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Association between dyslipidemia and early-onset preeclampsia in pregnant women at a national referral facility in Kenya

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Abstract

Background: Preeclampsia is a syndrome marked by hypertension that appears after 20 weeks of pregnancy and is linked to maternal and fetal complications. Physiological hyperlipidemia develops as the pregnancy proceeds, and lipids are taken up by the placenta to be used by the fetus. However, in preeclampsia, due to placental insufficiency, there is a decrease in lipid uptake, disrupting lipid metabolism.

Objective: To assess association between dyslipidemia and preeclampsia in pregnant women presenting at a national referral facility in Kenya.

Methods: This was a case-control study where 75 women presenting with preeclampsia and aged between 14 and 45 years with a gestational age of between 20 and 34 weeks were recruited as cases, and 75 age-matched pregnant women as controls. Medical data were obtained from their files, and a 5mL blood specimen was drawn for lipid profile analysis. Data were analyzed using STATA version 13 (Stata Corp Inc., USA). Chi-square was calculated to establish statistical significance. A p-value of <0.05 was considered significant.

Results: A majority, 78.8% of the cases, had high non-high-density lipoprotein cholesterol (HDL-C) compared with 58.7% of controls (p-value =0.02). Low HDL-C was reported in 4% of cases against 2.7% of controls (p-value =0.6.) High low-density lipoprotein cholesterol (LDL-C) was reported in 42.7% of cases compared to 45.3% of controls (p-value =0.7). Preeclampsia patients had high odds of dyslipidemia odds ratio (OR) 2.3, (95% CI 1.1-4.7, p-value = 0.04).

Conclusion: Dyslipidemia is more prevalent among women with preeclampsia than normotensives of the same gestational age. Non-HDL-C strongly correlates with atherogenic lipoproteins, and it could be elevated even when LDL-C is within normal reference range, thus making it a valuable marker of dyslipidemia in preeclampsia. There is an association between dyslipidemia and preeclampsia.

Keywords: dyslipidemia, eclampsia, normotensive, preeclampsia

Introduction

Preeclampsia is a multisystem condition marked by a new diagnosis of hypertension that appears after 20 weeks of pregnancy. It is classified according to its onset and severity; early-onset, when it occurs before 34 weeks of pregnancy, and late-onset after 34 weeks (1). Preeclampsia is classified as mild when the systolic blood pressure is >140 mmHg, diastolic blood pressure is >90 mmHg, and severe when the systolic blood pressure is >160 mmHg, and diastolic blood pressure is >110 mmHg (2). Severe preeclampsia may progress to cause multiple end-organ dysfunctions, manifesting as hemolysis, elevated liver enzymes, and low platelet count

(HELLP) syndrome (3). The pathological characteristic of preeclampsia observed is inadequate spiral artery remodeling leading to arterial spasm and endothelial dysfunction that may lead to maternal and fetal complications (4).

Dyslipidemia is a modifiable state of abnormal lipid metabolism manifesting with decreased serum levels of high-density lipoprotein cholesterol (HDL-C) and raised serum levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C) and paraoxonase-1 activity (5,6). Increased LDL-C and decreased HDL-C levels may result in an atherosclerotic state due to the accumulation of macrophages and increased inflammatory response within the arteries promoted by elevated LDL-C and oxidative stress due to the diminished antioxidant effect caused by decreased HDL-C (7). As pregnancy progresses, the demand for lipids increases to sustain the growth of the fetus with increasing plasma lipoproteins. Hormonal elevations of estrogen, progesterone, and human placental lactogen could also account for the lipid pattern observed in pregnancy (8). Dyslipidemia produces lipid peroxides and reactive oxygen species (ROS) in early pregnancy, increasing oxidative stress in the placenta (9). In preeclampsia, there is a decrease in antioxidant activity and an increase in lipid peroxides. Therefore, it has been postulated that oxidative stress markers may predict preeclampsia (10). Serum LDL-C and non-HDL-C are prooxidants that may be used as biomarkers of preeclampsia (11). This study assessed the association between dyslipidemia and preeclampsia in pregnant women at a national referral facility in Kenya.

Methods

Study design and setting

A prospective case-control study design was employed. The study setting was Kenyatta National Hospital's antenatal clinic and ward. Kenyatta National Hospital is Kenya's largest teaching, research, and training hospital. Its maternity unit handles approximately 20- 50 deliveries daily.

Study population

All pregnant women attending antenatal clinic aged between 14 and 45 years with gestational age between 20 and 34 weeks without preeclampsia were recruited. Cases with pathologies associated with secondary dyslipidemia (chronic liver disease, primary biliary cirrhosis, chronic kidney disease, nephrotic syndrome, Cushing syndrome, systemic lupus erythematosus, hypothyroidism, HIV, and diabetes) were excluded. Those who did not consent to the study were also excluded.

Sample size determination and sampling procedure

The sample size was determined using Kelsey et al.'s formula (12). The proportion of controls with dyslipidemia was specified at 73.7% (11), and the odds ratio for dyslipidemia in preeclampsia was 4.1 (13). The calculated sample size was 67 in each group. A markup of 10% was added, yielding a recalculated sample size of 74 in each group. The cases were consecutively sampled from the antenatal clinic and labor ward until the sample size was achieved. Controls were conveniently screened for eligibility criteria from the antenatal clinic and repeated until the sample size was achieved.

Sample collection and laboratory analysis

The principal investigator explained the procedure to the study participants before drawing 5mL of venous blood from the antecubital vein using plain vacutainer tubes. After collection, the specimens were placed in biohazard bags and transported to the laboratory in a secure sample transport box. The samples were analyzed at the Kenyatta National Hospital biochemistry laboratory using the Biolis 50i Superior (Tokyo, Boaki, Japan) with Dirui Kits (Shenzen Industrial Co., Ltd.). The lipid profile parameters were analyzed using the enzymatic colorimetric principle for quantification (14).

Data analysis

Data were entered and cleaned using Microsoft Excel 2016 (Microsoft Corp., Redmond, WA, USA) and transferred to STATA version 13 (Stata Corp Inc., USA) for analysis. Chi-square was calculated to establish statistical significance. A p-value of <0.05 was considered significant.

Ethical consideration

This study was approved by the Kenyatta National Hospital and University of Nairobi Ethics and Research Committee (registration number KNH-ERC/A/172). This study was voluntary, without any coercion or cash incentive given to the participants. Participants who were found to have total plasma cholesterol >7.5 mmol/l were brought to the attention of their attending clinician to inform their management since cholesterol >7.5 was indicative of primary hypercholesterolemia.

Results

Sociodemographic and medical characteristics

Data were collected over five months, from November 2020 to March 2021. During the study period, 75 cases and 75 controls with similar gestational ages were recruited. The mean age and gestational age for cases and controls was 29.7 (SD 6.2) and 30.2 (SD 5.2), and 29 (SD 4.0) and 28 (SD 4.0) weeks, respectively. Most participants were of low parity,

with para one having the highest frequency of 36.67% (Table 1).

Table 1: Sociodemographic and medical characteristics of the study participants at Kenyatta National Hospital

	Preeclampsia N (%)	Normal pregnancy N (%)	P-value
Age (years)			
Mean	29.7(SD 6.2)	30.3 (SD 5.2)	0.6
Occupation			
Employed	17 (22.7%)	20(26.7%)	0.1
Unemployed	36(48%)	23(30.7%)	
Business	19(25.3)	30(40%)	
Student	3(4%)	2(2.7%)	
Smoking history			
No	75(100%)	73(97.3%)	0.6
Yes	0(0%)	2(2.7%)	
Residence			
Rural	11(14.7%)	9(12%)	0.6
Urban	64(85.3%)	66(88%)	
Parity			
0	15 (20%)	15 (20%)	
1	23 (30.7%)	27 (36%)	
2	18 (24%)	14 (18.7%)	
3	11 (14.7)	14 (18.7%)	0.9
4	4 (5.3%)	3 (4%)	
> 4	4 (5.3%)	2 (2.6%)	
Previous live births	17 (22.7%)	19 (25.3%)	0.8
0	25 (33.3%)	30 (40%)	
1	21 (28%)	14 (18.7%)	
2	9 (12%)	8 (10.7 %)	
3	2 (2.7%)	3 (4%)	
4	1 (1.3%)	1 (1.3%)	
> 4			
Previous abortions	61 (83.1 %)	61 (81.3%)	0.9
0	10 (13.3%)	10 (13%)	
1	2 (2.7%)	3 (4%)	
2	1 (1.3%)	1 (1.3%)	
3	0	0	
4	1 (1.3%)	0	
> 4			
Gestational age (weeks)			
20-23+6	9 (12%)	11 (14.7%)	0.6
24-27+6	15 (20%)	18 (24%)	
28-31+6	26 (34.7%)	28 (37.3%)	
32-34	25 (33.3%)	18 (24%)	
BMI			
Underweight	1 (1.33%)	0	0.9
Normal	15 (20%)	19 (25.3%)	
Overweight	31 (41.3%)	31 (41.3%	
Obese	28 (37.3%)	25 (33.3)	
Contraceptive			
Hormonal	31 (41.3%)	25(33.3%)	0.3
Nonhormonal	4 (5.4 %)	9 (12%)	
None	40 (53.3%)	41 (54.7%)	

Prevalence of dyslipidemia

Most clients, 140 (71%), reported that they were not barred from using contraceptives by their denominations or religion. However, a minority, 57 (29%), seemed to support the idea that religion still barres women from using contraceptives. The prevalence of dyslipidemia in preeclampsia was higher at 80% compared with 64% in controls (Figure 1-2).

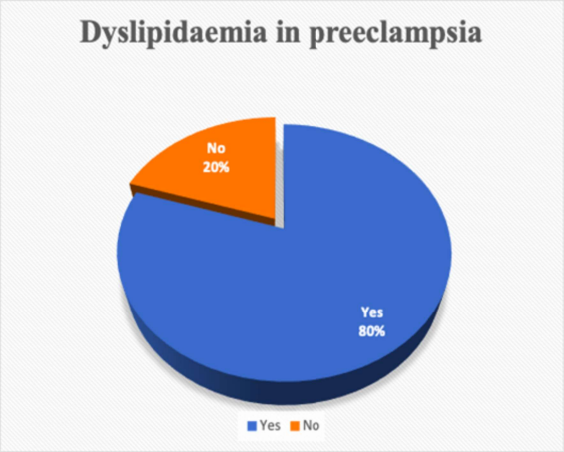

Figure 1: Prevalence of dyslipidemia in women with preeclampsia at Kenyatta National Hospital

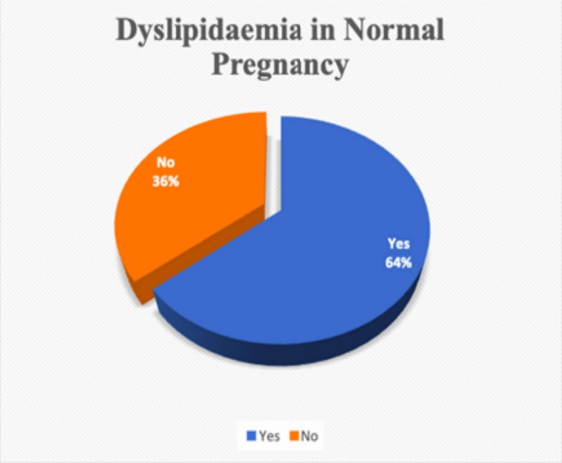

Figure 2: Prevalence of dyslipidemia in women with normal pregnancy at Kenyatta National Hospital

Association between dyslipidemia and preeclampisa

Dyslipidemia was established to be a risk factor for preeclampsia, odds ratio (OR) 2.3 (95% CI 1.1-4.7, p-value = 0.04). Patients with preeclampsia were 2.3 more likely to have dyslipidemia than normotensive patients (Table 2).

Table 2: Association between dyslipidemia and preeclampsia

	Pre-eclampsia	Normal pregnancy	Odds ratio	95% CI	P-value
Dyslipidemia	60	48	2.3	1.1 – 4.7	0.04
No dyslip-idemia	15	27			

Discussion

This study assessed high non-HDL-C, high LDL-C, and low HDL-C to determine the prevalence of dyslipidemia in preeclamptic and normotensive participants. This criterion established dyslipidemia in most, 80% of preeclamptic participants, against 64% of normotensive participants. Patients with dyslipidemia were 2.3 times more likely to develop preeclampsia (p-value = 0.04). HDL-C and LDL-C are elevated in normal pregnancy in a tight balance, indicating average utilization of lipoproteins (8,15). In preeclampsia, physiologic hyperlipidemia tends to shift toward a dyslipidemic pattern due to altered lipid metabolism observed in preeclampsia (12). A decrease in lipoprotein lipase activity yields an atherogenic picture where HDL-C is low while LDL-C remains elevated (16). In this study, participants with preeclampsia had a higher prevalence of dyslipidemia than normal pregnancies. This was similar to studies published elsewhere (13,16–18).

In this study, HDL-C and LDL-C were comparable at all cut-off points in both groups. HDL-C and LDL-C concentrations did not significantly differ in women with preeclampsia and normal pregnancy. From these findings, LDL-C and HDL-C do not seem reliable in assessing dyslipidemia in early-onset preeclampsia. These findings are comparable to other studies that found no significant differences between patients and healthy controls (19,20). Non–HDL-C is a calculated parameter obtained from total cholesterol and HDL-C reflecting levels of triglyceride-rich lipoproteins that may be difficult to measure directly. Non-HDL-C strongly correlates with atherogenic lipoproteins and can be used as a marker for dyslipidemia (21). With a p-value of 0.02, high non-HDL- C was determined to have a statistically significant link to preeclampsia. These findings align with those of a meta-analysis study, where non-HDL-C levels were observed to be greater in preeclampsia than in normotensive pregnancy (16). Another study also observed elevated non-HDL-C in patients with preeclampsia, despite normal LDL-C levels (22).

This study established a link between dyslipidemia and preeclampsia, with an odds ratio of 2.3 (95 % confidence interval 1.1-4.7, p-value = 0.04), consistent with an Iranian study that found an association between dyslipidemia with an odds ratio of 4 (13). Other studies have shown similar results, bolstering the theory that lipids may play a role in the development of preeclampsia (16,23,24).

Study strengths and limitations

This study is among the few on dyslipidemia in preeclampsia and adds to the knowledge pool, particularly in sub-Saharan Africa. As a prospective study, the coronavirus disease 2019 pandemic affected the data collection process. However, analyzable data were obtained.

Conclusion

Dyslipidemia is more prevalent among women with preeclampsia than normotensive women of the same gestational age. Non-HDL-C strongly correlates with atherogenic lipoproteins, and it could be elevated even when LDL-C is within reference levels, thus making it a potential marker of dyslipidemia in preeclampsia. There is an association between dyslipidemia and preeclampsia.

Recommendations

Non-HDL-C can be used as a marker of dyslipidemia in preeclampsia, providing a basis for screening and monitoring for preeclampsia. There is a need for further research on dyslipidemia in pregnancy and preeclampsia to create a baseline for management.

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Declarations

Conflict of interests

The authors declare no conflicts of interest.

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References

1. Raymond D, Peterson E. A critical review of early-onset and late-onset preeclampsia. *Obstet Gynecol Surv*. 2011;66(8):497-506. doi:10.1097/OGX.0b013e3182331028
2. Jasović-Siveska E, Jasović V. Prediction of mild and severe preeclampsia with blood pressure measurements in first and second trimester of pregnancy. *Ginekol Pol*. 2011;82(11):845-850
3. Pennington KA, Schlitt JM, Jackson DL, Schulz LC, Schust DJ. Preeclampsia: multiple approaches for a multifactorial disease. *Dis Model Mech*. 2012;5(1):9-18. doi:10.1242/dmm.008516
4. Uzan J, Carbonnel M, Piconne O, Asmar R, Ayoubi JM. Pre-eclampsia: pathophysiology, diagnosis, and management. *Vasc Health Risk Manag*. 2011;7:467-474. doi:10.2147/VHRM.S20181
5. Hedayatnia M, Asadi Z, Zare-Feyzabadi R, et al. Dyslipidemia and cardiovascular disease risk among the MASHAD study population. *Lipids Health Dis*. 2020;19(1):42. Published 2020 Mar 16. doi:10.1186/s12944-020-01204-y
6. Niroumand S, Khajedaluee M, Khadem-Rezaiyan M, et al. Atherogenic Index of Plasma (AIP): A marker of cardiovascular disease. *Med J Islam*

Repub Iran. 2015;29:240. Published 2015 Jul 25
7. Noubiap JJ, Bigna JJ, Nansseu JR, et al. Prevalence of dyslipidaemia among adults in Africa: a systematic review and meta-analysis [published correction appears in Lancet Glob Health. 2018 Dec 12;:]. *Lancet Glob Health*. 2018;6(9):e998-e1007. doi:10.1016/S2214-109X(18)30275-4
8. Grimes SB, Wild R. Effect of Pregnancy on Lipid Metabolism and Lipoprotein Levels. In: Feingold KR, Anawalt B, Boyce A, et al., eds. *Endotext*. South Dartmouth (MA): MDText.com, Inc.; February 20, 2018
9. Oguejiofor OC, Onwukwe CH, Odenigbo CU. Dyslipidemia in Nigeria: prevalence and pattern. *Ann Afr Med*. 2012;11(4):197-202. doi:10.4103/1596-3519.102846
10. Gupta S, Aziz N, Sekhon L, et al. Lipid peroxidation and antioxidant status in preeclampsia: a systematic review. *Obstet Gynecol Surv*. 2009;64(11):750-759. doi:10.1097/OGX.0b013e3181bea0ac
11. Nouhjah, S.; Shahbazian, H.; Jahanfar, S.; Shahbazian, N.; Jahanshahi, A.; Cheraghian, B.; Hardanipasand, L.; Moradi, M. Early Postpartum Lipid Profile in Women with and Without Gestational Diabetes Mellitus: Results of a Prospective Cohort Study. Iran. Red Crescent Med. J. 2017, 19
12. Kelsey, J.L., Whittemore, A.S., Evans, A.S. and Thompson, W.D. (1996) Methods of sampling and estimation of sample size. In: Kelsey, J.L., Whittemore, A.S., Evans, A.S. and Thompson, W.D., Eds., Methods in Observational Epidemiology, Oxford University Press, New York.
13. Hajar Sharami S, Abbasi Ranjbar Z, Alizadeh F, Kazemnejad E. The relationship of hyperlipidemia with maternal and neonatal outcomes in pregnancy: A cross-sectional study. *Int J Reprod Biomed*. 2019;17(10):739-748. Published 2019 Nov 7. doi:10.18502/ijrm.v17i10.5294
14. Richmond W. Analytical reviews in clinical biochemistry: the quantitative analysis of cholesterol. *Ann Clin Biochem*. 1992;29 (Pt 6):577-597. doi:10.1177/000456329202900601
15. Islam NAF, Chowdhury MAR, Kibria GM, Akhter S. Study Of Serum Lipid Profile In Pre-Eclampsia And Eclampsia. *Faridpur Med Coll J* 2010;5: 56-59
16. Spracklen CN, Saftlas AF, Triche EW, et al. Genetic Predisposition to Dyslipidemia and Risk of Preeclampsia. *Am J Hypertens*. 2015;28(7):915-923. doi:10.1093/ajh/hpu242
17. Siddiqui Ia. Maternal Serum Lipids in Women with Pre-eclampsia. *Ann Med Health Sci Res*. 2014;4(4):638-641. doi:10.4103/2141-9248.139358
18. Tesfa E, Nibret E, Munshea A. Maternal lipid profile and risk of pre-eclampsia in African pregnant women: A systematic review and meta-analysis. *PLoS One*. 2020;15(12):e0243538. Published 2020 Dec 23. doi:10.1371/journal.pone.0243538
19. Herrera E, Desoye G. Maternal and fetal lipid metabolism under normal and gestational diabetic conditions. *Horm Mol Biol Clin Investig*. 2016;26(2):109-127. doi:10.1515/hmbci-2015-0025
20. Fodor G. Primary prevention of CVD: treating dyslipidemia. American Family Physician. 2011 May 15;83(10):1207-8.
21. Pandeya A, Sharma M, Regmi P, Basukala A, Lamsal M. Pattern of dyslipidemia and evaluation of non-HDL cholesterol as a marker of risk factor for cardiovascular disease in type 2 diabetes mellitus. *Nepal Med Coll J*. 2012;14(4):278-282
22. Reena R, Usha S M R, Rupakala B M, Shetty H V, Role of non-HDL-cholesterol in evaluation of dyslipidemia in preeclampsia. *Int J Clin Biochem Res* 2019;6(3):369-374
23. Kanmani K, Subramanian S. Association of dyslipidemia in second trimester of pregnancy with preeclampsia. Int J Reprod Contracept Obstet Gynecol. 2018 Jan 12;7(2):435–41
24. Singh U, Yadav S, Mehrotra S, Natu SM, kumari K, Singh Yadav Y. Serum Lipid Profile in Early Pregnancy as a Predictor of Preeclampsia. *Int J Med Res Rev* 2013;1(2):55-2