

## Foetal Outcomes in Women with Pregnancy Related Acute Kidney Injury in a Referral Facility in Kenya

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### Abstract

**Background:** Pregnancy related acute kidney injury (PRAKI) is an obstetric complication, which can occur at any stage of pregnancy and in postpartum, often associated with significant adverse foetal outcomes.

**Objective:** To determine foetal outcomes among patients with PRAKI at Kenyatta National Hospital (KNH), Kenya.

**Methods:** We carried out a descriptive study on pregnant women with gestation age equal or above 28 weeks and postpartum women within six weeks after delivery who were admitted in labour ward or the post-natal wards at KNH. Study commenced following approval by the KNH- University of Nairobi Ethics and Research Committee. Data was obtained from both the patient and the medical records. Participants were followed up until discharge or for a maximum of two weeks. Patient management was at the discretion of attending clinician.

**Results:** A total of 66 participants with a mean age of 28 years and peak age between 26-30 years were enrolled into the study out of 2068 admissions. The prevalence of PRAKI was 3.2%. Sixty (91%) participants gave birth during the follow-up period and six remained pregnant past the two weeks after enrollment. Average gestation age at delivery was 35 weeks. Live infants were 43 (71.7%) and fresh still births were 17 (28.3%). Preterm births were the majority 33 (55%), of whom 23 were live infants and 10 were fresh still births. Comparing between participants and women without PRAKI, the ratio of fresh still births was 1:4 while the ratio of fresh still births among women without PRAKI was 1:23 deliveries.

**Conclusion:** We demonstrate an average gestation age of 35 weeks and a six (6) fold increase in fresh still births among women with pregnancy related acute kidney injury at KNH.

**Key Words:** PRAKI, KNH, Gestation age, Fresh still births, Kenya

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### I. Introduction

Pregnancy related acute kidney injury (PRAKI) is a rare obstetric complication that is poorly understood. PRAKI is characterized by rapid deterioration of renal functions within hours to days, in pregnancy or in the postpartum period, in women with previously healthy kidneys. It is often associated with significant foetal morbidity and mortality (1-10).

There is great diversity in the incidence of PRAKI and great variation in foetal outcomes across socioeconomic boundaries. The variability is also seen in different patient demographics and in the availability of healthcare services (3-5).

In the 1960s, PRAKI used to contribute 20-40% of all AKI in the general population. The incidence dropped to less than 3% worldwide following reduction of septic abortions and improvement in perinatal care in the 1980's. In the developed world, PRAKI contributes 0-1% of all the AKI in the general population and had decreased from 1:3000 to 1:20000 pregnancies. However, recent studies in the United States and Canada demonstrate a paradoxical rise in the incidence of PRAKI, a public health concern. In the United States, the incidence rose from 2.3 to 4.5 /10000 deliveries between 1998 and 2008, in Canada from 1.6 to 2.7/10000 between 2003 and 2010. The temporal rise in the incidence of PRAKI is associated with increase in lifestyle diseases related to obesity such as diabetes mellitus and hypertension and rising maternal age.

The rise in maternal age is attributed to advances in reproductive services and probably due to improved education of girls (4, 7, 8). Unfortunately, in the developing World, the incidence of PRAKI has remained high between 5-15% and contributes 5-20% of all AKI in the general population (1-12, 15-18).

The aetiologies of PRAKI include prerenal, renal and post renal causes, like those in the general population.

It has been observed that, approximately 75% of all cases of PRAKI are related to hypertensive disorders of pregnancy (preeclampsia, eclampsia, hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome, and thrombotic microangiopathies) and occur in third trimester and in the post-partum period (1-15,19).

Specific obstetric causes of PRAKI include obstetric hemorrhages, ureteral and bladder outlet obstruction, iatrogenic injuries of bladder and/or ureter and puerperal sepsis. Maternal characteristics such as, multifetal gestation and multiparity may also increase the risk and contribute towards development of PRAKI (1-4,6,14).

Owing to the anatomic and physiologic adaptations during pregnancy, PRAKI lacks international consensus for definition and diagnosis. Hence, diagnosis is based on combination of both clinical features and laboratory findings for the estimation of glomerular filtration rate (3,4, 6,12,19).

Pregnancy related acute kidney injury impacts negatively on foetal outcome regardless of the primary cause the AKI.

### **1.1 Foetal outcome in patients with PRAKI**

An opinion piece in the Lancet, published in 1975 stated:

‘Children of women with renal disease used to be born dangerously or not at all’ (14).

This is a statement that emphasized the impact of renal disease on the foetal outcome in women with kidney injury during pregnancy. Neonatal mortality is notably high in women with acute kidney injury during pregnancy according to Liu et al, (11) and Yuehong et al, (17) and the odds of perinatal mortality in women with PRAKI increases 3.4 fold compared to pregnancies in women without PRAKI (19). PRAKI is also associated with increase in other poor foetal outcomes such as premature births, small for gestational age and intrauterine growth restriction (2-9).

The actual factors responsible for the increase in foetal morbidity and mortality in PRAKI are not clear (1-4,7,18-19). However, the aetiology of foetal morbidity and mortality could be related to the primary cause of maternal acute kidney injury or directly related to uremia or both. Pyelonephritis is associated with increased risk of preterm deliveries whereas premature delivery of foetus is sometimes indicated in women with preeclampsia, in which case, the delivery of the placenta is therapeutic. The need for such early deliveries to save the mother may compromise foetal wellbeing (2-11,19-20). Prenatal blood pressure  $\geq 160/110$  mmHg and uric acid above  $363 \mu\text{mol/l}$ , common in preeclamptic women with PRAKI are independent risk factors for poor foetal outcomes (17-19). Bilateral compression of the ureters by the gravid uterus is a rare cause of PRAKI and is also associated with high foetal morbidity especially in multifetal gestation (20).

Foetal outcomes vary widely across socioeconomic settings (1-4,7,9,15,19-20). Studies in developing countries such as India and Malawi demonstrate high perinatal mortality ranging from 10-40% in women with PRAKI (8, 9, 16,19), while in developed countries like Canada as demonstrated in a study by Hildebrand et al (4), perinatal morbidity such as preterm deliveries, low birth weight and small for gestation was common at 35.6% in women with PRAKI requiring dialysis. However, in the same study, perinatal mortality was less than 2.7% in women with PRAKI compared with 0.8% in the general population (4).

We have no local publications on foetal outcome in patients with PRAKI in Kenya. Therefore, in this study we desired to find out what were the foetal outcomes in patients with PRAKI at K.N.H in Kenya.

## **II. Materials And Methods**

**2.1 Study design:** The design was a descriptive study

**2.2 Study site:** The study was carried out in the Department of Obstetrics and Gynecology, in Labour ward and Post-natal wards of KNH.

**2.3 Study population:** The target population consisted of pregnant women with gestation age equal to or above 28 weeks and postpartum women within six weeks after delivery admitted to the Labour ward or the post-natal wards of K.N.H.

**2.4 Inclusion criteria:** Pregnant women with gestation of  $\geq 28$  weeks and postpartum women within six weeks after delivery with a diagnosis of acute kidney injury or with deranged serum creatinine fulfilling the operational definition of PRAKI in any of the stated wards willing to sign consent to enroll in the study.

**2.5 Exclusion criteria:** Women with chronic kidney disease, or pregnant  $< 28$  weeks or in postpartum  $> 6$  weeks.

**2.6 Sampling method:** Consecutive patient sampling

**2.7 Ethical considerations:** The study commenced upon approval by the Ethics and Research Committee of KNH and University of Nairobi. Approval number: P635/11/2017

**2.8 Diagnosis of PRAKI:** Given the limitations in estimation of glomerular filtration rate (GFR) in pregnancy due to the physiologic adaptations and challenges in the use of 24-hour urine for creatinine clearance, rise in serum creatinine was used for estimation of GFR in this study. Hence PRAKI was defined using Kidney Disease Improving Global Outcomes (KDIGO) creatinine Criteria as increase of serum creatinine by  $\geq 26.5 \mu\text{mol/L}$  within 48 hours, or a similar rise in creatinine above upper limit of normal of the reference laboratory or increase in serum creatinine 1.5 times of the baseline within seven (7) days, assuming a normal GFR of 75mls/minute per  $1.73\text{m}^2$ .

Renal function tests are not part of the routine antenatal profile, so the patients did not have their pre pregnancy or early pregnancy baseline serum creatinine.

**2.9 Clinical methods:** The patient management was at the discretion of attending clinician. The principal investigator or the research assistant screened patients for deranged kidney function tests in the respective wards by looking through the file for laboratory results and applying the operational criteria for definition of PRAKI. Patients with results that fitted operational criteria for PRAKI were approached and introduced to the study. The study requirements were verbally introduced to each patient, by the principal investigator or the research assistant and permission was sought to access and extract information from the patient's medical file. Participants were informed that, benefits of participation would include sharing the interpretation of results with the patient and the primary healthcare provider for relevant intervention, that no risks, and that, participation in the study was voluntary. Those who consented to enroll into the study were assigned a study serial number placed on their medical record file for easy access. The medical records of each participant were then assessed, and verbal interviews were used for any necessary additional information. Follow up was until discharge or a maximum of two weeks which ever came first.

Captured baseline data included both demographic and clinical profile such as age, residence, marital and referral status, presenting complaint, past medical and obstetric history, obstetric and non-obstetric diagnosis and laboratory results such as full hemogram and kidney function tests.

The outcomes documented included both pregnancy and foetal outcomes. Pregnancy outcomes were: delivered or pregnancy on-going after two weeks of enrollment or until discharge, which ever came first. Mode of delivery as spontaneous vertex delivery or caesarian section. Foetal outcomes included gestation age at birth and status at birth. Delivery before 37 completed weeks was defined as premature birth. Status at birth was either life infant or fresh still birth.

**2.9 Data processing and analysis:** Raw data was screened, coded and entered into a password protected Computer. Statistical analysis was performed in Statistical Package for Social Sciences (SPSS) version 21.0 by a Statistician. Data were summarized into descriptive statistics, where, continuous variables were described in means or median and categorical variables were summarized into frequencies. Other results were presented in tables.

### III. Results

Sixty-six (3.2%) participants were enrolled into the study out of 2068 admissions. They were young women with mean age of 28 (SD 5.9) years, peak age, 26-30 years (34.8%) and age range of 15 to 44 years.

**Table 1 Age distribution among participants with PRAKI**

N=66		
Age in years	n	%
Below 20	6	9.1
21 – 25	18	27.3
26- 30	23	34.8
31-35	11	16.7
Above 35	8	12.1

Sixty pregnancies were delivered, 39 (65%) through spontaneous vertex delivery and 21 (35%) by caesarian section. The average gestation was 35 weeks. 33 (55%) were preterm infants. Life 43 (71.7%) were life infants and fresh still births were 17 (28.3%).

**Table 2: Foetal outcome in pregnancy related acute kidney injury at KNH**

Status of foetus at birth (N=60)			
Age at birth	Life infants n= 43	Fresh still births n=17	Total %
Preterm births < 37 weeks	23	10	33 (55.0)
Term births > 37 weeks	20	7	27 (45.0)
<b>Total</b>	<b>43 (71.7)</b>	<b>17 (28.3%)</b>	<b>60 (100)</b>

#### IV. Discussion

The incidence of PRAKI remains high in developing regions of the world and is associated with significant foetal morbidity and mortality. In this study, 66 participants were enrolled out of 2068 admissions in the labour ward and the postnatal wards. We demonstrate a prevalence of PRAKI of 3.2%. This prevalence was higher than a prevalence of 1.8% reported in India by Prakash et al, 2010 (7) and less than 8.1% in Malawi (10). These differences in prevalence between developing countries may be related to differences in risk factor profiles, patient selection and challenges in the definition of PRAKI.

Pregnancy related acute kidney injury is associated with increased perinatal morbidity such as premature deliveries and intrauterine growth restriction and increased mortality (1-7, 11, 13-18). The cause of which is related to the maternal factors leading to PRAKI and because of uremia (3-7, 19-20).

To the best of our knowledge, this was the first study to assess foetal outcomes in women with pregnancy related acute kidney injury in Kenya.

We demonstrate a mean gestational age of 35 weeks at delivery. The majority, 33 (55%) were preterm births born before 37 completed weeks. Fresh still births were 17 (28.3%) out of whom 10 were premature births. The rate of premature births in our study was higher than in Canada where prematurity was 32.5% premature infants but with no still births (4). Our findings were different from those from a study in India, where the rate of prematurity was much higher as reported by Mahesh et al, (16) with 89% preterm infants and 26% fresh still births.

Foetal mortality was notably high among participants in our study owing to various maternal complications including PRAKI. The number 17 (28.3%) of fresh still births were higher than 11.7% reported in Morocco by Kibbali et al (7) and lower than 41% reported in a study in India by Munna et al (9). The overall foetal mortality was comparatively higher than that reported in developed countries like Canada where there were no fresh still births and neonatal deaths were less than 2.7% (4). These differences in foetal outcome may be due to differences in maternal risk factor profile for PRAKI and socioeconomic differences in perinatal care.

The ratio of still births among the participants was 1:4 and the ratio of still births among patients without PRAKI in the same setting was 1:23.

We therefore demonstrate that, PRAKI was associated with six (6) fold increase in fresh still births. The 6-fold increase in fresh still births in our study was higher than reported from a meta-analysis by Liu et al, 2015 (11) where PRAKI was documented to cause a 3.9-fold increase in fresh still births. The high rate of fresh still births in our setting may be due to late referrals, high patient turnover and strained human resources within the facility. These findings may as well reflect differences in antenatal and perinatal care practices and the challenges in handling non-obstetric emergencies like acute kidney injury in resource strained setting.

#### V. Conclusion

We demonstrate average gestation age of 35 weeks at delivery and a six (6) fold increase in fresh still births among women with pregnancy related acute kidney injury at Kenyatta National Hospital.

#### Conflict of interest

The authors declare no conflict of interest

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