http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v12i08.14

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

A Study on relationship between Red Cell Distribution Width and High-Density Lipoprotein-Cholesterol in patients with Acute coronary syndrome in a tertiary care hospital

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Abstract

Introduction: *Acute coronary syndrome is a spectrum of disease consisting of ST segment elevated myocardial infarction (STEMI), non-ST segment elevated myocardial infarction (NSTEMI) and unstable angina where the blood flow to the heart is decreased. According to WHO, India contributes to one-fifth of the world's deaths due to cardiovascular disease. In recent times, the RDW has been used as a helpful marker in the diagnosis and prognosis of patients with acute coronary syndrome. However, the relationship between RDW, HDL-C, and ACS has yet to be identified properly.*

Aim: *To evaluate the association between HDL-C levels and the RDW among patients with ACS and to find its association with the various socio-demographic factors of the patient.*

Methods: *This hospital-based cross-sectional study was conducted in a tertiary care hospital in Puducherry between October 2023 and February 2024. Patients aged more than 18 with a diagnosis of acute coronary syndrome were included in the study. All the patients were subjected to a complete history followed by laboratory investigations, including the RDW, HDL-C, and troponin-I.*

Results: *A total of 62 patients participated in the study. The mean age of the patients with ACS was found to be 55.6 ± 3.4 years. The study didn't show any association between the age (p=0.753), gender (p=0.897), residence (p=0.517), Type-2 DM (p=-.924), hypertension (p=0.615), dyslipidemia (p=0.302), smoking (p=0.565), alcohol (p=0.593), ACS type (p=0.714), Troponin-I (p=0.916), HDL-C (p=0.517) and RBS (p=0.078) with the level of the RDW. However, the study showed a significant association between BMI and RDW levels (p<0.001), and there is a significant and negative correlation was noted between the RDW and HDL-C levels (p=0.038).*

Conclusion: *The study showed a significant and negative correlation between the HDL-C and the RDW among patients with acute coronary syndrome. The study recommends that the RDW be used as an additional marker in predicting the risk of ACS and diagnosing patients with ACS.*

Keywords: *acute coronary syndrome, RDW, HDL-C, demographic factors.*

Introduction

Acute coronary syndrome (ACS) is a disease in which the blood flow to the heart is decreased[1]. Acute coronary syndrome comprises three main disease components they are the ST segment elevated myocardial infarction (STEMI), non-ST segment elevated myocardial infarction(NSTEMI) and unstable angina[2]. And it is responsible for one-third of the deaths below 35 years of age. According to the World Health Organization (WHO), India contributes to one-fifth of the world's deaths due to cardiovascular disease in the younger population[3]. The results of the Global Burden of the Disease study showed that the death rate because of coronary vascular disease accounts for 272 deaths per one lakh population in India, which was found to be higher than the annual death rate globally, which was found to be only 235 death per lakh population[3].

Severable modifiable and non-modifiable risk factors have been identified to cause cardiovascular disease. The modifiable risk factors are hypertension, diabetes mellitus, smoking, alcohol and hypercholesteremia. In contrast, the non-modifiable risk factor for the causation of the disease is age, gender and family history of premature coronary artery disease[4]. Most patients with acute coronary syndrome present with chest pain or breathlessness radiating to the hand and the jaw. Some of the patients will present with anginal equivalent symptoms such as dyspnea, nausea, vomiting, diaphoresis and unexplained fatigue[5]. And atypical symptoms were found to be more commonly seen among the women and in elderly patients. Sometimes, the patients will have syncopal attacks. Most of the time, acute coronary syndrome is diagnosed based on clinical history, physical examination, electrocardiogram and the biochemical markers of the heart[6].

The red cell distribution width (RDW) is nothing but the measure of the red blood size heterogeneity, and it is reported as a part of the routine blood cell count[7]. In recent times, the RDW has been used as a helpful marker in the diagnosis and the prognosis of patients with acute coronary syndrome, but the relationship between the RDW and the ACS is not known. Studies have proposed some hypotheses responsible for the pathogenesis of the disease, such as microvascular dysfunction, anaemia, oxidative stress, high amounts of cholesterol, nutritional deficiency, and renal dysfunction[8,9]. Studies have shown that high RDW is associated with an increased risk of developing hypertension, atrial fibrillation, and stroke[10].

The anti-atherogenic effects of the High-Density Lipoprotein-Cholesterol (HDL-C) have been attributed to antioxidant and anti-inflammatory properties. So, lower levels of HDL-C have been associated with the increased development of acute coronary syndrome[11]. The relationship between low HDL-C and high RDW is not fully understood; however, few studies have shown the relation between low HDL-C and high RDW in the increased development of the ACS. So, these studies had been planned to correlate the HDL-C levels with the RDW among the patients with ACS and its association with the various socio-demographic factors of the patient.

Methods

Study Design

This hospital-based cross-sectional study was conducted among patients attending the outpatient and inpatient departments of general medicine in a tertiary care centre in Puducherry from October 2023 to February 2024.

Sampling

The mean red cell distribution width among the patients with no ST-segment elevated myocardial infarction and with unstable angina was found to be 14.6 + 1 and 13.6 +1.7, respectively.

Considering the confidence interval of 95% and the power of the study was 80%, the sample size was calculated to be 62. The sample size was calculated using the open Epi software, version 3. Patients with age more than 18 years old with a diagnosis of acute coronary syndrome were

included in the study, and patients with age less than 18 years old, pregnant women, lactating mothers and patients with malignancy were excluded from the study.

Interventions

After the informed and written consent, the patients were asked to inquire about the basic demographic details of the patients, such as name, age, gender, locality, and body mass index, followed by a brief history of the patient explored in that the patient was inquired about the presence of the type 2 diabetes mellitus, hypertension, dyslipidemia, smoking and alcoholic history and the presence of acute coronary syndrome were confirmed based on the electrocardiogram. Then, all the patients were subjected to a Troponin I card test. The patients were then evaluated on the red cell distribution width, the High-density lipoprotein – -cholesterol, and the random blood sugar level from the venous sample taken on the anti-cubital vein. All the samples were taken in the early morning on the same day of admission to the hospital within 2 hours, and all the samples were processed within one hour after taking the blood samples.

Ethical declaration

All the procedures performed in this study involving the human participants were done by the ethical standards of the Internal Human Ethics Committee and the Scientific Research Committee of the Sri Manakula Vinayagar Medical College and Hospital, Puducherry, Puducherry, via reference no. SMVMCH-EC/ECO/IL/07/2024 and National Research Committee, 1964. Helsinki Declaration and its latest amendments.

Statistical analysis

All the data were entered in Microsoft Excel and analysed via the SPSS software version 25.0. and the independent t-test was used to compare the means, and the p-value of <0.05 is considered statistically significant.

Results

A total of 62 patients participated in the study. The mean age of the patients with ACS was found to be 55.6 $\pm$ 3.4 years. About 88.7% of the patients who participated in the study were more than 45 years old, and more than half of the patients (67.7%) were males, whereas the female contributed 32.3% only. Nearly 71% of the patients were from rural areas, and about 59.7% had a BMI of less than 23. Type 2 DM was present in 46.8% of the patients, whereas hypertension and dyslipidemia were present in only 33.9% and 12.9% of the patients, respectively. Only 24.2% of the patients were smokers, and alcoholics contributed only 29%, as in Table 1.

Table 1: Socio-demographic details of the study participants (n=62)

Parameter	Frequency (n)	Percentage (%)
Age (in years)		
≤45	7	11.3
>45	55	88.7
Gender		
Male	42	67.7
Female	20	32.3
Residence		
Urban	18	29
Rural	44	71
BMI		
<23	37	59.7
>23	25	40.3
Type 2 Diabetes mellitus		
Present	29	46.8
Absent	33	53.2
Hypertension		
Present	21	33.9
Absent	41	66.1
Dyslipidemia		
Present	8	12.9
Absent	54	87.1
Smoking		
Smoker	15	24.2
Non-smoker	47	75.8
Alcohol history		
Alcoholic	18	29
non-alcoholic	44	71

According to the electrocardiogram, about 43.5% of the patients who participated in the study had STEMI, 41.9% had unstable angina, and 14.5% had NSTEM, as in Figure 1. Based on the

patient's laboratory parameters, about 58.1% of the patients were found positive for Troponin-I, and 66.1% had RDW of less than 14%, whereas 33.9% had RDW of more than 14%. In about 71% of the patients, HDL-C was found to be more than 35; in only 29% of the patients, it was found to be less than 35; and in 66.1% of the patients, it had a random blood sugar of more than 200, as in Table 2.

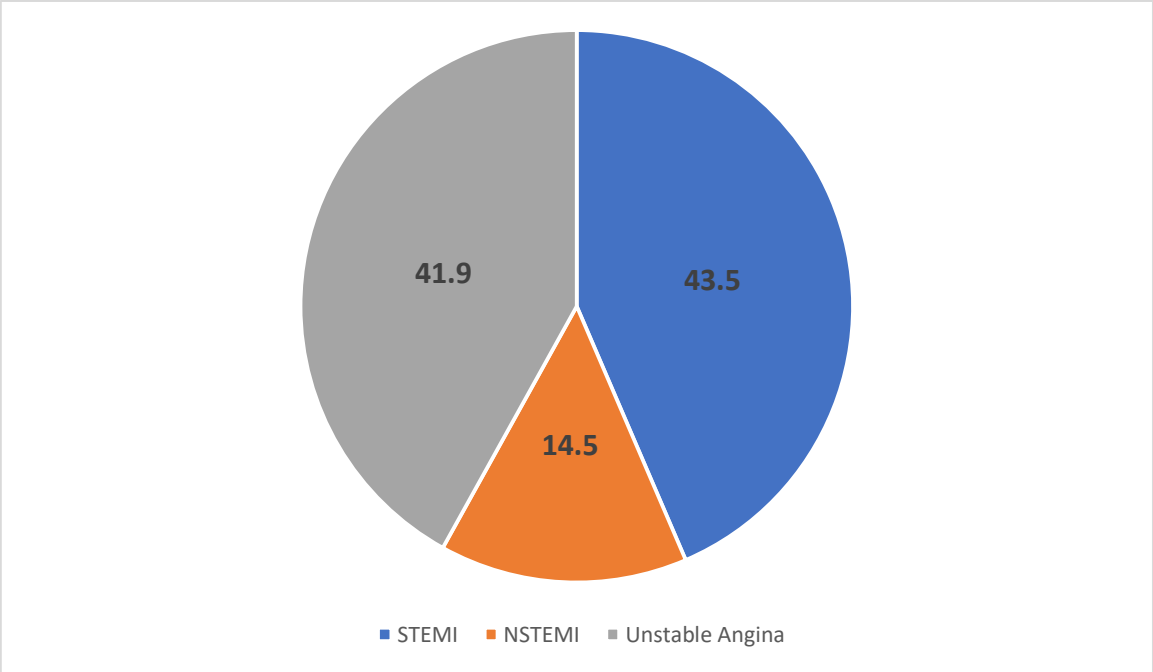

Figure 1: Types of ACS based on the Electrocardiogram

Table 2: Clinical and Laboratory characteristics of study participants

Variable	Frequency (n)	Percentage (%)
Troponin - I		
Positive	36	58.1
Negative	26	41.9
RDW		
<14	41	66.1
>14	21	33.9
HDL-C		
<35	30	48.4
>35	32	51.6
RBS		
<200	41	33.9
>200	21	66.1

On assessing the association between the various socio-demographic and the laboratory parameters of the patients with the level of the RDW, the study didn't show any association between the age (p=0.753), gender (p=0.897), residence (p=0.517), Type-2 DM (p=-.924), hypertension (p=0.615), dyslipidemia (p=0.302), smoking (p=0.565), alcohol (p=0.593), ACS type (p=0.714), Troponin-I (p=0.916), and RBS (p=0.078) with the level of the RDW. However, the study showed a significant association between BMI (P<0.001) and HDL-C (p<0.001) and RDW levels; the patients with a BMI less than 23 were found to have lower levels of RDW than the persons with a high BMI value, as in Table 3

Table 3: Association between various factors with the RDW

Parameter		Low RDW (<14)		High RDW (>14)		p-value
		n	%	n	%	
Age	≤45	5	8.1	2	3.2	0.753
	>45	36	58.1	19	30.6	
Gender	Male	28	45.2	14	22.6	0.897
	Female	13	21	7	11.3	
Residence	Urban	13	21	5	8.1	0.517
	Rural	28	45.2	16	25.8	
BMI	<23	31	50	6	9.7	<0.001
	>23	10	16.1	15	24.2	
Type 2 DM	Present	19	30.6	10	16.1	0.924
	Absent	22	35.5	11	17.7	
Hypertension	Present	13	21	8	12.9	0.615
	Absent	28	45.2	13	21	
Dyslipidemia	Present	4	6.5	4	6.5	0.302
	Absent	37	59.7	17	27.4	
Smoking	Smoker	9	14.5	6	9.7	0.565
	Non-smoker	32	51.6	15	24.2	
Alcohol	Alcoholic	11	17.7	7	11.3	0.593
	Non-alcoholic	30	48.4	14	22.6	
ACS type	STEMI	17	27.4	10	16.1	0.714
	NSTEMI	7	11.3	2	3.2	
	UA	17	27.4	9	14.5	
Troponin-I	Positive	24	38.7	12	19.4	0.916
	Negative	17	27.4	9	14.5	
HDL-C	<35	9	18	9	18	<0.001
	>35	32	64	0	0	
RBS	<200	24	38.7	17	27.4	0.078
	>200	17	27.4	4	6.5	

Upon assessing the RDW and the HDL-C correlation, the study showed a significant and negative correlation between the two variables with a p-value of 0.038, as shown in Table 4 and Figure 2.

Table 4: correlation between mean HDL-C level and RDW

Variable	Mean	SD	R-value	p-value
RDW	13.76	1.28	-0.625	<0.001
HDL-C	37.76	9.99		

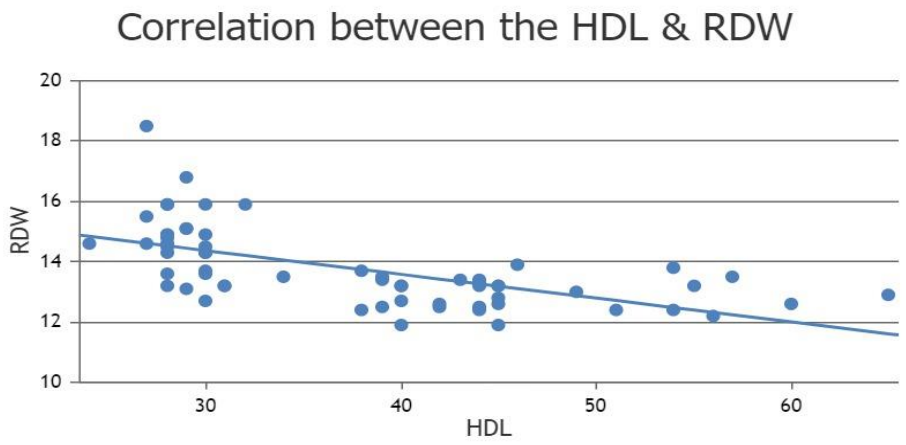

Figure 5: correlation between mean HDL-C level and RDW

Discussion

The red cell distribution width is a heterogenicity index of the cell sizes of the peripheral blood and was found to be independently correlated with several cardiac conditions. Due to the need for knowledge regarding its historical prognostic importance in various cardiac and vascular diseases, the RDW had been ignored previously beyond the evaluation of anaemia[12]. The increase in the RDW showed a profound dysregulation in the erythrocytes' homeostasis, attributed to various underlying metabolic abnormalities such as inflammation and oxidative stress. These proinflammatory cytokines will transform the bone marrow erythroid hematopoietic stem cells insensitive to erythropoietin, which increases the number of immature erythrocytes in peripheral blood, which leads to the increase in the increase in the RDW level[13]. The study by Chen et al.[14] showed that high levels of RDW are associated with an increased risk of mortality among patients even without cardiac diseases. The study by Patel et al.[15] also demonstrated that the RDW predicts mortality in older patients with or without age-related disease.

Based on demographic evaluation of the patients, our study showed that ACS is seen more commonly among patients over 45 (88.7%) and males (67.7%). Our study showed that the people living in rural areas (71%) were more commonly affected, and in our study, about 59.7% of the patients with low BMI were found to be more commonly affected by ACS. Similar to our study, the study by Dai X et al.[16] and Anh DT et al.[2] also showed that the incidence of ACS is more commonly seen in the increasing age of patients. The study by Redberg RF et al.[17] also showed that the incidence of ACS was more common in women. Krishnan MN et al.[10] showed that ACS was more commonly seen among patients from rural areas. However, the study by Moniruzzaman M et al.[18] and Park SJ et al.[19] showed that patients with higher BMI were found to be associated with ACS. In our study, about 46.8% of type-2 DM, 33.9% of hypertensive and 12.9% of dyslipidemia patients were found to have ACS. The study by Petrie JR et al. [20] showed that the various comorbidities such as diabetes, hypertension and dyslipidemia affect the outcomes of ACS patients.

Our study didn't show any association between the various demographic factors and the levels of the RDW. Similar to our study, the study by Xiong Ke et al.[21] didn't show any association between the various demographic factors such as gender, BMI, smoking, diabetes, hypertension, family history, past CABG, blood pressure and various laboratory parameters with the levels of the RDW. However, the study showed a significant association between age and the levels of RDW ($P<0.01$). However, the study by Talarico M et al.[22] showed an association between age ($p<0.01$), diabetes ($p=0.014$), dyslipidemia ($p=0.034$) and the various laboratory parameters. But the same study didn't find any association with gender (p-0.510), BMI (p-0.546), hypertension ($p=0.158$), active smoking (p-0.166) and the types of heart disease. The study by Zhao N et al.[23] also showed similar results. In our study, no correlation was noted between the type of the ACS and the levels of the RDW. Similar to our study, Xiong K et al.[21] didn't show any association between the RDW and the type of ACS.

Our study noted no significant association between the Troponin-I and the RDW levels ($p=0.916$). Still, the study by Lippi G. et al.[24] showed that combining the RDW with the troponin T improved the diagnostic sensitivity of the ACS to 99% compared to the other combined parameters. They concluded that the RDW levels were used to predict the severity of the coronary artery disease.

Our study showed a significant negative correlation between the HDL-C and the RDW levels with a p-value of <0.001. Similar to our study, the study by Raza also showed a negative and significant correlation between the HDL-C and the RDW. The study by Lippi G. et al.[25]

compared the lipid profile values across the RDW categories and showed that the RDW was negatively associated with the HDL-C level, similar to our study results. In another study, the investigator reported an increase in the mortality rate of ACS patients with above-normal RDW levels. The study by Avci E et al.[26] also showed similar results.

Limitation

The study was conducted in a single centre with relatively few patients. The inflammatory factors, malnutrition, natriuretic peptides, and other laboratory parameters may be associated with the increased RDW, which were not evaluated.

Conclusion

The study showed a relationship between the HDL-C and the RDW among patients with acute coronary syndrome. The study recommends that the RDW be used as an additional marker in predicting the risk of ACS and diagnosing patients with ACS. However, further studies are required to increase the understanding of the association between HDL-C and RDW in various study settings to diagnose the patient earlier and take necessary preventive measures and treatment to prevent disease occurrence.

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