Acute kidney injury in obstetrics: a five-year study in a tertiary centre

Sushma H. Papegowda, Pratima K. Devi*, Ranjit L. Singh, Agalya Muruganadam, Zikpuii L. Tochhawng

Department of Obstetrics and Gynecology, Regional Institute of Medical Sciences and Research, Imphal, Manipur, India

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*Correspondence:
Dr. Pratima K. Devi,
E-mail: pratimadutta09@gmail.com

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ABSTRACT

Background: Pregnancy Related Acute Kidney Injury (PRAKI) is a major cause of maternal and foetal morbidity and mortality in developing countries. The incidence has declined due to improvements in reproductive health but it is still associated with significant perinatal mortality and maternal morbidity. It may be due to decrease in renal perfusion or ischemic tubular necrosis from a variety of conditions encountered during pregnancy. Our study aims at determining the predisposing factors and causes of AKI during pregnancy and its impact on maternal and foetal outcome.

Methods: A retrospective cohort study over a period of 5 years was conducted on pregnant women with AKI as per inclusion and exclusion criteria. The detailed history, events, mode of delivery, cause leading to AKI, management, hospital stay, maternal and foetal outcome were studied in detail and evaluated. These patients were classified according to RIFLE criteria and were followed up for hospital stay and residual morbidities.

Results: The incidence of PRAKI in the study was 0.07% (36 out of 50,735 deliveries) and among obstetric ICU patients, it was 6.8%. Most of the majority of the cases were unbooked (66.7%) and multipara (61.1%). Maternal morbidity was seen in 66.7% and mortality was 27.8%. Poor foetal outcome was seen in 44.4%.

Conclusions: Haemorrhage is the most common cause of PRAKI, followed by toxemia of pregnancy and sepsis. Early detection and meticulous management of haemorrhage, hypertension and sepsis reduce the incidence of PRAKI and associated maternal mortality.

Keywords: Foetal outcome, Maternal outcome, Pregnancy related acute kidney injury, RIFLE criteria

INTRODUCTION

In pregnancy, acute renal injury usually occurs in women with previously healthy kidneys, but it can complicate the course of patients with pre-existing renal disease. The incidence has declined due to improvements in reproductive health and perinatal care but it is still associated with significant perinatal mortality and maternal morbidity.2

AKI is defined as any of the following

Increase in SCr. by ≥0.3 mg/dl (≥26.5 μmol/L) within 48 hours; or

Increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within prior 7 days; or

Urine volume <0.5 ml/kg/h for 6 hours.3
Acute kidney injury (AKI) is a heterogeneous syndrome defined by a rapid decline in the glomerular filtration rate (GFR).\textsuperscript{4} PRAKI (Pregnancy poses a challenge of different level to clinicians taking care of these patients).\textsuperscript{5} It is a major cause of maternal and foetal morbidity and mortality in developing countries.\textsuperscript{6} The incidence and the mortality associated with PRAKI have decreased in developed countries from 40% to 20% in 1960 to <10% in recent series mostly due to meticulous antenatal management.\textsuperscript{7} Female gender is as such increases the susceptibilities for non-specific AKI.\textsuperscript{3} PRAKI may be due to a decrease in renal perfusion or ischemic tubular necrosis from a variety of conditions.\textsuperscript{7} These include hyperemesis gravidarum, postpartum haemorrhage, hypertensive disorders, thrombotic microangiopathies, acute fatty liver of pregnancy, septic abortion, sepsis, acute fatty liver of pregnancy and complicated urinary tract infections.\textsuperscript{8} Recently reported incidence of postpartum AKI (PP-AKI) is 10.55% sepsis and haemorrhage being the commonest aetiologies.\textsuperscript{9}

**Incidence**

Incidence of pregnancy related AKI used to be 24-40% of all AKI in 60’s which decreased to 2-3% in 80’s.\textsuperscript{10} The incidence of PRAKI is a more common problem in the developing nations.\textsuperscript{11} The incidence of obstetric AKI has further declined over last 4 decades.\textsuperscript{12} The lesser incidence of this problem is due to the improvement in antenatal care and the reduction of septic abortion due to its legalisation.\textsuperscript{1,13,14} Socioeconomic factors contributing to PRAKI in the developing countries are mainly due to poverty, poor obstetrics care, lack of proper healthcare facilities and awareness of the condition, delayed referral process, multiparity, and the increasing population number.\textsuperscript{15} Some studies summarized that the incidence of PRAKI was 1.0% to 2.8% in developed nations versus 4%-26% in developing countries.\textsuperscript{1,2,15} A study from India revealed a decrease in PRAKI incidence from 22% between 1965 and 1974 to 9% between 1981 and 1986, which was the result of better obstetrical care and increased availability of medical facilities.\textsuperscript{16}

**Definitions and criteria**

**RIFLE:** Increase in SCr X 1.5 or GFR decrease >25%.\textsuperscript{17}

**AKIN:** Increase in SCr by ≥0.3 mg/dl or increase ≥150% to 200% (1.5 to 2-fold) from baseline within 48 hours.\textsuperscript{17}

| System       | Serum creatinine criteria                                                                 | Urine output                                    |
|--------------|-------------------------------------------------------------------------------------------|-------------------------------------------------|
| **RIFLE class** |                                                                                           |                                                  |
| Risk         | SCr increase to 1.5-fold or GFR decrease >25% from baseline                                 | <0.5 ml/kg/h for 6 hours                         |
| Injury       | SCr increase to 2-fold or GFR decrease >50% from baseline                                  | <0.5 ml/kg/h for 12 hours                        |
| Failure      | SCr increase to 3-fold or GFR decrease >75% from baseline                                  | Anuria for 12 hours                              |
|              | SCr ≥354 μmol/l (≥4 mg/dl) with an acute increase of at least 44 μmol/l (0.5 mg/dl)       |                                                 |
| **AKIN stage** |                                                                                           |                                                  |
| 1            | SCr increase ≥26.5 μmol/l (>0.3 mg/dl) or increase to 1.5-2 from baseline                 | <0.5 ml/kg/hr for 6 hours                        |
| 2            | SCr increase >2.0 to 3 fold from baseline                                                  | <0.5 ml/kg/hr for 12 hours                       |
| 3            | SCr increase >3-fold from baseline or SCr ≥354 μmol/l (≥4 mg/dl) with an acute increase of | <0.3 ml/kg/hr for 24 hours or anuria for 12 hours or need for RRT |
|              | at least 44 μmol/l (0.5 mg/dl) or need for RRT                                             |                                                 |

A RIFLE criterion stratifies AKI into five stages (Table 1). There are differences between the two systems. Time constraint is used in AKIN criteria whereas GFR decreases are used in RIFLE criteria.

**KDIGO:** Increase in SCr by ≥0.3 mg/dl within 48 hours or to ≥1.5 times the baseline, known or presumed to have occurred within prior 7 days.

**Aetiology\textsuperscript{19}**

**AKI during early pregnancy**

- Acute or massive blood loss
  - Abortion
  - Ruptured ectopic pregnancy
  - Hydatidiform mole
- Severe dehydration
  - Acute pyelonephritis
  - Hydatidiform mole
- Acute tubular necrosis (ATN)
  - Septic abortion.

**AKI during late pregnancy**

- Thrombotic microangiopathy
A. TTP - HUS  
B. Severe preeclampsia, HELLP syndrome  
- Renal cortical necrosis due to  
  a. APH: abruption placenta, placenta previa  
  b. Prolonged IUD  
  c. Amniotic fluid embolism  
- Intrinsic renal disease/autoimmune disease  
- Acute pyelonephritis  
- ATN  
  a. Septicaemia  
  b. Hypotension  
- Acute fatty liver of pregnancy  
- Obstructive causes.

**AKI during postpartum period**

- Massive blood loss due to PPH  
- Thrombotic microangiopathy  
  a. HELLP syndrome, preeclampsia  
- ATN  
  a. Puerperal sepsis  
- Postoperative AKI  
  a. Blood loss  
  b. Intraoperative hypotension.

**Pathogenesis**

The conditions that precipitate the deterioration in function may be pre-renal, renal parenchymal or post renal in origin.  

**Pre-renal failure**

A mild form of acute renal failure caused by moderate degrees of renal ischemia. It is reversible if renal perfusion is restored. Pre-renal azotemia is the most common form of AKI.

**Acute tubular necrosis**

This follows more prolonged ischemia. It is also reversible. Damage is limited to metabolically active tubular cells.

**Acute cortical necrosis**

This follows severe renal ischemia that causes disintegration of both glomeruli and tubules in the renal cortex. Although the process is irreversible, it is the incomplete or patchy variety that occurs more often in pregnancy.

**Three subsequent phases of AKI**

**Oliguria**

Urine output of <400 ml in 24 hours lasting days to weeks.

**Polyuria**

Markedly increased urine output lasting days to weeks. During this phase plasma urea and creatinine levels usually continue to rise. As large volumes of urine may be passed, careful attention must be given to fluid and electrolyte replacement. During this phase the renal tubular cells are recovering but not yet able to concentrate urine.

**Recovery**

Urine output reverts towards normal with complete or variable return of renal function.

The objective of this study was to determine the risk factors and to analyse the clinical spectrum and outcome of acute kidney injury (AKI) in obstetric patients.

**METHODS**

This was a retrospective cohort study conducted in patient department of obstetrics and gynaecology, Regional Institute of Medical Sciences, Imphal, Manipur, India.

This was a five-year study starting from March 2014 to February 2019 included 36 pregnant women who developed kidney injury due to pregnancy related causes.

**Inclusion criteria**

- Pregnant women admitted for safe confinement who later developed AKI  
- Pregnant women who were admitted for complications which later progressed to AKI  
- Patient giving consent for participating in the study.

**Exclusion criteria**

- Pregnant women with prior kidney failure  
- Chronic kidney disease patients  
- Pregnant women with medical disorder as a direct cause of AKI.

Sample size calculated using the formula \( n = \frac{z^2 \cdot p \cdot q}{L^2} \)

**Sampling method**

Convenience sampling was done to include all pregnant patients who developed acute kidney injury during the course of pregnancy.

**Study variables**

**Independent variables**

Age, religion, residence, education, occupation, parity, number of ANC check-ups, number of living issues, birth
spacing, booking status, history of abortion, age of menarche, past history, level of anaemia, renal function test, mode of delivery.

**Dependent variables**

Risk factors of AKI in pregnant women, foetal and maternal outcome.

**Study tools**

The case sheets of all the patients who developed acute kidney injury were analyzed in detail for the history, examination findings and investigations were studied.

**Procedure**

A retrospective cohort study over a period of 5 years was conducted on pregnant women admitted in Regional Institute of Medical Sciences and who met the criteria of AKI. The detailed history, events, mode of delivery, cause leading to AKI, management, hospital stay, maternal and foetal outcome were studied in detail and evaluated. These patients were classified according to RIFLE criteria and were followed up for hospital stay and residual morbidity.

**Statistical analysis**

Data was checked for consistency and completeness, and was entered and analyzed using SPSS version 21.0 IBM for Windows. Descriptive statistics such as frequency, percentage, mean and standard deviation were used. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

**RESULTS**

During the 5 years study, 50735 deliveries were conducted in RIMS among which 530 critical patients were admitted in Obstetrics ICU. Among those 536 critical patients AKI complicated the course of 36 patients representing an incidence of 6.8%. Among 36 patients, 10 patients had mortality, 26 patients recovered after prolonged hospital stay, 9 patients had to undergo dialysis at least once. Majority of the cases belonged to age group of more than 20 years (63.9%) as shown in Table 2.

| Age       | No. of patients | %   |
|-----------|-----------------|-----|
| ≤20 years | 13              | 36.1%|
| >20 years | 23              | 63.9%|
| Total     | 36              | 100.0%|

Most of these cases belonged to low socioeconomic status and rural area. Among these 38.9% cases were primigravida (Table 3).

| Parity    | No. of patients | %   |
|-----------|-----------------|-----|
| Primi     | 14              | 38.9%|
| Multi     | 22              | 61.1%|
| Total     | 36              | 100.0%|

| Residence    | No. of patients | %   |
|--------------|-----------------|-----|
| Urban        | 14              | 38.9%|
| Rural        | 22              | 61.1%|
| Total        | 36              | 100.0%|

Primigravida constitutes around 38.9% and multipara constitutes majority (61.1%). Among primigravida, toxaemia of pregnancy was found to be the leading cause whereas haemorrhage was the leading cause in multiparity women.

| Risk         | No. of patients | %   |
|--------------|-----------------|-----|
| Present      | 30              | 83.3%|
| Absent       | 6               | 16.7%|
| Total        | 36              | 100.0%|

Majority (66.7%) of cases were unbooked cases (Table 4). Inadequate antenatal visit is one of the main predisposing factors leading to complications during labour and hence causing poor pregnancy outcome (Figure 1). More than half (61.1%) of the cases belonged to rural area (Table 4). Poor access to health care facilities, poor management of complications and late
referral from the primary health centres were some of the reasons of having a poor pregnancy outcome among women from rural area.

Failure was observed in majority (66%) of patients with AKI (Table 7). 12 Patients among those diagnosed with failure stage of RIFLE criteria underwent renal dialysis.

It was observed renal tubular loss was seen in majority (66.7% as shown in Table 8) and majority of those patients with significant tubular loss progressed to End stage renal disease (Table 9).

End stage renal disease was observed in nearly quarter of cases (33.3%). Majority of the patients with end stage renal disease had maternal mortality (27.8%) as shown in Table 10.

It was observed that AKI had a mortality rate of 27.8% and majority (72.2%) of the patients were recovered. Majority of those patients with failure and ESRD had worst prognosis.

Poor foetal outcome was observed in nearly half of the cases (44.4% as shown in Table 11). Poor foetal outcome was seen in terms of abortion, IUD, Preterm birth and Neonatal mortality.

Anaemia was the most common laboratory finding which reflects the laboratory picture of haemorrhage and hence haemorrhage was the leading cause of AKI followed by leucocytosis and thrombocytopenia (Figure 2). Leucocytosis was seen in patients with infection. Thrombocytosis was a laboratory picture of HELLP syndrome and DIC.

Our study shows that the haemorrhage is the most common cause of AKI in obstetrics followed by toxemia...
of pregnancy and septicaemia (Figure 3). Cases with combination of toxaemia of pregnancy and haemorrhage or sepsis and haemorrhage had the worst prognosis.

![Figure 3: Distribution of cases according to the causes of AKI.](image)

**DISCUSSION**

Study reports AKI occurred in 36 patients out of 530 critical patients admitted in obstetrical HDU reflecting the incidence of PRAKI in our hospital as 6.8%. Out of those 36 patients 25% required dialysis. Study conducted by Jonard M et al, shows the similar percentage of patients who needed dialysis; however, incidence seems lesser in our study.4 Several demographic factors and meticulous management might have influenced the occurrence of obstetric AKI. Since we was a referral hospital, most of the cases were referred in last stage and hence were unbooked cases, most of patients had received NSAIDS in PHC, most of the abortions were due to abortions taken over the counter, septic abortions were due to late report and illegal abortions. Most of the unbooked cases had inadequate antenatal visits, one reason being people residing in hilly areas had difficulties for regular antenatal visits and some had home deliveries. Study shows that 67.7% of these patients were unbooked and had irregular antenatal consultation. Munib S et al, reported 84% who did not receive antenatal care and Gopani KR et al, reported 15.71% home deliveries.5,6

In this study 61.1% were from rural areas. Dambal A et al, reported 73.3% were from rural and Gopani KR et al, also reported 70% were from rural.7 Patients in rural areas would have delayed early access during the emergency even though toxaemia was more common in urban residency patients.

Multipara were 61.1% and this result was consistent with the study conducted by Dambal et al that showed 66.6% were multipara.

In 66.7% of obstetric AKI, stage of failure was found and 33.3% of the cases progressed to Loss and End stage renal disease of RIFLE criteria 83.3% of those with loss and end stage renal disease had mortality. Those patients who reported in early stage, progression to failure, loss and end stage renal disease was halted due to coverage of broad-spectrum antibiotic, fluid restriction and dialysis.

The haemorrhage is the most common cause of AKI in obstetrics followed by Toxemia of pregnancy and septicaemia. Haemorrhage associated with toxaemia of pregnancy or septicaemia had the worst prognosis and poor feto-maternal outcome.

**CONCLUSION**

Postpartum haemorrhage is the leading cause of AKI reflecting peripartum AKI accounts for maximum of Pregnancy related AKI. Toxaemia of pregnancy and septicaemia are the other main leading causes of PRAKI. Hence a good antenatal care, better access to health facilities, better intrapartum care, meticulous management of PPH, good coverage of antibiotic can reduce the incidence of obstetric AKI.

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