Nigerian Medical Journal
NIGERIA MEDICAL ASSOCIATION
Print ISSN 0300-1652, E-ISSN 2229-774X

Original Article

Small Dense Low-Density Lipoprotein (sdLDL) and Its Correlates among Pregnant Women in Juth

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Abstract

Background: Small dense low-density lipoprotein (sdLDL), an atherogenic LDL subfraction, raises cardiovascular risk and mortality. Pregnancy-induced hyperlipidemia supports fetal growth and alters lipoprotein metabolism, but data on sdLDL changes and correlations during pregnancy, especially in African populations, are limited. This study assessed sdLDL levels and their biochemical and biophysical associations among pregnant women at Jos University Teaching Hospital (JUTH).

Methodology: This cross-sectional study involved 190 pregnant women between 28 and 32 weeks of gestation who attended the metabolic clinic at JUTH. Fasting blood samples for sdLDL was quantified using the precipitation method of Hirano et al. Correlations between sdLDL and biochemical/biophysical parameters were assessed using Pearson's correlation coefficients, and group comparisons were performed between participants with high versus low sdLDL levels.

Results: The mean (SD) age of participants was 31.0 ± 6.2 years, and the mean BMI was 30.7 ± 6.3 kg/m². sdLDL levels averaged 0.7 ± 0.5 mmol/L. sdLDL showed a significant positive correlation with LDL-C ($r = 0.314$, $p < 0.001$) and a significant negative correlation with HDL-C ($r = –0.297$, $p < 0.001$). No significant relationships were observed between sdLDL and triglycerides, total cholesterol, fasting glucose, or blood pressure parameters ($p > 0.05$). Women with high sdLDL had higher LDL-C [2.8 ± 0.9 vs 2.3 ± 0.8 mmol/L; $p = 0.01$] **and** lower HDL-C [1.1 ± 0.4 vs 1.3 ± 0.4 mmol/L; $p < 0.01$] compared to those with low sdLDL.

Conclusion: Among pregnant women in Jos, sdLDL was significantly associated with LDL-C but inversely with HDL-C, showing no relationship to glucose or blood pressure. This suggests sdLDL changes in pregnancy are tied to lipoprotein metabolism, not glycemic or hemodynamic shifts.

Keywords: Small dense LDL, pregnancy, lipoprotein metabolism, atherogenic risk, HDL cholesterol, LDL cholesterol

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How to Cite Lukden MS, Imoh LC, Paul ME, Solomon ML, Olaniru OB, Luku PM. Small Dense Low-Density Lipoprotein (sdLDL) and Its Correlates among Pregnant Women in Juth. Niger Med J 2025; 66 (5): 1959-1966. https://doi.org/10.71480/nmj.v66i5.1115

Quick Response Code:

Introduction

The LDL particle is a crucial lipid fraction due to its unique rolein metabolism. While it subserves many physiological functions in the body, it has a strong atherogenic potential, depending on defects in its metabolism and clearance from the circulation(1).

The primary physiological role of the LDL particle is the transport of cholesterol from the liver to tissues in the body where cholesterol is needed(2). These cells contain LDL receptors and are found in the skin, adrenals, gonads, and liver, where they are involved inthe synthesis of vitamin D, adrenocortical hormones, sex hormones, and bile salts,respectively(2,3).

Two distinct variants of LDL have been identified based on particle size and density. They are the large buoyant LDL particle and the small dense LDL (sdLDL) particle, which have been shown to possess higher atherogenic potentials relative to the larger buoyant variant(4).

Pregnancy has been shown to cause increases in the plasma and, by extension, the placental concentration of cholesterol(2,5).There isa particularly high concentration ofplasma LDL, which is the main vehicle that transports cholesterol to the developing fetus for growth and development of tissues(6). Small, dense LDL, being a variant of LDL, is typically increased in pregnancy for the same reason, thereby increasing the atherogenic risk in pregnant women(7).

Studies in Africa show that while sdLDL levels are significantly elevated in acute coronary syndrome (ACS) patients and predict cardiovascular events, African ACS patients generally have lower sdLDL levels than other populations, possibly due to genetic and environmental factors (8).

A study on sdLDL among Chinese pregnant women showeda higher sdLDL/large buoyant LDL particle ratio in GDM patients, when compared with normoglycemic pregnant women(7). The study also noted a significant association between fasting plasma glucose and sdLDL levels. Some other studies among Caucasian populations have shown associations between maternal obesity and the risk of formation of sdLDL(9). These risks and correlates have not been well documented in studies among African populations(7).

Additionally, measuring sdLDL is quite challenging for lipidologists, as accurate values often require specialized technical assay methods, such as proton NMR spectroscopy, gradient gel electrophoresis, or high-performance liquid chromatography (HPLC). Consequently, some researchers have resorted to using lipid ratios (TC/HDL-C, TG/HDL-C, and LDL-C/HDL-C), particularly the TG/HDL-C ratio, as surrogate markers for sdLDL quantification(10,11).

A cheaper and relatively less cumbersome precipitation method of measurement of sdLDL,popularized by Hirano et al, shows good correlation with actual values of sdLDL obtained through more advanced assay methods. It is more objective than the use of ratios as surrogate markers for quantification of sdLDL(10).

There is limited data on sdLDL levels and their biochemical and biophysical correlates in pregnant women. Additionally, the significance and potential cardiometabolic risks of sdLDL, especially among pregnant women in Nigeria (JUTH), remain under-researched. Inthis study, we examined mid-pregnancy sdLDL levels, as assayed using the precipitation technique, among African women in a tertiary facility andtheir correlates,tounderstandtheir significanceand correlatesduring pregnancy(12,13).

Methods

The study was conducted at the metabolic clinic of the Chemical Pathology department in the Jos University Teaching Hospital (JUTH).The Department of Chemical Pathology runs a Metabolic clinic where screening for metabolic disorders, including OGTT,is performed.

Most of the patients served by the hospital and the metabolic clinic are residents of the Jos-Bukuru metropolis, and a few others are from remote areas of Plateau state.

Study Design

This observational, cross-sectional study was conducted among pregnant women attending antenatal care at Jos University Teaching Hospital.

Study Population

Pregnant women who were referred to the Metabolic Clinic of Jos University Teaching Hospital (JUTH) for OGTT due to presences of risk factors which include obesity/overweight, a previous diagnosis of gestational diabetes, impaired glucose tolerance, or impaired fasting glycaemia; family history of a first degree relative with T2DM; maternal age greater than 25 years;a previous pregnancy which resulted in a child with a high birth weight (> 90th centile, or > 4000g) and previous poor obstetric history(14,15).

However, some obstetric units in the hospital practice universal screening for HIP. All women who consented and met the study's inclusion criteria were included.

Inclusion Criteria

- Consenting pregnant women who were referred between 28 and 32 weeks of gestation for OGTT.

Exclusion Criteria

- Non-consenting pregnant women
- Pregnant women whose first Antenatal visit will be after 32 weeks of pregnancy.
- Women with an uncertain date of last menstrual period and no ultrasonographic estimation between 6 and 24 weeks of gestational age
- Women with multiple pregnancies.
- Women with a diagnosis of Diabetes Mellitus before the current pregnancy.
- Pregnant women are on drugs that affect glucose and lipid metabolism, such as steroids, beta-adrenergic blockers, and thiazide diuretics.

Ethical Consideration

Ethical approval for this study was obtained from the JUTH Institutional Research Ethical Committee (Approval No.: JUTH/DCS/IREC/127/XXXI/2396; Date: 24/02/2021).

Study Procedure

Participants underwent a 2-hour OGTT with a 75g glucose load (WHO standards), and blood samples for glucose and lipids (after an 8-hour fast) were collected. Blood pressure, weight, and height were measured at the same visit.

Participants underwent an 8-hour overnight fast before blood was collected in a department phlebotomy room. Using aseptic technique and the Vacutainer system, five milliliters were drawn: one sample for fasting plasma glucose and another for the sdLDL assay. All tests were performed on the Roche COBAS C111 autoanalyser, with sdLDL samples prepared by the precipitation method of Hirano et al. (Roche, 2025).

Results

Table 1a: Summary of clinical and biochemical characteristics of study population

PARAMETERS	FREQUENCY	PERCENT (%)
GDM	57	30
NORMOGLYCAEMIC	133	70
AGE Group:		
<25	84	44
25-35	91	48
>35	15	8
GRAVIDITY:		
1	32	17
2	36	19
3	36	19
4	34	18
5	52	27

Table 1b: Summary of clinical and biochemical characteristics of study population

PARAMETER	MEAN (SD)
AGE	31.0 (6.2)
Weight (Kg)	81.0 (18.0)
Systolic BP (mmHg)	111.3 (15.3)
Diastolic BP (mmHg)	68.0 (12.7)
Fasting glucose (mmol/L)	4.7 (0.62)
1-hour glucose (mmol/L)	7.0 (1.6)
2-hour glucose (mmol/L)	6.4 (1.5)
TG (mmol/L)	2.0 (0.5)
TC (mmol/L)	4.4 (1.0)
HDL (mmol/L)	1.3 (0.4)
LDL (mmol/L)	2.5 (0.9)
SDLDL (mmol/L)	0.7 (0.5)

Table 2: Correlation between SdLDL and biophysical and biochemical parameters

PARAMETERS	r	P-VALUE
sdLDL	1	
WEIGHT	-0.051	0.481
SYSTOLIC	-0.075	0.304
DIASTOLIC	-0.095	0.194
Fasting glucose (mmol/L)	0.02	0.785
1-hour glucose (mmol/L)	0.065	0.373
2-hour glucose (mmol/L)	0.047	0.517
TG	-0.006	0.929

TC	0.152	0.037
HDL	-0.297	<0.001
LDL	0.314	<0.001

Small dense LDL showed a weak negative correlation with weight, SBP, and DBP, and these were not significant. The correlation with glucose time point at 0-hr was (r=0.02), 1 hr (r=0.065), and 2-hr (r=0.047), and these correlations were not statistically significant, $p<0.05$.

Small dense LDL, however, correlated negatively with HDLc, r=0.297, and correlated with LDLc,r=0.314. This correlation was significant.

There was no correlation with TG and TC (see Table 2)

TABLE 3: Showing the relationship between biochemical and physical characteristics of participants with sdLDL

PARAMETERS	HIGH sdLDL	LOW sdLDL	P-VALUE
AGE	29.7 (6.7)	31.5 (5.9)	0.06
GRAVIDITY	3.4 (2.2)	3.8 (2.3)	0.213
WEIGHT	78.8 (18.3)	81.4 (17.9)	0.37
BMI (Kg/m^2)	30.3 (6.6)	31.0 (6.0)	0.427
SYSTOLIC (mmHg)	109.1 (15.1)	112.4 (15.3)	0.165
DIASTOLIC (mmHg)	66.9 (12.4)	68.4 (12.8)	0.466
Fasting glucose (mmol/L)	4.6 (0.6)	4.7 (0.6)	0.827
1-hour glucose (mmol/L)	6.9 (1.6)	6.8 (1.6)	0.738
2-hour glucose (mmol/L)	6.4 (1.4)	6.3 (1.5)	0.759
TG	1.5 (0.4)	1.5 (0.5)	0.598
TC	4.6 (1.0)	4.4 (0.9)	0.189
HDL	1.1 (0.4)	1.3 (0.4)	<0.001
LDL	2.8 (0.9)	2.3 (0.8)	0.001
TRIGINDEX2	8.6 (0.30)	8.6 (0.4)	0.565

There was no significant difference in age, gravidity, weight, BMI, SBP, and DBP among participants with low sdLDL and those with high sdLDL($p>0.05$). Also, fasting glucose, 1-hr, and 2-hr glucose values were similar in participants with low sdLDL and those with high sdLDL. However, HDL cholesterol was significantly lower in pregnant women with high sdLDL [1.1(0.4)] compared with participants with low sdLDL [1.3 (0.4)], $p< 0.01$

Also, LDLc was significantly higher [2.8 (0.9)] in pregnant women with high sdLDL compared with women who had lower sdLDL [2.3(0.8)]; $p =0.01$.

Triglycerides and TC levels were not significantly different between the 2 groups.

Discussion

This study assessed small dense low-density lipoprotein (sdLDL) levels and their biochemical and biophysical correlates among pregnant women in Jos University Teaching Hospital (JUTH).The mean age of participants (31.0 ± 6.2 years) and the predominance of multiparous women reflect the typical demographics of antenatal clinic attendees in similar sub-Saharan African settings (12). The overall lipid profile revealed physiological hyperlipidemia, a characteristic of normal pregnancy, which is believed to support fetal growth by increasing substrate availability for placental steroidogenesis and membrane synthesis (2,5).

The observed positive correlation between sdLDL and LDL-C ($r = 0.314$, $p < 0.001$) agrees with findings from previous studies showing that sdLDL constitutes a subfraction of total LDL, whose levels increase in parallel with total LDL concentrations during pregnancy(4,7). The rise in sdLDL among some participants likely results from pregnancy-driven metabolic changes, with estrogen and human placental lactogen increasing hepatic VLDL production and LDL remodeling (17).

Conversely, the inverse correlation between sdLDL and HDL-C ($r = –0.297$, $p < 0.001$) is consistent with the well-documented inverse relationship between atherogenic and protective lipoprotein fractions(18). Low HDL-C with high sdLDL suggests impaired reverse cholesterol transport and increased LDL oxidation, both contributing to endothelial dysfunction and atherosclerosis(3,10). This pattern has also been reported among non-pregnant adults with insulin resistance or metabolic syndrome(9,11).

Interestingly, sdLDL did not correlate significantly with triglycerides or total cholesterol in this study, contrary to the mechanistic link between elevated TG and sdLDL formation described in non-pregnant populations(1). This may be explained by the unique hormonal and metabolic milieu of pregnancy, where hypertriglyceridemia primarily results from estrogen-driven hepatic VLDL overproduction rather than the hepatic lipase–mediated lipoprotein remodeling that typically generates sdLDL(5).

sdLDL levels were not associated with any plasma glucose values, unlike studies in Chinese pregnant women, where sdLDL was higher in those with GDM and correlated with fasting glucose (7). The low sdLDL aligns with other African data (8). This lack of association may result from the cohort's low GDM prevalence (3%) and largely normal glucose levels, minimizing dysglycemia's effect on lipoprotein changes(14).

Comparison between women with high versus low sdLDL levels further demonstrated that those with elevated sdLDL had significantly lower HDL-C and higher LDL-C, confirming the unfavorable lipoprotein pattern observed in correlation analysis. Anthropometric indices (weight, BMI) and glycemic parameters, however, did not differ significantly between the two groups, suggesting that sdLDL alterations may occur independently of overt dyslipidemia or glucose intolerance during pregnancy (13).

The clinical implications of these findings are notable. Although pregnancy-associated hyperlipidemia is generally physiological, elevated sdLDL levels represent a potentially atherogenic lipid subfraction with enhanced susceptibility to oxidation, greater arterial wall penetration, and reduced affinity for LDL receptors (1,4). Elevated sdLDL, combined with reduced HDL-C, could predispose to endothelial dysfunction, preeclampsia, or increased future cardiovascular disease risk in predisposed women(3,9). Thus, sdLDL may serve as an early biomarker for adverse cardiometabolic risk in pregnancy, complementing conventional lipid measurements.

The limited number of GDM cases restricted subgroup analyses, while missing pre-pregnancy lipid profiles and dietary data further constrain the interpretation of sdLDL changes. Also, although the Hirano

precipitation method correlates with advanced techniques (10), its sensitivity may differ from reference methods. These factors represent key limitations of this study.

Despite these limitations, this study provides novel insight into sdLDL patterns among African pregnant women—a population in which such data are scarce(8). The findings underscore the need for larger, longitudinal studies to evaluate sdLDL trajectories across gestation and their potential impact on maternal and fetal outcomes.

Conclusion

This study's findings revealed that sdLDL was significantly positively correlated with LDL-C and negatively correlated with HDL-C, whereas no significant associations were observed with triglycerides (TG), total cholesterol (TC), glucose indices, or blood pressure parameters. The study provides important baseline data on sdLDL behavior among pregnant women in Nigeria (JUTH), a group with limited existing research. Future longitudinal and mechanistic studies should examine sdLDL dynamics across gestation, their links to maternal and fetal outcomes, and whether sdLDL measurement could be a useful marker of cardiometabolic risk in pregnancy care.

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