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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 postpartumperiod. It often impacts negatively on foetaloutcomes.*
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 post-natal wards at KNH. The study started afterit was approved by the KNH- University of Nairobi Ethics and Research Committee.Patient management was at the discretion of attending clinician.Data was obtained fromthe participants and their medical records. Followupwas until dischargeor for a maximum of two weeksfor those who remained in the wards.*
Results: *Total participantswere 66 out of2068 admissions. Their mean age was 28years with peak age between 26-30 years.The prevalence of PRAKI was 3.2%. Sixty (91%) participants weredelivered andsix pregnancies were ongoing past the follow-up period.The average gestation age at birth was 35 weeks. Forty-three (71.7%) were life 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 23deliveries.*
Conclusion: *Wetherefore 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 inpregnancy andor in the postpartum period. It is often associated with significant foetalmorbidity 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 inthe general population and had decreased from 1:3000 to 1:20000 pregnancies following reduction of septic abortions through improved obstetric care.However, recent studiesdone a decade ago in the United States and Canada demonstrated paradoxical increase in the incidence of PRAKI.In the United States,the incidence increased from2.3 to 4.5 /10000 deliveries between 1998 and 2008.In Canada, there was recorded increase in incidence from 1.6to2.7/10000 between 2003and 2010.The temporal change in the incidence of PRAKI isassociatedwith increase in lifestylerelated diseasessuch as hypertension and diabetes andadvanced maternal ageattributableto advances in reproductive healthservices (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 hydroureterand hydronephrosis from compression by the gravid uterus, theaetiologic factors of PRAKIare similar to those in the general population and can be categorized into three: i)Prerenal azotemiaarising 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, whichcontribute,approximately 75% ofall cases (4,6-15,18).

While maternal characteristics such asadvanced maternal age, multifetal gestation as reported in Canada (4) and multiparty in developing countries alsocontribute towards development of PRAKI (3,4,7, 14).
The diagnosis of PRAKIlacks 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 findingssuch as measurement of creatinine andor clinical features like determination of urinary output(3,4, 6,12,19).

1.1 Foetaloutcome in patients with PRAKI

Pregnancy related acute kidney injury remains a great threat to foetalwellbeing 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 foetalmorbidity 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 PRAKIremains unclear (1-4,7,18-19). However, theprimary cause of uremia in the mother could be the main contributing factor. Pyelonephritis increases the risk of preterm deliveries whereas premature delivery of foetusmay be indicated in preeclampsia and eclampsia since thedelivery of the placenta is in these conditions oftherapeuticbenefit.Unfortunately,such early delivery to safe the mother may compromise foetalsurvival (2-11,19-20).Uric acid above 363µmols/land prenatal blood pressureabove 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 Canadaperinatal mortality was less than 2.7% (4).However preterm deliveries, low birth weight and small for gestation was common at 35.6% inwomen with PRAKI requiring dialysis in the same study in Canada (4).

There are no local publications on foetalsurvival in patients with PRAKI in Kenya.Therefore, it was necessary to find outhow PRAKI impacted on the foetalsurvival inK.N.H 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 tothe 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 with deranged serum creatinine meeting the operational definition of PRAKI in any of the stated wards willing to sign consent tobe enrolledin 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
***2.8Diagnosis 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 usedfor 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 $\geq$ 26.5µmols/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 1.73m^2 .
Renal function tests are not part of the routine antenatal profile,so most of the patientsdid 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 operationaldiagnostic criteria for PRAKI were then approachedand introducedto the study. They were given verbal description of the study requirements and explained that,if they agreed to enroll 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 informedthat, 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 andfrom 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, maritalstatus, referralstatus, presentingcomplaint, 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 pregnancyand foetaloutcomes. Mode of delivery, gestation age and foetalstatus 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 life 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 (SD5.9) years and peak age between 26-30 years (34.8%). Age range was 15 to 44 years.

Table 1 Age distribution of Participants with PRAKI

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

Table2: Foetal outcome in PRAKI

Foetal status at birth (n=60)			
Age at birth	**Life infant n= 43**	**Fresh still birth n=17**	**Total %**
Preterm< 37 weeks	23	10	**33 (55.0)**
Term >37 weeks	20	7	**27 (45.0)**
Total	**43 (71.7)**	**17(28.3%)**	**60 (100)**

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 weekswith 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 ourstudy, 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 citeany 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.

Recent studies in developed world such as Canada and United States of America have demonstrated paradoxical rise in incidence of PRAKIfrom 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 asdiabetes mellitusand hypertensionand emerging advanced maternal age (4,5,7-9,16-20).

The study population consisted ofyoung womenwhose peak age wasbetween 26 to 30 years. The peak age compared withthat reported in India (10), Morocco (7), Malawi (9) and in manyother studies in the developing world (1-3,7-10) and lower than 30-39 years inCanada (4). Availability of advanced reproductive health technology in the developed world mayexplain differences in peak maternal age between developed 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 pregnancyare associated with increasedfoetal morbidity such as preterm deliveries, intrauterine growth retardation andincreased mortality (3-6 -17-21).The actual causeof thesesfoetal complications is thought to be related to both maternal and uremic factors (4,19-21).

We demonstrate average gestational ageat birthwas 35 weeks. Preterm infants werethe majority ,33 (55%). Foetal mortality was 17(28.3%),of whom 10 were preterm.The rateof prematurity in our study was higher than in Canada,whereHildebrand 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 was1:4 while the ratio of fresh still births amongnon-participants in the same setting was 1:23. Wetherefore demonstratesix (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 etal, 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 berelated toserious 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 authorsdeclare no conflict of interest

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