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RELATIONSHIP BETWEEN HIGH DENSITY LIPOPROTEIN (HDL) AND RED CELL DISTRIBUTION WIDTH (RDW) VALUE WITH THE DEGREE OF CORONARY HEART DISEASE

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Abstract

Background. Coronary heart disease causes the most deaths in the world. Coronary artery stenosis can be seen with angiography. A high RDW value is associated with the intimal-medial thickness of the atherosclerotic carotid artery. Recently, RDW was found to be a novel independent predictor of prognosis in patients with acute myocardial infarction or congestive heart failure, after percutaneous aortic valve implantation, and among patients with risk factors or coronary artery disease.

Aim. To see the relationship between HDL levels and RDW values with the degree of severity of coronary heart disease associated with this Gensini score, using an analytical observational method with a cross-sectional approach.

Methods. Analytical observational research with cross-sectional quantification method. A total of 48 subjects with coronary heart disease were examined for serum HDL levels and RDW values as well as coronary angiography examination. The severity of coronary artery stenosis was assessed by this gensini score which was then analyzed statistically

Results. Of the 48 patients with patient characteristics, 36 were male (75%), and 12 female (25%) were obtained. From laboratory examination, it was found that the mean HDL level was 41.68 with a standard deviation of 16.85 and the mean RDW value of the patients was 12.85 with a standard deviation of 0.86. The difference in HDL levels with the severity of CHD was associated with this gensini score, the value of $p = 0.001$ was obtained. By using the Spearman correlation, it was found that the correlation between HDL levels and this gensini score was $p = 0.002$ with a value of $r = -0.427$. With the unpaired T test assessing the difference in RDW value with the severity of CHD associated with this gensini score, the value of $p = 0.20$ was obtained. By using the Pearson correlation, the correlation between the RDW value and the gensini score is $p = 0.06$ with a value of $r = 0.27$.

Conclusion. From the research results, it is concluded that there is a significant relationship between HDL levels and there is no significant relationship between the RDW value and the degree of coronary severity in people with coronary heart disease.

Introduction

Coronary artery disease (CHD) is the leading cause of death and disability in developed countries. Although CHD mortality rates have declined over the past four decades in the United States (and elsewhere), CHD remains responsible for about one-third of all deaths in individuals over the age of 35. It is estimated that nearly half of all middle-aged men are aged and one-third of all deaths. Middle-aged women in the United States will develop several manifestations of CHD. Heart disease deaths have declined in the United States and in regions where economies and health care systems are relatively developed, but the experience is often very different around the world. Coronary artery disease is the number one cause of death in adults from both low- and middle-income countries and from high-income countries. At the turn of the century, it was reported that CHD deaths were expected to increase by about 29 percent in women and 48 percent in men in developed countries between 1990 and 2020. Estimates of the corresponding increases in developing countries are 120 percent in women and 137 percent in men. ¹

Red blood cell distribution width / *red cell distribution width* (RDW) is a measure of the variation in the size of circulating red blood cells (coefficient of variability of the volume of red blood cells) and are regularly reported as part of a complete blood count automatically. Recent studies have reported a strong independent association



INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

between RDW and prognosis in cardiopulmonary disorders such as coronary artery disease (CHD), acute myocardial infarction (AMI), acute and chronic heart failure, peripheral vascular disease, pulmonary embolism, as well as in the general population. ²

In 2007, Felker et al. first found that elevated RDW was an independent predictor of prognosis in heart failure patients, and investigators gradually found that RDW was closely related to cardiovascular disease prognosis. Recent studies have shown that elevated RDW is not only a predictor for poor prognosis of heart failure, CHD, and pulmonary hypertension, but also shows a predictive value for the prognosis of stable CHD patients who have undergone PCI therapy. ³

Uyarel et al showed that higher baseline RDW levels in patients with STEMI undergoing percutaneous primary coronary intervention were associated with an increased risk of hospitalization, long-term cardiovascular mortality and length of hospital stay. RDW has also been found to be an independent predictor of all-cause long-term death in patients with NSTEMI. Dabbah et al. Demonstrated a stratified positive independent association between baseline value and RDW expenditure and the risk of all-cause death and developing new-onset heart failure in patients with AMI. ²

Plasma HDL has been reported to protect against the early development of inflammatory atherosclerosis. It is believed that plasma HDL is involved in the cholesterol reverse transport process to remove plasma cholesterol, which contributes to its anti-atherosclerotic properties. ⁴ Intravenous injection of synthetic HDL reduces intima thickening and macrophage content after balloon injury in cholesterol-fed rabbits without changes in arterial total cholesterol levels. In addition, synthetic HDL was effective in inhibiting neointimal formation of cholesterol-fed rabbits during pre-treatment prior to positioning of the collar around the carotid artery. These observations suggest that HDL exerts a preventive effect on the formation of lesions caused by vascular injury. ⁵

Plasma high density lipoprotein (HDL) levels were inversely associated with cardiovascular morbidity and mortality. The most comprehensively studied function of HDL is reverse cholesterol transport. Other cardioprotective functions include antioxidant properties and its ability to increase the bioavailability of nitric oxide (NO). Recently, the anti-inflammatory effects of HDL, particularly in the endothelium, have been reported. ⁶

The values of HDL as a predictor of cardiovascular risk remains largely unchallenged. Many prospective studies from different racial and ethnic groups around the world have confirmed that HDL-C is a strong, consistent, and independent predictor of cardiovascular events. Strong data also exist regarding HDL-C as a predictor of cardiovascular events in secondary prevention settings in individuals who have been diagnosed with cardiovascular disease. In the statin era, the association of HDL-C with cardiovascular events in statin-treated patients is less clear. In some of the large clinical trials with statins, HDL-C treatment was a predictor of cardiovascular events, whereas others were not. In the JUPITER trial, HDL-C's ability to predict incident incidence in patients treated with high-dose statins was weak. However, in a large meta-analysis of eight statin trials, baseline HDL-C concentrations were highly predictive of subsequent cardiovascular events. ⁷

From the description above, several studies have shown that RDW and HDL can be used as biomarkers of CHD incidence. However, so far, there has been little research that has discussed this relationship, especially in North Sumatra. Apart from that, several studies also show some controversial results. From this phenomenon, the researchers were interested in examining the relationship between HDL levels and RDW values in patients with CHD

Research Methods

This research is an analytical study with a *cross sectional* design. The research was conducted from May to August 2019. The population was patients suffering from coronary heart disease who were hospitalized in the inpatient room of the Adam Malik General Hospital Medan and underwent angiography procedures. The sample in this study amounted to 48 people. The tool used to measure serum HDL levels is the Abbott Architect Plus 8200 and the tool used to measure RDW is Sysmex XN 1000. The severity of coronary lesions is checked to make use of n score GENSINI. Data were analyzed using the Pearson correlation test if the data were normally distributed and the Spearman correlation test if the data were not normally distributed with a confidence level of 95% ($\alpha = 0.05$).



Results

This research was conducted at the Laboratory of Clinical Pathology and at the Department of Cardiology and Vascular Medicine, Cardiology Inpatient Installation of H. Adam Malik Hospital Medan. Samples were collected from patients diagnosed with coronary heart disease who underwent coronary angiography at RSUP H. Adam Malik Medan from May 2019 to August 2019. The samples collected met the inclusion and exclusion criteria, as many as 48 patients were included in the study.

1. Patient Characteristics

In this study, the characteristics of patients based on gender were obtained as many as 36 men (75%), and 12 women (25%). This study was also obtained from the average value of the overall age of study patients was 57.45 years with a standard deviation of 8.86 and median values obtained 58 years of age to the youngest 36 years old and the oldest 81 years of age.

Table 1, Patient Characteristics by Gender

Variable	N	Percentage (%)
Gender		
Male	36	75
Female	12	25

Table 2, Patient Characteristics by Age

Variable	N	Percentage (%)	Mean \pm SD	Median (Min - Max)
Age				58.00
Age			57.45 \pm 8.86	(36.00 - 81.00)
Range				
30 – 39	2	4.2		
40 – 49	6	12.5		
50 – 59	21	43.5		
60 – 69	15	31.3		
70 – 79	3	6.3		
>80	1	2.1		

2. Preliminary Measurement Results HDL Levels, RDW Value, and Gensini Score

In this study, blood was collected to assess the HDL levels and RDW values of patients. From the results of the measurement by the tool, the mean value of HDL levels from all study patients was 41.68 mg / dL with a standard deviation of 16.85 and obtained a median value of 37 mg / dL with the lowest HDL level of 20 mg / dL and the highest HDL level of 80 mg / dL. For the RDW value, the mean RDW value of all study patients was 12.85 with a standard deviation of 0.86 and a median value of 12.70 mg / dL was obtained with the lowest RDW value of 10.9 and the highest RDW value of 15.1.

Table 3. Data on the initial measurement of HDL levels, RDW values, and Gensini scores

Variable	Mean \pm SD	Median (Min - Max)
HDL levels (mg/dL)	41.68 \pm 16.85	37.00 (20.00 - 80.00)
RDW levels	12.85 \pm 0.86	12.70 (10.90 - 15.10)
Gensini Score	47.75 \pm 21.62	52.00 (6.00 - 88.00)



INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

3. The difference between HDL levels and the severity of CHD was associated with this gensini score
 By using the *Mann-Whitney* test to assess the difference in HDL levels with the severity of CHD associated with this generator score, the value of $p = 0.001$ was obtained. This shows that there is a significant difference between HDL levels in the group with mild atherosclerosis and severe atherosclerosis group .

Table 4, Difference in HDL levels with the severity of CHD associated with the score GENSINI

	CHD severity (Gensini score)		p
	Mild athero Sclerosis (1 - 29)	Severe Athero sclerosis (≥ 30)	
HDL (Median (Min - Max))	67.50 (27.00 - 81.00)	33.00 (20.00 - 56.00)	0.001*
* Mann-Whitney Test			

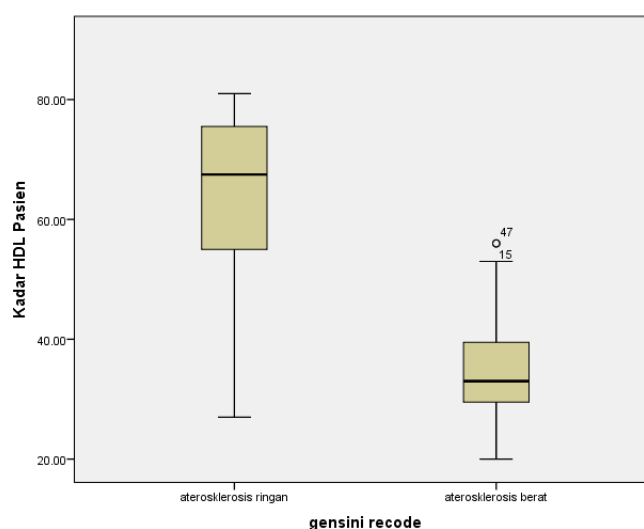


Figure 1, differences in HDL levels with the severity of CHD associated with this gensini score

4. Correlation of HDL levels with the severity of CHD is associated with this gensini score
 By using the Spearman Correlation test to assess the correlation between HDL levels and the severity of CHD associated with this generator score, the value of $p = 0.002$ with a value of $r = -0.427$ was obtained. This shows that there is a significant correlation between HDL levels and the group with the severity of CHD associated with this generator score with a moderate relationship strength level.

Table 5, Correlation of HDL levels with the severity of CHD associated with this gensini score

HDL Levels (Median (Min - Max))	Gensini score (Median (Min - Max))	P	r
37.00 (20.00 - 80.00)	52.00 (6.00 - 88.00)	0.002*	-.427

*Korelasi Spearman

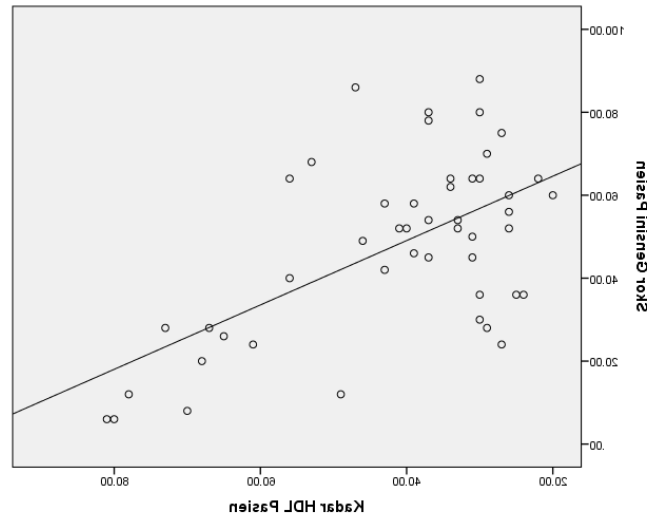


Figure 2 , Correlation of HDL levels with the severity of CHD associated with this gensini score

5. The difference in RDW value with the severity of CHD is associated with this gensini score

By using the unpaired T test to assess the difference in RDW value with the severity of CHD associated with this generator score, the value of $p = 0.20$ was obtained. This shows that there is no relationship between the RDW value in the group with mild atherosclerosis and severe atherosclerosis group .

Table 6 , Differences in RDW Value and CHD severity associated with this gensini score

	CHD severity (Gensini score)		p
	Mild Atero sclerosis (1 - 29)	Severe Atero sklerosis (≥ 30)	
RDW value (Mean \pm SD)	12.57 \pm 0.88	12.94 \pm 0.85	0.20*

* Unpaired T test

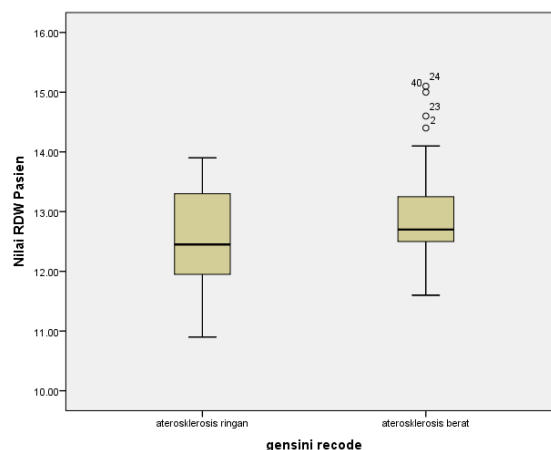


Figure 3 , Difference in RDW value with CHD severity associated with this generator score

6. The correlation of the RDW value with the severity of CHD is associated with this gensini score

By using the Pearson Correlation test to assess the correlation between the RDW value and the severity of CHD associated with this generator score, the value of $p = 0.06$ with $r = 0.27$ was obtained. This shows that there is no significant correlation between the RDW score and the group with the severity of CHD associated with this generator score with a very weak relationship strength level.



Table 7, Correlation of RDW Value with CHD severity associated with this gensini score

RDW value (Mean \pm SD)	Gensini score (Mean \pm SD)	p	r
12.85 \pm 0.86	47.75 \pm 21.62	0.06	0.27

*Pearson
correlation

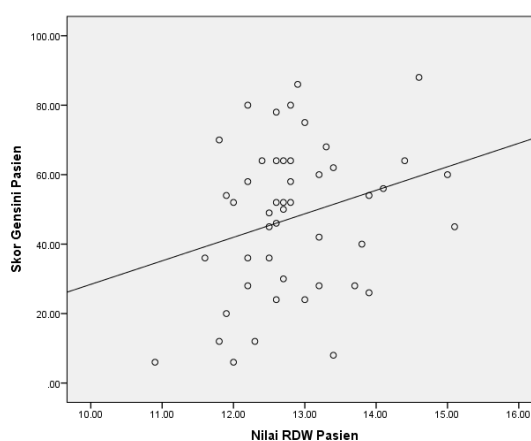


Figure 4, Correlation of RDW value with CHD severity associated with this gensini score

Discussion

This study is a *cross sectional study* which aims to determine the role of HDL levels and RDW values in assessing the severity of coronary arteries in coronary heart disease sufferers.

This research was conducted at the Department of Clinical Pathology and the Department of Cardiology and Vascular Medicine RSUP.H Adam Malik with consecutive sampling method in patients with coronary artery disease who underwent coronary angiography from May to July 2019. Of the 48 coronary heart disease patient undergoing coronary angiography obtained 75% are male and 25% are female. The mean age of patients with coronary heart disease in this study was 57.45 years. Research in Turkey in 2013 found that male gender ranks first in stable CHD patients (76%) with an older average age, which is 62 years.⁸ Similar results were also obtained by Çetin et al, where there were more male (70%) male coronary heart disease patients with an average age of 61 \pm 11.⁹ This is because the risk of coronary atherosclerosis is greater in men than women. Women are relatively more resistant to the disease until menopause, and then become just as vulnerable as men. The protective effect of estrogen is thought to explain the existence of women's immunity at the age before menopause, namely protecting blood vessels from damage. Age is the most important risk factor for CHD, as you get older, the risk of developing coronary heart disease is getting higher and generally starts at the age of 40 years and over. Individual susceptibility to coronary atherosclerosis increases with age, age 40-60 years the incidence of acute myocardial infarction increases fivefold.¹⁰

From the results of laboratory examinations, the average HDL level of all study patients was 41.68 mg / dL. In this study, it was found that the RDW value obtained by the mean RDW value of all study patients was 12.85, this is still within normal limits. This is in contrast to the study of Salvago et al, where they measured RDW in 456 consecutive patients with chest pain and acute coronary syndrome (ACS) who were admitted to the emergency



INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

department over a period of 1 year. Patients with a final diagnosis of ACS were found to have higher RDW scores than those without (15.1% versus 13.5%; $p < 0.001$).¹¹

Based on the results of laboratory tests and coronary angiography examinations, it was found that there was a significant difference in HDL levels between the Coronary Heart Disease group with a low Gensini score and the Coronary Heart Disease group with a High Gensini Score ($p = 0.001$). Likewise, when a correlation analysis was carried out between HDL levels and the severity of CHD associated with this generator score, it was obtained a significant value with moderate relationship strength ($p = 0.002$, $r = -0.427$). In patients with coronary heart disease, HDL levels do show values that tend to be lower than normal values, several prospective epidemiological studies have shown that there is a clear inverse relationship between a low serum HDL-C concentration and the risk of coronary heart disease.¹² Research by Kadi (2012) found that low HDL levels and high triglycerides were associated with poor coronary conditions ($p < 0.001$ and $p 0.015$). HDL is proven to have antiatherogenic properties, is protective of the endothelium, and increases the number and function of progenitor cells that play a role in the endothelium repair process.¹³ Similar results were also obtained in the research of Avci et al, 2018, where they conducted a study on patients with coronary heart disease who underwent angiography. As a result, they got a significant difference and correlation with the severity of coronary heart disease and the patient's HDL level.¹⁴

In this study, there was no significant difference in the RDW value between the Coronary Heart Disease group with a low Gensini score and the Coronary Heart Disease group with a High Gensini Score ($p = 0.2$). Likewise, when a correlation analysis was carried out between the RDW value and the severity of CHD associated with this generator score, it was obtained a value that was not significant with the strength of the weak relationship ($p = 0.06$, $r = 0.27$). This result is not in line with the study conducted by Akin et al, where they found a significant difference in the severity of acute myocardial infarction between the group with low RDW values and the group with high RDW values with $p < 0.001$.² This was also found in a study conducted by Celik et al, where the RDW value was significantly higher in diabetic CHD patients ($p < 0.001$). Patients with CHD who had an RDW value above the cut-off point also had a higher Gensini score, a higher percentage of obstructive CHD and triple-vessel disease ($p \leq 0.001$ for all).¹⁵

This can be caused because not only HDL and RDW can cause atherosclerosis, but can also be caused by increased blood fat levels, diabetes, hypertension, smoking habits, and obesity which have been recognized as risk factors for the occurrence of atherosclerosis.¹⁵

Conclusion

Based on the results of data analysis obtained in this study, it can be concluded that:

1. HDL levels are closely related and correlated with the severity of CHD associated with this generator score, so that the HDL level examination is useful for predicting the severity of Coronary Heart Disease. This examination is cheap and readily available, so that efforts can be made to monitoring HDL levels and therapy that aims to keep the stability lipid profiles do.
2. The RDW score was not associated and correlated closely with the severity of CHD associated with this generator score. Where checkup result of RDW and HDL were done once cannot describe the long-term inflammatory status and cannot describe the progression of coronary artery disease as a whole.
3. The incidence of CHD undergoing coronary angiography at RSUP H. Adam Malik was more male with an average age of 57 years

Suggestion

Examination of HDL levels is useful for predicting the severity of coronary heart disease. This examination is cheap and easy to obtain, so that efforts can be made to monitor HDL levels and therapy aimed at maintaining the stability of the lipid profile.

References

- [1] Lashmanados, U. (2010) 'Overview of Coronary Artery Disease', *Intechopan.com*, 1(1), pp. 3–14.
- [2] Akin, F. et al. (2013) 'Relation between red cell distribution width and severity of coronary artery disease in patients with acute myocardial infarction', *Angiology*, 64(8), pp. 592–596. doi: 10.1177/0003319712461931.
- [3] Liu, X. M. et al. (2015) 'Relationship between red blood cell distribution width and intermediate-term



INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

- mortality in elderly patients after percutaneous coronary intervention', *Journal of Geriatric Cardiology*, 12(1), pp. 17–22. doi: 10.11909/j.issn.1671-5411.2015.01.013.
- [4] Tolle, M. et al. (2008) 'HDL-associated lysosphingolipids inhibit NAD(P)H oxidase-dependent monocyte chemoattractant protein-1 production', *Arteriosclerosis, Thrombosis, and Vascular Biology*, 28(8), pp. 1542–1548. doi: 10.1161/ATVBAHA.107.161042.
- [5] Park, S. H. et al. (2003) 'Involvement of transcription factors in plasma HDL protection against TNF- α -induced vascular cell adhesion molecule-1 expression', *International Journal of Biochemistry and Cell Biology*, 35(2), pp. 168–182. doi: 10.1016/S1357-2725(02)00173-5.
- [6] Murphy, A. J. et al. (2008) 'High-density lipoprotein reduces the human monocyte inflammatory response', *Arteriosclerosis, Thrombosis, and Vascular Biology*, 28(11), pp. 2071–2077. doi: 10.1161/ATVBAHA.108.168690.
- [7] Rader, D. J. and Kees Hovingh, G. (2014) 'HDL and cardiovascular disease', *The Lancet*. Elsevier Ltd, 384(9943), pp. 618–625. doi: 10.1016/S0140-6736(14)61217-4.
- [8] Uysal, O. K., Turkoglu, C. and Sahin, D. . (2013) 'The Relationship Between Neutrophil-to-Lymphocyte Ratio and Coronary Collateral Circulation', *The Relationship Between Neutrophil-to-Lymphocyte Ratio and Coronary Collateral Circulation*, 21(4), pp. 329–333.
- [9] Çetin, M. et al. (2018) 'Red Blood Cell Distribution Width (RDW) and its Association with Coronary Atherosclerotic Burden in Patients with Stable Angina Pectoris', *European Journal of General Medicine*, 9(1), pp. 7–13. doi: 10.29333/ejgm/82548.
- [10] Libby, P. and Theroux, P. (2005) 'Pathophysiology of Coronary Artery Disease. Circulation', *Circulation Journal*, 111, pp. 3481–3488.
- [11] Salvagno, G. L. et al. (2015) 'Red blood cell distribution width: A simple parameter with multiple clinical applications', *Critical Reviews in Clinical Laboratory Sciences*. Informa Healthcare USA, Inc, 52(2), pp. 86–105. doi: 10.3109/10408363.2014.992064.
- [12] Kosmas, C. E. et al. (2018) 'High-density lipoprotein (HDL) functionality and its relevance to atherosclerotic cardiovascular disease', *Drugs in Context*, 7, pp. 1–9. doi: 10.7573/dic.212525.
- [13] Kadi, H. et al. (2012) 'The Relationship Between High-Density Lipoprotein Cholesterol and Coronary Collateral Circulation in Patients With Coronary Artery Disease', *Journal of Investigative Medicine*, 60(5), pp. 808–813. doi: 10.231/JIM.0b013e31824e980c.
- [14] Avci, E. et al. (2018) 'Relationship between high-density lipoprotein cholesterol and the red cell distribution width in patients with coronary artery disease', *Lipids in Health and Disease*. Lipids in Health and Disease, 17(1), pp. 4–9. doi: 10.1186/s12944-018-0709-5.
- [15] Celik, A. et al. (2017) 'Red cell distribution width is correlated with extensive coronary artery disease in patients with diabetes mellitus', *Cardiovascular Journal of Africa*, 28(5), pp. 319–323. doi: 10.5830/cvja-2017-015.
- [16] Ahmed, M. I. et al. (2018) 'Relationship between HDL-Cholesterol and Angiographic Severity of Coronary Artery Disease', *Bangladesh Heart Journal*, 33(1), pp. 32–38. doi: 10.3329/bhj.v33i1.37023.
- [17] Annema, W. and von Eckardstein, A. (2013) 'High-Density Lipoproteins', *Circulation Journal*, 77(10), pp. 2432–2448. doi: 10.1253/circj.CJ-13-1025.
- [18] Arbel, Y. et al. (2013) 'Red blood cell distribution width and the risk of cardiovascular morbidity and all-cause mortality: A population-based study', *Thrombosis and Haemostasis*, 111(2), pp. 300–307. doi: 10.1160/TH13-07-0567.
- [19] Aulakh, R. et al. (2009) 'Red cell distribution width (RDW) in the diagnosis of iron deficiency with microcytic hypochromic anemia', *Indian Journal of Pediatrics*, 76(3), pp. 265–268. doi: 10.1007/s12098-009-0014-4.
- [20] Bhatia, S. K. (2010) 'Coronary Artery Disease', *Biomaterials for Clinical Applications*, 1(1), pp. 23–49. doi: 10.1007/978-1-4419-6920-0.
- [21] Danese, E., Lippi, G. and Montagnana, M. (2015) 'Red blood cell distribution width and cardiovascular diseases', *J Thorac Dis*, 7(I), pp. 402–411. doi: 10.3978/j.issn.2072-1439.2015.10.04.
- [22] Eren, E., Yilmaz, N. and Aydin, O. (2012) 'High Density Lipoprotein and it's Dysfunction', *The Open Biochemistry Journal*, 6(1), pp. 78–93. doi: 10.2174/1874091x01206010078.
- [23] Fisher, E. A. et al. (2012) 'High-density lipoprotein function, dysfunction, and reverse cholesterol transport', *Arteriosclerosis, Thrombosis, and Vascular Biology*, 32(12), pp. 2813–2820. doi: 10.1161/ATVBAHA.112.300133.
- [24] Fisher, E. A. et al. (2012) 'High-density lipoprotein function, dysfunction, and reverse cholesterol transport', *Arteriosclerosis, Thrombosis, and Vascular Biology*, 32(12), pp. 2813–2820. doi: 10.1161/ATVBAHA.112.300133.



INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

- [25] Gordon, S. M. *et al.* (2011) 'High density lipoprotein: It's not just about lipid transport anymore', *Trends in Endocrinology and Metabolism*. Elsevier Ltd, 22(1), pp. 9–15. doi: 10.1016/j.tem.2010.10.001.
- [26] Li, N., Zhou, H. and Tang, Q. (2017) 'Red Blood Cell Distribution Width: A Novel Predictive Indicator for Cardiovascular and Cerebrovascular Diseases', *Disease Markers*. Hindawi, 2017(Mcv), pp. 1–23. doi: 10.1155/2017/7089493.
- [27] Li, W. *et al.* (2015) 'Association between red cell distribution width and the risk of heart events in patients with coronary artery disease', *Experimental and Therapeutic Medicine*, 9(4), pp. 1508–1514. doi: 10.3892/etm.2015.2244.
- [28] Li, Y. *et al.* (2015) 'Red Blood Cell Distribution Width is Independently Correlated with Diurnal QTc Variation in Patients with Coronary Heart Disease', *Medicine (United States)*, 94(23), p. e822. doi: 10.1097/MD.0000000000000822.
- [29] Libby, P. *et al.* (2014) 'Pathophysiology of Coronary Artery Disease', *American Heart Journal*, 1(1), pp. 1–9. doi: 10.1161/CIRCULATIONAHA.105.537878.
- [30] Patel, K. V. *et al.* (2009) 'Red blood cell distribution width and the risk of death in middle-aged and older adults', *Archives of Internal Medicine*, 169(5), pp. 515–523. doi: 10.1001/archintermed.2009.11.
- [31] Şahin, I. *et al.* (2015) 'Increased level of red cell distribution width is associated with poor coronary collateral circulation in patients with stable coronary artery disease', *Türk Kardiyoloji Dernegi Arsivi*, 43(2), pp. 123–130. doi: 10.5543/tkda.2015.24819.
- [32] Skjelbakken, T. *et al.* (2014) 'Red cell distribution width is associated with incident myocardial infarction in a general population: The tromsø study', *Journal of the American Heart Association*, 3(4), pp. 1–10. doi: 10.1161/JAHA.114.001109.
- [33] Subedi, B. H. *et al.* (2014) 'Current guidelines for high-density lipoprotein cholesterol in therapy and future directions.', *Vascular health and risk management*, 10, pp. 205–216.
- [34] Tonelli, M. *et al.* (2008) 'Relation between red blood cell distribution width and cardiovascular event rate in people with coronary disease', *Circulation*, 117(2), pp. 163–168. doi: 10.1161/CIRCULATIONAHA.107.727545.
- [35] Toth, P. P. *et al.* (2013) 'High-density lipoproteins: A consensus statement from the National Lipid Association', *Journal of Clinical Lipidology*. Mosby, Inc, 7(5), pp. 484–525. doi: 10.1016/j.jacl.2013.08.001
- [36] Tseliou, E. *et al.* (2014) 'Red Blood Cell Distribution Width Is a Significant Prognostic Marker in Advanced Heart Failure, Independent of Hemoglobin Levels', *Hellenic J Cardiol*, 55(1), pp. 457–461.
- [37] Zheng, C. and Aikawa, M. (2012) 'High density lipoprotein.', *Journal of the American College of Cardiology*. Elsevier Inc., 60(23), pp. 269–271. doi: 10.1016/j.jacc.2012.08.999.