

# Association of Lipid Profile with Disease Activity of Rheumatoid Arthritis Patients

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**ABSTRACT: Background:** Rheumatoid arthritis (RA) is a chronic autoimmune disease-causing systemic inflammation, joint destruction, and increased cardiovascular risk. Lipid profile abnormalities in early rheumatoid arthritis (RA) may contribute to premature atherosclerosis and an increased risk of early cardiovascular events. This study aim was to assess the relationship between lipid profile and disease activity in RA patients at a tertiary care hospital. **Methods:** This cross-sectional study was conducted in the Department of Medicine at Rajshahi Medical College Hospital (RMCH), Rajshahi, with 30 respondents (by ACR criteria) and severity assessment were done by DAS-28 (Disease Activity Score) score, through purposive sampling method. Participants were requested to perform a fasting lipid profile. Researcher were conducting the interview focusing demographic profile, clinical profile RA, and severity grading of RA by interview using a preformed structured questionnaire. **Results:** The study revealed that the mean age of participants was 39.07±9.82 years, female predominant. The mean (DAS-28) was 4.61±1.03, and the mean disease duration was 4.67±1.40 years. A significant negative correlation was observed between DAS28 (Disease Activity Score) and serum HDL cholesterol levels (Pearson's  $r = -0.470$ ,  $p = 0.009$ ), suggesting that as disease activity increases, HDL cholesterol levels decrease. However, LDL cholesterol levels were not significantly correlated with DAS28 (Pearson's  $r = -0.266$ ,  $p = 0.155$ ). **Conclusion:** In conclusion, these findings highlight the impact of RA disease severity on lipid metabolism, particularly HDL cholesterol levels, which may contribute to the increased cardiovascular risk in RA patients. Further research with a larger sample size is recommended to explore the underlying mechanisms and potential clinical interventions.

**Keywords:** Rheumatoid Arthritis, DAS-28, TC, HDL, LDL.

## Article at a glance:

**Study Purpose:** To examine the relationship between lipid profile levels and disease activity in rheumatoid arthritis patients at a tertiary hospital.

**Key findings:** Higher RA activity (DAS-28 score) was significantly linked with lower HDL levels, indicating altered lipid metabolism with inflammation.

**Newer findings:** The study reinforces that active RA reduces HDL levels, emphasizing cardiovascular monitoring even in early disease stages.

**Abbreviations:** RA – Rheumatoid Arthritis, DAS-28 – Disease Activity Score-28, HDL – High-Density Lipoprotein, LDL – Low-Density Lipoprotein, TC – Total Cholesterol

## INTRODUCTION

Rheumatoid arthritis (RA) is a symmetric, inflammatory, peripheral polyarthritis of indeterminate origin. It generally results in joint degradation via the deterioration of cartilage and bone.<sup>1</sup> Rheumatoid arthritis (RA) is a chronic autoimmune disorder, affecting around 0.5–1% of the

population. The pathogenic basis of rheumatoid arthritis (RA) is synovial inflammation, which subsequently deteriorates articular cartilage and bone tissue from the synovium, resulting in joint degeneration and impaired joint function in patients.<sup>2,3</sup> Furthermore, patients with rheumatoid arthritis demonstrate a greater incidence of

atherosclerosis in comparison to healthy controls, leading to a heightened occurrence of cardiovascular events, including stroke, myocardial infarctions, and cardiac fatalities, relative to the general population.<sup>1,4</sup> Extraarticular manifestations, such as cardiovascular diseases (CVD) and comorbidities, are common in rheumatoid arthritis (RA) and increase both the incidence and mortality rates among RA patients. The precise aetiology remains ambiguous; nonetheless, it is presently considered that genetic factors, autoimmune, environmental influences, and gut bacteria significantly contribute to the disease.<sup>5,6</sup> In addition to these well-established traits, recent studies reveal a substantial association between lipid metabolism and rheumatoid arthritis (RA). Lipids, the predominant class of cellular metabolites, are essential for energy supply and storage, cellular membrane construction, and signal transduction.<sup>7</sup> It is hypothesized that prolonged inflammation in rheumatoid arthritis may facilitate the progression of atherosclerosis. Conversely, the inhibition of inflammation may positively influence the prevention of subclinical atherosclerosis progression.<sup>8</sup> Furthermore, rheumatoid arthritis influences lipid levels. Consequently, modifications in serum lipids among rheumatoid arthritis patients are frequently noted in clinical assessments, resulting from the systemic inflammatory condition and pharmacological interventions for rheumatoid arthritis.<sup>9</sup> Typically, alterations in these lipid molecules entail a decrease in total cholesterol, low-density lipoprotein cholesterol (LDL), and high-density lipoprotein cholesterol (HDL) levels in untreated individuals prior to and during active phases.<sup>10</sup> Comparing RA patients to the control group, the apolipoprotein B (Apo B)/apolipoprotein A-1 (Apo A-1) ratio is likewise noticeably greater, and the serum lipoprotein (a) concentration rises noticeably.<sup>9</sup> The participation of prevalent pro-inflammatory cytokines, including interleukin-1 and interleukin-6, as well as tumor necrosis factor alpha (TNF- $\alpha$ ), contributes to the onset and advancement of both rheumatoid arthritis (RA) and atherosclerosis. A proinflammatory state results in a reduction of total cholesterol, HDL cholesterol, and LDL cholesterol in patients with rheumatoid arthritis.<sup>11</sup> Paradoxically, anti-inflammatory medications elevate total cholesterol, HDL cholesterol, and LDL cholesterol to varying extents in patients with rheumatoid arthritis.<sup>12</sup> Chronic inflammation induces oxidative alterations that modify HDL structure and diminish

apolipoprotein-A-I in individuals with active rheumatoid arthritis, impairing the typical anti-inflammatory, antioxidant, and cardioprotective roles of HDL cholesterol, which consequently becomes pro-inflammatory, thereby expediting endothelial dysfunction and plaque development.<sup>13</sup> Rheumatoid arthritis patients exhibit elevated risks of cardiovascular morbidity and mortality. Research demonstrates that the incidence of cardiovascular disease (CVD) is elevated by 48% in patients with rheumatoid arthritis (RA) relative to the general population.<sup>14</sup> Total cholesterol correlates with the risk of cardiovascular disease in rheumatoid arthritis, exhibiting a 3.3-fold increased risk when total cholesterol levels are below 4 mmol/L (155 mg/dL), whereas no elevated risk is shown when total cholesterol is equal to or greater than 4 mmol/L.<sup>15</sup> Some studies indicate that patients with rheumatoid arthritis experiencing acute myocardial infarction and ischemic stroke exhibit considerably reduced levels of total cholesterol. The European League Against Rheumatism recommends that the screening and management of rheumatoid arthritis patients encompass annual risk assessments, management of identified risk factors, and vigorous suppression of the inflammatory process to mitigate complications associated with rheumatoid arthritis.<sup>16</sup> Too far, it is unclear exactly how these changes in lipid patterns relate to the pathophysiology and inflammation of RA patients.<sup>1</sup> This study was conducted to assess the relationship between Lipid Profile and Disease Activity in patients with Rheumatoid Arthritis.

## METHODS

This cross-sectional study was carried out in the Department of Medicine of Rajshahi Medical College & Hospital, Rajshahi, Bangladesh. The Institutional Review Board of Rajshahi Medical College reviewed and approved the research protocol. In this study purposive sampling method was used, and data was collected from March 2021 to January 2023. A total of 30 (by ACR criteria) patients with confirmed diagnosis of RA who were attended in Department of Medicine ward, Rajshahi Medical College Hospital interviewed. A comprehensive history was obtained from each patient, and a thorough clinical examination, encompassing both articular and extra-articular assessments, as well as disease activity monitoring using DAS 28, was conducted. The 28-joint disease activity score (DAS 28) was used to assess disease activity.<sup>17-19</sup> Blood

samples were taken from the subjects after a 12-hour fast in order to evaluate their lipid profile, which included their levels of triglycerides (TG), total serum cholesterol (TC), low density lipoprotein cholesterol (LDL), high density lipoprotein cholesterol (HDL), and very low-density lipoprotein (VLDL). Data was entered into a structured case record form that had already been created. Following that, they were imported into the statistical program. SPSS Version 26.0 was used to conduct the analysis. Percentage was used to summarize the qualitative factors. The mean and Standard Deviation (SD) were used to summarize the quantitative variables. Depending on the type of data, tables, diagrams, and graphs were used to display it. Correlation coefficient test was carried out

to find out the relation between DAS 28 with lipid profile. One way ANOVA test was done to find out the relation between severity of RA and lipid profile.

## RESULTS

Results and observations of this study are given below in tables and figures. Among the participants majority were aged between 31 to 40 years 12(40.0%), mean age  $\pm$ SD was (39.07 $\pm$ 9.82) years. Male was 20% and female 80%. The majority resided in rural areas 17(56.6%) and 16(53.30%) of the respondents were homemakers (Table I).

**Table 1: Demographic characteristics of the respondents (n=30)**

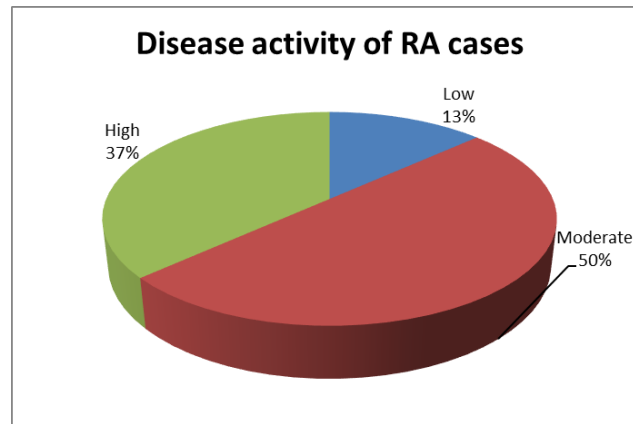
Characteristics	Percentage (%)
<b>Age groups (year)</b>	
18-30	6 (20)
31-40	12 (40)
41-50	8 (26.70)
51-60	4 (13.30)
Mean $\pm$ SD	39.07 $\pm$ 9.82
<b>Sex</b>	
Female	24 (80.0)
Male	6 (20.0)
<b>Residence</b>	
Rural	17 (56.6)
Urban	13 (43.3)
<b>Educational qualification</b>	
Illiterate	6(20.0)
Below HSC	7 (23.30)
SSC	6 (20.0)
HSC	7 (23.30)
Graduate and above	4 (13.30)
<b>Occupation</b>	
Student	2 (6.70)
Homemaker	16 (53.30)
Business	3 (10.0)
Farmer	1 (3.30)
Service holder	5 (16.70)

The mean height, weight and BMI of the study cases were 1.59 $\pm$ 0.05m, 57.50 $\pm$ 10.64 kg, and 22.86 $\pm$ 3.99 kg/m<sup>2</sup> respectively.

**Table 2: Mean height, weight and BMI of RA cases (n=30)**

Variable	Mean $\pm$ SD
Height (m)	1.59 $\pm$ 0.05
Weight (kg)	57.50 $\pm$ 10.64
BMI (kg/m <sup>2</sup> )	22.86 $\pm$ 3.99

Regarding disease severe activity of moderate disease activity, and 11 (36.67%) had high disease activity. rheumatoid arthritis 4 (13.33%) of the participants had low disease activity, 15 (50.0%) of the respondents had



**Figure 1: Mean height, Weight and BMI of RA Cases (n=30)**

The mean total cholesterol level was significantly lower in high disease activity subjects than in moderate and low disease activity subjects ( $P=0.003$ ). It averaged  $215.37 \pm 23.37$  mg/dl in the low,  $185.07 \pm 30.54$  mg/dl in the moderate, and  $157.27 \pm 21.96$  mg/dl in the high disease activity group. HDL cholesterol level was significantly lower in high disease activity subjects than in moderate and low disease activity subjects ( $P=0.001$ ), averaging  $49.50 \pm 5.07$  mg/dl in the low,  $46.87 \pm 9.69$  mg/dl in the

moderate, and  $33.18 \pm 8.32$  mg/dl in the high disease activity group. The mean LDL cholesterol level was similar across disease activity groups ( $P=0.103$ ), averaging  $109.75 \pm 16.82$  mg/dl in the low,  $111.87 \pm 12.61$  mg/dl in the moderate, and  $97.27 \pm 21.43$  mg/dl in the high disease activity group. The mean TC: HDL cholesterol ratio was similar across disease activity groups ( $P=0.389$ ), averaging  $4.39 \pm 0.78$  in the low,  $4.23 \pm 1.61$  in the moderate, and  $5.06 \pm 1.57$  in the high disease activity group.

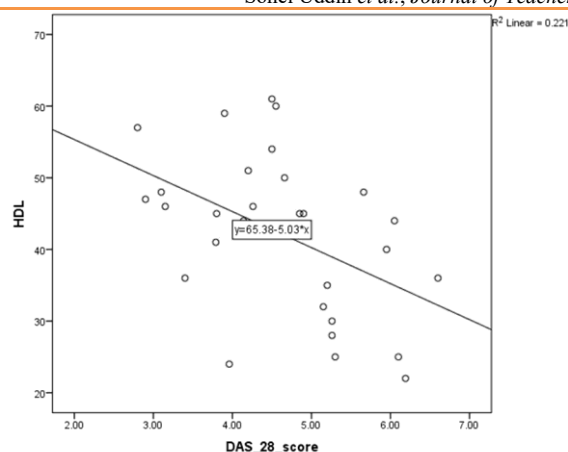
**Table 3: Relation between total cholesterol level and disease severity of RA (n=30).**

Variable	Low disease activity	Moderate disease activity	High disease activity	Overall	P value
Total cholesterol (mg/dl)	$215.37 \pm 23.37$	$185.07 \pm 30.54$	$157.27 \pm 21.96^*$	$178.87 \pm 32.40$	0.002
HDL cholesterol (mg/dl)	$49.50 \pm 5.07$	$46.87 \pm 9.69$	$33.18 \pm 8.32^*$	$42.20 \pm 11.02$	0.001
LDL Cholesterol (mg/dl)	$109.75 \pm 16.82$	$111.87 \pm 12.61$	$97.27 \pm 21.43$	$106.23 \pm 17.69$	0.103
TC: HDL-C	$4.39 \pm 0.78$	$4.23 \pm 1.61$	$5.06 \pm 1.57$	$4.57 \pm 1.52$	0.389

P value is determined by one way ANOVA test. Post-hoc analysis with Bonferroni adjustment done.

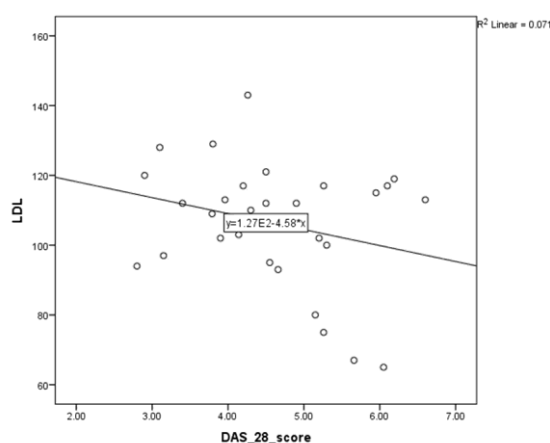
\*Denotes the significant difference between low disease activity and high disease activity.

! Denotes the significant difference between moderate disease activity and high disease activity.



**Figure 2: The correlation between DAS28 and serum levels of HDL**

The correlation analysis using Spearman's rho reveals a negative correlation between HDL and DAS 28 score (correlation coefficient = -0.047,  $p=0.009$ ) among the 30 participants.



**Figure 3: The correlation between DAS28 and serum levels of low-density LDL**

The correlation analysis using Spearman's rho reveals a negative correlation between LDL and DAS 28 score (correlation coefficient = -0.0266,  $p=0.155$ ) among the 30 participants.

## DISCUSSION

Patients with rheumatoid arthritis(RA) exhibited an atherogenic lipid profile, characterized by elevated total cholesterol and low-density lipoprotein cholesterol, alongside a decline in high-density lipoprotein cholesterol.<sup>21</sup> The TC/HDL ratio should ideally be less than four, while ratios exceeding five indicate an elevated risk of myocardial infarction.<sup>22</sup> The study aimed to evaluate the association between lipid profile and the disease activity of rheumatoid arthritis patients. The study uncovered a wide age distribution, with the majority falling within the 31-40 age groups (40.0%) and a mean age of  $39.07 \pm 9.82$  years. Study conducted by

Sakr found the mean age of their study cases  $40.50 \pm 12.60$  years, Study conducted by Kumar and co-researchers found the mean age  $42.07 \pm 10.60$  years.<sup>23, 24</sup> Another study conducted by Bhowmik and colleagues found 60% of their study in 31-50 years age group, 20% were in 20-30 years age group and 16% were in > 50 years age group which are consistent to the finding of this study.<sup>25</sup> The present study showed the male-to-female ratio of rheumatoid arthritis cases was determined to be 1:4. In the examined instances, a maximum of 24 (80%) were female, while only 6 (20%) were male. Study conducted by Malaviya and colleagues found 90.31% of their study cases female, study conducted by Kumar and co-researchers found 81.50% of their RA cases female and Sakr and co-researchers found 84% of their study cases female and all the findings are similar to the finding of this study.<sup>24-26</sup> The genes located on the female sex chromosome and the female sex hormones,



particularly estrogen, which modulate immune responses by promoting the survival of undesirable autoreactive clones, may account for the increased incidence observed in females.<sup>27</sup> The average height of the study subjects was  $1.59 \pm 0.05$  m, the average weight was  $57.50 \pm 10.64$  kg, and the average BMI was  $22.86 \pm 3.99$  kg/m<sup>2</sup>. The research by Velpula reported a mean BMI of  $22.82 \pm 4.66$  kg/m<sup>2</sup>, aligning with the findings of this study.<sup>28</sup> The mean disease activity score and duration of the disease were  $4.61 \pm 1.03$  and  $4.67 \pm 1.40$  years respectively. Study conducted by Movahedi also found the mean DAS-28 score  $4.70 \pm 1.30$ .<sup>26</sup> Study conducted by Hadda et.al also found the mean DAS score  $4.9 \pm 1.02$  and mean duration  $5.5 \pm 3.09$  years.<sup>29</sup> In this study the mean total cholesterol, LDL-C, HDL-C, and TG level  $178.87 \pm 32.40$  mg/dl,  $106.23 \pm 17.69$  mg/dl,  $42.20 \pm 11.02$  mg/dl and  $114.83 \pm 21.35$  mg/dl. These findings align by a couple of articles.<sup>30,31</sup> The mean total cholesterol and HDL cholesterol was statistically significantly lower among high disease activity cases than moderate and low disease activity cases ( $P=0.002$  and  $0.001$ ). Another study reported lower levels of HDL-C and TC, elevated blood concentrations of lipoprotein(a), and increased TC/HDL-C and LDL-C/HDL-C ratios in inactive and/or untreated illness compared to the general population.<sup>21</sup> These alterations in lipid profiles suggest a potential link between disease activity and dyslipidemia, which may have implications for cardiovascular risk in affected individuals. There was a negative correlation between total cholesterol, HDL and LDL and DAS 28 ( $r=0.171$ ,  $p=0.006$ ) and a positive correlation was found between TG and DAS 28 ( $r=-0.200$ ,  $p=0.290$ ). Similar result was found by Mullick et.al where they found negative correlation between total cholesterol, HDL and LDL and DAS 28 and a positive correlation was found between TG and DAS.<sup>32</sup>

## CONCLUSION

This study highlights the significant association between lipid profile abnormalities and disease activity in rheumatoid arthritis (RA) patients. Dyslipidemia, characterized by altered levels of total cholesterol, triglycerides, LDL, and HDL, appear to be linked with increased inflammatory burden and disease severity in RA. Overall, these findings highlight the impact of RA disease severity on lipid metabolism, particularly HDL cholesterol levels, which may contribute to the increased cardiovascular risk in RA patients. Further research with a larger

sample size is recommended to explore the underlying mechanisms and potential clinical interventions.

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**Conflict of Interest:** The authors declare no conflict of interest.

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