

LOW DENSITY LIPOPROTEIN (LDL) LEVELS, AGE, AND SEX AS RISK FACTORS FOR CORONARY HEART DISEASE INCIDENTS AT NGOERAH HOSPITAL

I Gede Pramaditya Wahyu Saputra¹, A.A. Ngurah Subawa², I Wayan Putu Sutirtha Yasa², Desak Gde Diah Dharma Santhi²

¹Medical Student, Faculty of Medicine, Udayana University

²Department of Clinical Pathology, Faculty of Medicine, Udayana University, RSUP Prof.dr.I.G.N.G. Ngoerah
e-mail: gedeptram46@gmail.com

ABSTRACT

Coronary heart disease (CHD) is the foremost cause of mortality in Indonesia and is closely related to atherosclerosis due to increased levels of low density lipoprotein (LDL). The risk of CHD increases with age and is generally higher in male than in female, especially before menopause. Therefore, this study sought to assess the role of LDL, age, and sex as risk factors for CHD at Ngoerah Hospital. A case-control study of 34 case and 34 control patients (2022–2024) was conducted using consecutive sampling from medical records. To identify risk factors for CHD, bivariate analysis was conducted using the Chi-square test, followed by multivariate analysis using multiple logistic regression. Among the 68 patients analyzed, the majority (41 patients, 60.3%) had high LDL levels. The sample characteristics were predominantly male (44 patients, 64.7%) and of older age (42 patients, 61.8%). Multivariate analysis revealed that patients with high LDL levels showed a 7.4-fold greater likelihood of developing CHD relative to those with low LDL levels (AOR = 7.4; CI 95% : 2.22–24.75; $p = 0.001$). Male patients was also significantly associated with CHD, with approximately 5.78 times higher odds compared to females (AOR = 5.78; CI 95% : 1.67–19.97; $p = 0.006$). Age did not show a significant relationship with CHD ($p = 0.65$).

Keywords : Coronary Heart Disease (CHD), Low Density Lipoprotein (LDL), Sex, Age

INTRODUCTION

Coronary heart disease (CHD) occurs when the coronary arteries responsible for supplying oxygen and blood to the myocardium become narrowed due to the formation of lipid plaques and thrombi via atherosclerosis.¹ This process will result in a lack of oxygen as well as nutrients supply to myocardium, thereby causing in impaired myocardial function and causes a decrease in perfusion of vital organs and the periphery.²

In the US, the mortality prevalence from heart disease is approximately 610,000, representing 1 in every 4 fatalities. Meanwhile, the number of patients experiencing CHD is 735,000, comprising 525,000 new CHD and 210,000 recurrent CHD.³

CHD is a multifactorial disease primarily caused by an unhealthy lifestyle, including unhealthy dietary patterns, sedentary behavior or insufficient physical activity, psychosocial stress, and exposure to toxic substances such as cigarette smoke.⁴ These lifestyles are known to be associated with many metabolic syndromes such as hypertension, dyslipidemia, and insulin resistance that

increases the risk of atherosclerosis formed in the coronary arteries of the heart.⁵

Among the secondary factors that contribute to atherosclerosis, dyslipidemia is considered a critical initial trigger. Lipids accumulation within the vascular intima, which triggers a localized inflammatory response, is strongly implicated in the pathogenesis of atherosclerosis. Lipids are distributed throughout the whole body via the bloodstream by binding to a specific protein, forming a complex known as lipoproteins. Lipoproteins is classified into two general types: low-density lipoprotein (LDL) and high-density lipoprotein (HDL). LDL primarily functions to transport cholesterol from the liver to peripheral tissues, whereas HDL removes excess cholesterol from peripheral tissues and returns it to the liver for excretion. Normally, LDL is rapidly cleared by LDL receptors on hepatocytes. However, when the amount of LDL in the plasma is excessively high, it can be deposited in the blood vessels, and the cholesterol components within it contribute to atherosclerosis.⁶

In cases of hyperlipidemia, the excessive amount of LDL in the vascular lumen can be transported into the vascular intima and is oxidized to form ox-LDL. This ox-

LDL then can trigger an inflammatory reaction by inducing inflammatory mediators that leads to plaque formation. Thrombosis can also occur due to the rupture of the blood vessel endothelium, often resulting from an unstable plaque burden.⁷ It is known that 40% of patients who have CHD have high cholesterol levels.⁸

Besides the levels of LDL, age and sex also play a role in increasing the risk of CHD. Older age contributes to increased exposure to toxins, and male also have lower estrogen levels than female, resulting in a less protective effect.

MATERIALS AND METHOD

A total of 68 patient recorded from the Ngoerah Hospital registry were analyzed for this analytical, observational case-control study. Data were collected over the 2022–2024 period using a non-probability, consecutive sampling technique. The case group in this study was patients with CHD while the control group was patients with diabetes mellitus who had never been diagnosed with CHD. The inclusion criteria for the case group were all males or females with a diagnosis of CHD, with complete information of LDL levels in the medical record. Participants were excluded from the case group if they had a history of consuming lipid-lowering drugs (statins, fibrates, niacin, high-dose omega-3 fatty acids, bile acid sequestrants, ezetimibe, PCSK9 inhibitors, bempedoic acid, and specialized drugs such as lomitapide or mipomersen) and incomplete medical records. The inclusion criteria for the control group were all males or females who had not been diagnosed with CHD, with complete information of LDL levels in medical records. The exclusion criteria for control group were patients with a history of consuming

lipid-lowering drugs (statins, fibrates, niacin, high-dose omega-3 fatty acids, bile acid sequestrants, ezetimibe, PCSK9 inhibitors, bempedoic acid, and specialized drugs such as lomitapide or mipomersen) and patients with incomplete medical records. The study received ethical clearance from the Research Ethics Committee, Faculty of Medicine, Udayana University (Reference No: [1246/UN14.2.2. VII.14/LT/2025]).

Data regarding age, sex, medical history, medication history, and LDL levels were retrospectively retrieved from electronic medical records. The LDL levels findings were grouped into low LDL level (LDL < 100 mg/dl) and high LDL level (LDL ≥ 100 mg/dl). Age was classified into two groups: younger age (≤ 55 years) and older age (> 55 years), while sex was categorized as male and female. The data then statistically processed with IBM SPSS® version 26. The data were analyzed in three stages: univariate analysis for sample characteristics, bivariate analysis using the Chi-square, and multiple logistic regression for multivariate analysis.

RESULTS

Within the 68 patients in total, the majority were male (64.7%) and the remainder were female (35.3%). The study population had a mean age of 58.5 ± 11.9 ranging from 25 to 91 years, where the majority are aged > 55 years (61.8%) and the rest are aged ≤ 55 years (38.2%). Laboratory examinations showed that the mean LDL level of patients was 122.22 ± 57.27 mg/dl ranging from 15 to 248 mg/dl, most of whom had high LDL levels (60.3%) while the rest had low LDL levels (39.7%). The characteristic of all patients is presented in **Table 1**.

Table 1. Characteristics of Study Subjects

General Characteristics		Results
Sex	Male n (%)	44 (64.7)
	Female n (%)	24 (35.3)
Age (Years)	Mean ± SD (range)	58.5 ± 11.9 (25-91)
Age Category	≤ 55 Years n (%)	26 (38.2)
	> 55 Years n (%)	42 (61.8)
LDL Levels (mg/dl)	Mean ± SD (range)	122.22 ± 57.27 (15-248)
LDL Category	Low n (%)	27 (39.7)
	High n (%)	41 (60.3)

Among the 34 CHD patients (the case group), the majority had high LDL levels (79.4%), were aged > 55 years (64.7%), and were male (79.4%). The remainder had low LDL levels (20.6%), were aged ≤ 55 years (35.3%), and were female (20.6%). Conversely, the 34 diabetes mellitus patients (the control group) exhibited different

characteristics. The majority of control group had low LDL levels (58.8%) and were aged > 55 years (58.8%), but the sex distribution were evenly split between male and female. The remainder had high LDL levels (41.2%) and were aged ≤ 55 years (41.2%). The distributions of LDL levels, age, and sex on each group is provided in **Table 2**.

Table 2. Distribution of LDL Levels, Age, and Sex Each on Case and Control Group

Variables	Control Group (DM)	Case Group (CHD)	Total n (%)
Low LDL	20 (58.8)	7 (20.6)	27 (39.7)
High LDL	14 (41.2)	27 (79.4)	41 (60.3)
Age ≤ 55 Years	14 (41.2)	12 (35.3)	26 (38.2)
Age > 55 Years	20 (58.8)	22 (64.7)	42 (61.8)
Male	17 (50)	27 (79.4)	44 (64.7)
Female	17 (50)	7 (20.6)	24 (35.3)

The relationships between each independent variable (LDL levels, age, and sex) and the dependent variable (CHD incidence) were examined using bivariate analysis. It was found that significant relationship between elevated LDL levels and CHD incidence was observed (OR = 5.51; 95% CI : 1.88–16.16; p = 0.001). A significant relationship was also found between male sex and the incidence of CHD (OR = 3.86; 95% CI : 1.32–11.24; p = 0.011). Conversely, there was no significant relationship found between age and the incidence of CHD, with a p-value of 0.62 (>0.05). A multivariate analysis then conducted using multiple logistic regression analysis to determine the joint relationship between LDL levels, age, and sex as risk factors for CHD, it was found that high LDL levels were significantly associated with the incidence of CHD. Patients with high LDL had 7.4 times higher odds to experiencing CHD than

patients with low LDL (AOR = 7.4; 95% CI : 2.22-24.75; p = 0.001). Male patients was also significant, with approximately 5.78 times higher likelihood of experiencing CHD than females (AOR = 5.78; 95% CI : 1.67-19.97; p = 0.006). Meanwhile, age did not show a significant association with the incidence of CHD (p = 0.65). The results of bivariate and multivariate analysis is presented in **Table 3**.

The Hosmer–Lemeshow test results showed a p-value of 0.35 (> 0.05), indicating that the data were suitable for analysis. The Nagelkerke R² value of 0.33 indicated that LDL levels, sex, and age explained the 33.3% of the variation in CHD incidence, while the remainder was explained by other factors that were not examine in this study. The logistic regression model feasibility test is summarized in **Table 4**.

Table 4. Logistic Regression Model Feasibility Test

Feasibility est	Results	P-value
Hosmer-Lemeshow	5.61	0.35
Nagelkerke R ²	0.33	-

DISCUSSION

This study provides strong empirical evidence regarding the relationship between LDL and CHD incidence at Ngoerah Hospital. Multiple logistic regression analysis also found that high LDL levels were 7.4 times more likely to develop CHD than patients with low LDL (AOR = 7.4; 95% CI : 2.22-24.75; $p = 0.001$). The findings of this study confirm that high LDL levels play a significant role in the pathogenesis of CHD in the local clinical setting.

The results of this study are consistent with several previous studies. A meta-analysis of 20 cohort studies with 1.2 million samples showed that patients with LDL levels of 130–159 mg/dL (RR = 1.26; 95% CI : 1.08–1.47) and those with LDL levels of ≥ 160 mg/dl (RR = 1.70; 95% CI : 1.35–2.14) had a high risk of developing CHD, in contrast to patients with LDL levels of 70–129 mg/dL, which were not associated with CHD events.⁹ The same study further noted that patients with LDL ≥ 160 mg/dl were associated with a significantly higher CHD-related mortality (RR = 2.03; 95%CI : 1.36–3.03) compared to patients with LDL levels of 70-129 mg/dl and 130-159 mg/dl.⁹ Further supporting findings from a large cohort study in Denmark, reported that at all ages, particularly in older patients (aged 70-100 years), the risk of CHD increased for every 1 mmol/l increase in LDL (HR 1.16, 95% CI : 1.12–1.21).¹⁰ In Indonesia, a study conducted at Pertamedika Ummi Rosnati Hospital in Aceh also found a significant relationship between high LDL levels and CHD based on the chi-square test ($p = 0.022$).¹¹ A descriptive study at Dr. Kariadi General Hospital Semarang also stated that 74% of CHD patients registered at the hospital in the 2016-2017 period had LDL levels > 100 mg/dl with an average of 126 mg/dl.

Table 3. Bivariate and Multivariate Analysis Results

Variables	OR (CI 95%)	Bivariate p-value	AOR (CI 95%)	Multivariate p-value
High LDL	5.51 (1.88–16.16)	0.001	7.40 (2.22–24.75)	0.001
Male Sex	3.86 (1.32–11.24)	0.011	5.78 (1.67–19.97)	0.006
Age (> 55 years)	1.28 (0.48–3.42)	0.062	1.30 (0.41–4.14)	0.065

The findings regarding sex as a risk factor for CHD are in line with epidemiological studies that reveal that 75% of CHD patients are found in male aged over 45 years, while the incidence in female only increases after the age of 50 years, when female experiencing menopause. This is primarily associated with the decreased estrogen levels in menopausal women, which is believed to reduce the level of CD8+ T cells that constitute a key factor in human immunity against chronic diseases. This is also explained by another theory that estrogen represent an important

¹² The consistency of the findings from various populations, both global and local, strengthens the external validity of the Ngoerah Hospital study.

Pathologically, the increased risk of coronary heart disease due to high LDL levels can be explained by LDL's role in initiating the formation of atherosclerotic plaque in the coronary arteries. Endothelial dysfunctions of coronary arteries triggered by physical stress, chemical substances, or oxidative stress enabling the transport of LDL from lumen space into intimal space of vessels.¹³ LDL subsequently trapped within the intimal space of blood vessels and binds to the extracellular matrix and is oxidized to ox-LDL. Ox-LDL can then release inflammatory mediators that facilitate monocyte adhesion to the intimal space, where these monocytes can differentiate into macrophages. The phagocytosis of ox-LDL by macrophages then occurs, resulting in the formation of foam cells. To maintain blood vessel integrity, foam cells promote smooth muscle proliferation in the intimal space and form a fibrous cap with the production of a collagen-rich extracellular matrix. This ongoing process leads to plaque formation that narrows the arterial lumen and, if ruptured, can trigger acute thrombosis that manifests as a myocardial infarction.^{1,14,15} This molecular process is the culmination of a pathogenesis cascade observed in 79.4% of CHD patients with high LDL levels. To assess the contribution of control factors other than LDL to CHD, multiple logistic regression analysis was also performed on the variables of sex and age.

An increased risk was observed in male patients based on multiple regression analysis, approximately 5.78 times higher risk of developing CHD compared to female (AOR = 5.78; 95% CI : 1.67-19.97; $p = 0.006$).

determinant in the production of antioxidants in the female body, especially NADPH oxidase (nicotinamide adenine dinucleotide phosphate-oxidase), specifically the p47 subunit and the level of Nox, as well as angiotensin II.^{16,17} However, unlike sex factor, multiple logistic regression analysis found no significant association between older age and the incidence of coronary heart disease at Ngoerah Hospital. This finding is inconsistent with a cohort study conducted in China with 39,259 subjects, which found that older age was associated with an increased likelihood of

developing coronary heart disease (OR =1.06; 95% CI : 1.05–1.06).¹⁸ The reason of this inconsistency finding is because the majority of patients in this study are patients of older age, limiting the analysis's ability to detect the risk gradient based on age. This relatively uniform age distribution subsequently rendered the analysis results insignificant.

The results of this study provide several clinical implications that can be applied locally, particularly at Ngoerah Hospital, regarding the diagnosis and treatment of CHD patients. As a first step, early screening of LDL lipid profiles is mandatory for patients at high risk of CHD. Patients with high LDL levels are required to achieve LDL levels of < 70–100 mg/dl according to international guidelines, with an absolute

reduction of $\geq 50\%$ for very high levels. LDL levels can be reduced through pharmacological interventions and lifestyle changes. Pharmacological therapy that can be given includes lipid-lowering drugs such as statin group (simvastatin, atorvastatin, rosuvastatin) which inhibits cholesterol production, where it has been proven that by reducing LDL level, the risk of CHD can be reduced. Not only is lipid-lowering medication administered, high-risk CHD patients must also be given education on medication adherence. This is an important finding to note, as the local setting itself demonstrated that 56% of CHD patients at Ngoerah Hospital during the period of January–June 2018 had high LDL levels (>100 mg/dL).¹⁹ Other risk factors also need to be considered, such as the need for adequate blood pressure control, given that most CHD patients at Ngoerah Hospital have hypertension as a comorbidity.²⁰ Although pharmacological therapy is the mainstay of dyslipidemia management, it is important to emphasize that holistic lifestyle modifications encompassing a healthy dietary pattern, regular physical activity, and cessation of smoking as the primary steps in implementing the prevention of CHD.

CONCLUSION AND RECOMMENDATION

Based on study conducted at Ngoerah Hospital, it was found that high LDL levels and male patients have a higher risk of developing CHD compared to patients with low LDL levels and female sex, whereas age did not have a relationship with CHD incidence. Through multiple logistic regression analysis, it was found that patients with high LDL were 7.4 times more likely to experience CHD than patients with low LDL (AOR = 7.4; 95% CI : 2.22–24.75; $p = 0.001$). Male patients was also significant, with approximately 5.78 times higher likelihood of experiencing CHD than females (AOR = 5.78; 95% CI : 1.67–19.97; $p = 0.006$). Meanwhile, age did not show a significant association with CHD incidence ($p=0.65$). The relationship between LDL and gender variables on CHD incidence is in line with previous research, in contrast to the age variable

which is not in line with previous descriptive research. The results of this study can be applied clinically at Ngoerah Hospital by implementing mandatory LDL screening rules for high-risk CHD patients and increasing education regarding compliance with LDL level control.

Subsequent research is recommended to involve a larger number of participants across a wider age spectrum to more clearly depict the risk distribution by age group. The analysis should also include other variables that play a significant role in CHD incidence, such as high blood pressure, DM, obesity, smoking habits, physical activity, and family history. This way, future research can provide a more comprehensive picture of CHD risk factors and support more effective prevention and management strategies.

REFERENCES

1. Björkegren JLM, Lusis AJ. Atherosclerosis: Recent developments. *Cell*. 2022;185(10):1630–45. doi:10.1016/j.cell.2022.04.004.
2. Wolf D, Ley K. Immunity and inflammation in atherosclerosis. *Circ Res*. 2019;124(2):315–27. doi:10.1161/CIRCRESAHA.118.31359
3. Lee YY, Rhee MH. Atherosclerosis. In: *Recent Advancements in Microbial Diversity: Macrophages and Their Role in Inflammation*. 2022. p. 265–75. doi:10.1016/B978-0-12-822368-0.00012-8.
4. Lechner K, von Schacky C, McKenzie AL, Worm N, Nixdorff U, Lechner B, et al. Lifestyle factors and high-risk atherosclerosis: pathways and mechanisms beyond traditional risk factors. *Eur J Prev Cardiol*. 2020;27(4):394–406. doi:10.1177/2047487319869400.
5. Ji X, Leng XY, Dong Y, Ma YH, Xu W, Cao XP, et al. Modifiable risk factors for carotid atherosclerosis: a meta-analysis and systematic review. *Ann Transl Med*. 2019;7(22):632. doi:10.21037/atm.2019.10.115.
6. Wolska A, Remaley AT. Measuring LDL-cholesterol: what is the best way to do it? *Curr Opin Cardiol*. 2020;35(4):405. doi:10.1097/HCO.0000000000000740.
7. Zhang S, Li L, Chen W, Xu S, Feng X, Zhang L. Natural products: the role and mechanism in low-density lipoprotein oxidation and atherosclerosis. *Phytother Res*. 2021;35(6):2945–67. doi:10.1002/ptr.7002.
8. Michos ED, McEvoy JW, Blumenthal RS. Lipid management for the prevention of atherosclerotic cardiovascular disease. *N Engl J Med*. 2019;381(16):1557–67. doi:10.1056/NEJMra1806939.
9. Peng K, Li X, Wang Z, Li M. Association of low-density lipoprotein cholesterol levels and outcomes in chronic kidney disease. *Medicine (Baltimore)*. 2022;101:e32003. doi:10.1097/MD.00000000000032003.
10. Mortensen MB, Nordestgaard BG. Elevated LDL cholesterol and increased risk of myocardial infarction and atherosclerotic cardiovascular disease in individuals aged 70–100 years: a contemporary primary prevention

- cohort. *Lancet*. 2020;396(10263):1644–52. doi:10.1016/S0140-6736(20)32233-9.
11. Hafiza R, Candra A, Lidiawati M. Hubungan hipertensi, kadar kolesterol total, dan kadar LDL terhadap penyakit jantung koroner di Poli Jantung Rumah Sakit Pertamedika Umami Rosnati Kota Banda Aceh. *J Ilmu Kedokt Kesehat*. 2024;11(10):1963–71.
 12. Muzakky MI, Ardianto P, Uddin I. Distribusi kadar LDL target pasca terapi statin pada pasien penyakit jantung koroner di RSUP Dr. Kariadi Semarang. *J Kedokt Diponegoro*. 2018;7(2):1081–7. doi:10.14710/dmj.v7i2.20855.
 13. Karani Y. HDL dan aterosklerosis. 2020;5(4).
 14. Souilhol C, Serbanovic-Canic J, Fragiadaki M, Chico TJ, Ridger V, Roddie H, et al. Endothelial responses to shear stress in atherosclerosis: a novel role for developmental genes. *Nat Rev Cardiol*. 2019;17(1):52–63. doi:10.1038/s41569-019-0239-5.
 15. Clyne AM. Endothelial response to glucose: dysfunction, metabolism, and transport. *Biochem Soc Trans*. 2021;49(1):313. doi:10.1042/BST20200611.
 16. Madonna R, Balistreri CR, De Rosa S, Muscoli S, Selvaggio S, Selvaggio G, et al. Impact of sex differences and diabetes on coronary atherosclerosis and ischemic heart disease. *J Clin Med*. 2019;8(1):98. doi:10.3390/jcm8010098.
 17. Marzà-Florensa A, Kiss P, Mohamed Youssef D, Jalali-Farahani S, Lanas F, di Cesare M, et al. Sex differences in acute coronary syndromes: a scoping review across the care continuum. *Glob Heart*. 2025;20(1):26. doi:10.5334/gh.1410.
 18. Wang Y, Li Y, Liu X, Zhang H, Abdulai T, Tu R, et al. Prevalence and influencing factors of coronary heart disease and stroke in Chinese rural adults: the Henan Rural Cohort Study. *Front Public Health*. 2020;7:411. doi:10.3389/fpubh.2019.00411.
 19. Utama FW, Herawati S, Wande IN. Gambaran rasio profil lipid pada pasien penyakit jantung koroner di RSUP Sanglah periode Januari–Juni 2018. *E-J Med Udayana*. 2021;10(4):23–8.
 20. Mahottama AA, Karmaya INM, Muliani. Prevalensi hipertensi pada penderita penyakit jantung koroner (PJK) di RSUP Sanglah Denpasar Maret – September 2019. *E-Jurnal Medika Udayana*. 2021;10(4):1–5. doi:10.24843/MU.2021.V10.i4.P01.

