East African Medical Journal Vol. 99 No. 1 January 2022
RENAL COMPLICATIONS AMONG WOMEN WITH SEVERE PREECLAMPSIA MANAGED AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA
Dr. Kelvin Mutwiri, Resident, Department of Reproductive Health, School of Medicine, Moi University, P.O Box 1941-60100 Embu. Dr. Peter Itsura, Lecturer, Department of Reproductive Health, School of Medicine, Moi University, Gynecologic Oncologist MTRH/Moi University, P.O Box 6116-30100 Eldoret. Dr. Philiph Tonui, Lecturer, Department of Reproductive Health, School of Medicine, Moi University, Gynecologic Oncologist MTRH/Moi University, P.O Box 7933-30100 Eldoret.

Corresponding author: Dr. Kelvin Mutwiri, Department of Reproductive Health, School of Medicine, Moi University. P.O Box 1941-60100 Embu Email: kelvinmutwiri@gmail.com.

RENAL COMPLICATIONS AMONG WOMEN WITH SEVERE PREECLAMPSIA MANAGED AT MOI TEACHING AND REFERRAL HOSPITAL, ELDORET, KENYA

K. Mutwiri, P. Itsura and P. Tonui

ABSTRACT

***Objective*: To evaluate renal complications of women managed for severe preeclampsia at MTRH, Eldoret.**
***Design*: Prospective cohort study.**
***Setting*: Moi Teaching and Referral Hospital (MTRH), Eldoret**
***Participants*: The study recruited 61 (exposed) women with severe preeclampsia and 121 (non- exposed) women without severe preeclampsia all at ≥28 weeks gestation.**
***Outcome*: Acute kidney injury (AKI) and their outcomes which included spontaneous kidney recovery, medical intervention without dialysis, need for dialysis, need for continued dialysis at 6 weeks post-partum.**
***Results*: Complete data for 175 participants (57 exposed and 118 non-exposed) was available for analysis. Mean age was 28.57 (18-43) years. The incidence of AKI among the exposed was 26.3% and 5.9% among the non-exposed. The exposed were more likely to develop AKI than the non-exposed (RR 4.4 [95% CI 1.92 – 10.27]). Among those who had AKI in the exposed group, 85.7% recovered with medical intervention (without dialysis) while 14.3% underwent dialysis. History of preeclampsia in previous pregnancy (RR 18.18[95% CI 2.26 – 157.95]) and diagnosis of severe preeclampsia at <37 weeks gestation (RR 0.02 [95% CI 0.01 – 0.70]) were statistically associated with AKI in severe preeclampsia.**
***Conclusion*: Incidence of AKI in patients with severe preeclampsia was 26.3%. Severe preeclampsia increased the risk of AKI 4.4 fold. Among those with AKI, 85.7% recovered with medical intervention while 14.3% underwent dialysis. Factors associated with AKI in severe preeclampsia were history of preeclampsia**

in previous pregnancy and diagnosis of severe preeclampsia at <37 weeks gestation.

INTRODUCTION

Preeclampsia is the occurrence of new onset hypertension (systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg) plus new onset proteinuria after 20 weeks gestation which affects 2-8% of all pregnancies (1). The incidence in Kenya is 2.3% (2). It is a leading cause of maternal and perinatal morbidity and mortality globally. Proteinuria is diagnosed as protein urine excretion of equal to or greater than 300mg in 24 hours (24-hour urine sample) or if the ratio of measured protein to creatinine in single voided urine is 0.3 or more (1).

Severe features of preeclampsia include; systolic blood pressure of ≥160 mm Hg or diastolic blood pressure of ≥110 mm Hg (or both), thrombocytopenia (platelet count of less than 100,000/micro liter), impaired liver functions (elevated liver enzymes to twice normal or severe persistent right upper quadrant or epigastric pains unresponsive to medication, with no other attributable cause), pulmonary edema, new onset cerebral or visual disturbance and progressive renal insufficiency (serum creatinine greater than 1.1 mg/dl or doubled serum concentration in the absence other renal disease) (1).

Acute kidney injury (AKI) is the rapid or abrupt decline in renal filtration function characterized by reduced urine output (0.5mls/kg/h for 6 hours) or increase in serum creatinine (>26.5mmol/l, or >1.5 times baseline) (3). AKI in pregnancy is a life-threatening complication associated with maternal and fetal loss of 30-60% (4). It has been noted to have two incidence peaks; the first peak is in the first trimester mostly attributed to septic abortion. The second peak is in the late third trimester and early post-partum period. The latter comprises 75% of cases of AKI in pregnancy and can be attributed to late obstetric complications such as preeclampsia and/or Hemolysis, Elevated Liver enzymes, and a Low Platelet (HELLP) syndrome. Preeclampsia causes renal injury by glomerular endotheliosis which involves swelling and detachment of glomerular endothelial cells. This in turn leads to capillary lumina obstruction secondary to subendothelial deposits (5).

AKI affects 16% of patients with severe preeclampsia (6). Outcomes of AKI in severe preeclampsia include spontaneous recovery, medical interventions, need for dialysis, progression to chronic kidney disease and need for renal transplant as well as related morbidities and mortalities (3). Indications for dialysis in patients who develop AKI include pulmonary edema, hyperkalemia, uremia, severe metabolic acidosis and hypervolemia (3).

Among patients with severe preeclampsia who developed AKI, 34% require dialysis while 2% develop persistent proteinuria suggestive of chronic kidney disease (6). Among women with preeclampsia 31% develop microalbuminuria, compared to 7% without, accounting to a fourfold increased risk of renal disease. There is an eight-fold risk in women with severe preeclampsia (7). In Moi Teaching and Referral Hospital (MTRH), there is no data on the renal complications and their outcomes in severe preeclampsia, thus a gap in knowledge on the same, a problem that this study sought to address.

The main objective of this study was to evaluate renal complications of women managed for severe preeclampsia at MTRH, Eldoret. The specific objectives included; To determine the incidence of AKI among women

with severe preeclampsia at MTRH, to evaluate AKI outcomes among women with severe preeclampsia at MTRH and to determine the factors associated with AKI in severe preeclampsia at MTRH.

MATERIALS AND METHODS

This was a prospective cohort study conducted at Riley Mother and Baby Hospital (RMBH) of the MTRH, Eldoret, Kenya. This is the second largest referral hospital in Kenya located in Eldoret, Uasin Gishu County, in Western Kenya (310 kilometers Northwest of Nairobi). It serves residents of Western Kenya, parts of Eastern Uganda and Southern Sudan with a population of approximately 24 million.

The target population comprised women who sought obstetric care at RMBH, MTRH and admitted for antenatal care and delivery. The study population comprised women with severe preeclampsia at a gestation of 28 weeks and above. It involved 61 women with severe preeclampsia (exposed group) and 121 without severe preeclampsia or other hypertensive disorders in pregnancy (non-exposed group) all at ≥28 weeks gestation and followed up to 6th week postpartum, a total of 182 participants. Patients with a history of chronic kidney disease and renal transplant in both groups were excluded. It was conducted from September 2019 to August 2020.

The exposed participants were selected using systematic sampling technique. In the year 2018 the estimated number of patients admitted with severe preeclampsia was 255 in MTRH. Hence the sampling interval was k = N/n = 255/61=4.1, thus every fourth patient with severe preeclampsia was selected to attain the desired sample size of 61. Two non-exposed participants matched for gestation age and parity were selected consecutively for every exposed participant to attain the desired sample size of 121. Matching for gestation age and parity was to ensure equal distribution of the same between the exposed and non-exposed. Recruitment was done in RMBH, MTRH at the admission desk or antenatal ward.

Severe preeclampsia was defined as blood pressure of either systolic of ≥160 mm Hg, diastolic of ≥110 mm Hg or both with proteinuria of 3+. AKI was defined as an increase in creatinine level by ≥26.5 mmol/l above the upper normal range.

Data was collected using a semi-structured questionnaire which was pretested prior to the commencement of the study to ensure that it was appropriately designed. Socio-demographic as well as the clinical characteristics were taken at recruitment. Initial creatinine levels were done at admission. Creatinine levels for the exposed were repeated after the admission as per MTRH protocol on severe preeclampsia, at week 2 and 6 postpartum. Creatinine levels for the non-exposed who had AKI were also repeated at week 2 and week 6 postpartum. All the participants were subjected to equal treatment based on their conditions as per respective MTRH protocols.

Data was analyzed using STATA 16. At descriptive level, data was analyzed separately for the exposed and the non-exposed. Age was summarized as mean and corresponding standard deviation. Categorical data such as education level, occupation, marital status, parity, gestation, blood pressure and history of preeclampsia in previous pregnancy were summarized as frequency and percentages. At bivariate level, Chi Square, Students t-tests and Fisher's exact test were done to compare AKI and other categorical variables such as age, occupation, education level, marital status, parity, gestation at diagnosis and history of preeclampsia in previous pregnancy. Variables

at bivariate analysis that were statistically significant were subjected to multivariable logistic regression to determine factors associated with AKI. Statistical significance was tested at P <0.05. All statistical analysis were performed at 95% confidence level.

Approval was obtained from Institutional Research and Ethics Committee (IREC) of Moi University. Permission to carry out the study was obtained from MTRH management and the Department of Reproductive Health. Upon acceptance to participate in the study, the participants signed a written informed consent. Confidentiality and anonymity of the respondents was maintained. There was no compensation of study participants.

RESULTS

Complete data for 175 participants (57 exposed and 118 non-exposed) was available for analysis. Mean age of participants was 28.57 (18-43) years. Majority of the participants had attained secondary education level (40.6%). Majority were unemployed (62.9%) and married (78.9%). Majority of them were multipara (58.3%) and had a gestational age of >37 weeks (60.6%). Majority did not have a history of severe preeclampsia in previous pregnancy / pregnancies (94.9%). Age, education level, occupation, marital status and parity were equally distributed among the exposed and the non-exposed (p>0.05). Gestation at diagnosis and history of preeclampsia in previous pregnancy varied significantly among the two groups. Tables 1 and 2 shows the socio-demographic and clinical characteristics respectively of the study participants.

The incidence of AKI in severe preeclampsia was 26.3% (15/57) and 5.9% (7/118) for the non-exposed. The exposed were 4.4 (95% CI 1.92 – 10.27) times more likely to develop AKI compared to the non-exposed.

Table 1

Socio-demographic characteristics of the study participants

Variable	Severe preeclampsia(n =57)	No severe preeclampsia (n=118)	Totals (n=175)	p-value
Age (years)				
Mean (SD)	29.19 (6.51)	28.26 (5.86)	28.57 (6.1)	0.344[t]
Range	19 – 43	18- 43	18-43	
Education level				
None	0 (0%)	5 (4.2%)	5 (2.9%)	0.487[f]
Primary	9 (15.8%)	20 (16.9%)	29 (16.6%)	
Secondary	20 (35.1%)	51 (43.2%)	71 (40.6%)	
Tertiary	28 (49.1%)	42 (35.6 %)	70 (40.0%)	
Occupation				
Unemployed	36 (63.2%)	74 (62.7%)	110 (62.9%)	0.877[c]
Self-employed	11 (19.3%)	26 (22.0%)	37 (21.1%)	
Formal employment	10 (17.5%)	18 (15.3%)	28 (16.0%)	
Marital status				
Married	45 (78.9%)	93 (78.8%)	138 (78.9%)	0.984[c]
Single	12 (21.1%)	25 (21.2%)	37 (21.1%)	

t t-tests, f Fisher's Exact test, c Chi Square.

Table 2

Clinical characteristics of the study participants

Variable	Severe preeclampsia (n=57)	No severe preeclampsia (n=118)	Totals (n=175)	p-value	
Parity					
Primigravida	19 (33.3%)	33 (28.0%)	52 (29.7%)	0.744[c]	
Multipara	32 (56.1%)	70 (59.3%)	102 (58.3%)		
Grand Multipara	6 (10.5%)	15 (12.7%)	21 (12.0%)		
Gestation at Diagnosis					
<37 weeks	29 (50.9%)	40 (33.9%)	69 (39.4%)	0.031[c]	
≥37 weeks	28 (49.1%)	78 (66.1%)	106 (60.6%)		
History of preeclampsia in previous pregnancy					
No	49 (86.0%)	117(99.1%)	166(94.9%)	0.001[f]	
Yes	8 (14.0%)	1 (0.9%)	9 (5.1%)		

c Chi Square, f Fisher's Exact test.

Among those with AKI, 14 (93.3%) required medical intervention (RR 0.42 [95% CI 0.02-8.42]) Of these, 12 (85.7%) recovered while 2 (14.3%) required dialysis (RR 1.20 [95% CI 0.08,16.4]). There was 1 recovery after dialysis and 1 continued with dialysis at 6 weeks post-partum (RR 0.33 [95% CI 0.06-1.86]). (Table 3).

Table 3

Outcomes of AKI among the study participants (overall N=22)

Variable	Severe preeclampsia (n=15)	No severe preeclampsia(n=7)	RR (95%CI)	P Value
Spontaneous kidney recovery without intervention				
No	14 (93.3%)	6 (85.7%)	Reference	
Yes	1 (6.7%)	1 (14.3%)	2.33 (0.12,4.37)	0.003
Need for medical intervention				
No	1 (6.7%)	1(14.3%)	Reference	
Yes	14 (93.3%)	6 (85.7%)	0.42 (0.02,8.42)	0.504
Requires dialysis				
No	12 (85.7%)	5 (83.3%)	Reference	
Yes	2 (14.3%)	1 (16.7%)	1.20 (0.08,16.4)	0.063
Outcome of dialysis				
Recovery	1 (50%)	1 (100%)	Reference	
Continuous dialysis	1 (50%)	0 (0%)	0.33 (0.06, 1.86)	0.901

The proportion of those who developed AKI was significantly high (p=0.009) among those with a gestation of <37 weeks (41.4%) compared with those with a gestation of ≥37 weeks (10.7%). Those with history of preeclampsia in previous pregnancies had higher proportion with AKI (62.5%) compared to those without (p=0.024) (table 4).

Table 4

AKI in severe preeclampsia by Socio-Demographic and clinical characteristics; Bivariate analysis

Variable	No AKI (n=42)	AKI (n=15)	p-value
Age (years)			
Mean (SD)	28.95 (6.56)	29.87 (6.57)	0.645[t]
Range	19 – 43	21- 43	
Education level			
Primary	6 (66.7%)	3 (33.3%)	0.719[f]
Secondary	14 (70%)	6 (30%)	
Tertiary	22 (78.6%)	6 (21.4%)	
Occupation			
Unemployed	26 (72.2%)	10 (27.8%)	>0.99[f]
Self-Employed	8 (72.7%)	3 (27.3%)	
Formal Employment	8 (80%)	2 (20%)	
Marital status			
Married	33 (73.3%)	12 (26.7%)	>0.99[f]
Single	9 (75%)	3 (25%)	
Parity			
Primigravida	14 (73.7%)	5 (26.3%)	>0.99[f]
Multipara	28 (73.7%)	10 (26.3%)	
Gestation at Diagnosis			
<37 weeks	17 (58.6%)	12 (41.4%)	0.009[c]
≥37 weeks	25 (89.3%)	3 (10.7%)	
History of preeclampsia in previous pregnancy			
No	39 (79.6%)	10 (20.4%)	0.024[f]
Yes	3 (37.5%)	5 (62.5%)	

t t-tests, f Fisher's Exact test, c Chi Square.

After logistic regression, gestation age at diagnosis (RR 0.02 [95% CI 0.01 – 0.70]) and history of preeclampsia in previous pregnancy (RR 18.18[95% CI 2.26 – 157.95]) were still statistically significant (table 5).

Table 5

AKI in severe preeclampsia; logistic regression

Variable	No AKI (n=42)	AKI (n=15)	RR	95% CI	p-value
Gestation at diagnosis					
<37 weeks	17 (58.6%)	12 (41.4%)	Ref		
≥37 weeks	25 (89.3%)	3 (10.7%)	0.02	0.01 – 0.70	0.001
History of preeclampsia in previous pregnancy					
No	39 (79.6%)	10 (20.4%)	Ref		
Yes	3 (37.5%)	5 (62.5%)	18.88	2.26 – 157.95	0.007
Adjusted Relative Risk					

None of the factors were significantly associated with AKI in the non-exposed group on bivariate analysis.

DISCUSSION

In this study, the incidence of AKI among the exposed was 26.3% (15/57) and 5.9% (7/118) for the non-exposed. The exposed were 4.4 (relative risk) (95% CI 1.92 – 10.27) times more likely to develop AKI compared to the non-exposed. This is in contrast to a study by Eswarrappa et al, in India who reported an incidence of 16% (6). The higher rate in this study could be attributed to the fact that the Indian study was conducted in a more developed country as compared to this study with better health seeking behaviors, better technology as well as more and better trained human resource. The findings of this study also contrast to the findings by Frances et al., who reported an incidence of 15.3% (8). The study was conducted in South Africa which is similarly a more developed country. The higher rate in this study as compared to the two studies above could also be attributed to possible concomitant uterine bleeding and sepsis, both of which can cause or worsen AKI. In the exposed group 85.7% of those receiving medical intervention recovered while 14.3% required dialysis. These findings are consistent with findings by Frances et al., and Drakeley et al., who reported 12.5% and 10% respectively required dialysis (8,9). They however contrast to Eswarrappa et al., who reported that 34% of the AKI cohort underwent dialysis (6). This difference may be attributed to lower threshold to do dialysis on AKI patients being a more developed country with better medical technology and human resource.

Gestation age at diagnosis was statistically significant as a factor associated with AKI in severe preeclampsia (RR 0.02 [95% CI 0.01 – 0.70]). Diagnosis at <37 weeks had a higher percentage of AKI (24.2%) compared to ≥37 weeks. This could be explained by the fact that diagnosis of patients with severe preeclampsia at advanced gestation age are delivered immediately on diagnosis, thus less exposed to the effect of the disease on the kidneys. History of preeclampsia in previous pregnancy was also statistically significant (RR 18.18[95% CI 2.26 – 157.95]). Frances I et al., showed preeclampsia in the previous pregnancy was the strongest predictor of AKI (odds ratio, 1.87; 95% CI 1.10–3.18) which is in keeping with the findings of this study (8). This maybe be due to possible subtle disease on kidneys of patients with history of preeclampsia in previous pregnancy thus predisposing them to AKI in the subsequent pregnancy.

The strength of this study design was that it was prospective cohort with 2 groups (exposed and non-exposed). This enabled a comparison of the 2 groups thus showing associations as well as relative risks of developing AKI in severe preeclampsia. Its limitations were that it was a hospital based study and may not be generalizable to the general population and that other confounders that may have affected or led to development and severity of AKI such as hemorrhage, sepsis or other preexisting conditions were not studied.

CONCLUSION

This study found that the incidence of AKI in severe preeclampsia was 26.3% and that severe preeclampsia increased the risk of developing AKI 4.4 fold. In the cohort that developed AKI in severe preeclampsia, 14.3% required dialysis. Further, it found that gestation of severe preeclampsia at <37 weeks gestation and history of preeclampsia in previous

pregnancy were both statistically associated with developing AKI in severe preeclampsia.

RECOMMENDATIONS

From the above findings and in the absence of indications for dialysis, medical intervention is recommended for the patients who develop AKI in severe preeclampsia. History of preeclampsia in previous pregnancy and diagnosis of severe preeclampsia at <37 weeks gestation can help predict AKI, hence enhance close follow up and management. Further research with larger populations to assess for other confounders that may contribute to AKI development and severity in severe preeclampsia is recommended.

REFERENCES

1. American College of Obstetricians and Gynecologists. (2019). ACOG Practice Bulletin: Clinical Management Guidelines for Obstetrician-Gynecologists Number 202, January 2019: Gestational Hypertension and Preeclampsia. Obstetrics and gynecology, 133(1), 1 - 25.
2. Itoh M., Were F., Owidhi M., Gutman J., (2017) Incidence of Pregnancy-Associated Hypertension and preeclampsia in a Cohort of Kenyan Women. Annals of Gynecology and Obstetrics volume 1 | issue 1 | DOI: 10.36959/468/456
3. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of chronic Kidney Disease: volume 3 | issue 1 | JANUARY 2013.
4. Jamie Szczepanski, Ashley Griffin, Sarah Novotny and Kedra Wallace- Acute Kidney Injury in Pregnancies Complicated with preeclampsia or HELLP Syndrome. Front. Med., 07 February 2020.
5. J. Prakash and V. C. Ganiger. Acute Kidney Injury in Pregnancy-specific Disorders. Indian J Nephrol. 2017 Jul-Aug; 27(4): 258–270
6. Eswarappa, M., Rakesh, M., Sonika, P., Snigdha, K., Midhun, M., Kaushik, K., Chennabasappa, G.K., & Sujeeth, B. (2017). Spectrum of renal injury in pregnancy-induced hypertension: Experience from a single center in India. Saudi J Kidney Dis Transpl, 28, 279-84.
7. McDonald, S. D., Han, Z., Walsh, M. W., Gerstein, H. C., & Devereaux, P. J. (2010). Kidney disease after preeclampsia: a systematic review and meta-analysis. American journal of kidney diseases, 55(6), 1026-1039.
8. Frances I. Conti-Ramsden, Hannah L. Nathan, Annemarie De greeff, David R. Hall, Paul T. Seed, Lucy C. Chappell, Andrew H. Shennan, K. Bramham. Pregnancy-Related Acute Kidney Injury in preeclampsia Risk Factors and Renal Outcomes. Hypertension. 2019 Nov;74(5):1144-1151.
9. Drakeley AJ, Le Roux PA, Anthony J, Penny J. Acute renal failure complicating severe preeclampsia requiring admission to an obstetric Intensive Care Unit. Am J Obstet Gynecol 2002; 186:253-6.