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Maternal Serum Lipids in Pre-Eclamptic and Normotensive Pregnant Women: A Case-Control Study

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Abstract

Background: Preeclampsia-eclampsia is a major contributor to maternal and fetal, morbidity and mortality especially in low to middle income countries. This hypertensive disorder of pregnancy remains a disease of theories due to its unclear etiology. We evaluated for possible associations between maternal serum lipids and preeclampsia. **Methods**: This was a prospective case-control study that recruited 60 consenting women diagnosed with preeclampsia (cases) and 60 normotensive healthy pregnant women (controls), matched for maternal age and gestational age over an 8-month period (18th June, 2014 to 18th February, 2015) at the Federal Teaching Hospital Ido-Ekiti, Nigeria. Cases and controls were recruited using the non-probability convenience sampling. Fasting venous blood samples were collected in both cases and controls and analyzed for serum total cholesterol (TC), triglycerides (TG), high density lipoproteins (HDL) and low density lipoproteins (LDL) using Randox standard enzymatic methods. Data obtained were analyzed using SPSS version 18 to compare and test for significance using Student t-test, Chi-square, and Pearson's correlation as the appropriate. Tests of association were determined using logistic regression models. The difference was considered significant at $P < 0.05$. **Findings:** The mean serum levels of TC, HDL and LDL were significantly ($p < 0.001$) higher in the pre-eclamptics (6.6 ± 2.9 mmol/L, 2.1 ± 1.0 mmol/L and 3.6 ± 2.6 mmol/L) than in normotensive women (4.5 ± 1.3 mmol/L, 1.5 ± 0.9 mmol/L and 2.2 ± 1.2 mmol/L) respectively. Mean serum level of triglycerides was increased in the pre-eclamptics (2.0 ± 1.0

mmol/L) compared to the controls (1.8 ± 0.6 mmo/L) (p = 0.089). Serum TC, TG and LDL were similar in women with mild preeclampsia when compared with women with severe preeclampsia. Correlation between maternal systolic and diastolic blood pressures and the serum lipids was not significant. Adjusted multivariate logistic regression analysis revealed that total cholesterol (OR = 4.363, 95% CI = 1.410 - 13.506, p = 0.011) and high density lipoproteins (OR = 3.247, 95% CI = 1.086 - 9.709, p = 0.035) are significant independent risk factors for preeclampsia. **Conclusion:** Elevated maternal serum lipids are associated with preeclampsia, however, the widespread lack of uniformity in the patterns of dyslipidemias in pre-eclamptics, across different populations, may suggest that serum lipids will not be a reliable predictor or severity marker of preeclampsia.

Keywords

Pregnancy and Serum Lipids, Serum Lipids and Preeclampsia, Preeclampsia

1. Introduction

Preeclampsia is a multi-systemic disorder that is peculiar to human pregnancy [1]. It is characterized by the occurrence of hypertension and significant proteinuria after the 20th week of gestation in a previously normotensive and non-proteinuric woman [1] [2]. It complicates 5% - 7% of pregnancies [1] [3]. It is one of the leading causes of maternal and perinatal morbidity and mortality [1] [2]. It is a complex disorder characterized by generalized vasospasm, intravascular volume contraction, reduced organ perfusion and activation of coagulation cascade. It precedes the onset of eclampsia in most cases [4] [5].

The aetiology of preeclampsia is still unknown almost a century after it was termed the disease of theories [5] [6]. However, several aspects of its pathology are clearer and can now be related to its clinical manifestation [7] [8].

Some reports have suggested that women likely to develop preeclampsia have marked increase in serum triglycerides, free fatty acids and low density lipoprotein concentration, which are evident as early as 16 - 18 weeks gestation [9] [10]. These low density lipoproteins (LDL) are more susceptible to oxidative modification and it is the generation of oxidative stress and in turn Reactive Oxygen Species (ROS) that is thought to be responsible for the cycle of events, which causes the vascular endothelial damage [10] [11]. In addition, altered lipid metabolism and synthesis have been shown to lead to a decrease in the prostaglandin I_2: Thromboxane A_2 ratio, which plays important contributory roles in the pathogenesis of preeclampsia. Studies among Caucasian women have suggested that maternal predisposition to preeclampsia may be linked with abnormal lipid metabolism [6] [9]. We therefore evaluated for associations between maternal serum lipids and preeclampsia in a black rural Nigerian population, where related studies are currently sparse.

2. Materials and Methods

This was a hospital-based, prospective, case-control study in the Obstetrics and Gynaecology department of the Federal Teaching Hospital Ido-Ekiti, Nigeria, over an 8-month period (18th June, 2014 to 18th February, 2015). Sixty consenting women with singleton pregnancy diagnosed with preeclampsia were recruited as cases and 60 normotensive, matched for maternal age and gestational age were recruited as controls. Both cases and controls were recruited using the non-probability convenience sampling from women receiving care in the study location.

Women with any of the following conditions; hepatic disease, acute or chronic infection, suspected fetal congenital abnormalities, multiple gestation, diabetes mellitus, pre-existing hypertension or other cardiovascular diseases, tthyrotoxicosis, chronic renal disease and women on drugs that could influence serum lipid levels were excluded from the study.

The diagnosis of preeclampsia was made when the blood pressure of the pregnant woman was 140/90 mmHg or more taken twice at least 4 hours apart with proteinuria of 2+ or more on urinalysis, after 20 weeks gestational age in a previously normotensive and non-proteinuric woman. Preeclampsia was classified as mild or severe. Mild preeclampsia was when the systolic blood pressure was ≥140 mmHg but <160 mmHg and diastolic blood pressure was ≥90 mmHg but <110 mmHg. Severe preeclampsia was diagnosed when the systolic blood pressure was ≥160 mmHg and diastolic blood pressure was ≥110 mmHg [1] [8]. Women who had features of HELLP syndrome (Haemolysis, Elevated Liver enzymes, and Low Platelets), oliguria (<400 ml/24 hour), cerebral and visual disturbances, pulmonary oedema, cyanosis, epigastric and right upper quadrant pain were classified as severe preeclampsia [8] [12] [13].

Blood samples were drawn on presentation to the hospital after 8 - 12 hours of fasting and analyzed for serum Total cholesterol (TC), LDL-cholesterol, Triglycerides (TG) and HDL-cholesterol using enzymatic estimation kits for Total Cholesterol, LDL-cholesterol, HDL-cholesterol and Triglycerides manufactured by Randox Laboratories Limited, United Kingdom [14]. The study reference ranges were Total Cholesterol (≤5.2 mmol/L), Triglycerides (0.5 - 1.7 mmol/L), HDL-cholesterol (1.1 - 1.7 mmol/L) and LDL-cholesterol (≤2.3 mmol/L).

Data were obtained and documented with the aid of a semi-structured proforma designed for the study and analyzed using International Business Machines (IBM) statistical package for social science (SPSS) version 18 (New York, USA). Variables were presented in frequency, percentages, means and standard deviation. The mean of two continuous variables were compared using independent Student t-test. Probability value (p-value) less than 0.05 was deemed significant. Pearson correlation coefficient was used to assess correlation between two continuous variables and tests of association were determined using logistic regression models. Ethical approval was obtained from the Health Research and Ethics Committee of the Federal Teaching Hospital Ido-Ekiti.

3. Results

Sixty (60) consenting women with preeclampsia and 60 normotensive healthy pregnant women had their serum total cholesterol, LDL, HDL and triglycerides determined. The mean age of the pre-eclamptic group was 32.2 ± 5.9 years, while that of the normotensive group was 31.0 ± 4.2 years (p = 0.190) (Table 1). Majority (85%) of the women with preeclampsia had some form of formal education while almost all the women (96.7%) in the control group had formal education (p < 0.001) (Table 1). The occupational distribution pattern between the two groups was similar, less than half of the cases (41.7%) and one-fifth of the controls (20%) were unemployed (p = 0.057) (Table 1).

Table 1. Comparison of socio-demographic characteristics of the study population.

Characteristics	Controls (n = 60)	Preeclampsia (n = 60)	χ^2	p-value
Age (years)	*n* (%)	*n* (%)		
≤19	0 (0.0)	2 (3.3)	10.366	**0.024****
20 - 24	5 (8.3)	5 (8.3)		
25 - 29	16 (26.7)	8 (13.3)		
30 - 34	29 (48.3)	22 (36.7)		
≥35	10 (16.7)	23 (38.4)		
Mean ± SD	31.0 ± 4.2	32.2 ± 5.9	−1.319	0.190*
Marital status				
Single	4 (6.7)	13 (21.7)	5.551	**0.018**
Married	56 (93.3)	47 (78.3)		
Ethnicity				
Yoruba	50 (83.3)	42 (70.0)		0.379**
Ibo	7 (11.7)	11 (18.3)		
Hausa	2 (3.3)	5 (8.3)		
Others	1 (1.7)	2 (3.3)		
Education				
None	2 (3.3)	9 (15.0)	17.852	**<0.001****
Primary	1 (1.7)	6 (10.0)		
Secondary	12 (20.0)	22 (36.7)		
Tertiary	45 (75.0)	23 (38.3)		
Occupation				
Civil servants	31 (51.7)	19 (31.7)	7.538	0.057
Traders	11 (18.3)	11 (18.3)		
Self-employed	6 (10.0)	5 (8.3)		
Unemployed	12 (20.0)	25 (41.7)		

χ^2 Chi square statistic; *Student t test; **Fisher's exact test; SD: Standard deviation.

Table 2 shows that the mean systolic and diastolic blood pressure at the time of recruitment was 162.5 ± 17.4 mmHg and 105.7 ± 13.2 mmHg respectively in the women with preeclampsia and 107.1 ± 10.3 mmHg and 66.0 ± 9.6 mmHg respectively in the normotensive controls. There was no statistically significant difference in maternal weight between the preeclamptic cases (72.8 ± 13.0 kg) and normotensive controls (72.5 ± 11.4 kg) (p = 0.914). About two-third (68.3%) of women with preeclampsia were unbooked compared to one-tenth (10%) in the control group (p < 0.001) (Table 2). Almost three-quarters (71.7%) of the pre-eclamptic women were primigravidae compared to less than one-quarter (23.3%) of the controls (p < 0.001). The mean parity for the case and control group was 0.5 ± 1.0 and 1.3 ± 1.1 respectively (p < 0.001) (Table 2).

The mean serum total cholesterol, HDL and LDL in preeclamptics (6.6 ± 2.9 mmol/L, 2.1 ± 1.0 mmol/L and 3.6 ± 2.6 mmol/L respectively) were significantly higher than in controls (4.5 ± 1.3 mmol/L, 1.5 ± 0.9 mmol/L and 2.2 ± 1.2 mmol/L respectively) (p < 0.001) (Table 3). Mean serum level of triglycerides was higher in the preeclamptic group (2.0 ± 1.0 mmol/L) than in controls (1.8 ± 0.6 mmo/L) (p = 0.089) (Table 3). Serum HDL was lower in women with severe preeclampsia (1.8 ± 0.4 mmol/L) than in women with mild preeclampsia (2.2 ± 1.0 mmol/L) (p = 0.047) (Table 4).

Table 2. Clinical and obstetric characteristics of the women.

Variables	Controls (n = 60)	Preeclampsia (n = 60)	T	p-value
Mean SBP (mmHg)	107.1 ± 10.3	162.5 ± 17.4	−21.172	**<0.001**
Mean DBP (mmHg)	66.0 ± 9.6	105.7 ± 13.2	−18.863	**<0.001**
Proteinuria				
Yes	0 (0.0)	60 (100.0)		**<0.001***
No	60 (100.0)	0 (0.0)		
Mean Weight (Kg)	72.5 ± 11.4	72.8 ± 13.0	−0.108	0.914
Gestational Age (wks)				
<28	5 (8.3)	1 (1.7)		
28 - 36	26 (43.3)	31 (51.7)		0.217*
>36	29 (48.4)	28 (46.7)		
Mean GA (wks)	35.3 ± 4.2	35.3 ± 3.8	−0.068	0.946
Booking status *n* (%)				
Booked	54 (90.0)	19 (31.7)	42.845	**<0.001****
Unbooked	6 (10.0)	41 (68.3)		
Parity *n* (%)				
Nulliparous	14 (23.3)	43 (71.7)		**<0.001***
1 - 4	45 (75.0)	13 (21.7)		
5 and above	1 (1.7)	4 (6.6)		
Mean parity	1.3 ± 1.1	0.5 ± 1.0	4.102	**<0.001**

*Fisher's exact test; **Chi-square test; GA: Gestational age; wks: weeks.

Table 3. Comparison of serum lipid in pre-eclamptic and normotensive women.

Serum Lipids	Controls	Preeclampsia	t	p-value
	(n = 60)	(n = 60)		
TC (mmol/L)	4.5 ± 1.3	6.6 ± 2.9	−5.026	**<0.001**
TG (mmol/L)	1.8 ± 0.6	2.0 ± 1.0	−1.717	0.089
HDL (mmol/L)	1.5 ± 0.9	2.1 ± 1.0	−3.862	**<0.001**
LDL (mmol/L)	2.2 ± 1.2	3.6 ± 2.6	−3.611	**<0.001**

t: student t-test; TC: Total Cholesterol; TG: Triglycerides; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein.

Table 4. Comparison of serum lipid among mild and severe pre-eclamptic women.

Serum Lipids	Mild	Severe	T	p-value
	(n = 30)	(n = 30)		
TC (mmol/L)	6.4 ± 3.5	6.8 ± 2.2	−0.625	0.534
TG (mmol/L)	1.8 ± 0.5	2.3 ± 1.4	−1.642	0.106
HDL (mmol/L)	2.2 ± 1.0	1.8 ± 0.4	2.034	**0.047**
LDL (mmol/L)	3.4 ± 3.0	3.8 ± 2.1	−0.603	0.549

t: student t-test; TC: Total Cholesterol; TG: Triglycerides; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein.

Correlation between all serum lipid values and both systolic and diastolic blood pressure in preeclamptic and normotensive women were poor and non-significant (Table 5). Association between elevated individual lipid values and preeclampsia were evaluated by using univariate unadjusted and multivariate adjusted (adjusted for confounders; age, education, parity, booking status and marital status) logistic regression analysis as seen in Table 6. Table 7 shows association between elevated serum lipids and severe preeclampsia.

4. Discussion

In this study, we observed significant increases in the serum total cholesterol, high density lipoproteins and low density lipoproteins in women with preeclampsia compared to normotensive pregnant women (Table 3). While the mean serum triglycerides level in preeclamptics was higher than in normotensive pregnant women, this was not statistically significant. Singh *et al.* in a related work in India similarly found that women who developed preeclampsia had increased levels of total cholesterol, triglyceride, HDL and LDL concentrations as compared with pregnant women who remained normotensive [15]. Alahakoon *et al.* also demonstrated that maternal TG levels are increased in preeclampsia [16]. Some other studies have demonstrated that serum TG and free fatty acid concentrations increased approximately twofold in women with preeclampsia relative to uncomplicated pregnancies with no effect on total cholesterol, HDL,

Table 5. Correlation between Serum Lipid and Blood pressure in cases and controls.

Variables	Controls		Preeclampsia	
	r	P-value	R	p-value
SBP vs.				
TC	−0.081	0.537	0.028	0.834
TG	−0.003	0.983	−0.010	0.937
HDL	0.003	0.981	−0.001	0.994
LDL	−0.094	0.477	0.124	0.344
DBP vs.				
TC	−0.070	0.595	0.076	0.565
TG	0.058	0.661	0.101	0.442
HDL	−0.119	0.364	−0.091	0.489
LDL	0.002	0.989	0.050	0.705

r: Pearson correlation coefficient.

Table 6. Logistic regression showing association between preeclampsia and increased maternal serum lipids.

Variables	OR (95% C.I.)	P value	aOR (95% C.I.)	p value
TC	4.369 (2.025 - 9.424)	**<0.001**	4.363 (1.410 - 13.506)	**0.011**
TG	1.397 (0.681 - 2.865)	0.362	2.142 (0.715 - 6.419)	0.174
HDL	2.413 (1.159 - 5.023)	**0.019**	3.247 (1.086 - 9.709)	**0.035**
LDL	2.591 (1.240 - 5.412)	**0.011**	2.735 (0.903 - 8.280)	0.075

OR: odds ratio; C.I.: confidence interval; aOR: adjusted odds ratio (age, education, parity, booking status and marital status); TC: Total Cholesterol; TG: Triglycerides; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein.

Table 7. Logistic regression showing association between severity of pre-eclampsia and increased maternal serum lipid.

Variables	OR (95% C.I.)	P value	aOR (95% C.I.)	p value
TC	3.286 (1.085 - 9.952)	**0.035**	4.033 (0.994 - 16.373)	0.051
TG	0.874 (0.316 - 2.418)	0.795	0.683 (0.208 - 2.243)	0.530
HDL	0.654 (0.229 - 1.864)	0.427	0.599 (0.179 - 2.002)	0.405
LDL	2.406 (0.816 - 7.095)	0.111	2.072 (0.582 - 7.378)	0.261

OR: odds ratio; C.I.: confidence interval; aOR: adjusted odds ratio (age, education, parity, booking status and marital status) TC: Total Cholesterol; TG: Triglycerides; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein.

and LDL [17] [18]. This is unlike our observation in this study and the reasons for these differences are unclear but may be attributable to racial, dietary and environmental differences.

The values of all four serum lipids in women with severe preeclampsia were

higher when compared to the normotensive women and similarly, so when compared with women with mild preeclampsia except for HDL which was lower in women with severe preeclampsia than in women with mild preeclampsia (**Table 3** and **Table 4**). This was similar to other studies which reported that; high serum total cholesterol, triglycerides, low density lipoproteins and reduced serum high density lipoprotein were associated with severe preeclampsia [19] [20]. However, some authors have reported no significant difference in serum lipid profile between normal, mild, and severe pre-eclamptic women [10]. Eman *et al.*, also reported significant increase in only triglycerides with no change in other serum lipids [21].

We found positive but negligible and insignificant correlation between serum lipids and blood pressure in both the preeclamptic and normotensive groups (**Table 5**). This was similar to a study done in Ibadan, Nigeria [9].

The lipid profile and associated preeclampsia risk and risk of severe preeclampsia) were evaluated by using univariate unadjusted and multivariate adjusted (adjusted for age, education, parity, booking status and marital status) logistic regression analysis (**Table 6** and **Table 7**). Following multivariate adjusted regression analysis, only serum total cholesterol and HDL were independently associated with preeclampsia (**Table 6**) however, none of the serum lipids was independently associated with developing severe preeclampsia (**Table 7**). This finding agreed with studies done in Ibadan and Indian hospitals [9] [15].

5. Conclusion

We therefore conclude that despite possible associations of elevated serum lipid values and preeclampsia, the widespread lack of uniformity in the patterns of dyslipidemias in preeclamptics, across different populations suggests that serum lipids may not be a reliable predictor or severity marker of preeclampsia. However, the finding on Triglyceride in this study will need further research.

Conflicts of Interest

The authors report no conflict of interest.

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