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Evaluation Of Liver Enzymes (ALP, ALT, AST and GGT) in Preeclamptic Pregnant Women in the Third Trimester Of Pregnancy

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Abstract.*Alkaline Phosphatase (ALP), Alanine Transaminase (ALT), Aspartate Transaminase (AST), and Gamma-Glutamyl Transferase (GGT) are liver enzymes commonly associated with liver dysfunction, and increased or decreased levels of these enzymes may be implicated in the pathophysiology of preeclampsia. This study aims to evaluate the levels of liver enzymes (ALP, ALT, AST, and GGT) in preeclamptic pregnant women in the third trimester of pregnancy. By analyzing these enzymes, the research seeks to identify potential early indicators of preeclampsia. Forty (40) consenting pregnant women were recruited from St. Philomina Catholic Hospital, Edo State, Nigeria. Blood samples were spun in a bucket centrifuge at 2500 RPM (rounds per minute) for 10 minutes, after which plasma was collected and stored frozen in plain sample bottles to be analyzed for liver enzymes (ALP, ALT, AST, and GGT) levels using the spectrophotometric method. Data obtained from the study were analyzed using Graph Pad Prism 9. Results were expressed as mean ± SEM, and a P-value of ≤ 0.05 was considered statistically significant. The present study showed a statistically significant increase in ALP, and a statistically significant decrease in liver enzymes such as ALT and AST were observed in preeclamptic women compared to normotensive pregnant women, indicating various underlying pathophysiological processes such as liver dysfunction.*

Keywords: *Alanine Transaminase (ALT), Alkaline Phosphatase (ALP), Aspartate Transaminase (AST), Gamma-GlutamylTransferase (GGT), Preeclampsia.*

1. INTRODUCTION

Liver dysfunction is a commonly observed feature in preeclampsia, a serious pregnancy complication that can lead to significant maternal and fetal health risks. Elevated levels of liver enzymes, such as Alkaline Phosphatase (ALP), Alanine Transaminase (ALT), Aspartate Transaminase (AST), and Gamma-Glutamyl Transferase (GGT), are frequently seen in women with preeclampsia. These enzymes are essential markers of liver function, and their abnormal levels may indicate liver damage or dysfunction, which plays a critical role in the progression of

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the disease. Understanding the relationship between liver enzyme levels and preeclampsia can offer valuable insights into the mechanisms underlying the disease and aid in the development of predictive tools for early diagnosis.

Preeclampsia is a complex and multifactorial condition characterized by elevated blood pressure and damage to multiple organs, including the kidneys, liver, and brain. It typically occurs after the 20th week of pregnancy and is defined by new-onset hypertension and proteinuria. In severe cases, preeclampsia can lead to organ failure, eclampsia, and even maternal or fetal death. With an incidence rate of 2-8% of pregnancies worldwide, preeclampsia remains one of the leading causes of maternal and fetal morbidity and mortality. Due to the potential for rapid deterioration of maternal health, early identification and monitoring are crucial for managing the condition and improving outcomes for both the mother and fetus.

Oxidative stress, inflammation, and impaired placental function are central to the pathophysiology of preeclampsia. The imbalance between pro- and antioxidant mechanisms in the body leads to endothelial dysfunction, which is a key factor in the development of hypertension and organ damage. Liver involvement is particularly notable in preeclamptic women, as it contributes to the development of liver dysfunction, one of the hallmark features of severe preeclampsia. Elevated liver enzymes, such as ALP, ALT, AST, and GGT, have been observed in preeclamptic women, suggesting that liver dysfunction may serve as an early indicator of the disease. These enzymes are involved in various biochemical processes within the liver, and their abnormal levels are thought to reflect underlying liver damage due to the disease.

Early detection of preeclampsia is vital for preventing adverse outcomes, as the condition can progress rapidly from mild symptoms to severe organ damage. Elevated liver enzyme levels can be used as a potential marker for identifying women at risk of developing preeclampsia or those already experiencing liver involvement. Since preeclampsia often develops without obvious symptoms in the early stages, utilizing liver enzymes as biomarkers could provide a non-invasive, cost-effective method for early diagnosis and monitoring of at-risk pregnancies. This is especially important in resource-limited settings, where access to advanced diagnostic tools may be limited.

This study aims to evaluate the levels of ALP, ALT, AST, and GGT in preeclamptic women during the third trimester of pregnancy to determine their potential role as early indicators of preeclampsia. By analyzing these liver enzymes, the research seeks to identify biomarkers that can predict the onset of preeclampsia before clinical symptoms become apparent. Understanding the

relationship between liver enzyme levels and preeclampsia will provide critical insights into the pathophysiology of the disease and contribute to the development of better diagnostic strategies and targeted interventions for managing preeclamptic pregnancies.

Related Works

Alkaline phosphatase (ALP) is an enzyme involved in metabolism and skeletal development, found in tissues like the liver, bones, and kidneys. Elevated ALP levels are commonly used in diagnostics for liver and bone disorders, while low levels may indicate conditions like hypophosphatasia or malnutrition [7]. ALP isoenzymes are specific to different tissues and help pinpoint the underlying cause of abnormalities [8].

Low-dose aspirin has been studied for preventing preeclampsia, with significant benefits when started before 16 weeks of pregnancy [9]. Aspirin doses of 75–81 mg/day are recommended by health organizations, though higher doses carry a risk of obstetric bleeding.

Low molecular weight heparins (LMWH) also show potential, but more research is needed Alanine transaminase (ALT) is a key enzyme for liver function, often elevated in liver damage or preeclampsia]. Aspartate transaminase (AST), while less specific to the liver, is also measured in liver tests to assess injury.

Gamma-glutamyl transferase (GGT) plays a role in detoxification and is used to assess liver diseases, alcohol use, and cardiovascular risk [14]. It may also serve as a biomarker for preeclampsia, though its clinical application is still under investigation [15].

2. MATERIALS AND METHODS

Geographical Description of the Study Area

This research was carried out among Third Trimester Pregnant women in St. Philomina Catholic Hospital, Edo State, Nigeria lies longitudinally at 04ºE and 43ºE and Latitude 05º44ºN and 07º34ºN. It geopolitical location is the South South and it has a population of 3.5 million people. Oredo land, Benin City, the State capital, is 100 km long. Edo State, South-South, Nigeria. Oredo is a Local Government Area of Edo State, Nigeria. Its headquarters are in the town, Benin city. It has an area of 502 km² and a population of 500,000 at the 2006 census.

Majority of which are civil servants, traders, businessmen/women, transporter, farmers, teachers/lecturers and students by occupation. Oredo, since after its designation as headquarters and as the host of Oba of Benin Palace, the town has grown into an urban center.

Research Design

Forty (40) consenting pregnant subjects were recruited from St. Philomina Catholic Hospital, Edo State. These subjects consisted of twenty (20) normotensive pregnant women in their third trimester of pregnancy with blood pressure between 120/80mmHg to 130/90 mm/Hg without presence of proteinuria and twenty (20) preeclamptic women in their third trimester of pregnancy classified as having preeclampsia according to their blood pressure measured was above 130/90 mm/Hg with the presence of proteinuria taken two consecutive times at presentation at the antenatal clinic of the hospital

Sample Size

The Population of study was determined using the formula;

$N= Z^2pq/d^2$

Where N= the desired sample size (when population is greater than 10,000)

Z= is a constant given as 1.96 (or more simply at 2.0) which corresponds to the 95% confidence level.

P= previous survery prevalence of 2.23%

q= 1.0-p

d= acceptable error 5%.

Where N= sample size, Z=1.96, p=0.1% (0.01) and d=5% (0.05)

N= 39.8 subject.

Therefore, the sample for this study is 40 respondents who are normotensive and preeclamptic pregnant women from Oredo town, Benin City.

Ethical Approval and Informed Consent

Ethical clearance (REC Approval No:RECC/10/2023(07)) was obtained from the Research Ethics Committee of St. Philomina Catholic Hospital, Edo State.

Written informed consent was obtained from subjects prior to commencement of the study.

Blood Sampling

10 milliliters (10 ml) of venous blood was drawn from consenting participants and placed in a lithium heparin sample bottles. Blood samples was spun in a bucket centrifuge at 2500 RPM (rounds per minute) for 10 minutes after which plasma was collected and stored frozen in plain sample bottles and was analyzed for Liver enzymes (aspartate aminotransaminase, Alkaline phosphatase, Gamma-glutamylTransferase and alanine transaminase,)

Experimental Protocols

After the subjects were identified and recruited into the study, they were taken to the lab where their vital signs was taken, after which blood samples were collected by venipuncture and taken to the chemistry laboratory for analysis.

Study Area/Population

The study were conducted for three months at St. Philomina Catholic Hospital, Edo State, Nigeria.

Inclusion Criteria

Normotensive and Preeclamptic pregnant women in the third trimester of pregnancy, within the age range of 25 to 35years was used for this study. Pregnant women were recruited for this study and women who had given birth before and were pregnant for the second time.

Exclusion Criteria

Normotensive and Preeclamptic pregnant women who were on drugs and with a known history of hyperlipidemia, gestational Diabetes and other comorbidity.

Biochemical Examination

Measurement of Liver Enzymes (ALP, ALT, AST and GGT)

by spectrophotometric method. Procedure. Liver enzymes (aspartate aminotransaminase, Alkaline phosphatase, Gamma-glutamylTransferase and alanine transaminase,) Analysis

Alanine Aminotransferase (ALT) (Thomas, 1998)

Alanine Aminotransferase (ALT) was determined by spectrophotometric method

Principle

α-Ketoglutarate reacts with L-alanine in the presence of ALT to form L-glutamate plus pyruvate. The pyruvate was used in the indicator reaction for a kinetic determination of the reduced form of nicotinamide adenine dinucleotide (NADH) consumption.

Procedure

0.1ml of samples was added to sample test tube while no sample was added to reagent blank test tube. 0.5ml of solution R1 was added to reagent blank and sample test tube. 0.1ml of distilled water was added to reagent blank test tube only. Was Mix and incubated for exactly 30min. at 37^0C. 0.5ml of solution R2 was added to reagent blank and sample test tube. Mix, allow to stand for exactly 20min at 20 to 25^0C. 5.0ml of Soduim hydroxide was added to reagent blank and sample test tube. Mix, read the absorbance of sample against the reagent blank after 5 min at Wavelength at 546.

Alkaline Phosphatase (ALP) (Thomas, 1998)

Alkaline Phosphatase (ALP) was determined by spectrophotometric method

Principle

In the presence of magnesium ions, p-nitrophenylphosphate is hydrolyzed by phosphatases to phosphate and p-nitrophenol. The rate of p-nitrophenol liberation is proportional to the ALP activity and can be measured photometrically

Procedure

1.0ml of deionized water was added to sample and standard test tube. 1 drop of substrate was added to sample and standard test tube. Mix and incubate 5min at 37^0C. 0.1ml of standard was added to standard test tube. 0.1ml samples was added to sample test tube. Mix and start the chromometer incubate for 20min at 37^0C. 5.0ml of colour developer was added to sample and standard test tube. Read at Wavelenght 550.

Aspartate Aminotransferase (AST) (Guder and Zawta, 2000)

Aspartate Aminotransferase (AST) was determined by spectrophotometric method.

Principle

α-Ketoglutarate reacts with L-aspartate in the presence of AST to form L-glutamate plus oxaloacetate. The indicator reaction uses the oxaloacetate for a kinetic determination of NADH consumption.

Procedure

0.1ml of samples was added to sample test tube while no sample was added to reagent blank test tube. 0.5ml of solution R1 was added to reagent blank and sample test tube. 0.1ml of distilled water was added to reagent blank test tube only. Mix and incubate for exectly 30min. at 37^0C. 0.5ml of solution R2 was added to reagent blank and sample test tube. Mix, allow to stand for exactly 20min at 20 to 25^0C. 5.0ml of Soduim hydroxide was added to reagent blank and sample test tube. Mix, read the absorbance of sample against the reagent blank after 5 min at Wavelength at 546.

Gamma Glutamyltransaminase (γ-GT)

(Schumann, Bonora, CeriottiandFerad, 2002)

Gamma Glutamyltransaminase (γ-GT) will be determined by spectrophotometric method.

Principle

In this rate method, L-γ-glutamyl-3-carboxy-4-nitroanilide is used as a substrate α and glycylglycine as a acceptor. The rate at which 5-amino-2-nitrobenzoate is liberated is proportional to γ-GT activity and is measured by an increase in absorbance.

Procedure

Add 0.1ml of sample to 1.0ml of reagent (20^0C,30^0C,37^0C). Mix, read initial absorbance and

Data Analysis

Data obtained from this study were analysed using Graph Pad Prism 9. Results generated were expressed as mean ± SEM and a P-value of ≤ 0.05 were considered satistically significant. The significance of difference among the groups were used to assess the repeated-measures analysis of variance (ANOVA). Independent students' t-test were used to compare normotensive and preelclamptic pregnant women groups.

3. RESULTS AND DISCUSSION

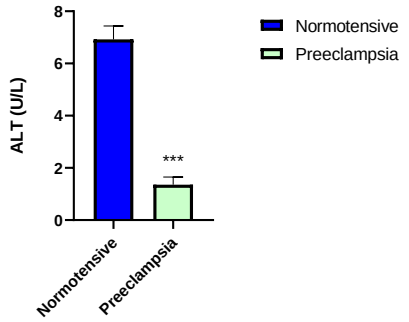

Figure 1: Mean ± SEM of Alanine Transaminases (ALT) activities in normotensive (n=20) and preeclampsia (n=20). The t-test was carried out to access any significant difference. * represents p<0.001**

Figure 1 shows that Alanine Transaminases (ALT) activities statistically decreased significantly (p< 0.05; <0.001) in pre-eclamptic women in their third trimester of pregnancy to 1.36 ± 0.29U/L when compared to Alanine Transaminases (ALT) level 6.920 ± 0.52 U/L in Normotensive pregnant women.When both groups where compared, this decreased was found to be statistically significant (p<0.05; <0.0001).

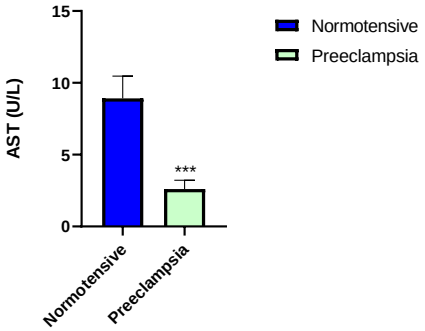

Figure 2: Mean ± SEM of Aspartate Transaminases (AST) activities in normotensive (n=20) and preeclampsia (n=20). The t-test was carried out to access any significant difference. * represents p<0.001**

Figure 2 shows the levels of Aspartate Transaminases (AST) activities in Normotensive and pre-eclamptic women in their third trimester of pregnancy. Aspartate Transaminases (AST) activities decreased significantly ($p< 0.05$; 0.0005) from 8.915 ± 1.55U/L in Normotensive women to 2.611 ± 0.606U/L in pre-eclamptic women. When both groups where compared, this decreased was found to be statistically significant ($p<0.05$; <0.0001).

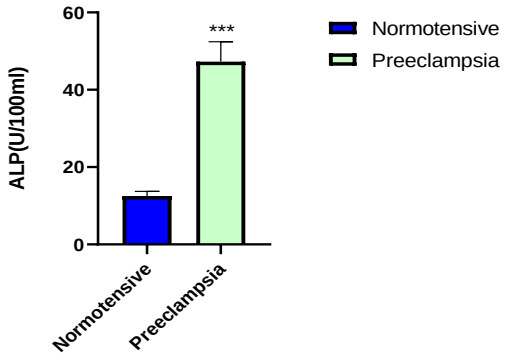

Figure 3: Mean ± SEM of Alkaline Phosphatase (ALP) activities in normotensive (n=20) and preeclampsia (n=20). The t-test was carried out to access any significant difference. * represents p<0.001**

Figure 3 shows the levels of Alkaline Phosphatase (ALP) activities in Normotensive and pre-eclamptic women in their third trimester of pregnancy. Alkaline Phosphatase (ALP) activities increased significantly ($p< 0.05$; <0.0001) from 12.54 ± 1.20U/100ml in Normotensive women to 47.27 ± 5.174U/100ml in pre-eclamptic women. When both groups where compared, this increase was found to be statistically significant ($p<0.05$; <0.0001).

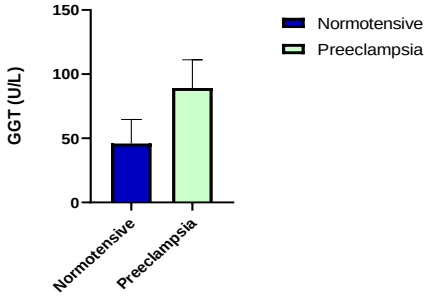

Figure 4: Mean ± SEM of Gamma GlutamylTransferase (GGT) level in normotensive (n=20) and preeclampsia (n=20). The t-test was carried out to access any significant difference.

Figure 4 shows the levels of Gamma GlutamylTransferase (GGT) in Normotensive and pre-eclamptic women in their third trimester of pregnancy. Gamma GlutamylTransferase (GGT) increased from 45.99 ± 18.66U/L in Normotensive women to 89.16 ± 21.97U/L in pre-eclamptic women. However, the increase was not statistically significantly ($p<0.05$; 0.1425)

4. DISCUSSION

ALT and AST are enzymes primarily found in the liver, and their levels are commonly used as indicators of liver function [16]. Figure 1 and Figure 2, there was significant decrease in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities observed in pre-eclamptic pregnant women compared to normotensive women this suggests potential implications for their predictive roles in preeclampsia. The decrease in ALT and AST activities in pre-eclamptic women may reflect impaired liver function, which is a common complication of severe preeclampsia. Previous studies have reported alterations in liver enzymes, including ALT and AST, in women with preeclampsia [2],[3]. Therefore, monitoring ALT and AST levels may provide valuable information for identifying women at risk of developing severe preeclampsia and guiding clinical management Liver involvement in preeclampsia can manifest as hepatic ischemia, necrosis, and impaired liver function [17]. ALP is an enzyme found in various tissues, including the liver, bones, and placenta [16] in Figure 3, the significant increase in alkaline phosphatase (ALP) activities observed in pre-eclamptic women compared to normotensive women suggests a potential predictive role for ALP in preeclampsia. Which corroborated the work of [18]. He reported that there was Elevated ALP levels in preeclamptic pregnant women and are indicative of liver dysfunction or placental abnormalities. In the context of preeclampsia,

Gamma-glutamyl transaminase (GGT) is another liver enzyme that is elevated in conditions affecting the biliary tract and liver function [16]. Figure 4 The non-significant increase in gamma-glutamyl transaminase (GGT) levels in pre-eclamptic women compared to normotensive pregnant women suggests a limited predictive role for GGT in preeclampsia .in contrast some previous studies have reported increased GGT levels in preeclampsia [19],[3], the lack of statistical significance in this present study suggests that GGT may not be a reliable predictor of preeclampsia. Overall, the observed changes in liver enzymes, including ALT, AST, ALP, and GGT, highlight the importance of assessing liver function in the prediction and management of preeclampsia.

CONCLUSION

The present study showed that there was statistically significant increase in ALP and statistically significant decrease in liver enzymes like ALT, AST were observed in preeclamptic women compared to normotensive pregnant women, indicating various underlying pathophysiological processes such as liver dysfunction. These findings suggest the potential implication of these liver enzymes in identifying and monitoring preeclampsia. However, level of gamma-glutamyl transaminase (GGT) did not show significant differences between preeclamptic and normotensive women, suggesting that this biomarkers may not be reliable implicator of preeclampsia based on the current study's findings. A limitation of this study is its small sample size of just 40 participants, which may not accurately reflect the broader population. The research was conducted at a single hospital during the third trimester of pregnancy, limiting its generalizability. Additionally, potential confounding factors such as diet, pre-existing medical conditions, or genetic variations were not considered, which could influence liver enzyme levels. The use of the spectrophotometric method for enzyme analysis also carries the risk of technical variability, which may affect the reliability of the results.

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