

## Maternal characteristics of women with Pregnancy Related Acute Kidney Injury at Kenyatta National Hospital, Kenya

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**Abstract:** Background: Pregnancy is a physiologic state that can become complicated by pregnancy related acute kidney injury (PRAKI) which may occur at any stage of pregnancy and in postpartum, in previously healthy women. It is associated with variable obstetric outcomes often with significant but preventable foeto-maternal morbidity and mortality.

Objective: To determine maternal characteristics of in-patients with PRAKI at Kenyatta National Hospital (KNH), Nairobi, Kenya

Methods: We carried out a descriptive study on in-patient pregnant women with gestation age of 28 completed weeks or more and postpartum women within six weeks after delivery admitted in labour ward or the post-natal wards at KNH. Study started after approval by the KNH- University of Nairobi Ethics and Research Committee. Data was obtained from the patient through verbal interviews and from the medical records using a pretested data capture form. The participants were followed up for a maximum of two weeks or until discharge. The patient management was left at the discretion of attending clinician.

Results: We enrolled 66 (3.2%) participants out of 2068 admissions. The mean age was 28 (SD 5.9) years with peak age between 26-30 years. Forty-two were referred from other health facilities. Nineteen (27.8%) had pre-pregnancy medical conditions mainly cardiovascular and all participants developed obstetric complication(s). Hypertensive disorders of pregnancy were the main associated factors. Sixty (91%) participants were delivered within two weeks after enrollment. The average gestation age at delivery was 35 weeks. Twenty-one (35%) were delivered through caesarian section. Live infants were 43 (71.7%) and fresh still births were 17 (28.3%). The ratio of fresh still births among participants was 1:4 while the ratio of fresh still births among women without PRAKI was 1:23 deliveries.

Conclusion and recommendations: This study demonstrated prevalence of pregnancy related acute kidney injury was 3.2% at K.N.H. The main associated factors were hypertensive disorders of pregnancy. Participants with PRAKI were characterized with increased premature deliveries and a six (6) fold increase in fresh still births. There is need for screening, monitoring and close follow-up of women with hypertensive disorders in pregnancy and related kidney complications.

**Key Words:** PRAKI, KNH, hypertensive disorders of pregnancy, still births, Kenya

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### I. Introduction

Pregnancy related acute kidney injury (PRAKI) is one of the most serious complications of pregnancy, a bimodal disease occurring in early pregnancy in relation to septic abortions and hyperemesis gravidarum and in late pregnancy and early postpartum period due to hypertensive disorders, obstetric hemorrhages and periperal sepsis. It is associated with adverse maternal and foetal outcomes (1-10).

#### 1.1 Incidence of PRAKI

The incidence of PRAKI had declined significantly from 20-40% in 1960s to about 3% Worldwide in the 1980s following improvement in perinatal care, however it remains a serious public health issue in developing countries (3-5). Maternal risk profile vary greatly across socioeconomic boundaries, such that, in the developed world, PRAKI contributes 0-1% of the AKI in the general population while, in the developing World, the incidence of PRAKI contributes up to 5-20% of all AKI in the general population (2,4-5,16).

In the last decade, studies in the United States of America and Canada have demonstrated a paradoxical rise in the incidence of PRAKI where in United States, the incidence rose between 1998 and 2008 from 2.3 to 4.5 /10000 deliveries, while in Canada, the rise between 2003 and 2010 was from 1.6 to 2.7 /10000. The temporal rise

in the incidence of PRAKI is thought to be associated with the evolution of risk profile; where advanced maternal age, multifetal gestation and lifestyle diseases such as diabetes mellitus and hypertension are on the rise in developed world (2).

The rise in maternal age is attributed to advances in reproductive technology and probably due to education of the girl child. In the developing countries, the incidence of PRAKI has however remained high at 5-15% (1-8,10-17). The persistent high incidence is mainly due to late diagnosis and management of hypertensive disorders of pregnancy, cardiogenic shock and obstetric hemorrhages (1-10, 13,15).

### **1.2 The aetiology of Pregnancy related acute kidney injury**

The risk factors for PRAKI are like those in the non-pregnant population and include prerenal, renal and post renal factors. Prerenal aetiologies arise from volume depletion as a result of hyperemesis gravidarum and obstetric hemorrhages. Intrinsic /renal factors involve the tubulointerstitium, the glomerular and the blood vessels often in combination. Post renal causes arise from the physiologic adaptations during pregnancy, such as, physiologic hydronephrosis and hydronephroses which may predispose to anuria, stasis and ascending infection (1-6,15).

Up to 75% of PRAKI occur in third trimester and in the early post-partum period and are mainly related to hypertensive disorders of pregnancy which often present with overlapping features (1,5-8,12,14,24).

### **1.3 Definition of AKI in Pregnancy**

The wide range of criteria used for definition of AKI in the general population lack utility in PRAKI owing to the physiologic adaptations of pregnancy characterized by increase in blood volume decreased systemic vascular resistance and increased cardiac output with subsequent hyperfiltration and reduction in serum creatinine. Hence PRAKI lacks international consensus for definition and diagnosis. The estimation of glomerular filtration rate is based on combination of both laboratory and clinical findings (5,6,8,10,14,19,23).

### **1.4 Outcomes of PRAKI**

Complete renal recovery is achievable if patients with PRAKI receive an appropriate and timely management. However, some patients become entirely dependent on dialysis due to lack of adequate initial resuscitation and consequently late initiation of dialysis.

Risk factor profile may determine the outcome. Severe preeclampsia is associated with maternal and fetal complications. While advanced maternal age may predispose to obstetric hemorrhages and increased risk of cardiovascular disease (12,5,8,12-20). However, PRAKI from whichever etiology is associated with poor foetal outcomes (11).

There is paucity of data on maternal characteristic in patients with PRAKI and no local publications on the same. We then desired to determine the maternal characteristics of patients with PRAKI at KNH in Kenya

## **II. Materials And Methods**

2.1 Study design: The design was a descriptive study

2.2 Study setting: The study was done in the Labour ward and Post-natal wards of KNH

2.3 Study population: We targeted pregnant women with gestation age of 28 completed weeks and above and postpartum women who were within six weeks after delivery.

2.4 Inclusion criteria: We included pregnant women with gestation of  $\geq 28$  weeks and women in postpartum within six weeks with deranged serum creatinine which fulfilled the operational definition of PRAKI consenting to enroll in the study.

2.5 Exclusion criteria: Women known to have chronic renal disease, or with gestation less than 28 weeks and women in postpartum beyond six weeks after delivery.

2.6 Sampling method: Consecutive patient sampling

2.7 Study ethics considerations: The study began after approval by KNH and University of Nairobi Ethics and Research Committee. Approval number: P635/11/2017

2.8 Clinical methods: Patient management was left at the discretion of attending clinician. The principal investigator (PI) and or the research assistant carried out screening through the patient files for laboratory reports on daily basis. They were able to identify patients with deranged renal function tests in the respective wards. Such patients were approached by the PI or the assistant and verbal introduction to the study was done. The patients were explained that if they

enrolled into the study, they would be subjected to verbal interviews and their medical records would be accessed for information. They were informed that benefits of participation included shared interpretation of results with the patient and the primary healthcare provider for intervention. There were no risks involved and participation was voluntary. Data capture forms were used to extract data from the file and from the participant. Followup was until discharge or a maximum of two weeks which ever came first.

2.8.1 Outcomes

Outcomes were defined regarding maternal, renal and foetal status and were recorded at discharge or at end of two weeks as follows:

Maternal - Pregnancy on going or delivered, mode of delivery and status as dead or alive

Fetal outcome –Age at birth and status at birth –Life infant or Freshstill birth

Renal –Management- conservative or Dialyzed

2.9 Data processing and analysis: Afterscreening and coding the data was entered into a password protected Computer. Statistical analysis was performed by a Statistician in Statistical Package for Social Sciences (SPSS) version 21.0. Descriptive statistics were applied to summarize the findings. Continuous variables were described in means or median and Categorical variables were summarized into frequencies. Other statistical test results were presented in tables and figures.

III. Results

A total of sixty-six (3.2%) participants were enrolled out of 2068 admissions. The mean age was 28 (SD5.9) years. Age range was 15 to 44 years. Majority (62.1%) lived in urban area and 63.6% were referral

**Table 1: Maternal demographics and other characteristics of participants**

Characteristics N=66	n	%
<b>Age in years</b>		
≤20	6	9.1
21-25	18	27.3
26-30	23	34.8
31-35	11	16.7
≥35	8	12.1
<b>Residence</b>		
Urban (Nairobi)	41	62.1
Rural	25	37.9
<b>Referred</b>	42	63.6
• From Rural	24	57.1
• From Urban	18	42.9
<b>Marital status</b>		
• Married	63	95.5
• Single	2	3.0
• Underage	1	1.5
<b>Parity</b>		
• Primigravida	7	10.6
• Multigravida	59	89.4
<b>ANC attendance</b>	62	94%
<b>Mode of delivery n=60</b>		
• SVD	39	65
• CS	21	35
<b>Time of onset of PRAKI</b>		
• Antepartum	49	74.2
• Post-partum	17	25.8
<b>Gestation Age at Delivery</b>		
• < 37weeks	33	55.0
• >37 weeks	27	45.0
<b>Need for hemodialysis</b>		
• Yes	19	28.8
• No	47	71.2

Nineteen (28.8%) had pre-pregnancy conditions which were predominantly cardiovascular diseases. HIV infection were 15.8% as shown in table 2 below

**Table 2 Pre-pregnancy medical conditions of the study participants**

Pre- pregnancy conditions	n=19
Hypertension	10
Valvular heart disease	4
Dilated cardiomyopathy	2
HIV	3

The main obstetric conditions predisposing to PRAKI hypertensive disorders of pregnancy 53(80.3%). Other conditions were as shown in table 3 below

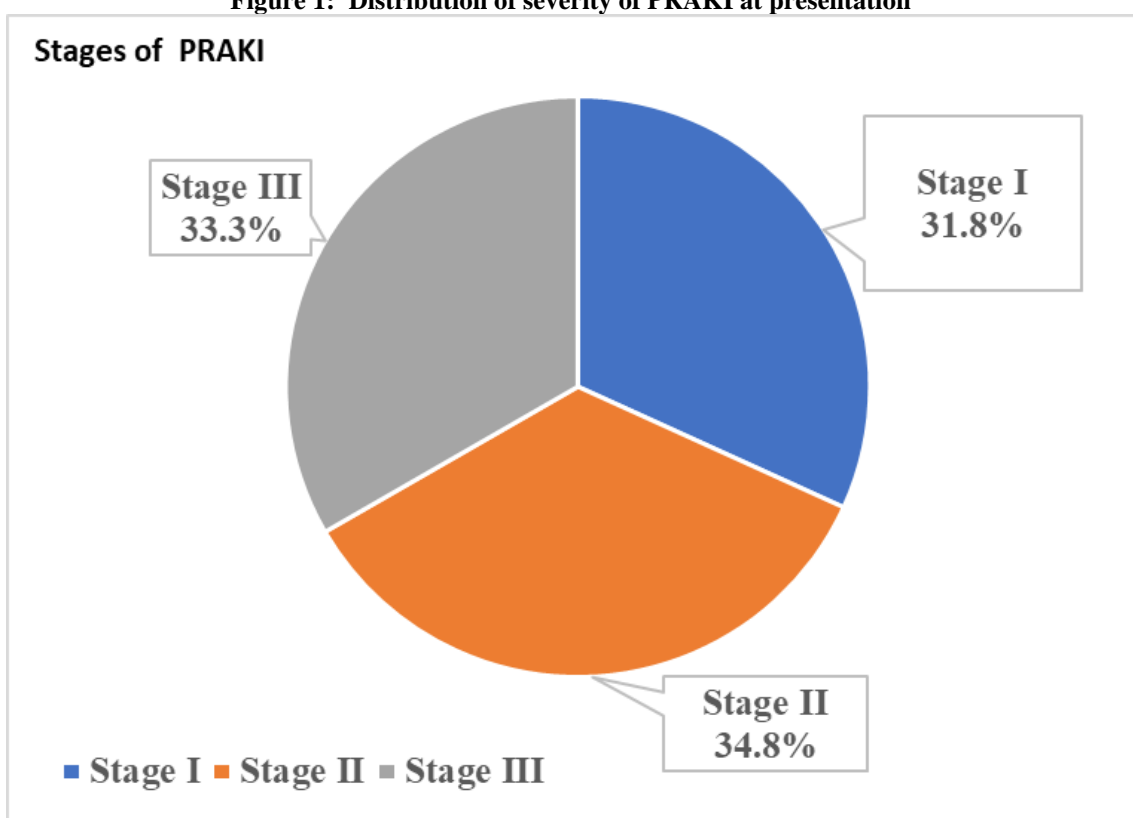
**Table 3 Obstetric conditions among the study participants**

Morbid Condition N=66	n
Hypertensive disorders	53
• Preeclampsia	28
• Eclampsia	8
• HELLP syndrome	17
Volume loss	9
• PPH	6
• APH	1
• Hyperemesis gravidarum	2
Puerperal sepsis	2
Bladder and Urethral injuries	2

The average gestation age at birth was 35 weeks. 33 (55.0%) were born prematurely while 27(45.0%) were term. Live births were 43(71.7%) and fresh still births were 17(28.3%).

The study demonstrated an even distribution of severity of PRAKI at presentation as shown in Figure 1 below

**Figure 1: Distribution of severity of PRAKI at presentation**



**Stage 1:** Serum Creatinine 1.5 to 1.9 times of baseline: **Stage 11:** Serum Creatinine 2.0 to 2.9 times of baseline: **Stage 111:** Serum Creatinine 3.0 times of baseline or Need for Dialysis

#### IV. Discussion

##### Main Findings

Sixty-six participant were enrolled out of 2068 admissions. We demonstrate a prevalence of 3.2%. The mean age of the study participants was 28 (SD5.9) years and peak age of 26 to 30 years. 41 (62.1%) were urban residents and 42 (63.6%) were referred with complications. Fifty-nine were multigravida and 62 attended antenatal clinic. Sixty (90.9%) pregnancies were delivered. Majority 39 (65%) delivered spontaneously. The mean gestation age at delivery was 35 weeks. Thirty-three pregnancies were delivered prematurely. Forty-nine (74.2%) developed PRAKI in antepartum period. The severity of PRAKI at presentation was evenly distributed across stages 1, 11 and 111. Nineteen (28.8%) needed hemodialysis. The main associated factors were hypertensive disorders. Three participants had HIV infection. All participants were noted to have associated obstetric condition(s). No maternal mortality was documented among participants during the follow-up period.

**Comparison with other studies**In our study, the prevalence of PRAKI was 3.2%, a prevalence that was higher than a prevalence of 1.8% reported in India by Prakash et al, 2010 (20) and lower than the prevalence of 8.1% reported in Malawi by Cooke et al, in a similar setting (12). Differences in patient selection and associated factors may explain differences in prevalence, where in some studies, women with pregnancies of all ages were included while in our study, only women in third trimester were enrolled.

**The mean age** of the study participants was 28 years, which was comparable to mean age reported in studies in Morocco (18) and, in India (24) **Peak age.** The peak age was similar to peak age reported in other studies in the developing world (1,3,4,7,12,17-21) and lower than peak age of 30-39 years reported in Canada (2). Differences in peak age between developing and developed world may be due to differences in risk factor profile.

**Residence** Most 41(62.1%) of the participants were urban residents from Nairobi City with near proximity and easy access to KNH, while 25(37.9%) lived in the rural areas 24 of whom were referred to KNH. Our results were similar to findings in a study by Kibali et al in Morocco (18) where urban residents were 59% and rural residents were 41%. Our results sharply contrast with the findings in Canada where Hildebrand et al (2) found participants resident in rural areas were 9.6%. These differences may be explained by the fact that in developing countries, specialized services are concentrated in the urban settings while in developed countries healthcare services are evenly available in all settings (2).

#### **Pre pregnancy factors**

Cardiovascular disorders mainly; chronic hypertension 10(16.7%), valvular heart disease 4(6.1%) and dilated cardiomyopathy 2 (3%) were main the associated pre pregnancy factors in patients with PRAKI. With HIV infection were 3 (4.5%). Comparing our results with a study in Canada (2) their percentage of preexisting hypertensive diseases was 5.3% with no valvular heart disease. These study findings demonstrate differences in patient characteristics in deferent socioeconomic settings

#### **Obstetric factors**

We observed that, all participants had obstetric complication(s), predominantly, hypertensive disorders namely, preeclampsia 42.4%, eclampsia 12.1% and HELLP syndrome 25.8%. The preeclampsia spectrum of disorders remains the main risk factor for PRAKI in the world (1-8,12,13, 14,17,18,25).

Volume loss mainly from obstetric hemorrhage occurred in 10.6% which compared with observations made in Malawi 11.5%, (12) and Morocco 9.1% (18) and lower than in Canada 17.6% by Hildebrand et al, (2). These differences in obstetric volume loss between the developing and the developed countries may be due to differences in availability of resuscitation services.

In this study, no maternal mortalities were documented over the study period.

Concomitant with the decrease in the incidence of PRAKI, maternal mortality associated with PRAKI has significantly decreased worldwide (4,5,12). Recent studies from China and India reported maternal mortality rate associated with PRAKI of 4.0% and 5.8%, respectively as compared with a rate of 20% during the 1980s (8,17).

Our study findings compare with those of a study done in Malawi by Cooke et al, 2018 (12) where no maternal mortality was documented in a similar study setting. Our findings contrasted the findings of studies done in Morocco and India where maternal mortality was 11.4% and 15% respectively (18,19). Findings of this study and that in Malawi may reflect a declining maternal mortality in developing countries.

Pregnancy related acute kidney injury is associated with increased deliveries through Caesarian sections and increased rate of foetal mortality (1-3,7,8,11- 18,24,25). We demonstrate a ratio of 1.4:1 between CS in PRAKI patients to CS in non PRAKI patients. The increased need for operational delivery may be contributed by the fact that, delivery of the placenta and the foetus is therapeutic in preeclampsia/eclampsia (1-6,8,12). In our study Caesarian deliveries were 35%, were higher than 25.5% reported in Canada where hypertensive disorders were also noted to be lower than in our study (2).

According to Liu et al (13), the odds of foetal mortality increases to 4.9-fold in PRAKI when compared to non- PRAKI women. In our study we demonstrate 17(28.3%) fresh still births a rate higher than 15.9% reported in Morocco (18) and lower than 41% reported in India (21). Our results are a sharp contrast to the findings reported in Canada by Hildebrand et al (2) where no still births were reported. We also demonstrate a 6-fold increase in fresh still birth among women with PRAKI compared to those without PRAKI, where ratio of still births among participants was 1:4 and among non-participant was 1:23. Our finding was higher than 4.9 fold that documented by Liu et al, 2015(13) in a meta-analysis in China. The high rate of fresh still births in our setting may be explained by late referrals and strained health care resources.

#### **Need for dialysis**

Forty-seven 72.1% participants were managed conservatively and nineteen (28.8%) needed renal replacement therapy. The need for dialysis in our study was higher compared to, 16.2% by Cooke et al (12) in Malawi and lower than another site in Morocco (18) where the need for dialysis was 38.6%. The indications for

dialysis are similar in patients with PRAKI, but the time to initiation of therapy may vary depending on the healthcare facility and availability of dialysis services.

## V. Conclusion

The prevalence of PRAKI from this study was 3.2%. The participants were mainly referred young multi gravid women most of who delivered prematurely with a 6-fold increase in fresh still births. The main associated factors were hypertensive disorders of pregnancy. Majority were managed conservatively and about a third were dialyzed

## Limitations

1 Generalizability The study population was limited to women with viable pregnancies above 28 completed weeks, so these results are not generalizable to patients with PRAKI in early pregnancy. Longer follow-up of the participant would have been useful in assessing the long-term impact of this condition on morbidity, mortality, and dialysis dependency.

### 2. Information Bias

The laboratory information obtained from the medical record originated from different laboratories whose uniformity of quality could not be ascertained.

### 3. Confounding factors

There was a great overlap in the associated factors where in about 50% of the participants had more than one pre pregnancy and pregnancy related factors.

## Conflict of interest

The authors declare no conflict of interest

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