Impact of Pregnancy Related Acute Kidney Injury on foetalsurvival: a single Centre Experience in Kenya

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Abstract: Background: Pregnancy related acute kidney injury (PRAKI) is a heterogenous obstetric complication, which can occur at any stage during pregnancy and in postpartum period. It often impacts negatively on foetal outcomes.

Objective: To determine impact of PRAKI on foetal outcomes at Kenyatta National Hospital (KNH), Nairobi.

Methods: We carried out a descriptive study on women with viable pregnancies, gestation age equal to, or above 28 weeks and postpartum women within six weeks after delivery admitted in labour ward or the postnatal wards at KNH. The study started after it was approved by the KNH- University of Nairobi Ethics and Research Committee. Patient management was at the discretion of attending clinician. Data was obtained from the participants and their medical records. Followup was until discharge for a maximum of two weeks for those who remained in the wards.

Results: Total participants were 66 out of 2068 admissions. Their mean age was 28 years with peak age between 26-30 years. The prevalence of PRAKI was 3.2%. Sixty (91%) participants were delivered and six pregnancies were ongoing past the follow-up period. The average gestation age at birth was 35 weeks. Forty-three (71.7%) were live infants while 17 (28.3%) were fresh still births. Comparing between participant women with PRAKI and women without PRAKI, the ratio of fresh still births among participants was 1:4 and the ratio of fresh still births among women without PRAKI was 1 in 23 deliveries.

Conclusion: We therefore demonstrate that pregnancy related acute kidney injury was associated with a six (6) fold increase in fresh still births at Kenyatta National Hospital in Kenya.

Key Words: PRAKI, KNH, Preterm births, Fresh still births, Nairobi, Kenya

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I. Introduction

Pregnancy related acute kidney injury (PRAKI) is a worldwide obstetric complication in previously healthy women characterized by rapid deterioration of kidney functions in pregnancy and/or in the postpartum period. It is often associated with significant foetal morbidity and mortality (1-4).

The incidence of PRAKI varies widely in different socioeconomic and demographic settings (3). In the developed world, PRAKI had been reported to contribute less than 1% of all the AKI in the general population and had decreased from 1:3000 to 1:20000 pregnancies following reduction of septic abortions through improved obstetric care. However, recent studies done a decade ago in the United States and Canada demonstrated paradoxical increase in the incidence of PRAKI. In the United States, the incidence increased from 2.3 to 4.5 /10000 deliveries between 1998 and 2008. In Canada, there was recorded increase in incidence from 1.6 to 2.7 /100000 between 2003 and 2010. The temporal change in the incidence of PRAKI is associated with increase in lifestylerelated diseases such as hypertension and diabetes and advanced maternal age attributable to advances in reproductive health services (4, 7). Unfortunately, the incidence of PRAKI in the developing world, has remained high and contributes 5-20% of all AKI in the general population, which may also reflect the status of reproductive health services in developing world (7, 9-12).

Despite the physiologic changes in pregnancy such as increase in vascular volume by 30% and anatomic adaptations including increase in kidney size by 1-1.5 cm and development of transient hydroureter and hydropnephrosis from compression by the gravid uterus, theaetiologic factors of PRAKI are similar to those in the general population and can be categorized into three: i)Prerenal azotemia arising from volume loss leading toischaemia.

ii) Intrinsic/Renal- involving the tubulointerstitium and the glomerular iii) Post renal causes constituting obstructive uropathy arising from obstruction by the gravid uterus (6).

The overall main cause of PRAKI in many parts of the world are related to hypertensive disorders of pregnancy, such as preeclampsia, eclampsia, hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome, which contribute approximately 75% of all cases (4, 6, 15, 18).
While maternal characteristics such as advanced maternal age, multifetal gestation as reported in Canada (4) and multiparty in developing countries also contribute towards development of PRAKI (3,4,7, 14). The diagnosis of PRAKI lacks international consensus owing to the physiologic and hemodynamic adaptations during pregnancy which are characterized by increase in vascular volume and hyperfiltration. Therefore the estimation of glomerular filtration rate is based on combination of both laboratory findings such as measurement of creatinine and/or clinical features like determination of urinary output(3,4, 6,12,19).

1.1 Foetal outcome in patients with PRAKI

Pregnancy related acute kidney injury remains a great threat to foetal wellbeing as exemplified by an opinion piece in the Lancet, published in 1975 which stated: ‘Children of women with renal disease used to be born dangerously or not at all’(12). The statement emphasized how renal disease in pregnancy affected the foetus in utero and at birth. Acute kidney injury in pregnancy is associated with serious foetal morbidity such as premature births, small for gestational age and intrauterine growth restriction (2-9) and 3.9-fold increase in perinatal mortality (13). The mechanisms responsible for the increase in foetal morbidity and mortality in PRAKI remain unclear (1-4,7,18-19). However, the primary cause of uremia in the mother could be the main contributing factor. Pyelonephritis increases the risk of preterm deliveries whereas premature delivery of foetus may be indicated in preeclampsia and eclampsia since the delivery of the placenta is in these conditions of therapeutic benefic. Unfortunately, such early delivery to save the mother may compromise foetal survival (2-11,19-20). Uric acid above 363µmols/land prenatal blood pressure above 160/110 mmHg are independent risk factors for poor fetal outcomes (17-18). Bilateral ureteric compression by the gravid uterus, a rare cause of PRAKI especially in women with multifetal gestation is also associated with poor foetal outcomes (20).

Foetal outcomes have been shown to vary widely across socioeconomic settings in women with PRAKI (1-4,7,9,15-19,20). Studies in developing world such as India and Africa demonstrate high perinatal mortality ranging from 10-40% in women with PRAKI (8, 9, 16,19), while in developed countries like Canada perinatal mortality was less than 2.7% (4). However preterm deliveries, low birth weight and small for gestation was common at 35.6% in women with PRAKI requiring dialysis in the same study in Canada (4). There are no local publications on foetal survival in patients with PRAKI in Kenya. Therefore, it was necessary to find out how PRAKI impacted on the foetal survival in KNH a referral facility 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 Labour ward and Post-natal wards of KNH.

2.3 Study population: The study population were pregnant women with gestation age equal to or above 28 weeks and postpartum women within six weeks after delivery, who were admitted to the Labour ward or the post-natal wards of KNH.

2.4 Inclusion criteria: Pregnant women with gestation of ≥28 weeks and postpartum women within six weeks with deranged serum creatinine meeting the operational definition of PRAKI in any of the stated wards willing to sign consent to enrol in the study.

2.5 Exclusion criteria: Women with chronic kidney disease, or pregnant with gestation age less than 28 weeks or in postpartum for more than six 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: Due to the limitations in estimation of GFR in pregnancy as a result of 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 ≥ 26.5µmols/L within 48 hours, or a similar rise in creatinine above normal limit of the reference laboratory or an increase in serum creatinine 1.5 times of the baseline within seven (7) days, assuming a normal GFR of 75mls/minute per 1.73m². Renal function tests are not part of the routine antenatal profile, so most of the patients did not have their pre pregnancy or early pregnancy baseline serum creatinine.

2.9 Clinical methods: Patient management was left at the discretion of attending clinician. The principal investigator and or the research assistant identified patients with deranged renal function tests in the respective wards by screening through the file for laboratory reports on daily basis and applying the operational criteria for definition of PRAKI. Women whose results fitted the operational diagnostic criteria for PRAKI were then approached and introduced to the study. They were given verbal description of the study requirements and explained that, if they agreed to enrol into the study, the principal investigator or the research assistant would carry out verbal interviews and will need permission to access and extract information from the patient’s medical file and that the benefits will include sharing the interpretation of results with the patient and the
primary healthcare provider for relevant medical intervention. The patient was also informed that, there were no risks involved and that participation in the study was voluntary and withdrawal from the study would not compromise service delivery. Those who consented to enroll into the study were registered and assigned a study serial number which was placed on the cover of their medical record file for easy access. Their medical records were then assessed, and data capture form was used to extract demographic and clinical data from the file and from the patient through verbal interviews. Follow up was until discharge or a maximum of two weeks which ever came first.

Baseline data included demographic profile of the participant and clinical profile including age, residence, marital status, referral status, presenting complaint, past medical and obstetric history, current obstetric and non-obstetric diagnosis and results of physical examination and laboratory findings including full hemogram, renal function tests and liver function tests were also noted. The outcomes documented included both pregnancy and foetal outcomes. Mode of delivery, gestation age and foetal status at birth. Pregnancy outcome was categorized into delivered or pregnancy on going after two week follow up or until discharge, which ever came first, mode of delivery as spontaneous vertex delivery or caesarian section. Foetal outcome included gestation age at birth, delivery before 37 completed weeks was considered premature birth. Status at birth was categorized as live infant or as fresh still birth.

Maternal status - a life or dead was also documented at the end of two-week follow-up or at discharge which ever came first.

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. Descriptive statistics were used to summarize the findings where continuous variables were described in means or median and categorical variables were summarized into frequencies. Other statistical test results were presented in tables.

III. Results
A total of 66 (3.2%) participants were enrolled into the study out of 2068 admissions. The participants were mainly young women whose mean age was 28 (SD 5.9) years and peak age between 26 - 30 years (34.8%). Age range was 15 to 44 years.

<table>
<thead>
<tr>
<th>Age in years</th>
<th>n</th>
<th>%</th>
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<tbody>
<tr>
<td>≤ 20</td>
<td>6</td>
<td>9.1</td>
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<tr>
<td>21 – 25</td>
<td>18</td>
<td>27.3</td>
</tr>
<tr>
<td>26 - 30</td>
<td>23</td>
<td>34.8</td>
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<tr>
<td>31 - 35</td>
<td>11</td>
<td>16.7</td>
</tr>
<tr>
<td>&gt; 35</td>
<td>8</td>
<td>12.1</td>
</tr>
</tbody>
</table>

Table 1: Age distribution of Participants with PRAKI

Table2: Foetal outcome in PRAKI

<table>
<thead>
<tr>
<th>Age at birth</th>
<th>Life infant n=43</th>
<th>Fresh still birth n=17</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preterm&lt;37 weeks</td>
<td>23</td>
<td>10</td>
<td>33 (55.0)</td>
</tr>
<tr>
<td>Term&gt;37 weeks</td>
<td>20</td>
<td>7</td>
<td>27 (45.0)</td>
</tr>
<tr>
<td>Total</td>
<td>43 (71.7)</td>
<td>17 (28.3)</td>
<td>60 (100)</td>
</tr>
</tbody>
</table>

A total of 60 pregnancies were delivered and six were ongoing as at the end of follow up period. Delivered by spontaneous vertex delivery were 39 (65%) and by caesarian section were 21 (35%). The average gestation age at birth was 35 weeks with 33 (55%) preterm infants. Life infants were 43 (71.7%) and fresh still births were 17 (28.3%). The ratio of fresh till birth among participants was 1:4.

IV. Discussion
In our study, we enrolled sixty-six participants out of a total of 2068 admissions. We therefore demonstrate prevalence of PRAKI of 3.2%. Our prevalence was higher than a prevalence of 1.8% reported in India by Prakash et al., 2010 (5) and lower than 8.1% reported in Malawi by Cooke et al. (9) in a similar study setting. Differences in prevalence in the developing countries may be explained by differences in criteria for patient selection. We did not cite any past publications on prevalence of PRAKI in Kenya, as such we could not comment on any change in the local prevalence of PRAKI in Kenya.
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Recent studies in developed world such as Canada and United States of America have demonstrated paradoxical rise in incidence of PRAKI from 1.6 to 2.7% and 2.3 to 4.5% respectively. The increase in incidence of PRAKI is related to increase in lifestyle diseases such as diabetes mellitus and hypertension and emerging advanced maternal age (4,5,7,9,16-20).

The study population consisted of young women whose peak age was between 26 to 30 years. The peak age compared with that reported in India (10), Morocco (7), Malawi (9) and in many other studies in the developing world (1-3,7-10) and lower than 30-39 years in Canada (4). Availability of advanced reproductive health technology in the developed world may explain differences in peak maternal age between developing and developing world(4).

To the best of our knowledge, this was the first study to determine the impact of PRAKI on foetal outcome in Kenya

Renal complications in pregnancy are associated with increased foetal morbidity such as preterm deliveries, intrauterine growth retardation and increased mortality (3-6,17-21). The actual cause of these foetal complications is thought to be related to both maternal and uremic factors (4,19-21).

We demonstrate average gestational age at birth 35 weeks. Preterm infants were the majority (55%). Foetal mortality was 17(28.3%), of whom 10 were preterm. The rate of prematurity in our study was higher than in Canada, where Hildebrand et al. (4) reported 32.5% premature infants however without stillbirths. While in a study in India, the rate of prematurity was higher as reported by Mahesh et al. (15) where preterm infants were 89% and fresh still births were 26%.

Among the study participants, the ratio of fresh still births was 1:4 while the ratio of fresh still births among non-participants in the same setting was 1:2.3. Wetherefore demonstrates a 6-fold increase in fresh still births.

The rate of fresh still births in this study was higher than reports 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 foetal mortality in our setting may be related to serious maternal complications at presentation and strained human resources.

V. Conclusion

Pregnancy related acute kidney injury was associated with increased premature deliveries with average gestation age of 35 weeks and asix (6) fold increase in fresh still births.

Conflict of interest

The authors declare no conflict of interest

References


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