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Lipid ratios improve early detection of atherosclerotic cardiovascular disease in women with hypertensive disorders in pregnancy

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Abstract

In a normal healthy pregnancy, increased lipid profiles help to encourage fetal development, but in hypertensive disorders in pregnancy, these changes in lipid profiles are amplified, which may predispose these women to atherosclerotic cardiovascular disease. The study's aim was to determine the alteration in lipid profile levels of women with hypertensive disorders in pregnancy and also calculate their atherogenic risk ratios, with the view to improving the predictive capacity of the lipid assay for the risk of arteriosclerosis and cardiovascular incidence. This study enlisted 190 participants, which included 124 pregnant women with preeclampsia, 30 pregnant women with pregnancy-induced hypertension, and 36 pregnant women with normal blood pressure who served as controls. Lipid profile was determined via the enzymatic method from blood samples obtained from the participants. When compared to normotensive control study participants, patients with hypertensive disorders in pregnancy had a slight increase in total cholesterol and LDL cholesterol, as well as a substantial difference in triglyceride levels. Despite minor increases in total and LDL cholesterol levels, the case group's mean atherogenic index plasma, atherogenic coefficient, and Castelli risk index I and II were all higher than the control group's. Individual lipid parameter measurements were found to be ineffective in evaluating the relative contribution of lipids to cardiovascular risk in pregnant patients with hypertensive disorders. Lipid ratios, also known as atherogenic indices, were found to be more effective in assessing the relative contribution of lipids to cardiovascular risk.

Keywords: dyslipidemia, atherogenic indices, hypertensive disorders in pregnancy, preeclampsia, lipid profile

1. Introduction

Hypertensive disorders in pregnancy (HDP) represent a group of conditions that are related to high blood pressure while pregnant. Preeclampsia/eclampsia, gestational hypertension without proteinuria, chronic hypertension, and preeclampsia superimposed on chronic hypertension all fall under the HDP umbrella (1). They are characterized by hypertension in pregnancy, regardless of gestational age, with or without proteinuria, and/or convulsions. It is a leading cause of maternal and feto-maternal morbidity and mortality, particularly in developing countries (1).

Globally, 2.73% of women suffer from HDP while the incidence of chronic hypertension, preeclampsia, and eclampsia are 0.29%, 2.16% and 0.28%, respectively (2). Hypertensive disorders in pregnancy are found to be more common in Africa, affecting one out of every ten women (3). In Nigeria, it is estimated that 5-10% of pregnancies are complicated by hypertensive disorders in pregnancy (HDP), which leads to more antenatal admissions than any other condition (4-6).

In healthy normotensive pregnancy, there is an increase in lipid production which helps to promote fetal growth. Studies have shown that these changes in lipid profile are amplified in hypertensive disorders in pregnancy and may predispose these women to atherosclerotic cardiovascular disease (7-9). The dyslipidemia trend seen in preeclampsia and gestational hypertension may also predispose these women to cardiovascular disease in the future (7, 10, 11).

The study's aim was to determine the alteration in lipid profile levels of women with hypertensive disorders in pregnancy and also calculate their atherogenic risk ratios, with the view to improving the predictive capacity of the lipid assay for the risk of arteriosclerosis and cardiovascular incidence.

2. Participants and Methods

A total of 190 people took part in this study. Participants' blood pressure was measured in the sitting position with a mercury

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sphygmomanometer after 10 minutes of rest.

2.1. Study Population

Pregnant normotensive women served as a control group in the study. The study also included women of reproductive age (18-45 years) who were currently pregnant and had been diagnosed with pregnancy-induced hypertension and preeclampsia. The last menstrual cycle, pregnancy test strip, and obstetrics scan results were used to determine pregnancy which was then divided into trimesters. The second trimester covered from fourteen to twenty-six weeks, and the third trimester from twenty-seven weeks and more. Preeclampsia was defined as having blood pressure of 140/90 mmHg or higher on at least two occasions separated by six hours and accompanied by significant proteinuria (300 mm/l or 500 mm/24 hrs) in the absence of a urinary tract infection in a previously normotensive woman, whereas pregnancy induced hypertension was defined as having blood pressure of 140/90 mmHg or higher on at least two occasions separated by six hours and in the absence of proteinuria (12).

Women below the ages of 18 and above the ages of 45 were excluded from the study. Women in the reproductive age group (18 to 45 years) who were not pregnant were also excluded. Also excluded from the study were women with a history of chronic hypertension, diabetes, chronic renal failure, or congestive heart failure, as well as those who met the inclusion criteria but declined to give consent.

2.2. Methodology

A venipuncture was used to collect approximately 2 mL of blood into a simple tube. Before being centrifuged for 15 minutes at 3000 rpm, the entire blood was able to clot and retract. The serum was extracted into 5ml plain tubes with a Pasteur pipette and stored at -20ºC before biochemical analysis. The lipid analysis was performed using an enzymatic method (13) with Randox Laboratory Limited reagents and the standard operating assay technique.

The blood lipid indexes were calculated using the following equations;

Friedewald equation for LDL Chol. = TC – (TG/5) – HDL Chol. (mg/dL)

Atherogenic index of plasma, AIP = Log TG / HDLChol.

Atherogenic coefficient, AC = Non HDL Chol / HDL Chol.

Non-HDL cholesterol, NHDL = Total Chol – HDL Chol

Very low-density lipoprotein, VLDL = trıglycerıdes / 5

Castelli Risk Index I, (CRI I) = TC / HDL Chol.

Castelli Risk Index II, (CRI II) = LDLC / HDLC

2.3. Ethical Clearance

This was obtained from Edo State Hospitals Management Board, Nigeria, with reference number A.723/56 dated September 16, 2014.

2.4. Statistical Analyses

The data obtained in the study were statistically analyzed using SPSS® version-21. The results were presented using percentages and the mean of repeated data. Correspondence studies were used to demonstrate a link between certain parameters and the participants' lipid status.

3. Results

Majority of the participants in the preeclampsia group was 31 – 35 yrs (44%), compared to 42% in the normotensive group and 20% in the negative control group (Figure 1). Demographic data of respondents as presented on Table 1 showed that majority of the participants were pre-eclamptic in their first marriage (74.2%). Similarly, in pregnancy-induced hypertension (PIH) (100%) and the normotensive group (91.7%), participants were majorly in their first marriage.

Table 2 shows results of lipid profiles of respondents presented on the basis of trimesters. Total cholesterol in the preeclamptic group was higher during the third trimester (211. 13 mg/dl) than in the second trimester (205.76 mg/dl). Similarly, triglyceride levels were lower during the second than at the 3rd trimester. Although significant differences in total cholesterol levels during the third trimester showed differences in concentration among the various study groups ($p>0.05$), no observable differences were recorded. Differences in HDL-cholesterol were minimal irrespective of trimester.

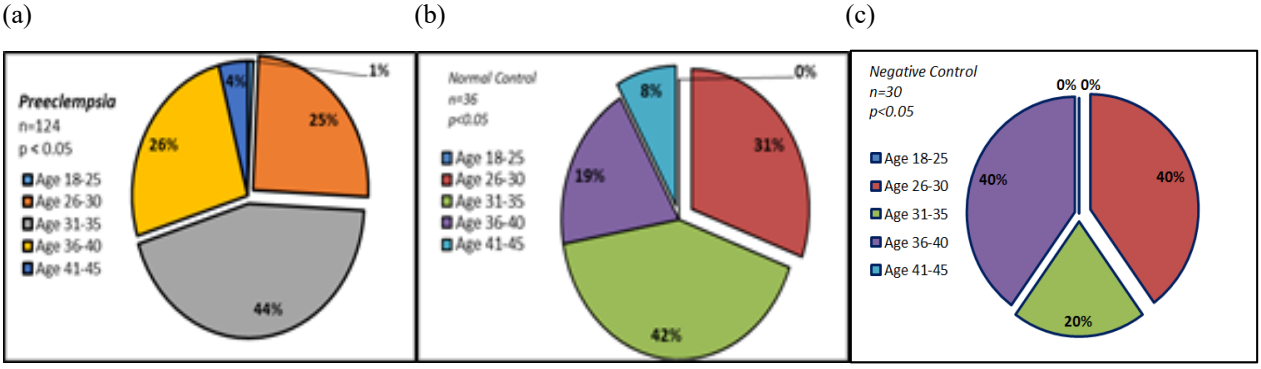

Fig. 1. Age groups of (a) pre-eclamptic and (b) control and (c) PIH respondents

Table 1. Demographic data of respondents

Queries	Preeclampsia cases (A) n (%) (N=124)	Control cases(B) n (%) (N=36)	PIH(C) n (%) (N=30)	(A+B)	(A+C)	(B+C)
				p-values		
Marital status						
Single	3 (2.4)	2 (5.6)	0	0.323	0.032*	0.041*
First Marriage	92 (74.2)	33 (91.7)	10 (100)	0.041	0.006*	0.032*
Remarried	29 (23.4)	1 (2.8)	0	0.013	0.027	0.072
Educational status						
None	4 (3.2)	0	0	0	0	0
Primary	17 (13.7)	3 (8.3)	3 (30)	0.442	0.441	0.989
Secondary	47 (37.9)	16 (44.5)	3 (30)	0.110	0028*	0.001*
Post-secondary	56 (45.2)	17 (47.2)	4 (40)	0.142	0.146	0.083
Job status						
Employed	102 (82.3)	27 (97.5)	8 (80)	0.192	0.892	0.173
Unemployed	22 (17.7)	9 (2.5)	2 (20)	0.014	0.070	0.009*

Table 2. Lipid profiles of respondents presented on the basis of trimesters. Only means of replicates have been presented

Queries	Trimester	Preeclampsia cases (A)	Control cases(B)	PIH(C)			
		(n=62)	(n=16)	(n=15)	(A+B)	(A+C)	(B+C)
					p-values		
Total Cholesterol	Second	205.76	195.435	196.574	0.364	0.626	0.734
	Third	211.131	202.815	213.22	0.354	0	0.012
Triglycerides	Second	156.029	113.631	135.648	0.002	0.369	0.326
	Third	153.431	130.352	200.942	0.015	0.01	0.006
HDL Cholesterol	Second	34.435	37.8	39.068	0.081	0.115	0.092
	Third	36.654	35.67	33.404	0.599	0	0
LDL Cholesterol	Second	145.86	135.735	130.376	0.244	0.26	0.261
	Third	145.56	141.085	128.98	0.607	0	0

Grouped data (totals) for Lipid profiles for assessment of dyslipidaemia in respondents, presented irrespective of trimester was determined (Table 3). Total cholesterol in the preeclamptic group was 208.44 mg/dl and 202.13 mg/dl in the PIH group ($p>0.05$). No significant differences in total cholesterol was reported between normotensive group (199.53 mg/dl) and the preeclamptoc group ($p>0.05$). triglycerides ranged from 122.92 – 154.73 mg/dl ($p<0.05$). The lowest triglyceride was reported in the Control group (122.92 mg/dl) ($p<0.05$). Based on severity of disease, only two categories of people were presented – mild and severe. No significant values in lipid profiles as separated by disease severity was reported (Table 4). No significant differences in lipid profiles was also reported on the basis of BMI (Table 5).

Lipid ratios of the study participants have been presented on Table 6. Generally, the preeclamptic group, antherogenic index plasma ratio (AIP) was highest (0.64) compared to that in the control (0.53) and PIH (0.60) groups respectively. During the second trimester, AIP was highest in preeclampsia. But during the third trimester, AIP was highest in PIH. The normotensive individuals had lowest AIP ratios at both trimesters. Similar ratios were reported in non-HDL, AC, and VLDL. While leveraging on lipid ratios separted on the basis of severity of preeclampsia, results showed AIP was highest in participants with severe preelclampsia (0.65) compared to mild preeclampsia (0.62). VLDL was also higher in severe preeclampsia. However, Non-HDL, AC, CRI-I and CRI-II respectively were higher in mild preeclampsia compared to severe preeclampsia (Table 6).

Table 3: Grouped data (totals) for Lipid profiles for assessment of dyslipidaemia respondents, presented irrespective of trimester

Queries	Preeclampsia cases (A)	Control cases(B)	PIH(C)			
	(µ±SEM)	(µ±SEM)	(µ±SEM)	p-value	p-value	p-value
	(mg/dl)	(mg/dl)	(mg/dl)	(A+B)	(A+C)	(B+C)
	(n=124)	(n=36)	(n=30)			
Total Cholesterol	208.44±3.39	199.53±5.97	202.13±21.21	0.21	0.307	0.209
Triglycerides	154.73±3.96	122.92±5.52	134.51±12.62	0	0.009	0.163
HDL Cholesterol	35.14±0.61	36.61±1.32	33.63	0.425	0.31	0.325
LDL Cholesterol	142.17±2.85	138.83±5.48	141.63	0.129	0.337	0.243

Table 4: Lipid profiles of preeclamptic subjects separated on the basis of severity of disease

Lipid profiles	Groups	N	Mean	Std. Error Mean	p-value
Total Cholesterol	Mild	39	209.94	5.02	0.718
	Severe	84	207.27	4.43	
Triglycerides	Mild	39	147.39	5.60	0.229
	Severe	84	157.72	5.20	
HDL Cholesterol	Mild	39	35.275	1.06	0.865
	Severe	84	35.498	0.74	
LDL Cholesterol	Mild	39	151.61	5.11	0.153
	Severe	84	145.83	6.22	

Table 5: Comparing Lipid profiles of preeclamptic subjects separated on the basis of BMI

	Group 1 – Normal vs Overweight						Group 2 – Normal vs Obese				
		N	Mean	SEM	p-value			N	Mean	SEM	p-value
Total Cholesterol	Normal	23	214.46	8.697	0.522		Normal	23	214.46	8.697	0.324
	Overweight	71	208.69	4.265			Obese	30	203.26	7.252	
Triglycerides	Normal	23	157.079	9.418	0.994		Normal	23	157.08	9.418	0.469
	Overweight	71	157.004	4.994			Obese	30	147.55	8.86	
HDL Cholesterol	Normal	23	33.8522	1.435	0.317		Normal	23	33.852	1.435	0.108
	Overweight	71	35.4573	0.78			Obese	30	37.051	1.31	
LDL Cholesterol	Normal	23	150.512	7.817	0.514		Normal	23	150.51	7.817	0.403
	Overweight	71	145.738	3.292			Obese	30	141.96	6.558	

Table 6: Lipid ratios of study participants

	AIP	NonHDL	AC	VLDL	CRI-I	CRI-II
General						
Preeclampsia	0.64	173	4.94	30.8	5.94	4.06
Control	0.53	163	4.53	24.4	5.53	3.85
PIH	0.6	168.37	5.01	26.8	6.01	4.21
At 2nd Trimester						
Preeclampsia	0.66	171.33	4.98	31.21	5.98	4.07
Control	0.48	157.64	4.17	22.73	5.17	3.57
PIH	0.54	157.51	4.03	27.13	5.03	3.34
At 3rd Trimester						
Preeclampsia	0.62	174.48	4.76	30.69	5.76	3.92
Control	0.56	167.15	4.69	26.07	5.69	3.96
PIH	0.78	179.82	5.38	40.19	6.38	4.18
Severity of Preeclampsia						
Mild preeclampsia	0.62	174.67	4.95	29.48	5.95	4.12
Severe preeclampsia	0.65	171.77	4.84	31.54	5.84	3.95

Note: AIP atherogenic index plasma, NonHDL non-HDL cholesterol, AC atherogenic coefficient, VLDL very low density lipoprotein, CRI-I Casterlly risk index-I, CRI-II Casterlly risk index-II

4. Discussion

In order to enhance the predictive ability of lipid profile assays for atherosclerotic cardiovascular disease, the current study used various lipid ratios or "atherogenic indices" to evaluate the risk of atherosclerosis and dyslipidemia in hypertensive disorders in pregnancy. When compared to normotensive control study participants, patients with hypertensive disorders in pregnancy had a slight increase in total cholesterol and LDL cholesterol, as well as a substantial difference in triglyceride levels. A substantial increase in serum triglyceride concentration in pre-eclampsia has been reported in previous research (14-16). A lipid profile that is abnormal is associated to atherosclerosis and has a direct effect on endothelial dysfunction (17).

This research aims to better understand the potential for early detection and prevention of cardiovascular disease in pregnant women with hypertension using lipid profile data. The researchers used lipid ratios, also known as atherogenic indices, to assess the risk of atherosclerotic cardiovascular disease in the case study because the lipid profile showed only minor changes. Despite the minor rise in total and LDL cholesterol levels, the case group's mean atherogenic index plasma (AIP) was higher than the control groups. AIP is a plasma atherogenicity marker that has been proposed. Higher AIP levels have been linked to an increased risk of cardiovascular disease (18). For its high correlation with apolipoprotein B levels, non-HDL cholesterol is believed to be a good surrogate marker for total apolipoprotein B. (19). On the other hand, standardized apolipoprotein B measurements are not always available in routine clinical procedures. As a result, the atherogenic coefficient, which is a simple ratio of non-HDL and HDL cholesterol, may be useful in determining whether a person is at risk of cardiovascular disease. In our current study, the atherogenic coefficient was also higher in the case study than in the control group, implying that pregnant women with hypertensive disorders face a higher cardiovascular risk.

Previous study has found that the cardiac risk ratio (TC/HDL), also known as the Castelli Risk Index I (CRI I), is significantly elevated in preeclamptic women (20-22). In the current study, we found an increase in Castelli risk index I and II in patients with hypertensive disease during pregnancy, despite minor changes in their lipid profile.

In pregnant patients with hypertension, lipid ratios, also known as atherogenic indices, were found to be more effective than individual lipid parameter measurements in determining the relative contribution of lipids to cardiovascular risk. Lipid ratios may aid in the early detection and prevention of atherosclerotic cardiovascular disease in women with hypertensive disorders during pregnancy, despite minor changes in their lipid profile levels.

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Conflict of interest

The authors declare no conflict of interest

References

1. Albertini RJ. Accumulation of somatic mutations in proliferating T cell clones from children treated for leukemia Leukemia, 2001; 15, 1898–1905.
2. Allain CC, Poon LS, Chan CSG, Richmond W, Fu PC. Enzymatic determination of Total Serum Cholesterol. Clinical Chemistry, 1974; 20(4): 470-475.
3. Audu LR, Ekele BA. A ten-year review of maternal mortality in Sokoto, northern Nigeria. West Afr J Med, 1995; 21,74 – 76.
4. Banaczek Z, Wojeicka-Jagodzinska J. Concentration of lipids lipoprotein in serum of women with pregnancy induced hypertension. Ginekologia Polska, 2002; 66(2),72-75.
5. Baker AM, Klein RL, Moss KL, et al. Maternal serum dyslipidemia occurs early in pregnancy in women with mild but not severe preeclampsia. Am J Obstet Gynecol, 2009; 201,293e1-4
6. Begum Z, Ara I, Shah ABS. Association between lipid profile pre-eclampsia. Ibrahim Card Med J, 2011; 1(1),41–44.
7. Brizzi P, Tonolo G, Esposito F, et al. Lipoprotein metabolism during normal pregnancy. Am J Obstet Gynecol, 1999; 181,430 – 434.
8. Belo L, Caslake M, Gaffney D, et al. Changes in LDL size HDL concentration in normal preeclamptic pregnancies. Atherosclerosis, 2011; 162,425-32.
9. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Catherine YS. Williams Obstetrics 23rd ed. New York, Mc Graw Hill Companies; Chapter, Hypertensive disorders in pregnancy; 2010; pp 706–56.
10. Dobiasova, M Frohlich, J. The plasma parameter log (TG/HDL-C) as an atherogenic index,correlation with lipoprotein particle size esterification rate in apoB-lipoprotein-depleted plasma (FERHDL). Clinical Biochemistry, 2001; 34,583–588.
11. De J, Mukhopadhyay AK, Saha PK. Study of serum lipid profile in pregnancy induced hypertension. Indian Journal of Clinical Biochemistry, 2000; 21(2),165–68.
12. Abalos E, Cuesta C, Carroli G, et al. Pre-eclampsia, eclampsia adverse maternal perinatal outcomes, a secondary analysis of the World Health Organization Multicountry Survey on Maternal Newborn Health. BJOG 2014; 121(Suppl 1), 14–24.
13. Dutta DC, Konar HL. Hypertensive disorders in pregnancy, In, Textbook of Obstetrics 5th ed, New Central Book Agency; 2001.
14. Emuveyan E. Pregnancy induced hypertension. Trop J Obstet Gynaecol., 1995; 12, 8–11.
15. Itam IH, Ekabule JE. A review of pregnancy outcome in women with eclampsia at the University of Calabar Teaching Hospital, Calabar Trop J Obstet Gynaecol. 2002; 18, 66–68.
16. Enquobahrie DA, Williams MA, Butler CL, et al. Maternal plasma lipid concentrations in early pregnancy risk of preeclampsia Am J Hypertens, 2004; 7,574 – 581.
17. Myers JE, Baxer PN. Hypertension diseases eclampsia. Curr Opin Obstet Gynecol, 2002; 14,119–125.
18. Noubiap JJ, Bigna JJ, Nyaga UF, et al. The burden of hypertensive disorders of pregnancy in Africa, a systematic review meta-analysis. J Clin Hypertens, 2019; 21(4), 479–488.
19. Pushparaj JL, Subramanyam G. Dyslipidemia in pre-eclampsia-risk factor for future maternal cardiovascular diseases. Journal of

Evolution of Medical Dental Sciences, 2012; 1(4),487–95.

20. Sattar N, Clark P, Greer IA et al. Lipoprotein (a) levels in normal pregnancy in pregnancy complicated with preeclampsia Atherosclerosis, 2000; 148 (2), 407-411.

21. Steer PJ. Turnbull's Obstetrics Geoffrey Chamberlain, 3rd Edition Churchill, Livingstone. 2001

22. Third report of the National Cholesterol Education Program (NCEP) expert panel on Detection, Evaluation Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report *National Cholesterol Education Program* [online] 2002 Sep Available from, URL, http,//wwwnhlbinihgov/guidelines/cholesterol/atp3fullpdf