Renal Data from Asia–Africa

Pregnancy-related Acute Kidney Injury: Etiologies and Short-term Outcomes in a Tertiary Hospital in Southwest Nigeria

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ABSTRACT. Although the incidence of pregnancy-related acute kidney injury (PRAKI) is declining in developing countries, it still remains a major cause of maternal and fetal morbidity and mortality. The aim of this study was to determine the etiologies, short-term outcomes, and their predictors in patients with PRAKI managed in a tertiary health facility in Southwest Nigeria over a four-year period. This was a four-year retrospective review of clinical records of patients managed for PRAKI in University of Medical Sciences Teaching Hospital, Ondo State, Nigeria. Thirty-two women with a mean age of 31.09 ± 7.50 years had PRAKI during the period reviewed. Twenty-four (75%) patients were multiparous and PRAKI was most common in the postpartum period (56.3%). Twenty-three patients (71.9%) were in RIFLE Stage 3, 24 (75%) received blood transfusion, 5 (15.6%) required intensive care unit (ICU) care, 24 (75%) needed dialysis while 19 (59.4%) had hemodialysis. The common causes of PRAKI were obstetric hemorrhage in 16 (50%), sepsis in seven (21.9%), and eclampsia in six (18.8%). Maternal and fetal mortality were 34.4% and 50% respectively. Seventeen (53.1%) had full renal recovery and only one (3.1%) became dialysis dependent. Significant factors that were associated with maternal mortality were admission to ICU (P = 0.01), hypotension (P = 0.02), and impaired consciousness (P <0.001) PRAKI is still relatively common and significantly contributes to maternal and perinatal mortality in Nigeria. Obstetric hemorrhage which is the most common cause of PRAKI is preventable and treatable. There is a need for physicians to effectively prevent and manage obstetric hemorrhage.

Introduction

Acute kidney injury (AKI) is the abrupt loss of kidney function that results in the retention of urea and other nitrogenous waste products, dysregulation of extracellular volume and electrolytes. 1 AKI occurring during pregnancy or puerperium is termed pregnancy-related AKI (PRAKI). The incidence of PRAKI has declined significantly over the second half of the 20th century; 2 with a low incidence of 1.5%–2.8% in developed countries 3 and higher incidence of 15%–20% in developing countries. 4 Although the incidence of PRAKI is declining in deve-
loping countries, it still remains a major cause of maternal and fetal morbidity and mortality. Maternal mortality from PRAKI reported in several studies, ranged between 20% and 67%, which is higher than earlier reports of 9%–55%. The maternal mortality rate is still relatively high in Nigeria with 814 deaths/100,000 live births as at 2015. Maternal mortality in Nigeria accounts for about 10% of the global cases of maternal mortality despite a global reduction in maternal mortality rate by 45% between 1990 and 2013. PRAKI which is preventable and treatable is a significant contributor to maternal mortality in developing countries like Nigeria.

The etiology of PRAKI varies widely depending on the stage of pregnancy and the country involved. Septic abortion is the most common cause of AKI in early pregnancy, whereas toxemia of pregnancy, hemorrhage, and ischemic damage, acute tubular necrosis occur in late pregnancy. In developing countries, sepsis and hemorrhage account for greater than of cases of PRAKI, in contrast to developeed countries where chronic hypertension, renal disease, preeclampsia, and eclampsia are important causes.

Determining the etiology and outcomes of PRAKI will serve as an audit of the current medical practice with the aim of identifying areas of deficiencies, improving practice, and reducing the burden of PRAKI. The aim of this study was to determine the etiologies and short-term outcomes in patients with PRAKI managed at University of Medical Sciences Teaching Hospital, Ondo State in Southwest Nigeria, over a four-year period.

Methods

This was a retrospective review of patients managed for PRAKI at our center over four years between May 2014 and April 2018. The case files of all patients managed for PRAKI during this period were retrieved. Patients’ data were retrieved from their hospital notes using a structured proforma. Information retrieved included patients’ socio-demographic data, socioeconomic status, referral hospital, symptoms at presentation, obstetric history, etiology of PRAKI, investigation results, treatment given, and outcomes. Patients with underlying chronic kidney disease were excluded from the study.

Definition of terms

AKI was defined on the basis of Risk, Injury, Failure, Loss of function, and End-stage renal disease (RIFLE) criteria. PRAKI was defined as AKI diagnosed anytime during pregnancy or postpartum period (first 6 weeks’ post-delivery).

Preeclampsia was defined as blood pressure reading ≥140/90 mm Hg diagnosed for the first time after 24 weeks of gestation with ≥2+ proteinuria on the dipstick.

Eclampsia was defined as the presence of new-onset grand mal seizures in a woman with preeclampsia.

Sepsis was defined as per the criteria laid down by the American College of Chest Physicians. Sepsis is the clinical syndrome that results from a dysregulated inflammatory response to an infection that is non-resolving and deleterious, often leading to organ dysfunction. Sepsis was defined as the presence (probable or documented) of infection together with systemic manifestations of infection.

Outcomes

Evaluated outcomes included maternal and perinatal mortality, full renal recovery, continuous requirement of renal replacement therapy (RRT), discharged against medical advice (DAMA) and referral to another hospital. Full renal recovery was defined as a decline in serum creatinine to ≤0.0 mg/dL within six weeks of diagnosis of AKI.

Ethical approval was obtained from the Ethics and Research Committee of University of Medical Sciences, Ondo State.

Statistical Analysis

Data generated were analyzed using the Statistical Package for Social Sciences version 17.0 (SPSS Inc., Chicago, IL, USA). Results
were presented in tabular form. Discrete variables were presented as frequency and percentages. Continuous variables were presented as means and standard deviation. Chi-square test and Fisher’s exact test were used to determine the significance of observed differences for categorical variables where appropriate.

**Results**

Thirty-two females who had PRAKI were studied. The age of patients ranged from 19 to 47 years with a mean of 31.09 ± 7.50 years. Majority of our patients (84.4%) were Christians, while only five (15.6%) were Muslims. Twenty-seven (84.4%) were in low socioeconomic class. Twenty-six (81.3%) were married, five (15.6%) were single, and one (3.1%) had separated from her spouse. Twenty-two (78.1%) patients were referred from a secondary health facility, while five (15.6%) were from tertiary health facilities (Table 1).

Eight (25%) patients were primipara, and 24 (75%) were multipara. PRAKI was most common in the postpartum period (56.3%) and third trimester (34.4%). Majority (71.9%) were in RIFLE Stage 3. Twenty-four (75%) patients received blood transfusion, 5 (15.6%) required intensive care unit (ICU) care, 24 (75%) needed dialysis, and 19 (59.4%) had hemodialysis (HD) (Table 1).

At presentation, the mean packed cell volume, white blood cell count, serum creatinine, and urea were 23.38% ± 8.13%, 17,497 ± 12,692 cells/mm³, 5.72 ± 3.46 mg/dL, and 23.20 ± 12.63 mg/dL, respectively. The mean hospital stay, HD sessions, and units of blood transfusion were 10.7 ± 7.8 days, 2.66 ± 1.96 sessions, and 5.81 ± 5.19 units, respectively (Table 2).

The common clinical features at presentation were oliguria (87.1%), breathlessness (67.7%), body swelling (64.5%), fever (61.3%), and jaundice (35.5%) (Figure 1).

The common causes of PRAKI were obstetric hemorrhage in 16 (50%), sepsis in seven (21.9%), and eclampsia in six (18.8%) (Figure 2).

One (3.1%) patient became dialysis dependent while 17 (53.1%) had full renal recovery, two (6.3%) discharged against medical advice, one (3.1%) was referred to another facility and 11 deaths were recorded giving a maternal mortality rate of 34.4% (Figure 3). Fetal death

| Parameters | N (%)/Mean (SD) |
|------------|-----------------|
| Religion   |                 |
| Christianity | 27 (84.4)     |
| Islam      | 5 (15.6)       |
| Marital status |             |
| Single     | 5 (15.6)       |
| Married    | 26 (81.3)      |
| Separated  | 1 (3.1)        |
| Socio-economic status |
| Low        | 27 (84.4)      |
| Middle     | 5 (15.6)       |
| Referral facility |
| Traditional birth attendant | 1 (3.1)      |
| Secondary  | 25 (78.1)      |
| Tertiary   | 5 (15.6)       |
| Not Stated | 1 (3.1)        |
| Parity     |                 |
| Primipara  | 8 (25.0)       |
| Multipara  | 24 (75.0)      |
| Pregnancy outcome |
| Terminated | 3 (9.4)        |
| Delivered  | 29 (90.6)      |
| Delivery modality |
| Spontaneous vaginal delivery | 9 (30.1)     |
| Cesarean Section | 20 (69.9) |
| Time of diagnosis of PRAKI |
| 1st trimester | 3 (9.4)       |
| 3rd trimester | 11 (34.4)    |
| Postpartum | 18 (56.3)      |
| RIFLE stage |                 |
| Risk       | 2 (6.3)        |
| Injury     | 7 (21.9)       |
| Failure    | 23 (71.9)      |
| Required hemodialysis | 24 (75.0)  |
| Received hemodialysis treatment | 19 (59.4) |
| Received blood transfusion | 26 (81.3) |
| Admitted to ICU | 5 (15.6) |

SD: Standard deviation, PRAKI: Pregnancy-related acute kidney injury, ICU: Intensive care unit.
Table 2. Laboratory and clinical characteristics of the study population.

| Parameter                          | Mean (SD)     |
|------------------------------------|---------------|
| Packed cell volume (%)             | 23.38±8.13    |
| White blood cells (cells/mm$^3$)   | 17,497±12,692 |
| Creatinine (mg/dL)                 | 5.72±3.46     |
| Urea (mg/dL)                       | 23.20±12.63   |
| Potassium (mmol/L)                 | 4.72±1.14     |
| Sodium (mmol/L)                    | 134.40±8.42   |
| Bicarbonate (mmol/L)               | 14.82±4.66    |
| Chloride (mmol/L)                  | 112.53±8.81   |
| The onset of symptoms (days)       | 2.71±1.97     |
| Hospital stay (days)               | 10.7±7.8      |
| Number of HD session               | 2.66±1.96     |
| Blood transfusion (units)          | 5.81±5.19     |

SD: Standard deviation, HD: Hemodialysis.

Figure 1. Common clinical features at presentation.

Figure 2. Etiologies of pregnancy-related acute kidney injury ($n = 32$).
occurred in 50% women with PRAKI.

Significant factors that were associated with maternal mortality were admission to ICU (P = 0.01), hypotension (P = 0.02), and impaired consciousness (P ≤0.001) (Table 3).

**Discussion**

PRAKI is still relatively common in developing countries and has devastating consequences on both maternal and fetal survival. The mean age of the study population was 31 ± 7 years, which is comparable to reports from other studies. The age range of patients in our study was 19–47 years which is at variance with 17–35 years reported by Aminu et al and 15–30 years reported by Makusidi et al.6 The higher age range in our study compared to the other studies may be related to the culture of early marriage that is common in northern Nigeria compared to southwestern Nigeria.

Multigravid women were more commonly affected by PRAKI in this study which is similar to some studies but at variance to reports by Makusidi et al and Eswarappa et al who reported that primigravid women were more affected. Majority of the patients in this study belong to low socioeconomic class which may be a contributing factor to developing AKI. Low socioeconomic status has been

| Factors                        | Full renal recovery Number (%) | Death Number (%) | P       |
|--------------------------------|--------------------------------|------------------|---------|
| Impaired consciousness         | 0 (0)                          | 8 (72.7)         | <0.001  |
| No                             | 17 (100)                       | 3 (27.3)         |         |
| Hypotension                    | 1 (5.9)                        | 5 (45.5)         | 0.02    |
| No                             | 16 (94.1)                      | 6 (54.5)         |         |
| ICU admission                  | 0 (0)                          | 5 (45.5)         | 0.01    |
| No                             | 17 (100)                       | 6 (54.5)         |         |
| Breathlessness                 | 8 (47.1)                       | 10 (90.9)        | 0.04    |
| No                             | 9 (52.9)                       | 1 (9.1)          |         |

ICU: Intensive care unit.
reported as an established factor which contribute to non-utilization or inadequate use of antenatal services in Nigeria.\textsuperscript{26,27} Furthermore, Grams et al\textsuperscript{28} reported low socioeconomic status as a risk factor for AKI in the general population.

PRAKI was most common in the postpartum period (56.3%) and third trimester (34.4%) which is similar to findings of Paudyal et al\textsuperscript{29} in Nepal and Najar et al\textsuperscript{8} in India. Reports from northern Nigeria and Pakistan, however, showed the highest prevalence of PRAKI in the third trimester.\textsuperscript{6,14,30} The most common presenting symptom of our patients was oliguria which is similar to other reports.\textsuperscript{6,14} This may be related to the fact that obstetric hemorrhage was the most common cause of PRAKI in these studies; causing inadequate renal perfusion and subsequent oliguria from pre-renal AKI.

Obstetric hemorrhage was the most common cause of PRAKI in our study similar to previous studies from Nigeria\textsuperscript{6,14} but at variance with findings from other studies\textsuperscript{29,31} where preeclampsia-eclampsia was reported as the most common cause of PRAKI. Preeclampsia and eclampsia were not common etiologies of PRAKI in our study as seen in some studies from Asia.\textsuperscript{24,32} This may be due to the fact that we had fewer primigravida women; a known risk factor for preeclampsia/eclampsia compared to these other studies.

Among our PRAKI patients whose etiology was obstetric hemorrhage, a significant proportion were delivered through cesarean section (CS). In addition, about 50% of all patients delivered through CS had bleeding significant to cause hemodynamic disturbances. This may suggest gaps in patients’ resuscitation prior to surgery, intraoperative and postoperative monitoring for features of shock. There is a need for obstetricians managing pregnant women to promptly detect and correct significant blood loss during the surgery. Furthermore, our blood transfusion services must be strengthened so that blood is always readily available for use.

PRAKI is still a major cause of maternal and fetal morbidity and mortality. Maternal mortality in our study was 34.4%. This is comparable to 30.8% reported by Aminu et al\textsuperscript{14} but lower than 45% reported by Makusidi et al\textsuperscript{b} and 66.6% reported by Okunola et al\textsuperscript{7} The higher mortality in these studies compared to ours may be due to the fact that they studied dialysis requiring PRAKI patients which may suggest that they had more ill patients. However, the mortality reported in all these studies from Nigeria is far higher than those recently reported in Casablanca, different parts of India where it was not more than 20%.\textsuperscript{23,25,32,33} Fetal mortality was 50% in this study which is very high. Most other studies from outside Nigeria reported a lower rate of 5.5%–26.2%.\textsuperscript{23,25,32,33} PRAKI, therefore, contributes significantly to perinatal mortality in Nigeria.

Factors that were significantly associated with maternal mortality in this study were hypotension, impaired consciousness and ICU admission which is similar to previous reports on AKI from pregnancy and non-pregnancy related causes.\textsuperscript{24,32,34} All the patients who presented with refractory shock despite attempt at fluid resuscitation and those who were managed in ICU due to their critical condition died. This brings to the fore the need to improve our obstetric health care in Nigeria to reduce this associated mortality. Physicians also need to do more toward the management of early stages of shock before it becomes irreversible.

Complete renal recovery was seen in about 53.1% of our patients which is comparable to findings of previous studies that showed that between 42% and 61% of PRAKI patients had complete renal recovery.\textsuperscript{4,35,36} This is however lower than 65% reported by Aminu et al\textsuperscript{14} whose study population consisted of patients with less severe PRAKI.

**Conclusion**

PRAKI is still relatively common and significantly contributes to maternal and perinatal mortality in Nigeria. Significant factors associated with maternal mortality are ICU admission, shock, impaired consciousness, and elevated white cell count. Obstetric hemorrhage
which is the most common cause of PRAKI is preventable and treatable. There is a need for obstetricians to effectively prevent and manage obstetric hemorrhage.

Conflict of interest: None declared.

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