TMJ
Original research
Published by OJS
Doi: 10.4314/tmj.v33i3.539.g298
OPEN ACCESS JOURNAL

Prevalence, Risk Factors and Short-term Outcomes of Acute Kidney Injury in Women with Obstetric Complications in Dar es Salaam, Tanzania

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Abstract

Introduction

In keeping abreast with the International Society of Nephrology "0by25" initiative that aims at achieving zero preventable deaths from Acute Kidney Injury (AKI) by the year 2025, we investigated on Pregnancy-Related Acute Kidney Injury (PRAKI), a potentially preventable cause of AKI but still commonly reported in developing countries as a significant contributor to both maternal and fetal morbidity and mortality. In this study, we report on the prevalence, risk factors and outcomes of PRAKI among pregnant women with obstetric complications at Muhimbili National Hospital (MNH), Dar es Salaam, Tanzania.

Methodology

This was a hospital-based descriptive cross-sectional study involving women with obstetric complications in late pregnancy at MNH, Dar es Salaam, Tanzania from August 2015 to February 2016. Acute Kidney Injury Network (AKIN) criterion was used to define acute kidney injury (AKI). Data analysis was done using the Statistical Package of Social Sciences (SPSS) version 23.

Results

During the study period a total of 5448 deliveries occurred at MNH amongst whom 1150 (21.1%) women had obstetric complications. Overall, AKI occurred in 99(8.6%) and was stage-wise categorized into AKIN Stage I in 55/99(55.5%), Stage II in 8/99(8.1%), and Stage III in 36/99 (36.4%). Hemolysis, Elevated Liver enzymes, Low Platelet count (HELLP) syndrome and severe pre-eclampsia were the most frequent obstetric complications among patients with PRAKI. PRAKI was associated with advanced maternal age, being HIV positive, having history of hypertension and/or having elevated blood pressure, albuminuria and having anemia detected during antenatal clinic (ANC) visits. Among patients who developed PRAKI; hemodialysis therapy was offered to 6/99(6.1%) patients who after several rounds of therapy were able to recover their renal function; 66/99 (66.7%) had partial recovery of renal function whereas 27/99 (27.3%) had complete spontaneous recovery of their renal function without need of hemodialysis therapy. On considering fetal outcome; PRAKI was associated with delivering a stillbirth baby.

Conclusion

In this novel study on PRAKI in Tanzania, we found that PRAKI is common among women with obstetric complications and strong associated with advanced maternal age, being HIV positive, having history of hypertension, albuminuria or anemia detected during antenatal clinic visits. Early recognition and treatment of PRAKI may help prevent associated poor maternal and fetal outcomes and in a broader sense, it a significant step forward into achieving the ISN "0by25" global initiative in Tanzania.

Keywords: *Acute Kidney Injury, Women with Obstetric Complications, Tanzania.*

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Introduction

The International Society of Nephrology (ISN) “0by25” initiative targets at achieving zero preventable deaths from Acute Kidney Injury (AKI) by the year 2025 with a special emphasis on developing countries where morbidity and mortality attributed to preventable AKI is still unacceptably high (1). The incidence of pregnancy-related acute kidney injury (PRAKI) differs significantly between developed and developing countries. Estimated incidence in developed countries is 1 in 20,000 (0.005%) births while that in developing countries occurs in up to a quarter of women with obstetric complications (2, 3). Poverty, lack of awareness and difficulty in accessing obstetric care account for this observed difference between developed and under-developed countries (4).

PRAKI may occur at any stage of pregnancy, both ante-partum or post-partum. Presence of obstetric complications during pregnancy, delivery or puerperium such as antepartum hemorrhage, pre-eclampsia, eclampsia, postpartum hemorrhage or sepsis increase the incidence of AKI in pregnancy (5).

Despite being a potentially preventable condition, PRAKI connotes high risk of progression to bilateral renal cortical necrosis and, consequently, to chronic kidney disease (6). The World Health Organization (WHO) regions that are overburdened with obstetric complications such as Sub Saharan Africa need to focus on preventing PRAKI as it contributes up to 30% of the causes of (potentially preventable) AKI in these populations (4, 7).

PRAKI is a frequent cause of maternal and fetal morbidity and mortality in developing countries (8). In general, mortality associated with AKI seems to be variably increasing with advanced age, greater degree of illness, severity at presentation, presence of chronic kidney disease, need for mechanical ventilation, hypotension or need for inotropic support (9,10). Furthermore, degree of change in serum creatinine, need for dialysis and prolonged duration of oliguria are all associated with increased rate of dialysis dependency (10). To improve maternal and fetal health, prevention and timely treatment of PRAKI is therefore warranted. In this study, we determined the prevalence of PRAKI among women with obstetric complications, teased out associated risk factors and reported on short-term (maternal and fetal) outcomes at MNH, Dar es Salaam, Tanzania which in this context, serves as a proxy for a wider WHO Sub Saharan region.

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Materials and Methods

Study population and design

This was a cross-sectional descriptive study conducted among women with obstetrical complications from their 28th week of pregnancy to early postpartum period (up to 7 days post-delivery) admitted in the obstetric wards at the Muhimbili National Hospital between August 2015 and February 2016. Muhimbili National Hospital is a tertiary referral and teaching hospital situated in Dar es Salaam, Tanzania. The Maternity Block at MNH consists of 7 wards out of which four wards are dedicated to admission of women with antenatal and postnatal complications. The remaining three wards are the labor ward, postnatal ward for normal deliveries and an obstetric ICU for patients with severe pre-eclampsia, eclampsia and critical maternal conditions.

Obstetrics Complications

A broader definition of obstetrical complications entails complications occurring during pregnancy, delivery or puerperium. In this study we included women with hypertensive disorders of pregnancy (i.e. pregnancy induced hypertension, pre-eclampsia and eclampsia), severe anemia, hemorrhages (antepartum and postpartum), HELLP (Hemolysis, Elevated Liver enzymes and Low Platelets) and infections (intrapartum and postpartum sepsis and severe malaria etc.).

Data collection process

We collected data by interviewing women and/or their next of kin using a pre-tested investigator- administered questionnaire. Additional information related to their clinical progress during antenatal (ANC) visits was obtained from their respective standard Reproductive and Child Health (RCH) cards. We recorded gravidity, gestational age at first ANC booking visit, number of ANC visits made; blood pressure, presence of anemia, albuminuria and lower limb edema during pregnancy as well as HIV status. Patients were also interrogated on past history of established kidney disease (excluded if known to have chronic kidney disease), hypertension, diabetes mellitus, HIV infection, liver disease and chronic obstructive pulmonary disease (COPD).

Patients were screened for clinical and laboratory evidence of AKI. Urine output was obtained from a patient's urine output chart and recorded at admission, 6, 12, and 24 hours. Serum creatinine level at admission was retrieved from patients' records computer system. For patients without such results, blood samples were taken by the investigator and research

assistants on the day of admission and were tested at the hospital's laboratory. Serum creatinine level was repeated within 48 hours from baseline. The diagnosis of AKI was made based on two serum creatinine values taken within 48 hours with an increase in serum creatinine of ≥26.4 µmol/l or a percentage increase in serum creatinine of ≥50% (1.5× baseline value) or a urine output of <0.5ml/kg/hr for more than 6 hours according to the AKIN diagnostic criteria (11,12).

During data analysis, we decided to define AKI based on increase in serum creatinine only and dropped the definition based on urine output largely due to potential inaccuracies and inconsistencies that might have happened during collection of timed urine output.

Patient care and outcomes

Patients who were diagnosed to have PRAKI were managed by the nephrologist on call. Hemodialysis was offered whenever indicated. Patients were visited regularly until discharge from the hospital. Fetal outcomes were recorded and maternal PRAKI outcomes (complete or partial recovery of renal function) or deaths were recorded at discharge.

Complete recovery from Acute Kidney Injury was declared when serum creatinine values returned to normal ranges at discharge from ward. Partial recovery was declared when serum creatinine values showed improvement but did not return to normal range.

Statistical methods

Data were coded and initially entered into a Microsoft excel spread sheet and then transferred into IBM® SPSS® version 23 for analysis. Categorical data were summarized as frequencies and proportions. Statistical associations were tested using chi-square test. Univariate and multivariable logistic regression analysis were performed to evaluate for associated factors. Multivariable analysis was performed using variables which had a p-value of <0.2 in the univariate analysis (13). A two-tailed p-value <0.05 was considered statistically significant.

Ethical considerations

Ethical clearance and permission to conduct the study were sought from the Senate Research and Publications Committee of Muhimbili University of Health and Allied Sciences and the Muhimbili National Hospital research administrative office, respectively. Verbal and written informed consent were obtained from patients and or their next of kin. Care was provided to all patients according to the hospital guidelines.

Results

During the six-month study period (August 2015 to February 2016), 5448 deliveries were conducted at Muhimbili National Hospital out of which 1150 (21.1%) women had obstetric complications and were eligible for enrollment into this study (Figure 1). The overall mean age was 28.0 ± 6.7 years, 95.1% were married, only 26.5% had were educated beyond primary school level (Table 1) , majority (43.0%) were in their second or third pregnancy, had normal blood pressure (70.6%) at enrollment and only 4.5% were them known to be HIV positive status.

Table 1: Socio-demographic characteristics of women with obstetric complications at Muhimbili National Hospital, Dar es Salaam, Tanzania (N= 1150)

Demographic Parameter	n(%)
Age group (years)	
≤ 20	193 (16.8)
21 to 25	246 (21.4)
26 to 30	299 (26.0)
31 to 35	242 (21.0)
≥ 36	170 (14.8)
Marital status	
Single	48 (4.2)
Married	1094 (95.1)
Divorced/separated	8 (0.7)
Level of Education	
No formal education	51(4.4)
Primary school	795 (69.1)
Secondary school	224 (19.5)
Higher education	80 (7.0)
Occupation	
Civil servant	123 (10.7)
Business/Self-employed	529 (46.0)
Housewife	407 (35.4)
Peasant	91 (7.9)

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Prevalence of PRAKI

Prevalence of PRAKI among women with obstetric complications was 8.6% (99/1150), and was further categorized according to AKIN criteria into Stage I 55/99(55.5%), II 8/99(8.1%), and III 36/99(36.4%) respectively. The overall mean age (±SD) for all patients was 28.0 ± 6.6 years. The mean age of patients with AKI was 30 ± 5.9 years which was significantly higher compared to the mean age of patients with no AKI which was 27 ± 6.6 years (p = 0.002).

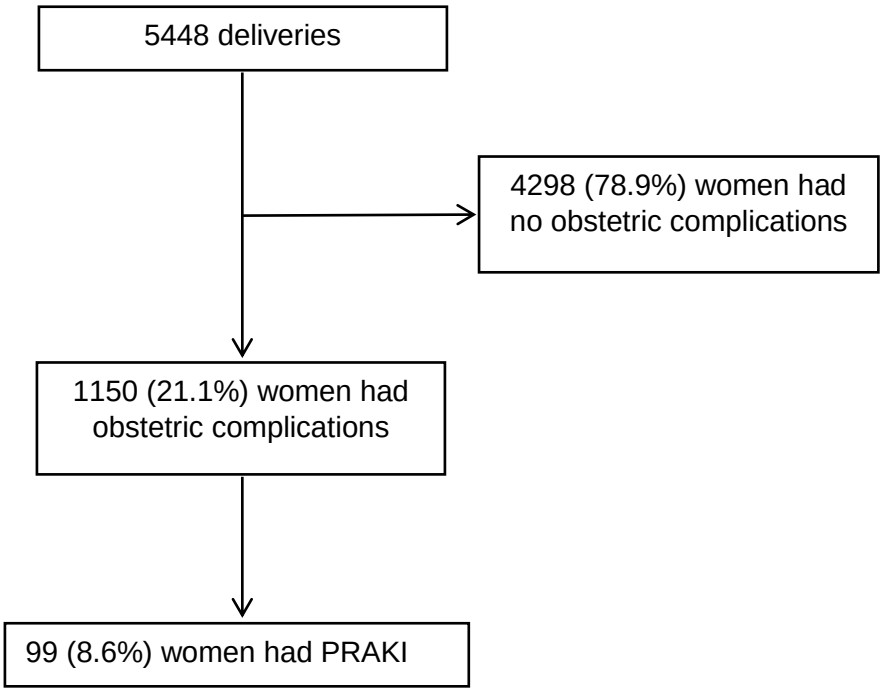

Figure 1. Flow diagram showing our selection process to women with PRAKI at Muhimbili National Hospital

Obstetric complications in patients with PRAKI

Of the 99 women with AKI, 27 (27.3%) had HELLP syndrome, 21 (21.2%) had severe pre-eclampsia, and 15 (15.2%) had postpartum hemorrhage. Most common obstetric complications were; hypertensive disorders of pregnancy 41/99 (41.4%), HELLP syndrome 27/99 (27.3%) and peri-partum hemorrhage 19/99 (19.2%) (Figure 2).

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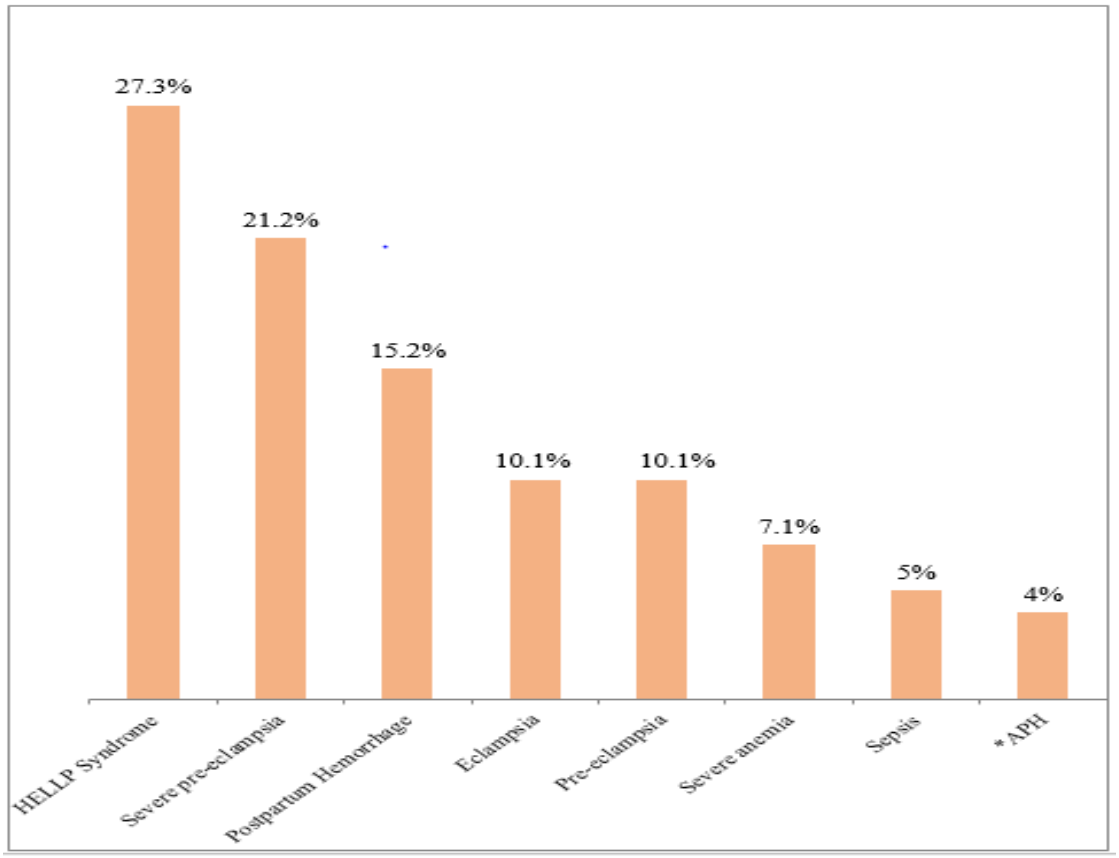

Figure 2. Obstetric complications among women with PRAKI at Muhimbili National Hospital

**APH-Antepartum hemorrhage, HELLP-Hemolysis, Elevated liver enzymes, Low platelet*

*** Pre-eclampsia, Eclampsia and Severe Pre-eclampsia are clinically distinct conditions of the same continuum*

Factors associated with PRAKI among women with obstetric complications

In univariate analysis, PRAKI was significantly associated with advanced maternal age, increased gravidity, being hypertensive, anaemic and HIV positive status among other factors. In multivariable analysis, independent factors for PRAKI included; maternal age, HIV infection, and detection of high blood pressure and/or albuminuria during ANC visit (Table 2).

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Table 2: Factors associated with AKI among women with obstetric complications at Muhimbili National Hospital, Dar es Salaam, Tanzania

Variable	Total	AKI, n (%)	OR (95% CI)	p-value	AOR (95% CI)	p-value
Age groups (years)						
≤ 20	193	3 (1.6)	ref		ref	
21 to 25	246	18 (7.3)	5.00 (1.45 – 17.23)	0.01	4.92 (1.37 -17.61)	0.01
26 to 30	299	25 (8.4)	5.78 (1.72 – 19.41)	0.005	4.53 (1.24 – 16.53)	0.02
31 to 35	242	21 (8.7)	6.02 (1.77 – 20.49)	0.004	4.36 (1.13 – 16.75)	0.03
≥ 36	170	32 (18.8)	14.69 (4.41 – 48.93)	<0.001	9.93 (2.58 – 38.23)	0.001
Gravidity						
1	398	19 (4.8)	ref		ref	
2-3	495	42 (8.5)	1.85 (1.06 – 3.23)	0.03	1.32 (0.69 – 2.52)	0.4
4 and above	257	38 (14.8)	3.46 (1.95 – 6.15)	<0.001	1.74 (0.82 – 3.71)	0.2
Blood pressure at ANC						
Normal BP	808	46 (5.7)	ref		ref	
High BP	337	51 (15.1)	2.95 (1.94 – 4.50)	<0.001	4.54 (2.65 – 7.78)	<0.001
Albuminuria						
Absent	1098	89 (8.1)	ref		ref	
Present	47	8 (17.0)	2.33 (1.05 – 5.13)	0.04	2.76 (1.12 – 6.82)	0.03
Hemoglobin status						
Normal	634	42 (6.6)	ref		ref	
Anemic	511	55 (10.8)	1.70 (1.12 – 2.59)	0.01	1.69 (1.05 – 2.71)	0.03
Hypertension						
No	648	62 (9.6)	ref		ref	
Yes	502	37 (7.4)	0.75 (0.49 – 1.15)	0.2	0.32 (0.18 -0.57)	<0.001
Diabetes Mellitus						
No	1142	97 (8.5)	ref		ref	
Yes	8	2 (25.0)	3.59 (0.72 – 18.03)	0.1	2.49 (0.46 – 13.56)	0.3
HIV infection						
No	1098	89 (8.1)	ref		ref	
Yes	52	10 (19.2)	2.70 (1.31 – 5.56)	0.007	2.40 (1.05 – 5.52)	0.04

Management of women with obstetric complications and maternal outcomes at discharge

Of the 99 women with PRAKI, 9/99 (9.1%) had indications for dialysis of which 6/99 (6.1%) were offered hemodialysis therapy. The remaining 3 patients with indications for hemodialysis could not be offered the therapy due to lack of hemodialysis machines dedicated for patients who were HIV and Hepatitis B positive at the time when this research was carried out. Therefore 93/99 (93.9%) of women with PRAKI were managed conservatively. Clinical indications for hemodialysis included; electrolyte imbalance, uremic

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complications and volume overload unresponsive to medical treatment. Out of 99 women with PRAKI, deaths occurred in 4% and 27 (27.3%) had complete recovery of renal function at discharge from hospital (Figure 3).

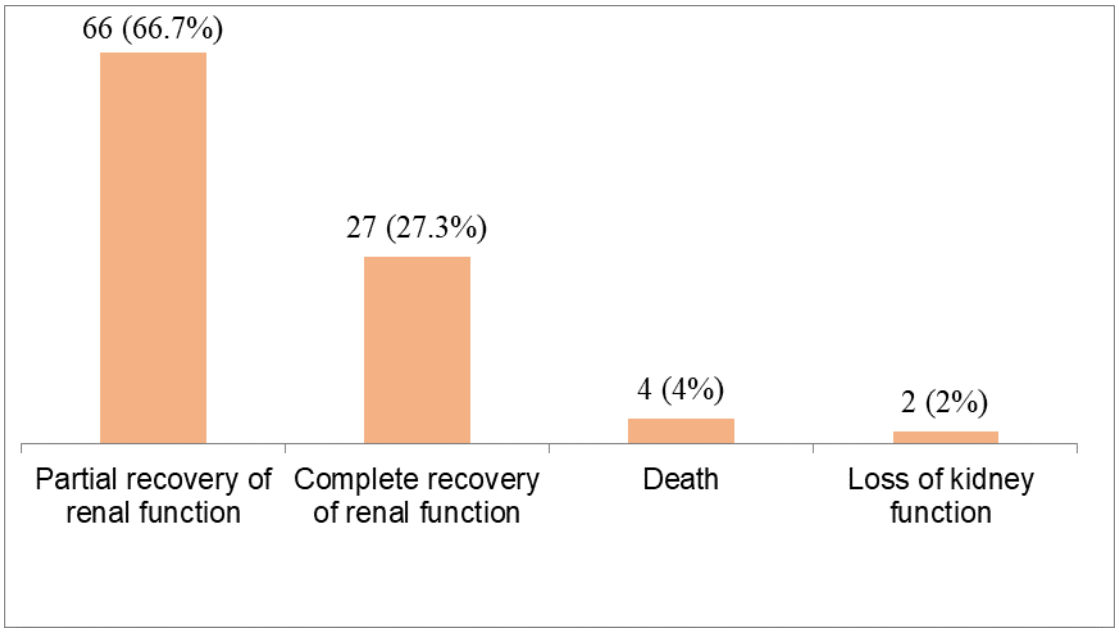

Figure 3. Maternal outcomes at discharge among patients with PRAKI at Muhimbili National Hospital (n=99)

Association between AKI and fetal outcomes

Stillbirths occurred in 47/99 (47.5%) of women with PRAKI, as opposed to 81/976 (8.3%) stillbirths among women without AKI, p<0.001(Figure 4).

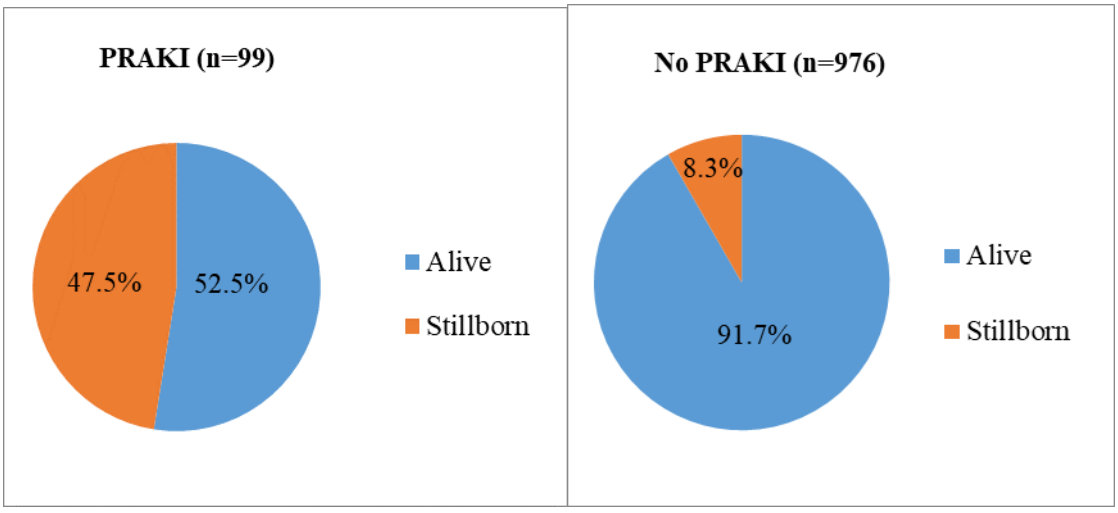

Figure 4. Association between PRAKI and fetal outcomes among women with obstetric complications admitted at Muhimbili National Hospital (N=1075)

Discussion

In this study, we report the prevalence of PRAKI of 8.6% among women with obstetric complications and found it to be associated with increasing maternal age, HIV positive status, high blood pressure, albuminuria and anemia detected during ANC visits. Further, we found that PRAKI is significantly associated with worse fetal outcomes.

The prevalence of AKI among women with obstetric complications in this study was comparable to that reported from other centers (6,12,14). The observed prevalence of AKI may be over-estimation due to referral bias as Muhimbili National Hospital is a tertiary referral hospital where over a fifth of all women who give birth experience obstetric complications and are therefore at an increased risk of developing PRAKI.

Severe preeclampsia (with or without HELLP syndrome), eclampsia and or preeclampsia were risk factors for PRAKI in our study. This is consistent with findings form other developing countries where hypertensive disorders of pregnancy represented the main risk of developing PRAKI (10,15,16,17). Hemorrhage (antepartum or postpartum) was noted in 19.2% of women with PRAKI similar to that reported by Prakash et al who reported hemorrhage as a cause of PRAKI in 18.8% (18). However, in contrast to our findings, Naqvi et al. reported uterine hemorrhage as a dominant cause (58%) of PRAKI (19). High blood pressure and anemia during pregnancy can compromise the ability to tolerate obstetric complications such as hemorrhage during delivery (20).

Women with advanced age resulted into higher odds of PRAKI comparable with an earlier study by Arryhani et al (10). Advanced maternal age, hypertensive disorders of pregnancy and bleeding complications are all associated with increased perinatal complications (21). Further, we found that lack of antenatal clinic attendance and presence of high blood pressure, albuminuria and anemia during pregnancy were significantly associated with PRAKI.

Sub-optimal access and prompt antenatal care still prevails in developing countries and can significantly influence early recognition of high risk pregnancies. In a study done in north India, Patel et al. reported 53.3% women with PRAKI had not received any antenatal care during pregnancy and had undergone traditional birth attendant assisted home delivery (22). Similarly, Bentata et al. noted 67.4% of women with PRAKI lacked prenatal care (23). Limited access to prenatal care is more than a medical problem and is attributed to socio-cultural and economic barriers.

In resource-limited settings like ours, access to hemodialysis therapy is yet another hurdle that women with PRAKI have to surmount. In this study, hemodialysis therapy was offered to

only (6.1%) of those who developed PRAKI. Other studies have reported higher rates of hemodialysis in PRAKI (3,10,15,16,18). The relatively low percentage of pregnant women with AKI requiring dialysis in our study may be explained on one hand, by the fact that over half (55.5%) of them were categorized as being in AKIN stage 1 in which renal function is still preserved and diuresis is maintained, and on the other hand, by stringent criteria for initiation of dialysis in our setting at the time when this study was being conducted. Furthermore, failure to initiate dialysis in some patients who had indications added to the observed lower proportion of patients who received hemodialysis therapy.

We found that at discharge from hospital, about two-thirds of women with PRAKI had partial recovery of renal function, 27.3% had complete recovery of renal function whilst the remaining 2% had loss of kidney function. These findings are in contrast to other studies on PRAKI that have reported that over 50% of women with PRAKI had complete recovery of renal function (6,10,14–16,18,24). We hypothesize that the lower proportion of complete recovery at discharge in our study could be due to premature discharge of patients with PRAKI before full recovery. Ideally, kidney function should be evaluated at 3 months post AKI to determine if full recovery (e GFR ≥60ml/min), partial recovery (e GFR 15-59ml/min) or loss of kidney function (e GFR<15ml/min) has occurred.

Due to loss of follow-up, it is difficult to wait for 3 months post discharge to classify renal recovery, henceforth in this current study, we decided to classify renal recovery at point of discharge (albeit this might be too early) to minimize loss of follow up at 3 months. Therefore, the differences in the duration of follow up might in part explain the varying proportions of recovery of renal function observed in different studies.

In our study mortality among women with PRAKI was much lower when compared to that reported in other developing countries (15-20%) (6,10,14–16,18,24). Again, we hypothesize this may be due to the fact most women with PRAKI were in AKIN stage 1. Perinatal mortality in women with PRAKI was comparable to findings from other studies, this justifies that PRAKI is an important risk factor of perinatal mortality (16,25).

Study limitations

There is a potential for some recall bias as some information (e.g. status of co-morbidities) was inquired from patients themselves (e.g. history of kidney disease, HIV infection, diabetes or hypertension). Also, as pointed above, classifying renal recovery at point of discharge might be too early as compared to the ideal timing (3 months post AKI). This might lead to over or under estimation of the proportions of recovery. However, as stated in the

title, this study explored on short-term outcomes and was not designed to follow up patients upon discharge from the hospital. It is thus desirable to design and conduct a similar study but with a longer follow-up time to explore the full extent of maternal outcomes as well as fetal outcomes.

Conclusion

Pregnancy-related acute kidney injury (PRAKI) is common among women with obstetric complications and is associated with harbingers such as advanced maternal age, having high blood pressure, albuminuria or anemia as detected during antenatal clinic visits. Therefore offering optimal antenatal care by early detection and management of conditions such as anemia, albuminuria and hypertension might reduce the incidence of PRAKI and improve maternal and fetal outcomes.

Data Availability

The data supporting this study is available upon request from the author

Conflicts of Interest

The authors declare no conflict of interest

Funding Statement

This work emanates from academic requirements, so no funding was received.

Acknowledgement

We extend our sincere gratitude to the patients who consented and voluntarily participated in this study.

Author contributions

PR and EA conceived the study, collected data, carried out data analysis and developed the first draft. PK, TB and JM rephrased, formatted and proofread several versions of the manuscript. FF and OK read the final version and provided overall leadership of the research project.

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