



LDL/HDL Ratio and Coronary Heart Disease in Employees of Shiraz University of Medical Sciences

Saeid Zare ¹, Seyed Jalil Masoumi ^{2,3,4,*}, Maryam Karimi Jaberi ¹, Andishe Hamedei ¹, Hadis Salimi ⁵, Atefeh Torabi Ardekani ⁶, Jafar Hassanzadeh ^{7,**}

¹ Student Research Committee, Shiraz University of Medical Sciences, Shiraz, Iran

² Department of Clinical Nutrition, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran

³ Gastroenterohepatology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

⁴ Nutrition Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

⁵ Non-Communicable Diseases Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

⁶ Center for Cohort Study of Shiraz University of Medical Sciences Employees' Health, Shiraz University of Medical Sciences, Shiraz, Iran

⁷ Research Center for Health Sciences, Institute of Health, School of Health, Department of Epidemiology, Shiraz University of Medical Sciences, Shiraz, Iran

* **Corresponding Author:** Department of Clinical Nutrition, Nutrition Research Center, School of Nutrition and Food Sciences, Gastroenterohepatology Research Center, Shiraz University of Medical Science, Shiraz, Iran. Email: masoumi7415@gmail.com

** **Corresponding Author:** Department of Epidemiology, Research Center for Health Sciences, School of Health, Shiraz University of Medical Sciences, Shiraz, Iran. Email: jafarabolhasan@yahoo.com

Received: 10 December, 2025; Revised: 13 May, 2026; Accepted: 24 May, 2026

Abstract

Background: Cardiovascular diseases are the leading cause of mortality in Iran, and dyslipidemia is a major contributor to cardiometabolic risk.

Objectives: This study assessed the discriminatory ability of the low-density lipoprotein/high-density lipoprotein (LDL/HDL) ratio for prevalent coronary heart disease (CHD) in participants in the Shiraz University of Medical Sciences Employee Cohort Study.

Methods: This cross-sectional analysis was conducted from 2017 to 2020 among 7,100 university employees aged 20 - 70 years. Eligibility criteria included active employment and the ability to complete questionnaires; individuals unwilling to participate or those with incomplete medical records were excluded. Coronary heart disease status was determined based on physician-documented diagnoses or self-report. Demographic, anthropometric, and biochemical data, including LDL, HDL, total cholesterol, triglycerides, fasting blood glucose, blood urea nitrogen, and creatinine, were obtained from standardized medical records and laboratory reports using validated protocols. Lipid ratios, including LDL/HDL, were calculated. Multivariable logistic regression was used to estimate adjusted odds ratios while controlling for age, sex, hypertension, diabetes, and other major confounders. The discriminatory performance of lipid indices was evaluated using receiver operating characteristic (ROC) curve analysis. Analyses were performed using SPSS version 26 and Python (scikit-learn), with $P < 0.05$ considered statistically significant.

Results: Of the 7,100 participants, 332 had prevalent CHD. Age, hypertension, and fasting blood glucose were independently associated with CHD (all $P < 0.05$). The LDL/HDL ratio demonstrated the highest discriminatory performance among the lipid indices (area under the curve [AUC] = 0.677; 95% CI, 0.644 - 0.710), with an optimal cutoff of 2.19 (63% sensitivity and 61% specificity). Higher LDL/HDL ratios were significantly associated with greater clustering of cardiometabolic risk factors ($P < 0.001$).

Conclusions: The LDL/HDL ratio is a simple, readily available index derived from routine lipid profiles that reflects the clustering of cardiometabolic risk factors and is associated with prevalent CHD in this working population. These findings may help inform workplace health monitoring and cardiovascular risk assessment. Study limitations include the cross-sectional design, reliance on self-reported CHD, and the single-institution cohort, which may limit the generalizability of the findings.

Keywords: Coronary Heart Disease, LDL/HDL Ratio, Cardiovascular Risk Prediction, Workplace Health Monitoring

1. Background

Cardiovascular diseases, particularly coronary heart disease (CHD), remain among the leading causes of death and disability worldwide (1). According to the Global Burden of Disease report, an estimated 19.41 million deaths

worldwide were attributed to cardiovascular diseases in 2021, with a prevalence exceeding 612 million. The age-standardized mortality rate was reported as 235 deaths per 100,000 population. These statistics indicate that cardiovascular diseases continue to impose a substantial global public health burden, with the highest mortality

rates observed in Central Asia, Eastern Europe, North Africa, and the Middle East (2, 3).

A similar trend has been observed in Iran. According to the Global Burden of Disease Study, cardiovascular diseases have been the leading cause of death in the country over the past 3 decades, accounting for a substantial proportion of years of life lost and years lived with disability (4). National and regional cohort studies, including the Kharameh cohort in southern Iran, have also shown an increasing prevalence of cardiovascular diseases, with classic risk factors such as diabetes, hypertension, obesity, and dyslipidemia contributing substantially to this trend (5).

Among these factors, lipid disorders are particularly important because changes in blood cholesterol levels are directly related to atherosclerosis (6). Low-density lipoprotein (LDL) cholesterol is considered atherogenic, and elevated levels are associated with lipid deposition in the vascular wall and the formation of atherosclerotic plaques (7). In contrast, high-density lipoprotein (HDL) cholesterol plays a protective role by removing cholesterol from the vascular wall and transporting it to the liver for excretion (8, 9). Recent studies have shown that the LDL/HDL ratio may be a more accurate indicator of coronary artery disease risk because it simultaneously accounts for the atherogenic effects of LDL and the protective effects of HDL (6).

Epidemiological evidence suggests that a higher LDL/HDL ratio is associated with greater coronary disease severity and unfavorable cardiometabolic profiles. For example, a study in China of patients with myocardial ischemia reported that the LDL/HDL ratio was more strongly associated with the severity of coronary atherosclerosis than LDL cholesterol or HDL cholesterol alone (10). Recent evidence indicates that lipid ratios such as LDL/HDL may provide better discrimination of CHD than isolated lipid parameters because they integrate atherogenic and protective lipid components (1). European studies have also reported significant cross-sectional associations between this ratio and the burden of cardiovascular disease (11).

2. Objectives

Given the potential relevance of this index, examining the association between the LDL/HDL ratio and prevalent CHD in different populations may help characterize cardiometabolic risk profiles. In Iran, data on this ratio among academic staff and working populations are limited. Therefore, this study aimed to investigate the association and discriminatory ability of the LDL/HDL ratio

in relation to prevalent CHD among employees of Shiraz University of Medical Sciences.

3. Methods

3.1. Study Design and Participants

This cross-sectional study was conducted as part of the first phase of the Center for Monitoring and Promoting Employee Health at Shiraz University of Medical Sciences. The study included 7,100 employees aged 20 - 70 years, of whom 332 had prevalent CHD. Coronary heart disease status was defined based on either physician-documented diagnoses in medical records or participant self-report of a previous physician diagnosis. This cohort is part of the Persian National Cohort (12) and represents one of the first 3 centers established for employee health monitoring in Iran. Inclusion criteria included official, contract, and temporary employees. Exclusion criteria were unwillingness to participate or inability to understand the questionnaire.

3.2. Data Collection

Data were collected using a demographic questionnaire that recorded age, sex, marital status, educational level, weight, and height. Laboratory data, including LDL, HDL, total cholesterol (TC), triglycerides (TG), blood urea nitrogen (BUN), creatinine (Cr), glucose (GLU), and lipid ratios such as LDL/HDL, were extracted from the medical records.

3.3. Statistical Analysis

Statistical analyses were conducted using SPSS version 26. Continuous variables were reported as mean $\pm$ standard deviation, and groups were compared using independent-samples *t*-tests or nonparametric equivalents. Categorical variables were reported as percentages and compared using the chi-square test. Pearson correlation analysis was used to assess associations between continuous variables. Simple and multiple logistic regression models were used to evaluate associations between prevalent CHD and lipid profiles (TC, LDL, TG, HDL, GLU, BUN, and Cr), as well as the LDL/HDL ratio, after adjustment for major confounders. The discriminatory ability of lipid indices in relation to prevalent CHD was assessed using ROC curve analysis, and the optimal cutoff was determined using the Youden Index. Receiver operating characteristic curves were generated in Python using the scikit-learn library, which provided AUC calculations and graphical visualization of the diagnostic performance of each lipid marker. A *P* value < 0.05 was considered statistically significant.

Table 1. Comparison of Demographic and Clinical Variables Between the CHD and Non-CHD Groups ^a

Variables	CHD: Yes (n = 332)	CHD: No (n = 6754)	P Value
Age	45.29 ± 7.50	40.53 ± 7.12	< 0.001
Gender			0.06
Male	159 (47.9)	2886 (42.7)	
Female	173 (52.1)	3868 (57.3)	
Marital status			0.001
Single	45 (13.6)	1402 (20.8)	
Married	287 (86.4)	5352 (79.2)	
Educational level			< 0.001
Low (≤ high school diploma)	119 (35.8)	1766 (26.2)	
Intermediate (associate or bachelor's degree)	154 (46.4)	3740 (55.4)	
High (≥ master's degree)	59 (17.8)	1247 (18.5)	
Smoking status			0.04
No	302 (91)	6331 (93.7)	
Yes	30 (9)	423 (6.3)	
Hypertension			< 0.001
Yes	68 (20.5)	377 (5.6)	
No	264 (79.5)	6377 (94.4)	
Hypolipidemic drug use			0.81
No	319 (96.1)	6457 (95.6)	
Yes	13 (3.9)	297 (4.4)	
Body Mass Index (kg/m²)			0.02
Underweight (BMI < 18.5)	2 (0.6)	79 (1.2)	
Normal (18.5 ≤ BMI < 23.9)	49 (14.8)	1335 (19.8)	
Overweight (24 ≤ BMI < 27.9)	130 (39.2)	2755 (40.8)	
Obese (BMI ≥ 28.0)	151 (45.5)	2585 (38.3)	
LDL/HDL	2.24 ± 0.66	2.27 ± 0.70	0.55
LDL-C	100.67 ± 25.25	100.46 ± 24.70	0.88
HDL-C	46.30 ± 10.01	46.11 ± 10.16	0.73
TC	175.19 ± 35.58	173.46 ± 34.10	0.36
TG	150.88 ± 90.37	135.18 ± 83.74	< 0.001
Cr	1.006 ± 0.20	0.97 ± 0.18	< 0.001
GLU	99.54 ± 34.98	92.26 ± 19.11	< 0.001
BUN	13.27 ± 3.55	13.24 ± 3.27	0.84

^a Values are expressed as mean ± SD or No. (%). Abbreviations: BMI, Body Mass Index; BUN, blood urea nitrogen; CHD, coronary heart disease; Cr, creatinine; GLU, glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

4. Results

4.1. Participant Characteristics

The study included 7,100 participants (3,035 men and 4,047 women; mean age, 40.7 ± 7.2 years). No significant differences were observed between participants with and without prevalent CHD with respect to sex, use of lipid-lowering medications, LDL, HDL, TC, or BUN (Table 1). In contrast, older age, lower educational attainment, smoking, hypertension, obesity, elevated TG, increased Cr,

and higher blood glucose were associated with a higher prevalence of CHD (Table 1).

4.2. Logistic Regression Analysis

In both univariate and multivariate analyses, age (OR = 1.07), hypertension (OR = 2.50), and blood glucose (OR = 1.004) remained independently associated with prevalent CHD. Owing to multicollinearity among LDL-C, HDL-C, and the LDL/HDL ratio, separate multivariate models were constructed. Although the crude comparison in Table 1 showed no significant difference in the mean LDL/HDL ratio between the CHD and non-CHD groups (P = 0.55), the

Table 2. Logistic Regression Results for Demographic, Clinical, and Biochemical Variables in Relation to CHD ^a

Variables	Univariate OR (95% CI)	P-Value	Multivariate OR (95% CI)	P-Value
Age	1.09 (1.07 - 1.10)	< 0.001	1.07 (1.05 - 1.09)	< 0.001
Gender				
Female	0.81 (0.65 - 1.01)	0.06	1.09 (0.81 - 1.45)	0.55
Marital status				
Married	1.67 (1.21 - 2.30)	0.001	1.24 (0.89 - 1.75)	0.19
Educational level				
Intermediate (associate or bachelor's degree)	0.61 (0.47 - 0.78)	< 0.001	0.83 (0.64 - 1.09)	0.19
High (≥ master's degree)	0.70 (0.50 - 0.96)		0.83 (0.59 - 1.16)	0.29
Smoking status				
Yes	1.48 (1.008 - 2.19)	0.04	1.28 (0.84 - 1.97)	0.24
Hypertension				
Yes	4.36 (3.27 - 5.80)	< 0.001	2.50 (1.87 - 3.50)	< 0.001
Hypolipidemic drug use				
Yes	0.88 (0.50 - 1.58)	0.81	0.96 (0.53 - 1.71)	0.89
BMI (kg/m ²)	1.04 (1.01 - 1.07)	0.02	1.01 (0.98 - 1.04)	0.35
LDL/HDL	0.95 (0.81 - 1.11)	0.55	1.35 (1.10 - 1.65)	0.004
LDL-C	1.00 (0.99 - 1.005)	0.88	1.01 (0.98 - 1.03)	0.36
HDL-C	1.002 (0.99 - 1.01)	0.73	0.97 (0.93 - 1.01)	0.12
TC	1.001 (0.99 - 1.005)	0.36	0.99 (0.98 - 1.01)	0.92
TG	1.002 (1.001 - 1.003)	< 0.001	1.001 (0.99 - 1.003)	0.32
Cr	2.01 (1.23 - 3.27)	< 0.001	1.46 (0.88 - 2.41)	0.13
GLU	1.01 (1.007 - 1.01)	< 0.001	1.004 (1.001 - 1.008)	0.02
BUN	1.003 (0.97 - 1.03)	0.84	0.98 (0.95 - 1.02)	0.49

^a Values are expressed as 95% CI. Abbreviations: BMI, Body Mass Index; BUN, blood urea nitrogen; CHD, coronary heart disease; CI, confidence interval; Cr, creatinine; GLU, glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; OR, odds ratio; TC, total cholesterol; TG, triglycerides.

ratio was significantly associated with prevalent CHD after adjustment in separate models. This finding likely reflects confounding and multicollinearity among lipid variables; adjustment for major cardiometabolic factors and isolation of the ratio from its individual components revealed its independent association with CHD. In the model that included only the LDL/HDL ratio, a higher ratio was positively associated with CHD, whereas LDL-C and HDL-C showed no significant independent associations when modeled separately. Other variables, including sex, marital status, educational level, smoking status, lipid-lowering medication use, BMI, TC, TG, Cr, and BUN, also showed no independent associations in their respective models (Table 2).

4.3. Correlation and Discriminatory Analyses

As shown in Figure 1, the LDL/HDL ratio demonstrated statistically significant correlations with several metabolic indices, including LDL, TC, TG, and HDL. Its strong positive correlation with LDL and negative correlation with HDL highlight the descriptive value of this ratio for summarizing participants' lipid status.

The ROC analysis of LDL-C, HDL-C, and the LDL/HDL ratio is presented in Figure 2. The LDL/HDL ratio showed greater discriminatory ability than LDL-C or HDL-C alone. The AUC for the LDL/HDL ratio was 0.677 (95% CI, 0.644 - 0.710), representing the highest discriminatory performance among the indices. The optimal cutoff was 2.19, yielding 63% sensitivity and 61% specificity. For LDL-C, the AUC was 0.576 (95% CI, 0.541 - 0.611), with an optimal cutoff of 105.52 mg/dL (58% sensitivity and 58% specificity). For HDL-C, the AUC was 0.591 (95% CI, 0.556 - 0.626), with an optimal cutoff of 46.24 mg/dL (59% sensitivity and 60% specificity).

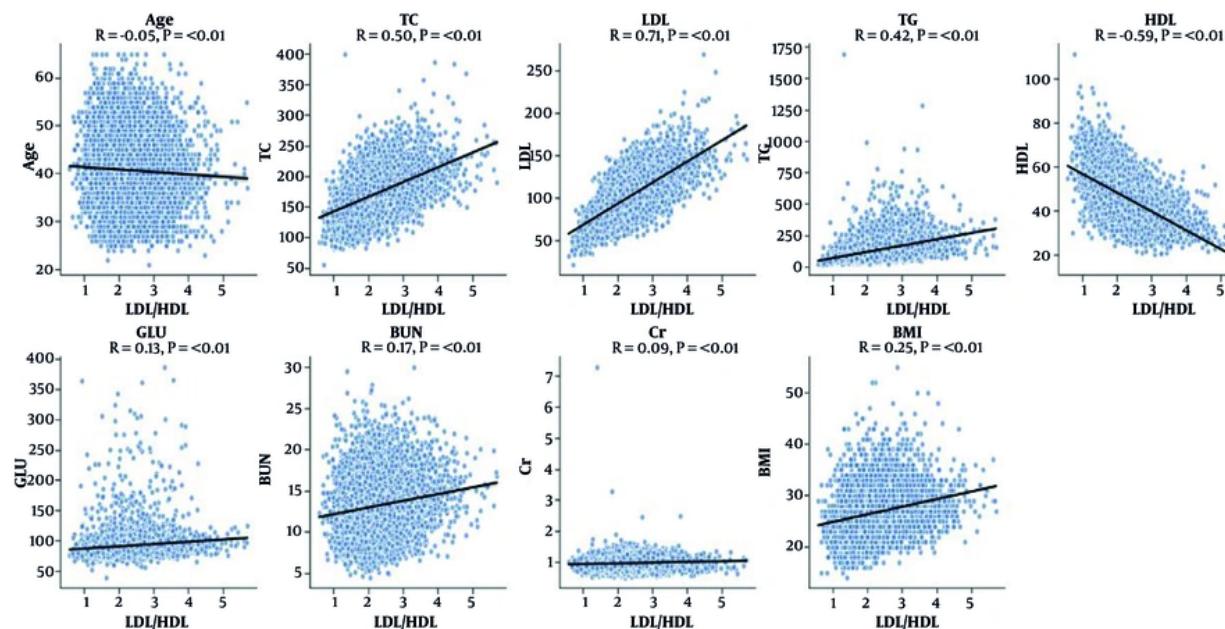


Figure 1. Correlation Between the LDL/HDL Ratio and Metabolic Health Indicators

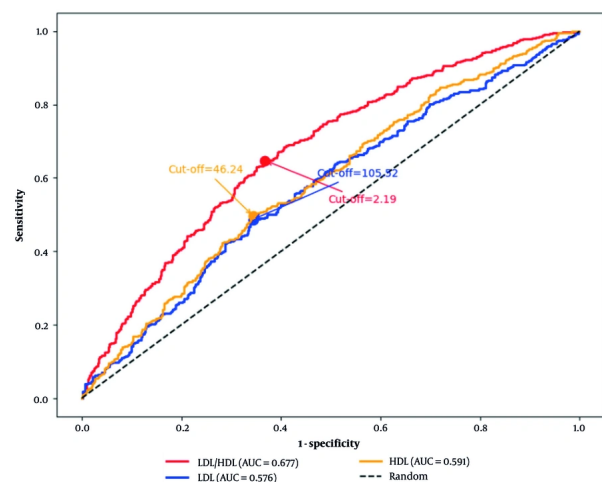


Figure 2. Comparative ROC Analysis of LDL, HDL, and the LDL/HDL Ratio for CHD Diagnosis

4.4. Clinical and Metabolic Differences by LDL/HDL Cutoff

Participants were divided into 2 groups based on the LDL/HDL cutoff of 2.19. The prevalence of CHD and associated cardiometabolic factors was compared between the groups (Table 3). Participants with LDL/HDL ≥ 2.19 had a higher prevalence of CHD and were more likely to be male, married, and smokers. This group also included a higher proportion of participants with lower educational attainment. BMI distributions differed significantly, with more participants classified as overweight or obese in the group with LDL/HDL ≥ 2.19 than in the group with LDL/HDL < 2.19 . The group with LDL/HDL ≥ 2.19 also had higher LDL-C, TC, TG, Cr, GLU, and BUN levels and lower HDL-C levels.

5. Discussion

This study evaluated the association between the LDL/HDL ratio and prevalent CHD in an occupational cohort with relatively favorable health profiles. Although dyslipidemia is a well-established contributor to cardiovascular disease (6, 13, 14), our findings indicate a more nuanced pattern in this population. The LDL/HDL ratio was positively associated with CHD when modeled independently to address multicollinearity (OR = 1.35; 95% CI, 1.10 - 1.65), but its relative contribution was weaker than those of age, hypertension, and fasting glucose. This pattern is biologically plausible given the close

Table 3. Clinical and Metabolic Differences Between Participants Above and Below the Optimal LDL/HDL Cutoff^a

Variables	LDL/HDL < 2.19 (n = 1901)	LDL/HDL ≥ 2.19 (n = 5199)	P-Value
Age	40.46 ± 7.25	41.05 ± 7.17	0.002
Gender			< 0.001
Male	470 (24.7)	2583 (49.7)	
Female	1431 (75.3)	2616 (50.3)	
Marital status			< 0.001
Single	828 (23.5)	624 (17.4)	
Married	2695 (76.5)	2953 (82.6)	
Educational level			< 0.001
Low (≤ high school diploma)	830 (23.6)	1060 (29.6)	
Intermediate (associate or bachelor's degree)	2007 (57.0)	1892 (52.9)	
High (≥ master's degree)	686 (19.5)	624 (17.4)	
Smoking status			< 0.001
No	1824 (95.9)	4822 (92.7)	
Yes	77 (4.1)	377 (7.3)	
Hypertension			0.04
Yes	200 (5.7)	245 (6.9)	
No	3320 (94.3)	3326 (93.1)	
Hypolipidemic drug use			0.20
No	3380 (95.9)	3410 (95.3)	
Yes	143 (4.1)	167 (4.7)	
Body Mass Index (kg/m²)			< 0.001
Underweight (BMI < 18.5)	74 (2.1)	7 (0.2)	
Normal (18.5 ≤ BMI < 23.9)	934 (26.5)	452 (12.6)	
Overweight (24 ≤ BMI < 27.9)	1439 (40.8)	1455 (40.7)	
Obese (BMI ≥ 28.0)	1076 (30.5)	1663 (46.5)	
LDL/HDL			
LDL-C	86.48 ± 18.16	114.28 ± 22.52	< 0.001
HDL-C	51.21 ± 9.94	41.10 ± 7.53	< 0.001
TC	159.97 ± 29.46	186.94 ± 33.25	< 0.001
TG	105.57 ± 66.33	165.87 ± 88.95	< 0.001
Cr	0.95 ± 0.19	0.99 ± 0.17	< 0.001
GLU	90.40 ± 17.96	94.79 ± 21.95	< 0.001
BUN	12.78 ± 3.27	13.70 ± 3.24	< 0.001

^a Values are expressed as mean ± SD or No. (%). Abbreviations: BMI, Body Mass Index; BUN, blood urea nitrogen; Cr, creatinine; GLU, glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

interrelationship among lipid metabolism, glucose homeostasis (15, 16), and blood pressure regulation (17).

This finding contrasts with several previous reports identifying the LDL/HDL ratio as a strong independent marker associated with CHD, often retaining high statistical significance after extensive adjustment for multiple risk factors (6, 18, 19). For example, studies in general populations or high-risk clinical settings have frequently reported that the LDL/HDL ratio demonstrates better discriminatory ability and stronger associations with CHD than isolated lipid parameters (20, 21). The more limited effect observed in the present cohort may be

explained by the relatively healthy worker population and restricted variability in cardiometabolic risk factors, consistent with the healthy worker effect (22-24). In such settings, reduced exposure variability can attenuate observed associations between lipid indices and disease outcomes.

Among all lipid measures, the LDL/HDL ratio showed the highest discriminatory capacity, although its discriminatory ability was modest (AUC = 0.677) (25). Rather than indicating strong diagnostic utility, this result suggests that the ratio reflects the clustering of cardiometabolic abnormalities rather than acting as an

isolated disease discriminator. Participants with an LDL/HDL ratio ≥ 2.19 had a higher burden of adverse metabolic traits, including obesity, smoking, and hypertension, supporting its role as an integrated marker of metabolic dysregulation rather than a stand-alone predictor (26).

Current clinical guidelines emphasize non-HDL cholesterol and apolipoprotein B as more robust risk markers (27, 28), limiting the clinical applicability of the LDL/HDL ratio in routine practice. In this study, multivariable models confirmed an independent association between the LDL/HDL ratio and prevalent CHD after adjustment; however, this association remained secondary to traditional risk factors, particularly age, hypertension, and glycemic status.

After multicollinearity was addressed by modeling the LDL/HDL ratio independently of LDL-C and HDL-C, the ratio was positively associated with prevalent CHD. Although this finding may appear inconsistent with the crude comparison in Table 1, in which no significant difference was observed between groups, the discrepancy is expected because unadjusted comparisons do not account for confounding or intercorrelations among lipid variables. After adjustment for major cardiometabolic factors, the LDL/HDL ratio remained independently associated with prevalent CHD; however, its effect size was weaker than those of age, hypertension, and fasting glucose.

The observed pattern suggests that the LDL/HDL ratio primarily reflects underlying metabolic dysregulation rather than acting as a dominant independent determinant of CHD in this cohort. This interpretation is consistent with its biological role as an integrated indicator of opposing atherogenic and antiatherogenic lipid effects (6) and with previous studies reporting associations between the LDL/HDL ratio and CHD severity, plaque characteristics, and stenosis burden (19, 20, 29, 30).

The relatively modest discriminatory performance observed in the ROC analysis (31), compared with the regression results, likely reflects methodological differences because ROC curves evaluate discrimination without adjustment, whereas multivariable models estimate independent associations (23). In this occupational cohort, the influence of lipid indices appears attenuated, likely because of limited variability in risk-factor distribution and the healthy worker effect (24), resulting in a stronger apparent contribution of traditional factors such as hypertension and glycemic status.

CHD classification based on medical records or self-report may have introduced misclassification bias, and the

absence of apolipoprotein-based markers limited comparisons with more contemporary lipid indices (32). Overall, these findings support interpreting the LDL/HDL ratio as a marker of metabolic risk clustering rather than as a primary independent predictor of prevalent CHD in this population.

5.1. Strengths and Limitations

This study has several strengths. First, the relatively large sample of 7,100 participants increased statistical power and improved the precision of the estimated associations. The use of data from an established cohort within the PERSIAN Cohort framework also enhanced methodological rigor because data collection followed standardized protocols and validated procedures. Second, the study incorporated a comprehensive set of demographic, anthropometric, and biochemical variables, allowing adjustment for important cardiometabolic confounders such as age, hypertension, blood glucose, BMI, and smoking. Third, the analysis combined logistic regression, correlation analysis, and ROC curve analysis. Receiver operating characteristic analysis enabled evaluation of the discriminatory ability of the LDL/HDL ratio compared with individual lipid parameters, providing additional insight into its potential utility as a risk-stratification marker. Another strength was the evaluation of the LDL/HDL ratio in a working population. Occupational cohorts are relatively understudied in cardiovascular epidemiology in Iran, and this study contributes evidence regarding cardiometabolic risk patterns among university employees. Finally, identifying a data-driven optimal LDL/HDL cutoff of 2.19 provides a useful reference point for future epidemiological and workplace health-monitoring studies.

Several limitations should be considered. First, the cross-sectional design precludes causal inference because exposure and outcome were assessed simultaneously; therefore, it is not possible to determine whether the observed lipid profiles preceded CHD. Second, CHD status was partly based on self-reported physician diagnoses, which may have introduced recall bias or misclassification. Although medical records were used when available, some reporting error cannot be excluded. Third, the study population consisted exclusively of employees of a single university medical system. This relatively homogeneous occupational group may not represent the general population, and the healthy worker effect could have led to underestimation of associations between lipid abnormalities and cardiovascular disease. Finally, residual confounding cannot be excluded. Information on certain lifestyle and clinical factors, such as diet, physical activity, medication adherence, and duration of lipid-lowering

therapy, was unavailable or incompletely captured and may have influenced the observed associations.

5.2. Conclusions

In this relatively healthy and homogeneous occupational cohort, the LDL/HDL ratio primarily reflected the clustering of adverse cardiometabolic traits rather than serving as a strong independent marker of prevalent CHD. Its moderate discriminatory ability suggests potential utility for identifying higher-risk subgroups in research or occupational settings, but it should not replace guideline-endorsed lipid markers in clinical practice. These findings emphasize the importance of considering population characteristics and underlying metabolic factors when interpreting lipid ratios and highlight the need for studies in more diverse populations to clarify their association with cardiometabolic outcomes.

Given the cross-sectional design, the absence of apolipoprotein-based markers, and the possibility of residual confounding, these results should be interpreted cautiously and viewed as descriptive rather than inferential. Future longitudinal studies in more heterogeneous populations incorporating broader lipid and metabolic profiling may further clarify how this ratio fits within the overall cardiometabolic risk landscape.

Acknowledgements

This article is based on a master's thesis. We sincerely thank all staff members of Shiraz University of Medical Sciences who participated in the study and the cohort team for their invaluable contributions to data collection, management, and overall support.

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: S. Z.: Conceptualization, study design, and data analysis; S. J. M.: Data curation and data provision; M. K. J.: Manuscript drafting; A. H.: Manuscript drafting and revision; A. T.: Data curation and data provision; H. S.: Manuscript drafting and revision; J. H.: Conceptualization, study design, manuscript revision, and supervision.

Conflict of Interests Statement: The authors declare that they have no Conflict of Interest.

Data Availability: The dataset presented in the study is available on request from the corresponding author

during submission or after publication.

Ethical Approval: This research is extracted from an MSC dissertation under the supervision of Dr. Jafar Hassanzadeh. The ethics committee of Shiraz University of Medical Sciences has also approved it (IR.SUMS.SCHEANUT.REC.1402.123).

Funding/Support: The authors declare that they have no funding source.

Informed Consent: This study was derived from the Employees of Shiraz University of Medical Sciences cohort. We used data from that cohort, and participants provided informed consent.

References

1. Seyithanoğlu M, Kizildag B, Gulmez R, Cagri Aykan A. Monocyte/HDL cholesterol ratio and atherogenic indexes as predictors of coronary artery disease severity and angiography need in patients undergoing coronary CT angiography. *Ij Radiology*. 2025;22(1). <https://doi.org/10.5812/iranjradiol-157636>.
2. Aringazina A, Kuandikov T, Arkhipov V. Burden of the cardiovascular diseases in Central Asia. *Central Asian journal of global health*. 2018;7(1):321. [PubMed ID: 30863664]. [PubMed Central ID: PMC6393056]. <https://doi.org/10.5195/cajgh.2018.321>.
3. Soleimani H, Nasrollahizadeh A, Nasrollahizadeh A, Razeghian I, Molaei MM, Hakim D, et al. Cardiovascular disease burden in the North Africa and Middle East region: an analysis of the global burden of disease study 1990 - 2021. *BMC Cardiovascular Disorders*. 2024;24(1). 712. [PubMed ID: 39702074]. [PubMed Central ID: PMC11657751]. <https://doi.org/10.1186/s12872-024-04390-0>.
4. Heidari-Foroosan M, Farshbafnadi M, Golestani A, Younesian S, Jafari H, Rashidi MM, et al. National and Subnational Burden of Cardiovascular Diseases in Iran from 1990 to 2021: Results from Global Burden of Diseases 2021 study. *Global Heart*. 2025;20(1). 43. [PubMed ID: 40386247]. [PubMed Central ID: PMC12083073]. <https://doi.org/10.5334/gh.1429>.
5. Baeradeh N, Ghodussi Johari M, Moftakhar L, Rezaeianzadeh R, Hosseini SV, Rezaianzadeh A. The prevalence and predictors of cardiovascular diseases in Kherameh cohort study: a population-based study on 10,663 people in southern Iran. *BMC cardiovascular disorders*. 2022;22(1). 244. [PubMed ID: 35643460]. [PubMed Central ID: PMC9148515]. <https://doi.org/10.1186/s12872-022-02683-w>.
6. Sun T, Chen M, Shen H, PingYin, Fan L, Chen X, et al. Predictive value of LDL/HDL ratio in coronary atherosclerotic heart disease. *BMC Cardiovascular Disorders*. 2022;22(1). 273. [PubMed ID: 35715736]. [PubMed Central ID: PMC9206383]. <https://doi.org/10.1186/s12872-022-02706-6>.
7. Ferrieres J, De Ferrari GM, Hermans MP, Elisaf M, Toth PP, Horack M, et al. Predictors of LDL-cholesterol target value attainment differ in acute and chronic coronary heart disease patients: results from DYSIS II Europe. *European journal of preventive cardiology*. 2018;25(18):1966-76. [PubMed ID: 30335504]. <https://doi.org/10.1177/2047487318806359>.
8. Ling Y, Jiang J, Wu B, Gao X. Serum triglyceride, high-density lipoprotein cholesterol, apolipoprotein B, and coronary heart disease in a Chinese population undergoing coronary angiography. *Journal of clinical lipidology*. 2017;11(3):646-56. [PubMed ID: 28506386]. <https://doi.org/10.1016/j.jacl.2017.02.017>.

9. Chary A, Tohidi M, Hashemini M, Golmohammadi M, Haji Hosseini R, Hedayati M, et al. Association Between HDL2-C and HDL3-C with Cardiovascular Disease: A Nested Case-Control Study in an Iranian Population. *International journal of endocrinology and metabolism*. 2023;**22**(1). e141550. [PubMed ID: 38665147]. [PubMed Central ID: PMC11041996]. <https://doi.org/10.5812/ijem-141550>.
10. Xu J, Jing C, Yingxian L, Ying S, Lin J, Shaodi Y, et al. The effect of LDL-C/HDL-C ratio on severity of coronary artery disease and 2-year long-term prognosis in patients with premature coronary heart disease—a multicenter, observational results. *European Heart Journal*. 2023;**44**(Supplement_2). ehad655.1441. <https://doi.org/10.1093/eurheartj/ehad655.1441>.
11. God M, Manola S, Jurin I, Novak A, Hadzibegovic I, Pavlovic N, et al. Correlation between LDL/HDL-cholesterol ratio and long term prognosis after acute coronary syndrome and severity of coronary artery disease. *European Heart Journal*. 2024;**45**(Supplement_1). ehae666. <https://doi.org/10.1093/eurheartj/ehae666.1338>.
12. Poustchi H, Eghtesad S, Kamangar F, Etemadi A, Keshtkar AA, Hekmatdoost A, et al. Prospective epidemiological research studies in Iran (the PERSIAN Cohort Study): rationale, objectives, and design. *American journal of epidemiology*. 2018;**187**(4):647-55. [PubMed ID: 29145581]. [PubMed Central ID: PMC6279089]. <https://doi.org/10.1093/aje/kwx314>.
13. Bittner V. Perspectives on dyslipidemia and coronary heart disease in women. *Journal of the American College of Cardiology*. 2005;**46**(9):1628-35. [PubMed ID: 16256860]. <https://doi.org/10.1016/j.jacc.2005.05.089>.
14. Leon AS, Bronas UG. Dyslipidemia and risk of coronary heart disease: role of lifestyle approaches for its management. *American journal of lifestyle medicine*. 2009;**3**(4):257-73. <https://doi.org/10.1177/1559827609334518>.
15. Chen L, Chen XW, Huang X, Song BL, Wang Y, Wang Y. Regulation of glucose and lipid metabolism in health and disease. *Science China life sciences*. 2019;**62**(11):1420-58. [PubMed ID: 31686320]. <https://doi.org/10.1007/s11427-019-1563-3>.
16. Taskinen MR, Borén J. New insights into the pathophysiology of dyslipidemia in type 2 diabetes. *Atherosclerosis*. 2015;**239**(2):483-95. [PubMed ID: 25706066]. <https://doi.org/10.1016/j.atherosclerosis.2015.01.039>.
17. Deshmukh M, Lee HW, McFarlane SI, Whaley-Connell A. Antihypertensive medications and their effects on lipid metabolism. *Current Diabetes Reports*. 2008;**8**(3):214-20. [PubMed ID: 18625119]. <https://doi.org/10.1007/s11892-008-0037-7>.
18. Yuan S, Pu T, Wang Z, Li L, Gao P, Zhang L, et al. Correlation between neutrophil/lymphocyte ratio combined with low-density lipoprotein cholesterol/high-density lipoprotein cholesterol ratio and severity of coronary artery disease in patients with acute coronary syndrome. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue*. 2022;**34**(3):274-279. [PubMed ID: 35574745]. <https://doi.org/10.3760/cma.j.cn121430-20211008-01441>.
19. Yuan S, Li L, Pu T, Fan X, Wang Z, Xie P, et al. The relationship between NLR, LDL-C/HDL-C, NHR and coronary artery disease. *Plos one*. 2024;**19**(7). e0290805. [PubMed ID: 38985788]. [PubMed Central ID: PMC11236180]. <https://doi.org/10.1371/journal.pone.0290805>.
20. Jiang Y, Zhang L, Gu Z. LDL-C/HDL-C ratio as a predictor of atherosclerosis in the Japanese population: insights from a cross-sectional study. *BMC Cardiovascular Disorders*. 2025;**25**(1). 333. [PubMed ID: 40295965]. [PubMed Central ID: PMC12039290]. <https://doi.org/10.1186/s12872-025-04792-8>.
21. Gao P, Wen X, Ou Q, Zhang J. Which one of LDL-C/HDL-C ratio and non-HDL-C can better predict the severity of coronary artery disease in STEMI patients. *BMC Cardiovascular Disorders*. 2022;**22**(1). 318. [PubMed ID: 35843962]. [PubMed Central ID: PMC9288699]. <https://doi.org/10.1186/s12872-022-02760-0>.
22. Harrell FE. Multivariable Modeling Strategies. In: *Regression Modeling Strategies*. Springer Series in Statistics. Springer. 2015;**Cham**:63-102. https://doi.org/10.1007/978-3-319-19425-7_4.
23. Rothman KJ. The origin of Modern Epidemiology, the book. *European Journal of Epidemiology*. 2021;**36**(8):763-5. [PubMed ID: 34453632]. [PubMed Central ID: PMC8397859]. <https://doi.org/10.1007/s10654-021-00790-0>.
24. Li CY, Sung FC. A review of the healthy worker effect in occupational epidemiology. *Occupational medicine*. 1999;**49**(4):225-9. [PubMed ID: 10474913]. <https://doi.org/10.1093/occmed/49.4.225>.
25. Hosmer DW, Lemeshow S, Sturdivant RX. *Applied logistic regression*. Applied logistic regression: John Wiley & Sons; 2013. <https://doi.org/10.1002/9781118548387>.
26. Cersosimo E, DeFronzo RA. Insulin resistance and endothelial dysfunction: the road map to cardiovascular diseases. *Diabetes/metabolism research and reviews*. 2006;**22**(6):423-36. [PubMed ID: 16506274]. <https://doi.org/10.1002/dmrr.634>.
27. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS). *European heart journal*. 2020;**41**(1):111-88. [PubMed ID: 31504418]. <https://doi.org/10.1093/eurheartj/ehz455>.
28. Quispe R, Brownstein AJ, Sathiyakumar V, Park J, Chang B, Sajja A, et al. Utility of non-HDL-C and apoB targets in the context of new more aggressive lipid guidelines. *American Journal of Preventive Cardiology*. 2021;**7**. 100203. [PubMed ID: 34611642]. [PubMed Central ID: PMC8387302]. <https://doi.org/10.1016/j.ajpc.2021.100203>.
29. Xu JJ, Chen J, Liu YX, Song Y, Jiang L, Yan SD, et al. The impact of LDL-C/HDL-C ratio on severity of coronary artery disease and 2-year outcome in patients with premature coronary heart disease: results of a prospective, multicenter, observational cohort study. *Zhonghua Xin Xue Guan Bing Za Zhi*. 2023;**51**(7):702-708. [PubMed ID: 37460423]. <https://doi.org/10.3760/cma.j.cn112148-20230128-00043>.
30. Wu Z, Li X, Wen Q, Tao B, Qiu B, Zhang Q, et al. Serum LDL-C/HDL-C ratio and the risk of carotid plaques: a longitudinal study. *BMC Cardiovascular Disorders*. 2022;**22**(1). 501. [PubMed ID: 36434516]. [PubMed Central ID: PMC9700971]. <https://doi.org/10.1186/s12872-022-02942-w>.
31. Cook NR. Use and misuse of the receiver operating characteristic curve in risk prediction. *Circulation*. 2007;**115**(7):928-35. [PubMed ID: 17309939]. <https://doi.org/10.1161/CIRCULATIONAHA.106.672402>.
32. Zhang J, Liu M, Gao J, Tian X, Song Y, Zhang H, et al. ApoB/ApoA-I is associated with major cardiovascular events and readmission risk of patients after percutaneous coronary intervention in one year. *Scientific Reports*. 2025;**15**(1). 996. [PubMed ID: 39762288]. [PubMed Central ID: PMC11704328]. <https://doi.org/10.1038/s41598-024-84092-x>.