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Research Article

Aetiology and Prognosis in Pregnancy Related Acute Renal Failure

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ABSTRACT

Acute renal failure (ARF) is a major complication during pregnancy and is associated with high mortality rate. Acute kidney injury continues to be common in developing countries. We conducted this study to determine the major aetiological factors for pregnancy related acute renal failure (PRARF) in the present setting due to its changing pattern from yester years by detailed study of the clinical profile of obstetric acute renal failure. The study also aims to determine maternal and perinatal outcome in PRARF and prognosis in dialysis instituted patients.

Objectives of the Study

1. *To identify the aetiological factors and study the clinical profile of pregnancy related acute renal failure*
2. *To study the maternal and perinatal outcome in pregnancy related acute renal failure*
3. *To identify the incidence of dialysis requiring patients in obstetric acute renal failure and its outcome*

Materials and Methods

Study design: *Prospective study*
Study setting: *Department of Obstetrics and Gynaecology, Govt. Medical College, Kottayam.*
Study period: *June 2012 to June 2014*

The outcomes of the pregnancies in 50 women who presented with pregnancy related acute renal failure and received their obstetrical care were evaluated, 12 major aetiological factors for development of PRARF were identified. A total of 10 maternal death of PRARF, 22 still births (IUD) and 5 neonatal deaths accounting for 27 perinatal deaths were found. Dialysis was instituted in four patients with PRARF of which three patients expired and only one survived.

Keywords (MeSH): *Acute renal failure, Acute Kidney Injury, Pregnancy, Renal Cortical Necrosis*

INTRODUCTION

Obstetric Acute Renal Failure although rare is an important health concern as it directly and indirectly contributes significantly to maternal mortality. In recent years, there has been a marked decline in cases of ARF related to obstetric cases and the current incidence is probably less than 0.01%. [(1) (2)] This decrease has been attributed chiefly to the

decline in the number of septic abortions, improvements in prenatal care with clinicians ready to intervene quickly and aggressively in situations that could potentially lead to renal failure. Such situations include placental abruption, preeclampsia, pyelonephritis, postpartum haemorrhage, systemic infections, dehydration and/or hypotension. Two entities associated uniquely with pregnancy acute fatty liver and idiopathic postpartum renal failure (hemolytic uremic syndrome) are fortunately rare. [3]

For the most part, Obstetric ARF occurs in women with preexisting renal disease (ARF superimposed on chronic kidney disease). [4] Before uremic or oliguria is associated to ARF, obstruction of urinary tract must be excluded by ultrasound. This is particularly pertinent in obstetric practice, since it is too easy to damage the urinary tract when performing emergency surgery for obstetric disasters such as postpartum haemorrhage which are themselves causes of ARF.[5][6] ARF in pregnancy follows a bimodal distribution. There are peaks in the first trimester (related to unregulated and/or septic abortion) and late third trimester (related to obstetric compilations). Sepsis secondary to illegal abortion, now less common in industrialized nations is still a common cause of renal failure worldwide. Milder forms are observed in industrialized countries and only 1 case in 15,000 pregnancies requires dialysis.[7]

Physiological changes occurring in pregnancy involve nearly every organ system and the kidneys are no exception.[8] Renal plasma flow increases by 50-70% in pregnancy and this change is most pronounced in the first two trimesters.[7][9]This is one of the factors that lead to an increased glomerular filtration rate. The GFR peaks at around 13th week of pregnancy and can reach levels up to 150% of normal. Therefore both BUN, S.creatinine levels and plasma markers of GFR are decreased. This decrease has clinical significance in that a normal BUN or creatinine level in a pregnant female may actually indicate underlying renal disease. [10]All the physiological changes maximize by the end of the second trimester and then start to return to prepartum level where as changes in the anatomy take up to 3 months postpartum to subside.[7]

ARF is conventionally and conveniently divided into 3 categories: Prerenal, Intrinsic (renal) and Postrenal. Prerenal causes include the hypovolemic states like: -Haemorrhage, Volume depletion from gastrointestinal or renal loses, burns, fluid sequestration or low cardiac output state, Systemic vasodilation (eg: sepsis, anaphylaxis), Disseminated intravascular coagulation.[7]

Intrinsic pathology may be Acute Tubular Necrosis (ATN) or Cortical necrosis (ACN). ATN is the most common pathologic finding for ARF in pregnancy.[11]ATN typically occurs after an acute ischaemic or toxic event. Ischaemic ATN is often considered to be a continuum of prerenalazotemia, indeed the causes of the two conditions are identical. In pregnancy these causes are often related haemorrhage, abruption placentae, amniotic fluid embolism and retained dead fetus. Nephrotoxic drugs like Gentamycin are administered in pregnancy especially in pyelonephritis which can result in acute tubular necrosis.[12] The presentation of cortical necrosis is similar to that of severe degree of ATN and is differentiated only by arteriogram and/or biopsy. It was a common finding in ARF because of septic abortion. No specific treatment for cortical necrosis is available.Post renal causes i.e., obstructions are rare but must be considered in all patients with ARF because of the ease of reversibility. Diagnosis however may be difficult.[7]

Renal Failure can occur in septic abortion/ septic shock and in Acute Pyelonephritis (AP). The oliguric phase in women with tubular necrosis due to septic abortion may last 3 weeks or more and anuria may occur in this period.[5]

Hypertensive disorders of pregnancy like severe preeclampsia, eclampsia, HELLP syndrome and superimposed preeclampsia and acute fatty liver of pregnancy[13] are the important contributors to ARF in pregnancy and to maternal mortality and morbidity. In severe preeclampsia, acute renal failure from acute tubular necrosis may develop. Such kidney failure is characterized by oliguria or

anuria and rapidly developing azotermia (approximately 1mg/dL increase in S.creatinine per day). Rarely irreversible renal cortical necrosis developed.[14]

Acute renal failure also can occur in miscellaneous causes like HaemolyticUraemic Syndrome (HUS), after intraamniotic saline administration, after amniotic fluid embolism, collagen disorders or accidents unrelated to pregnancy such as bacterial endocarditis, drug ingestion and incompatible blood transfusions.[15]

AIMS AND OBJECTIVES

1. To determine the major aetiological factors of PRARF in our institution
2. To find out the maternal and perinatal outcome in PRARF and prognosis in dialysis instituted patients

MATERIALS AND METHODS

This is a prospective study performed in the Department of Obstetrics and Gynaecology, Government Medical College, Kottayam during the period June 2012 to June 2014 after approval from the ethical committee Government Medical College, Kottayam. Proper informed consent was obtained from all the patients after explaining the benefits of the study.

STUDY POPULATION

Women who presented with pregnancy related acute renal failure and received their received their obstetrical care in Obstetrics and Gynaecology Department, Medical College, Kottayam.

INCLUSION CRITERIA

1. Patients who developed pregnancy related acute renal failure (PRARF) during pregnancy and within 6 weeks of delivery.
2. Patients with acute renal failure superimposed on chronic renal disease

EXCLUSION CRITERIA

1. Those patients who developed acute renal failure beyond 6 weeks of delivery

METHODS OF STUDY

The outcomes of pregnancies in 50 women who presented with pregnancy related acute renal failure and received their obstetrical care during the study period were evaluated. All the pregnant women who developed ARF underwent standardized obstetrical and nephrological evaluations. Their perinatal outcome was also studied. The outcome of their newborn admitted to intensive care unit (SCNU) was determined from health records. Definitions of PRARF and outcomes were determined by consensus between obstetrician and nephrologists before data collection. Data were obtained from independent review of health and clinical records. Baseline data were collected before review of outcomes and included maternal age, socio economic class, parity status, singleton/ multiple gestation, previous history of medical disorders like chronic hypertension/overt diabetes/renal disease and the gestational age/postpartum period at the presentation with acute renal failure.

In this study pregnancy related acute renal failure is defined as sudden reduction in urine output (<400mL/day) or elevated creatinine more than 0.8mg% in the antenatal and peripartum period (upto 6 weeks after delivery) and more than 1.2mg% on follow up. The basic aetiological factor for development of acute renal failure was evaluated and proportion analyzed statistically. Adverse events and laboratory parameter derangements during antepartum, peripartum and postpartum periods were recorded. The clinical presentations and abnormality in laboratory investigations were evaluated. Maternal outcome was studied in terms of need for termination of pregnancy, mode of termination, maternal morbidity and mortality and requirement for institution of dialysis or steroid therapy. The relation between elevation of serum creatinine and maternal outcome in terms of maternal mortality were evaluated. The renal parameters at which dialysis was instituted, the method of dialysis and its outcome studied. Time taken for maternal renal parameters to revert to normal after standardized care was also studied. The proportion of prerenal causes, acute tubular necrosis and acute cortical necrosis as aetiological factors for PRARF were also evaluated. Neonatal outcomes were defined in terms of still birth neonatal death

preterm deliveries and low birth weight babies. The proportion of intensive care unit admission for live born neonates was also determined.

STATISTICAL ANALYSIS

Statistical analysis were performed for the 1. Majoraetiological factors of pregnancy related acute renal failure, 2. Clinical profile of PRARF, 3. Maternal and perinatal outcome in PRARF, 4.Incidence of dialysis requiring acute renal failure and its outcome. Data was initially entered into an excel file and was entered into SPSS software data variable. Potential aetiological factors of PRARF are examined with chi square test. Maternal mortality following PRARF are analyzed statistically. Statistical analysis was performed with unpaired 't' test. $P<0.05$ was accepted as the level of statistical significance.

RESULTS

A total of 50 cases during the study period were included.

Table 1: Patient characteristic

Age	27.5±4.7
Gestational age	32±4.6
Parity	
Nullipara	34 (68)
Multi Para	16(32)
Presentation	
Antenatal	39(78)
Postnatal	11(22)
Socioeconomic status	
Low	44(88)
High	6(12)

Mean age= 27.5±4.7

The youngest patient who developed PRARF in this group was 20 years and the oldest was 38 years. Majority of patients were nulliparous or primipara. Mean gestational age at presentation with PRARF is 32 weeks. 88% of patients who developed PRARF belong to low socioeconomic status.

Table 2: Aetiological factors

Major Aetiological factors		95% confidence limits
Severe preeclampsia	10(20)	8.9-31.0
HELLP Syndrome	8(16)	6.0-26.0
Eclampsia	6(12)	3.0-21.0
Abruption	6(12)	3.0-21.0
PPH	5(10)	1.7-18.3
AFLP	3(6)	0-12.6
Hepatitis E	3(6)	0-12.6
Sepsis/Acute pyelonephritis	2(4)	0-12.6

Hypertensive disorders like severe preeclampsia, HELLP syndrome and eclampsia are the major aetiological factors. Abruption and postpartum haemorrhage are significant contributors. AFLP, HUS, Hepatitis and Sepsis are less common causes of PRARF.

Table 3: Causes of PRARF

Causes of PRARF		
Prerenal cause	49(96)	94-99
Acute tubular necrosis	44(88)	81-98
Acute cortical necrosis	1(2)	0-6

Prerenal causes contribute in 98% of cases, ATN 90%, ACN 2%. Prerenal cause results in ATN in 82% of cases.

Table 4: Clinical profile

Clinical Profile		
Hypertension	36(72)	60-84
Oliguria	33(66)	53-79
Edema	29(58)	44-72
Bleeding manifestation	26(52)	39-67
Pallor	21(42)	29-56
Altered LFT	16(32)	20-46
Jaundice	13(26)	14-39
Hypotension	12(24)	12-37
Seizures	8(16)	6-27
Fever	8(16)	6-27

The most common clinical features seen in patients with PRARF are hypertension, oliguria, edema and bleeding manifestation.

Table 5: Maternal morbidity

PRARF and Maternal Outcome		
ICU care	28(56)	42-70
Multi organ dysfunction (MODS)	27(54)	40-68
Dialysis	4(8)	0-16

Of the 50 patients with PRARF, 20 patients required ICU care for more than a week, 27 patients developed MODS and 4 patients required institution of dialysis.

Table 6: Occurrence of PRARF

Occurrence of PRARF	Yes	No	Survived	Maternal death
Preterm	30(100)	0(0)	27(90)	3(10)
Term	9(50)	9(50)	8(88.9)	1(11.1)
Antenatal			35(89.7)	4(10.3)
Postpartumday1	6(100)	0(0)	5(45.5)	6(54.5)
Postpartumday2	4(66.7)	2(33.3)		
Postpartum day3	1(20)	4(80)		

There is a strong relation with maternal outcome and gestational age.

Chi square value: 10.66, p value: 0.007

Table 7: S creatinine

S creatinine	Survived	Maternal death	
<1.4	21(84)	4(16)	
>1.5	13(68.4)	6(31.6)	0.287

There is strong relation between S.creatinine elevation and maternal death. For S.creatinine elevation of 2 mg%, there is 71.4% mortality and S.creatinine more than 2.5% mortality increases to 80%.

Chi square: 14.37, p value: 0.003

Table 8: Perinatal death

Perinatal death	Yes	No	
<1.4	18(58.1)	13(41.9)	
>1.5	8(38.1)	13(61.9)	0.258

There is no relationship between S.creatinine elevation and perinatal death.

**Figures within bracket indicates percentage*

For all tables Fishers Exact test was done.

DISCUSSION

Obstetric Acute Renal failure accounts for almost 14% of total cases of ARF in most parts of India. Pregnancy related ARF may comprise upto 25% of referrals to dialysis centres in developing countries and is associated with significant maternal and fetal mortality. The incidence of PRARF still remaining 9-25% is developing countries mostly due to late referral of pregnancy related complications. The incidence of PRARF in the developed countries is 1-2.8%.

The reason of the lower incidence in developed countries is the prevention of pregnancy complic-ations and early and more effective treatment of preeclampsia. Septic abortion is not observed any more in developed countries and the rates are declining is developed countries. There was no case of septic abortion as a cause of ARF in this study.

In the present study 82% of cases were due to complication in late pregnancy and 12% due to postpartum complications. This is in contrast with the study conducted by K.R.Goplani, P.R. Shah et al in India in which 59.7% patients were reported to have ARF in early pregnancy. This appears to be due to legalization of abortion. In our study, hypertensive disorders of pregnancy were the most important aetiological factors contributing to 52% of cases of PRARF. Of these HELLP syndrome accounted for 16% cases, eclampsia 12% and severe pre eclampsia for 20% cases. Abruption accounted for 12% cases and PPH for 10% cases. Gopalan et al study on etiology and course of PRARF concluded incidence of HELLP syndrome and preeclampsia in 28.5%. APH as 14.2%, PPH as 24.2%, post abortal sepsis as 20% and puerperal sepsis 61.4% in PRARF. The other important causes for PRARF in our study are puerperal sepsis; AFLP, HUS and hepatitis to complicating pregnancy.

In our study, incidence of pre-renal causes was 98%, leading to acute tubular necrosis in 90% cases and acute cortical nercosis only in 2%. Patients with an underlying renal disease may have increased maternal and fetal morbidity and mortality, one such case was that a superimposed preeclampsia lupus nephritis with APLA syndrome in this study. P.R. Shah, D.N. Gera et al incidence of cortical necrosis was 14.28% in India is contrast to the Western countries where post abortal ARF leading to cortical necrosis is rare (1.5%).

In our study maternal mortality was 20%. The outcome in our series was comparable to that reported in other studies. Kumar et al recently reported a maternal mortality rate in PRARF of 24%. In previous studies conducted in India, it was approximately 30%. The declining trend appears to be the result of aseptic delivery parches and early management of antipartum and postpartum haemorrhages. The outcome is improving also probably due to early recognition and prompt

termination of pregnancy in complication like HELLP syndrome, AFLA etc. Sepsis, thrombocytopenia, DIC and liver involvement (MODS) were associated with significant maternal mortality.

The management of ARF following abruption or PPH is similar to ARF in non-pregnant subjects an exception being that haemorrhage may be concealed. This fact is often underestimated and even moderate blood loss can have deleterious effects on the kidneys, therefore blood should be replaced, patients with HELLP syndrome and postpartum HUS may benefit the platelet transfusion, fresh frozen plasma or even plasma exchange or plasmapheresis. Also component therapy can improve the outcome.

SUMMARY AND CONCLUSION

1) Pregnancy related acute renal failure though rare is still associated with considerable maternal mortality and morbidity rates. Twelve aetiological factors for development of pregnancy related acute renal failure were identified in our study group. Hypertensive disorders were the most important aetiological factors contributing to 52% of cases of PRARF in this study group. Of these HELLP syndrome contributed to 16% of cases and Eclampsia to 12% of cases.
2) There were 10 maternal deaths accounting for 20% maternal mortality rate. Survival rate was 80%. Among the maternal survivors, the average time taken for maternal parameter to return to baseline value was 1.68 weeks.
3) There was 1 case of post renal transplant who developed ARF in early pregnancy following UTI and deterioration of renal function test but resolved with dialysis and rest of pregnancy and delivery went uneventually.
4) Strict perinatal and antenatal care, risk stratification during pregnancy and judiciously timed institution of dialytic support inPRARF can improve the prognosis in pregnancy related acute renal failure.

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DECLARATION

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