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Promising Markers of Preeclampsia : Cardiac Troponin 1 and Brain Natriuretic Peptide in Third Trimester Pregnant Women

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Abstract *Cardiac Troponin1 (cTn1) is a protein released into the bloodstream following cardiac damage and Brain Natriuretic Peptide (BNP) is a hormone released by the heart in response to ventricular stretch and pressure overload. This study aims to investigate the predictive role of cTn1 and BNP in preeclamptic pregnant women in the third trimester of pregnancy. Forty (40) consenting pregnant women were recruited from St. Philomina Catholic Hospital, Edo State, Nigeria. 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 Cardiac Troponin 1(cTn1) and Brain Natriuretic Peptide (BNP) by fluorescence immunoassay. 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 statistically significant. The present study showed that there was statistically significant increase in Brain Natriuretic Peptide (BNP) in preeclamptic women compared to normotensive pregnant women, indicating various underlying pathophysiological processes. These findings suggest the potential predictive roles of this cardiac marker in identifying and monitoring preeclampsia.*

Keywords: *Brain Natriuretic Peptide (BNP), Cardiac Troponin1 (cTn1), Preeclampsia*

1. INTRODUCTION

Preeclampsia is a complex and multifactorial pregnancy complication characterized by high blood pressure and damage to organs such as the kidneys, liver, and brain. It affects approximately 2-8% of pregnancies worldwide, making it a leading cause of maternal and fetal morbidity and mortality. Early detection and prediction of preeclampsia are crucial to prevent severe complications and ensure timely interventions.

Recent studies have highlighted the potential of cardiac biomarkers in predicting preeclampsia. Brain Natriuretic Peptide (BNP) and Cardiac Troponin 1 (cTn1) have emerged as promising biomarkers due to their association with cardiac dysfunction and preeclampsia pathophysiology. BNP is a hormone released by the heart in response to ventricular stretch and pressure overload, while cTn1 is a protein released into the bloodstream following cardiac damage.

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Elevated levels of BNP and cTn1 have been observed in preeclamptic women, suggesting their potential role in predicting preeclampsia. This study aims to investigate the predictive role of BNP and cTn1 in preeclamptic pregnant women in the third trimester of pregnancy. By analyzing these biomarkers, this research seeks to identify potential early indicators of preeclampsia, enabling timely interventions and improving maternal and fetal outcomes.

The use of BNP and cTn1 as predictors of preeclampsia offers a promising approach, as they are widely available and cost-effective biomarkers. This study's focus on these biomarkers provides a nuanced understanding of their predictive role, enabling healthcare providers to make informed decisions and improve patient care. Furthermore, the study's findings will have implications for the development of personalized medicine approaches to preeclampsia diagnosis and management.

2. RELATED WORKS

Cardiac troponins, specifically cardiac troponin I (cTnI) and cardiac troponin T (cTnT), are essential proteins that regulate heart muscle contraction and serve as highly specific biomarkers for cardiac injury, particularly during myocardial infarction (MI). These proteins are released into the bloodstream when the heart muscle is damaged, providing a highly sensitive and specific means for diagnosing acute coronary syndromes (ACS) [8]. Prior to the discovery of cardiac troponins, markers like creatine kinase-MB (CK-MB) were used, but these lacked the specificity that troponins offer. The development of assays distinguishing cardiac troponins from skeletal muscle forms has significantly improved the detection of myocardial injury.

Troponins regulate contraction by interacting with actin and myosin filaments in response to calcium. Troponin C (TnC) binds calcium to initiate contraction, while troponin I (TnI) inhibits actin-myosin interaction in the absence of calcium, and troponin T (TnT) anchors the complex to tropomyosin. Both cTnI and cTnT are specific to cardiac muscle, making them reliable markers for myocardial injury. These markers are critical for diagnosing myocardial infarction, with cTnT rising slightly earlier and remaining elevated longer than cTnI, offering insight into the timing and extent of injury.

Beyond acute myocardial infarction, elevated troponin levels can indicate conditions like heart failure, myocarditis, and sepsis. Research into high-sensitivity assays has enabled the detection of even minor myocardial injuries, improving diagnostic and prognostic accuracy.

Troponin levels are also used to assess the risk of future cardiovascular events and the severity of chronic conditions like heart failure and chronic kidney disease. High-sensitivity assays have revolutionized early detection and clinical decision-making by identifying minor troponin elevations that might otherwise be missed.

In pregnancy, troponins can be elevated in conditions like preeclampsia and pregnancy-induced hypertension, which can cause myocardial stress. Elevated troponin levels in these cases highlight the cardiovascular strain associated with hypertensive disorders during pregnancy. A study by found high-sensitivity cardiac troponin I levels in a significant proportion of pregnant women, particularly those with hypertensive disorders, emphasizing the relevance of troponins in pregnancy-related cardiovascular monitoring.

In addition, Brain Natriuretic Peptide (BNP), a hormone released in response to myocardial stress, also plays a critical role in diagnosing heart failure. BNP and its inactive fragment NT-proBNP are widely used as biomarkers, with elevated levels correlating with heart failure severity and aiding diagnosis, particularly in patients with acute dyspnea. While BNP levels are also elevated in conditions such as pulmonary hypertension and chronic obstructive pulmonary disease (COPD), they may not always correlate with pulmonary function, highlighting the complexity of BNP's role in respiratory diseases.

3. 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’s 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

Fourty (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 cardiac markers (Brain natriuretic peptide and Cardiac troponin 1).

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 Brain natriuretic peptide and Cardiac troponin 1 by fluorescence immuno assay.

Procedure

Step 1: Preparation: Prior to the testing, the test cassette, detection buffer and specimen was allowed to equilibrate at room temperature. The ID chip was inserted into the chip port of the instrument after the ID chip was confirmed to be consistent with the batch number of test cassette

Step 2: Sampling: Plasma sample of 75 µL was drawn with transfer pipette and added to the buffer tube.

Step 3: Loading: The sample mixture of 75 µL was loaded into the sample well of the test cassette.

Step 4: Testing: The standard test mode was used in which the test device was inserted onto the test cassette holder of FIA Meter right after adding sample mixture to the sample well and "Test botton" was been pressed to start testing. The reaction time was 3 minutes.

Step 5: Reading result: Results were displayed on the main screen of meter and was printed out by pressing "Print".

Step 6: Withdraw: The used test kit was discarded according to local regulations and procedure after released from the meter.

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.

4. RESULTS

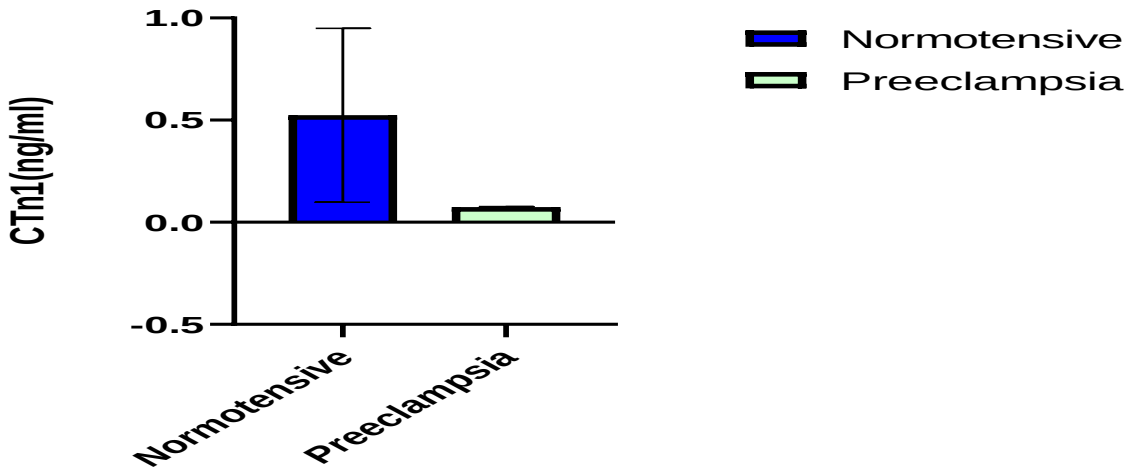

Figure 1: Mean ± SEM of Cardiac Troponin 1(CTn1) level in normotensive (n=20) and preeclampsia (n=20). The t-test was carried out to access any significant difference.

Figure 2: shows the levels of Cardiac Troponin 1(CTn1) in Normotensive and pre-eclamptic women in their third trimester of pregnancy. Cardiac Troponine 1 (CTn1) decreased from 0.524 ± 0.43ng/ml in Normotensive women to 0.07 ± 0.003ng/ml in pre-eclamptic women. However, when both means were compared, there was no statistically significant difference observed (p> 0.05; 0.2976)

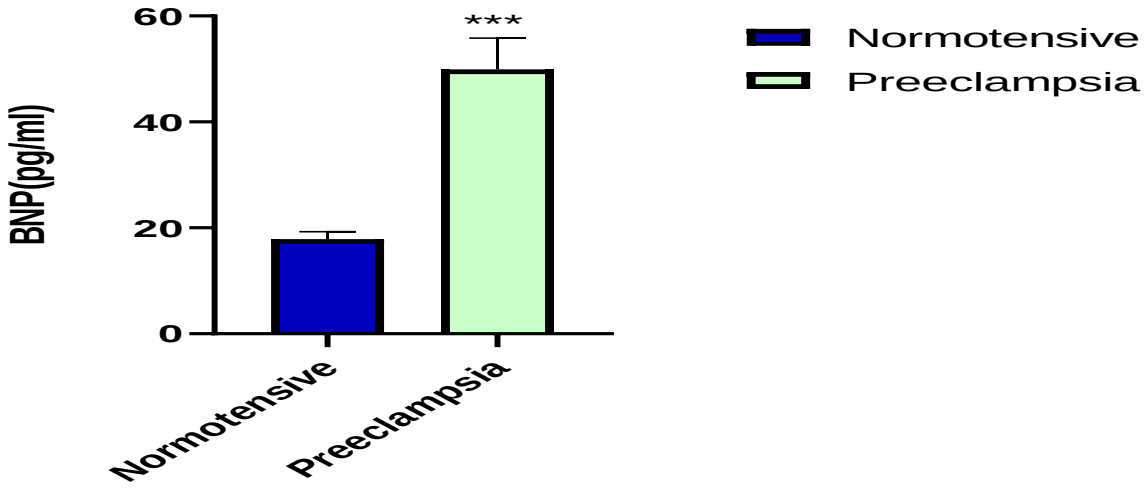

Figure 2: Mean ± SEM of Brain Natriuretic Peptide (BNP) level in normotensive (n=20) and preeclampsia (n=20). The t-test was carried out to access any significant difference. *** represents $p<0.001$

Figure 2 shows the levels of Brain Natriuretic Peptide (BNP) in Normotensive and pre-eclamptic women in their third trimester of pregnancy. BNP increased significantly ($p<0.05$; <0.0001) from 17.86 ± 1.44pg/ml in Normotensive women to 49.91 ± 5.91pg/ml in pre-eclamptic women.

5. DISCUSSION

Cardiac Troponin I (CTnI) is a protein that is released when the heart muscle is damaged. It is a biomarker for myocardial infarction (heart attack) and is used to diagnose and monitor heart damage. Elevated levels of CTnI in the blood can indicate myocardial infarction, even if other tests such as electrocardiogram (ECG) are normal. Brain Natriuretic Peptide (BNP) is a hormone produced by the brain in response to heart failure. It helps to regulate fluid balance and blood pressure by increasing urine production and reducing blood volume. Elevated levels of BNP in the blood can indicate heart failure, and it is used to diagnose and monitor the condition. BNP also inhibits the sympathetic nervous system and the activities of several other hormone systems, including the renin-angiotensin-aldosterone system. Figure 1 the contrasting findings regarding cardiac troponin I (CTnI) level in normotensive and pre-eclamptic women provide valuable insights in the predictive roles in preeclampsia. Although CTnI level decreased in pre-eclampticwomen compared to normotensive women, the difference was not statistically significant. This suggests that CTnI may not be a reliable predictor of preeclampsia. Studies have

reported conflicting results regarding the association between CTnI and preeclampsia. Some studies have found elevated CTnI levels in women with preeclampsia, indicating myocardial injury or dysfunction, while others have reported no significant difference in CTnI levels between normotensive and pre-eclamptic wome. Figure 2, the significant increase in BNP level in pre-eclampticwomen compared to normotensive women suggests a potential predictive role of BNP in preeclampsia. Elevated BNP level have been consistently reported in women with preeclampsia [33]. The increase in BNP level reflects the cardiac dysfunction and hemodynamic changes. BNP is a marker of cardiac stress and is elevated in conditions associated with increased cardiac workload, such as preeclampsia. characteristic of preeclampsia, including increased vascular resistance and fluid retention. Therefore, while CTnI may not be a reliable predictor of preeclampsia, elevated BNP level could serve as a valuable potential biomarker in the prediction of women at high risk of developing preeclampsia.

6. CONCLUSION

The present study showed that there was statistically significant increase in Brain Natriuretic Peptide (BNP) in preeclamptic women compared to normotensive pregnant women, indicating various underlying pathophysiological processes. These findings suggest the potential predictive roles of this cardiac marker in identifying and monitoring preeclampsia. However, level of cardiac troponine I (CTnI), suggesting that this cardiac marker may not be reliable predictors of preeclampsia based on the current study's findings.

A limitation of this study is its relatively small sample size of 40 participants, which may limit the generalizability of the findings to a larger population. Additionally, the study focused only on women in the third trimester of pregnancy, which might not account for early changes in biomarkers that could be useful for the early detection of preeclampsia. Furthermore, the cross-sectional design of the study does not allow for assessing the temporal relationship between biomarker levels and the development of preeclampsia.

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