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[VOL. 12 NO. 1, APRIL 2024](#)

## TABLE OF CONTENTS

### Articles

<a href="#">AI-SPOT: a Novel Artificial Intelligence-enabled Sport Optimization Tracker to Enhance Performance and Prevent Injury in Elite Footballers</a> Aaron Chen Angus, Dinesh Sirisena	<a href="#">PDF</a> 1–11
<a href="#">The Relationship Level of Self-medication Knowledge with Rationality of Drug Use in Adolescents</a> Muhammad Cariefzi Zahdffa Kusuma, Meiyanti Meiyanti	<a href="#">PDF</a> 12–17
<a href="#">Patient Safety Incident Reporting Challenges in Indonesian Private Hospitals</a> Ekorini Listiowati, Merita Arini, Mochamad Iqbal Nurmansyah, Emma Rachmawati, Agus Samsudin	<a href="#">PDF</a> 18–25
<a href="#">Vitamin D Levels and Their Correlation with Predisposing Factors and Estimated Fetal Weight in Third Trimester of Pregnancy: an Observational Study</a> Dwiwahju Dian Indahwati, Diana Krisanti Jasaputra, Arief Budiono, Julia Windi Gunadi, Ronny Lesmana, Steven Zerine Putra Kusmawan	<a href="#">PDF</a> 26–30
<a href="#">Epidemiologic Spatial Analysis of a Tuberculosis Incidence in Bandung City in 2021</a> Dony Septriana Rosady, Nysa Ro Aina Zulfa, Sony Bagja Pratama	<a href="#">PDF</a> 31–36
<a href="#">Ethnomedicinal Plants Used for Treatment of Infectious Diseases by Dayak Ethnic in Borneo, Indonesia</a> Nawan Nawan, Septi Handayani, Agnes Immanuela Toemon	<a href="#">PDF</a> 37–45
<a href="#">Blood Pressure, Total Cholesterol, and Triglycerides Associated with Cardiovascular Risk Score in Low 25-Hydroxy Vitamin D Level among Online Motorcycle Drivers, Jakarta, Indonesia</a> Joice Viladelvia Kalumpiu, Elly Herwana, Yenny Yenny, Kurniasari Kurniasari	<a href="#">PDF</a> 46–53
<a href="#">Correlation of NLR and D-dimer Levels with Clinical Severity of COVID-19 and Determination of Cut-off Values at a Hospital in Cirebon</a> Fitria Ratna Sari, Rika Nilapsari	<a href="#">PDF</a> 54–62
<a href="#">Bacteriological and Antibiotic Susceptibility Profile of Urinary Tract Infection among Online Motorcycle Drivers in Jakarta, Indonesia</a> Ida Effendi, Thomas Robertus, Jihan Samira, Arleen Devita, Widyasari Kumala, Isa Bella	<a href="#">PDF</a> 63–68
<a href="#">Ruang Sehat: Innovating Portable Lactation Pods for Wellness Tourism Using Design Thinking Method in Yogyakarta</a> Giyawati Yulilania Okinarum, Venny Vidayanti, Sri Hasta Mulyani	<a href="#">PDF</a> 69–75
<a href="#">Clinicopathological Characteristics of Breast Cancer at Cibabat Regional General Hospital in 2022–2023</a> Meike Rachmawati, Nuzirwan Acang, Wida Purbaningsih, Rian Robian, Adhi Nugraha, Rina Melati,	<a href="#">PDF</a> 76–81

**Blood Pressure, total cholesterol, and triglycerides associated with cardiovascular risk score in low 25-hydroxy vitamin d level among online motorcycle drivers, Jakarta,**

# Indonesia

*by* Elly Herwana

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# Blood Pressure, Total Cholesterol, and Triglycerides Associated with Cardiovascular Risk Score in Low 25-Hydroxy Vitamin D Level among Online Motorcycle Drivers, Jakarta, Indonesia

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## Abstract

Low 25-hydroxy vitamin D is associated with many chronic diseases, such as coronary heart disease. Online motorcycle drivers spend prolonged hours on the road and may face many stressors and occupational hazards that can create the development of cardiovascular disease. This study aims to determine factors contributing to cardiovascular risk among online motorcycle drivers. This study was an observational analytic with a cross-sectional design. Data were collected in September 2022 with consecutive random sampling methods for 114 subjects at Universitas Trisakti Jakarta. The ages of the subjects ranged from 25 to 62 years. Cardiovascular risk was assessed based on the Jakarta Cardiovascular Risk Score (JAKVAS). The data collection included physical examination and blood biochemistry (lipid profile, fasting blood glucose, and 25(OH)D). The data were analyzed using chi-square test with  $p < 0.05$ . The majority of subjects were male 83 (72.8%). On blood pressure examination, mean systolic blood pressure was  $128.9 \pm 16.7$  mmHg, and diastolic blood pressure was  $83.7 \pm 11.9$  mmHg. The mean cardiovascular risk was  $4.4 \pm 2.8$ , and 52.6% had a high-risk score. All subjects had low 25(OH)D serum levels, with mean 25(OH)D serum levels of  $18 \pm 5.7$  ranging between 6.9 and 29.8. Among online motorcycle drivers, there was a significant association between blood pressure, total cholesterol, and triglyceride with cardiovascular risk scores in low 25-hydroxy vitamin D levels. Blood pressure, total cholesterol, and triglyceride could affect cardiovascular health in low 25-hydroxy vitamin D levels among online motorcycle drivers.

**Keywords:** 25-hydroxy vitamin D, blood pressure, Jakarta Cardiovascular Risk Score, lipid profile, online motorcycle drivers

## Introduction

Vitamin D plays a significant role in supporting overall health. Vitamin D deficiency is a widespread health issue that affects the world. The global prevalence of deficiency serum 25(OH)D was 15.7% between 2000 and 2022.<sup>1</sup> Unequivocally, Indonesia, as a tropical country, has a high prevalence of vitamin D deficiency. Pulungan et al.<sup>2</sup> and Poh et al.,<sup>3</sup> showed that vitamin D deficiency in Indonesia was 44.6% and 94.4%, respectively. Insufficient exposure to sunlight and low intake of vitamin D are two leading causes of vitamin D deficiency, and it can contribute to an increased risk of chronic disease, such as cardiovascular disease, cancer, diabetes mellitus, etc.<sup>4</sup>

Coronary heart disease (CHD) or coronary artery disease (CAD) is the most common cardiovascular dysfunction disease, and its

prevalence is approximately 5–8% worldwide.<sup>5</sup> In Indonesia, the Basic Health Research data 2018 showed that 1.5% of Indonesians suffered from CHD, with death reaching 2.9%.<sup>6</sup> Siadat et al.<sup>7</sup> showed an association of 25(OH)D serum deficiency and coronary artery disease with cardiovascular risk factors. Its risk rises to 5.8 times (1.77–18.94) higher than in people with an average 25(OH)D serum level. Measurement of serum 25(OH)D levels has not been widely carried out in Indonesia, especially for online motorcycle drivers (*ojek* online) who are exposed to sunlight every day. Online motorcycle driving is a job that is now in great demand by the people of Indonesia, and there are still not many published studies on this job. Drivers spend prolonged hours on the road and may face many stressors and occupational hazards that can develop cardiovascular risk factors.<sup>8</sup> Drivers with high-risk cardiovascular disease had a higher



likelihood of crash and death.<sup>9,10</sup>

Preventing CHD through early detection of risk factors and efforts to control them are very important. Risk factors for CHD include modified and non-modified risk factors. Previous studies have documented that age, gender, hypertension, diabetes, hyperlipidemia, alcohol intake, low physical activity, and long duration of work were cardiovascular risks for drivers. Blood pressure and biochemical parameters are essential in determining a person's cardiovascular risk. Studies showed that biochemical parameters such as blood sugar, lipid profile, and even 25(OH)D status were often used to analyze cardiovascular risk.<sup>18</sup>

This article aims to determine the relationship factors contributing to cardiovascular risk in online motorcycle drivers with low 25(OH)D levels.

## Methods

It is an analytic observational study with a cross-sectional design conducted in September 2022. The selection of research subjects used consecutive non-random sampling techniques. The study inclusion criteria were male and female online motorcycle drivers aged 25–64 years, willing to participate, and signed informed consent. Exclusion criteria were having a cognitive impairment, a history of cardiovascular disease, not fully completing the questionnaire, having normal to high serum 25(OH)D level ( $\geq 30$  ng/ml), and having a high a high low-density lipoprotein cholesterol (LDL-C)  $\geq 300$  mg/dl. The study subjects who met the inclusion and exclusion criteria were asked to come to the study location after an overnight fast of 12 hours before blood collection for laboratory examination. Data were collected by interview using a demographic characteristics questionnaire and Jakarta's Cardiovascular Risk Score (JAKVAS) instrument adapted from the Framingham risk score. Jakarta's Cardiovascular Risk Score is based on the Indonesian population and is used for cardiovascular risk stratification in developing countries. It has been shown to have a sensitivity of 77.9%, a specificity of 90%, a positive predictive value of 92.2%, and a negative predictive value of 72.8%.<sup>12</sup> It consists of 7 items (gender, age, blood pressure, body mass index, smoking behavior, diabetes, and physical activity), and the level of risks was divided into

three categories: low risk if the score was (–)7–1, moderate risk if the score was 2–4, and high risk if the score was  $\geq 5$ . Two previously trained nurses performed physical examination of height, weight, waist circumference, blood pressure (with a mercury sphygmomanometer), and blood sample collection.

Laboratory examinations were performed using blood samples of 10 ml each to determine fasting glucose, lipid profile, and 25(OH)D. The 25(OH)D level was determined by indirect competitive chemiluminescence immunoassay (CLIA).<sup>13</sup> Vitamin D deficiency was defined as a serum 25(OH)D level below 20 ng/ml or 50 nmol/l. A 25(OH)D level in the range of 21–29 ng/ml (52–72 nmol/l) was designated vitamin D insufficiency, while a level of  $\geq 30$  ng/ml was deemed sufficient.<sup>14</sup> The laboratory examinations were performed at Prodia Laboratories, Jakarta. The Friedewald equation determines LDL-C. The equation subtracts high-density lipoprotein cholesterol (HDL-C) and a fixed ratio of triglycerides/5.

The sample size was determined using the infinite-finite population formula with a 95% significance level of 1.96. The prevalence for counting samples was 1.5%, with a measurement accuracy of 0.05%. The minimal sample size was 109, rounded upwards to 114. The data processing used SPSS for Windows version 29.0. Descriptive statistical analysis (frequency, percentage, mean, standard deviation, minimal, and maximal) was used to display subjects' characteristics and biochemical parameters. The bivariate data analysis used a chi-square test with a significance level of  $< 0.05$ .

This research protocol has passed a research ethics review from the Research Ethics Committee of the Faculty of Medicine, Universitas Trisakti number 163/KER/FK/VIII/2022.

## Results

One hundred twenty-four (124) online motorcycle drivers aged 25–64 agreed to participate in this study, with 10 subjects who did not meet the inclusion criteria excluded. The univariate analysis was used to determine the subjects' characteristics and biochemical parameter distribution.

Table 1 shows the data characteristics of 114 study subjects. The mean subjects were aged  $38 \pm 7.8$  years, with a waist circumference of  $89 \pm 13$

**Table 1 Distribution of Features and Characteristics of the Subjects**

Characteristics	n=114	%	Mean (SD)	Min–Max
Age (years)			38 (7.8)	25–62
Gender				
Male	83	72.8		
Female	31	27.2		
Waist circumference (cm)			89 (13.0)	60–128
Duration of being an online motorcycle driver (years)				
<5	51	44.7		
5–10	60	52.6		
>10	3	2.6		
Smoking				
Never	26	22.8		
Ex-smoker	9	69.3		
Smoker	79	7.9		
Physical activity				
Never	36	31.6		
Low	59	51.8		
Medium	19	16.7		
High	0	0		
Blood pressure status				
Systolic (mmHg)			128.9 (16.7)	87–174
<140	91	79.8		
≥140	23	20.2		
Diastolic (mmHg)			86.7 (11.9)	60–127
<90	66	57.9		
≥90	48	42.1		
Jakarta's Cardiovascular Risk Score			4.4 (2.8)	(–4)–14
Low risk	16	14.0		
Moderate risk	38	33.3		
High risk	60	52.6		

cm. The majority of them were male; 83 (72.8%) and 60 (52.6%) subjects had been working as online motorcycle drivers for 5–10 years. On blood pressure examination, mean systolic blood pressure (SBP) was 128.9±16.7 mmHg, and diastolic blood pressure (DBP) was 86.7±11.9 mmHg. Based on Jakarta's Cardiovascular Risk Score, the online motorcycle drivers participating in this study had a mean cardiovascular risk of 4.4±2.8, and 60 (52.6%) had high-risk scores.

Table 2 shows biochemical parameters from 114 online motorcycle drivers. Lipid profile, i.e., the level of total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride, were standard in most subjects (except LDL-C). Mean total cholesterol were 184.6±30.1, HDL 45±9.9, LDL 109.6±26.3, and triglyceride 151.5±94.2. The mean fasting glucose was

82.5±31.7, and 103 (90.4%) subjects had average fasting glucose. All subjects had low 25(OH)D serum levels, with mean 25(OH)D serum levels of 18±5.7 ranging between 6.9 and 29.8.

Table 3 shows a significant association between blood pressure, triglycerides, total cholesterol, and Jakarta Cardiovascular Risk Score with p-value <0.005. Meanwhile, the relationship between HDL, LDL, and fasting glucose with Jakarta Cardiovascular Risk Score was found to have no significant association.

## Discussion

Jakarta's Cardiovascular Risk Score (JAKVAS) is an instrument that predicts the risk of cardiovascular events in the next ten years. Our study showed that % prevalence in the high-

**Table 2 Biochemical Parameters**

Characteristics	n=114	%	Mean (SD)	Min–Max
Total cholesterol (mg/dl)			184.6 (30.1)	130–296
<200	82	71.9		
≥200	32	28.1		
HDL cholesterol (mg/dl)			45 (9.9)	22–68
<40	41	36.0		
≥40	73	64.0		
LDL cholesterol (mg/dl)			109.6 (26.3)	44.4–184.4
<100	44	36.1		
≥100	78	63.9		
Triglycerides (mg/dl)			151.5 (94.2)	44–581
<150	71	62.3		
≥150	43	37.7		
Fasting glucose (mg/dl)			82.5 (31.7)	57–290
<100	103	90.4		
≥100	11	9.6		
25(OH)D status			18 (5.7)	6.9–29.8

risk category based on JAKVAS was 52.6%. This prevalence is different from a study conducted on athletes, which only shows a prevalence of 3.85% in the high-risk category,<sup>15</sup> and on health cadres,

who also have a high-risk outcome category of only 11.7%.<sup>16</sup> Work-related cardiovascular risk factors can significantly impact an individual's health. Our research was conducted on online

**Table 3 Blood Pressure, Biochemical Parameters, and Cardiovascular Risk Profile**

Variables	Jakarta Cardiovascular Risk Score			p
	Low n (%)	Moderate n (%)	High n (%)	
Blood pressure (mmHg)				
Systolic				
<140	14 (15.4)	36 (39.6)	41 (45.1)	0.005*
≥140	2 (8.7)	2 (8.7)	19 (82.6)	
Diastolic				
<90	11 (16.7)	29 (43.9)	26 (39.4)	0.004*
≥90	5 (10.4)	9 (18.8)	34 (70.8)	
Total cholesterol (mg/dl)				
<200	16 (19.5)	27 (32.9)	39 (47.6)	0.021*
≥200	0 (0)	11 (34.4)	21 (65.6)	
HDL cholesterol (mg/dl)				
<40	3 (7.3)	16 (39.0)	22 (53.7)	0.260*
≥40	13 (17.8)	22 (30.1)	38 (52.1)	
LDL cholesterol (mg/dl)				
<100	8 (18.6)	12 (27.9)	23 (53.5)	0.439*
≥100	8 (11.3)	26 (36.6)	37 (52.1)	
Triglycerides (mg/dl)				
<150	14 (20.0)	28 (40.0)	28 (40.0)	0.002*
≥150	2 (4.5)	10 (22.7)	32 (72.7)	
Fasting glucose (mg/dl)				
<100	15 (14.6)	34 (33.0)	54 (52.4)	1.000*
≥100	1 (9.1)	4 (36.4)	6 (54.5)	

Note: \*chi-square test, \*Fisher test, significant p<0.05



motorcycle drivers who had a sizable percentage of smoking at 69.3% and low physical activity (never-low category) at 83.4%. At the same time, studies on athletes found that physical activity was quite high (optimum-excessive category), reaching >95%, and smokers only 35.9%. A survey of health cadres also showed that smokers comprise only 2.3% of the population, and moderate physical activity is 90.9%.

A meta-analysis study in 2017, conducted by Hackshaw et al.<sup>17</sup> on 141 cohort studies, showed men and women who smoked about one cigarette per day had a 48% and 57% higher risk of heart disease than non-smokers, respectively. Cigarettes have adrenergic effects, which result in an increased heart rate, inotropic status, coronary microvascular resistance, and reduced insulin sensitivity. It affects blood pressure, heart rate, and lipid profile and results in the development of atherosclerotic changes, narrowing of the vascular lumen, endothelial dysfunction, and impaired response of coronary blood flow.<sup>18</sup> A systematic review in 2022 by Gonzalez-Jaramillo et al.<sup>19</sup> with 33,576 patients from nine prospective cohort studies showed that higher levels of physical activity were associated with lower mortality risk and cardiovascular risk. Regular physical activity can help strengthen the heart muscle, improve blood flow, and enhance the heart's ability to use oxygen.<sup>20</sup>

This study found a significant relationship between systolic and diastolic blood pressure with cardiovascular risk. A recent cohort study by Whelton et al.,<sup>21</sup> which included 1,457 subjects, found that for every 10 mmHg increase in systolic blood pressure, there was a 53% higher risk for atherosclerotic cardiovascular disease. High systolic blood pressure alters the dynamics of normal blood flow and encourages plaque formation. Its increased shear stress in arteries disrupts endothelial function, which can cause reduced production of nitric oxide and trigger inflammatory response, leading to the formation of atherosclerosis.<sup>22</sup> Although both systolic and diastolic blood pressure have been reported to be associated with future cardiovascular risk, the association of DBP with cardiovascular risk diminishes with age as vascular compliance is attenuated. High diastolic blood pressure leads to increased arterial resistance, compromising the delivery of oxygen and nutrients to the heart muscle and can lead to endothelial dysfunction.<sup>23</sup> A systematic review and meta-analysis by

Okamoto et al.<sup>24</sup> suggest that reducing DBP to 80 mmHg or less would significantly reduce coronary revascularization and heart failure but potentially cause hypotension in CHD patients.

This study had a significant association between total cholesterol and cardiovascular risk ( $p=0.021$ ). This study was in line with Pe et al.,<sup>25</sup> and Jeong et al.,<sup>26</sup> which showed that raised total cholesterol is a strong risk factor for CHD. The fundamental process that causes CHD is atherosclerosis. It occurs when cholesterol and other substances accumulate within the walls of arteries, forming plaques. Total cholesterol is transported in blood as low-density lipoprotein or LDL-C (about 70%) and high-density lipoprotein or HDL-C (about 30%). Increased levels of total cholesterol, especially LDL-C, might increase the development of atherosclerosis by increasing the amount of cholesterol deposited in the artery walls. High LDL-C particles penetrate the arterial walls, attracting immune cells and inflammation. This process causes fatty plaques to develop over time, which narrows the arteries and reduces blood flow to the heart.<sup>27</sup>

Many studies stated that there was a relationship between cholesterol levels and cardiovascular risk.<sup>28</sup> But in this study we found no significant association between LDL or HDL-C with cardiovascular risk ( $p=0.439$  and  $p=0.260$ , respectively). A current literature study also found that low-density lipoprotein cholesterol (LDL-C) does not cause cardiovascular disease. It said that people with low cholesterol levels became just as atherosclerotic as people with high levels, and their risk of suffering from cardiovascular disease (CVD) is the same or higher.<sup>29</sup> It is important to note that the relationship between LDL-C and cardiovascular risk is complex and influenced by other factors such as inflammation, genetics, and individual patient characteristics. In this study, LDL-C levels were not obtained from blood tests but were determined using the Friedewald formula. The Friedewald equation is commonly used to estimate LDL-C levels. However, it has some limitations and weaknesses that can affect its accuracy, particularly at high triglyceride and/or low LDL-C values where inaccuracy in VLDL-C estimation using a "one size fits all approach" constitutes a more significant proportion of estimated LDL-C.<sup>30</sup>

Low levels of HDL-C predict increased cardiovascular risk because HDL-C has a protective role in heart and blood vessel health.



The positive effect of HDL is due to its role in reverse cholesterol transport and removing excess cholesterol from the body.<sup>31</sup> However, data from several cohorts have revealed a plateau in the inverse association above certain HDL-C levels, and there is even a suggestion of increased cardiovascular outcomes in those with high HDLs-C.<sup>32,33</sup>

This study found a significant association between triglycerides and cardiovascular risk ( $p=0.002$ ). High triglyceride levels are often associated<sup>18</sup> with other lipid abnormalities, such as low levels of high-density lipoprotein (HDL) cholesterol and small, dense, low-density lipoprotein (LDL) particles. These lipid abnormalities contribute to the development of atherosclerosis, the underlying process of CHD. High triglyceride levels can also trigger inflammation and oxidative stress within the blood vessels. It can contribute to the damage of the endothelial lining, which lines the blood vessel walls, making them more susceptible to plaque formation. Elevated triglyceride levels are often associated with reduced clearance of triglyceride-rich lipoproteins from the bloodstream. It can result from various factors, including impaired lipoprotein lipase activity, an enzyme that breaks down triglycerides. Reduced clearance leads to the accumulation of these lipoproteins and their remnants, contributing to the development of atherosclerosis.<sup>34,35</sup>

<sup>37</sup> This study was conducted in a population with low levels of 25(OH)D. Vitamin D is involved in<sup>31</sup> regulating the synthesis of cholesterol in the body. Studies have shown that vitamin D deficiency may be associated with dyslipidemia (total cholesterol, HDL-C, LDL-C<sup>34</sup> and triglycerides).<sup>36,37</sup> It has been proposed that vitamin D may reduce the production of LDL-C in the liver and increase the expression of LDL receptors, which helps remove LDL-C from the bloodstream. Vitamin D plays a role in regulating lipid metabolism, including the synthesis and breakdown of cholesterol. Both vitamin D deficiency<sup>36</sup> and dyslipidemia (abnormal lipid levels) are associated with increased inflammation and oxidative stress. Vitamin D deficiency may contribute to systemic inflammation, impacting lipid metabolism and altering cholesterol levels.<sup>36,38</sup>

This study found no association between fasting glucose level and cardiovascular risk ( $p=1.000$ ). It might be due to differences in the study's cutoff point for fasting blood sugar.

<sup>8</sup> Research conducted by Park et al.<sup>39</sup> showed the relationships between fasting glucose levels and CVD risks generally followed J-shape curves, with the lowest risk in the glucose range of 85–99 mg/dl. As fasting glucose levels increased to  $\geq 110$  mg/dl, risks for atherosclerotic cardiovascular disease increased.<sup>39</sup> <sup>31</sup> High fasting glucose levels can contribute to endothelial dysfunction, a condition in which the<sup>33</sup> inner lining of blood vessels becomes impaired. Endothelial dysfunction is a critical early step in the development of atherosclerosis and promotes inflammation within blood vessels, contributing to the progression of CVD.<sup>40</sup> High fasting glucose levels also can lead to increased production of reactive oxygen species, causing oxidative stress. Oxidative stress damages blood vessels, promotes inflammation, and accelerates the development of atherosclerosis, thus increasing cardiovascular risk.<sup>41</sup> Both high fasting glucose levels and vitamin D deficiency have<sup>25</sup> been associated with increased inflammation and oxidative stress. Chronic inflammation and oxidative stress can contribute to insulin resistance and impaired glucose metabolism.<sup>42</sup>

## Conclusions

There was a significant relationship between blood pressure, total cholesterol, and triglycerides and the Jakarta Cardiovascular Risk Score in low 25-hydroxy vitamin D levels among online motorcycle drivers in Jakarta. Early detection of<sup>1</sup> blood pressure, total cholesterol, and triglycerides can prevent the increasing risk of cardiovascular disease.

## Conflict of Interest

All authors have disclosed any actual or potential competing interests regarding the submitted article and the nature of those interests.

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## RESEARCH ARTICLE

## Blood Pressure, Total Cholesterol, and Triglycerides Associated with Cardiovascular Risk Score in Low 25-Hydroxy Vitamin D Level among Online Motorcycle Drivers, Jakarta, Indonesia

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### Abstract

Low 25-hydroxy vitamin D is associated with many chronic diseases, such as coronary heart disease. Online motorcycle drivers spend prolonged hours on the road and may face many stressors and occupational hazards that can create the development of cardiovascular disease. This study aims to determine factors contributing to cardiovascular risk among online motorcycle drivers. This study was an observational analytic with a cross-sectional design. Data were collected in September 2022 with consecutive random sampling methods for 114 subjects at Universitas Trisakti Jakarta. The ages of the subjects ranged from 25 to 62 years. Cardiovascular risk was assessed based on the Jakarta Cardiovascular Risk Score (JAKVAS). The data collection included physical examination and blood biochemistry (lipid profile, fasting blood glucose, and 25(OH)D). The data were analyzed using a chi-square test with  $p < 0.05$ . The majority of subjects were male 83 (72.8%). On blood pressure examination, mean systolic blood pressure was  $128.9 \pm 16.7$  mmHg, and diastolic blood pressure was  $86.7 \pm 11.9$  mmHg. The mean cardiovascular risk was  $4.4 \pm 2.8$ , and 52.6% had a high-risk score. All subjects had low 25(OH)D serum levels, with mean 25(OH)D serum levels of  $18 \pm 5.7$  ranging between 6.9 and 29.8. Among online motorcycle drivers, there was a significant association between blood pressure, total cholesterol, and triglyceride with cardiovascular risk scores in low 25-hydroxy vitamin D levels. Blood pressure, total cholesterol, and triglyceride could affect cardiovascular health in low 25-hydroxy vitamin D levels among online motorcycle drivers.

**Keywords:** 25-hydroxy vitamin D, blood pressure, Jakarta Cardiovascular Risk Score, lipid profile, online motorcycle drivers

### Introduction

Vitamin D plays a significant role in supporting overall health. Vitamin D deficiency is a widespread health issue that affects the world. The global prevalence of deficiency serum 25(OH)D was 15.7% between 2000 and 2022.<sup>1</sup> Unexpectedly, Indonesia, as a tropical country, has a high prevalence of vitamin D deficiency. Pulungan et al.<sup>2</sup> and Poh et al.,<sup>3</sup> showed that vitamin D deficiency in Indonesia was 44.6% and 94.4%, respectively. Insufficient exposure to sunlight and low intake of vitamin D are two leading causes of vitamin D deficiency, and it can contribute to an increased risk of chronic disease, such as cardiovascular disease, cancer, diabetes mellitus, etc.<sup>4</sup>

Coronary heart disease (CHD) or coronary artery disease (CAD) is the most common cardiovascular dysfunction disease, and its

prevalence is approximately 5–8% worldwide.<sup>5</sup> In Indonesia, the Basic Health Research data 2018 showed that 1.5% of Indonesians suffered from CHD, with death reaching 12.9%.<sup>6</sup> Siadat et al.<sup>7</sup> showed an association of 25(OH)D serum deficiency and coronary artery disease with cardiovascular risk factors. Its risk rises to 5.8 times (1.77–18.94) higher than in people with an average 25(OH)D serum level. Measurement of serum 25(OH)D levels has not been widely carried out in Indonesia, especially for online motorcycle drivers (*ojek* online) who are exposed to sunlight every day. Online motorcycle driving is a job that is now in great demand by the people of Indonesia, and there are still not many published studies on this job. Drivers spend prolonged hours on the road and may face many stressors and occupational hazards that can develop cardiovascular risk factors.<sup>8</sup> Drivers with high-risk cardiovascular disease had a higher





likelihood of crash and death.<sup>9,10</sup>

Preventing CHD through early detection of risk factors and efforts to control them are very important. Risk factors for CHD include modified and non-modified risk factors. Previous studies have documented that age, gender, hypertension, diabetes, hyperlipidemia, alcohol intake, low physical activity, and long duration of work were cardiovascular risks for drivers. Blood pressure and biochemical parameters are essential in determining a person's cardiovascular risk. Studies showed that biochemical parameters such as blood sugar, lipid profile, and even 25(OH)D status were often used to analyze cardiovascular risk.<sup>8,11</sup>

This article aims to determine the relationship factors contributing to cardiovascular risk in online motorcycle drivers with low 25(OH)D levels.

## Methods

It is an analytic observational study with a cross-sectional design conducted in September 2022. The selection of research subjects used consecutive non-random sampling techniques. The study inclusion criteria were male and female online motorcycle drivers aged 25–64 years, willing to participate, and signed informed consent. Exclusion criteria were having a cognitive impairment, a history of cardiovascular disease, not fully completing the questionnaire, having normal to high serum 25(OH)D level ( $\geq 30$  ng/ml), and having a high low-density lipoprotein cholesterol (LDL-C)  $\geq 300$  mg/dl. The study subjects who met the inclusion and exclusion criteria were asked to come to the study location after an overnight fast of 12 hours before blood collection for laboratory examination. Data were collected by interview using a demographic characteristics questionnaire and Jakarta's Cardiovascular Risk Score (JAKVAS) instrument adapted from the Framingham risk score. Jakarta's Cardiovascular Risk Score is based on the Indonesian population and is used for cardiovascular risk stratification in developing countries. It has been shown to have a sensitivity of 77.9%, a specificity of 90%, a positive predictive value of 92.2%, and a negative predictive value of 72.8%.<sup>12</sup> It consists of 7 items (gender, age, blood pressure, body mass index, smoking behavior, diabetes, and physical activity), and the level of risks was divided into

three categories: low risk if the score was  $(-)-7-1$ , moderate risk if the score was 2–4, and high risk if the score was  $\geq 5$ . Two previously trained nurses performed physical examinations of height, weight, waist circumference, blood pressure (with a mercury sphygmomanometer), and blood sample collection.

Laboratory examinations were performed using blood samples of 10 ml each to determine fasting glucose, lipid profile, and 25(OH)D. The 25(OH)D level was determined by indirect competitive chemiluminescence immunoassay (CLIA).<sup>13</sup> Vitamin D deficiency was defined as a serum 25(OH)D level below 20 ng/ml or 50 nmol/l. A 25(OH)D level in the range of 21–29 ng/ml (52–72 nmol/l) was designated vitamin D insufficiency, while a level of  $\geq 30$  ng/ml was deemed sufficient.<sup>14</sup> The laboratory examinations were performed at Prodia Laboratories, Jakarta. The Friedewald equation determines LDL-C. The equation subtracts high-density lipoprotein cholesterol (HDL-C) and a fixed ratio of triglycerides/5.

The sample size was determined using the infinite-finite population formula with a 95% significance level of 1.96. The prevalence for counting samples was 1.5%, with a measurement accuracy of 0.05%. The minimal sample size was 109, rounded upwards to 114. The data processing used SPSS for Windows version 29.0. Descriptive statistical analysis (frequency, percentage, mean, standard deviation, minimal, and maximal) was used to display subjects' characteristics and biochemical parameters. The bivariate data analysis used a chi-square test with a significance level of  $< 0.05$ .

This research protocol has passed a research ethics review from the Research Ethics Committee of the Faculty of Medicine, Universitas Trisakti number 163/KER/FK/VIII/2022.

## Results

One hundred twenty-four (124) online motorcycle drivers aged 25–64 agreed to participate in this study, with 10 subjects who did not meet the inclusion criteria excluded. The univariate analysis was used to determine the subjects' characteristics and biochemical parameter distribution.

Table 1 shows the data characteristics of 114 study subjects. The mean subjects were aged  $38 \pm 7.8$  years, with a waist circumference of  $89 \pm 13$

Table 1 Distribution of Features and Characteristics of the Subjects

Characteristics	n=114	%	Mean (SD)	Min–Max
Age (years)			38 (7.8)	25–62
Gender				
Male	83	72.8		
Female	31	27.2		
Waist circumference (cm)			89 (13.0)	60–128
Duration of being an online motorcycle driver (years)				
<5	51	44.7		
5–10	60	52.6		
>10	3	2.6		
Smoking				
Never	26	22.8		
Ex-smoker	9	69.3		
Smoker	79	7.9		
Physical activity				
Never	36	31.6		
Low	59	51.8		
Medium	19	16.7		
High	0	0		
Blood pressure status				
Systolic (mmHg)			128.9 (16.7)	87–174
<140	91	79.8		
≥140	23	20.2		
Diastolic (mmHg)			86.7 (11.9)	60–127
<90	66	57.9		
≥90	48	42.1		
Jakarta Cardiovascular Risk Score			4.4 (2.8)	(–4)–14
Low risk	16	14.0		
Moderate risk	38	33.3		
High risk	60	52.6		

cm. The majority of them were male; 83 (72.8%) and 60 (52.6%) subjects had been working as online motorcycle drivers for 5–10 years. On blood pressure examination, mean systolic blood pressure (SBP) was 128.9±16.7 mmHg, and diastolic blood pressure (DBP) was 86.7±11.9 mmHg. Based on Jakarta's Cardiovascular Risk Score, the online motorcycle drivers participating in this study had a mean cardiovascular risk of 4.4±2.8, and 60 (52.6%) had high-risk scores.

Table 2 shows biochemical parameters from 114 online motorcycle drivers. Lipid profile, i.e., the level of total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride, were standard in most subjects (except LDL-C). Mean total cholesterol was 184.6±30.1, HDL 45±9.9, LDL 109.6±26.3, and triglyceride 151.5±94.2. The mean fasting glucose was

82.5±31.7, and 103 (90.4%) subjects had average fasting glucose. All subjects had low 25(OH)D serum levels, with mean 25(OH)D serum levels of 18±5.7 ranging between 6.9 and 29.8.

Table 3 shows a significant association between blood pressure, triglycerides, total cholesterol, and Jakarta Cardiovascular Risk Score with p-value <0.005. Meanwhile, the relationship between HDL, LDL, and fasting glucose with Jakarta Cardiovascular Risk Score was found to have no significant association.

Discussion

Jakarta's Cardiovascular Risk Score (JAKVAS) is an instrument that predicts the risk of cardiovascular events in the next ten years. Our study showed that % prevalence in the high-

**Table 2 Biochemical Parameters**

Characteristics	n=114	%	Mean (SD)	Min–Max
Total cholesterol (mg/dl)			184.6 (30.1)	130–296
<200	82	71.9		
≥200	32	28.1		
HDL cholesterol (mg/dl)			45 (9.9)	22–68
<40	41	36.0		
≥40	73	64.0		
LDL cholesterol (mg/dl)			109.6 (26.3)	44.4–184.4
<100	44	36.1		
≥100	78	63.9		
Triglycerides (mg/dl)			151.5 (94.2)	44–581
<150	71	62.3		
≥150	43	37.7		
Fasting glucose (mg/dl)			82.5 (31.7)	57–290
<100	103	90.4		
≥100	11	9.6		
25(OH)D status			18 (5.7)	6.9–29.8

risk category based on JAKVAS was 52.6%. This prevalence is different from a study conducted on athletes, which only shows a prevalence of 3.85% in the high-risk category,<sup>15</sup> and on health cadres,

who also have a high-risk outcome category of only 11.7%.<sup>16</sup> Work-related cardiovascular risk factors can significantly impact an individual's health. Our research was conducted on online

**Table 3 Blood Pressure, Biochemical Parameters, and Cardiovascular Risk Profile**

Variables	Jakarta Cardiovascular Risk Score			p
	Low n (%)	Moderate n (%)	High n (%)	
Blood pressure (mmHg)				
Systolic				
<140	14 (15.4)	36 (39.6)	41 (45.1)	0.005*
≥140	2 (8.7)	2 (8.7)	19 (82.6)	
Diastolic				
<90	11 (16.7)	29 (43.9)	26 (39.4)	0.004*
≥90	5 (10.4)	9 (18.8)	34 (70.8)	
Total cholesterol (mg/dl)				
<200	16 (19.5)	27 (32.9)	39 (47.6)	0.021*
≥200	0 (0)	11 (34.4)	21 (65.6)	
HDL cholesterol (mg/dl)				
<40	3 (7.3)	16 (39.0)	22 (53.7)	0.260*
≥40	13 (17.8)	22 (30.1)	38 (52.1)	
LDL cholesterol (mg/dl)				
<100	8 (18.6)	12 (27.9)	23 (53.5)	0.439*
≥100	8 (11.3)	26 (36.6)	37 (52.1)	
Triglycerides (mg/dl)				
<150	14 (20.0)	28 (40.0)	28 (40.0)	0.002*
≥150	2 (4.5)	10 (22.7)	32 (72.7)	
Fasting glucose (mg/dl)				
<100	15 (14.6)	34 (33.0)	54 (52.4)	1.000#
≥100	1 (9.1)	4 (36.4)	6 (54.5)	

Note: \*chi-square test, #Fisher test, significant p<0.05

motorcycle drivers who had a sizable percentage of smoking at 69.3% and low physical activity (never-low category) at 83.4%. At the same time, studies on athletes found that physical activity was quite high (optimum-excessive category), reaching >95%, and smokers only 35.9%. A survey of health cadres also showed that smokers comprise only 2.3% of the population, and moderate physical activity is 90.9%.

A meta-analysis study in 2017, conducted by Hackshaw et al.<sup>17</sup> on 141 cohort studies, showed men and women who smoked about one cigarette per day had a 48% and 57% higher risk of heart disease than non-smokers, respectively. Cigarettes have adrenergic effects, which result in an increased heart rate, inotropic status, coronary microvascular resistance, and reduced insulin sensitivity. It affects blood pressure, heart rate, and lipid profile and results in the development of atherosclerotic changes, narrowing of the vascular lumen, endothelial dysfunction, and impaired response of coronary blood flow.<sup>18</sup> A systematic review in 2022 by Gonzalez-Jaramillo et al.<sup>19</sup> with 33,576 patients from nine prospective cohort studies showed that higher levels of physical activity were associated with a lower mortality risk and cardiovascular risk. Regular physical activity can help strengthen the heart muscle, improve blood flow, and enhance the heart's ability to use oxygen.<sup>20</sup>

This study found a significant relationship between systolic and diastolic blood pressure with cardiovascular risk. A recent cohort study by Whelthorn et al.,<sup>21</sup> which included 1,457 subjects, found that for every 10 mmHg increase in systolic blood pressure, there was a 53% higher risk for atherosclerotic cardiovascular disease. High systolic blood pressure alters the dynamics of normal blood flow and encourages plaque formation. Its increased shear stress in arteries disrupts endothelial function, which can cause reduced production of nitric oxide and trigger inflammatory responses, leading to the formation of atherosclerosis.<sup>22</sup> Although both systolic and diastolic blood pressure have been reported to be associated with future cardiovascular risk, the association of DBP with cardiovascular risk diminishes with age as vascular compliance is attenuated. High diastolic blood pressure leads to increased arterial resistance, compromising the delivery of oxygen and nutrients to the heart muscle and can lead to endothelial dysfunction.<sup>23</sup> A systematic review and meta-analysis by

Okamoto et al.<sup>24</sup> suggest that reducing DBP to 80 mmHg or less would significantly reduce coronary revascularization and heart failure but potentially cause hypotension in CHD patients.

This study had a significant association between total cholesterol and cardiovascular risk ( $p=0.021$ ). This study was in line with Peters et al.,<sup>25</sup> and Jeong et al.,<sup>26</sup> which showed that raised total cholesterol is a strong risk factor for CHD. The fundamental process that causes CHD is atherosclerosis. It occurs when cholesterol and other substances accumulate within the walls of arteries, forming plaques. Total cholesterol is transported in blood as low-density lipoprotein or LDL-C (about 70%) and high-density lipoprotein or HDL-C (about 30%). Increased levels of total cholesterol, especially LDL-C, might increase the development of atherosclerosis by increasing the amount of cholesterol deposited in the artery walls. High LDL-C particles penetrate the arterial walls, attracting immune cells and inflammation. This process causes fatty plaques to develop over time, which narrows the arteries and reduces blood flow to the heart.<sup>27</sup>

Many studies stated that there was a relationship between cholesterol levels and cardiovascular risk.<sup>28</sup> But in this study we found no significant association between LDL or HDL-C with cardiovascular risk ( $p=0.439$  and  $p=0.260$ , respectively). A current literature study also found that low-density lipoprotein cholesterol (LDL-C) does not cause cardiovascular disease. It said that people with low cholesterol levels became just as atherosclerotic as people with high levels, and their risk of suffering from cardiovascular disease (CVD) is the same or higher.<sup>29</sup> It is important to note that the relationship between LDL-C and cardiovascular risk is complex and influenced by other factors such as inflammation, genetics, and individual patient characteristics. In this study, LDL-C levels were not obtained from blood tests but were determined using the Friedewald formula. The Friedewald equation is commonly used to estimate LDL-C levels. However, it has some limitations and weaknesses that can affect its accuracy, particularly at high triglyceride and/or low LDL-C values where inaccuracy in VLDL-C estimation using a "one size fits all approach" constitutes a more significant proportion of estimated LDL-C.<sup>30</sup>

Low levels of HDL-C predict increased cardiovascular risk because HDL-C has a protective role in heart and blood vessel health.



The positive effect of HDL is due to its role in reverse cholesterol transport and removing excess cholesterol from the body.<sup>31</sup> However, data from several cohorts have revealed a plateau in the inverse association above certain HDL-C levels, and there is even a suggestion of increased cardiovascular outcomes in those with high HDLs-C.<sup>32,33</sup>

This study found a significant association between triglycerides and cardiovascular risk ( $p=0.002$ ). High triglyceride levels are often associated with other lipid abnormalities, such as low levels of high-density lipoprotein (HDL) cholesterol and small, dense, low-density lipoprotein (LDL) particles. These lipid abnormalities contribute to the development of atherosclerosis, the underlying process of CHD. High triglyceride levels can also trigger inflammation and oxidative stress within the blood vessels. It can contribute to the damage of the endothelial lining, which lines the blood vessel walls, making them more susceptible to plaque formation. Elevated triglyceride levels are often associated with reduced clearance of triglyceride-rich lipoproteins from the bloodstream. It can result from various factors, including impaired lipoprotein lipase activity, an enzyme that breaks down triglycerides. Reduced clearance leads to the accumulation of these lipoproteins and their remnants, contributing to the development of atherosclerosis.<sup>34,35</sup>

This study was conducted in a population with low levels of 25(OH)D. Vitamin D is involved in regulating the synthesis of cholesterol in the body. Studies have shown that vitamin D deficiency may be associated with dyslipidemia (total cholesterol, HDL-C, LDL-C, and triglycerides).<sup>36,37</sup> It has been proposed that vitamin D may reduce the production of LDL-C in the liver and increase the expression of LDL receptors, which helps remove LDL-C from the bloodstream. Vitamin D plays a role in regulating lipid metabolism, including the synthesis and breakdown of cholesterol. Both vitamin D deficiency and dyslipidemia (abnormal lipid levels) are associated with increased inflammation and oxidative stress. Vitamin D deficiency may contribute to systemic inflammation, impacting lipid metabolism and altering cholesterol levels.<sup>38</sup>

This study found no association between fasting glucose level and cardiovascular risk ( $p=1.000$ ). It might be due to differences in the study's cutoff point for fasting blood sugar.

Research conducted by Park et al.<sup>39</sup> showed the relationships between fasting glucose levels and CVD risks generally followed J-shape curves, with the lowest risk in the glucose range of 85–99 mg/dl. As fasting glucose levels increased to  $\geq 110$  mg/dl, risks for atherosclerotic cardiovascular disease increased.<sup>39</sup> High fasting glucose levels can contribute to endothelial dysfunction, a condition in which the inner lining of blood vessels becomes impaired. Endothelial dysfunction is a critical early step in the development of atherosclerosis and promotes inflammation within blood vessels, contributing to the progression of CVD.<sup>40</sup> High fasting glucose levels also can lead to increased production of reactive oxygen species, causing oxidative stress. Oxidative stress damages blood vessels, promotes inflammation, and accelerates the development of atherosclerosis, thus increasing cardiovascular risk.<sup>41</sup> Both high fasting glucose levels and vitamin D deficiency have been associated with increased inflammation and oxidative stress. Chronic inflammation and oxidative stress can contribute to insulin resistance and impaired glucose metabolism.<sup>42</sup>

## Conclusions

There was a significant relationship between blood pressure, total cholesterol, and triglycerides and the Jakarta Cardiovascular Risk Score in low 25-hydroxy vitamin D levels among online motorcycle drivers in Jakarta. Early detection of blood pressure, total cholesterol, and triglycerides can prevent the increasing risk of cardiovascular disease.

## Conflict of Interest

All authors have disclosed any actual or potential competing interests regarding the submitted article and the nature of those interests.

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