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Maternal Lipid Profile in Preeclampsia: Case-Control Study

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Preeclampsia has continued to be a challenge especially in the areas of understanding the pathogenesis and prevention or treatment of the disease. Previous reports on the relationship between maternal lipids and preeclampsia have varied as its role in the aetiopathogenesis of pre-eclampsia is not clearly defined. This study aimed at comparing the lipid profile in preeclampsia with that in normotensive pregnancy. It also examined for any relationship between an abnormal profile and severe disease.
Methods: This was a prospective case-control study. It was conducted among pregnant women who presented for routine antenatal care and those seen in the emergency room of the obstetrics unit of a tertiary institution in Lagos, Nigeria. The duration of the study was 6 months as it took place between May 2015 to October 2015. Pregnant women in their second half of pregnancy, diagnosed to have pre-eclampsia and, who gave consent were consecutively recruited as cases and pregnant women with similar age and gestational age, who had normal blood pressure were also selected as controls within the study period. The Maternal lipid profile was assayed using an

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enzyme-based assay kit and analysed according to the manufacturer's instructions. All participants were followed up till delivery.

Results: One hundred and seventy pregnant women in the third trimester of pregnancy participated in this study. They were within 18 – 45 years of age. More of the participants were nulliparous. Eighty-five of them had pre-eclampsia and constituted the study group while 85 were normotensive in the control group. The mean age was similar in both groups (control=29.59 ± 4.50 years versus pre-eclampsia=29.73 ± 5.10 years). The gestational ages at blood sampling of the patients in this study ranged between 27 – 40 weeks. The analysis of data revealed that the level of total cholesterol, triglycerides, low-density lipoprotein and very-low-density lipoprotein was higher in the cases compared with the control. This difference was statistically significant because the calculated P-value was <0.05. The level of high-density lipoprotein was lower in those with pre-eclampsia. Serum cholesterol and low-density lipoprotein were significantly higher (P-value= 0.04) in those with severe disease. A significant positive relationship was observed between mean arterial blood pressure and abnormal levels of lipids.

Conclusion: An abnormal pattern of lipid profile was observed in women with preeclampsia and this was more marked in those with severe disease. A larger multi-centre study will be required to substantiate this finding.

Keywords: Preeclampsia; lipid profile; pregnancy.

1. INTRODUCTION

Pre-eclampsia is a disorder in pregnancy characterised by new-onset hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman. Globally, it complicates 2-8% of all pregnancies [1] and is a major cause of maternal and perinatal morbidity and mortality [1,2].

In Nigeria, it is documented to affect 6% [3] and 11% [4] respectively of all pregnancies. Worldwide, preeclampsia/eclampsia is reported to be responsible for 10%-15% of maternal deaths [1] and continues to be a leading cause of indicated preterm delivery [1,2]. In Nigeria, maternal deaths resulting from the disease is reported to be between 11% and 46.4% [3-5].

The aetiology of preeclampsia is yet to be fully known. It has been proposed "that abnormal placental implantation interacts with additional maternal factors (such as dyslipidaemia, genetic, immune and vascular disorders as well as oxidative stress)" [6-8].

Research findings in cardiovascular diseases suggest that endothelial health is influenced by normal levels of serum lipids, so that significant alterations may cause endothelial dysfunction [9,10] which is a salient feature of pre-eclampsia [11].

Recent studies suggest that altered levels of serum lipids may be associated with an increased risk of preeclampsia, but the findings have, however, been inconsistent [12-15].

A meta-analysis of studies on maternal serum triglyceride levels and pre-eclampsia, suggest that high levels of triglycerides may be a risk factor and/or predictor for pre-eclampsia [16]. In another report, most of the lipids were elevated in all the trimesters of pregnancy except for HDL-C which increased in the 3rd trimester [16]. Whereas, Vandjert et.al. "did not find any significant difference in the level of lipids in their study" [17] others reported variable alteration in concentration in women with pre-eclampsia [18-19].

A meta-analysis of studies on maternal serum triglyceride levels and pre-eclampsia, suggest that high levels of triglycerides may be a risk factor and/or predictor for pre-eclampsia. [16] In another report, most of the lipids were elevated in all the trimesters of pregnancy except for HDL-C which increased in the 3rd trimester [16].

1.1 Rationale of Study

Pre-eclampsia has remained a significant public health challenge especially in developing countries contributing to maternal, fetal and neonatal morbidity and mortality. Maternal mortality ratio of 814 per 100,000 live births in Nigeria [20] remains one of the highest in the world and pre-eclampsia/eclampsia is a major contributor to this alarming statistics. The cause of pre-eclampsia is not fully known. The study of serum lipid abnormality in the pathogenesis of

pre-eclampsia is one of the current research focus in understanding the disease. Research findings have been conflicting. Few of these studies were conducted here in Nigeria [17,18]. Establishing an association between maternal dyslipidaemia and pre-eclampsia may be clinically useful because maternal lipid levels can be readily assayed in the laboratories here and could serve as a cost-effective screening method for identifying women who are at risk of severe disease. This will help in the initiation of appropriate preventive and management options.

Aim of study: To evaluate the serum lipid profile of patients with pre-eclampsia and to determine if there is any difference in lipid profiles compared with that in healthy normotensive pregnant women in Lagos State University Teaching Hospital, Nigeria.

To determine if the serum lipid levels correlate with severity of pre-eclampsia.

2. SUBJECTS AND METHODS

This was a prospective case-control study. It was carried out among patients who presented for routine antenatal care and those seen in the emergency room of the obstetrics unit of the Lagos State University, Teaching Hospital, Lagos, Nigeria. The duration of the study was 6 months as it took place between May 2015 to October 2015. Pregnant women in their second half of pregnancy, diagnosed to have pre-eclampsia and, who gave consent were consecutively recruited as cases and matched for age and gestational age with those with normal blood pressure was controls within the study period. Pregnant women with multiple gestation, chronic hypertension, molar pregnancy, cardiac disease, renal disease, human immunodeficiency virus, liver disease, history of dyslipidaemia or any other medical condition in pregnancy were excluded.

Pre-eclampsia was diagnosed when systolic and/or diastolic blood pressure measured on two occasions about 4-6 hours apart was ≥ 140mmHg and ≥ 90mmHg respectively and the presence of proteinuria of ≥0.3g/dl or ≥1+ on qualitative urine analysis using dipsticks [21]. Severe preeclampsia was defined as the presence of elevated blood pressure ≥160/110 mmHg, proteinuria≥ 5g/24 hours, or the presence of maternal complications like eclampsia, HELLP (haemolysis, elevated liver enzymes and low platelets) syndrome, disseminated intravascular coagulopathy, renal failure or any other end organ damage.

The blood sample was drawn from a superficial vein in each patient and collected into plain sample bottles after an overnight fast. Each sample was allowed to clot and retract. It was then centrifuged at 2500ramps/minute for 5 minutes. The sera were separated into cryovials and stored at -8^{o}c till analysed. Analysis for serum total cholesterol, triglycerides and HDL- C was done using ERBA -5 semi auto analyzer and by an enzymatic process. Serum LDL-C was estimated using Frederickson-Friedewald formula where “LDL-C = TC – (HDL-C+ VLDL-C) and, VLDL-C = 1/5 of TG” [14, 21]. A diagnosis of dyslipidaemia was made if total cholesterol >200mg/dl, low-density cholesterol >100mg/dl, high-density lipoprotein <50mg and triglyceride >150 mg/dl.[22].

Table 1. Socio-demographic of patients

VARIABLES	PRE-ECLAMPSIA N = 85	CONTROL N = 85	P-VALUE
AGE (YEARS)			
MEAN ± SD	29.73 ± 5.10	29.59 ± 4.50	0.0856
RANGE	18 – 45.	18 – 45.	
SOCIAL CLASS			
LOW	47(55.3%)	29 (34.1%)	
MIDDLE	38 (44.7%)	56 (65.9%)	0.0087
UPPER	0	0	
BOOKING STATUS			
BOOKED	37 (43.5%)	70 (82.4%)	0.0000015
UNBOOKED	48 (56.5%)	15 (17.6)%	
PARITY			
0	41 (48.2%)	45 (52.9%)	
1-4	41 (48.2%).	36 (42.4%)	0.7212
5 AND ABOVE	3 (3.5%)	4 (4.7%)	

The sociodemographic information for each patient which includes age, highest educational level, occupation (including husband's), religion, tribe, gestational age and clinical details was collected from case file and entered into a proforma. The socioeconomic status was determined using the method by Olusanya et al. [23]. The analysis of the data generated was done using the statistical package for social sciences (SPSS) version 17.0. Descriptive statistics which include: frequencies and percentages, mean ±standard deviation or median± interquartile range was done depending on the normality of distribution. Continuous variables were compared using the Student's t-test or an analysis of variance depending on whether they were 2 or ≥3 levels and categorical variables compared with the Chi-square test. Scatter plots and Pearson's correlation was plotted to examine for any relationships. Statistical significance was set at a p-value less than 0.05.

3. RESULTS

One hundred and seventy pregnant women in the 2nd half of pregnancy participated in this study. They were within 18 – 45 years of age. Eighty-five of them had pre-eclampsia and constituted the study group while 85 were normotensive in the control group. The mean age was similar in both groups (control=29.59 ± 4.50 years versus pre-eclampsia=29.73 ± 5.10 years). More of the controls (65.9%) were from the middle socio-economic class while slightly more than half (55.3%) of the pre-eclamptics were from the lower socio-economic class. None of the participants was from the upper socio-economic class. The difference in the distribution of tribes and religion between both group were not significant. More than half of the participants were nulliparous in the control group compared to those with preeclampsia (52.9% vs 48.2%), this difference, however, was not significant statistically. The gestational ages at blood sampling of the patients in this study ranged between 27 – 40 weeks. The gestational ages and BMI of the cases (34.09 ± 3.89 weeks; 30.10 ± 1.89 kg/m^2) and those in the control group (34.14 ± 3.53 weeks; 30.23 ± 1.92) were comparable. The mean of the DBP, SBP, and MAP for the cases were 108.00 ± 12.60, 170 ± 19.06, 128.79 ± 13.57 respectively, whereas, for the controls, it was 65.48 ± 9.79, 108.65 ± 10.28, and 79.84 ± 8.45 respectively. The differences observed were statistically significant Table 2.

Analysis of the lipid parameters (Table 3) revealed that the mean serum levels of the lipids were TC (255.2±36.7mg/dl), TG (278.1±62.0mg/dl), HDL-C (54.1±13.2mg/dl), LDL-C (174±39.1mg/dl) and VLDL-C (24.4±5.4mg/dl) respectively in the cases. The corresponding levels in the controls were TC (205.0±22.0.0mg/dl), TG (207.3±31.9mg/dl), HDL-C (64.6±9.7mg/dl), LDL-C (122.6±15.5mg/dl) and VLDL-C (18.2±2.7mg/dl) respectively. From the results, pre-eclampsia is seen to be associated with higher serum levels of all of the lipids studied except HDL-C whose level was lower and the difference was statistically significant with a P-value =0.0001.

The assessment for a possible relationship between the lipid profiles and disease severity revealed, patients with severe pre-eclampsia had statistically significant higher levels of mean TC (268.4±34.4 vs 234.6±30.2mg/dl; p=0.0001) and LDL-C (187.6±28.6 vs 153.5±44.9mg/dl; p=0.0001) than those with mild pre-eclampsia. The levels of TG (279. ±62.0 vs 274.6±31.9mg/dl; p=0.6707) are similar in both groups. However, HDL-C was significantly lower in mild (50.7±12.8mg/dl) compared with severe (56.5+13.1mg/dl) preeclampsia in this study with a P-value of 0.041 (Table 4).

Table 2. Clinical characteristics of the patients

VARIABLES MEAN ± SD	PRE-ECLAMPSIA N = 85	CONTROL N = 85	P-VALUE.
GESTATIONAL AGE (WEEKS)	34.09 ± 3.89	34.14 ± 3.53	0.9343
RANGE	27 – 40.	27 – 40.	
BODY MASS INDEX KG/M^2	30.10 ± 1.89	30.23 ± 1.92	0.5854
MEAN SYSTOLIC BP	170 ± 19.06	108.65 ± 10.28	0.0000
MEAN DIASTOLIC BP	108.00 ± 12.60	65.48 ± 9.79	0.0000
MABP	128.79 ± 13.57	79.84 ± 8.45	0.0000

Table 3. Mean level of lipid parameters in the two groups

LIPID PARAMETERS(MG/DL) MEAN ± SD	PRE-ECLAMPSIA N = 85	CONTROL N = 85	P-VALUE.
TC	255.2 ± 36.7	205.0 ± 22.0	0.0000
TG	278.1 ± 62.0	207.3 ± 31.9	0.0000
HDL-C	54.1 ± 13.2	64.6 ± 9.7	0.0000
LDL-C	174.0± 39.1	122.6 ± 15.5	0.0000
VLDL	24.4± 5.4	18.2± 2.7	0.0000

Table 4. Relationship between mean levels of lipid parameters and severity of pre-eclampsia

LIPID PARAMETERS(MG/DL) MEAN ± SD	SEVERE PRE-ECLAMPSIA N = 52	MILD PRE-ECLAMPSIA N = 33	P-VALUE
TC	268.4 ± 34.4	234.3 ± 30.2	0.0000
TG	279.2 ± 62.0	274.6± 31.9	0.6707
H DL-C	56.5 ± 13.1	50.7 ± 12.8	0.0410
LDL-C	187.6 ± 28.6	153.5 ± 44.9	0.0001
VLDL –C	24.4 ± 5.8	24.0 ± 4.6	0.6707

Table 5. Pearson's correlation examining the association between maternal serum lipids and mean arterial blood pressure

Lipid fractions in (MG/DL)	Pearson's correlation coefficient (R)	P-VALUE
TC	0.669	0.0000
TG	0.593	0.000
HDL-C	0.295	0.000
LDL-C	0.698	0.000
VLDL-C	0.593	0.000

Using Pearson's correlation, the mean arterial blood pressure was observed to rise with increasing maternal serum levels of total cholesterol (r=0.669; p=0.0001), triglycerides (r= 0.593; p=0.0001), low-density lipoprotein (r= 0.698; p=0.0001), and very low-density lipoprotein (r=0.593; p= 0.0001) respectively. However, it was lowered as high-density lipoprotein increased (r=0.295; p=0.0001) Table 5.

4. DISCUSSION

This study examined the serum lipid profile in preeclampsia compared with healthy normotensive pregnant women and a possible association between abnormal lipid profile and severe disease. The participants were drawn from a normal population. A higher number of the women with preeclampsia were nulliparous which is expected as the disease entity is more common in the first pregnancy [4].

In this study, the serum levels of most of the lipids were observed to significantly increase in pregnancy. The increase was marked in women with pre-eclampsia than normotensives. The level of HDL-C in both groups was within the normal limit. In comparison with the control, the level was lower in those with preeclampsia. Similar lipid profile variations in preeclampsia have been reported in other studies [13,14,24,25,26]. A meta-analysis of studies examining lipids in pregnancy documented "increased levels of total cholesterol, triglycerides, low-density lipoprotein and other non-high-density lipoproteins with a significantly reduced level of high-density lipoprotein in the third trimesters in preeclampsia" [27]. These observations were different from that of Olalare et al, [18] who reported no difference.

The women with severe pre-eclampsia had a higher level of total cholesterol and low-density lipoprotein compared with those who had mild preeclampsia in our study. This observation was similar to that reported by Spracklen et al. [28]. An elevated level of total cholesterol and low-density lipoprotein may therefore, be an indicator of worsening disease. Spracklen et al. documented that "high-density lipoprotein was lower in women with severe pre-

eclampsia compared with mild preeclampsia" [28]. We did not observe this difference in our study. We observed a corresponding increase between triglycerides, total cholesterol, low-density lipoprotein and mean arterial blood pressure in preeclampsia.

Pregnancy is associated with insulin resistance and, the reverse transport of cholesterol causes a decrease in HDL-C which may account for the increased total cholesterol in pregnancy [29]. Low-density lipoprotein transports cholesterol to the peripheral tissues and has been implicated in atherosclerosis and cardiovascular disease [30]. Preeclampsia is suggested to result from dysregulation of hepatic lipase and lipoprotein lipase leading to dyslipidaemia. The excessive accretion of lipids within endothelial cells alters the level of prostacyclin which could lead to endothelial dysfunction and oxidative stress, factors implicated as initiators of preeclampsia [31,32]. The altered levels of insulin, lipids and, other factors implicated in the development of the metabolic syndrome have been observed to persist in women who had preeclampsia suggesting a causal relationship between both entities [33].

5. CONCLUSION

Lipid profile abnormality was observed in preeclampsia and was marked in those with severe disease. Screening for dyslipidaemias from the 2nd half of pregnancy may be considered for early identification and management. However, a larger scaled multi-centre study will be needed to further elucidate the association.

6. LIMITATION OF STUDY

The sample size and being an institution-based study are limitations of this study. As a result, findings may not be representative of the larger population and generalizable. The reference values used are not pregnancy-specific and may exaggerate the values of the lipids studied.

CONSENT

The patients were fully briefed on the protocol and written informed consent was obtained before recruitment into the study. This research was done at no added costs to the participants.

ETHICAL APPROVAL

Ethical Approval for this study was obtained from the Research and Ethics Committee of Lagos State University Teaching Hospital, Ikeja. Lagos state (REF.NO:LREC/10/06/505).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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