Incidence and Predictors of Acute Kidney Injury Among Women With Severe Pre-eclampsia at Mbarara Regional Referral Hospital

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Abstract

Background

The presence of acute kidney injury (AKI) in pre-eclampsia complicates treatment including; increasing length of hospital stay and a need to access services like dialysis which are largely expensive in resource-limited settings. We aimed to determine incidence and predictors of acute kidney injury among women with severe pre-eclampsia at Mbarara Regional Referral Hospital in southwestern Uganda.

Methods

We carried out a hospital-based prospective cohort study from 16 November 2018 to 18 April 2019, among pregnant women with severe preeclampsia followed up in the hospital. We enrolled 70 mothers with severe pre-eclampsia and eclampsia; we excluded patients with a history of chronic renal disease, chronic hypertension, and gestational hypertension.

Data on socio-demographics, laboratory parameters, health system, obstetric and medical factors were collected. Baseline serum creatinine, complete blood count, and CD4 T-cell count were all done at admission (0-hour). Second serum creatinine was done at 48-hours to determine the presence of AKI. AKI was defined as a rise in serum creatinine of 0.3mg/dl or more from the baseline. The proportion of women diagnosed with acute kidney injury among the total number of women with severe pre-eclampsia was reported as incidence proportion. Univariate and multivariate logistic regression was used to establish the association of acute kidney injury and severe pre-eclampsia.

Results

Incidence of acute kidney injury was high (41.4%) among women with severe pre-eclampsia. Antenatal care attendance was protective 0.36 (0.16, 0.80), $p < 0.013$ at bivariate analysis but had no statistical significance at multivariate analysis. Eclampsia was an independent risk factor for acute kidney injury. (aRR 2.74 (1.06, 7.08), $P < 0.037$).

Conclusion

The incidence of acute kidney injury in patients with preeclampsia is high.

Eclampsia is an independent risk factor of acute kidney injury.

Introduction

Acute Kidney Injury (AKI) is defined as an abnormality of the excretory function of the kidney characterized by an accumulation of nitrogenous waste which includes urea and creatinine(1). AKI normally happens in hours, days, or weeks and is potentially reversible. The diagnosis of AKI is normally made on history, measurement of kidney function, and detection of urine abnormalities.

Incidence and factors associated with acute kidney injury in women with severe pre-eclampsia vary. Severe renal impairment occurs frequently when pre-eclampsia is complicated by abruption placentae or hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome (2). A history of pre-eclampsia in previous pregnancies increases the risk of acute kidney injury by 3 while this risk is increased to 5 if two or more previous pregnancies were complicated by pre-eclampsia(3).

The most common causes of AKI in pregnancy are preeclampsia and eclampsia, which can ultimately lead to an increase in maternal mortality rates(4). In Africa, AKI is a challenging problem because of the burden of disease, the late presentation of patients to health care facilities, and the lack of resources to support patients with established AKI in many countries(5).

The presence of AKI in pre-eclampsia complicates the treatment including increasing the length of hospital stay, the need to access services like dialysis which are largely expensive. It is therefore paramount to know the incidence and predictors of AKI in the setting of Mbarara Regional Referral Hospital in Southwestern Uganda in mothers admitted with severe pre-eclampsia.

Study Design, Setting And Population:

We prospectively enrolled 70 participants on the maternity ward at Mbarara Regional Referral Hospital (MRRH) to determine the incidence and predictors of acute kidney injury in mothers admitted with severe pre-eclampsia. MRRH is a public regional referral hospital that serves as a teaching hospital for Mbarara University of Science and Technology. The hospital serves as a referral for the western region of Uganda but also receives patients from refugee camps of Rwanda, Congo, and Burundi. The hospital offers specialized services, employs eleven obstetricians and 32 midwives together with resident doctors who perform over 10,000 deliveries annually. The hospital also can perform laboratory tests including chemistries, urinalysis, and ultrasonography among others. A resident nephrologist in the hospital can perform acute hemodialysis for patients who require the service.

The study population consisted of all women having severe pre-eclampsia and eclampsia between November 2018 to April 2019. We included all women who were diagnosed with severe pre-eclampsia/eclampsia defined as high blood pressure ($\geq 140/90$ mmHg) plus one or more of the following symptoms of severity (headache, epigastric pain, blurring of vision, convulsions, and proteinuria plus 2 or 3 on urine dipstick). Women who had a history or documentation of chronic renal disease and chronic hypertension and gestational hypertension were excluded. Eligible women were recruited until the sample size was attained. Consent was obtained and blood samples were taken for baseline renal function tests. After 48 hours another sample was drawn for a 2nd creatinine. A difference of serum creatinine ≥ 0.3 mg/dl from the baseline was considered AKI and patients were followed up by the study team while in hospital from the time of admission to when they were discharged. The sample size was estimated based on the Fleiss formula (1981) for cohort studies.

The major outcome variable of the study was acute kidney injury. The primary exposure variable was severe pre-eclampsia while the secondary exposure variables were sociodemographic factors, healthcare

system factors, obstetric factors which included gravidity/parity, gestation age at diagnosis of pre-eclampsia and admission to the hospital, postpartum hemorrhage, antepartum hemorrhage, eclampsia, HELLP syndrome and previous history of pre-eclampsia. The medical factors were a history of diabetes, hypertension, and HIV infection.

Statistical analysis

Data was captured using Redcap, and exported to Excel. All analyses were performed using Stata software Version 13.0. Continuous variables such as age were presented as means and standard deviation for normally distributed variables or median and interquartile range for variables not normally distributed. The incidence proportion of AKI was derived as the proportion of women diagnosed with acute kidney injury among the total number of women with severe pre-eclampsia/eclampsia. Bivariate and multivariate logistic regression models were used to identify predictors of acute kidney injury. Predictor variables were variables with relative risk. Additional variables were included if on bivariate analysis they demonstrated a correlation with the outcome of interest (acute kidney injury) with a *P*-value <0.05. Backward stepwise elimination was used to create the final model, and all variables with *P*-values <0.05 in the final model were considered significant independent factors associated with acute kidney injury.

Results

A total of 4547 obstetrics and gynecology admissions were conducted during the study period, out of which 75 met the inclusion criteria. Among those eligible, some participants refused to participate while others escaped from the hospital before official discharge. 70 participants were recruited.

The mean age of our study participants was 27.5(±6.4) years with 87.1% of them being married. 65.7% of the participants were housewives and 76.7% of the participants were referred from lower health facilities. A majority (85.3%) reported having attended antenatal care clinics. The commonest gestational age at delivery was 36 weeks and above. HELLP syndrome accounted for 27.1% of cases while 21.4% had eclampsia. The mean systolic blood pressure was 166 (±28.5) while the diastolic was 108(±16.8) mmHg. The mean baseline creatinine was 0.9mg/dl (±0.3). 68.6% of the participants had proteinuria and the mean hemoglobin level was 11.3g/dl (±2.4). The details of the participants' baseline characteristics are shown in

Table 1: **Baseline characteristics of study participants**

Characteristics	Overall N=70 N (%)
Age, in years, mean (SD)	27.5(±6.4)
Education category	
None	26 (37.1)
Primary	20 (28.6)
Marital status	
Married	61 (87.1)
Housewife	46 (65.7)
Referring facility	
HC III and IV	39 (76.5)
Obstetric factors	
Multigravida	51 (72.9)
ANC attendance, yes (N=68)	58 (85.3)
Gestational age at diagnosis	
20 - 28 weeks	12 (17.1)
28 - 34 weeks	18 (25.7)
34 - 36 weeks	12 (17.1)
36 weeks & above	28 (40.0)
Abruption placenta	4 (5.7)
HELLP syndrome	19 (27.1)
Eclampsia	15 (21.4)
Laboratory parameters	
Haemoglobin in g/dl, mean (SD)	11.3 (±2.4)
< 10 g/dl	13 (18.6)
> 10g/dl	57 (81.4)
Proteinuria	48(68.6)
Baseline creatinine at admission in mg/dl, mean (SD)	0.90 (±0.3)
HIV status, positive	5 (7.1)

SBP at admission in mmHg, mean (SD)	166 ($\pm$ 28.5)
DBP at admission in mmHg, mean (SD)	108.8 ($\pm$ 16.8)

Abbreviations: HC Health Center, ANC Antenatal Care, HIV Human Immunodeficiency Virus, HELLP-Hemolysis Elevated Liver Enzymes Low platelets, SBP Systolic Blood pressure, DBP Diastolic Blood pressure

Incidence of Acute Kidney Injury

The incidence of acute kidney injury among women with severe pre-eclampsia/ eclampsia was 29/70 (41.4%) and is diagrammatically represented in **figure 1**.

Predictors of acute kidney injury in logistic regression (both univariate multivariate analysis)

Antenatal care attendance was protective with a crude risk ratio of 0.36 (0.16, 0.80), $p < 0.013$ in bivariate analysis but there was no statistical significance at multivariate analysis. Eclampsia was an independent risk factor of acute kidney injury (aRR 2.74, 95% CI 1.06 - 7.08, $P < 0.037$). The details of the predictors of acute kidney injury among women with pre-eclampsia are shown in **table 2**.

Table 2: Predictors of acute kidney injury by logistic regression

Abbreviations: ANC Antenatal Care, HIV Human Immunodeficiency Virus, SBP Systolic Blood Pressure, DBP Diastolic Blood Pressure

Discussion

In this prospective study, our main goal was to establish the incidence and predictors of AKI

among mothers admitted with pre-eclampsia admitted at the maternity ward of Mbarara Regional

Referral Hospital (MRRH). We found a high cumulative incidence of AKI of 41.4%, and

eclampsia as the main independent predictor of AKI, within 48 hours after admission. Our findings were lower than what was reported among severe preeclampsia/eclampsia patients in Cameroon among whom 66.7% developed acute kidney injury. This could be because a majority (72.5%) of the enrolled participants in the study done in Cameroon had eclampsia (6) compared to our study which had only 21.4% patients with eclampsia. Furthermore, the Cameroon study was conducted in an intensive care unit and also had 7 years of follow-up. Data from developed countries suggests lower rates of AKI, with estimates as low as 1-2.8% (7). However, in developing countries, the incidence of AKI is high ranging from 36% to 66.7% (8, 9), Cameroon (66.7%)(10), Morocco (66.7%)(11). The high incidence of AKI in developing countries may be attributed to the late presentation of patients to hospitals for care.

In our study eclampsia was the main independent predictor of AKI (aRR 2.74, (5%CI 1.06 - 7.08,

Characteristic	Bivariate analysis	p-value	Multivariate analysis	P-value
	cRR (95%CI)		aRR (95%CI)	
Age (each year)	1.022(0.97,1.08)	0.444	1.00(0.90,1.11)	0.991
ANC attendance				
No	Ref		Ref	
Yes	0.36 (0.16,0.80)	0.013	0.49 (0.16 ,1.54)	0.221
Eclampsia				
No	Ref		Ref	
Yes	2.24 (1.06,4.74)	0.035	2.74 (1.06,7.08)	0.037
HIV status				
Negative	Ref		Ref	
Positive	1.95(0.26,14.43)	0.514	2.01 (0.26,15.62)	0.506
SBP>160 or DBP>110				
No	Ref		Ref	
Yes	1.27 (0.59,2.72)	0.545	2.41 (0.81,7.18)	0.115
Gravidity				
2 or less	Ref			
3 or more	1.51(0.70,3.25)	0.291	0.87(0.11,6.75)	0.897
Parity				
2 or less	Ref			
3 or more	1.94(0.92,4.11)	0.381	1.83(0.31,10.96)	0.510
Gestational age at delivery				
20-28	Ref		Ref	
28-34	0.47(0.13,1.61)	0.228	0.72(0.13,3.93)	0.708
34 or more	0.64(0.29,1.43)	0.281	0.74(0.23,2.31)	0.600

P<0.037). This is in agreement with a prospective hospital-based study done in India which revealed that acute kidney injury was common among patients with eclampsia as high as 25 – 50% (12). This may be so because pre-eclampsia and eclampsia are associated with glomerular endotheliosis which decreases the glomerular filtration rate and renal blood flow. An increase in renal vascular resistance predisposes patients to AKI which is characterized by proteinuria and renal failure.

In our study, we noted that antenatal care attendance was associated with a reduction in the incidence of acute kidney injury compared to non-attendance; crude risk ratio 0.36, 95% C.I, 0.16-0.80, p-value 0.013. However, this was not significant at multivariate analysis and there was no association between the number of times the mothers attended antenatal care and the incidence of AKI. There is evidence to suggest that women with severe pre-eclampsia who present with severe complications are likely to have attended ANC fewer times than those without major complications ([Manandhar et al., 2013](#)). This may be so because antenatal attendance is associated with early detection of disease and timely intervention due to the structured routine screening of blood pressure and urine protein during antenatal visits.

However, some studies found no association between the number of times of antenatal care attendance and the severity of pre-eclampsia on presentation (13, 14). This may be because the disease progression pattern is most times unpredictable and acute complications can occur without warning symptoms.

The inability to use measure more sensitive renal biomarkers for the diagnosis of AKI was one of our study limitations. Serum creatinine takes time to rise and may lead to late detection of AKI.

Urine output is not routinely monitored quantitatively unless in very sick or catheterized patients.

Conclusion

The incidence of acute kidney injury in patients with pre-eclampsia/eclampsia is high (41.4%).

The presence of eclampsia in patients admitted with severe pre-eclampsia is associated with the development of AKI within 48 hours after hospitalization. We recommend a larger prospective study that will include the use of biomarkers for acute kidney injury and closer monitoring and management of mothers with eclampsia for features of acute kidney injury.

Abbreviations

AKI:	Acute Kidney Injury
ALP:	Alkaline phosphatase
AST:	Aspartate aminotransferase
ALT:	Alanine aminotransferase
ATN:	Acute tubular necrosis
CBC:	Complete blood cell count
CKD:	Chronic kidney diseases
eGFR:	Estimated Glomerular filtration rate

HELLP: Hemolysis, elevated liver enzymes and low platelet syndrome

LFT: Liver function test

MRRH: Mbarara Regional Referral Hospital

MUST: Mbarara University of science and Technology

OBS/GYN: Obstetrics and Gynecology

RFT: Renal function test

Declarations

Author Details

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Author contributions

All authors named in this manuscript have contributed substantially to this work and meet the criteria for authorship. MH, RM and RM took part in initial concept design, proposal writing, data collection, data interpretation, manuscript writing/revision, and approval of final work.

GW, SO, HML contributed towards data interpretation, revision of the manuscript, and approval of final work. NR contributed towards manuscript writing/revision.

Competing interests

The authors declare that they have no competing interests.

Ethics approval and Informed consent

This study was approved by the Mbarara University of Science and Technology's faculty review board and institutional ethics review board, and Uganda national council for science and technology. We confirm that all eligible participants or their caregivers provided informed consent to participate in this study and that the study got approval from the necessary bodies. All methods in this study were carried out in accordance with relevant guidelines and regulations.

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Figures

Figure 1

Incidence of acute kidney injury among mothers with pre-eclampsia