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Original article

Small Dense Low-Density Lipoprotein as a Predictive Biomarker for Atherosclerosis at the National Heart Centre – Tajura, Libya

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Abstract
Atherosclerosis is a chronic inflammatory vascular disease and one of the leading causes of cardiovascular morbidity and mortality worldwide. It represents the pathological basis of acute coronary syndromes (ACS), including ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina. Small dense low-density lipoprotein (sdLDL) has recently gained attention as a highly atherogenic lipid fraction associated with endothelial dysfunction, plaque instability, and increased cardiovascular risk. This study aimed to evaluate the role of sdLDL as a predictive biomarker for atherosclerosis among Libyan patients attending the National Heart Center, Tajura. A cross-sectional study was conducted on 88 participants, including 68 patients diagnosed with atherosclerosis and 20 apparently healthy controls. Serum sdLDL levels were measured using enzyme-linked immunosorbent assay (ELISA), while lipid profile parameters—including LDL, HDL, total cholesterol, and triglycerides—were analyzed using the Roche Cobas Integra 400 plus automated analyzer. The findings demonstrated that sdLDL levels were higher among patients compared to controls, with 20.6% of patients having elevated sdLDL compared to none of the controls ($p = 0.033$). HDL levels were significantly lower among patients ($p = 0.011$), whereas triglyceride levels were significantly higher ($p = 0.0097$). A statistically significant positive correlation was identified between triglycerides and sdLDL in the patient group ($r = 1.770$, $p = 0.034$). In conclusion, sdLDL is a valuable biomarker for predicting atherosclerosis and cardiovascular risk in the Libyan population, and its assessment alongside conventional lipid parameters may improve early diagnosis and risk stratification.
Keyword. sdLDL, Atherosclerosis, Lipid profile, Cardiovascular risk Biomarker, Libya.

Introduction

Atherosclerosis is a chronic and widespread vascular disease that forms the pathological basis for most cases of coronary heart disease and ischemic stroke, making it one of the leading causes of morbidity and mortality worldwide [1]. It develops through a chronic inflammatory process affecting medium- and large-sized arteries, leading to structural and functional changes in the vessel wall. The atherosclerotic process begins with the penetration of lipid proteins—particularly LDL—into the intimal layer, where they undergo oxidation and trigger a complex inflammatory response involving endothelial cells, monocytes, and smooth muscle cells, resulting in plaque formation [2].

Global Burden of Disease analyses indicate that cardiovascular diseases associated with atherosclerosis continue to rank first among causes of death worldwide, with the burden remaining most severe in low- and middle-income countries [3]. In the Middle East and North Africa region, cardiovascular diseases have become the leading cause of death, driven by rising rates of obesity, metabolic syndrome, diabetes, hypertension, and smoking [4]. In Libya, available studies point to a substantial burden of cardiovascular diseases and high prevalence of risk factors, suggesting a hidden burden of atherosclerosis that is often undetected until acute coronary or cerebral complications arise [5].

Small dense low-density lipoprotein (sdLDL)—a LDL subfamily featuring smaller, denser particles (~15–20 nm)—is markedly more atherogenic than large buoyant LDL, even at comparable LDL-C levels [6]. sdLDL particles penetrate the arterial endothelium more easily, are less efficiently cleared by LDL receptors, are more susceptible to oxidative modification, and remain in circulation longer. These properties render sdLDL a potent driver of endothelial dysfunction and plaque formation. Classic studies by Austin et al. showed that individuals with Pattern B (sdLDL-dominant) LDL distribution had approximately three-fold higher coronary artery disease risk compared to Pattern A individuals [7].

Despite growing evidence of sdLDL clinical significance, its measurement is not yet routinely incorporated into cardiovascular risk assessment, especially in the Libyan population. This study is among the first in Arab countries to focus on sdLDL in patients with atherosclerosis, aiming to bridge this knowledge gap [8].

Classic and contemporary studies demonstrate that sdLDL associates more tightly with atherosclerosis than total LDL, whether in incidence/progression or subclinical imaging markers such as carotid intima-media thickness (CIMT) and arterial calcification [7, 9]. Early work by Austin et al. using gradient gel electrophoresis defined two LDL patterns: Pattern A (large buoyant LDL) and Pattern B (sdLDL dominant), with Pattern B individuals showing approximately three-fold higher coronary artery disease risk despite

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similar total LDL-C [7]. Berneis and Krauss subsequently demonstrated that Pattern B tightly links insulin resistance, elevated triglycerides, low HDL, and metabolic syndrome [10].

Multiple studies tested sdLDL relationships with CIMT. A Japanese longitudinal study showed sdLDL-C to be a stronger 5-year CIMT progression predictor than LDL-C, with sdLDL-C and sdLDL-C/LDL-C ratio remaining the top lipid correlates of CIMT increase after adjustment for traditional risk factors [11]. Regarding coronary artery calcium (CAC), elevated sdLDL-C was linked to higher CAC presence and advanced scores even after LDL-C adjustment [12].

Large prospective cohorts provide strong evidence that sdLDL predicts cardiovascular disease risk independently of traditional LDL-C. The ARIC (Atherosclerosis Risk in Communities) study, involving over 11,000 participants followed for approximately 10–11 years, showed that the highest sdLDL-C quartile had clearly elevated incident coronary heart disease (CHD) risk compared to the lowest, even among individuals with LDL-C <100 mg/dL [13]. The Framingham Offspring Study demonstrated that sdLDL-C was the best single lipid predictor of incident ASCVD, surpassing direct LDL-C and other atherogenic lipid markers [14].

In type 2 diabetes, sdLDL-C elevation is near-universal; diabetic patients show higher sdLDL-C levels linking to greater atherosclerosis severity and higher ASCVD risk versus non-diabetics at the same LDL-C [15]. Metabolic syndrome studies position sdLDL as a near "lipid fingerprint," rising with high triglycerides, low HDL-C, and increased waist circumference [16]. Hypertension often coexists with sdLDL-associated dyslipidemia, with the highest sdLDL-C hypertensives demonstrating greater CIMT and coronary calcification compared to peers with matched LDL-C [17].

ACS patient studies reveal markedly higher sdLDL in STEMI, NSTEMI, and unstable angina versus healthy or non-ischemic chest pain patients [18]. The pivotal Sekimoto 2021 study in statin-treated ACS patients found that elevated on-treatment sdLDL-C was clearly linked to rapid non-culprit lesion progression and increased cardiovascular events despite LDL-C control [19]. A 2023 North African study—among the first measuring sdLDL in a North African ACS sample—reported significant sdLDL elevation in ACS versus healthy controls and confirmed a shift toward atherogenic Pattern B [20].

Beyond biological marker status, sdLDL functions as a true predictive biomarker, improving cardiovascular risk models when added to classical equations and often surpassing non-HDL-C, ApoB, and LDL-P in risk reclassification, especially in metabolic disorder and residual risk categories [14, 21]. The Bekbossynova 2025 Spandidos review confirms sdLDL-C as an independent predictor of cardiovascular events and subclinical atherosclerosis after adjustment for non-HDL-C and ApoB [12].

Despite numerous Libyan studies on traditional risk factors (obesity, hypertension, diabetes, smoking) and metabolic syndrome, virtually no published work examines sdLDL specifically as an atherogenic biomarker or links it to coronary severity or ACS risk in the Libyan community [8]. This study is positioned to fill this critical evidence gap. This study aims to explore the role of sdLDL as a biomarker for atherosclerosis in the Libyan population by analyzing its levels in cardiovascular patients attending the National Heart Center – Tajoura.

Methods

Study Design and Target Population

A cross-sectional study was conducted at the National Heart Center, Tajura, Tripoli. The target population included male and female patients diagnosed with atherosclerosis, aged 20–80 years. The total sample comprised 88 participants: 68 patients diagnosed with atherosclerosis and 20 apparently healthy individuals who served as age-matched controls.

Sample Collection and Storage

Blood samples were collected from patients by venipuncture. Serum samples were separated and stored at −80°C until biochemical analysis. The stored samples were used for sdLDL measurement and lipid profile determination.

Data Collection

Questionnaire Interview

A structured face-to-face questionnaire interview was used to collect demographic and clinical data, including age, sex, smoking status, family history of cardiovascular disease, history of hypertension, diabetes mellitus, and lipid-lowering drug use.

Body Mass Index (BMI)

BMI was calculated as body weight in kilograms divided by height in meters squared (kg/m²). Participants were classified as: underweight (<18.5 kg/m²), normal weight (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), or obese (≥30.0 kg/m²).

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Materials

Table 1. Chemicals and kits used in this study.

Reagent	Supplier
LDL	COBAS INTEGRA® 400plus
Cholesterol	COBAS INTEGRA® 400plus
Triglycerides	COBAS INTEGRA® 400plus
HDL	COBAS INTEGRA® 400plus
sdLDL	Fine Test Company (ELISA)

Methods

Roche Cobas Integra 400 plus

The Roche Cobas Integra 400 plus was used for automated diagnostic clinical chemistry testing, equipped with FP photometer (fluorescence polarimetry), absorbance photometer, and ISE (Ion-Selective Electrode) module.

Determination of Serum LDL

LDL-cholesterol was measured using a homogeneous enzymatic colorimetric assay (selective miscellany solubilization with nonionic detergent). In the presence of Mg^{2+}, a sugar compound selectively reduces the enzymatic reaction of VLDL and chylomicrons, enabling selective LDL-cholesterol determination. Color intensity of the blue Quinone imine dye is proportional to LDL-cholesterol concentration, determined at absorbance 583 nm. Normal reference: <130 mg/dL.

Determination of Serum Cholesterol

Total cholesterol was determined using the enzymatic colorimetric CHOD/PAP method. Cholesterol esterase hydrolyzes cholesterol esters; cholesterol oxidase catalyzes oxidation to form H_2O_2; in the presence of peroxidase, H_2O_2 couples with phenol and 4-aminoantipyrine to form a red-colored Quinone imine dye measured at 520 nm. Normal reference: <200 mg/dL.

Determination of Serum Triglycerides

Triglycerides were determined after enzymatic splitting with lipoprotein lipase. The indicator is a Quinone imine dye generated from 4-aminoantipyrine and 4-chlorophenol by hydrogen peroxide under peroxidase catalysis, measured at 512 nm. Normal reference: <200 mg/dL.

Determination of Serum HDL

HDL-cholesterol was determined using a homogeneous enzymatic colorimetric assay. In the presence of magnesium sulfate and dextran sulfate, LDL, VLDL, and chylomicrons form water-soluble complexes resistant to PEG-modified enzymes. HDL-cholesterol is then determined enzymatically with absorbance measured at 583 nm. Normal references: males >35 mg/dL, females >45 mg/dL.

Determination of Serum sdLDL (ELISA)

The sdLDL ELISA method (Fine Test Company) is a sandwich enzyme-linked immunosorbent assay for quantitative in vitro diagnostic measurement of sdLDL in serum. Anti-sdLDL antibody was pre-coated onto 96-well plates. Biotin-conjugated anti-sdLDL antibody served as the detection antibody. Standards were prepared as serial dilutions (20, 10, 5, 2.5, 1.25, 0.625, 0.312, and 0 nmol/mL). After incubation (90 min at 37°C), biotin-labeled antibody was added (60 min), followed by HRP-Streptavidin (30 min), then TMB substrate (10–20 min in dark). Absorbance was read at 450 nm. Normal references by age: 21–54 years: 0.329–1.249 nmol/mL; 55–75 years: 0.326–1.337 nmol/mL.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics version 29.0.10. Continuous variables were expressed as mean ± standard deviation; categorical variables were summarized as frequencies and percentages. The independent samples t-test was used to compare means between two groups; one-way ANOVA was applied for comparisons involving more than two groups. The chi-square test assessed associations between categorical variables; Fisher's Exact test was applied when expected cell counts were less than 5. Pearson correlation coefficient evaluated relationships between continuous variables, particularly between sdLDL and other lipid profile parameters. A p-value of less than 0.05 was considered statistically significant; all analyses were conducted using two-tailed tests.

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Results and discussion

Demographic Characteristics

Table 2. Distribution of gender among patients and controls.

Gender	Patients n	Patients %	Controls n	Controls %
Female	34	50.0	7	35.0
Male	34	50.0	13	65.0

Chi-square = 0.860, p-value = 0.354 (not significant).

The distribution of gender showed an equal split among patients (50.0% female, 50.0% male), while controls had a higher proportion of males (65.0%). No statistically significant difference was observed between groups ($x^2 = 0.860$, $p = 0.354$), indicating that gender did not serve as a confounding variable in this study.

Table 3. Distribution of age groups among patients and controls.

Age Group	Patients n	Patients %	Controls n	Controls %
<40	1	1.5	6	30.0
40–49	7	10.3	6	30.0
50–59	16	23.5	5	25.0
60–69	20	29.4	0	0.0
≥70	24	35.3	3	15.0

Chi-square = 27.847, p-value < 0.001 (statistically significant).*

The majority of patients were aged ≥70 years (35.3%) and 60–69 years (29.4%), whereas controls were mainly distributed within younger age categories. A statistically significant difference was observed between patients and controls regarding age distribution ($x^2 = 27.847$, $p < 0.001$), reflecting the known association between advancing age and atherosclerosis development.

Table 4. Distribution of BMI groups among patients and controls.

BMI Group	Patients n	Patients %	Controls n	Controls %
Underweight	1	1.5	0	0.0
Normal	14	20.6	9	45.0
Overweight	27	39.7	11	55.0
Obese	26	38.2	0	0.0

Chi-square = 12.302, p-value = 0.006 (statistically significant).*

Overweight and obese participants constituted the majority of patients (39.7% and 38.2%, respectively), whereas no obese participants were found in the control group. The statistically significant difference in BMI distribution ($x^2 = 12.302$, $p = 0.006$) underscores the well-established contribution of excess body weight to atherosclerosis through metabolic dysregulation, including elevated sdLDL production.

Medical History

Table 5. Distribution of medical history variables among patients and controls.

Variable	Patients (n=68)	Controls (n=20)	x^2	p-value
Hypertension (Yes)	53 (77.9%)	0 (0.0%)	56.21	<0.001*
Diabetes Mellitus (Yes)	46 (67.6%)	0 (0.0%)	45.33	<0.001*
Lipid-lowering Drug Use (Yes)	48 (70.6%)	0 (0.0%)	48.90	<0.001*
Complications (Yes)	50 (73.5%)	0 (0.0%)	52.44	<0.001*
Family History (Yes)	3 (4.4%)	0 (0.0%)	0.91	0.340

** Statistically significant (p < 0.05).*

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Hypertension (77.9%), diabetes mellitus (67.6%), and lipid-lowering drug use (70.6%) were significantly more prevalent among patients compared to controls (all $p < 0.001$). Of patients using lipid-lowering drugs, the majority had been on treatment for more than 5 years (35.3%). Cardiovascular complications occurred in 73.5% of patients, with ischemic heart disease/coronary artery disease/ACS being most prevalent (44.1%), followed by heart failure (22.1%), chronic kidney disease (14.7%), and cerebrovascular accidents (7.4%). No statistically significant difference was found between groups regarding family history of disease ($p = 0.34$).

Biomarker Distribution (Fisher's Exact Test)

Table 6. Distribution of LDL levels among patients and controls.

LDL Level	Patients n	Patients %	Controls n	Controls %
Low	0	0.0	0	0.0
Normal	59	86.8	20	100.0
High	9	13.2	0	0.0

Fisher's Exact Test p-value = 0.444 (not significant).

Table 7. Distribution of HDL levels among patients and controls.

HDL Level	Patients n	Patients %	Controls n	Controls %
Low	36	52.9	4	20.0
Normal	32	47.1	16	80.0
High	0	0.0	0	0.0

Fisher's Exact Test p-value = 0.011 (statistically significant).*

Table 8. Distribution of total cholesterol (CHO) levels among patients and controls.

CHO Level	Patients n	Patients %	Controls n	Controls %
Low	0	0.0	0	0.0
Normal	57	83.8	20	100.0
High	11	16.2	0	0.0

Fisher's Exact Test p-value = 0.283 (not significant).

Table 9. Distribution of triglyceride (TAG) levels among patients and controls.

TAG Level	Patients n	Patients %	Controls n	Controls %
Low	0	0.0	0	0.0
Normal	51	75.0	20	100.0
High	17	25.0	0	0.0

Fisher's Exact Test p-value = 0.010* (statistically significant).

Table 10. Distribution of sdLDL levels among patients and controls.

sdLDL Level	Patients n	Patients %	Controls n	Controls %
Low	0	0.0	0	0.0
Normal	54	79.4	20	100.0
High	14	20.6	0	0.0

Fisher's Exact Test p-value = 0.033 (statistically significant).*

HDL levels were significantly lower in patients compared to controls ($p = 0.011$), and triglyceride levels were significantly higher ($p = 0.010$). Notably, 20.6% of patients had elevated sdLDL compared to none of the controls ($p = 0.033$). with a statistically significant difference ($p = 0.033$). In contrast, LDL and total cholesterol did not differ significantly between groups ($p > 0.05$), demonstrating the limited sensitivity of conventional lipid parameters in detecting atherogenic dyslipidemia in this population.

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Descriptive Statistics of Lipid Profile

Table 11. Descriptive statistics summary of lipid profile differences between patients and controls.

Variable	Patients (Mean ± SD)	Controls (Mean ± SD)	t-test	p-value
Total Cholesterol (mg/dL)	156.69 ± 52.81	150.25 ± 22.76	0.776	0.220
Triglycerides (mg/dL)	158.71 ± 72.47	112.00 ± 28.71	-4.23	0.003*
HDL (mg/dL)	41.15 ± 16.66	43.65 ± 8.13	-0.90	0.184
LDL (mg/dL)	79.75 ± 39.50	88.55 ± 21.87	1.264	0.107
sdLDL (nmol/mL)	1.12 ± 1.09	0.90 ± 0.17	1.592	0.058

** Statistically significant (p < 0.05).*

Triglyceride levels were significantly higher in patients compared to controls (158.71 ± 72.47 vs. 112.00 ± 28.71 mg/dL, p = 0.003). Although mean sdLDL was higher in patients (1.12 ± 1.09 nmol/mL) versus controls (0.90 ± 0.17 nmol/mL), the difference did not reach statistical significance in the continuous t-test (p = 0.058), likely reflecting the relatively small sample size and confounding effect of lipid-lowering drug use in 70.6% of patients, which would be expected to reduce measured sdLDL levels. Total cholesterol, HDL, and LDL showed no significant differences between groups.

Co-occurrence of High sdLDL with Other Lipid Abnormalities

Table 12. Co-occurrence of high sdLDL with other lipid abnormalities among patients (Fisher's Exact Test).

Lipid Biomarker	High sdLDL (n = 14)	p-value	Statistical Interpretation
LDL	3 (21.4%)	0.214	Weak co-occurrence
HDL (low)	0 (0.0%)	1.000	No co-occurrence
Total Cholesterol	4 (28.6%)	0.286	Low co-occurrence
Triglycerides (TAG)	13 (92.9%)	0.001*	Very strong co-occurrence

** Statistically significant (p < 0.05).*

Among the 14 patients with elevated sdLDL, 92.9% also had elevated triglycerides (p = 0.001), indicating a very strong and statistically significant co-occurrence. This finding is consistent with the well-established metabolic pathway through which hypertriglyceridemia drives CETP-mediated lipid exchange and hepatic lipase activity, ultimately generating small dense LDL particles. No significant co-occurrence was observed between elevated sdLDL and elevated LDL, total cholesterol, or low HDL levels.

Correlation of sdLDL with Lipid Profile Parameters

Table 13. Pearson correlation coefficients between sdLDL and other lipid parameters in patients and controls.

Variable	r (Patients)	p (Patients)	r (Controls)	p (Controls)
Total Cholesterol	-0.002	0.492	-0.109	0.326
Triglycerides	1.770	0.034*	0.204	0.197
HDL	-0.092	0.228	0.040	0.434
LDL	-0.001	0.496	-0.080	0.371

** Statistically significant (p < 0.05).*

In the patient group, triglycerides showed a statistically significant positive correlation with sdLDL (r = 1.770, p = 0.034). All other lipid parameters showed non-significant correlations in both groups. These findings reinforce the metabolic link between hypertriglyceridemia and elevated sdLDL, consistent with Hori et al. [22] (r = 0.67, p < 0.001 in ACS patients) and Cho et al. [23] (triglycerides as the principal sdLDL determinant in metabolic syndrome).

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Risk Factors for sdLDL Levels

Table 14. Descriptive statistics summary of demographic characteristics and medical history as risk factors for sdLDL levels.

Variable	Category	sdLDL Mean ± SD	Test	p-value
Gender	Male	1.24 ± 1.52	t = 0.93	0.358
	Female	0.99 ± 0.33		
Age Group	<50 years	0.91 ± 0.22	F = 0.76	0.474
	50–64 years	0.95 ± 0.30		
	≥65 years	1.27 ± 1.48		
Smoking	Yes	1.11 ± 0.23	t = -0.02	0.985
	No	1.12 ± 1.15		
BMI	Normal	1.02 ± 0.34	F = 1.82	0.171
	Overweight	1.42 ± 1.68		
	Obese	0.86 ± 0.29		
Hypertension	Yes	1.18 ± 1.24	t = 0.86	0.395
Diabetes Mellitus	Yes	1.14 ± 1.30	t = 0.23	0.822
Family History	Yes	0.95 ± 0.28	t = -0.31	0.759

None of the demographic or medical history variables showed a statistically significant effect on sdLDL levels (all p > 0.05).

No statistically significant associations were observed between sdLDL levels and any demographic or clinical variable. Although males and individuals aged ≥65 years exhibited slightly higher sdLDL values, and overweight participants showed the highest sdLDL mean, these differences were not statistically significant. This may be explained by the relatively small sample size and the confounding effect of lipid-lowering drug use. Previous studies by Shen et al. [24] and Shoji et al. [25] reported significant sdLDL elevation in males, elderly individuals, smokers, and hypertensives; discrepancies may reflect differences in sample size, ethnicity, and clinical status.

Discussion

The present study demonstrated that patients with atherosclerosis exhibited a significantly higher prevalence of elevated sdLDL (20.6%) compared to controls (0.0%, p = 0.033). These findings are consistent with Otrante et al. [20], who reported significantly higher sdLDL concentrations in ACS patients versus healthy controls in a North African population (0.303 ± 0.478 vs. 0.023 ± 0.043 mmol/L, p < 0.001), and with Ikezaki et al. [14], who demonstrated sdLDL-C as a strong predictor of ASCVD (hazard ratio = 1.42, p < 0.0001).

The sole lipid parameter significantly correlated with sdLDL was triglycerides (r = 1.770, p = 0.034). Furthermore, 92.9% of patients with elevated sdLDL also had elevated triglycerides (p = 0.001). This strong relationship is supported by Hori et al. [22] and Cho et al. [23], who identified triglycerides as the dominant determinant of sdLDL concentration. The metabolic mechanism is well established: hypertriglyceridemia drives CETP-mediated neutral lipid exchange and hepatic lipase activity, progressively removing triglycerides and phospholipids from LDL particles to generate the characteristic small, dense, cholesterol-depleted phenotype.

Conventional lipid parameters (LDL, HDL, total cholesterol) did not differ significantly between groups, consistent with Hirano et al. [26], who observed elevated sdLDL among coronary heart disease patients without significant differences in LDL-C, suggesting sdLDL provides additive information beyond routine lipid measurements. Shoji et al. [25] further demonstrated that sdLDL-C had a stronger relationship with carotid intima-media thickness than LDL-C or triglycerides after adjustment for conventional cardiovascular risk factors. Saether et al. [27] showed that patients with significant coronary artery disease had 30% higher sdLDL concentrations than those with non-significant coronary atherosclerosis, despite similar conventional cholesterol levels.

The absence of significant associations between sdLDL and demographic or clinical variables may be attributed to the limited sample size and the confounding effect of lipid-lowering drug use, present in 70.6% of patients. Overall, these results support the hypothesis that sdLDL, particularly in the context of

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elevated triglycerides, is a more sensitive indicator of atherogenic dyslipidemia than conventional LDL-C in this Libyan population.

Conclusion

This study aimed to evaluate the role of sdLDL as a biomarker for predicting the risk of atherosclerosis among patients attending the National Heart Center – Tajoura. The findings demonstrated that sdLDL levels were higher among patients with atherosclerosis compared to the control group, suggesting a potential role of this biomarker in the early identification of individuals at increased risk, particularly in patients who may present with a normal conventional lipid profile. In addition, the study revealed significantly elevated triglyceride levels among the patient group, along with a statistically significant positive correlation between triglycerides and sdLDL levels, indicating a close relationship between abnormalities in triglyceride metabolism and the formation of small dense LDL particles—considered more atherogenic and more likely to contribute to atherosclerosis progression. Furthermore, significant differences were observed between patients and controls regarding age, BMI, hypertension, diabetes mellitus, lipid-lowering drug use, and disease complications, highlighting the contribution of traditional cardiovascular risk factors to atherosclerosis development. Overall, these findings support the potential value of sdLDL as an additional biomarker alongside conventional lipid profile parameters for improving cardiovascular risk assessment and facilitating early detection of atherosclerosis. Further large-scale prospective studies are recommended to confirm its clinical significance within the Libyan population.

Study limitations

1. The relatively small sample size, particularly in the control group, may have affected the statistical power of the study.
2. The use of a cross-sectional study design limits the ability to establish causal relationships between elevated sdLDL levels and the development of atherosclerosis.
3. The study was conducted at a single healthcare institution, which may limit the generalizability of the findings.
4. A proportion of patients were using lipid-lowering medications, which may have influenced the biochemical measurements.
5. Some potential influencing factors, such as dietary habits, genetic factors, and physical activity levels, were not evaluated.
6. The study relied on laboratory measurements obtained during a specific time period without long-term follow-up.

Recommendations

1. Future studies should be conducted using larger and more representative sample sizes to increase statistical power and improve the accuracy of the findings.
2. Multicenter studies involving different regions across Libya are recommended to enhance the generalizability of the results to the broader Libyan population.
3. Future longitudinal studies should be carried out to determine the causal relationship between elevated sdLDL levels and the development of atherosclerosis and cardiovascular complications.
4. The effect of lipid-lowering medications on sdLDL levels should be investigated separately to avoid their influence as potential confounding factors.
5. Further research should expand on factors associated with sdLDL formation, such as insulin resistance, dietary habits, genetic factors, and physical activity levels.
6. It is recommended that sdLDL be included in specialized cardiovascular risk assessment research, particularly among patients who present with normal conventional lipid profile results despite having persistent high-risk factors.

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