ASSESSMENT OF CHARACTERISTICS OF PATIENTS WITH PREGNANCY RELATED ACUTE KIDNEY INJURY IN KENYATTA NATIONAL HOSPITAL

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DEDICATION

To my beloved husband Patrick and my children Waeni, Ndanu and Mumo.

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ABBREVIATIONS

AKI	Acute kidney injury
APH	Antepartum hemorrhage
BP	Blood Pressure
Cr	Creatinine
CKD	Chronic kidney disease
DCM	Dilated Cardiomyopathy
DM	Diabetes Mellitus
E	Electrolytes
eGFR	Estimated Glomerular Filtration Rate
ESRD	End Stage Renal Disease
FBC	Full blood count
g/dl	Grams per decilitre
Hb	Hemoglobin
HELLP	Hemolysis Elevated Liver Enzymes Low Platelets
HIV	Human immunodeficiency virus
HIVAN	Human immunodeficiency associated nephropathy
HTN	Hypertension
HUS	Hemolytic uremic syndrome
K+	Potassium ions
KDIGO	Kidney Disease: Improving Global Outcome
KNH	Kenyatta National Hospital
MDRD	Modification of diet in renal disease
Na+	Sodium ions
PE	Pulmonary embolism
Plts	Platelets
PPH	Postpartum hemorrhage
PR	Pulse rate
PRAKI	Pregnancy related acute kidney injury
RH	Rhesus factor
RPR	Rapid Plasma Reagin
RR	Respiratory rate
RRT	Renal replacement therapy
SPSS	Statistical package for social sciences
SVD	Spontaneous vertex delivery
TBC	Total blood count
TMA	Thrombotic microangiopathy
UECs	Urea, Creatinine, Electrolytes
WBC	White cell count

OPERATIONAL DEFINITION OF PRAKI

Given the limitations in estimation of 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 and PRAKI was defined as increase of serum creatinine by ≥ 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 the patients did not have their pre pregnancy or early pregnancy baseline serum creatinine.

ABSTRACT

Background:

Pregnancy related acute kidney injury (PRAKI) remains a grave complication of pregnancy. Studies on patient characteristics are few and demonstrate diverse patient features.

Objective:

To determine the demographic and clinical characteristics of patients with PRAKI at Kenyatta National Hospital (K.N.H)

Methods:

We carried out a descriptive study on women with gestation age equal to or above 28 weeks and on women in postpartum, within six weeks after delivery. The principal investigator or study assistant introduced study requirements to patients with diagnosis of PRAKI. After consent, clinical and demographic information was obtained from participants through verbal interviews and from medical records using a data capture form. Follow up was until discharge or maximum of two weeks which ever came first. Management of patients was at the discretion of the attending clinician.

Results

Out of 2068 admissions, 66 participants were enrolled into the study. The prevalence of PRAKI was 3.2%. The mean age was 28 years with peak age between 26-30 years. Forty-two (63.6%) were referred from other health facilities, of whom, 24(57.1%) were from rural areas. Nineteen (27.8%) had pre-pregnancy medical conditions, predominantly cardiovascular.

All participants developed one or more obstetric complication: -preeclampsia 28(42.4%), eclampsia eight (9.1%) and hemolysis with elevated liver enzyme low platelet (HELLP) syndrome 17(25.8%). Sixty (91%) pregnancies were delivered. Average gestation age at delivery was 35 weeks, with 33(55%) preterm births, of whom, 10 (30.3%) were fresh still births. Severity of PRAKI at presentation was evenly distributed across stages 1 to 111. Forty-one (62.1%) participants improved on conservative management and 25(37.9%) worsened, of whom, 19 (76.0%) were dialyzed. No maternal mortality was reported during the study.

Conclusion: We demonstrate a prevalence of PRAKI of 3.2% in K.N.H. Hypertensive disorders were the main associated factors. There was high rate of premature births and a six-fold increase in fresh still births among participants.

Chapter one

1.0 Introduction

Acute kidney injury (AKI) is a clinical syndrome characterized by impairment of the excretory functions of the kidney resulting in retention of fluid and waste products in the body. Pregnancy related acute kidney injury (PRAKI) is a rare obstetric complication that is poorly understood, characterized by rapid deterioration of renal functions within hours to days, in pregnancy or in the postpartum period, in otherwise healthy women. It is often associated with significant maternal and foetal morbidity and mortality (1, 2).

Despite paucity of data on incidence and patient characteristics, the few studies done show diversity in the incidence of PRAKI across socioeconomic boundaries. This variation is due to differences in patient demographics, comorbid disease burdens and quality of healthcare services (3). In the developed world, PRAKI contributes 0-1% of all the AKI in the general population while in the developing world PRAKI contributes between 5-20% of all AKI occurring in the general population (4, 5). Recent studies have demonstrated rising trends in the incidence of AKI in the general population and a paradoxical rise in the incidence of PRAKI in developed world which is attributable to increase in lifestyle diseases such as hypertension and diabetes mellitus and rising maternal age due to advances in reproductive services (1-5, 7, 8).

The aetiologies of PRAKI are similar to those in the general population and include pre-renal causes, interstitial and glomerular diseases and post renal causes (2, 4,6 ,12).

During pregnancy, renal and systemic adaptations are associated with decrease in serum creatinine and development of physiologic hydronephrosis and hydroureter which limit use of creatinine clearance or urine output for estimation of glomerular filtration rate. Hence, diagnosis of PRAKI is based on combination of clinical and laboratory parameters (3, 6,10,12,13).

Small derangement in serum creatinine in pregnancy may be associated with profound kidney injury (1-8).

The principles of prevention and management of PRAKI require early identification and treatment of the underlying cause, prevention of further damage and supportive care (2,4,8).

Chapter two

2.0 Literature review

2.1. Physiological changes in pregnancy

During pregnancy, there are both anatomic and physiologic changes in the kidney (4, 6) where the kidney size increases by 1 - 1.5cm and volume increases by up to 30% (3-6). Physiologic hydroureter and hydronephrosis develops in 43% to 100% of pregnant women (6) which is due to the influence of hormones:- progesterone and estrogens and also obstruction by the gravid uterus. The physiologic changes also predispose to, urinary tract infection and pyelonephritis as a result of urinary stasis (2, 6). Pregnancy is also associated with increased production of vasodilators such as prostacyclin and nitrous oxide and relative resistance to vasopressors like angiotensin II, norepinephrine and vasopressin. These changes lead to reduction of systemic vascular resistance (2, 6, 7). Vasodilatation leads to fall of blood pressure by 10mmHg during the first 24 weeks of pregnancy which triggers compensatory increase in cardiac output, plasma volume and renal plasma flow by 80% with subsequent increase in glomerular filtration rate (GFR) by 50% (3,6).These renal and systemic adaptations results in decrease in serum creatinine, urea and uric acid values (6).Tubular functions are also altered and results in glucosuria ,proteinuria , low serum osmolality and low sodium levels (2-7).

2.2 Measurement of kidney function in pregnancy

There is no gold standard for estimation of GFR in pregnant women owing to the physiologic adaptations in pregnancy and it remains an area of research (3, 5). Hyper filtration in pregnancy results in a physiologic decrease in serum creatinine concentration by an average of 35µmol/L (6). This renders estimations of glomerular filtration rate based on serum creatinine concentration inaccurate, however most parameters tend to normalize in third trimester (3-7).

The application of Cockcroft-Gault equation and the Modification of Diet in Renal Disease (MDRD) equations underestimates glomerular filtration rate by 25% in pregnant women with and without preeclampsia(7).

The chronic kidney disease (CKD)-Epidemiology equation, which was developed to provide a more accurate estimate of glomerular filtration rate among patients with higher

glomerular filtration rates, underestimates GFR to a similar degree as the MDRD equation (5 -7,19-22).

Use of 24-hour urine collection for calculation of creatinine clearance is the preferred method for estimation of GFR in pregnant women, however, imprecise due to the delay between urine formation and collection that results from urinary stasis with arising from compression of the ureters by the uterus (3, 6, 7,21-22).

Considering these limitations, assessment of kidney function in pregnancy is determined by examining patient's clinical features and trends in serum creatinine concentration (4,8).

2.3 Acute kidney injury

Acute Kidney Injury is a clinical syndrome characterized by the abrupt decline of renal filtration function that results in the retention of urea and other metabolic waste products in the body , with dysregulation of fluid and electrolyte balance (1- 5).

2.3.1 Pregnancy related acute kidney injury

Pregnancy related acute kidney injury is a complex disease entity that is characterized by rapid deterioration (within hours to days) of renal functions in pregnancy, during child birth and /or the postpartum period. It is associated with significant maternal and fetal morbidity and mortality (1-5, 8-18, 23-32).

2.4 Epidemiology of pregnancy related acute kidney injury

There is no international consensus in the definition of PRAKI and its true epidemiology is not well characterized (1, 3-5). However, the incidence of PRAKI has been shown to vary widely across socioeconomic boundaries and has decreased markedly in the past 60 years, from 20–40% in 1960s to less than 3% Worldwide. This was due to reduction in septic abortions and improvement of perinatal care (4, 5, 8-10). Similarly, the proportion of all AKI cases accounted for by pregnancy related causes has dropped from 20-40% down to 2-10% over the same period of time (3-5, 8-12,33-46).

In the developed countries, the incidence of PRAKI has decreased from 1:3000 to 1:20000 following the disappearance of septic abortion and improvement of perinatal care and contributes 0 -1% of all cases of AKI in the general population (2-4, 8-9,33-39). However, in developing countries, the incidence of PRAKI has remained high and ranges from

5–15% and contributes 5-20% of all AKI occurring in the general population (4, 10, 12,39 ,46). Recent studies in North American populations have demonstrated a paradoxical increase in incidence of PRAKI , from 2.3 to 4.5 per 10,000 in the United States, between 1998 and 2008 with a P<0.05, and in Canada between 2003 and 2010 where the incidence of PRAKI increased from 1.6 to 2.7 per 10,000 deliveries, P < 0.05 (9).This temporal increase was associated with pregnancies in women with advanced age and lifestyle diseases such as hypertension , diabetes mellitus and chronic renal disease (1-5,8, 9, 13).

Hildebrand et al. (4) found that most patients with PRAKI in Canada, were due to, preeclampsia in the postpartum period and the women had been delivered through Caesarean section and that maternal mortality was 4.3%.

In China, Chunhong et al. (14), found, the incidence of PRAKI was 0.81% and most 79.3% of the women were in the third trimester and PRAKI was mainly due to preeclampsia (14). In another study in China by Liu et al, found the incidence of PRAKI was 0.12% among the Han ethnicity, and most were due to obstetric hemorrhage (15).

In India Najar et al (16), reported incidence of PRAKI was 7%, of which 50% were due to septic abortions and 20% were due to obstetric hemorrhage. Maternal mortality rate was at 20%, while in a prospective observational study done between January 2010 and December 2014 by Jeyachandran et al , involving 130 patients, the incidence of PRAKI was 7.8%, of which 68% were in the post-partum period. Sepsis was the main cause of PRAKI, accounting for 39% of the causes, and preeclampsia 21%. Ninety six percent (96%) required dialysis; mortality rate was 8% (17).

In Morocco, Kabbali et al, found in 2010, in a study including 44 patients the incidence of PRAKI was 0.66%, of which 61.1% occurred in the third trimester and of those, 64% were due to preeclampsia .Poor prognosis was associated with age above 38years. Hemodialysis was needed in 38.6% of the cases. Maternal mortality rate was 11.4% (18).These findings reflect the variability in patient characteristics and outcome.

2.5 Etiology of acute kidney injury in pregnancy

2.5.1 Pre-renal causes of PRAKI

2.5.1.1 Hypovolemia and ischemic injury

Pre-renal azotemia is the most common form of AKI which arises mainly from volume depletion. In pregnancy, volume depletion can occur in early pregnancy as a result hyperemesis gravidarum or septic shock from spontaneous or induced abortion, and hemorrhage from ruptured ectopic pregnancy. While in late pregnancy, volume depletion results from obstetric hemorrhages (antepartum and postpartum), cardiogenic shock due to amniotic fluid embolism and sepsis. Rapid fluid repletion restores glomerular blood flow and improves renal functions (1-6, 8,12).

2.5.1.2 Hypertensive disorders of pregnancy

Hypertension, defined as a blood pressure more than 140/90 mm Hg, is the most common medical complication of pregnancy, it occurs in 6-8% of all pregnancies and is common in young primiparous women and older multiparous women (1-4, 8). Preeclampsia (PE) is the new onset of hypertension with proteinuria and or end-organ dysfunction after 20 weeks of pregnancy in a previously normotensive patient and is the most common cause of AKI in pregnancy (1-5,8). Pathogenesis of PE is not fully understood and is thought to result from placental insufficiency in early pregnancy leading to imbalance between pro angiogenic proteins such as vascular endothelial growth factor and placental growth factors and anti-angiogenic factors like soluble endogelin and fms -like tyrosine kinase (3). This factor imbalance leads to endothelial injury, systemic vasoconstriction, reduced glomerular perfusion and ischaemia (1-3, 5, 14).

The incidence of preeclampsia increases with advanced age, chronic hypertension, diabetes mellitus, chronic kidney disease and multifeotal gestation, which are known risk factors for PRAKI (3, 8). The impact of PE on the mother extends beyond pregnancy and women who have had PE develop persistent proteinuria and have a relative risk of 4.7 of progressing to chronic kidney disease and also end stage kidney disease (3, 5).

2.5.2 Intrinsic causes of PRAKI

Intrinsic renal injury involves the vessels, the tubulointerstitium, the glomerular or a combination of these structures (8, 10, 12). Tubular and interstitial injury is caused by sustained ischaemia arising from the prerenal causes or toxins. Vascular injury may be caused by hypertension or thrombotic microangiopathy (TMA). Hemolysis Elevated Liver Enzymes Low Platelets (HELLP) syndrome- a variant or a severe complication of PE which occurs in pregnancy or early postpartum, is frequently associated with hypertension and proteinuria except for a 20% of patients who do not have features of PE (3,5,8). Pathogenesis is not clear; however, it is thought to originate from poor placentation in early pregnancy with release of anti-angiogenic factors such as soluble endogelin and soluble fms-like tyrosine kinase -1 which cause endothelial injury, systemic vasoconstriction, hypertension and proteinuria as in PE (3,8). AKI occurs in 7-36% of patients with HELLP syndrome (1, 4, 8).

Toxins both endogenous such as myoglobin, hemoglobin and intra tubular crystal and exogenous such as drugs and herbs may as well contribute to intrinsic kidney injury in pregnancy by causing direct tubular and interstitial injury (3, 4, 5).

2.5.3 Post renal causes of PRAKI

Physiologic hydronephrosis and hydroureter are common in pregnancy and severe cases may lead to urinary stasis, oliguria and anuria (6). The gravid uterus and presence of polyhydramnios may cause obstructive uropathy whereas increased production of vitamin D may result in hypercalciuria and increase the risk of nephrolithiasis and urinary tract infection. Although these changes resolve upon delivery, some patients may present with features of PRAKI and may require ureteric stenting before delivery (4, 6).

2.6 Pregnancy and the underlying renal disease

Patients with chronic kidney disease have reduced fertility, however, those who get pregnant experience worsening hypertension and proteinuria and a decrease in GFR which may not be noticed due to the renal hyper filtration of pregnancy (3,4).These women are also at an increased risk of fetal loss, intrauterine growth retardation, and premature labor compared to women with normal renal functions. In chronic kidney disease high maternal blood urea nitrogen (BUN) levels act as an osmotic diuretic in the fetal kidney and can cause early labor and fetal loss (2-6, 12).

2.7 Diagnostic approach for PRAKI

There is a wide range of criteria for definition of AKI in the general population which lack specificity and sensitivity in definition of PRAKI due to the physiologic changes in pregnancy. As such, diagnostic definition is not universally conceptualized and the diagnosis of AKI in pregnancy is based on combination of clinical findings, careful interpretation of serum creatinine values, presence of oliguria or anuria and or need for dialysis (3,4, 8, 22).

The Risk, Injury, Failure, Loss of function and End Stage Renal Disease (RIFLE) criteria defines both increasing severity and outcomes where severity is based on increase in serum creatinine while the outcomes (Loss of function and ESRD) are based on the duration of loss of the renal functions. It is commonly used for definition of AKI in general population , however in pregnancy, the RIFLE criteria has various limitations such as need for baseline serum creatinine which are not routinely available in the pregnant women who are otherwise healthy (22) . In addition, full stage description of the RIFLE criteria may not be useful in pregnancy since most women with CKD have low fertility with poor early outcomes for both mother and foetus and the definition of ESRD requires a longer duration >90 days compared to AKI which may happen within hours(12,22). The RIFLE criteria also do not capture small changes in serum creatinine which in pregnancy, may be associated with profound kidney damage (8, 22). The Acute Kidney Injury Network (AKIN) criteria for AKI requires an absolute increament in serum creatinine ≥ 26.5 µmols/l within 48 hours and requires definition after volume status has been restored and obstructive causes excluded where as in pregnancy obstructive causes may not be ruled out or excluded. Urine criteria is not accurate in pregnancy due to physiologic hydro ureter and hydro nephrosis. The Kidney Disease Improving Global Outcomes (KDIGO) defined the clinical practice guidelines for AKI (8, 22). Where, AKI was defined as an increase in the serum creatinine by 1.5 times above the baseline within 7 days or urine output of less than 0.5 mL/kg per hour for more than 6 hours. Subsequently, the definition was extended to include an increase in serum creatinine by ≥26.5µmols/l which was found to be independently associated with mortality (22). So KDIGO clinical practice guidelines criteria stands out, in that, increase in serum creatinine by 26.5 µmols/L is independently associated with mortality and also recommends the highest staging system for severity of AKI (4,8,22).

Studies performed to evaluate and compare the accuracy of the formulae used to estimate GFR, the modification of diet in renal disease (MDRD) and the Cockcroft-Gault equations demonstrated inaccuracy in assessing GFR in pregnancy (19-21). The Cockcroft-Gault equation overestimated the GFR, the MDRD equation underestimated the real GFR value by about 40 ml/min (6, 19-23).

In an attempt to use creatinine clearance for estimation of GFR in pregnancy, Guo et al. (21) demonstrated a negative correlation between serum cystatin C and 24-hour urine creatinine clearance when compared with serum creatinine and uric acid in normal pregnancies and severe preeclampsia. On the contrary, it was found that the serum cystatin C did not correlate with inulin clearance in pregnancy and in postpartum. Therefore, the use of cystatin C for measurement of GFR in pregnancy is not recommended (4, 5, 6, 19-22).

Use of serum creatinine before pregnancy or in early pregnancy would be useful for comparison for patients who develop risk factors for PRAKI during pregnancy , but since pre pregnancy or early pregnancy serum creatinine is not routinely done, PRAKI is likely to be missed until symptoms are profound (8,12,).

Below is a table with a summary of the various criteria used for definition and staging of acute kidney injury.

Table 1 Summary of various definitions and staging criteria for acute kidney injury

Definition of AKI
Serum creatinine criteria Urine output criteria

RIFLE (4,22)	AKIN	KDIGO (22)	URINE OUTPUT
Increase in serum creatinine by> 50%in <7 days	Increase in serum creatinine of 26.5µmols/L or >50% in <48hours	Increase in serum creatinine by 26.5µmols/L in <48 hrs or by >50% which is known or presumed to have occurred <7days	Urine output of <0.5ml/kg/hour for>6hrs
Class/Stage of AKI			
Risk - Increase in serum creatinine to 1.5 fold of baseline or decrease in GFR by >25% **Injury** - increase in Serum creatinine to 2 fold or decrease in GFR by >50% **Failure -**increase of serum creatinine to 3 fold or >354 µmols/L decrease in GFR by >75% **Loss -**persistent loss of function >4 weeks **ESRD -** >90 days	**Stage 1** Increase in serum creatinine by ≥26.5µmols/L in ,<48hrs **Stage 2** serum creatinine >2.0-3.0 fold from baseline **Stage 3** serum creatinie increase >3 fold or >354 µmols/L Or need for RRT	**Stage 1** Increase in Serum creatinine of ≥26.5 µmol/L, or by 1.5 to 1.9 fold of baseline **Stage 2** serum Creatinine >2.0 to 2.9 fold **Stage 3** Serum creatinine >3.0 times fold or above ≥353.6 µmol/L >24 hrs or Need for RRT	<0.5ml/kg/hr for 6hrs <0.5ml/kg/hr for 12 hrs <0.3ml/kg/for 24 hrs or need for RRT or anuria for ≥ 12 hrs

Only one criteria need to be met either the serum creatinine or the urine criteria**.**

There are however small differences observed between the four systems (12).

2.7.1 Operational definition of PRAKI

Given the limitations in estimation of 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 and PRAKI was defined as increase of serum creatinine by ≥ 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 were not part of the routine antenatal profile, so patients did not have their pre pregnancy or early pregnancy baseline serum creatinine.

2.7.2. The staging of PRAKI

Definition of AKI according to the KDIGO criteria is; increase in serum creatinine by 26.5 µmol/L within 48 hours; or an increase in serum creatinine to more than or equal to 1.5 times of baseline, which is known or presumed to have occurred within the last 7 days or a urinary output/ volume of less than 0.5 mL/kg/h for 6 hours (1,3,4,8,12,22). For staging purposes, patients should be staged according to the criteria that give them the highest stage and the KDIGO criteria is mainly used for practice, research and public health(22).Staging of PRAKI like AKI in general population is important in assessing severity of kidney injury and deciding the method of treatment (2, 4,12 , 22). Therefore, applying the KDIGO staging criteria for PRAKI, the stages are as follows

Stage 1 Increase in Serum creatinine of ≥26.5 µmol/L within 48 hours, or increase in Serum creatinine 1.5 to 1.9 times above baseline,
Urine output <0.5 mL/kg /hr for more than 6 hour

Stage 2 Creatinine increased 2.0 to 2.9 times; or
Urine output <0.5 mL/kg for 12 hours

Stage 3 Serum creatinine increased 3.0 times above baseline; or increase
Above ≥353.6 µmol/L for more than 24 hours or
Initiation of renal replacement therapy or
Urine output <0.3 mL/kg for 24 hours or anuria for more than 12hrs (14, 22).

2.8 Management of pregnancy related acute kidney injury

Approach to management of PRAKI include treatment of the obstetric complications, supportive measures to preserve renal functions and or renal replacement therapy (12). Renal replacement therapy is mandatory for patients with deteriorating renal functions despite the resuscitatory measures (1-4, 8, 14). Indications for dialysis are the same as for patients in the general population. However higher dialysis dose of more than 20 hours per week is recommended since it has been shown to improve fetal survival (3, 5, 8, 24).

2. 8.1 Outcome of pregnancy related acute kidney injury

The outcome of PRAKI may be described in terms of maternal, fetal and renal outcomes (18);

2.8.2. Fetomaternal outcome

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 — not at all if their doctors had their way' (26).

This is a brief emphasis of what used to be the fetal outcome in patient with acute kidney injury in pregnancy. Pregnancy related acute kidney injury is associated with a 4.9 increase in fresh still births and 4.5-fold increase in maternal death (10,12).

A meta-analysis by Youxia et al., reviewed that, PRAKI was associated with high maternal mortality of 13.3% compared to 4.2% in those without PRAKI, and was also associated with longer duration of stay in the intensive care unit (ICU) . Pregnancy related acute kidney injury was associated with 1.49 fold increase in Caesarean section (CS) deliveries compared to those without PRAKI. Fetal outcomes were associated with birth at lower gestational age and lower birth weights with high rates of still births 29.8% compared to 6.0% of those without PRAKI (25).

2.8.3 Renal outcome

Renal outcomes are variable and include; complete recovery where serum creatinine falls to pre-injury state, partial recovery–serum creatinine remains above threshold and dialysis dependence evaluated at 90 days from injury (1-4,8, 11-18,23-46). Data obtained from

eight studies on kidney outcome in patients with PRAKI showed that 2.4 % of the women progressed to ESRD (25).

Table 2 summarizes outcomes of PRAKI from studies from different parts of the world.

Table 2 Summary of outcome of PRAKI

Reference	Number of patients.	Country	Foetal mortality %	Maternal mortality %	Reversed %	Partial recovery %	Dialysis Depended %
Hildebrand et al (4)	188	Canada	<2.7	4.3	96.1	none	3.9
Krishna et al (24)	98	India	11.0	18.4	61	none	20
Kabbali et al (18)	44	Morocco	15.9	11.4	66	23	11.7
Prakash et. al (8)	85	India	31.8	20	69.4	5.9	0.85
Chunhong et al (14)	343	China	17.1	4.08	not reported	not reported	6.1
Munna et al (29)	60	India	41.7	15	Not reported	Not reported	8.4
Cooke et al (30)	26	Malawi	13.8	nil	84.6	15.4	nil

2.9 Study justification

Pregnancy related acute kidney injury is associated with significant maternal and foetal morbidity and mortality and is a risk factor for chronic kidney disease (1-3, 15, 22, 25). Recent studies demonstrate rising trends in the incidence of AKI due to increase in lifestyle diseases such as obesity, hypertension and diabetes mellitus, which are independent risk factors for PRAKI (1-4,9,12, 13). Pregnancy related acute kidney injury is preventable. Identification of associated factors with early institution of therapy has been shown to be the most important measure in preventing PRAKI (4,5,8).

There is worldwide paucity of data on patient characteristics, risk factors and patterns of outcome of PRAKI and the studies done are limited to small sample sizes and demonstrate wide variation in patient characteristics across socioeconomic boundaries (4, 8, 15,38).

This study had not been done in Kenya and there was no local data on disease burden, patient characteristics and patterns of outcome and findings from other studies do not

necessarily represent the situation in Kenya. Therefore, there was need to carry out this study to describe the patient characteristics.

The findings of this study may form a basis for change of policy towards inclusion of renal function test in the antenatal care plan in order to facilitate early diagnosis and early institution of therapy in PRAKI and therefore reduce maternal and foetal morbidity and mortality.

2.9.1 Research question

What are the characteristics of patients with pregnancy related acute kidney injury at K.N.H?

2.9.2 Broad objective

To determine the demographic and clinical characteristics of patients with PRAKI in late pregnancy and early postpartum period among women admitted at K.N.H

2.9.2.1 Specific objectives

2.9.2.1.1 Primary objective

1. To determine the pre-morbid and morbid characteristics among patients with PRAKI at presentation.
2. To stage the severity of PRAKI at presentation

2.9.2.1.2 Secondary objectives

1. To document the short term maternal, pregnancy and foetal outcome within two weeks

2. To determine the trends of serum creatinine and need for dialysis within two weeks

Chapter three

3.0 Materials and methods

3.1 Study design

The design was a descriptive study

3.2 Study site

The study was carried out in the Kenyatta National Hospital in the Department of Obstetrics and Gynecology, in the Labour ward and Post-natal wards -Ground Floor (GF) A and B, Ward 1A and Ward 1D.

Kenyatta National Hospital is located off Ngong Road in Nairobi City, Kenya. It caters for referral and primary care services of all specialties. It has a bed capacity of about 1800.

Kenyatta National Hospital is the main referral facility in East and Central Africa with a well-established Department of Obstetrics and Gynecology which caters for women with reproductive needs and related medical conditions such as those arising from complications of pregnancy and child birth.

3.3 Study period

The study was carried out between 6th July and September 7th, 2018.

3.4 Study population

The target population was made up of pregnant women with gestation of 28 weeks and above and postpartum women within six weeks after delivery admitted at Labour ward or the post natal wards of K.N.H.

3.5 Case definition

Pregnancy related acute kidney injury was defined according to KDIGO serum creatinine criteria for AKI, assuming a normal GFR of 75mls/minute per 1.73m^2 as any woman, pregnant ≥28 weeks or postpartum within six weeks, admitted at the Labour ward or the postnatal wards with an increase in serum creatinine by

i) ≥ 26.5µmols/L above baseline, within 48 hours, or
ii) ≥ 26.5µmols/L above upper limit of normal or
iii) 1.5 times of the baseline within seven (7) days

3.6 Patient selection

3.6.1 Inclusion criteria

Pregnant women with gestation of ≥28 weeks and postpartum women within six weeks with a diagnosis of acute kidney injury or with deranged serum creatinine meeting the operational definition of PRAKI in any of the stated wards willing to sign consent were enrolled in the study.

3.6.2 Exclusion criteria

Women with chronic kidney disease and those who declined consent were excluded

3.7 Sample size estimation

According to KNH medical records and a preparatory pilot study done for one week, approximately eight to ten patients with PRAKI were admitted weekly in the respective wards. This implied that an estimated 32-40 AKI patients were admitted monthly. The sample size calculation was then obtained using the Daniel's formula for finite population. Sample size was calculated using the (Daniel, 1999) formula;

$$n = \frac{Z^2 x\ P(1-P)}{d^2}$$

Where,
n = Desired sample size
Z = value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)
P = expected true proportion (estimated at 11.7%, from a prospective observation study conducted by Munna L.P. et al (2013) over a period of one year at the Nephrology unit in collaboration with department of Obstetrics and Gynaecology, King George's Medical University, India; looking at acute renal failure cases, found that 11.7% of them were due to pregnancy related acute kidney injury (29).
d = desired precision (0.05)

$$n_0 = \frac{1.96^2 x\ 0.117(1-0.117)}{0.05^2} = 159$$

Adjusting the sample size for finite populations less than 10,000

$$nf = \frac{n_0}{1 + \frac{n_0 - 1}{N}} = \frac{156}{1 + \frac{156 - 1}{60}} = 44$$

Minimum of 44 patients were to be sampled during the study period.

3.8 Sampling method

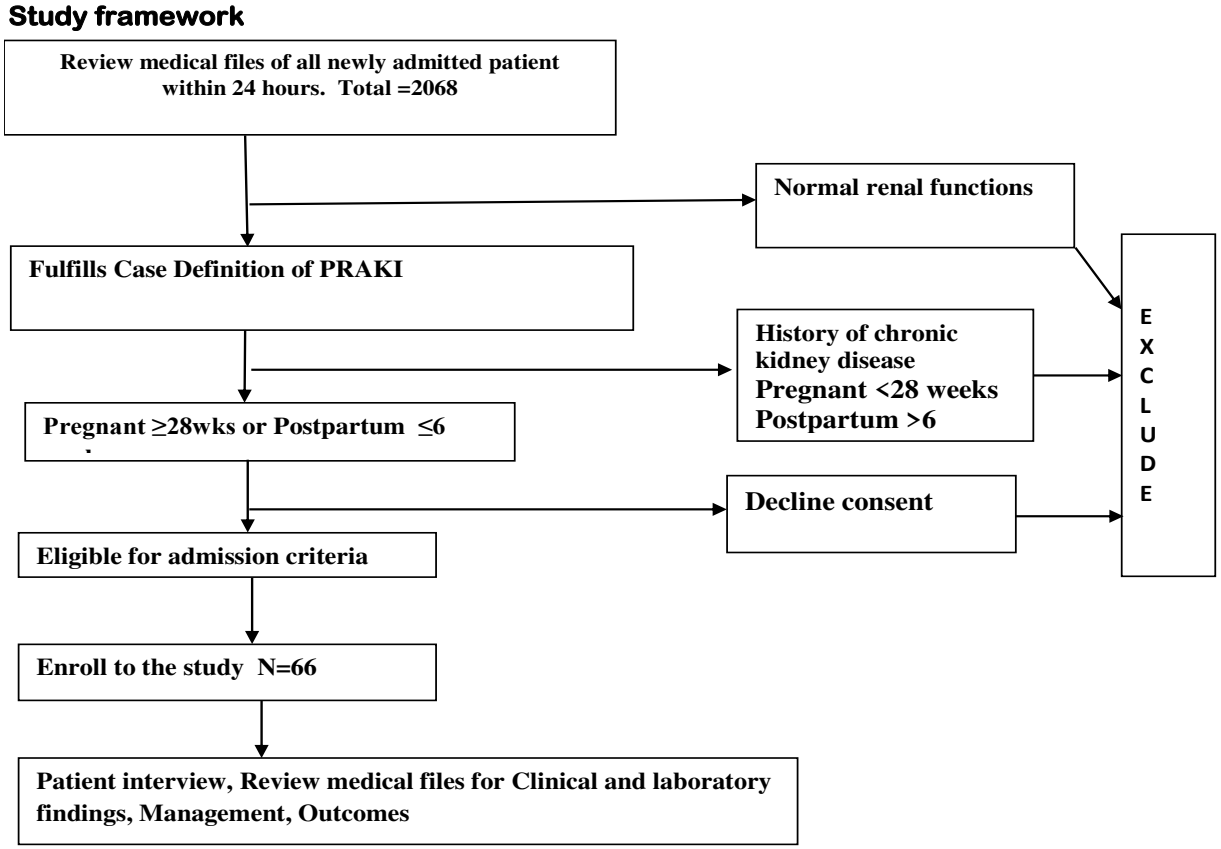
Consecutive patient sampling

3.8.1 Patient screening and recruitment

Patients were screened for eligibility by the principal investigator or the research assistant who was a Registered Clinical Officer, within 24 hours of admission or of documented change in condition for those previously stable in the wards. The admission register was used to identify new admissions and the nurses' hand over book, which contained daily patient updates, was used to identify patients who developed AKI while in the wards.

Patient medical records were then assessed for file diagnosis of AKI or for laboratory results with deranged renal function. The results were subjected to the operational definition of PRAKI. Those eligible were then approached for enrollment into the study. The study requirements were explained to each patient or their guardian for those below 18 years. Those who accepted to participate in the study were required to sign an informed consent form to enroll in the study.

3.8.2 Study frame work



3.9 .0 Clinical methods

Patient management was at the discretion of attending clinician. The principal investigator or the research assistant on daily basis, searched for patients with deranged renal function tests within 24 hours of admission. They also searched for in- patients in the respective wards who developed renal derangements after admission by looking at their renal test reports. Each of the deranged renal laboratory reports were then subjected to the operational definition of PRAKI.

Patients whose renal laboratory report fulfilled the operational definition of PRAKI were then approached and introduced to the study. They were given detailed verbal description of the study requirements. It was explained to them that, if they agreed to enroll into the study ,there will be verbal interviews and need to access and extract information from the patient's medical file .They were also informed that, benefits will include sharing the interpretation of results with the patient and the primary healthcare provider for relevant intervention. The patients were 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 assigned a study serial number which was placed on the front outer cover of their medical record file for easy access. Their medical records were then assessed, and data capture form labelled with the participant's serial number and hospital inpatient number 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.

The following information was obtained from the patient and the records.

Demographic data: Age in years, marital status, residence and referral status

Antenatal Clinic findings: Hb, HIV status –positive, negative or unknown

Presenting complaint:

Current diagnosis: Obstetric and/or medical

Past Medical history:

Obstetric History: Parity, Gravidity, Gestational age in weeks, or days postpartum, Preeclampsia, eclampsia, HELLP syndrome, TTP, HUS, Acute fatty liver of pregnancy, Gestational diabetes, Gestational hypertension

Surgical history: Ureteric ligation, bladder injury, urethral injury

Physical findings: Blood pressure in mmHg, Pulse Rate in beats/minute, Respiratory rate in breaths per minute, Temperature in degrees Celsius, Pallor, Jaundice, Oedema, Facial Puffiness

Laboratory data: The following laboratory data was recorded from the medical file

Total blood count-White blood cells, Hemoglobin, Platelets

Renal function tests -Urea, Sodium and Potassium ions and Serum Creatinine

Stage of PRAKI at presentation was derived from the renal function results by applying the KDIGO severity criteria as follows:

Stage 1 Serum creatinine 1.5 to 1.9 times baseline; or ≥26.5 micromol/L increase in serum creatinine above upper limit of reference normal

Stage 2 Serum Creatinine increased 2.0 to 2.9 times of baseline

Stage 3 Creatinine increased 3.0 times or Initiation of renal replacement therapy.

Outcome –This part of information was recorded at discharge or at end of two weeks.

Maternal - Pregnancy on going or delivered during follow up, if delivered

Mode of delivery- SVD or CS

Maternal status -Alive or dead
Fetal outcome –Age at birth in weeks

Foetal status at birth –Life infant or Fresh still birth

Mode of management: Conservative or need for dialysis

Trends of serum creatinine -Improved- if severity downstages,

- Progressed –if severity upstages

-Static - if no change in severity,

Indications for dialysis –Hyperkalemia, fluid overload, uremia or combined factors

Verbal interview was carried out to obtain any relevant information that may not have been captured in the medical record file.

The above data was entered the Data capture forms using ink pen.

3.9.1 Quality assurance

The research assistant was trained on the administration of the data capture form

by the principal investigator prior to commencement of the study.

3.9.2 Study variables

Independent variables	**Dependent variables**
▪ Socio-demographic data ▪ Medical and Obstetric History ▪ Present medical and obstetric conditions	▪ Severity of PRAKI ▪ Mode of renal management ▪ Outcome Maternal - Pregnancy status -Mode of delivery -Status -Alive or Dead Foetal -Gestation age at birth -Status at birth-live infant or FSB

3.9.3 Regulation and administration

The study commenced upon approval by the Ethics and Research Committee of Kenyatta National Hospital and University of Nairobi. Approval number: P635/11/2017

Confidentiality was maintained. The diagnosis and the stage of PRAKI were communicated to the patient and the primary health care provider

3.9.4 Study limitations

Participants presented baseline laboratory results from various laboratories whose validity could not be ascertained.

3.9.5 Data management

3.9.5.1 Data processing and analysis

The raw data was screened, coded, 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 where described in means or median and Categorical variables were summarized into frequencies. Other statistical test results were presented in tables.

CHAPTER FOUR

4.0 Results

A total of sixty six (3.2%) participants were enrolled out of 2068 admissions during the study period. The mean age was 28 (SD5.9) years., age range was 15 to 44 years.

Table 3 Demographic characteristics of the study participants

Characteristics N=66	**n**	**%**
Age in years		
≤20	6	9.1
21-25	18	27.3
26-30	23	34.8
31-35	11	16.7
≥35	8	12.1
Residence		
Urban (Nairobi)	41	62.1
Rural	25	37.9
Referred	**42**	**63.6**

Rural	24	57.1
Urban	18	42.9

Nineteen (28.8%) had premorbid conditions which were predominantly cardiovascular diseases. HIV infection were 15.8% as shown in table 4 below

Table 4 Premorbid conditions of the study participants

Premorbid conditions	**n=19**
Hypertension	10
Valvular heart disease	4
Dilated cardiomyopathy	2
HIV	3

The predominant morbid/obstetric condition associated with development of PRAKI were mainly hypertensive disorders of pregnancy 53(80.3%). While volume loss, puerperal sepsis and injuries were as shown in table 5 below

Table 5 Morbid /obstetric conditions among the study participants

Morbid Condition N=66	n
Hypertensive disorders	**53**
Preeclampsia	28
Eclampsia	8
HELLP syndrome	17
Volume loss	**9**
Puerperal sepsis	**2**
Bladder and Urethral injuries	**2**

The study demonstrated even distribution of severity at presentation as shown in figure 1.

Figure 1 Distribution of severity of PRAKI at presentation

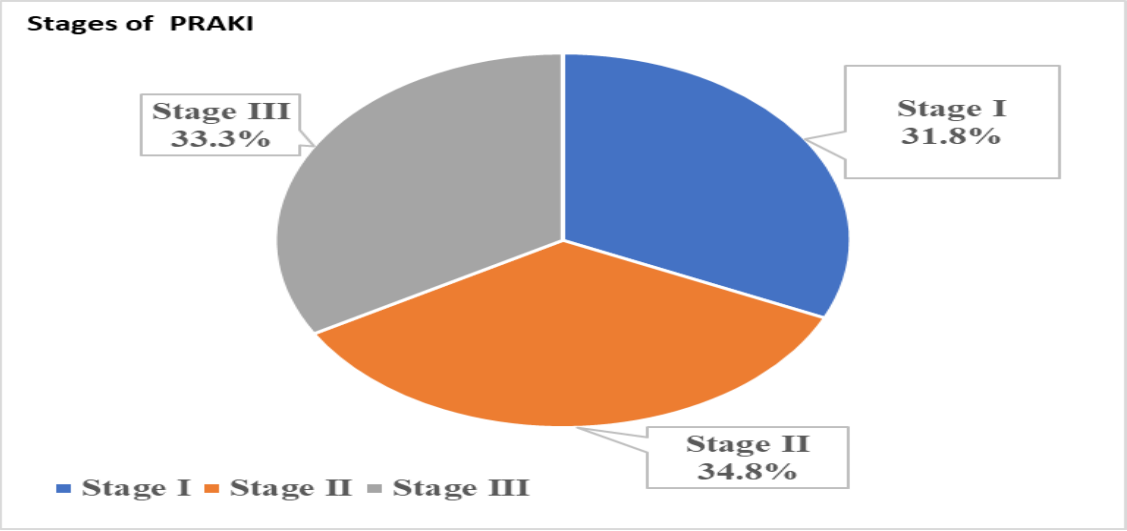


Table 6: Time of onset of PRAKI

	Antepartum	Postpartum
Stage		
Stage 1	16(76.2%)	5(23.8%)
Stage 11	19(82.6%)	4(17.4%)
Stage 111	14(63.6%)	8(36.4%)

Table 7: Maternal and Pregnancy Outcome in PRAKI

Of the 66 participants enrolled**,** 60 were delivered and six remained pregnant as at the end of follow up period. Of those delivered ,39(65 %) were delivered through spontaneous vertex delivery while 21(35%) were delivered through caesarian section, of whom 18(85.7%) were emergency caesarian sections. No maternal mortality was reported during the study period

Outcome	**n**	**%**
Pregnancy status Ongoing	6	9.1
Delivered	60	90.9
Mode of Delivery(n=60) SVD	39	65%
CS	21	35%

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%).

Table 8: Foetal outcome in PRAKI

Foetal status at birth (n=60)					
Age at birth	**Live infant n= 43**	**%**	**Fresh still birth n=17**	**%**	**Total %**
Preterm< 37 weeks	23	(53.5)	10	(58.8)	**33 (55.0)**
Term >37 weeks	20	(46.5)	7	(41.2)	**27(45.0)**
Total	**43**	**(71.7)**	**17**	**(28.3)**	**60(100)**

Table 9: Trends of serum creatinine of PRAKI

Forty-one (62.1%) improved while 25(37.8%) worsened during the follow up period. Majority (48.0%) of those who worsened were in Stage 111 at presentation

Stages of PRAKI				
Trends of serum creatinine	**Stage 1**	**Stage 11**	**Stage 111**	**Total**
Improved	16(39.0%)	15(36.6%)	10(24.4%)	**41**
Worsened	5(20.0%)	8(32.0%)	12(48.0%)	**25**

Table 10: Need for dialysis in PRAKI

Forty-seven (72.2%) were managed conservatively while 19(28.8%) were dialyzed.

	Stage of PRAKI			Total
	Stage 1	Stage 2	Stage 3	
Need for dialysis	2(10.5%)	3(15.8%)	14(73.7%)	19
No need for dialysis	19(40.4%)	20(42.6%)	8(17.0%)	47

Table 11: Indication for dialysis in participants with PRAKI

The main indication for dialysis was fluid overload

Reasons for Dialysis (n=19)	**n**	**%**
Fluid overload	12	63.2
Uremia	5	26.3
Resistant Hyperkalemia	1	5.3
Metabolic acidosis	1	5.3

CHAPTER FIVE

5.0 Discussion

To the best of our knowledge, this was the first study in Kenya to assess the characteristics of patients with pregnancy related acute kidney injury and the first to determine the prevalence, associated risk factors, mode of management and short-term foetal and maternal outcomes. We demonstrate that, out of 2068 admissions during the study period, 66 (3.2%) were managed for pregnancy related acute kidney injury.

Most of the participants were referrals from other health facilities mainly from the rural areas. The participants were young women with a mean age of 28 years. About a third had pre-pregnancy medical conditions which were predominantly cardiovascular diseases: - hypertension, valvular heart disease and dilated cardiomyopathy. The same patients were also noted to complicate with preeclampsia spectrum of diseases.

The most common associated cause of PRAKI were hypertensive disorders of pregnancy with a small contribution from volume loss, sepsis and injuries. Pregnancy related acute kidney injury was associated with high rate of premature births and poor foetal outcomes.

We documented an even distribution of severity of PRAKI at presentation. Majority of those who presented with stage 111 AKI, deteriorated and were dialyzed.

No maternal mortality was documented among the participants during the study period.

The incidence of PRAKI is increasing in tandem with the global increase in the incidence of AKI in the general population. Patient characteristics and outcome vary widely across demographic and socioeconomic settings (1-4,10,12,18,28,34,35,38). We did not identify any publications on previous studies in Kenya on prevalence of PRAKI so we could not state whether there was change in prevalence in Kenya or not.

However, comparing our study findings with publications of similar studies done in other developing countries in Africa such as Morocco and Malawi, the prevalence of PRAKI varies widely. In Morocco the prevalence was 0.66% (18) and Malawi 8.1% (30). Similar variation was noted in studies done in China and in India where the prevalence was 0.8 % (14) and 7.8% (17) respectively. Our findings were within the range of findings in these countries, however, below the global incidence range of 5-15% in developing countries. (4,10,12,39). Our findings fit in the global trend of decline of PRAKI since the 1960s.

The mean age of the participants was 28 years ,which was comparable to mean age reported in studies in Morocco (18),in India (24) ,Republic of South Africa (31) and in Pakistan(34).The peak age of 26 to 30 years was similar to the peak age in various studies in the world (18, 23,25,30,31,44) and lower than peak age of 30-39 years in Canada. High maternal age in the developed world, is reported to be due to availability of advanced reproductive technology, where older women can get pregnant through facilitated conception while such services are scarcely available in the developing world where most women conceive naturally (4).

Most 42(62.1%) participants were resident in the City of Nairobi while the minority 25(37.9%) lived in the rural areas. Forty-two (63.6%) had been referred from other healthcare facilities of whom, 24(57.1%) were from the rural areas. These results compare with findings in a study in Morocco by Kiballi et al (18) where participants from urban setting were 59% and from the rural areas were 41% and contrast study findings in Canada where participants from rural residence was 9.6% (4). In our setting, and other developing countries, specialized services are more concentrated in the urban areas and patients must be moved from rural to urban areas to receive services. This is in sharp contrast to developed countries like Canada where healthcare services are widely available and only a small percentage of patients are referred to other centers for specialized care (4).

Compared to the total admissions in the study setting, we noted that all women who developed PRAKI had obstetric complication(s) and only 19 (28.8%) had preexisting medical condition(s), mainly cardiovascular; of which, hypertension 52.6% and valvular heart disease 21.0% while a minority, 15.7% had HIV infection. In a similar study in Canada (4) prevalence of preexisting medical conditions was lower at 11.2% of which hypertension 5.3%, diabetes mellitus 2.7% and chronic kidney disease 4.3%. These

differences in study findings demonstrate differences in patient characteristics in deferent demographic and socioeconomic settings.

Of the obstetric complications, hypertensive disorders namely, preeclampsia (52.8%), eclampsia (15,1%) and HELLP syndrome (32.1%) were the main associated risk factors of PRAKI. The preeclampsia spectrum of diseases bears their pathobiology from the placental tissue and remain the main risk factor for PRAKI as evidenced by observations from this study and many studies in the world (1-5,8,12, 14-15,18,25,30,31,35, 38, 44,46).

Obstetric hemorrhage occurred in seven (10.6%) which compared to observations in Malawi 11.5%, (30) and Morocco 9.1% (18) and lower than in Canada 17.6% (4). The differences in obstetric hemorrhage between the developing countries and the developed country may be due to differences in practices and availability of resuscitation services. Two (3.0%) participants developed PRAKI due to volume loss from hyperemesis gravidarum both at gestation age of 31/40weeks. This was an uncommon finding since most hyperemesis occur in first trimester (10, 12).

Concomitant with decrease in incidence of PRAKI, maternal mortality associated with PRAKI has also decreased worldwide (4,5,12,39-45). Studies from China and India recently reported maternal mortality rate of 4.0% and 5.8% respectively as compared with a rate of 20% in the 1980s (8,17). In this study, no maternal mortalities were documented over the study period.

Our study findings compare with those of a study done in Malawi by Cooke et al, 2018 (30) 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 (18,29). Findings of this study and that in Malawi may reflect a declining maternal mortality in developing countries but do not necessarily mean that there are no maternal mortalities associated with PRAKI.

Pregnancy related acute kidney injury is associated with increased operational deliveries and increased rate of foetal loss (3,6,15,25,44). We found the ratio between CS in PRAKI patients to CS in non PRAKI patients was 1.4:1 The increase in operational delivery may be explained by the fact that, delivery of the foetus and the placenta is therapeutic in hypertensive disorders of pregnancy, which, as explained earlier are the most common possible etiologies of PRAKI as documented in this study and others (5,8,12). This may also explain why premature deliveries were noted to be higher than term deliveries at a ratio of 1.2:1in our study. The rate of CS deliveries in our study was 31.8%, was lower compared to findings by Mohamed et al (44) where CS deliveries were at 40.5%, however higher than Canada as reported by Hildebrand et al at 25.5% where the rate of hypertensive disorders was noted to be lower than our findings (4).

Pregnancy related acute kidney injury is also associated with increased foetal morbidity and mortality. The odds of perinatal deaths increase 3.4-4.9-fold when compared to pregnancies without PRAKI (15,25,33). We documented 17(28.3%) fresh still births which was higher than 15.9% reported by Kibbali et al in Morocco (18) and lower than

41% reported by Munna et al in India (29) .Our findings contrast the findings reported by Hildebrandt et al in Canada where no still births were reported (4). These findings may reflect differences in antenatal and perinatal care practices and also the challenges in handling non obstetric emergencies like acute kidney injury in resource strained setting.

The ratio of fresh still births among the study participants was 1:4. This ratio was much higher than that in the women without PRAKI which was at 1:23, in the same institution during the study period. Therefore, PRAKI increased the risk of fresh still birth by six (6) fold. This finding was higher than that documented by Liu et al, 2015(15) from review of literature in China, where, PRAKI was documented to cause a 4.9-fold increase in fresh still births. The high rate of fresh still births in our setting may be due to high patient numbers and inadequate facility to handle high emergency turn over.

We demonstrate even distribution of PRAKI at presentation across the severity levels where, stage 1 were 31.8%, stage 11; 34.8% and stage 111, 33.3%. This was in sharp contrast to observation in Pakistan by Bokhari (34) where majority (80%) presented in stage 111AKI while the rest were equally distributed between stages 1 and 11. The differences in severity at presentation may reflect various influencing factors such as: - risk factors of PRAKI and differences in time taken from onset of AKI to diagnosis.

The long-term renal outcome could not be ascertained in this study due to the short follow up period of two weeks. However, in the short term, less severe PRAKI, mostly in stages I and 11, were managed conservatively and 42 (62.1%) participants improvement while 25(37.9%) worsened, of whom, nineteen (28.8%) required renal replacement therapy which was mainly due to fluid overload (63.2%).

Most of the participant on dialysis remained on dialysis as at the end of follow up period. The need for dialysis in our study was higher compared to 16% documented by Randeere et al (31) in the Republic of South Africa, 16.2% by Cooke et al(30) in Malawi and Mohamed et al in Morocco (44) where 16.2% were dialyzed and lower than another site in Morocco (18) and in Pakistan(34) where the need for dialysis was 38.6% and 68.3% respectively.

The indications for dialysis may be similar among patients with PRAKI, but the time to initiation of therapy may vary depending on the healthcare facility and availability of dialysis service.

Conclusion

The prevalence of PRAKI from this study at KNH is 3.2%. The main associated factors were hypertensive disorders of pregnancy. There was six (6) fold increase in fresh still births among patients with PRAKI.

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Appendices

Appendix 1: Data Capture Form for pregnancy related acute kidney injury for

ASSESSMENT OF THE CHARCTERISTICS OF PATIENTS WITH PREGNANCY RELATED ACUTE KIDNEY FAILURE AT THE KENYATTA NATIONAL HOSPITAL

Part 1

Patient Demographics

In-Patient number…… Study number ……Ward …… Age in years.....

Residence……..Marital status…….. Referred from peripheral facility

Presenting complaint …….Obstetric Diagnosis ……Other Diagnoses……..

Past medical history

Hypertension	
Cardiac disease	
Diabetes mellitus	
Anemia	
Chronic kidney disease	
Glomerular disease	

Obstetric History

Parity	
Gravidity	
Gestation age ….. /40 weeks	
Gestational Hypertension	
Preeclampsia	
Eclampsia	
Gestational Diabetes	

Surgical history: Ureteric ligation, bladder injury or urethral injury

Physical findings: **Date**

BP								
PR								
RR								
Temp.								
Oedema								
Facial puffiness								

BP: Blood pressure, PR: Pulse rate, RR: Respiratory rate

Part 11 Laboratory Data

Booking Parameters: Hb …… g/dl, HIV Status …….

Date

TBC								
Hb								
Plts								
WBC								
U/E/C								
Urea								
Na+								
K+								
Creatinine								

Footnotes:

TBC: Total blood count, Hb Hemoglobin, WBC. White blood cell count, Plts Platelets,

UECs: U Urea, E Electrolytes, Creatinine C, K+ Potassium ions , Na+ Sodium ions

Part 111

Stage of AKI at presentation as per the KDIGO criteria …….

Management:

Drugs……

Conservative …… or Dialysis …….

Part 1V

Outcome –to be documented at discharge or at end of two week follow up

Maternal i) Pregnancy ongoing or

ii) Delivered –SVD…….or CS ……..

iii) Maternal status Alive……. or Dead ……

Foetal i) Age at birth

ii)Status at birth - life infant or fresh still birth

Renal-Trends of serum creatinine ……

1) Improved if severity of PRAKI changes to a lower stage
2) Worsened if severity of PRAKI advances to a higher stage
3) Static if severity of PRAKI does not change

-Need for dialysis due to either –

1) Resistant hyperkalemia,
2) Metabolic acidosis,
3) Fluid overload and pulmonary oedema
4) Uremic - Encephalopathy, Pericarditis,
   - Coagulopathy, Gastritis or
5) Combination of two or more factors

Appendix 2: Consent explanation

ASSESSMENT OF THE CHARACTERISTICS OF PATIENTS WITH PREGNANCY RELATED ACUTE KIDNEY FAILURE AT THE KENYATTA NATIONAL HOSPITAL

My name is Dr. JAYNE MUENI KIVAI a post graduate student in the Department of Internal Medicine and Therapeutics, University Of Nairobi.

I am the principal investigator conducting a research study on patients with pregnancy related acute kidney injury, who are admitted in the wards in the Department of Reproductive Health, at Kenyatta National Hospital in Labour ward, Ground Floor A and B, Wards 1A and 1D.

Purpose of the study.

This is a non- interventional study aiming at describing the characteristics of women with acute kidney injury in pregnancy, during labour and up to six weeks after delivery. The study will assess the socio-demographic, clinical, and laboratory characteristics. Acute kidney injury is a state, (which can occur to any one,) in which the kidneys do not function well and fail to adequately filter and remove waste and water from the body, so the waste and water accumulate within the body and cause harm to all organs in the body.

Procedures

If you agree to participate in this study or in the case of a minor, you as the parent / guardian of minor accept that she should participate in the study, there will be a request that:

The patient or in the case of a minor, the patient's parent/guardian answers questions relating to their (patient's) socio demographics, past and present medical history and will also search for clinical information from your medical file. The study will not extend your stay in hospital or make you pay for the investigations.

Risks

There will be no risks.

Benefits

1. The interpretation of the results in the file will be explained to you the patient and in case of a minor, to the guardian/parent and the same results' interpretation, will be shared with the primary doctor for your management.
2. For those with kidney dysfunction, caregivers will be informed so as to institute appropriate management.

Confidentiality

Strict confidentiality will be maintained and all the data obtained will be securely stored and used for purposes of this study only.

Conclusion

Participation in this study is voluntary and you, the patient or in the case of a minor, her guardian/parent, is free to withdraw at any time during the course of this study period. You or your parent's/ guardian's refusal to participate or withdrawal from the study will not in any way affect the quality of your/ her treatment. Kindly note that apart from the benefits outlined above, there will be no monetary compensation for your participation or the participation of your child, in the study. Your stay in the ward and time of discharge will be determined by your primary doctor.

If you have any questions concerning the study kindly contact any of the following

1. Dr. JAYNE MUENI KIVAI Cell phone number 0722763160
   DEPARTMENT OF INTERNAL MEDICINE AND THERAPEUTICS,
   UNIVERSITY OF NAIROBI

2. PROF. JOSHUA K. KAYIMA Telephone number 020 4915041
   ASSOCIATE PROFESSOR /NEPHROLOGIST
   DEPARTMENT OF INTERNAL MEDICINE AND THERAPEUTICS
   UNIVERSITY OF NAIROBI

3. DR.WERE A.J.O Telephone number 020 4915041
   CONSULTANT PHYSICIAN /NEPHROLOGIST
   DEPARTMENT OF INTERNAL MEDICINE AND THERAPEUTICS
   UNIVERSITY OF NAIROBI
4. The secretary
   KNH-UoN ERC
   Telephone number 2726300 ext.44102

Appendix 3: Consent form – adults (18 years and above)

I…… …….. After reading the consent explanation form and having been explained to by Dr. KIVAI JAYNE MUENI (the principal investigator) do voluntarily agree to take part in this study on ASSESSMENT OF THE CHARCTERISTICS OF PATIENTS WITH PREGNANCY RELATED ACUTE KIDNEY FAILURE AT THE KENYATTA NATIONAL HOSPITAL.

I am also aware that I can withdraw from this study without losing any benefits or the quality of management of my medical problem.

Signed/ Thumbprint…… ……Date……. Contacts: Patient Tel……

Physical address …….. ……Next of kin/ Caretakers……..

Name……Tel……Relationship……

I confirm that I have explained to the patient the details of the consent explanation form.

Signed……. Date…… (interviewer)

Appendix 4: Consent form – minors (below 18 years)

I……parent/guardian to …….. …….after reading the consent explanation form and having been explained to by Dr. KIVAI JAYNE MUENI (the principal investigator) do voluntarily agree to have my daughter take part in this study ASSESSMENT OF THE CHARCTERISTICS OF PATIENTS WITH PREGNANCY RELATED ACUTE KIDNEY AT KENYATTA NATIONAL HOSPITAL .I am also aware that I can withdraw my child from this study without her losing any benefits or affecting the quality of management of her medical problem.

Sign/thumb print…… Date……Telephone contacts (of parent/guardian)……

I confirm that I have explained to the parent/ guardian the contents of the consent explanation form. Signed…… Date ….……. (Interviewer)

Appendix 5: Maelezo ya kibali

ASSESSMENT OF THE CHARCTERISTICS OF PATIENTS WITH PREGNANCY RELATED ACUTE KIDNEY FAILURE AT THE KENYATTA NATIONAL HOSPITAL

Jina langu ni Dk. JAYNE MUENI KIVAI mwanafunzi aliyehitimu katika Idara ya Dawa na Matibabu ya Ndani, Chuo Kikuu cha Nairobi.

Mimi ni mfuatiliaji mkuu anayefanya utafiti wa utafiti kwa wagonjwa walio na jeraha kubwa ya figo kuhusiana na ujauzito, ambao wanaingizwa kwenye kata katika Idara ya Afya ya Uzazi, Kliniki ya Taifa ya Kenyatta katika kata ya kujifungua , Ground Floor A na B, Kata 1A na 1D.

Kusudi la utafiti

Hii ni utafiti usioingilia kati ambao unalenga kuelezea sifa za wanawake wenye uharibifu wa figo papo hapo wakati wa ujauzito, wakati wa kujifungua na hadi wiki sita baada ya kujifungua. Utafiti huo pia utachunguza tabia za jamii, za kliniki, na za maabara. Kujeruhiwa kwa figo kali ni hali (ambayo inaweza kutokea kwa mtu yeyote), ambayo figo hazifanyi kazi vizuri na hushindwa kuchuja na kutosha taka na maji kutoka kwenye mwili, hivyo taka na maji hujilimbikiza ndani ya mwili na kusababisha madhara kwa viungo vyote katika mwili.

Taratibu

Ikiwa unakubali kushiriki katika utafiti huu au katika kesi ya mdogo, wewe kama mzazi / mlezi wa mdogo kukubali kwamba anapaswa kushiriki katika utafiti, kutakuwa na ombi kwamba:

Mgonjwa au katika kesi ya mdogo, mzazi / mlezi wa mgonjwa anajibu maswali yanayohusiana na idadi ya watu (ya mgonjwa) ya historia ya matibabu, historia ya matibabu ya sasa na ya sasa na kutafuta habari za kliniki kutoka kwenye faili yako ya matibabu . Utafiti hauongezi kupumzika kwako katika hospitali au kukupa malipo ya uchunguzi.

Hatari. Hakutakuwa na hatari yoyote

Faida

1. ufafanuzi wa matokeo katika faili utakuelezea mgonjwa na kwa upande wa mdogo , mlezi wake / mzazi na sawa atashirikiwa na daktari wa msingi kwa usmamizi wako.
2. Kwa wale wenye matatizo ya figo, wasaidizi watatambuliwa kama vile kuanzisha usimamizi sahihi.

Usiri

Usiri thabiti utahifadhiwa na data zote zilizopatikana zitahifadhiwa na kutumika kwa ajili ya utafiti huu tu.

Hitimisho

Kushiriki katika utafiti huu ni kwa hiari na wewe, mgonjwa au katika kesi ya mdogo, mlezi wake / mzazi, ni huru kujiondoa wakati wowote wakati wa kipindi hiki cha utafiti. Wewe au kukataa kwa mzazi wako / mlezi wako kushiriki au kujiondoa kutoka kwenye

utafiti hautaathiri ubora wa matibabu yako kwa namna yoyote. Tafadhali kumbuka kwamba mbali na faida zilizotajwa hapo juu, hakutakuwa na fidia ya fedha kwa ushiriki wako au ushiriki wa mtoto wako, katika utafiti. Kukaa kwako katika kata na wakati wa kutokwa utatambuliwa na daktari wako wa msingi.

Ikiwa una maswali yoyote kuhusu utafiti unaweza kuwasiliana na wafuatao

1. Dk. JAYNE MUENI KIVAI Namba ya simu ya mkononi 0722763160
   DEPARTMENT OF INTERNAL MEDICINE AND THERAPEUTICS
   UNIVERSITY OF NAIROBI

2. PROF. JOSHUA K. KAYIMA Namba ya simu 020 4915041
   CONSULTANT PHYSICIAN /NEPHROLOGIST
   DEPARTMENT OF INTERNAL MEDICINE AND THERAPEUTICS
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   UNIVERSITY OF NAIROBI
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   Telephone number 2726300 ext.44102

Appendix 6: **Fomu ya shahili – watu wazima (miaka 18 na zaidi)**

ASSESSMENT OF THE CHARCTERISTICS OF PATIENTS WITH PREGNANCY RELATED ACUTE KIDNEY FAILURE AT THE KENYATTA NATIONAL HOSPITAL

Mimi.....Baada ya kusoma fomu ya ufafanuzi wa ridhaa na kuelezewa na Dk. KIVAI JAYNE MUENI (mfuatiliaji mkuu) kwa hiari wanakubali kushiriki katika utafiti huu juu ya utafiti juu ya wagonjwa walio na mimba ya ugonjwa wa figo papo hapo(ASSESSMENT OF THE CHARCTERISTICS OF PATIENTS WITH PREGNANCY RELATED ACUTE KIDNEY INJURY AT THE KENYATTA NATIONAL HOSPITAL) ambao wanaingizwa kwenye kata katika Idara ya Afya ya Uzazi,Hospitali ya Taifa ya Kenyatta

Ninajua pia kwamba ninaweza kujiondoa kwenye utafiti huu bila kupoteza faida yoyote au ubora wa usimamizi wa shida yangu ya matibabu.

Ishara / kuchapisha kidole..... Tarehe.....

Mawasiliano: Mgonjwa Tel.....Anwani ya kimwili…….. Karibu na jamaa /wahudumia: Jina..... Tel..... Uhusiano……..

Ninahakikishia kwamba nimewaelezea mgonjwa maelezo ya fomu ya maelezo ya idhini. Iliyotumwa.....Dha..... (mhojiwaji)

Appendix 7: Fomu ya shahili – watoto (miaka chini ya 18)

ASSESSMENT OF THE CHARCTERISTICS OF PATIENTS WITH PREGNANCY RELATED ACUTE KIDNEY FAILURE AT THE KENYATTA NATIONAL HOSPITAL

Baada ya kusoma fomu ya ufafanuzi wa ridhaa na kuelezewa na Dk. KIVAI JAYNE MUENI (mfuatiliaji mkuu) kwa hiari wanakubali kushiriki katika utafiti huu juu ya utafiti juu ya wagonjwa walio na mimba ya ugonjwa wa figo papo hapo,(ASSESSMENT OF THE CHARCTERISTICS OF PATIENTS WITH PREGNANCY RELATED ACUTE KIDNEY AT KENYATTA NATIONAL) ambao wanaingizwa kwenye kata katika Idara ya Afya ya Uzazi,Hospitali ya Taifa ya Kenyatta.

Ninajua pia kwamba ninaweza kujiondoa kwenye utafiti huu bila kupoteza faida yoyote au ubora wa usimamizi wa shida yangu ya matibabu.

Ishara / kuchapisha kidole..... Tarehe.....

Mawasiliano: Mgonjwa Tel.....Anwani ya kimwili…….

Karibu na jamaa /wahudumia Jina..... Tel.....

Uhusiano.....

Jina..... Simu..... Uhusiano..... Ninahakikishia kwamba nimewaelezea mgonjwa maelezo ya fomu ya maelezo ya idhini.

Iliyotumwa.....Dha..... (mhojiwaji).