

MATERNAL FASTING BLOOD LIPIDS: A MARKER OF SEVERITY OF PRE-ECLAMPSIA IN JOS, NORTH-CENTRAL NIGERIA

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ABSTRACT

Background: Pre-eclampsia is a common medical disorder of pregnancy, in Nigeria, and has been reported to be characterized by blood lipid derangements with oxidative stress and endothelial dysfunction.

Objective

Methods and materials: This was comparative cross-sectional study, amongst women with Preeclampsia. Fasting venous blood samples were taken into plain vacuitainers and analyzed in batches after —days for serum lipids using Cobas C-III Roche auto analyzer machine. The data were analysed using Epi-info version 3.5.4 The duration of study was for about seven month's period

Results: The mean serum levels of triglycerides in mild pre-eclampsia was 1.13 ± 0.50 mmo/L, while in severe pre-eclampsia $= 2.22 \pm 0.92$ mmo/L, p -value $= 0.00001$. Other lipid components: Total cholesterol, High density lipoprotein, Low density lipoprotein were not significantly different in the two studied groups ($p > 0.005$) Multiple linear regressions model revealed serum triglycerides had the highest standardized absolute coefficient of 0.332 and lead value of 0.591.

Conclusion: Serum triglycerides alone, appear to be a significant predictor of severity of pre-eclampsia; hence can serve as a surveillance tool during conservative management of pre-eclampsia.

Key Words: Maternal, Serum, lipids, Pre-eclampsia, Triglycerides, Total cholesterol, Low-density lipoprotein and High-density Lipoprotein

Introduction:

Pre-eclampsia is a potentially life threatening medical disorder of human pregnancy that complicates 2.0% to 16.7% of pregnancies in Nigeria¹ and is associated with significant maternal and perinatal morbidity and mortality¹. Pre-eclampsia usually develops after 20th week of gestation and thereafter potentially affects multiplicity of human body organs such as the brain, eyes, lungs, liver and the kidneys¹. Pre-eclampsia can be defined as new onset hypertension (Blood Pressure 140mmHg/90mmHg). Accompanied by proteinuria ++ or more in a strip dip test or total protein excretion of 300mg/dL in a 24 hour urine collection¹. In the absence of intervention, the mother is at significant risk of seizures (eclampsia) pulmonary, renal, hepatic damages, stroke and possible death. Pre-eclampsia is a known main risk factor for cardio-vascular disease later in life for both the mother and the baby¹.

Maternal vascular endothelial dysfunction is the hallmark in the pathophysiology of pre-eclampsia². This occurs in relation to increased levels of circulating lipids, which result in accumulation of these lipids within the endothelial cells, leading to impediment to the release of prostacyclin, resulting in oxidative stress and cascade of events in vascular endothelial dysfunction and release of more lipids particularly triglycerides, total cholesterol, low density lipoprotein and very low density lipoprotein^{2,3}. A meta-analysis on the relationship between maternal serum triglycerides levels and pre-eclampsia, found that women with pre-eclampsia had significantly higher levels of triglycerides than normotensive women³. Although numerous studies suggests that a dyslipidemia pattern that showed increased total cholesterol, triglycerides, and low-density lipoprotein-cholesterol along with decreased high-density

lipoprotein-cholesterol concentrations, may be associated with an increased risk of pre-eclampsia, results are inconsistent and inconclusive³. Many of these studies had small sample sizes, the gestational age of the time of the lipid measurement varied, making it difficult to compare findings across the studies. Therefore, we conducted comparative cross-sectional study to examine the link between maternal serum lipids and pre-eclampsia³.

Materials and Methods

This study was conducted at the Jos University Teaching Hospital, North-central, Nigeria. The sampled populations were obtained from the antenatal clinic and antenatal ward. A total of one hundred pregnant women with confirmed singleton gestation were placed into two groups (Mild Pre-eclampsia and Severe preeclampsia). Each of the groups consisted of fifty pregnant women, who were recruited based on non-probability convenient sampling method. The two groups were matched for age in years, parity, gestational age in weeks based on ultrasonography and Body Mass Index in Kg/M². The basis for the diagnosis of Mild pre-eclampsia follows newly identified blood pressure measurement (aided by mercury sphygmomanometer) of minimum 140 mmHg systolic but not up to 160mmHg and at least 90 mmHg but not upto 110mmHg diastolic blood pressure after 20th weeks of gestation, taken in sitting position, done twice, at least 4-6 hours apart. The diagnosis of proteinuria was based on newly identified urine dipstick test of at least 2+, after the 20th week of gestation, with the use of COMBI-URISCREEN reagent strip. A newly identified blood pressure measurement of at least 160 mmHg systolic and 110 mmHg diastolic pressures, alongside newly identified proteinuria of at least 3+, after the 20th week of gestation, was considered

severe Preeclampsia. In order to measure the maternal serum lipids, Five milliliter (5 mL) of fasting blood sample was collected via the ante-cubital vein from the sampled populations, by the use of plain vacuitainers with appropriate biosafety measures, The samples were thereafter centrifuged at 4000 revolutions per minute (rpm) for 10 minutes and each serum sample separated was transferred into a new appropriately labeled sample container (cryovials) and stored at -70°C refrigerator until the time-please state storage duration of analysis for serum lipids. The biochemical analysis was done for total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL) using the appropriate reagent kits for Cobas C – 111® Autoanalyser The Low density

lipoprotein was calculated using the Friedewald's formula. The data obtained was analyzed using Epi-info version 3.5.4 from CDC Atlanta, Georgia. The Mean Value, Standard deviation and their variations were determined. Student t-test was used to test for their mean difference and also to determine statistical significant difference for the continuous data. The level of significance was set at $P < 0.05$.

Ethical Consideration: This study was undertaken after due approval from the ethical and research committee of the Jos University Teaching Hospital (JUTH). Informed consent was duly obtained from all subjects who participated in the study after they were duly counseled about the study.

RESULTS

Results obtained from this study are summarized in three tables below

Table 1: Relationship of Age, BMI and Gestational Age in the studied population----

| Factors | % / Mean(Sd) | | Student t-test | P-Value |
|------------------------------|--------------|------------|----------------|---------------|
| | Mild | Severe | | |
| Age (Years) | 28.90 ±4.1 | 29.10 ±5.9 | 0.003 | 0.99(>0.05) |
| <29yrs | 65.2% | 34.8% | 0.911 | 0.340(>0.05) |
| =29yrs | 51.9% | 48.1% | | |
| Mean BMI(Kg/m ²) | 23.3 ±3.5 | 34.0 ±4.2 | 2.400 | 0.002(<0.05) |
| Mean Gestational Age(Weeks) | 33.31± 3.8 | 33.05± 2.8 | 0.270 | 0.7919(>0.05) |

N values not clear

Table 2: Mean Serum lipids components between mild and severe Pre-eclamptic group

| Lipid components | % / Mean (Std) | | Student t-test | P-Value |
|--|----------------|------------|----------------|---------|
| | Mild | Severe | | |
| Mean Serum levels of (Total Cholesterol) | 4.44±1.0 | 4.69±0.95 | 0.857 | 0.396 |
| Mean Serum Levels of Triglycerides | 1.13 ±0.50 | 2.22±0.92 | 5.406 | 0.00001 |
| Mean Serum Levels of HDLc | 0.83 ±0.31 | 0.74 ±0.26 | 1.12 | 0.27 |
| Mean Calculated Levels of LDLc | 1.89 ±0.39 | 1.78±0.37 | 1.05 | 0.30 |

Table 3: Multiple Linear Regression Model

| Model | Unstandardized Coefficients | | Standardized Coefficients | t-test | P-Value | 95.0% Confidence Interval for B | |
|--------------------------------|-----------------------------|----------------|---------------------------|--------|---------|---------------------------------|-------------|
| | B | Standard Error | Beta | | | Lower Bound | Upper Bound |
| (Constant) | 1.117 | .368 | | 3.033 | .004 | .375 | 1.859 |
| Serum levels Total Cholesterol | .041 | .062 | .080 | .659 | .514 | -.084 | .166 |
| Serum Levels of Triglycerides | .332 | .065 | .591 | 5.071 | 0.0002 | .200 | .464 |
| Serum Levels of HDLc | -.167 | .202 | -.098 | -.826 | .413 | -.575 | .241 |
| Calculated Levels of LDLc | -.150 | .162 | -.116 | -.931 | .357 | -.476 | .175 |

a. Dependent Variable: Severity of preeclampsia

DISCUSSION

This study revealed that age distribution of the studied population was between 28.90 ± 4.1 years and 29.10 ± 5.9 years for those with mild and severe preeclampsia respectively, reflecting a reproductive aged population. The subgroup differ significantly in terms of their Body mass index (BMI) where women with severe preeclampsia had higher mean BMI indicating obesity compared with mild preeclampsia with a normal mean BMI. Elevated serum triglyceride, as seen in this study, is a feature of maternal obesity, metabolic syndrome and long term cardiovascular⁴

Also there was a significant reduction in maternal serum HDL (0.83 ± 0.31 mmol/L versus 0.74 ± 0.26 mmol/L) i.e. Mild preeclampsia and severe preeclampsia respectively, but it was not statistically significant. However, in the severe Preeclampsia subgroup, maternal serum Triglycerides alone was found to be significantly elevated (1.13 ± 0.50 versus 2.22 ± 0.92). Further analysis with multiple linear regression analysis (Table 4) also showed that, maternal serum Triglycerides appeared to be the one of the significant predictor of the severity of preeclampsia in the studied population. Table 4 shows that maternal serum triglycerides contributes more to the model since it has the highest coefficient of 0.332 and also the lead value of 0.591 absolute standardized coefficients.

Our study is at variance with work done by Timalsina S et.al⁵ who reported lipid parameters are poor markers of severity of preeclampsia. This difference in findings may be due to some other factors including dietary and environmental.

Our finding depicting elevated serum triglycerides is similar to the case-control study by Abubakar et.al⁶ from North-eastern Nigeria, Islam NAF et.al⁷ from Bangladesh. However these separate studies did not report relationship between severity

of preeclampsia and maternal serum lipids in the subgroup of preeclampsia but rather focused on association between maternal serum lipids and preeclampsia for which serum triglycerides was included in this association. IA Siddiqui et.al⁸ reported that women, from their study who had preeclampsia had higher triglyceride levels compared with non-pregnant women and other measured lipid component in their study did differ significantly in the two groups. Conversely, K. Rajyalakshmi et.al⁹ found no statistical significant difference in serum lipid concentration between preeclampsia women and normal pregnant women.

Our study is in line with Cassandra N.S et.al³ in a systematic review and meta-analysis who demonstrated that women who develop preeclampsia have elevated levels of Total cholesterol, Non-HDL-c and Triglycerides during all trimesters of pregnancy as well as lower levels of HDL-c during the third trimester. However, it differs with our study in that serum Total cholesterol was not found to be significantly different in the groups and subgroups and Non-HDL-c was not part of the component measured in our study. Hypertriglyceridemia is well documented as an endothelial disruptor in atherosclerosis¹⁰ and is a potential candidate for endothelial dysfunction seen in this disease¹⁰ The findings from our study is also in agreement with studies done by Onuegbu AJ et.al¹¹ and Lima VJ et.al¹²

Based on our findings, maternal serum triglycerides can be adopted as a biochemical tool in the monitoring protocol of pregnant women with preeclampsia on conservative management. The maternal serum Triglycerides can be used along side other biochemical markers such as serum uric acid¹³, creatinine and electrolytes amongst others, to detect worsening pathological process of preeclampsia while carrying out conservative management of

preeclampsia. In a study to assess the level of uric acid level in maternal circulation during normal pregnancy and found that uric acid was significantly higher in pregnant women than in non-pregnant women¹⁴

CONCLUSION

This study has revealed higher levels of maternal serum triglycerides among women with severe preeclampsia compared with those with mild preeclampsia. It is not clear at this point if this finding is from the cause of the preeclampsia or effect of the disease progression. It is therefore noted that elevated serum triglycerides among women with severe preeclampsia can be used to determine worsening maternal condition and hence can serve in antepartum monitoring parameter. This may also guide timing of delivery of the foetus during conservative management of preeclampsia.

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