Original Article

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Outcomes and Associated Factors of Pregnancy Related Acute Kidney Injury: A Retrospective Longitudinal Study

Others Section

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ABSTRACT

Introduction: In developing countries, the incidence of Pregnancy-Related Acute Kidney Injury (PRAKI) has significantly decreased over the past three decades. However, it remains a major contributor to maternal and foetal morbidity and mortality.

Aim: This retrospective longitudinal study aims to determine the aetiology, outcomes, and factors associated with maternal-foetal outcomes of PRAKI.

Materials and Methods: The study was conducted at a tertiary care Medical College Hospital in Dharwad district, Karnataka, India. It included patients with AKI during pregnancy and the peripartum period, admitted between January 2014 and December 2021. A total of 156 subjects at risk of PRAKI were identified. Data was collected from the Medical Records Department (MRD), and three months of patient follow-up data were also collected. PRAKI diagnosis and staging were done using the Acute Kidney Injury Network (AKIN) criteria. Primary outcomes included the need for dialysis, renal recovery, renal biopsy findings, and development of CKD. Secondary outcomes were maternal and foetal mortality and birth weight. Data analysis was performed using Statistical Package for Social Sciences (SPSS) version 21.0.

Results: The mean age of the participants was 26.34±4.67 years. The most common cause of PRAKI was Pregnancy Induced Hypertension (PIH) (75 cases, 48.1%), followed by sepsis (67 cases, 42.90%), and Haemolysis, Elevated Liver enzymes, Low Platelet count (HELLP) syndrome (32 cases, 20.50%). Out of the 156 PRAKI patients, one-fourth (42 cases, 26.92%) required haemodialysis, 126 (93%) achieved complete renal recovery, 12 (7.6%) required renal biopsy, 9 (6.6%) developed chronic kidney disease, and 3 (2.2%) developed End-Stage Renal Disease (ESRD). Maternal mortality was observed in 21 patients (13.46%), and foetal mortality occurred in 47 patients (31%) out of 156 perinatal outcomes.

Conclusion: PRAKI was associated with poor maternal and neonatal outcomes. PIH, followed by sepsis, remained the leading cause of PRAKI. Immediate referral of patients to a higher centre and comprehensive antenatal care in peripheral areas can reduce the overall health and economic burden.

Keywords: Maternal mortality, Perinatal mortality, Renal biopsy, Renal recovery

INTRODUCTION

Acute Kidney Injury (AKI) is a rare but potentially dangerous condition that can complicate pregnancy. The incidence of PRAKI has significantly declined in recent decades due to efforts to legalise abortion and improved obstetric care. In 1960, the occurrence of PRAKI was around 20-40%, but it has decreased to less than 10% in recent years (2005) [1]. In developed countries, the incidence has further declined to a range of 1 to 2.8% due to the decline in septic abortions and improved perinatal care [2,3]. However, PRAKI remains prevalent in developing countries, with an incidence between 4.2% and 15% [4,5]. Nephrologists and the entire medical team face significant challenges in managing women with AKI during pregnancy.

In developing countries, obstetric renal failure occurs with two peaks. The first peak happens between the eighth and sixteenth week of gestation and is associated with septic abortions. The second peak occurs later in pregnancy and is linked to obstetric complications such as pre-eclampsia, abruptio placentae, uterine haemorrhage, and puerperal sepsis [4]. AKI caused by Thrombotic Microangiopathy (TMA) has been increasingly reported in recent years [6]. Approximately 25% of patients with PRAKI require referral to a dialysis centre due to the distinct etiological spectrum [7]. Pregnancy accounts for 20% of AKI cases and is associated with increased rates of foetal or neonatal mortality (39%) and maternal mortality (20%) [8]. Maternal mortality not only poses a public health problem but also affects the socio-economic growth of the country [9]. Existing literature from various parts of India has reported varying causes and outcomes, reflecting the heterogeneity of the study population in terms of geographic-ethnic characteristics, knowledge and awareness, and access to tertiary healthcare systems [4,6,8,10]. However, there is a lack of literature addressing these issues in the present study area. This study aims to determine the aetiology, dialysis requirement, renal recovery, and development of Chronic Kidney Disease (CKD) in PRAKI, as previous studies have predominantly focused on renal failure requiring dialysis [4-6]. Therefore, the objective of this study is to determine the aetiology, outcomes, and factors associated with maternal-foetal outcomes of PRAKI.

MATERIALS AND METHODS

This retrospective longitudinal study was conducted among 156 pregnant women with PRAKI who were admitted to a tertiary care centre in the Dharwad district of Karnataka, India. The study received clearance from the Institutional Ethics Committee (IEC No-SDMIEC/2021/90). The study was planned in January 2021 and executed over eight months, with the longitudinal component involving follow-up data at three months (until May 2021). The retrospective component involved gathering data from the Medical Records Department (MRD) of patients with PRAKI who were referred to the selected study hospital. All patients admitted during the study period were included in the study as it was time-bound.

Inclusion criteria: Patients with AKI during pregnancy and the peripartum period who were in the selected study hospital from January 2014 to December 2020, and whose data was complete, were included in the study.

Exclusion criteria: Patients with pre-existing kidney disease were excluded from the study.

Procedure

Complete data, including follow-up data, was collected from the MRD and recorded in a pre-designed semi-structured proforma. The proforma was validated by a group of five nephrologists to ensure comprehensive clinical history collection. The proforma included information on the patient's antenatal care, such as the number of pregnancies, previous pregnancy outcomes, and any history of renal illness or hypertension. Additionally, prior medical and treatment histories, including surgical and obstetric histories, were recorded.

Renal biopsy was recommended in cases of prolonged acute renal failure (oliguria for more than four weeks) or persistent proteinuria (after twelve weeks postpartum). The findings from renal biopsies, the need for dialysis, maternal mortality, and foetal outcomes were all observed. Written consent was obtained from patients who were able to come to the hospital, while consent forms were sent by post to those who were unable to come, and signed forms were collected from them.

The primary outcomes of this study were the need for dialysis, renal recovery, renal biopsy findings, and factors leading to the development of CKD. The secondary outcomes were factors related to maternal and foetal mortality and birth weight.

STATISTICAL ANALYSIS

Data entry was performed using Microsoft Excel, and data analysis was conducted using SPSS version 21.0. Descriptive analysis involved the use of frequency and proportion for categorical data, while mean and standard deviation were used for quantitative variables. Cross-tabulation and comparison of proportions were employed to determine the relationship between explanatory variables and categorical outcomes.

RESULTS

A total of 156 subjects (mean age 26.34±4.67 years) were included and analysed in the study. Among them, 58 (37.18%) were primigravida, while 98 (62.82%) were multigravida. The majority of participants had a normal vaginal delivery (96; 61.50%), while the remaining delivered through caesarean section (60; 38.50%).

In [Table/Fig-1], out of the 156 participants, 75 (48.1%) had Pregnancy-Induced Hypertension (PIH), 67 (42.9%) had sepsis on presentation, and 18 (11.54%) cases of obstetric haemorrhage were found to have PRAKI as the aetiology. Six (3.8%) participants presented with PRAKI in early pregnancy, while 150 (96%) presented during the peripartum period. According to AKIN staging, the majority of participants (81; 51.92%) were in AKI stage three, followed by stage one (40; 25.64%) and stage two (35; 22.4%).

Aetiology of PRAKI (N=156)*	Frequency (%)
Obstetric haemorrhage (Antepartum/Postpartum)	18 (11.54%)
Sepsis (Post-abortion/Puerperal)	67 (42.90%)
Pregnancy induced HTN	75 (48.10%)
HELLP syndrome	32 (20.50%)
Acute fatty liver of pregnancy	14 (9.00%)
Atypical haemolytic uraemic syndrome	2 (1.30%)
Multiple aetiology of PRAKI	
Obstetric haemorrhage and HELLP	1 (0.64%)
Obstetric haemorrhage and pregnancy induced HTN	2 (1.28%)
Obstetric haemorrhage, sepsis and HELLP	2 (1.28%)
Obstetric haemorrhage, sepsis and pregnancy induced HTN	2 (1.28%)
Obstetric haemorrhage and sepsis	5 (3.21%)

[Table/Fig-1]: Aetiological factors for pregnancy-related acute renal failure.
*Multiple aetiology; HTN: Hypertension; HELLP: Haemolysis, elevated liver enzymes, low platelet count; PRAKI: Pregnancy-related acute kidney injury

In [Table/Fig-2], maternal mortality was observed in 21 (13.46%) patients, with 6 (28.6%) of them requiring haemodialysis and 15 (71.4%) not requiring haemodialysis. Approximately one-fourth of the patients (42; 26.92%) required haemodialysis, with an average number of dialysis sessions being 4.76±3.39 (ranging from 1 to 15 sessions). Only 11 (26.83%) out of 42 patients required dialysis in the first month. A total of 9 (5.8%) patients developed chronic kidney disease over time.

Maternal outcome	No. of patients (%)
Death	21 (13.46)
Survived	135 (86.53)
Need for dialysis	42 (26.92)
Complete renal recovery	126 (93.3)
Chronic kidney disease	9 (6.6)
End stage renal disease	3 (2.22)
Underwent renal biopsy	12 (7.6)

[Table/Fig-2]: Maternal outcome parameters in the study population (N=156).

[Table/Fig-3] discusses the foetal parameters and outcomes. Only 103 (66.1%) of the births were documented as live births, while 26 (16.6%) were intrauterine deaths. Among live births, one-fourth of them (27; 26.2%) were low birth weight babies.

Foetal parameters	Frequency (%)
Perinatal outcome (N=156)	
Abortion	6 (3.84)
Intrauterine death	26 (16.6)
Still birth	21 (13.4)
Live	103 (66.1)
Birth weight (N=103)	
Very low birth weight	7 (6.79)
Low birth weight	27 (26.2)
Normal weight	69 (66.99)

[Table/Fig-3]: Foetal outcome parameters in the study population.

[Table/Fig-4] presents the histopathological spectrum of renal biopsy findings in PRAKI patients. Out of the 156 PRAKI patients, 12 required renal biopsy. Among them, four patients had Acute Tubular Necrosis (ATN), two (16.7%) had Acute Cortical Necrosis (ACN), and two had TMA.

Renal biopsy reports (N=12)	Frequency (%)
Acute Tubular Necrosis (ATN)	4 (33.33)
IgA nephropathy	3 (25)
Acute Cortical Necrosis (ACN)	2 (16.77)
Thrombotic Microangiopathy (TMA)	2 (16.77)
Chronic interstitial nephritis	1 (8.33)

[Table/Fig-4]: Histopathological Spectrum of Renal Biopsy of the PRAKI patients.

[Table/Fig-5] provides information on the incidence of PRAKI among different etiological factors, the mean age of patients with PRAKI, distribution of maternal characteristics, and maternal outcomes.

DISCUSSION

PRAKI has a significant impact on healthcare in developing countries, leading to increased maternal morbidity and mortality [3,11,12]. The objectives of this study were to determine the aetiology, requirement for dialysis, renal recovery, and development of CKD among PRAKI patients, as most previous studies have focused exclusively on renal failure requiring dialysis [Table/Fig-6] [4,5,8,13,14].

Aetiology of PRAKI	Mean age (years)	Primi Gravida* (%)	Multi Gravida* (%)	Maternal mortality* (%)	Haemodialysis (%)	CKD* (%)	Renal recovery* (%)
Obstetric haemorrhage (Antepartum/Postpartum) (N=18)	26.16±4.57	7 (38.9)	11 (61.1)	3 (16.67)	8 (44.4)	2 (16.7)	13 (72.2)
Sepsis (Post Abortion/Puerperal) (N=67)	26.23±4.76	25 (37.3)	42 (62.7)	13 (19.4)	25 (37.31)	2 (3)	52 (77.6)
PIH (N=75)	25.79±4.26	31 (41.3)	44 (58.7)	8 (10.67)	18 (24)	2 (2.7)	65 (86.7)
HELLP Syndrome (N=32)	26.34±3.98	14 (43.8)	18 (56.2)	3 (9.38)	8 (25)	1 (3.1)	28 (87.5)
Pregnancy aHUS (N=2)	30.50±9.19	1 (50)	1 (50)	0 (0)	2 (100)	2 (100)	0
AFLP (N=14)	28.57±5.80	3 (21.4)	11 (78.6)	3 (21.43)	3 (21.43)	0	11 (78.6)

[Table/Fig-5]: Aetiology, course and outcome of Pregnancy-Related Acute Kidney Injury (PRAKI).
*Multiple aetiology; CKD: Chronic kidney disease; PIH: Pregnancy induced HTN; aHUS: Atypical haemolytic uraemic syndrome; HELLP: Haemolysis, elevated liver enzymes, low platelet count; AFLP: Acute fatty liver of pregnancy

Authors with year of publication	Place of study	Total patients of AKI (N)	Incidence of PRAKI (%)
Chugh KS et al., (1989) [13]	Artificial Kidney Unit of the Postgraduate Institute of Medical Education and Research, Chandigarh	1862	14.5
Prakash J et al., (2010) [8]	Sir Sunderlal Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi	59	13.9
Kilari S et al., (2006) [14]	Sher-i-Kashmir Institute of Medical Sciences, Srinagar, JK	41	4.3
Goplani K et al., (2008) [5]	Institute of Kidney Disease and Research Centre and Dr. HL Trivedi Institute of Transplantation Sciences, Civil Hospital, Asarwa, Ahmedabad, Gujarat, India	772	9.6
Saini S et al., (2020) [4]	Institute of Post-Graduate Medical Education and Research and Seth Sukhlal Karnani Memorial Hospital, Kolkata, West Bengal, India	449	16.5
Present study	Tertiary care centre in the Dharwad district of Karnataka	5234	2.98

[Table/Fig-6]: Incidence of PRAKI in various studies [4,5,8,13,14].

The frequency distribution of PRAKI is bimodal, with a decrease in the incidence of AKI in the first trimester due to better obstetric care, health education, and stricter implementation of abortion laws [4]. However, the demographic profile of the patients in this study is similar to that of other studies conducted by Saini S et al., Gattani V, and Shah MK [4,6]. This could be attributed to the location of the tertiary care centre, which attracts referrals from surrounding rural areas with lower rates of antenatal care compared to urban areas [9].

Pregnancy-Induced Hypertension (PIH) is the major contributor to PRAKI (48.1%), followed by puerperal sepsis and obstetric haemorrhage. The incidence of Acute Fatty Liver of Pregnancy (AFLP) is increasing compared to other studies, indicating the increasing incidence of hypertension and diabetes as comorbidities in older pregnant women. However, sepsis-associated AKI has become less common due to improved obstetric care, changes in lifestyle, and stricter abortion laws [4-6]. The incidence of PRAKI in pre-eclampsia and PIH patients varies from 14-68% in the literature [10,11]. Among patients requiring dialysis, sepsis patients (37.31%) had a higher proportion than PIH patients (24%) [Table/Fig-7] [4-6,8,12].

Obstetric haemorrhage ranked fourth among the most frequent causes of PRAKI (11.54%) in this study, which is lower than previous estimates of 20-40% [7,14]. Postpartum haemorrhage following cesarean section, often accompanied by sepsis, increased the case fatality rate, highlighting the importance of monitoring perinatal and postnatal services in peripheral healthcare centres.

Approximately 26% of the patients in this study required dialysis support during hospitalisation. Nine out of 156 patients developed CKD, with three progressing to End-Stage Renal Disease (ESRD). Of the 135 patients, 126 (93.3%) experienced complete renal function recovery. The higher recovery rate observed in this study could be attributed to early diagnosis and prompt treatment of AKI. Other studies conducted in different regions of India reported a renal function recovery rate of 40-70% [6-8].

Maternal mortality was observed in 21 (13%) PRAKI patients in this study [Table/Fig-2], with 6 (28.6%) of them requiring haemodialysis and 15 (71.4%) not requiring haemodialysis. Similar mortality rates between 15% and 30% have been reported in other studies by Mahesh E et al., and Prakash J et al., [12,15].

The study also found a perinatal mortality rate of 16.6%, with 13.4% stillbirths, 30% foetal deaths, and 6.79% very low birth weight infants [Table/Fig-3]. These results are consistent with the reported aetiology of maternal mortality and morbidities among PRAKI patients. Other studies by Gul A et al., and Drakeley AJ et al., have reported perinatal mortality rates ranging from 26-38%, highlighting the need for comprehensive antenatal care and prompt referral to tertiary care centres [11,16]. The renal biopsy findings in this study showed ATN as the most common feature (33%) among the 12 patients who underwent biopsy, whereas another study by Sani S et al., reported TMA as the most common finding (54%), followed by ATN [4]. Two CKD patients in this study had TMA, and two had ACN, indicating poor renal recovery with these histological findings.

Author	Region	Duration of the study	Numbers (PRAKI)	Incidence (%)	Sepsis (%)	PE/E %)	Hmg (%)	CR %	PR (%)	NR (%)	Death (%) Maternal
Goplani K et al., [5]	Gujarat	2004 -2006	70	9.06	61.42	28.6		54.3	12.9	14.2	18.57
Mahesh E et al., [12]	Karnataka	2005 -2014	165	1.56	59	56					20
Prakash J et al., [8]	Uttar Pradesh	2006 -2008	85	1.78	24.7	35.3		69.4	5.88		20
Gattani V and Shah MK [6]	Ahmedabad	2014 -2015	96	56.26	63.54	22.9		43.7	16.67	19.7	19.79
Saini S et al., [4]	Kolkata	2015 -2016	81	15	49	12		39	16	33	25
Present study	Dharwad Karnataka	2014 to 2021	156	2.98	42.9	48.1	11.5	91	6.7	2.2	13.5

[Table/Fig-7]: PRAKI-comparison with previous studies.

Limitation(s)

The present study was a record-based study and was limited to a single hospital setting. As a result, the generalisability of the study results is restricted.

Here's a revised version of the text with improved grammar and presentation.

CONCLUSION(S)

PRAKI is associated with poor maternal and neonatal outcomes. PIH, followed by sepsis, remains a leading cause of AKI and is associated with poorer outcomes. Therefore, it is essential to identify patients with these conditions and refer those with deteriorating renal function to a higher centre early on. Improving antenatal care, preventing PIH, and increasing awareness about sepsis prevention in healthcare institutions located in peripheral areas can help reduce the burden of PRAKI.

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