Original Article

Lipid Profile and High Maternal Body Mass Index is Associated with Preeclampsia: A Case-Control Study of the Cape Coast Metropolis

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Abstract

Background: Preeclampsia is a leading cause of maternal mortality worldwide and a serious health problem that affects the majority of women. **Aim:** We investigated the association between lipid profile and maternal obesity among preeclamptic women in the Cape Coast Metropolis. **Subject and Methods:** This case–control study involved 60 preeclamptics and 50 healthy pregnant controls matched for age and gestational weeks consecutively recruited from two major hospitals in the Cape Coast Metropolis. Blood samples were collected after overnight fasting and enzymatic spectrophotometric tests used to estimate lipid concentrations. The independent samples *t*-test, Chi-square, and Pearson's correlation were used in the analysis of data gathered. **Results:** Serum triglyceride (TG) ($P = 0.04$), very low density lipoprotein (VLDL) ($P = 0.02$), TC ($P = 0.01$) and low density lipoprotein (LDL) ($P = 0.03$) levels were higher in preeclamptic participants than in the controls. High density lipoprotein concentration showed no significant variation between the two groups ($P = 0.83$). Preeclamptic women were more obese ($P = 0.07$). High body mass index (OR = 1.501; CI = 0.926-2.106, $P = 0.01$), high TG level (OR = 5.026; CI = 0.794-31.818, $P = 0.01$), were associated with preeclampsia. **Conclusion:** Lipid abnormalities, mostly elevated levels of TG, TC, LDL, and VLDL are present in preeclamptics. High TG levels and maternal obesity are associated with preeclampsia among pregnant women in the Cape Coast Metropolis.

Keywords: Body mass index, Dyslipidemia, High blood pressure, Pre-eclampsia, Proteinuria

Introduction

Preeclampsia is a hypertensive disorder of pregnancy whose etiology though ill-understood has been linked with the stimulation of the regulatory systems of inflammation and endothelial function beyond tolerable physiological limits in normal pregnancy. This condition still remains a leading cause of maternal mortality worldwide and a serious health problem that affects the majority of women in the presence of numerous preventive and management strategies.[1] Across the globe, the incidence rate of preeclampsia currently stands at 2-10%.[2] The incidence rate in Ghana is currently pegged around 7%.[3,4]

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The etiology of preeclampsia still remains unknown with several theories trying to identify the exact cause. However, the following theories on the pathogenesis of preeclampsia: Placental ischemia, genetics, immune maladaptation, and oxidative stress hypotheses have received worldwide acclaim.[5] The oxidative stress theory seems to be the most popular among the theories and has been linked with the lipid abnormalities and vascular dysfunction seen in preeclampsia. Consequently, several studies have linked dyslipidemia, characterized by abnormal levels of high density lipoprotein (HDL), low density lipoprotein (LDL), TC, triglycerides (TGs) and very low density lipoprotein (VLDL), with an increased risk of preeclampsia.[6-8] Substantial variations have been identified in the lipid parameters of preeclamptics compared with normal pregnant women. These variations make preeclamptics more vulnerable to lipoprotein oxidation a major etiology of this condition. Furthermore, abnormalities in lipoprotein metabolism lead to cardiovascular consequences and proteinuria, a predictive marker of preeclampsia.[9] These arguments emphasize the

important role played by dyslipidemia in the pathogenesis of preeclampsia and subsequently eclampsia. However, there is a paucity of data on the lipid levels of preeclamptics in Ghana as earlier studies conducted by Turpin *et al.*, (2008) focused on pregnancy induced hypertension (PIH). The aim of this study is to determine the lipid profile and identify the association between the lipid levels and maternal body mass index (BMI) of preeclamptic women in the Cape Coast Metropolis.

Subjects and Methods

Study design/study site

This case-control study was carried out from January to April 2013, at the maternity wards of the Central Regional Hospital and the University of Cape Coast Hospital in the Cape Coast Metropolis of the Central Region of Ghana. Cape Coast covers a total land mass of 9,826 km^2 (2223.9843 acres) with an estimated population of 1,805,488 (population census of Ghana, 2010).

Study population

A total of 110 pregnant participants comprising 60 preeclamptics and 50 healthy normotensive controls matched for age and gestational age were recruited using a consecutive sampling method. A standard pretested questionnaire was used to obtain information on demographic data, family history of hypertension, parity, and gravidity.

Inclusion and exclusion criteria

Participants with gestational age 20 weeks or more, with elevated blood pressure (≥140/90 mmHg) and dipstick proteinuria (>++) were recruited as subjects. Healthy pregnant women, of similar ages as the cases receiving antenatal care at the maternity units of the hospitals were recruited as controls. Women with other hypertensive disorders of pregnancy such as eclampsia, and other conditions such as diabetes, chronic hypertension, autoimmune disease or renal disease were excluded.

Ethical consent

Ethical approval was obtained from the Institutional Review Board of the University of Cape Coast (IRB/UCC), and the Institutional Ethics Committees of the hospitals. Informed consent was also obtained from all participants before enrollment into the study.

Anthropometric measurements

Patients were made to stand without their sandals, bags or anything of significant weight on the weighing scale (Hospibrand ZT-120, Huaiyin medical instruments Co. Ltd, China) and against the meter rule (Huanan measuring tape). The weight was read to the nearest 0.1 kg and recorded. The value for the height was recorded to the nearest 0.1 cm and then converted to meters. The BMI was calculated using formula (weight/height squared) and expressed in kg/m^2.

Blood pressure measurement

Trained personnel used a mercury sphygmomanometer (Accoson, England) and a stethoscope to measure the blood pressure of participants in accordance with recommendations of the American Heart Association.[10] The procedure was repeated for each patient between 5 and 10 min. Mean values of duplicate measurements were recorded as the blood pressure.

Urine collection and determination of proteinuria

Participants provided 10-20 ml freshly voided early morning urine in clean, wide mouth and leak proof containers. Semi quantitative proteinuria was immediately assessed using dipstick (CYBOW™ DFI Co. Ltd., Gimhae-City, Republic of Korea). Proteinuria was defined as the presence of urinary protein in concentrations more than 2+ on urine dipstick.

Blood sample

A volume of 5 ml of venous blood samples was collected from participants after an overnight fast (8-12 h) and immediately transferred into vacutainer plain tubes. The clotted sample was centrifuged at 500 g for 5 min and the serum stored at -80°C in cryovials until assayed.

Biochemical analysis

Serum TG, total cholesterol (TC), and HDL-C levels were estimated by enzymatic techniques with Fortress biochemistry kits (Unit 2C Antrim Technology Park, Antrim, BT41 1QS, UK) on Labmate 5i semi auto biochemistry analyzer (Labmate (Asia) Pvt. Ltd). Serum VLDL, LDL-C levels (mmol/l) was calculated using the Friedewald's formula: [11]

Statistical analysis

Independent *t*-test was used to compare mean scores between preeclamptics and controls. Chi-square was used to test the association between categorical outcome variables. Correlations between proteinuria and both clinical and biochemical parameters were made using Pearson's correlation coefficient test. The odds ratio of the association between preeclampsia and BMI were performed with multivariate logistic regression. $P < 0.05$ were considered as statistically significant. Data were analyzed with Statistical Package for Social Sciences (SPSS version 16 SPSS Inc. Chicago, USA).

Results

Sociodemographic and clinical characteristics of study participants are shown in Table 1. Women with preeclampsia had significantly higher BMI compared with the controls ($P = 0.01$). Obesity was associated with preeclampsia as preeclamptic women were more obese (30.0%; 18/60) than controls (4%; 8/50), Mean parity ($P = 0.27$) and age ($P = 0.26$) were not significantly different in preeclamptics compared with healthy pregnant controls.

Table 2 summarizes the clinical and biochemical characteristics of the participants. The mean levels of TG, VLDL, LDL-C, and TC were significantly higher in preeclamptic women than in normotensive controls ($P = 0.04$; 0.02; 0.03; <0.01). Though mean HDL-C was higher in controls than in preeclamptic women the differences were of no statistical significance ($P = 0.83$).

Correlation of demographic, clinical, and biochemical parameters of participants are shown in Table 3. Proteinuria positively correlated with SBP ($r = 0.569$, $P < 0.01$), DBP ($r = 0.429$, $P < 0.01$), LDL ($r = 0.377$, $P < 0.01$) and TC ($r = 0.409$, $P < 0.01$). A similar relationship was observed between DBP and TC ($r = 0.369$, $P < 0.01$), BMI and SBP ($r = 0.259$, $P = 0.02$), BMI and DBP ($r = 0.234$ $P = 0.04$). SBP was significant ($P < 0.01$; 0.02; 0.01) and positively associated with DBP, LDL, and TC.

Multivariate logistic regression of factors associated with preeclampsia is shown in Table 4. High BMI odds ratio (OR = 1.501; CI = 0.926-2.106, $P = 0.01$) and high TG level (OR = 5.026; CI = 0.794-31.818, $P = 0.01$) were significantly associated with the presence of preeclampsia. However, parity ($P = 0.41$) and TC ($P = 1.00$) and were not significantly associated with preeclampsia among our participants.

Table 1: Sociodemographic and clinical characteristic of study subjects

Variable	*n* (%)		*P* value
	Preeclamptics (*n*=60)	Control (*n*=50)	
Age, mean (SD)	29.3 (5.2)	28.0 (5.2)	0.26
Age range (years)			
<20	6 (10.0)	5 (10.0)	0.27
21-25	9 (15.0)	15 (30.0)	
26-30	25 (41.7)	15 (30.0)	
31-35	10 (16.7)	10 (20.0)	
36-40	10 (16.7)	5 (10.0)	
BMI (kg/m²) mean (SD)	29.4 (2.8)	27.0 (2.1)	0.01
BMI *n* (%)			
<18.5 (underweight)	0 (0.0)	0 (0.0)	0.02
18.5-24.9	2 (6.7)	35 (70.0)	
25-29.9	40 (70.0)	11 (22.0)	
>30	18 (30.0)	4 (8.0)	
Parity mean (SD)	2.0 (1.4)	1.6 (1.3)	0.27
Gravida			
Primigavida	43 (90.3)	47 (94.0)	0.11
Multigravida	17 (9.7)	3 (6.0)	

BMI: Body mass index, SD: Standard deviation

Table 2: Clinical and biochemical characteristic of the participants

Variables	Preeclamptic (*n*=60)	Controls (*n*=50)	*P* value
Lipid profile (mmol/l)			
TG	5.1 (1.6)	2.2 (1.6)	0.04
TC	7.6 (2.2)	3.0 (1.8)	<0.01
HDL-C	2.4 (5.9)	2.6 (1.7)	0.83
LDL-C	3.6 (1.9)	2.1 (1.4)	0.03
VLDL	2.41 (1.0)	1.0 (1.0)	0.02

TG: Triglycerides, TC: Total cholesterol, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein-cholesterol, VLDL: Very low density lipoprotein

Discussion

We assessed the association between lipid profile and maternal BMI among preeclamptic women in the Cape Coast Metropolis. Our results showed that serum lipid levels (TG, TC, LDL, and VLDL) were higher among our preeclamptic subjects; and hypertriglyceridemia and high BMI were independently associated with preeclampsia.

Increased obesity among preeclamptic women has been related to implications for prenatal care and supervision of the delivery. Participants with preeclampsia were more obese than the healthy controls [Table 1] in agreement with the finding of Sharami *et al.*,[12] who alluded that women with preeclampsia had higher BMI than controls. The pathophysiological mechanism behind the increased BMI in preeclampsia is not fully understood though increased insulin resistance and a state of inflammation associated with obesity are likely important contributing factors.[13]

Several studies have identified the crucial role played by abnormal lipid at different stages of pregnancy in the pathogenesis of preeclampsia.[6,7,14] In this study, we observed elevated levels of the lipid parameters (TC, TG VLDL, and LDL) with reduced levels of HDL in the preeclamptic participants compared with the controls [Table 2]. The serum concentration of TC was significantly increased in the preeclamptics compared with the normal pregnant women [Table 2]. This is in conformity with the results of earlier studies.[5,15]

Furthermore, our preeclamptics had high levels of TG, which corroborates the reports of Gratacós *et al.*,[9] and Evrüke *et al.*,[16] but contradicts the observations made by Turpin *et al.*,[3] among Ghanaian women with pregnancy induced hypertension. Hypertriglyceridemia in preeclampsia have been attributed to insulin resistance due to obesity, hyperestrogenemia and reduced lipoprotein lipase activity in pregnancy.[17,18] Hypertriglyceridemia also leads to increased serum levels of VLDL as observed in this study [Table 2] and in earlier studies.[19,20] VLDL transports TG in peripheral blood thus the resultant high levels of VLDL in hypertriglyceridemia.

Variations in the serum lipid concentrations have been attributed to hormonal changes that occur during pregnancy. Serum levels of LDL were significantly elevated in the preeclamptic women compared to normal pregnant controls [Table 2] in agreement with the works of Gratacós *et al.*,[9] and Wakatsuki *et al.*,[14] The concentration of HDL however did not differ significantly

Table 3: Correlation of demographic, clinical, and biochemical parameters of participants

Variable	BMI	SBP	DBP	Parity	LDL	HDL	TC	TG	VLDL	PRT
BMI										
R	1	0.259*	0.234*	−0.009	0.149	−0.002	0.158	0.159	0.158	0.105
P value		0.02	0.04	0.94	0.18	0.99	0.16	0.16	0.16	0.35
SBP										
R		1	0.879**	0.044	0.255*	0.077	0.283*	−0.049	−0.049	0.569**
P value			<0.01	0.70	0.02	0.49	0.01	0.66	0.66	<0.01
DBP										
R			1	0.048	0.222*	0.028	0.369**	−0.044	−0.044	0.429**
P value				0.67	0.05	0.81	<0.01	0.70	0.70	<0.01
Parity										
R				1	−0.067	0.152	−0.179	0.054	0.055	−0.020
P value					0.55	0.18	0.11	0.63	0.63	0.86
LDL										
R					1	−0.243*	0.624**	0.140	0.140	0.377**
P value						0.03	<0.01	0.21	0.21	<0.01
HDL										
R						1	−0.094	−0.057	−0.057	−0.574
P value							0.40	0.61	0.61	0.01
TC										
R							1	0.018	0.018	0.409**
P value								0.87	0.83	<0.01
TG										
R								1	0.999**	0.049
P value									<0.01	0.94
VLDL										
R									1	0.049
P value										0.94
PRT										
R										1
P value										

*Correlation=Statistically significant at $P<0.05$, **Correlation=Statistically significant at $P<0.01$, *r*=Correlation coefficient. PRT: Proteinuria, BMI: Body mass index, TC: Total cholesterol, TG: Triglycerides, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, VLDL: Very low density lipoprotein

in the preeclamptics compared to the controls [Table 2]. This finding contradicts the high levels observed among PIH women in Kumasi, Ghana by Turpin *et al.*,[3] and the low level recorded by Islam *et al.*,[21] but agrees with the works of Wakatsuki *et al.*,[14] and Lima *et al.*,[22] who observed no changes in HDL-C levels among preeclamptic women compared with normal controls. The discrepancies recorded in the levels of HDL-C among our participants compared to earlier studies could be premised on the fact that whereas Turpin *et al*. studied women with PIH, Islam *et al*., included both preeclamptics and eclamptics in his case control study.

The cause of the increased levels of LDL recorded among our participants remains unclear as no correlation existed between maternal BMI and LDL-C [Table 2]. However, studies conducted by Salameh and Mastrogiannis,[23] have associated increased LDL-C levels to elevated estrogen and progesterone levels in preeclampsia.

Our findings from correlation studies [Table 3] confirmed suggestions that LDL, TC, and HDL may be involved in the endothelial damage associated with the pathogenesis of preeclampsia. Endothelial dysfunction, mostly associated with oxidation of LDL, leads to the formation of glomerular lesions and subsequently proteinuria, which is associated with preeclampsia as well as give an indication of its severity.

Obesity and abnormal lipid levels, especially TG contribute to the development of preeclampsia, which is characterized by proteinuria and high blood pressure, through endothelial dysfunction.[22] When we controlled for age and other confounders through multivariate logistic regression analysis the preeclamptic participants were obese (OR = 1.501; CI = 0.926–2.106; $P = 0.01$) and had hypertriglyceridemia (OR = 5.026; CI = 0.794–31.818; $P = <0.01$) [Table 4]. The risk posed by elevated TG levels in the development of preeclampsia as reported in this study confirms earlier evidence in cohort studies which indicated that the risk of preeclampsia was four times higher in women with elevated levels of TG, than in women with normal TG.[24] It also reaffirmed the argument that maternal obesity is independently associated with the development of placental endothelial dysfunction and ultimately preeclampsia.[12]

The variation in study design coupled with the small sample employed could explain the insignificant differences in

Table 4: Multivariate logistic regression of factors associated with preeclampsia

Variables	Regression coefficient (β)	OR (95% CI)	*P* value
High BMI	0.334	1.501 (0.926-2.106)	0.01
Parity	0.267	1.306 (0.691-2.469)	0.41
High TG	1.615	5.026 (0.794-31.818)	0.01
TC	21.202	0 (0.00-0.00)	1.00

OR: Odd ratio, TC: Total cholesterol, TG: Triglycerides, BMI: Body mass index, CI: Confidence interval

the parity of the cases compared to the controls. Second, the single determination of lipids as employed in this study instead of serial measurements in the course of the pregnancy as employed in longitudinal studies may lead to misleading data.

Conclusion

Lipid abnormalities mostly elevated levels of TG, TC, LDL, and VLDL are present in preeclamptics. The high TG levels and BMI are associated with preeclampsia during pregnancy. Thus, it is incumbent on health caregivers to ensure that women of childbearing age adopt healthy lifestyles so as to control their weight and lipid levels, especially TGs to reduce their risk of developing preeclampsia.

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