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Multifactorial Risk Assessment: LDL Level, Fasting Blood Glucose, Uric Acid, Triglycerides, and TG/HDL Ratio as Predictors of Framingham Risk Score for Hard Coronary Heart Disease

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Abstract*. The Framingham Risk Score (FRS) assesses coronary heart disease (CHD) risk and predicts acute coronary events. Metabolic markers like LDL cholesterol, fasting blood glucose, uric acid, triglycerides, and TG/HDL ratio play critical roles in atherosclerosis and cardiovascular risk. Elevated LDL cholesterol, fasting blood glucose, and uric acid contribute to plaque formation, inflammation, and vascular damage, while high triglycerides and low HDL cholesterol exacerbate atherogenesis. This study explores the relationship between these markers and FRS to enhance CHD risk prediction and support targeted cardiovascular interventions. This study analyzed LDL cholesterol, fasting blood glucose, uric acid, triglycerides, and TG/HDL ratio with Framingham Risk Score in 85 participants, excluding those with incomplete data or chronic illnesses. The analysis found significant correlations between metabolic parameters and the 10-year myocardial infarction risk. LDL cholesterol, triglycerides, and uric acid showed moderate positive associations with cardiovascular outcomes, while the triglyceride-to-HDL ratio and fasting blood glucose had weaker but significant correlations. These findings highlight lipid profiles and metabolic markers as key contributors to cardiovascular risk. This study highlights significant correlations between LDL cholesterol, fasting blood glucose, uric acid, triglycerides, and the triglyceride/HDL ratio with 10-year cardiovascular risk. These findings emphasize the importance of lipid profiles, glycemic control, and metabolic markers in predicting coronary outcomes and guiding targeted preventive interventions for improved cardiovascular risk management.*

Keywords: *Framingham; Hard coronary heart disease; Lipid panel; Predictor parameter*

Abstrak. Skor Risiko Framingham (Framingham Risk Score/FRS) digunakan untuk menilai risiko penyakit jantung koroner (PJK) dan memprediksi kejadian koroner akut. Penanda metabolik seperti kolesterol LDL, glukosa darah puasa, asam urat, trigliserida, dan rasio TG/HDL memainkan peran penting dalam proses aterosklerosis dan risiko kardiovaskular. Peningkatan kadar kolesterol LDL, glukosa darah puasa, dan asam urat berkontribusi terhadap pembentukan plak, peradangan, dan kerusakan vaskular, sementara kadar trigliserida yang tinggi dan HDL yang rendah memperburuk proses aterogenesis. Penelitian ini bertujuan untuk mengetahui hubungan antara kolesterol LDL, glukosa darah puasa, asam urat, trigliserida, dan rasio TG/HDL terhadap Skor Risiko Framingham dalam memperkirakan risiko penyakit jantung koroner secara lebih akurat dan mendukung intervensi pencegahan yang lebih tepat sasaran. Penelitian ini dilakukan pada 85 partisipan, dengan mengecualikan individu yang memiliki data tidak lengkap atau penyakit kronis. Analisis menunjukkan korelasi yang signifikan antara parameter metabolik dan risiko infark miokard 10 tahun. Kolesterol LDL, trigliserida, dan asam urat menunjukkan hubungan positif yang sedang dengan hasil kardiovaskular, sementara rasio trigliserida terhadap HDL dan glukosa darah puasa menunjukkan korelasi yang lebih lemah namun tetap signifikan. Penelitian ini menekankan korelasi signifikan antara kolesterol LDL, glukosa darah puasa, asam urat, trigliserida, dan rasio TG/HDL dengan risiko kardiovaskular dalam 10 tahun. Hasil ini menggarisbawahi pentingnya kontrol lipid, glikemik, dan status metabolik dalam memprediksi kejadian koroner serta mendukung intervensi pencegahan yang terarah untuk meningkatkan manajemen risiko kardiovaskular.

Kata kunci: Penyakit Jantung Koroner Berat; Panel Lipid; Parameter Prediktif; Skor Risiko Framingham

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1. INTRODUCTION

Cardiovascular diseases (CVDs) remain a leading cause of morbidity and mortality worldwide. The Framingham Risk Score (FRS) provides a widely used tool for assessing the risk of coronary heart disease (CHD) and predicting severe coronary events, such as myocardial infarction and coronary death. Key metabolic and biochemical markers, including LDL cholesterol, Fasting Blood Glucose, uric acid, triglycerides, and triglyceride-to-HDL cholesterol (TG/HDL) ratio, significantly influence the development of atherosclerosis and coronary artery disease. (Bosomworth & Fcfp, 2011; Brindle et al., 2003; Kasim et al., 2023)

LDL cholesterol, or "bad cholesterol," plays a central role in atherosclerosis by promoting plaque buildup in arterial walls. Elevated fasting blood glucose, a hallmark of diabetes and prediabetes, exacerbates cardiovascular risk by inducing glycation, inflammation, and oxidative stress, which damage blood vessels and impair vascular function. (Ference et al., 2017) Uric acid, while commonly linked to gout, contributes to cardiovascular pathology through inflammatory activation, oxidative stress, and endothelial dysfunction. High triglycerides and low HDL cholesterol levels, markers of dyslipidemia, further increase cardiovascular risk by promoting atherogenesis and impairing cholesterol clearance. Together, these factors accelerate the progression of atherosclerosis and increase the risk of acute coronary events. (Gidding & Allen, 2019)

By investigating the correlation between these markers and the Framingham Risk Score, this study seeks to clarify their collective impact on cardiovascular risk. Understanding these relationships will enhance predictive models for CHD and support targeted interventions in high-risk populations, ultimately reducing the burden of cardiovascular disease.

2. LITERATURE REVIEW

Elevated LDL cholesterol, often called "bad cholesterol," plays a central role in the development of atherosclerosis, the primary mechanism underlying coronary heart disease (CHD). High LDL levels lead to the accumulation of cholesterol in arterial walls, forming fatty plaques that narrow the arteries and reduce blood flow to the heart and other organs. (Ajoolabady et al., 2024) This process, called atherosclerosis, increases the risk of ischemia, angina, myocardial infarction, and other cardiovascular events. Systematically, LDL particles penetrate the endothelial lining of blood vessels, where they become oxidized. Oxidized LDL is highly atherogenic, triggering inflammatory responses that attract macrophages and form foam cells, the building blocks of atherosclerotic plaques. (Gaggini et al., 2022) Additionally,

oxidized LDL promotes endothelial dysfunction by reducing nitric oxide bioavailability, impairing vascular tone, and initiating inflammation. Over time, unstable plaques, often rich in oxidized LDL, may rupture, leading to thrombosis and complete arterial blockage, causing a heart attack or stroke. (Qiao et al., 2022)

Hypertriglyceridemia likely contributes to cardiovascular risk by promoting endothelial dysfunction, increasing pro-inflammatory responses, and influencing the formation of small, dense LDL particles. Elevated triglyceride levels, or hypertriglyceridemia, are strongly associated with an increased risk of cardiovascular disease (CVD) due to several underlying mechanisms. (Soffer et al., 2024) High triglycerides contribute to endothelial dysfunction by reducing nitric oxide availability, leading to impaired vascular tone and increased vascular stiffness. Triglyceride-rich lipoproteins, such as very-low-density lipoproteins (VLDL) and their remnants, also stimulate the release of pro-inflammatory cytokines, creating a pro-inflammatory environment that promotes atherosclerosis. (Singh & Singh, 2016) Furthermore, elevated triglycerides facilitate the formation of small, dense LDL particles, which are highly atherogenic because they more easily penetrate arterial walls, are prone to oxidation, and drive plaque development. Triglyceride-rich lipoprotein remnants directly infiltrate arterial walls, contributing to foam cell formation and plaque progression. Hypertriglyceridemia is also a hallmark of metabolic syndrome, which includes insulin resistance, abdominal obesity, hypertension, and dyslipidemia, all of which synergistically increase cardiovascular risk. (Miller et al., 2011)

Elevated uric acid levels, or hyperuricemia, contribute to oxidative stress, endothelial dysfunction, and chronic inflammation, all of which are key mechanisms in the development of coronary heart disease (CHD). Hyperuricemia promotes oxidative stress by generating reactive oxygen species (ROS), which damage endothelial cells and reduce nitric oxide bioavailability, impairing vascular relaxation and increasing vascular stiffness. Additionally, uric acid activates the NLRP3 inflammasome, triggering the release of pro-inflammatory cytokines such as interleukin-1β (IL-1β) and interleukin-18 (IL-18), which accelerate atherosclerotic plaque formation and destabilization. (Borghi & Piani, 2021; Maloberti et al., 2020; Muiesan et al., 2016)

Hyperglycemia also promotes chronic inflammation in the blood vessels, leading to endothelial dysfunction, atherosclerosis, and higher blood pressure. Additionally, high glucose levels generate reactive oxygen species (ROS), which damage blood vessel walls and impair blood flow, further raising cardiovascular risk. (C. Park et al., 2013)

3. METHODS

This study aimed to assess the correlation between LDL cholesterol levels, fasting blood glucose, uric acid, triglycerides, and the triglyceride/HDL ratio with the Framingham Risk Score for Hard Coronary Heart Disease. The research was conducted in Kelurahan Krendang, West Jakarta, and involved 85 participants who met the inclusion and exclusion criteria. Participants aged 30 years or older and willing to provide informed consent were included. Researchers excluded individuals with incomplete clinical or biochemical data or those with chronic illnesses such as cancer or renal failure, as these conditions could confound cardiovascular risk evaluations.

Researchers collected data by measuring LDL cholesterol, triglycerides, and the triglyceride/HDL ratio using the Nesco Lipid Monitoring System. Fasting Blood Glucose and uric acid levels were analyzed using Fora 6. Participants fasted for 8–10 hours before measurements to ensure accuracy.

The Framingham Risk Score was calculated to estimate the 10-year risk of developing cardiovascular disease (CVD). Key factors included age, gender, total cholesterol, high-density lipoprotein (HDL) cholesterol, systolic blood pressure, use of antihypertensive medication, smoking status, and diabetes status. Age, gender, antihypertensive medication use, and smoking status were determined through structured interviews, while HDL and total cholesterol levels were measured using the Nesco Lipid Monitoring System. Blood pressure was assessed following standard physical examination protocols

Spearman's correlation test was used to evaluate the relationship between the biomarkers and the Framingham Risk Score for Hard Coronary Heart Disease. Researchers considered statistical significance at a p-value threshold of <0.05. This study received ethical approval from the Tarumanagara University Human Research Ethics Committee.

4. RESULT AND DISCUSSION

The study population predominantly consisted of females, accounting for 95.3% of participants, with males comprising only 4.7%. The mean age of the participants was 41.40 years, with a median age of 39 years and a range of 30 to 71 years. The largest age group was 30–39 years, representing 55.29% of the population, followed by the 40–49 years group at 24.71%. Key clinical parameters included a mean LDL level of 112.59 mg/dL and a median of 114 mg/dL (range: 47–183 mg/dL). Fasting blood glucose levels had a mean of 91.89 mg/dL and a median of 85 mg/dL (range: 68–268 mg/dL). Uric acid levels averaged 3.93 mg/dL with a median of 3.8 mg/dL (range: 2.7–6.2 mg/dL). Triglyceride levels showed a

mean of 131.68 mg/dL and a median of 109 mg/dL (range: 47–394 mg/dL). The TG/HDL ratio had a mean of 4.07 and a median of 3.94 (range: 2.15–7.78). These findings provide critical insights into the demographic and metabolic profiles of the study participants. (Table 1)

Table 1. Characteristics of Research Results

Parameter	N (%)	Mean (SD)	Med (Min - Max)
Gender			
• Female	81 (95.3)		
• Male	4 (4.7)		
Age		41.40 (1.07)	39 (30 – 71)
• 30 – 39 years	47 (55.29)		
• 40 – 49 years	21 (24.71)		
• 50 – 59 years	10 (11.76)		
• 60 – 69 years	6 (7.06)		
• 70 – 79 years	1 (1.18)		
LDL Level		112.59 (2.92)	114 (47 – 183)
Fasting Blood Glucose		91.89 (3.17)	85 (68 – 268)
Uric Acid		3.93 (0.07)	3.8 (2.7 – 6.2)
Triglycerides		131.68 (6.92)	109 (47 – 394)
TG/HDL Ratio		4.07 (0.13)	3.94 (2.15 – 7.78)

The analysis revealed significant correlations between various metabolic parameters and the 10-year risk of myocardial infarction (MI) or death, as estimated by the Framingham Risk Score for hard coronary heart disease. Low-density lipoprotein (LDL) levels showed a moderate positive correlation with the 10-year risk ($r = 0.408$, $p < 0.001$), highlighting its strong association with cardiovascular outcomes. Triglycerides exhibited a similar correlation ($r = 0.403$, $p < 0.001$), reinforcing their role in cardiovascular risk. Uric acid levels also demonstrated a moderate positive correlation ($r = 0.386$, $p < 0.001$), while the triglyceride-to-HDL ratio displayed a weaker but still significant correlation ($r = 0.297$, $p = 0.006$). Additionally, fasting blood glucose levels showed a statistically significant but weaker association ($r = 0.231$, $p = 0.034$). These findings emphasize the importance of addressing lipid profiles, uric acid, and fasting blood glucose as potential contributors to long-term cardiovascular risk. (Table 2)

Table 2. Correlation Between Metabolic Parameters and 10-Year Cardiovascular Risk

Parameter N =85	10-year risk of MI or death for this patient (Framingham Risk Score for Hard Coronary Heart Disease)	
	r-correlation (Spearman)	*p*-value
Low Dense Lipoprotein (LDL)	0,408	<0,001
Fasting Blood Glucose	0,231	0,034
Uric Acid	0,386	<0,001
Triglyceride	0,403	<0,001
Ratio triglyceride/HDL	0,297	0,006

The findings in this table highlight the significant role of metabolic parameters in predicting the 10-year risk of myocardial infarction (MI) or death, as estimated by the Framingham Risk Score for hard coronary heart disease. LDL levels show the strongest correlation ($r = 0.408$, $p < 0.001$), emphasizing the critical role of cholesterol regulation in cardiovascular risk. This result aligns with existing evidence that elevated LDL levels are a major contributor to atherosclerosis and subsequent coronary heart disease.

The significance of LDL cholesterol as a predictor of cardiovascular risk is well-documented. Epidemiological studies, such as the Framingham Heart Study, consistently demonstrate that higher LDL levels strongly correlate with increased cardiovascular events. Interventional trials, including those involving statin therapy, further support this relationship, showing that lowering LDL levels significantly reduces the incidence of major cardiovascular events. (Hilvo et al., 2022) For instance, a meta-analysis by the Cholesterol Treatment Trialists' Collaboration revealed a 22% reduction in cardiovascular events for every 1 mmol/L (39 mg/dL) decrease in LDL cholesterol. Consequently, clinical guidelines prioritize LDL cholesterol as a key target for therapy, recommending lifestyle modifications and pharmacological treatments, such as statins, ezetimibe, and PCSK9 inhibitors, to achieve LDL reductions. In high-risk individuals, aggressive lowering of LDL to below 70 mg/dL is often advised to prevent adverse outcomes. The strong correlation observed in this study reinforces the critical role of LDL cholesterol in cardiovascular risk and highlights the importance of effective LDL management in reducing the burden of coronary heart disease. (Burger et al., 2024; Zheutlin et al., 2024)

Triglyceride levels also exhibit a robust positive correlation, reinforcing their well-established association with cardiovascular outcomes. Epidemiological studies have consistently demonstrated that elevated triglyceride levels are an independent risk factor for cardiovascular events, particularly when combined with low HDL or high LDL cholesterol levels. (Sarwar et al., 2007) For instance, the Copenhagen City Heart Study identified hypertriglyceridemia as a significant predictor of myocardial infarction and coronary artery disease. (Harchaoui et al., 2009) Genetic evidence from Mendelian randomization studies supports a causal relationship between elevated triglycerides and CVD risk. (Singh & Singh, 2016) While traditional triglyceride-lowering therapies, such as fibrates, have shown mixed results, newer therapies like icosapent ethyl, a high-purity EPA omega-3 fatty acid, have demonstrated significant reductions in cardiovascular events among patients with elevated triglycerides. (Miller et al., 2011)

The significant correlation between triglycerides and cardiovascular risk observed in this study highlights the need for targeted interventions to address hypertriglyceridemia. (Harchaoui et al., 2009) Lifestyle modifications, including dietary changes, regular exercise, and weight loss, remain the first-line approach for managing elevated triglyceride levels. Pharmacological treatments, such as fibrates, omega-3 fatty acids, and statins, may also benefit high-risk patients. (Marston et al., 2019) The triglyceride-to-HDL ratio, a marker of insulin resistance and cardiovascular risk, further emphasizes the clinical importance of triglyceride management. These findings support the inclusion of triglyceride reduction in comprehensive cardiovascular risk management strategies, particularly for individuals with other metabolic abnormalities. (Nelson et al., 2020)

The triglyceride-to-HDL cholesterol (TG/HDL) ratio has gained recognition as a significant marker for metabolic and cardiovascular health, with this study demonstrating a statistically significant correlation between the ratio and cardiovascular risk. This finding underscores its clinical importance, particularly in identifying individuals at risk for dyslipidemia, insulin resistance, and related cardiovascular complications. The TG/HDL ratio reflects the balance between pro-atherogenic and anti-atherogenic lipids, with elevated triglycerides and reduced HDL cholesterol often indicating atherogenic dyslipidemia. This lipid profile is strongly linked to the presence of small, dense LDL particles, which are highly atherogenic and contribute to plaque formation in the arteries. (Da Luz et al., 2008) Furthermore, a high TG/HDL ratio serves as a surrogate marker for insulin resistance, a key feature of metabolic syndrome that impairs the regulation of triglyceride metabolism, resulting in increased triglyceride synthesis and decreased HDL levels. These imbalances promote endothelial dysfunction, chronic inflammation, and atherosclerosis. (Kosmas et al., 2023)

Numerous studies support the association of the TG/HDL ratio with cardiovascular risk. Large-scale population studies, such as NHANES, have demonstrated that an elevated TG/HDL ratio predicts adverse cardiovascular outcomes and is strongly correlated with insulin resistance. (Kosmas et al., 2023) Its predictive value extends across diverse populations, although risk thresholds may vary based on ethnicity and gender. For instance, a TG/HDL ratio above 3.5 often indicates increased cardiovascular risk in Western populations, while lower thresholds may apply to Asian populations. (Martínez-Marroquín et al., 2023) Additionally, the TG/HDL ratio has been proposed as a marker of residual cardiovascular risk in patients receiving LDL cholesterol-lowering therapy, identifying those

who may benefit from interventions targeting triglycerides and HDL cholesterol. (B. Park et al., 2021)

This study highlights the importance of addressing an imbalanced TG/HDL ratio in cardiovascular risk management. Lifestyle modifications, including weight loss, regular physical activity, and dietary changes such as reducing refined carbohydrate intake and increasing omega-3 fatty acids, effectively lower the TG/HDL ratio. Pharmacological treatments, including fibrates, niacin, and omega-3 fatty acids, may also help optimize the lipid profile in patients with persistent dyslipidemia despite statin therapy. By focusing on reducing the TG/HDL ratio, clinicians can address underlying metabolic disturbances contributing to cardiovascular disease and improve outcomes for high-risk populations. These findings reinforce the growing recognition of the TG/HDL ratio as a critical marker in cardiovascular risk stratification and management. (Kosmas et al., 2023; Martínez-Marroquín et al., 2023; B. Park et al., 2021)

Uric acid, a byproduct of purine metabolism, plays a significant role in cardiovascular disease (CVD), as demonstrated by this study's moderate positive correlation ($r = 0.386$, $p < 0.001$) between uric acid levels and 10-year cardiovascular risk. Epidemiological studies consistently show an independent association between hyperuricemia and cardiovascular events, including myocardial infarction and stroke. Clinical observations further link elevated uric acid levels with hypertension, chronic kidney disease, and arterial stiffness, which are all major CVD risk factors. (Akashi et al., 2023) Experimental models also reveal that lowering uric acid levels improves endothelial function, reduces blood pressure, and decreases vascular inflammation, suggesting a potential causal role for uric acid in cardiovascular pathology. (Chien et al., 2005) Pharmacological agents such as allopurinol and febuxostat, which lower uric acid levels, have shown promise in reducing cardiovascular events in preliminary studies, although large-scale trials are needed to confirm these findings. Lifestyle modifications, including reducing dietary purine intake, avoiding excessive alcohol consumption, and achieving healthy weight loss, remain effective strategies for managing hyperuricemia and potentially reducing cardiovascular risk. (Sosa et al., 2024)

This study reinforces the importance of evaluating uric acid levels as part of cardiovascular risk assessments. Elevated uric acid may serve not only as a biomarker for identifying high-risk individuals but also as a potential therapeutic target for cardiovascular risk reduction. By addressing hyperuricemia, clinicians can mitigate its effects on oxidative stress, inflammation, and endothelial dysfunction, offering a novel approach to lowering the burden of CVD. (Feig et al., 2008; Gagliardi et al., 2009; Yu & Cheng, 2020)

Fasting blood glucose (FBG) is a crucial indicator of metabolic health and cardiovascular risk, though it shows a weaker correlation with cardiovascular disease compared to other markers like lipids and uric acid. A moderate but statistically significant relationship exists between FBG and cardiovascular risk, pointing to its role in conditions like diabetes and impaired glucose metabolism. (Zuo et al., 2022) Elevated blood glucose contributes to vascular inflammation, oxidative stress, and the formation of advanced glycation end-products (AGEs), all of which increase cardiovascular risk. AGEs also accumulate in tissues, stiffening arteries and exacerbating plaque formation. While lipids, especially LDL cholesterol and triglycerides, and uric acid are more strongly associated with cardiovascular disease, FBG remains an important parameter in a comprehensive cardiovascular risk assessment, particularly in identifying individuals at risk for type 2 diabetes. (Bjørnholt et al., 1999) Managing elevated FBG through lifestyle changes or medication can help reduce cardiovascular risk by preventing or controlling diabetes-related complications. Thus, even with a weaker correlation, FBG plays a vital role in evaluating and managing cardiovascular health. (Barr et al., 2007)

5. CONCLUSION

This study found substantial associations between particular clinical characteristics and the 10-year risk of myocardial infarction or death, as measured by the Framingham Risk Score for Hard Coronary Heart Disease. LDL cholesterol, fasting blood glucose, uric acid, triglycerides, and the triglyceride-to-HDL ratio were all strong predictors of cardiovascular risk. These results highlight the importance of lipid profiles, glycemic management, and metabolic indicators in predicting cardiovascular outcomes. Regular monitoring of these markers may improve risk stratification and provide focused therapies to lower coronary heart disease risk.

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