LABORATORY FACTORS ASSOCIATED WITH MORTALITY AMONG PATIENTS WITH ECLAMPSIA AT THE KENYATTA NATIONAL HOSPITAL, NAIROBI, KENYA.

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Key Words: eclampsia; maternal mortality; Kenyatta National Hospital; Nairobi, Kenya; laboratory factors

ABSTRACT

Background: Eclampsia contributes significantly to maternal and neonatal morbidity and mortality both locally and globally. Identifying risk factors for mortality in women with eclampsia at KNH would serve to try and ameliorate these catastrophic outcomes.

Objective: To determine and compare the laboratory findings associated with mortality in women managed for eclampsia at KNH between 2007 and 2014.

Design: A hospital-based case control study. Cases were women who were managed for eclampsia and died while controls were those who survived eclampsia.

Results: A total of 262 records of patients with eclampsia managed at KNH between 1st January 2007 and 31st December 2014 were retrieved. Compared to controls, cases were older and less educated. Patients aged above 34 years had significantly higher odds of death compared to those between 14 and 24 years (OR 4.03; 95% CI 1.70 - 9.56; p= 0.002). Normal haemoglobin levels offered some protection against death (OR 0.37; 95% CI 0.14 – 0.95, p= 0.116). High creatinine levels significantly increased the odds of death, (OR 7.30; 95% CI 2.50 – 21.4; p< 0.001). High aspartate transferase (AST) levels were significantly associated with death (OR 5.14; 95% CI 1.12 – 23.49, p= 0.005). There was no significant association between death and potassium levels, alanine transaminase levels (ALT), educational attainment or marital status.

Conclusion: Patients on management for eclampsia at KNH aged above 34 years with elevated AST and creatinine levels had increased risk of mortality.

INTRODUCTION

Pre-eclampsia and eclampsia are associated with adverse obstetric outcomes. The ability to predict risk factors for mortality may help to ameliorate these catastrophic outcomes. Globally, millions of women and children die from preventable causes, with 99% of these occurring in developing countries. Maternal mortality contributes substantially to this burden (1). Hypertension is the second commonest medical complication of pregnancy, affecting up to ten percent of pregnancies (2, 3, 4). It contributes up to 14% maternal mortality globally. In Africa, the Maternal Mortality ratio (MMR) is at 600 per 100,000 live births, which is significantly higher than that in North America (5). In Kenya, it stands at 362 per 100,000 live births, a far cry from the 2015 Millennium Development Goal target of 147 per 100,000 live births (5).

Several risk factors have been shown to significantly impact on mortality in eclampsia. These include liver dysfunction, diastolic blood pressure >115 mmHg, anemia, being comatose, having thrombocytopenia, acute renal failure, cerebral edema, intracranial hemorrhage or pulmonary edema (6, 7). This study aimed to identify factors that are associated with maternal mortality in patients with eclampsia in KNH so as to predict and possibly prevent this outcome. Presently, there is a hiatus of published literature in this area in Kenya.

METHODS

Study Design: A hospital-based case-control study.

Study population: Cases were women who died of eclampsia. Controls were those who survived eclampsia. Factors associated with mortality were compared between the two groups.

Setting: The Kenyatta Hospital (KNH), which is the largest teaching and referral hospital in Kenya. It handles more than 120 cases of eclampsia per year. Following the initial review in Casualty, those with eclampsia before gestational viability are managed in the acute gynaecological ward, while the rest are transferred to the acute room in labour ward. Patients with renal dysfunction are reviewed by the renal unit team as required. Patients requiring critical care are transferred to the critical care unit, with a focus on multidisciplinary management to optimise the chances of survival. The management of eclampsia in KNH is shown in Box 1.

Study Population: Eclamptics managed in KNH between 1st January 2007 and 31st December 2014 who had a gestation of at least twenty weeks and availability of information of outcome in terms of death or survival were included. Those with incidental/ accidental causes of mortality were excluded.

Sample Size: The Kirkwood et al formula (8) for detection of difference in proportions was used with

Box 1: Management of Patients with Eclampsia at Kenyatta National Hospital

- Assess the airway, breathing, circulation and vital signs.
- Lay the patient in the recovery position to reduce risk of injury and administer oxygen by mask at 4-6L/ min.
- Insert two large bore IV cannulae and a Foley catheter.
- Administer Magnesium Sulphate (MgSO4) at a loading dose of 4g of 20% solution intravenously (IV) over 5 minutes.
- If convulsions recur within 15 minutes of initial dosing, add 2g of 20% MgSO4 solution IV over 5 minutes.
- The maintenance dose is administered as 1g of 20% MgSO4 solution per hour by continuous IV infusion until 24 hours after delivery or after the last convulsion, whichever occurs last.
- Definitive management of eclampsia is delivery.
- If convulsions are controlled and the fetus is mature with a good Bishop score, induce and augment labour.
- Conservative management may be considered in very early pregnancy in addition to steroid therapy for lung maturation.
- If convulsions are not controlled in a reasonable amount of time (6-8hrs), provider-initiated delivery is indicated irrespective of gestation.
- Management is multidisciplinary involving renal and critical care teams and physiotherapists, with laboratory and radiological support.

a Case/ Control ratio of 1:2, at 80% power, 95% significance and a 10% contingency to cater for incomplete records. The final sample size calculated was 240 (80 cases and 160 controls).

Study variables: The exposure and outcome variables are shown in Box 2.

Box 2: Exposure and outcome variables
Exposure variables: ALT/ AST levels, Haemoglobin; Haematocrit; Platelet Count; LDH levels; Bilirubin levels; Urea levels; Creatinine levels; electrolyte levels **Outcome variables:** Vital status: Alive or dead

Data Management and Analysis: Data were collected using a closed ended pre-tested data extraction form developed using third trimester reference ranges (9), checked for completeness and correctness and entered into Microsoft Access with in-built consistency and validation checks. Data were then exported to STATA Version 12.0 for analysis and relevant tests of statistical significance were applied.

Ethics: This study was approved by KNH/ University of Nairobi (UON) Ethics and Review Committee (Ref: KNH-ERC/A/346). Since it was a retrospective review of patient records, no patient contact was made, hence no need for informed consent.

RESULTS:

A total of 262 records of eclamptics managed at KNH were retrieved for the study. Out of these, 61 cases, 199 controls were analysable for this study. Two records were missing outcome data and were thus excluded. Table 1 shows the socio-demographic characteristics of the study population. The cases and controls showed significant differences in age, education and marital status. Overall, the cases were older and less educated.

The laboratory parameters of the study population are shown in Table 2. There were significantly different urea and creatinine levels. Normonatremia and normokalemia were protective. Anemia was more common among the cases, though the difference was not significant.

Table 1: Socio-demographic characteristics of patients with eclampsia managed in Kenyatta National Hospital between 2007 and 2014

Parameter	Cases N=61 n (%)	Controls N=199 n (%)	p-value
Age			
≤18 years	4 (7)	21 (11)	
19 – 23	13 (21)	73 (37)	0.017
24 – 28	16 (26)	53 (27)	
29 – 33	12 (20)	30 (15)	
>33 years	16 (26)	22 (11)	
Education			
None	4(7)	5(3)	
Primary	13(21)	48(24)	
Secondary	13(21)	64(32)	0.026
Post-secondary	7(12)	38(19)	
Missing	24(39)	44(22)	
Marital status			
Single	10(16)	48(24)	0.001
Married	44(72)	148(74)	
Unknown	7(12)	3(2)	

There was a lot of missing data on various laboratory parameters, ranging from 16 to 67%.

The associations between the exposure variables and mortality among cases and controls are shown in Table 3. Patients aged above 34 years had significantly higher odds of death (OR 4.03; 95% CI 1.70 – 9.56; p 0.002). Normal haemoglobin levels offered significant protection against death (OR 0.37; 95% CI 0.14 – 0.95, p 0.039), whereas high creatinine levels were significantly associated with mortality (OR 7.30; 95% CI 2.50 – 21.4; p <0.001). High AST levels were significantly associated with death (OR 5.90, 95% CI 1.72 – 20.26, p 0.005). There were no significant associations among death and potassium levels, ALT levels, education levels or marital status.

Table 2: Laboratory findings of patients with eclampsia managed in Kenyatta National Hospital between 2007 and 2014

Parameter	Cases N=61 n (%)	Controls N=199 n (%)	p-value
Lowest recorded Haemoglobin levels			0.116
<7	10(16)	20(10)	
7-10	20(33)	62(31)	
>10	14(23)	76(38)	
Unknown	17(28)	41(21)	
Lowest recorded Platelet levels			0.067
≤100	13(21)	28(14)	
>100	25(41)	115(58)	
Unknown	23(38)	56(28)	
Highest recorded Aspartate Transaminase (AST) levels			0.001
<33	3(5)	52(26)	
≥33	31(51)	91(46)	
Unknown	27(44)	56(28)	
Highest recorded Alanine Transaminase (ALT) levels			0.012
<33	12(20)	74(37)	
≥33	21(34)	69(35)	
Unknown	28(46)	56(28)	
Highest recorded Urea levels			0.017
<3.9	14(23)	86(43)	
≥3.9	31(51)	73(37)	
Unknown	16(26)	40(20)	
Highest recorded Creatinine levels			<0.001
<80	4(7)	64(32)	
≥80	42(69)	92(46)	
Unknown	15(25)	43(22)	
Highest recorded Potassium levels			<0.001
<3.3	8(13)	8(4)	
3.3 to 5.1	26(43)	107(54)	
>5.1	17(28)	18(9)	
Unknown	10(16)	66(33)	
Highest recorded Sodium levels			<0.001
<130	4(7)	11(6)	
130 to 148	31(51)	114(57)	
>148	15(25)	8(4)	
Unknown	11(18)	66(33)	
Highest recorded Chloride levels			0.600
<97	2(3)	5(2.5)	
97 to 109	14(23)	37(19)	
>109	4(7)	24(12)	
Unknown	41(67)	133(67)	

Table 3: Associations between exposure variables and mortality among cases and controls

Parameter	Cases N=61 n (%)	Controls N=199 n (%)	OR (95% CI)	P value
Marital Status				
Single	10(19)	48(25)	1.00	
Married	44(82)	148(76)	1.43(0.67 – 3.05)	0.359
Age				
15 to 24 years	18(30)	106(53)	1.00	
24 to 34 years	30(50)	74(37)	2.39(1.24 – 4.60)	0.009
>34 years	13(21)	19(10)	4.03(1.70 – 9.56)	0.002
Level of Education				
Primary	17(46)	53(34)	1.00	
Post primary	20(54)	102(66)	0.61(0.30 – 1.26)	0.184
Hemoglobin levels				
<7	10(23)	20(13)	1.00	
7-10	20(46)	62(40)	0.65(0.26 – 1.60)	0.346
>10	14(32)	76(48)	0.37(0.14 – 0.95)	0.039
Lowest Platelet Levels				
≤100	13(34)	28(20)	1.00	
>100	25(66)	115(80)	0.47(0.21 – 1.03)	0.059
Highest Aspartate Transaminase (AST) Levels				
<33	3(9)	52(36)	1.00	
≥33	31(91)	91(64)	5.90(1.72 – 20.26)	0.005
Highest Alanine Transaminase (ALT) Levels				
<33	12(36)	74(52)	1.00	
≥33	21(64)	69(48)	1.88(0.86 – 4.10)	0.114
Highest Urea Levels				
<2.9	14(31)	86(54)	1.00	
≥2.9	31(69)	73(46)	2.61(1.29 – 5.27)	0.008
Highest Creatinine Levels				
<80	4(9)	64(41)	1.00	
≥80	42(91)	92(59)	7.30(2.50 – 21.4)	<0.001
Highest Potassium Levels				
<3.3	8(16)	8(6)	1.00	
3.3 to 5.1	26(51)	107(81)	0.24(0.08 – 0.71)	0.010
>5.1	17(33)	18(14)	0.94(0.29 – 3.08)	0.925
Highest Sodium levels				
<130	4(8)	11(8)	1.00	
130 to 148	31(62)	114(85)	0.75(0.22 – 2.51)	0.638
>148	15(30)	8(6)	5.16(1.23 – 21.6)	0.025

DISCUSSION

This study found that high AST and creatinine levels and age above 34years were significantly associated with mortality among the study population. However, having normal haemoglobin levels conferred significant protection against fatality. This is congruent with other data from Turkey and Morocco (6, 7). The extremely high frequency of missing data precluded analysis of bilirubin, chloride and lactate dehydrogenase levels.

The main strength of this study was the ability to retrospectively analyse trends over a long period of time, whereas its main limitation was the high frequency of missing information in the patient records.

CONCLUSION AND RECOMMENDATIONS:

In conclusion, patients with eclampsia at KNH aged above 34 years with elevated AST and creatinine levels are at significantly increased risk of mortality. It is recommended that patient documentation and monitoring need to be optimized so as to facilitate more judicious management in order to reduce the mortality among these patients.

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The specific SORT IT programme which resulted in this publication was developed and implemented by the University of Nairobi, Department of Obstetrics and Gynaecology, Nairobi, Kenya with financial support from WHO/TDR.

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Conflict of interest: None to declare.

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POLICY BRIEF

LABORATORY FACTORS ASSOCIATED WITH ECLAMPSIA AT THE KENYATTA NATIONAL HOSPITAL, NAIROBI, KENYA.

PROBLEM STATEMENT

Eclampsia is the new onset of convulsions in a woman with high blood pressure in pregnancy in the absence of another cause. Pre-eclampsia and eclampsia are associated with adverse obstetric outcomes. The ability to predict risk factors for mortality may help to ameliorate these catastrophic outcomes.

Globally, millions of women and children die from preventable causes, with 99% of these occurring in developing countries. Maternal mortality contributes substantially to this burden (1). Hypertension contributes up to 14% maternal mortality globally. In Africa, the Maternal Mortality ratio (MMR) is at 600 per 100,000 live births (5). In Kenya, it stands at 362 per 100,000 live births, a far cry from the 2015 Millennium Development Goal target of 147 per 100,000 live births (5).

Several risk factors have been shown to significantly impact on mortality in eclampsia. These include liver dysfunction, diastolic blood pressure >115 mmHg, anemia, being comatose, having thrombocytopenia, acute renal failure, cerebral edema, intracranial hemorrhage or pulmonary edema (6, 7).

Eclampsia can occur prenatally, intrapartum or postpartum. This can culminate in death or lead to end organ damage with sequalae such as stroke, blindness, physical injuries from falls, injury to baby and compromise of the unborn baby.

PRIORITY ACTIONS

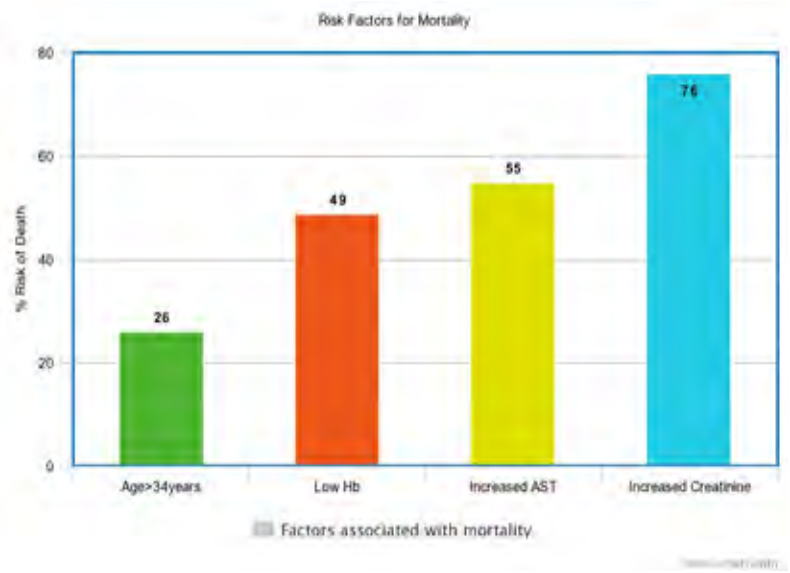
1. Increase laboratory capacity to ensure adequate monitoring of blood, liver and kidney functions in patients with Eclampsia.
2. Develop a standard data collection form to capture all relevant information regarding eclamptic patients at and after admission.

FACTORS INFLUENCING MATERNAL MORTALITY FROM ECLAMPSIA

This study found that high AST and creatinine levels and age above 34years were significantly associated with mortality among the study population. However, having normal haemoglobin levels conferred significant protection against fatality.

The extremely high frequency of missing data precluded analysis of bilirubin, chloride and lactate dehydrogenase levels

Factors associated with increased risk of death among eclamptics



WHAT THE DATA INDICATES

1. Patients aged above 34 years had a 26% risk of mortality
2. Normal haemoglobin levels offered significant protection against death
3. Patients with high creatinine and AST levels (kidney and liver dysfunction) were much more likely to die

IMPLICATIONS

1. **Better monitoring would lead to better quality response and thus decrease risk of death.**
2. **Better documentation would increase quality of care and quality of referrals.**
3. **If nothing is done, more and more patients will continue to needlessly die from eclampsia, which is both preventable and treatable.**

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