF has decreased in the west [1] Septic abortion has virtually disappeared[4] and the incidence of bilateral renal cortical necrosis has also decreased markedly[2] But in the developing countries the incidence remains high. Improved prenatal care, septic abortion prevention, legalization of abortion, early recognition and better management of obstetric complications as well as enhanced overall access to health care facilities, have led to the decreased incidence of ARF in pregnancy in the developed countries.[1,3,4,7,8]

In India Pregnancy related ARF constituted 4.24 % and 7% of ARF done recently.[1,3] Pregnancy related acute renal failure involves women of reproductive age group who are otherwise normal . Every effort has to be done to prevent and optimize the management of this disorder, so that we can meet the same reduction in maternal morbidity and mortality as the western countries.

Materials and Methods

All patients admitted in nephrology ward fulfilling the criteria of pregnancy related acute renal failure (PR-ARF) were selected for the study. Informed consent was taken from the patient and or the guardian. Demographic characteristics were recorded. Clinical examination and investigations were performed to rule out chronic kidney disease, hypertension and diabetes mellitus. Dialysis, antibiotics and related treatment including blood transfusion, removal of retained products of conception (RPOC) were carried out if indicated. The variables of interest were maternal and fetal outcome, associated clinical and laboratory findings and outcome of treatment given to patient. All the information was collected in a structured Performa

ARF was diagnosed on basis of clinical and laboratory findings. Sudden oliguria (urine less than 400 ml in24 hrs) or anuria or serum creatinine increased above 1.5mg/dl.

Complete recovery was defined as renal function returning to normal. Whereas, partial improvement was defined when serum Creatinine decreased below 2 mg/dl and patient was not dialysis dependent. Irreversible renal failure when the patient remained dialysis dependent after 3 months.

Acute tubular necrosis (ATN) was suspected with history of hypovolemia, APH, PPH, abruption placentae, hypotension and transfusion reaction. Sepsis was diagnosed in presence of fever ≥ 38.5 C, respiratory rate >20/min, pulse rate>90/min, WBC counts ≥ 12000 cells/mL ± DIC, positive blood cultures, retained products of conception and/ or organ hypoperfusion.[7]

Preeclampsia was diagnosed if hypertension and proteinuria occurred after 20 weeks of gestation, progressing to eclampsia when seizures occurred.

Indications for dialysis were volume overload, hyperkalemia, metabolic acidosis, uremic encephalopathy, severe uremia. Renal biopsy was performed in selected patients when renal function did not recover after 4 weeks.

Data analysis procedure: Data was collected and analyzed in SPSS version 16.0 Mean + standard deviation was computed for all quantitative variables, age, gestational age, initial and final creatinine, duration of hospital stay blood, indices like hemoglobin, WBC. Frequency and percentage was computed for all qualitative variables like sign and symptoms, primary diagnosis, outcome of treatment, maternal and fetal outcome with acute renal failure

Results

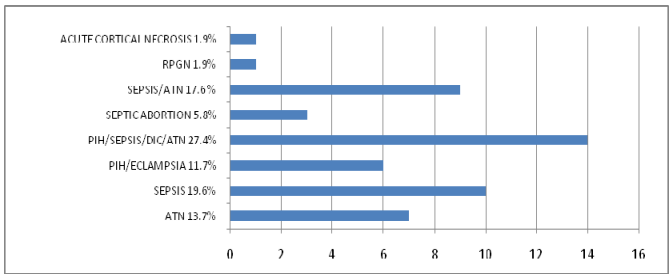
Total cases of acute renal failure admitted during the period of study were 346. Out of 56 pregnant women, 51 met the inclusion criteria of PR-ARF. Pregnancy related acute renal failure (PR-ARF) accounted for 14.7% of total ARF. Minimum age of subject was 18 years and maximum was 42 years with mean age 28 years. The mean number of pregnancies was 4.14, out of which 6/51 (11.7 %) were primigravida and 45/51 (88.2 %) were multigravida. Pregnancy related ARF was seen mostly in third trimester/post partum, 46/51 (90.2 %). Demographic data, signs and symptoms and causes of pregnancy related acute renal failure along with maternal outcome are listed in Table I. Causes of PR-ARF were multi factorial in the majority patients. More than one etiological factor was present in many patients, sepsis / DIC / abruption / ATN along with preeclampsia. Overall sepsis/DIC was the most common etiological factor 33/51 (64.7%). Hemorrhage was present in 23/51 (45.0 %) out of which, APH in 8/51 (15.6 %) and PPH in 15/51 (29.4%). Maximum serum creatinine level measured was 25.9 mg %. Metabolic acidosis was present among 39/51 (76.6 %)

Table I: Demographics, signs and symptoms, etiology, maternal outcome

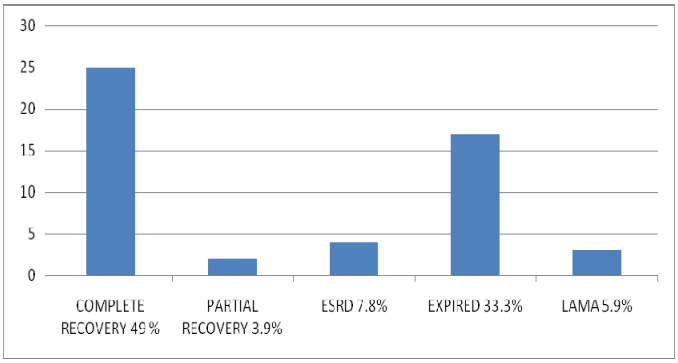
Variable	Frequency (N=51)	Percent
No Ante natal care	39	76.5
Vaginal Delivery	32	62.7
Caesarian Section	15	29.4
Laprotomy(tubal pregnancy)	1	1.96
Mid wife/Dai handling	17	33.3
Removal of RPOC	15	29.4
Bad obstetric history / Rec. abortions	16	31.3
Hospital delivery	40	78.4
Dialysis	39	76.5
Sign and Symptoms		
Altered Loc/fever	19	37.3
Fits	12	23.5
Pallor	45	88.2
Jaundice	11	21.6
Blood loss	23	45.0
Hypotension	24	47.1
Oligoanuric	25	49.1
Sepsis/DIC	33	64.7
Maternal Outcome		
Complete recovery	25	49.0
Partial recovery	2	3.9
Irreversible renal failure	4	7.8
Expired	17	33.3
Left against medical advice	3	5.9
Diagnosis		
Acute Tubular Necrosis (ATN)	7	13.7
Puerperal Sepsis	10	19.6
Pre Eclampsia / Eclampsia/HELLP	6	11.7
PIH, sepsis / DIC / Blood loss	14	27.4
septic abortion	3	5.8
SEPSIS, ATN(APH/PPH)	9	17.6
RPGN	1	1.9
CAN	1	1.9PRA RF

While only 12/51 (23.5 %) had sepsis / respiratory alkalosis. 33/51 (64.7%). Thrombocytopenia was present in 30/51 (58.8%) patients. 14/51 (28.1%) of the patients presented with hyperkalemia with maximum serum potassium 8 mEq/L. Lowest hemoglobin was 3 mg/dl 45/51 (91.1%) patients had a high WBC count. Hospital delivery was conducted in 40/51 (78.4%) versus home delivery 11/51 (21.6 %). 16/51(31.3%) women had a bad obstetrical history with recurrent fetal losses in 13/51(25.4 %) patients. Removal of retained products of conception (RPOC) was performed in a total 15/51(29.4%), it was needed after vaginal delivery in 11/51(21.5 %) patients and after cesarean section in 2/51 (3.9 %) patients and in 2/51 (3.9%) patients with septic abortion. In two particular patients removal of RPOC was done twice and when presented still had RPOC and severe sepsis and both patients expired. Major surgical interventions were performed in 8/51(15.6%). Three patients underwent obstetric hysterectomy (two had it after C.S). Explorative Laprotomy for ectopic pregnancy, ruptured uterus, rectovaginal fistula needing colostomy and in two post C.S. patients with PPH. Mean hospital stay was 11.69 days, maximum stay was 35 days. Renal biopsy was performed in three cases; it revealed ACN, RPGN and endotheliosis respectively. 16/51(31.3%) women had a bad obstetrical history with recurrent fetal losses in 13/51(25.4 %) patients.

In fetal outcome, alive fetus were delivered in 22/51 (43.1%), Intrauterine death in 14/51 (27.4 %), Still birth in 8/51(15.7%), Abortion in 4/51 (7.8%), Dead after delivery in 2/51 (3.9%) and ruptured ectopic pregnancy 1/51 (2.0%)



Graph no: I Etiologies of Pregnancy related Acute Renal Failure (pr-ARF).



Graph no: II Maternal Outcome Acute Renal failure (PR-ARF).

Table no II: Comparison with other Pregnancy related Acute Renal failure (PR-ARF) studies.

	Akhtar etal 2004	Altintepe et Al 2005	Kumar etal 2006	Goplani etal 2008	Current study 2010
%PR- ARF	7-10%	12.7 %	4.3 %	9.0 %	14.7%
Sepsis	24 %	13 %	39 %	61 %	64.7%
PET/HELLP	23 %	44 %	24 %	28 %	39.2%
Septic abortion	6 cases	14 %	9.7 %	20%	5.8%
Maternal mortality	18 %	8 %	24.3%	18.5 %	33.3%

Discussion

Pregnancy-related acute renal failure (PR-ARF) in the current study accounted for 14.7 % of ARF. Other researchers from Pakistan reported PR-ARF recently 1 % [9], whereas older studies mentioned as high as 24 %,and 18% respectively.[10,11] Statistics from other developing countries were Bangladesh 11% [12], Ethopia 55% [13], Nigeria 25.7%.[14] In India recent studies reported by Kumar et al 4.3% b 1 ,Goplani et al 9.06% [4],and remotely by Chugh et al in 1987 reported 14.5%[15] and the same author reported it in 1976 still higher figure of 22.1%.[16] In recent years, there has been a marked decline in the incidence of ARF associated with pregnancy in developed countries; 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 decreased to 6.3% in 1989-97.[17] Post-abortal sepsis in India was reported 59.7 % in 1976 [16] and in recent study published in 2008 was 20.0%[4], whereas in current study 3/51 (5.8%) patients had septic abortion and accounted for 5.8% of PR-ARF and 0.8% of ARF in one year.

ARF in pregnancy is associated with a high risk for maternal mortality (9-55%).[8] Mortality in recent Indian studies was reported 24%[1], 20% [3] 18.5%.[4] Maternal mortality in some recent studies from Pakistan akhter et al (2004) 18%[18], Hassan et al from (2007) was 16.2% [19], munib et al; (2008) 12.5%.[6] In our study Maternal outcome showed much higher mortality 17/51 (33.3%).

Renal cortical necrosis is an uncommon cause of ARF, and carries a high mortality. Obstetric complications are the most common cause of renal cortical necrosis. [20] In the current study majority of the patients had more than one etiological factor, sepsis being the most common factor. Preeclampsia was complicated by abruption placentae causing bleeding with hemodynamic instability (APH, ATN) and DIC, IUD and sometimes associated sepsis mostly being caused by RPOC. Preeclampsia per se was responsible in very few cases. Other factors were persistent fits which can cause rhabdomyolysis, mismatched transfusions. Many of the hemodynamically unstable received potentially nephrotoxic drugs like NSAID, antibiotics. Renal failure is unusual even with severe cases of preeclampsia unless there is significant bleeding with hemodynamic instability or marked disseminated intravascular coagulation (DIC).[2] ARF in preeclampsia occurs only when associated with other obstetric complications such as abruptio placentae or when preeclampsia progressed to HELLP.[21- 24] This was very much consistent with the current study. PR-ARF is associated with substantial maternal and fetal mortality, [25] and fetal outcome in our study showed the same.

Majority of the patients belonged to low socioeconomic background and had been referred to our hospital from small peripheral cities 43/51 (84.3 %).Total live births at PIMS in one year duration were 11952, and only 4/51 patients of PR-ARF had delivered at the obstetric unit of PIMS. Another 5 patients were referred from other hospitals of Islamabad. Patients came from as far as Gilgit and Afghanistan. The high rate of obstetric complications, sepsis, and retained products of conception implies that the level of antenatal and perinatal care needs much improvement. The problem of dai handling still remains and needs to be addressed. There is dire need for improving education and training of primary medical care personnel. Prompt diagnosis of high risk individuals and timely referral to tertiary medical care facilities. Surprisingly women with bad obstetrical history and recurrent fetal losses were never investigated. Moreover there was lack of family planning (the maximum number of pregnancy was 13) and the problem of unwanted pregnancies.

Conclusion

Most common cause of pregnancy related acute renal failure is PIH associated with other risk factors like abruption, IUD, DIC and RPOC. Sepsis is the main contributory factor in PR-ARF. No antenatal care and Dai handling was seen in most of patients. Pregnancy related acute renal failure has a very high maternal mortality and morbidity.

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