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Effect of Magnesium Sulphate on Hepatic Biomarkers in Pre-eclamptic Patients in Selected Tertiary Hospitals in Osun State South Western Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. The work emanated from the M.Sc. thesis of author SOA. Authors SOA and MFA conceived and designed the study. Author SOA carried out all laboratory works and wrote the first draft of the manuscript. Author JOI managed the literature searches, performed the statistical analysis and wrote the final draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Aims: This study investigated the effect of magnesium sulphate ($MgSO_4$) on hepatic biomarkers in the management of pre-eclampsia in Osun State, Nigeria. This was with a view to providing scientific support for the use of $MgSO_4$ in the management of pre-eclampsia, and also to investigate likely adverse effects of $MgSO_4$ on the biological functions of the liver.

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Study Design: One-factor, two controls - six test groups quasi - experimental design.
Place and Duration of Study: Department of Biochemistry, Ekiti State University, Ado-Ekiti, Ekiti State, Nigeria, between November 2013 and July 2014.
Methodology: A total of two hundred and sixty (260) consenting subjects were recruited for the study, and were grouped into normotensive pregnant women at 2nd and 3rd trimesters (n=20/trimester), pre-eclamptic women not on $MgSO_4$ at 2nd and 3rd trimesters (n=10/trimester) and pre-eclamptic women on $MgSO_4$ at 2nd and 3rd trimesters (n=60/trimester). Also normotensive pregnant women at post-partum (n=20) and pre-eclamptic women on $MgSO_4$ at post-partum (n=60). Blood samples (5 mL venous blood) were collected, centrifuged and stored as plasma before subjection to biochemical analysis. Blood plasma was analyzed for hepatic biomarker using standard Enzyme Linked Immunosorbent Assay (ELISA) and Spectrophotometric methods.
Results: The results showed no significant difference in hepatic biomarkers of pre-eclamptic women on $MgSO_4$ when compared with pre-eclamptic women not on $MgSO_4$ at both second and third trimesters. The results however showed that, comparing the hepatic biomarkers between normotensive pregnant women at post-partum and pre-eclamptic pregnant women on $MgSO_4$ also at post-partum, gave almost the same pattern with comparison between normotensive and pre-eclamptic women not on $MgSO_4$, but for albumin in which there was no significant difference in the mean plasma level.
Conclusion: The results obtained from this work revealed that $MgSO_4$ is devoid of any adverse effects on liver functions of pre-eclamptic women. This study further support its existing use as an anti-convulsant in the management of pre-eclampsia.

Keywords: Pre-eclampsia; magnesium sulphate; hepatic biomarkers.

1. INTRODUCTION

Pre-eclampsia is a pregnancy associated medical complication characterized by elevated blood pressure (hypertension), oedema, organ damage and significantly increased urine protein after 20th week of pregnancy, and various cardiovascular, hepatic, renal and haematological changes in an earlier normotensive pregnant woman. It is otherwise known as Pregnancy Induced Hypertension (PIH). It is a life threatening disorder that can occur during pregnancy and at post-partum, which if left untreated could progress and results into a very severe condition of 'eclampsia' known as occurrence of more severe seizures during pregnancy [1]. Meanwhile, eclampsia is a common cause of maternal mortality worldwide but particularly in the developing countries like Nigeria. It is estimated that every year eclampsia is associated with about 50,000 maternal deaths worldwide, most of which occur in developing countries [2,3].

Several management methods had been applied to prevent and treat the complications of hypertension in pregnancy. Therapeutic drug management has been a major prescription used by health providers in suppressing the effects of this pregnancy associated medical disorder at point of care in health institutions [4].

Magnesium sulphate ($MgSO_4$) is one of the possible therapeutic drugs used in the management and treatment of seizure associated with pregnancy induced hypertension. The dosage (intravascular injection) is 4 g (20 mL of 20% solution in saline) at a rate of 1g/5 min. over 5-20 min. Maintenance regime (intravascular injection) is 1 to 2 g/ hour in 100 mL of maintenance solution following last convulsion [4]. It is an effective seizure prophylaxis that acts by causing fall in blood pressure and opposes calcium dependent arterial constriction to relieve vasoconstrictions. It increases cardiac output through its activity to antagonize increase in intracellular calcium concentration initiated by ischemia, and thus could prevent cell damage and death. Magnesium sulphate is preferred because it possesses lower placental transfer thereby reversing the condition of placental abruption when taken by pre-eclamptic women [5]. The use of $MgSO_4$ in patients with severe pre-eclampsia reduces the risk of progression to eclampsia by more than half and reduced maternal mortality [6]. Also, the effect of $MgSO_4$ on perinatal outcomes has also been demonstrated to significantly improve outcomes for newborns compared to phenytoin [7].

The Magpie trial tried to address the main fear of toxicity in the use of $MgSO_4$. Toxicity of $MgSO_4$ was monitored using clinical parameters. The

parameters that were monitored are the knee jerk, respiratory rates (which should normally be more than 16/minute), and urine output (which should normally be more than 25 ml/l). The first warning of toxicity is loss of the knee jerk which occurs at serum magnesium level of 3.5 to 5 mmol/l. Respiratory paralysis occurs at 5 to 6.5 mmol/l, cardiac conduction is altered at more than 7.5 mmol/l while cardiac arrest occurs when serum magnesium exceeds 12.5 mmol/l [8].

Biomarkers are substances (like chemicals, enzymes, molecules, indicators or signals) produced by a cell, tissue and organ normally, or produced for the purpose of monitoring response to foreign compounds (like drugs, chemicals or substances), and treatment progress [9]. Furthermore, biomarkers exhibit some characteristics that make them significant such as specificity and sensitivity. Specificity in the sense that their presence or changes is an indicative of a particular effect, and sensitivity to show that something must have happen to the cell, tissue and organ before the biomarkers' appearance [10]. These characteristics have made biomarkers significant in screening, diagnosis, treatment and monitoring the activity of tissue and organ [11]. The liver is an organ in the body that performs many functions essential for life. It is a major and body's largest organ that processes, and stores metabolites like amino acids, carbohydrates, lipids, vitamins and minerals. In addition, many of the proteins, coagulation factors and transport proteins are synthesized and processed by the liver. The liver is the primary site of detoxification of exogenous compounds such as drugs, toxins and endogenously the site for conjugation and metabolism (Dereck et al. [12]).

Liver biomarkers are used as an important medical aid to detect any injury or damage the liver is exposed to, and they are of significant importance in the development of new therapeutics for prevention, treatment and management of a broad range of diseases the liver is exposed to as hepatoxicity or liver injury and dysfunctions (Obembe et al., [13]). Some of the biomarkers of importance include total protein, albumin, prothrombin, alanine aminotransferase, alkaline phosphatase, alphafetoprotein, bilirubin, gamma-glutamyl transferase, fibrinogen, platelets count, and amylase (Macfarlene, [14]).

This study investigated the effect of $MgSO_4$ on hepatic biomarkers in the management of pre-eclampsia in Osun State, Nigeria. This was with a view to further provide, or otherwise, scientific support for the use of $MgSO_4$ in the management of pre-eclampsia, and also to investigate likely adverse effects of $MgSO_4$ on the biological functions of the liver.

2. METHODS

2.1 Experimental Design and Grouping of Subjects

Quasi-experimental design method was utilized in this study and subjects were divided into eight (8) groups:

i. Group 1 was 2nd Trimester Normotensive Pregnant Women;
ii. Group 2 was 3rd Trimester Normotensive Pregnant Women;
iii. Group 3 was 2nd Trimester Pre-eclamptic Women not on $MgSO_4$;
iv. Group 4 was 3rd Trimester Pre-eclamptic Women not on $MgSO_4$;
v. Group 5 was 2nd Trimester Pre-eclamptic Women on $MgSO_4$;
vi. Group 6 was 3rd Trimester Pre-eclamptic Women on $MgSO_4$;
vii. Group 7 was Post-partum Normotensive Pregnant Women;
viii. Group 8 was Post-partum Pre-eclamptic Women on $MgSO_4$.

2.2 Sampling Areas

Six major hospitals located in various parts of Osun State, South Western Nigeria were used for the purpose of this research. Majority of pregnant women in Osun State attend these hospitals because of their proximity and qualitative health care delivery. The hospitals included:

i. Obafemi Awolowo University Teaching Hospital Complex, Ile-Ife.
ii. Wesley Guild Hospital, Ilesa.
iii. Ladoke Akintola University Teaching Hospital, Osogbo.
iv. Osun State General Hospital, Asubiaro, Osogbo.
v. The General (Osun State) Hospital, Iwo.
vi. Seventh- Day Hospital, Ile-Ife.

2.3 Recruitment of Subjects

A total of two hundred and sixty (260) consenting subjects were enrolled. The Postgraduate Ethical

Committee of the Faculty of Science, Ekiti State University, Ado-Ekiti, Ekiti State, Nigeria, approved the research work. The subjects consisted of normotensive pregnant women at 2^{nd} and 3^{rd} trimesters (n=20/trimester), pre-eclamptic women not on $MgSO_4$ at 2^{nd} and 3^{rd} trimesters (n=10/trimester), pre-eclamptic women on $MgSO_4$ at 2^{nd} and 3^{rd} trimesters (n=60/trimester), normotensive pregnant women at post-partum (n=20) and pre-eclamptic women on $MgSO_4$ at post-partum (n=60) were recruited for this research and their samples were processed for analysis within 72 hours of collection employing standard diagnostic techniques. The study was approved by the Ethical review of the study.

2.4 Method of Selection of Subjects

The subjects who participated in this project were selected according to the following criteria:

i. Visiting antenatal clinic to seek consent of the subjects in groups 1-6 (Pregnant and Pre-eclamptic women), and post-natal ward for subjects in groups 7-8 (Post-partum subjects);
ii. Obtaining brief clinical history from all subjects using questionnaire to take care of age, body mass index, gestational age (20 weeks and above) and other personal information;
iii. Measurement of the subjects' blood pressure was done using sphygmomanometer, and ensuring subjects in groups 3-6 and 8 have readings greater or around 140 mmHg systolic and 90 mmHg diastolic measurement, while subjects in groups 1,2 and 7 have normal blood pressure readings;
iv. Ensuring subjects in groups 5, 6 and 8 were on magnesium sulphate drug while subjects in groups 3 and 4 were not on magnesium sulphate drug, and subject in groups 1, 2 and 7 were not on any anti-hypertensives therapy;
v. Noticing the presence of oedema and proteinuria through rapid urine check for subjects in groups 3, 6 and 8 which are absent in subjects in other groups.

2.5 Collection of Blood Samples

2.5.1 Blood sample

About 10 mL of venous blood was collected from each subject and distributed into lithium heparin bottle (6 mL), sodium citrate bottle (2 mL) and Ethylene Diamine Tetra-acetic Acid bottle (2 mL) respectively.

2.5.2 Preparation of blood plasma

The blood samples (in lithium heparin bottle) were separated as plasma into plain labeled bottles after spinning in a centrifuge at 4,000 rpm for 20 min. The haematological samples were stored at 4℃ for analysis of platelets counts, prothrombin, and fibrinogen.

2.6 Determination of Concentration of Plasma Total Protein

Plasma total protein concentration was determined spectrophotometrically using biuret method [15].

2.7 Determination of Concentration of Plasma Albumin

Plasma albumin concentration was determined spectrophotometrically using dye binding method [15].

2.8 Determination of Prothrombin Time

Prothrombin time was determined according to the procedure reported by Quick [16].

2.9 Assay of Plasma Alkaline Phosphatase (ALP) activity

Alkaline phosphatase activity was assayed spectrophotometrically according to enzymatic method of Henry [17].

2.10 Estimation of Plasma Alpha-fetoprotein (AFP) Concentration

Concentration of alpha-fetoprotein was estimated using enzyme linked immunosorbent assay (ELISA) method [18].

2.11 Assay of Plasma Alanine Aminotransferase (ALT) Activity

This was assayed spectrophotometrically using enzymatic method [19].

2.12 Estimation of Plasma Levels of Bilirubin [Total and Conjugated]

Plasma bilirubin concentration was estimated spectrophotometrically according to Jendrassik's method of Cheesbrough [15].

2.13 Assay of Plasma Gamma-Glutamyl Transferase (GGT) Activity

This was assayed using enzymatic method [18].

2.14 Determination of Plasma Fibrinogen Concentration

Plasma levels of fibrinogen in all the samples collected were carried out according to clot-weight method [20].

2.15 Estimation of Platelets

Platelets were counted according to ammonium oxalate reagent method [15].

2.16 Assay of Plasma Amylase Activity

This was assayed using enzymatic method [21].

2.17 Statistical Analysis

Results are expressed as mean ± SEM. Statistical difference was determined by one-way analysis of variance (ANOVA) followed by a post hoc test (Student Newman-Keuls Test (SNK)). Difference was considered statistically significant with $p < 0.05$. Computer software Graph pad PRISM® version 3.00 was used for the analysis.

3. RESULTS

This study showed that pre-eclamptic women at 2nd and 3rd trimesters had significant increases in plasma prothrombin, alkaline phosphatase, alphafetoprotein and gamma-glutamyl transferase, and significant decreases in albumin and platelet when compared with normotensive pregnant women. There was no significant difference in same comparison in other investigated hepatic biomarkers (see Tables 1 and 2).

The results also showed no significant difference in hepatic biomarkers of pre-eclamptic women on $MgSO_4$ compared with pre-eclamptic women not on $MgSO_4$ at both second and third trimesters (see Tables 3 and 4).

The results however showed that, comparing the hepatic biomarkers between normotensive pregnant women at post-partum and pre-eclamptic pregnant women on $MgSO_4$ also at post-partum, gave almost the same pattern with comparison between normotensive and pre-eclamptic women not on $MgSO_4$, but for albumin in which there was no significant difference in the mean plasma level (see Table 5).

4. DISCUSSION

The results revealed a non-significant decrease in plasma concentrations of total protein and albumin in pre-eclamptic pregnant women at 2nd trimester, while at 3rd trimester, total protein was non-significantly raised when compared with the normotensive groups. Similar observations have been reported by Gray and Baron [22] and Edward et al., [23]. This result could be due to coupling effects of increased synthesis of proteins (endogenous, plasma and glycoproteins) by hepatocyte and proteinuria in pre-eclamptic individuals. However, plasma concentration of total protein was non-significantly decreased while albumin was non-significantly raised in pre-eclamptic pregnant women treated with $MgSO_4$ at both 2nd and 3rd trimesters, as well as 3-6 days post-partum when compared with same groups that were not on $MgSO_4$ treatment. This could be due to effect of $MgSO_4$ as a seizure prophylaxis that helps in prevention of endothelial damages to the hepatocytes that normally occur in pre-eclampsia to oppose transcellular transport of proteins through the tight junctions leading to reduced total protein and increased synthesis of albumin [24].

The formation time of prothrombin was observed to be significantly prolonged in pre-eclamptic women when compared with the normotensive pregnant women. The prolonged prothrombin formation could be linked to possible hepatocyte damage and necrosis from endothelial dysfunctions in pre-eclampsia. This is as reported by Edward, et al. [23]. However, the prothrombin time was non-significantly reduced in pre-eclamptic pregnant women treated with $MgSO_4$ at both 2nd and 3rd trimesters, and at post-partum when compared with similar groups not on $MgSO_4$ treatment. This reduction in prothrombin formation could be due to effects of $MgSO_4$ in the prevention of endothelial damages to the hepatocytes that normally occur as a result of pre-eclampsia, by opposing transcellular transport of proteins (glycoproteins) through the tight junctions leading to quick prothrombin formation. This gives similar observation with the report of Munjuluri et al. [24].

Table 1. Hepatic biomarkers in normotensive pregnant women at Second Trimester [A] and pre-eclamptic women not on $MgSO_4$ at Second Trimester [B]

Group	TP (g/L)	ALB (g/L)	PROTH (sec)	ALP (IU/L)	AFP (IU/mL)	ALT (IU/L)	TB (umol/L)	CB (umol/L)	GGT (U/L)	FIB (g/L)	PLT (/mm^3)	AMY (IU/L)
A (n=20)	76.20±2.69	35.30±1.04	22.50±0.47	171.10±6. 20	41.60±2.06	18.60±1.80	36.20±4.21	7.90±0.98	34.50±2.53	4.90±0.16	194,200.00±7,948.16	195.40±18.72
B (n=10)	73.40±2.40	30.60±0.40	24.60±0.48	193.00±4. 03	124.60±5.80	21.20±1.65	41.40±1.25	8.40±0.51	51.00±1.61	5.50±0.22	104,600.00±1,802.37	250.60±19.36
Levels of significance	P>0.05	P<0.001	P<0.05	P<0.01	P<0.001	P>0.05	P>0.05	P>0.05	P<0.05	P>0.05	P<0.001	P>0.05

Table showed Means ± Standard error of mean (SEM), Differences between means and the Level of significance (P<0.001, P>0.05). TP = Total protein, ALB = Albumin, PROTH = Prothrombin, ALP = Alkaline phosphatase, AFP = Alphafetoprotein, ALT = Alanine aminotransferase, TB = Total bilirubin, CB = Conjugated bilirubin, GGT = Gamma-glutamyl transferase, FIB = Fibrinogen, PLT = Platelet, AMY = Amylase

Table 2. Hepatic biomarkers in normotensive pregnant women at Third Trimester [C] and pre-eclamptic women not on $MgSO_4$ at Third Trimester [D]

Group	TP (g/L)	ALB (g/L)	PROTH (sec)	ALP (IU/L)	AFP (IU/mL)	ALT (IU/L)	TB (umol/L)	CB (umol/L)	GGT (U/L)	FIB (g/L)	PLT (/mm^3)	AMY (IU/L)
C (n=20)	79.70±1.26	36.70±0.92	22.50±0.47	150.30±8. 76	48.00±3.42	17.10±2.15	34.40±3.67	8.50±0.85	42.20 ±3.42	4.90±0.16	208,800.00±8,567.12	217.40±24.79
D (n=10)	81.40±1.50	31.00±0.71	25.70±0.44	224.20±12 .73	90.00±2.80	33.80±1.96	42.20±2.67	9.60±0.51	68.80±3. 42	5.60±0.23	108,400.00±2,416.52	271.20±11.38
Levels of significance	P>0.05	P<0.001	P<0.001	P<0.05	P<0.001	P>0.05	P>0.05	P>0.05	P<0.001	P>0.05	P<0.001	P> 0.05

Table showed Means ± Standard error of mean (SEM), Differences between means and the Level of significance (P<0.001, P>0.05). TP = Total protein, ALB = Albumin, PROTH = Prothrombin, ALP = Alkaline phosphatase, AFP = Alphafetoprotein, ALT = Alanine aminotransferase, TB = Total bilirubin, CB = Conjugated bilirubin, GGT = Gamma-glutamyl transferase, FIB = Fibrinogen, PLT = Platelet, AMY = Amylase

Table 3. Hepatic biomarkers in pre-eclamptic women not on $MgSO_4$ at Second Trimester [B] and pre-eclamptic women on $MgSO_4$ at Second Trimester [E]

Group	TP (g/L)	ALB (g/L)	PROTH (sec)	ALP (IU/L)	AFP (IU/mL)	ALT (IU/L)	TB (umol/L)	CB (umol/L)	GGT (U/L)	FIB (g/L)	PLT (/mm^3)	AMY (IU/L)
B (n=10)	73.40±2.40	30.60±0.40	24.60±0.48	193.00±4. 03	124.60±5.80	21.20±1.65	41.40±1.25	8.40±0.51	51.00±1.61	5.50±0.2 2	104,600.00±1,802.37	250.60±19.36
E (n=60)	72.30±1.64	31.80±0.45	24.40±0.17	191.10±8. 66	119.80±2.05	20.30±1.48	40.80±1.14	8.20±0.39	50.30±1.90	5.40±0.0 6	105,583.30±1,495.24	248.30±16.52
Levels of significance	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05

Table showed Means ± Standard error of mean (SEM), Differences between means and the Level of significance (P<0.05). TP = Total protein, ALB = Albumin, PROTH = Prothrombin, ALP = Alkaline phosphatase, AFP = Alphafetoprotein, ALT = Alanine aminotransferase, TB = Total bilirubin, CB = Conjugated bilirubin, GGT = Gamma-glutamyl transferase, FIB = Fibrinogen, PLT = Platelet, AMY = Amylase

Table 4. Hepatic biomarkers in pre-eclamptic women not on $MgSO_4$ at Third Trimester [D] and pre-eclamptic women on $MgSO_4$ at Third Trimester [F]

Group	TP (g/L)	ALB (g/L)	PROTH (sec)	ALP (IU/L)	AFP (IU/mL)	ALT (IU/L)	TB (umol/L)	CB (umol/L)	GGT (U/L)	FIB (g/L)	PLT (/mm^3)	AMY (IU/L)
D (n=10)	81.40±1.50	31.00±0.71	25.70±0.44	224.20±12.73	90.00±2.80	33.80±1.96	42.20±2.67	9.60±0.51	68.80±3.42	5.60±0.23	108,400.00±2,416.52	271.20±11.38
F (n=60)	80.70±1.37	32.30±0.39	24.50±0.12	223.00±10.68	87.90±2.01	33.40±5.55	41.60±1.12	7.90±0.44	68.60±2.01	5.50±0.06	109,550.00±1,352.21	269.20±13.52
Levels of significance	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P>0.05

Table showed Means ± Standard error of mean (SEM), Differences between means and the Level of significance (P<0.05). TP = Total protein, ALB = Albumin, PROTH = Prothrombin, ALP = Alkaline phosphatase, AFP = Alphafetoprotein, ALT = Alanine aminotransferase, TB = Total bilirubin, CB = Conjugated bilirubin, GGT = Gamma-glutamyl transferase, FIB = Fibrinogen, PLT = Platelet, AMY = Amylase.

Table 5. Hepatic biomarkers in normotensive pregnant women at Post-partum [G] and pre-eclamptic women on $MgSO_4$ at Post-partum [H]

Group	TP (g/L)	ALB (g/L)	PROTH (sec)	ALP (IU/L)	AFP (IU/mL)	ALT (IU/L)	TB (umol/L)	CB (umol/L)	GGT (U/L)	FIB (g/L)	PLT (/mm^3)	AMY (IU/L)
G (n=20)	66.50±3.00	34.00±1.36	20.60±0.60	105.20±8. 22	32.50±2.66	9.30±2.40	27.20±1.93	5.80±0.60	32.50±2.47	2.80±0.28	191,700.00±7,161.71	139.00±16.48
H (n=60)	71.40±1.25	34.50±0.49	23.10±0.18	192.30±10 .70	69.50±2.26	17.90±0.66	31.50±1.17	7.40±0.70	34.60±1.42	5.40±0.06	166,850.00±4,242.63	159.30±9.24
Levels of significance	P>0.05	P>0.05	P<0.001	P<0.001	P<0.001	P>0.05	P>0.05	P>0.05	P>0.05	P<0.001	P<0.01	P>0.05

Table showed Means ± Standard error of mean (SEM), Differences between means and the Level of significance (P<0.001, P<0.01, P<0.05). TP = Total protein, ALB = Albumin, PROTH = Prothrombin, ALP = Alkaline phosphatase, AFP = Alphafetoprotein, ALT = Alanine aminotransferase, TB = Total bilirubin, CB = Conjugated bilirubin, GGT = Gamma-glutamyl transferase, FIB = Fibrinogen, PLT = Platelet, AMY = Amylase

The plasma activities of alkaline phosphatase and gamma-glutamyl transferase were significantly increased while that of alanine aminotransferase was non-significantly raised when compared with the normotensive pregnant groups. This result could be linked to possible hepatic necrosis in pre-eclampsia [25]. In other way round, non-significant decreased activities of plasma alkaline phosphatase, gamma-glutamyl transferase and alanine aminotransferase were seen in pre-eclamptic pregnant women treated with $MgSO_4$ at both 2nd and 3rd trimesters, as well as 3-6 days post-partum when compared with similar group not on $MgSO_4$ treatment. The reduced enzyme activities again confirm $MgSO_4$ as angiotensin converting enzyme inhibitor that opposes the action of angiotensin converting enzyme by preventing hepatic necrosis to decrease plasma alkaline phosphatase, gamma-glutamyl transferase and alanine aminotransferase activities [26].

Results obtained from this study indicated that alphafetoprotein concentration was significantly raised in pre-eclamptic women than the normotensive groups. Phyllis et al. [1] has given similar reports. The increase in alphafetoprotein might be due to the production of alphafetoprotein as a response to foetal and neonatal development by liver in pre-eclampsia. However, the plasma concentration of alphafetoprotein was non-significantly reduced in pre-eclamptic pregnant women treated with $MgSO_4$ at both 2nd and 3rd trimesters, and at post-partum when compared with pre-eclamptic pregnant women that were not on $MgSO_4$ treatment. The decrease is in agreement with report of Munjuluri et al. [24]. This reduction in alphafetoprotein could be due to effect of $MgSO_4$ as a seizure prophylaxis in the prevention of alphafetoprotein production by liver that normally occur as a result of pre-eclampsia, thereby opposing transcellular transport of proteins (glycoproteins) through the tight junctions leading to decreased synthesis of alphafetoprotein.

Plasma bilirubin (total and conjugated) concentration was non-significantly elevated in pre-eclamptic women when compared with the normotensive groups. This hyperbilirubinaemia may be due to hepatic necrosis in pre-eclampsia causing continuous red cell haemolysis for bilirubin synthesis and decreased conjugated bilirubin excretion [27]. However, a non-significant decreased bilirubin concentration (total and conjugated) was observed in pre-eclamptic pregnant women treated with $MgSO_4$ at both 2nd and 3rd trimesters, as well as 3-6 days post-partum when compared with pre-eclamptic pregnant women that were not on $MgSO_4$ treatment. The hypobilirubinaemia may be due to the effect of $MgSO_4$ as a good cell membrane protector (neuroprotective) agent that decrease cellular disruption and oedema from pinocytosis associated with pre-eclampsia whose actions also causes reduced erythrocyte destruction for bilirubin synthesis and conjugation [5].

Plasma concentration of fibrinogen was significantly raised in pre-eclamptic women during pregnancy and at post-partum when compared with the normotensive groups. The elevated fibrinogen concentration might be due to acute inflammation or cell injury, immunological and biological injury (which include infection) to hepatocytes in pre-eclampsia. Similar observation has been reported by Bolarin and Bolarin, [28]. However, plasma concentration of fibrinogen was decreased non-significantly in pre-eclamptic pregnant women treated with $MgSO_4$ at both 2nd and 3rd trimesters, and after delivery when compared with their counterparts that were not on $MgSO_4$ treatment. The reduction in fibrinogen concentration confirm that $MgSO_4$ treatment may help in the prevention of endothelial damages to the hepatocytes that normally occur as a result of pre-eclampsia by opposing transcellular transport of proteins (glycoproteins) through the tight junctions leading to reduced fibrinogen concentration [24].

Platelet count was significantly reduced in pre-eclamptic women when compared with normotensive pregnant women. Similar observation has been reported by Furuhjelm, [29]. This reduced platelet count could be attributed to hepatocyte damage from endothelial dysfunction in pre-eclamptic women that facilitates reduced fibrinolytic activity by the liver cells to initiates thrombocytopenia. On the other hand, platelet count was non-significantly raised in pre-eclamptic pregnant women treated with $MgSO_4$ at both 2nd and 3rd trimesters, and after delivery when compared with their counterparts. From this result, it can be deduced that $MgSO_4$ may help in preventing endothelial damages to the hepatocytes that normally occur as a result of pre-eclampsia leading to increased fibrinolytic activity by the liver cells for increase platelets synthesis [30].

Amylase activity was non-significantly raised in pre-eclamptic women when compared with the

normotensive groups. Similar report has been made by Bolarin and Bolarin, [28]. This could be attributed to hepatic vascular obstruction in pre-eclampsia for increase plasma amylase activity. Findings afterward revealed a non-significant decreased plasma activity of amylase in pre-eclamptic pregnant women treated with $MgSO_4$ at both 2nd and 3rd trimesters, and at post-partum when compared with pre-eclamptic pregnant women that were not on $MgSO_4$ treatment. This is in agreement with the report of Witlin et al., [26]. This finding shows that magnesium sulphate may prevent vascular blockages and damages by stimulating production of prostacyclin (a vasodilator) by endothelial cells causing vasodilation for reduced plasma activity of amylase.

5. CONCLUSION

The results obtained from this work revealed that $MgSO_4$ is devoid of any adverse effects on liver function which support its existing usage as an anti-convulsant in the management and treatment of pre-eclampsia.

CONSENT

All authors declare that written informed consent was obtained from all the subjects studied in this work.

ETHICAL APPROVAL

The Postgraduate Ethical Committee of the Faculty of Science, Ekiti State University, Ado-Ekiti, Ekiti State, Nigeria, approved the research work.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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