Pattern of liver enzymes and maternal outcome in eclamptic patients admitted to the Intensive Care Unit, University College Hospital, Nigeria

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ABSTRACT

Introduction: Eclampsia, a hypertensive disorder, is one of the leading causes of maternal mortality in developing countries like Nigeria. We evaluated the relationship between the pattern of liver enzymes and maternal mortality in eclamptic women.

Method: A retrospective study of 55 eclamptic women admitted to the Intensive Care Unit (ICU), University College Hospital, Nigeria, was conducted. Data were obtained on their demographic, obstetric, and clinical characteristics, liver enzyme patterns, and maternal outcome. Analysis was by descriptive statistics, univariate analysis, and non-parametric tests with level of significance set at $p<0.05$.

Results: Maternal deaths occurred in 27.3% and elevation of liver enzymes was observed more among the dead patients compared with those who survived. Alanine aminotransferase (ALT) was the most commonly elevated liver enzyme, occurring in almost all (90.9%) the patients. Maternal mortality was significantly associated with age ($p=0.001$), saturated oxygen levels ($p=0.007$), elevated alkaline phosphatase ($p=0.008$), alanine aminotransferase ($p=0.013$), aspartate aminotransferase ($p=0.016$), and total bilirubin ($p<0.001$).

Conclusion: Maternal mortality due to eclampsia was clinically associated with age, elevated liver enzymes and a lower serum level of total bilirubin. Liver transaminases are therefore important prognostic indicators associated with eclampsia.

Keywords: eclampsia, liver enzymes, maternal outcome, ICU, Nigeria

INTRODUCTION

Eclampsia is one of the clinical manifestations of a hypertensive disorder of pregnancy. The American College of Obstetricians and Gynaecologists guidelines include elevation of liver enzymes as a criterion for the diagnosis of pre-eclampsia/eclampsia.[1] The difference between pre-eclampsia and eclampsia is that a woman with eclampsia has had a seizure.

Liver Function Tests (LFTs) evaluate liver and biliary system functions. They provide insights into coagulation, haemolysis, nutrition and bone turnover and are useful for monitoring the prognosis of pre-eclampsia/eclampsia.[2] LFT abnormalities occur in 3% to 30% of pregnancies and are associated with poor maternal and foetal outcomes.[3,4]

In Nigeria, institution-based studies reported an overall incidence between 1.1% and 4.0% of eclampsia.[5,6] Eclampsia continues to be one of the leading causes of maternal and perinatal morbidity and mortality, accounting for about 20% to 36.9% of the total maternal deaths.[7-9]

Eclampsia causes stillbirths, increased Caesarean Section deliveries, and intensive care unit admissions.[5] Haemolysis with elevated liver enzymes and low platelets (HELLP) syndrome, which complicates severe pre-eclampsia, is a consequence of liver damage. Determination of LFTs has proved useful in monitoring pre-eclampsia/eclampsia syndrome.[10]

This study examined the patterns of liver enzymes in women admitted under obstetric care to the ICU to assess it as a predictor of maternal mortality.

METHOD

A retrospective study was conducted among eclamptic women admitted to the Intensive Care Unit of the University College Hospital, Nigeria from 1st February, 2020 to 31st January, 2022. Data were obtained from the medical records of all eclampsia cases admitted to ICU within the study period.

Demographic, obstetric, and clinical characteristics, liver enzyme patterns, and maternal outcome were obtained using a proforma. Eclampsia was defined as seizures associated with hypertension (>140/90 mmHg) and proteinuria (at least +1 detectable by dipstick). Maternal death was defined as death during pregnancy or within 42 days of the termination of pregnancy, irrespective of the duration and site of the pregnancy. Booking status was used to classify pregnant women into those who registered and had antenatal care services during pregnancy (booked) and those who did not (unbooked). It is a vital component of antenatal care as health care providers use the occasion to collect basic medical information that will form the basis to care for the patient throughout pregnancy, delivery and postnatal care. Other features of complications were defined as associated diagnosis of pulmonary oedema, renal failure, unconsciousness, stroke, HELLP syndrome, and sepsis.

The liver enzymes were classified based on the standard reference values: Alkaline phosphatase (ALP) (42–98 U/L), Gamma-glutamyl transferase (GGT) (< 30 U/L), Aspartate aminotransferase (AST) (13–35 U/L), Alanine aminotransferase (ALT) (7–35 U/L), Total protein (60–78 g/L), Total bilirubin (5–21 µmol/L) and Albumin (35–52G/L).

Normally distributed data were summarised as mean ± standard deviation, while data that were not normally distributed as median (interquartile range). Kruskal-Wallis and Mann-Whitney tests were appropriately used to determine if there was an association between variables and outcome (maternal death and others - discharged and discharged against medical advice). A $p < 0.05$ was considered statistically significant. Those discharged against medical advice were removed from the final analysis.

RESULTS

A total of 55 eclamptic patients were admitted into ICU during the study period. Their mean age ± (SD) was 29.7 ± (6.11) years and were mainly primigravidae (36.4%). Just under half (45.5%) had antepartum eclampsia, 18.2% had postpartum eclampsia, and 16.4% had antepartum eclampsia complicated with HELLP syndrome (Table 1).

Table 1. Participants' characteristics (N=55)

Characteristics		n (%)
Age (years)	≤ 20	4 (7.3)
	21 – 30	31 (56.4)
	> 30	20 (36.4)
Marital status	Single	6 (10.9)
	Married	49 (89.1)
Education	Secondary/lower	45(81.8)
	Tertiary	10 (18.2)
Occupation	Employed	14 (25.5)
	Self-employed	29 (52.8)
	Unemployed	5 (9.1)
	Schooling	7 (12.7)
Booking status	Booked	10 (18.2)
	Unbooked	45 (81.8)
Parity	0	15 (27.3)
	1 – 4	33 (60.0)
	> 5	7 (12.7)
Gestational age (weeks)	(Mean ± SD)	34.6 ± 4.10
Multiple pregnancy	Yes	5 (9.1)
	No	50 (90.9)
Diagnosis	Antepartum eclampsia alone	25 (45.5)
	Intrapartum eclampsia alone	6 (10.9)
	Postpartum eclampsia alone	10 (18.2)
	Antepartum eclampsia complicated with HELLP and other features*	9 (16.4)
	Others**	5 (9.1)

**Other features-pulmonary oedema, renal failure, unconsciousness, stroke, and sepsis*

***Others- Intrapartum and Postpartum eclampsia with other features*

Clinical and laboratory investigations were abnormal in almost all the patients, revealing elevations in ALP, AST, ALT, and GGT (Table 2).

Maternal deaths occurred while on admission in 27.3% and was mainly due to acute kidney failure (26.7%), pulmonary oedema, septic shock, and hepatic encephalopathy (20.0%) (Figure. 1).

Table 2. Participants clinical and laboratory characteristics (N=55)

Variables	Mean ± SD/Median (IQR)
Pulse	111.7 ± 18.28
Respiratory rate	31.7 ± 7.94
Systolic Blood Pressure	157.5 ± 30.51
Diastolic Blood Pressure	98.8 ± 22.09
Oxygen saturation (SP02)	95.3 ± 6.46
Temperature oC	37.3 ± 1.38
Packed Cell Volume	30.5 ± 7.78
Platelets (× 105 /L)	46 (130), Range = 94 – 268
Urea (mmol/L)	54.4 ± 5.34
Creatinine (µmol/L)	1.3 (1.9); Range = 0.6 - 9.0
Liver function tests	
ALP (U/L)	191 (122); Range = 68 – 1103
AST (U/L)	65 (49); Range = 10 – 6442
ALT (U/L)	56 (47); Range = 10 – 3045
GGT (U/L)	36 (73); Range = 19 – 521
TP (g/dL)	5.8 (1.53); Range = 3.2 - 7.9
ALB (g/dL)	2.9 (0.75); Range = 1.1 - 22.6
TBIL(µmoles/L)	0.5 (2.62); Range = 0.09 - 412

Alkaline Phosphatase (ALP), Gamma-glutamyl transferase (GGT), Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Total protein (TP), Total Bilirubin (TBIL), Albumin (ALB).

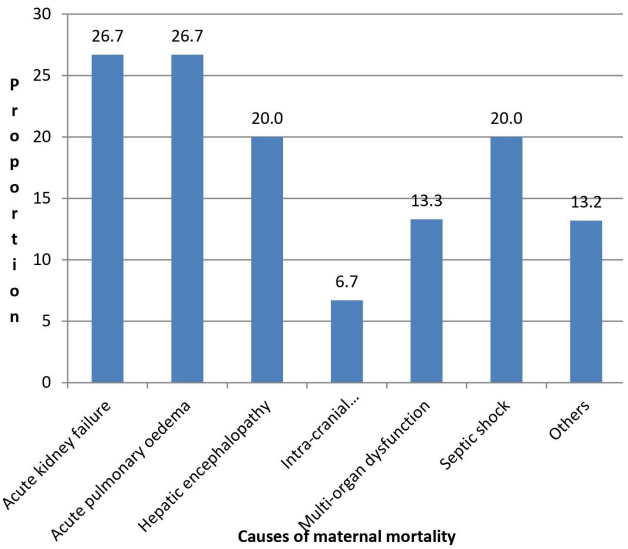

Figure 1. Causes of Maternal Mortality

ALT elevation was the most common abnormality, occurring in 90.9% of the patients. This was followed by AST (89.1%), and ALP (76.4%). All the liver enzymes were elevated in the dead patients compared with the survivors. The least frequently occurring abnormality was GGT in 32.7% of the patients (Table 3).

There was a significant association of SPO2, elevated ALP, AST, ALT, and total bilirubin levels with maternal outcome ($p<0.05$), (Table 4).

A significant association was found between age ($p=0.001$) and maternal outcome (Table 5).

DISCUSSION

Liver transaminases (ALP, AST, ALT, and GGT) are good indicators for the prognosis of eclampsia.[10,11] Their raised levels are due to the anaemic hypoxic effect of eclampsia on the liver. Monitoring of liver function is crucial in disease progression and could be prognostic.

In our study, elevation of liver transaminases ranked higher among the liver enzymes, and ALP, AST, and ALT were clinically associated with maternal death. AST and ALT elevation ranked highest, with AST being more elevated than ALT. These findings agree with previous reports and were attributed to haemolysis and renal insufficiency.[2,4,11]

Elevated GGT was not significantly associated with maternal death. This is similar to findings in a previous study.[12] However, GGT is a useful biochemical marker in revealing the severity of preeclampsia and specifies endothelial vascular damage.

The plasma total protein was high in our study and this is not unexpected because eclampsia with abnormal liver function is associated with higher proteinuria and increased maternal complications than those with normal liver function.[3] Total bilirubin activity decreases with gestational age due to haemodilution in all women. The decrease in serum total bilirubin levels, which was found to be significantly associated with maternal death may be connected to the fluid retention in severe eclampsia. Additionally, high blood pressure (BP) values are associated with preeclampsia/eclampsia death.[11,13]

SPO2 by pulse oximetry was the only maternal vital sign significantly associated with mortality. It has been previously reported that SPO2 by pulse oximetry helps in the assessment of maternal risk in women admitted to hospital with preeclampsia and that a value ≤ 93%[14] or ≤95%[15] confers particular risk or results in adverse outcomes.

Antepartum eclampsia was the dominant diagnosis,

Table 3. Pattern of Elevated liver enzymes between the survivors and dead (N=55)

Variable	Outcome		Total n (%)
	Died n (%)	Survived n (%)	
ALP (U/L)	14 (93.3)	28 (71.8)	42 (76.4)
AST (U/L)	14 (93.3)	35 (87.5)	49 (89.1)
ALT (U/L)	14 (93.3)	36 (90.0)	50 (90.9)
GGT (U/L)	9 (60.0)	9 (22.5)	18 (32.7)
TP (g/dL)	10 (66.7)	22 (55.0)	32 (58.2)
ALB (g/dL)	10 (66.7)	16 (40.0)	26 (47.3)
TBIL(µmoles/L)	14 (100.0)	35 (87.5)	49 (90.7)

Table 4. Association between maternal vitals, LFTs and outcome

Variable (n=53)	p-value
SBP	0.670
DBP	0.596
SPO2	0.007
ALP (U/L)	0.008
AST (U/L)	0.016
ALT (U/L)	0.013
GGT	0.057
Total protein	0.903
Total bilirubin (µmoles/L)	<0.001

Table 5. Association between maternal characteristics and outcome

Variable	p-value
Age	0.001*
Education	0.561
Occupation	0.204*
Parity	0.298*
Booking status	0.832
Referral status	0.653
Diagnosis	0.181*

**= Kruskal-Wallis Test*

a finding consistent with another Nigerian study.[16] The majority of women studied were unbooked and demonstrated poor health-seeking behaviour, along with the observed late referral. This is in keeping with the National Demographic Health Survey report that a third of Nigerian pregnant women did not receive antenatal care, thus exposing them to a higher risk of maternal mortality.[9]

The mean gestation age of eclamptic patients was 34.1±4.78 weeks. This agrees with previous studies with reports of a higher proportion of deaths among pregnant women with abnormal liver function tests between 30 and 40 gestational weeks.[4,13]

The maternal mortality rate of 27.3% in our study falls within the 20% to 36.9% previously reported in Nigeria.[7,8] The commonest causes of death were acute kidney failure and acute pulmonary oedema, intra-cranial haemorrhage, septic shock, and hepatic encephalopathy, which is in line with the report of other researchers.[17]

One of the strengths of this study is that a higher proportion of the women were discharged despite the abnormal liver function test readings, thus, implying that maternal mortality is not always the outcome of abnormal liver function test results. On the other hand, the study is limited by its small sample size.

CONCLUSION

Maternal mortality due to eclampsia was more prevalent with elevated ALP and low total bilirubin, however, maternal death could still occur due to other complications even in the presence of hypobilirubinaemia. The significant effect of low serum bilirubin on maternal outcome indicates that there might be a change in pattern of liver function test at presentation in this category of women, we therefore suggest that in managing women with eclampsia, any deviation from the normal values of liver enzymes should not be ignored but considered as equally important.

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