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Assessing Dyslipidemia Through Non-High-Density Lipoprotein (HDL) Cholesterol: A Moroccan Study at Mohammed VI University Hospital

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Abstract

Background: Non-high-density lipoprotein cholesterol (non-HDL-C) includes all atherogenic lipoproteins and is recognized by international guidelines as a secondary therapeutic target, particularly in patients with hypertriglyceridemia. Despite its simplicity and lack of additional analytical cost, its use remains limited in routine clinical laboratory practice.

Objective: To assess the distribution of non-HDL-C in a large population of patients undergoing lipid testing, to analyze its concordance with low-density lipoprotein cholesterol (LDL-C), and to evaluate its added value in the presence of hypertriglyceridemia.

Materials and methods: A monocentric, retrospective, observational study was conducted in the Central Biochemistry Laboratory of Mohammed VI University Hospital, Oujda, using data extracted from the laboratory information system for lipid profiles performed between January 1 and August 7, 2024. A total of 4,790 lipid profiles from 4,095 distinct patients were analyzed. Non-numeric results or results associated with preanalytical or analytical nonconformities were excluded. Non-HDL-C was calculated as total cholesterol (TC) minus HDL-C. Lipid parameters were described, correlations were assessed using Spearman's coefficient, LDL-C/non-HDL-C concordance was assessed using Cohen's kappa, and factors associated with elevated non-HDL-C were analyzed using binary logistic regression.

Results: Mean non-HDL-C concentration was 1.34 ± 0.45 g/L. The prevalence of elevated non-HDL-C was 49.5%, 36.2%, and 24.2% using thresholds of 1.30, 1.45, and 1.60 g/L, respectively. Non-HDL-C was very strongly correlated with TC ($\rho = 0.954$) and LDL-C ($\rho = 0.926$). Concordance between LDL-C ⩾ 1.30 g/L and non-HDL-C ⩾ 1.60 g/L was 91.4% ($\kappa = 0.771$). Discordance, defined as normal LDL-C with elevated non-HDL-C, was observed in 3.5% of lipid profiles and was concentrated among patients with TG ⩾ 1.50 g/L.

Conclusion: Non-HDL-C is strongly correlated with LDL-C but provides complementary information in patients with hypertriglyceridemia. Its calculation requires no additional analytical cost, and systematic reporting of non-HDL-C in lipid profiles may improve the biological identification of atherogenic lipid patterns in clinical laboratory practice.

Categories: Nutrition, Cardiology, Pathology
Keywords: cardiovascular risk, clinical biochemistry, dyslipidemia, hypertriglyceridemia, ldl cholesterol, non-hdl cholesterol

Introduction

Cardiovascular diseases (CVDs) are the leading cause of death worldwide, causing an estimated 19.8 million deaths in 2022, or approximately 32% of all global deaths [1]. This major public-health burden reinforces the need for simple, accessible tools to improve cardiovascular risk stratification. Dyslipidemia is one of the major modifiable risk factors for atherosclerosis because it promotes the accumulation of atherogenic lipoproteins within the vascular wall. Cardiovascular prevention therefore relies on early identification and management of lipid abnormalities. Conventional lipid profile parameters, particularly total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG), remain central to risk assessment and therapeutic monitoring [2-4].

LDL-C has historically been considered the primary therapeutic target in international guidelines [2,4]. Numerous interventional and genetic studies have shown that LDL-C reduction is associated with a significant reduction in cardiovascular events and that LDL-containing particles play a causal role in atherosclerotic CVD [3]. However, LDL-C does not fully reflect all circulating atherogenic lipoproteins. In

particular, TG-rich lipoproteins, such as very-low-density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), and their remnants, contribute to residual atherogenic risk [5-7].

Non-HDL-C, calculated by subtracting HDL-C from TC, represents the total amount of cholesterol contained in all atherogenic lipoproteins, not only LDL but also VLDL, IDL, remnant particles, and lipoprotein(a) [8,9]. Clinically, this makes non-HDL-C a broader marker of atherogenic cholesterol burden than LDL-C alone. Unlike Friedewald-calculated LDL-C, non-HDL-C is not directly dependent on the TG term in the equation and remains particularly useful when TG is elevated, especially in mild-to-moderate hypertriglyceridemia [6,9,10]. Its simplicity, reproducibility, and absence of additional analytical cost make it an attractive marker for routine laboratory reporting [9].

Recent European and American guidelines recognize non-HDL-C as a secondary treatment target after LDL-C and recommend its use for cardiovascular risk assessment, particularly in patients with hypertriglyceridemia, diabetes, obesity, or metabolic syndrome [2,4,9]. Several studies have suggested that non-HDL-C may be a better predictor of residual cardiovascular risk than LDL-C in selected populations, especially when TG-rich lipoproteins are increased [8,11-13].

Despite these recommendations, non-HDL-C remains underused in daily clinical laboratory practice [9]. In many institutions, lipid reports still emphasize LDL-C, although non-HDL-C can be calculated immediately from already measured parameters. This matters clinically because LDL-C and non-HDL-C can be discordant, and patients with normal LDL-C but elevated non-HDL-C may retain residual atherogenic risk [12,13]. In Morocco and, more broadly, in North Africa, data on non-HDL-C remain scarce. Global pooled analyses provide national estimates of mean non-HDL-C derived from population surveys [14], whereas available Moroccan lipid studies have mainly focused on selected populations, such as patients with type 2 diabetes, and have reported conventional lipid parameters and ratios [15]. To our knowledge, the distribution of non-HDL-C in routine laboratory practice and its concordance with LDL-C according to TG levels have not been described in a large Moroccan hospital population. Such local data are needed to determine whether systematic reporting of non-HDL-C would be useful in Moroccan clinical laboratories.

The primary objective of this study was to assess the distribution of non-HDL-C in a large population of patients undergoing lipid testing in the central laboratory of Mohammed VI University Hospital, Oujda. Secondary objectives were to describe the prevalence of elevated non-HDL-C using different thresholds, to study its variation according to age and gender, to evaluate its correlations with other lipid parameters, to assess its concordance with LDL-C, to examine its contribution to hypertriglyceridemia, and to identify biological and demographic factors associated with its elevation.

Materials And Methods

Study design and population

This was a monocentric, retrospective, observational study conducted in the Biochemistry Laboratory of Mohammed VI University Hospital, Oujda, Morocco. Biological data from lipid profiles performed between January 1, 2024, and August 7, 2024 were extracted from the laboratory information system.

All lipid profiles, including at least TC and HDL-C measurements, were considered for analysis. Non-numeric results were excluded when they corresponded, according to the laboratory information system, to a preanalytical or analytical nonconformity, such as hemolyzed, icteric, or markedly lipemic samples, non-interpretable results, technical errors, or lack of biological validation. Patients receiving lipid-lowering therapy or presenting intercurrent diseases could not be systematically excluded because these clinical data were not available in the biological database; this was considered a major limitation of the study. The main non-HDL-C analysis was performed only in patients with simultaneous TC and HDL-C measurements.

Analytical methods and quality control

Assays were performed on ARCHITECT cSystems analyzers (Abbott, Abbott Park, IL, USA), according to the manufacturer's instructions and the laboratory's standard operating procedures [16]. TC, HDL-C, LDL-C, and TG values were obtained from the routine lipid profile generated on the ARCHITECT platform. HDL-C was measured using the Ultra HDL reagent (Abbott). Internal quality control was based on at least two control levels and monitored using Levey-Jennings charts [17]. Calibration was performed at each reagent lot change or when required by quality-control results [18]. The laboratory participates in the Bio-Rad External Quality Assessment Services (EQAS) clinical chemistry program.

Biological parameters

The lipid parameters studied were TC, HDL-C, LDL-C, TG, and non-HDL-C. Non-HDL-C was calculated as follows: non-HDL-C = TC − HDL-C

LDL-C reported by the laboratory was calculated using the Friedewald formula [19] only when the conditions for its application were met, notably TG < 4.00 g/L and no biological evidence suggestive of chylomicronemia

or major interference. A clinically important limitation of calculated LDL-C is that its reliability decreases in hypertriglyceridemia, particularly when TG exceed 2.00 g/L; therefore, LDL-C values in this subgroup were interpreted with caution [9,10].

Definitions of lipid abnormalities

LDL-C ⩾ 1.30 g/L: descriptive threshold used to identify profiles requiring biological attention; it was not considered a universal therapeutic target. Elevated non-HDL-C: ⩾ 1.30 g/L, ⩾ 1.45 g/L, and ⩾ 1.60 g/L. These thresholds were used as graded descriptive thresholds covering values commonly used in clinical and epidemiological practice; they do not replace individualized targets based on global cardiovascular risk [2,4,20]. Hypertriglyceridemia: TG ⩾ 1.50 g/L; severe hypertriglyceridemia: TG ⩾ 2.00 g/L; low HDL-C: < 0.40 g/L in men and < 0.50 g/L in women. Atherogenic dyslipidemia was defined as the association of hypertriglyceridemia (TG ⩾ 1.50 g/L) and low HDL-C.

Variables and data limitations

Demographic variables included age and gender. Biological variables included TC, HDL-C, LDL-C, TG, and non-HDL-C. Patients were divided into six age groups (<18 years, 18-29 years, 30-44 years, 45-59 years, 60-74 years, and ⩾75 years) to assess changes in non-HDL-C according to age. Individual clinical information (cardiovascular history, diabetes, obesity, smoking, lipid-lowering therapy, or intercurrent disease) was not available in the laboratory extraction, preventing multivariable adjustment for these major confounders.

Statistical analysis

Statistical analyses were performed using Python (version 3.12, Python Software Foundation, Fredericksburg, VA, USA). Quantitative variables were described according to their distribution. Variables compatible with a normal distribution were summarized as mean ± standard deviation (SD), whereas non-normally distributed quantitative variables were summarized as median and interquartile range (IQR: Q1-Q3), with extreme values when appropriate. Qualitative variables were expressed as counts and percentages.

Distribution normality was assessed before comparative analyses, and statistical tests were selected according to the distribution of the data. Because lipid parameters, particularly TG, were not systematically normally distributed, comparisons between two groups were performed using the Mann-Whitney test, while comparisons among several age classes were performed using the Kruskal-Wallis test. Associations between non-HDL-C and other lipid parameters were assessed using Spearman's correlation coefficient.

The unit of analysis was the lipid profile, defined as all lipid parameters requested for the same patient on the same day. Because some patients were tested more than once during the study period, the 4,790 profiles included 695 repeat profiles (14.5%) from 542 patients. When a parameter was reported more than once within the same profile, the mean value was used. Descriptive, correlation, and concordance analyses were performed on all profiles. To account for within-patient correlation in the logistic regression, 95% confidence intervals were estimated using cluster-robust (sandwich) standard errors, with the patient as the cluster. In addition, a sensitivity analysis restricted to the first lipid profile of each patient (n = 4,095) was performed for the main correlation, concordance, and regression analyses. Gender distribution was described at the patient level.

The dichotomous comparison between LDL-C ⩾ 1.30 g/L and non-HDL-C ⩾ 1.60 g/L was used to assess qualitative concordance and was evaluated using Cohen's kappa coefficient [21]. A quantitative Bland-Altman analysis would have been useful to assess systematic bias between LDL-C and non-HDL-C [22]; however, it was not performed and is therefore presented as a methodological limitation. Factors associated with elevated non-HDL-C (⩾ 1.60 g/L) were studied using binary logistic regression; results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). Crude ORs were first calculated for each variable. A multivariable model including the variables available in the database (age ⩾ 45 years, gender, and hypertriglyceridemia) was then fitted; because the two TG thresholds overlap, separate models were fitted for TG ⩾ 1.50 g/L and TG ⩾ 2.00 g/L. The models could not be adjusted for comorbidities or treatments. No prior sample-size calculation was performed because the study used all available lipid profiles during the study period; therefore, confidence-interval width was used to assess estimate precision. All tests were two-sided, and $p < 0.05$ was considered statistically significant.

Ethical considerations

This retrospective study was conducted using anonymized biological data extracted from the laboratory information system. Analyses were performed in accordance with ethical principles applicable to biomedical research and confidentiality requirements for patient data. The study protocol was approved by the Ethics Committee for Biomedical Research of the Faculty of Medicine and Pharmacy, Mohammed First University, Oujda, Morocco (approval number 21).

Results

Study population

During the period from January 1 to August 7, 2024, 21,628 individual lipid test results (5,304 TC, 5,120 HDL-C, 5,005 LDL-C, and 6,199 TG), corresponding to 6,260 lipid profiles, were extracted from the laboratory database. Eight non-numeric results corresponding to analytical or preanalytical nonconformities were excluded.

Among the 6,260 available lipid profiles, 4,790 included simultaneous TC and HDL-C measurements, allowing calculation of non-HDL-C; the remaining 1,470 profiles were excluded from the non-HDL-C analysis. The 4,790 analyzed profiles came from 4,095 distinct patients; 695 profiles (14.5%) were therefore repeat measurements: 3,553 patients had a single profile, and 542 had two or more (445 had two, 69 had three, and 28 had four or more). The patients included 2,380 women (58.1%) and 1,715 men (41.9%). The mean age was 51.4 ± 18.7 years, with a median of 55 years (IQR: 38-65 years).

Description of lipid parameters

The main characteristics of lipid parameters are presented in Table *1*. Mean TC concentration was 1.76 ± 0.48 g/L, mean HDL-C was 0.42 ± 0.13 g/L, and mean LDL-C was 1.08 ± 0.40 g/L. The mean TG concentration was 1.30 ± 0.91 g/L. Non-HDL-C had a mean value of 1.34 ± 0.45 g/L and a median of 1.29 g/L (IQR: 1.04-1.59 g/L).

Parameter	Mean ± SD (g/L)
Total cholesterol	1.76 ± 0.48
HDL-C	0.42 ± 0.13
LDL-C	1.08 ± 0.40
Triglycerides	1.30 ± 0.91
Non-HDL-C	1.34 ± 0.45

TABLE 1: Main characteristics of lipid parameters.

LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol

Prevalence of lipid abnormalities

The prevalence of LDL-C ⩾ 1.30 g/L was 25.9%. Depending on the threshold used, the proportion of patients with elevated non-HDL-C was 49.5% for ⩾ 1.30 g/L, 36.2% for ⩾ 1.45 g/L, and 24.2% for ⩾ 1.60 g/L.

Hypertriglyceridemia (TG ⩾ 1.50 g/L) was observed in 27.4% of patients, while 12.4% had TG ⩾ 2.00 g/L. Low HDL-C was found in 62.4% of lipid profiles and atherogenic dyslipidemia in 21.6% of cases. This high prevalence of low HDL-C should be interpreted with caution, as it depends on laboratory reference values and the hospital-based profile of the study population.

Comparison according to gender

The concentrations of the main lipid parameters differed significantly according to gender in this hospital-based sample. Women showed higher observed TC, HDL-C, LDL-C, and non-HDL-C values than men (all $p < 0.001$), a finding that should be interpreted in light of potential differences in age distribution, menopausal status, and hospital recruitment. Median non-HDL-C was 1.37 g/L in women versus 1.21 g/L in men ($p < 0.001$). TG were also slightly higher in women ($p = 0.016$).

Variation of non-HDL-C according to age

Non-HDL-C varied significantly according to age group ($p < 0.001$). The highest concentrations were observed among patients aged 45-59 years, with a mean of 1.43 g/L and a median of 1.42 g/L. A moderate decrease was subsequently observed after 60 years of age.

Correlations between non-HDL-C and other lipid parameters

Non-HDL-C was very strongly correlated with TC ($\rho = 0.954$) and LDL-C ($\rho = 0.926$). A moderate correlation was found with TG ($\rho = 0.510$), whereas correlations with HDL-C ($\rho = 0.188$) and age ($\rho = 0.067$) were weak.

Concordance between LDL-C and non-HDL-C

Among the 4,774 lipid profiles with simultaneous LDL-C and non-HDL-C values, the comparison between LDL-C ⩾ 1.30 g/L and non-HDL-C ⩾ 1.60 g/L showed substantial concordance, with an overall agreement of 91.4% and a Cohen's kappa coefficient of 0.771.

Discordance between the two parameters was observed in a limited but clinically relevant proportion of patients. Thus, 165 of the 4,774 profiles (3.5%) had normal LDL-C with elevated non-HDL-C, while 246 profiles (5.2%) had elevated LDL-C despite non-HDL-C below the selected threshold.

Contribution of non-HDL-C in hypertriglyceridemia

The distribution of the 165 discordant profiles (normal LDL-C/elevated non-HDL-C) across mutually exclusive TG categories is shown in Table *2* and Figure *1*. No discordance of this type was observed among profiles with TG < 1.50 g/L (0 of 3,468). Overall, 164 of the 1,302 profiles with TG ⩾ 1.50 g/L (12.6%) were discordant: 21 of 715 (2.9%) in the 1.50-1.99 g/L category and 143 of 587 (24.4%) when TG was ⩾ 2.00 g/L; the remaining discordant profiles had no TG value. Thus, 86.7% of all discordant profiles occurred in patients with TG ⩾ 2.00 g/L, confirming the value of stratification according to TG.

TG category (g/L)	Lipid profiles, n	Normal LDL-C/elevated non-HDL-C, n (%)	Share of all discordant profiles, %
< 1.50	3,468	0 (0.0)	0.0
1.50-1.99	715	21 (2.9)	12.7
≥ 2.00	587	143 (24.4)	86.7
TG not available	4	1 (25.0)	0.6
Total	4,774	165 (3.5)	100

TABLE 2: Distribution of profiles with normal LDL-C (< 1.30 g/L) and elevated non-HDL-C (≥ 1.60 g/L) across triglyceride categories.

LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol

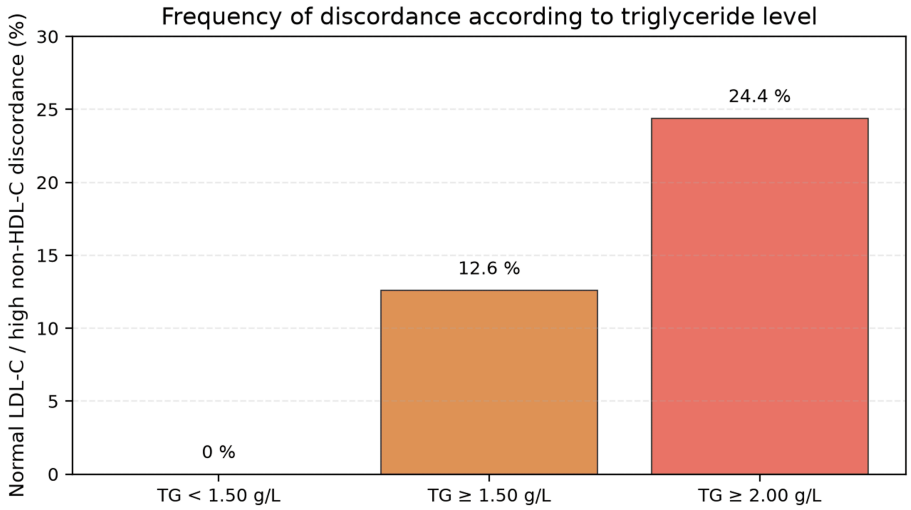


FIGURE 1: Frequency of normal LDL-C/elevated non-HDL-C discordance according to TG concentrations.

LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol; TG: triglycerides

The frequency of non-HDL-C ⩾ 1.60 g/L increased in parallel with TG concentrations: 15.4% in patients with TG < 1.50 g/L, 47.6% in those with TG ⩾ 1.50 g/L, and 56.3% when TG was ⩾ 2.00 g/L.

Factors associated with elevated non-HDL-C

In crude logistic regression analysis, age ⩾ 45 years was associated with an increased likelihood of non-HDL-C ⩾ 1.60 g/L (OR = 1.75; 95% CI: 1.51-2.03). Hypertriglyceridemia was the strongest associated factor, with a crude OR of 5.00 (95% CI: 4.34-5.77) for TG ⩾ 1.50 g/L and 5.27 (95% CI: 4.41-6.30) for TG ⩾ 2.00 g/L, whereas male gender was associated with a lower probability of elevated non-HDL-C (OR = 0.63; 95% CI: 0.55-0.72). In the multivariable model with cluster-robust CIs, these associations persisted: age ⩾ 45 years (adjusted OR = 1.56; 95% CI: 1.31-1.85), male gender (adjusted OR = 0.62; 95% CI: 0.53-0.73), and TG ⩾ 1.50 g/L (adjusted OR = 4.93; 95% CI: 4.24-5.74). In the model including TG ⩾ 2.00 g/L instead, the adjusted OR for TG was 5.52 (95% CI: 4.54-6.70). These ORs should be interpreted as incompletely adjusted biological associations because major clinical variables, including diabetes, obesity, smoking status, lipid-lowering treatment, and cardiovascular history, were not available.

Sensitivity analysis restricted to one profile per patient

When the analysis was restricted to the first lipid profile of each patient (n = 4,095), results were virtually unchanged. Non-HDL-C remained very strongly correlated with TC (ρ = 0.953) and LDL-C (ρ = 0.931). Concordance between LDL-C ⩾ 1.30 g/L and non-HDL-C ⩾ 1.60 g/L was 91.5% (κ = 0.777; n = 4,082); 132 profiles (3.2%) showed normal LDL-C with elevated non-HDL-C; and the adjusted OR for TG ⩾ 1.50 g/L was 4.84 (95% CI: 4.14-5.66).

Discussion

This study shows that non-HDL-C can be calculated in most patients undergoing a standard lipid profile without additional analytical cost. The results demonstrate a high prevalence of elevated non-HDL-C, a strong correlation with LDL-C, and a clinically relevant discordance between these two parameters among patients with hypertriglyceridemia. Hypertriglyceridemia was the factor most strongly associated with elevated non-HDL-C (adjusted OR = 4.93 for TG ⩾ 1.50 g/L). This OR describes a statistical association in a retrospective, cross-sectional dataset with limited adjustment for clinical confounders; it should not be interpreted as a five-fold increase in risk or as evidence of a causal relationship. Part of this association is also structural, because the cholesterol carried by TG-rich lipoproteins, which increases with TG, is itself a component of non-HDL-C [5-7,9].

These findings suggest that non-HDL-C is not merely a substitute for LDL-C; rather, it provides complementary information for identifying patients with increased atherogenic lipid burden when TG is elevated. This observation is consistent with international recommendations, which consider non-HDL-C as a secondary target, especially in patients with hypertriglyceridemia, diabetes, obesity, or metabolic syndrome [2,4,9].

In our study, non-HDL-C was very strongly correlated with TC (ρ = 0.954) and LDL-C (ρ = 0.926). These findings were expected, as LDL is the main circulating atherogenic cholesterol fraction in most populations. Similar correlation coefficients have been reported in several studies evaluating the performance of non-HDL-C [8,11,12].

Despite this strong correlation, LDL-C and non-HDL-C do not measure exactly the same lipid compartment. LDL-C estimates only the cholesterol transported by LDL particles, whereas non-HDL-C represents the TC content of potentially atherogenic lipoproteins, including LDL, VLDL, IDL, remnant particles, and lipoprotein(a). Thus, non-HDL-C more comprehensively reflects global atherogenic burden than LDL-C alone [7-9,13].

Although overall concordance between LDL-C and non-HDL-C was high in our series (91.4%; κ = 0.771), biological discordance persisted in a clinically relevant proportion of patients. In particular, 3.5% of lipid profiles had normal LDL-C with elevated non-HDL-C, suggesting potential underestimation of atherogenic burden when LDL-C alone is considered.

This proportion is lower than that reported by Du et al., who observed more frequent discordance in a population with nonalcoholic fatty liver disease, characterized by a high prevalence of metabolic disturbances [23]. In contrast, our study was based on a more heterogeneous hospital population not selected for a particular metabolic phenotype, which may explain the lower overall discordance rate. The results of van Deventer et al. also support the value of non-HDL-C for risk classification, particularly when TG are elevated, although their approach relied on comparison with reference methods in a dyslipidemic population, making direct comparison with our series cautious [11].

One of the main findings of this study is the marked increase in LDL-C/non-HDL-C discordance among patients with hypertriglyceridemia. No patient with TG < 1.50 g/L had discordance of the type normal LDL-C/elevated non-HDL-C. Discordance remained uncommon in the 1.50-1.99 g/L category (2.9%) but reached nearly one-quarter of profiles when TG was ⩾ 2.00 g/L, and almost nine in ten discordant profiles occurred in this subgroup. This stratification shows that discordance is not evenly distributed across the population but is concentrated in the subgroup in which calculated LDL-C is most likely to underestimate atherogenic burden.

From a pathophysiological standpoint, hypertriglyceridemia is associated with an increase in TG-rich lipoproteins and their remnants, which are included in non-HDL-C but are imperfectly reflected by calculated LDL-C [5-7]. This supports the practical value of non-HDL-C without repeating the detailed mechanisms already described in the introduction.

These results have practical implications for clinical laboratories. Non-HDL-C calculation requires no additional testing because it is obtained automatically from TC and HDL-C. Reporting non-HDL-C in routine lipid profiles could therefore help identify additional atherogenic lipid abnormalities without additional analytical cost [9,24]. However, identifying additional lipid abnormalities is not equivalent to demonstrating improved cardiovascular risk prediction. Because this study did not assess cardiovascular outcomes or include longitudinal follow-up, the potential clinical benefit of routine non-HDL-C reporting is suggested by our laboratory findings but was not directly demonstrated.

In addition, nearly one in four patients had non-HDL-C ⩾ 1.60 g/L, and a significant proportion of subjects considered to have normal LDL-C were reclassified, at the laboratory level, as having elevated atherogenic cholesterol burden when non-HDL-C was taken into account. These findings are consistent with international recommendations proposing non-HDL-C as a secondary treatment target, while emphasizing that thresholds should be interpreted according to global cardiovascular risk rather than as universal goals [2,4,9,20].

The ORs from the logistic regression must be interpreted in light of the clinical variables that were not available. Diabetes, obesity, and metabolic syndrome are associated with both hypertriglyceridemia and higher non-HDL-C; their omission is likely to inflate the OR for TG, part of which may reflect these shared metabolic conditions. Conversely, lipid-lowering therapy lowers non-HDL-C and is more often prescribed to older patients and to those with diabetes or known CVD; its omission could bias the association with age toward the null and modify the apparent association with gender. Smoking may also affect HDL-C and TG. Because the direction and magnitude of these biases cannot be quantified from our data, the reported ORs should be regarded as incompletely adjusted, descriptive associations that characterize this population, not as independent risk estimates or as predictors applicable to individual patients. In addition, because elevated non-HDL-C was common (24.2%), the ORs overestimate the corresponding prevalence ratios.

Strengths and limitations

This study has several strengths. It is based on a large sample of nearly 4,800 lipid profiles corresponding to more than 4,000 patients, reflecting routine practice in a university hospital laboratory. The analysis simultaneously assessed non-HDL-C distribution, correlations with other lipid parameters, concordance with LDL-C, and factors associated with its elevation.

Several limitations should nevertheless be acknowledged. First, this was a single-center retrospective study, which may limit the generalizability of the findings. Second, because of the retrospective design, risk factors could not be formally evaluated; clinical information such as cardiovascular history, diabetes, obesity, smoking, lipid-lowering therapy, or intercurrent diseases was not available. The regression model was therefore underadjusted, and ORs should be interpreted cautiously as biological associations rather than fully adjusted risk estimates, as discussed above. Third, the unit of analysis was the lipid profile, and 695 of the 4,790 profiles (14.5%) were repeat measurements; the correlation and concordance estimates therefore include non-independent observations. However, cluster-robust CIs in the regression and a sensitivity analysis restricted to one profile per patient gave virtually identical results. Fourth, selection bias is likely. The population consisted of hospital patients referred for lipid testing, who probably have a higher prevalence of metabolic and CVD than the general population, and 1,470 of the 6,260 available profiles were excluded because TC and HDL-C had not been measured simultaneously. Prevalence estimates should therefore not be extrapolated to the general Moroccan population. Fifth, LDL-C was calculated using the Friedewald formula when applicable, but its reliability may decrease in hypertriglyceridemia, particularly among patients with TG > 2.00 g/L [9,10]. Sixth, the non-HDL-C thresholds used were descriptive and derived from general clinical benchmarks; their specific relevance in the Moroccan population should be confirmed by studies incorporating cardiovascular risk and clinical follow-up. Seventh, concordance was assessed using kappa based on dichotomous thresholds [21]; a quantitative Bland-Altman analysis would have been informative to evaluate systematic bias between LDL-C and non-HDL-C [22], but was not performed. Eighth, no cardiovascular outcomes or longitudinal follow-up were available. This study therefore describes lipid abnormalities identified at the laboratory level and cannot establish whether non-HDL-C improves cardiovascular risk prediction or whether its routine reporting improves clinical outcomes. Finally, the high prevalence of low HDL-C and the higher non-HDL-C values observed in women could be influenced by laboratory reference values, age, menopausal status, or hospital recruitment bias.

Conclusions

This study shows that non-HDL-C is a simple and readily available laboratory indicator of atherogenic lipid burden. Although strongly correlated with LDL-C, it identified an additional subgroup of lipid profiles, concentrated among patients with hypertriglyceridemia, in which LDL-C alone may underestimate atherogenic cholesterol. These findings describe additional lipid abnormalities detected at the laboratory

level; they do not demonstrate improved cardiovascular risk prediction, because cardiovascular outcomes and longitudinal follow-up were not assessed. The potential benefit of systematically reporting non-HDL-C alongside LDL-C, which requires no additional analytical cost, is therefore suggested by these laboratory findings but should be confirmed by prospective studies including clinical data and cardiovascular outcomes. In the meantime, non-HDL-C should be interpreted according to individual cardiovascular risk and recommended therapeutic targets.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Acquisition, analysis, or interpretation of data: Boutayna Elrhaffouli, Hicham Ezzaidi, Dounia EL Moujtahide, Elhoucine Sebbar, Mohammed Choukri

Drafting of the manuscript: Boutayna Elrhaffouli, Hicham Ezzaidi, Dounia EL Moujtahide, Elhoucine Sebbar, Mohammed Choukri

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Supervision: Dounia EL Moujtahide, Elhoucine Sebbar, Mohammed Choukri

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Ethics Committee for Biomedical Research of the Faculty of Medicine and Pharmacy, Mohammed First University issued approval 21. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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