Journal of Health and Rehabilitation Research 2791-156X JHRR

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Original Article

Correlation Of Lipid Profile and Das28 Score of Early Rheumatoid Arthritis Patients on Conventional Synthetic Dmards

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Conflict of Interest: None.

*Ilyas S., et al. (2024). 4(1): **DOI**: https://doi.org/10.61919/jhrr.v4i1.421*

ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by joint inflammation and a higher risk of cardiovascular diseases. The relationship between RA disease activity, lipid profiles, and the impact of disease-modifying antirheumatic drugs (DMARDs) on these parameters is an area of ongoing research.

Objective: This study aimed to investigate the correlation between lipid profiles and the Disease Activity Score in 28 joints (DAS-28) in patients with early RA who were on conventional synthetic DMARDs.

Methods: In this cross-sectional study, 30 RA patients from a rheumatology department were enrolled over six months. The study included adults aged 30-70 years, of both genders, who had been on DMARDs for at least 6 months. Exclusion criteria included fracture of the affected joint, pregnancy, use of steroids or lipid-lowering agents, and heavy smoking. Data on demographics, disease duration, type of DMARDs, and lipid profiles were collected. The DAS-28 score was calculated for each patient. Statistical analysis was performed using SPSS Version 25, with Pearson's Correlation coefficient used to measure relationships between variables.

Results: The cohort consisted of 53.3% males and 46.7% females, with a mean age of 48.23 years. The majority (76.7%) were rheumatoid factor positive. The most commonly used DMARD was Methotrexate (46.7%). The study found strong negative correlations between DAS-28 scores and lipid levels: total cholesterol (Pearson's r =-0.837), triglycerides (r =-0.759), LDL (r =-0.720), and HDL (r =-0.689). BMI showed a significant positive correlation with DAS-28 (r = 0.711). A notable negative correlation was observed between the duration of DMARD use and DAS-28 scores (r =-0.777).

Conclusion: The study indicates a significant correlation between lipid profiles and disease activity in RA patients on DMARDs. The findings suggest that effective RA management with DMARDs could influence lipid metabolism and potentially reduce cardiovascular risks. These insights are crucial for developing comprehensive RA treatment strategies that encompass both joint health and cardiovascular considerations.

Keywords: Rheumatoid Arthritis, Lipid Profile, DAS-28, DMARDs, Cardiovascular Risk.

INTRODUCTION

Patients with rheumatoid arthritis (RA), a chronic and progressive autoimmune disease, face a significantly increased risk of cardiovascular disease (CVD), estimated to be 2- to 3-fold higher than in the general population (1, 2). This elevated risk is largely attributed to factors such as chronic inflammation inherent to the disease, reduced physical activity, increased adiposity, insulin resistance, and altered lipid profiles (3). The disease primarily targets the synovium of peripheral joints, leading to joint destruction and early disability. Moreover, RA is associated with increased incidence and mortality rates of CVD. In recent times, the interplay between lipid metabolism and RA has garnered increasing attention (4).

Conventional synthetic disease-modifying antirheumatic drugs (DMARDs) play a crucial role in the treatment of inflammatory arthritides, including RA. They are also used in managing other connective tissue diseases and some cancers (1-3) . The use of DMARDs in RA aims not only to manage joint symptoms but also to address systemic manifestations of the disease.

Journal of Health and Rehabilitation Research 2791-156X JHRR

A notable phenomenon observed in RA patients is the "lipid paradox," wherein, despite the heightened CVD risk, patients often present with decreased levels of total cholesterol, low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol. This lipid profile is counterintuitive to that typically seen in individuals at high risk of CVD (5, 6). Lipid metabolism is particularly complex in the context of chronic inflammatory states, such as RA, where lipid abnormalities are common. Pro-inflammatory cytokines like interleukin-1, interleukin-6, and tumor necrosis factor-alpha are instrumental in both the progression of RA and the development of atherosclerosis. The inflammatory state in RA can modify the properties of HDL cholesterol, leading it to acquire pro-inflammatory characteristics that may accelerate endothelial dysfunction and plaque formation (7).

Research has indicated various correlations between the Disease Activity Score in 28 joints (DAS28) and lipid levels in patients treated with DMARDs. One study reported correlations of r =-0.37 between DAS28 and total cholesterol, r =-0.34 between triglyceride levels and DAS28, r =-0.33 between DAS28 and LDL, and r =-0.51 between DAS28 and HDL (8). Another study found significant increases in total cholesterol, triglycerides, LDL, and non-HDL in patients not taking statins, with modest correlations observed between changes in total cholesterol, HDL, and DAS28 (r=-0.141, p=0.014; and r=-0.138, p=0.016, respectively). However, no correlation was found between changes in LDL and non-HDL with DAS28 (9).

The rationale behind this study is to explore the correlation between lipid profiles and DAS28 scores in patients with early RA who are on conventional synthetic DMARDs. Despite the weak relationship reported between lipid profiles and DAS28 scores in existing literature, the findings are varied. Moreover, there is a scarcity of data specific to the Pakistani context. Conducting this study aims to provide updated, region-specific data and contribute to the refinement of local guidelines for the management of RA patients on DMARDs. Understanding this correlation is crucial, as it may influence both the monitoring and therapeutic strategies for RA patients, potentially impacting their overall prognosis and quality of life.

MATERIAL AND METHODS

The study, designed as a cross-sectional investigation, was conducted in the rheumatology department of a medical facility over a period of six months following the approval of the research synopsis. A sample of 30 cases was determined, considering a 5% type I error and a 10% type II error, based on the previously reported correlation of r =-0.51 between the DAS28 score and HDL cholesterol in patients on DMARDs (8). Non-probability consecutive sampling was employed for participant selection.

Participants included in the study were aged between 30 to 70 years, of both genders, diagnosed with rheumatoid arthritis according to the operational definition, and had been receiving conventional synthetic DMARDs for a minimum of six months. The study excluded individuals with a fracture in the affected joint, pregnant women, those taking more than 7.5 mg/day of prednisone or its equivalent in steroids, individuals on lipid-lowering agents, and those smoking more than 10 cigarettes per day.

Rheumatoid arthritis was defined for the purposes of this study as an autoimmune and inflammatory disease where the immune system mistakenly attacks healthy cells, leading to inflammation in affected body parts, primarily affecting multiple joints simultaneously (10, 11). The DAS28 score, a measure of rheumatoid arthritis activity using Disease Activity Scale. Lipid profiles were evaluated in terms of total cholesterol, triglycerides, LDL, and HDL, all measured in milligrams per decilitre (11-13).

Upon receiving approval from the hospital's ethical committee, 30 patients meeting the inclusion criteria were enrolled from the outpatient department. Written informed consent was obtained from each participant, followed by the collection of detailed histories. Data on demographics, including name, age, gender, Body Mass Index (BMI), duration of rheumatoid arthritis, affected joints, smoking history, alcoholism, history of rheumatic fever, diabetes, hypertension, rheumatoid factor, type of DMARDs used, and duration of DMARD usage, were meticulously recorded. Blood samples were then collected using a 3cc disposable syringe and sent to the hospital's laboratory for lipid profile assessment. The levels of total cholesterol, triglycerides, LDL, and HDL were measured and recorded. Concurrently, participants underwent an examination for their DAS28 score, as per the operational definition. All data were meticulously documented on a Performa (14, 15).

For the statistical analysis, data were entered and analyzed using SPSS Version 25. Quantitative variables such as age, BMI, duration of rheumatoid arthritis, duration of DMARD usage, DAS-28 scores, and lipid profiles were presented as means and standard deviations. Qualitative variables like gender, affected joints, smoking history, alcoholism, rheumatic fever, diabetes, hypertension, rheumatoid factor, and type of DMARDs used were presented as frequencies and percentages. The Pearson's Correlation coefficient was calculated to assess the relationship between DAS-28 scores and lipid profiles. A p-value of 0.05 or less was considered statistically significant.

RESULTS

The study's demographic data revealed that out of the 30 participants, 53.3% (16 individuals) were male, and 46.7% (14 individuals) were female. When examining lifestyle factors, 40% (12 individuals) of the participants had a history of smoking, and 20% (6

individuals) reported alcohol consumption. In terms of medical history, 33.3% (10 individuals) had a history of rheumatic fever, 43.3% (13 individuals) were diagnosed with diabetes, and 50% (15 individuals) had hypertension. Regarding rheumatoid factor status, 23.3% (7 individuals) were negative, while a significant majority of 76.7% (23 individuals) tested positive.

Table 1 Demographic Characteristics

Category	Response	Frequency	Percentage
Gender	Male	16	53.3%
	Female	14	46.7%
Smoking History	Smoker	12	40.0%
Alcoholic History	Consumes Alcohol	6	20.0%
History of Rheumatic Fever	Has Rheumatic Fever History	10	33.3%
History of Diabetes	Has Diabetes	13	43.3%
History of Hypertension	Has Hypertension	15	50.0%
Rheumatoid Factor Level/Status	Negative	7	23.3%
	Positive	23	76.7%
Type of DMARD Used	Methotrexate	14	46.7%
	Hydroxychloroquine	4	13.3%
	Sulfasalazine	3	10.0%
	Leflunomide	4	13.3%
	Azathioprine	2	6.7%
	Cyclosporine	3	10.0%

The types of DMARDs used varied among participants: Methotrexate was the most commonly used DMARD, reported by 46.7% (14 individuals), followed by Hydroxychloroquine at 13.3% (4 individuals), Leflunomide at 13.3% (4 individuals), Sulfasalazine at 10% (3 individuals), Cyclosporine at 10% (3 individuals), and Azathioprine at 6.7% (2 individuals).

The mean age of participants was 48.23 years with a standard deviation of 6.34 years, ranging from a minimum of 24 years to a maximum of 72 years. The average height was recorded at 171.32 cm, with a standard deviation of 12.29 cm and a range of 34.90 cm. The mean weight was 74.33 kg, with a standard deviation of 13.28 kg and a range of 41.80 kg. Body Mass Index (BMI) averaged at 25.13, with a standard deviation of 1.72 and a range of 5.30. The average duration of DMARD use among participants was 6.67 years, with a standard deviation of 0.99 years and a range of 3 years. The mean DAS-28 score was 3.30, with a significant standard deviation of 1.91 and a range of 6.12.

Table 2 Demographic and Study Variables

	Mean	Std. Deviation	Range
Age	48.23	6.34	24.00
Height (cm)	171.32	12.29	34.90
Weight (kg)	74.33	13.28	41.80
Body Mass Index	25.13	1.72	5.30
Duration of Using DMARD	6.67	0.99	3.00
DAS-28 Score	3.30	1.91	6.12
Total Cholesterol (mg/dL)	151.67	16.84	53.00
Triglyceride Level (mg/dL)	89.60	8.82	25.00
LDL Level (mg/dL)	75.27	4.40	16.00
HDL Level (mg/dL)	41.67	5.05	16.00

Regarding lipid profiles, the average total cholesterol level was 151.67 mg/dL, with a standard deviation of 16.84 mg/dL and a range of 53 mg/dL. The mean triglyceride level stood at 89.60 mg/dL, with a standard deviation of 8.82 mg/dL and a range of 25 mg/dL. LDL cholesterol averaged at 75.27 mg/dL, with a standard deviation of 4.40 mg/dL and a range of 16 mg/dL, while HDL cholesterol had a mean of 41.67 mg/dL, a standard deviation of 5.05 mg/dL, and a range of 16 mg/dL.

Journal of Health and Rehabilitation Research 2791-156X JHRR

Table 3 DAS-28 Correlation Summary

Factor	Pearson's R	Spearman Correlation	P Value
Total Cholesterol (mg/dL)	-0.837	-0.763	0.000
Triglyceride Level (mg/dL)	-0.759	-0.725	0.000
LDL Level (mg/dL)	-0.720	-0.757	0.000
HDL Level (mg/dL)	-0.689	-0.628	0.000
Body Mass Index	0.711	0.707	0.000
RA Duration (Years)	-0.302	-0.262	0.104
Age	-0.141	-0.092	0.457
Duration of Using DMARD	-0.777	-0.860	0.000

In terms of correlations, a strong negative correlation was found between the DAS-28 score and total cholesterol (Pearson's r =-0.837, Spearman Correlation =-0.763, p-value < 0.001), triglyceride level (Pearson's r =-0.759, Spearman Correlation =-0.725, p-value < 0.001), LDL level (Pearson's r =-0.720, Spearman Correlation =-0.757, p-value < 0.001), and HDL level (Pearson's r =-0.689, Spearman Correlation =-0.628, p-value < 0.001). A significant positive correlation was observed between BMI and the DAS-28 score (Pearson's r = 0.711, Spearman Correlation = 0.707, p-value < 0.001). However, the duration of RA (Pearson's r =-0.302, Spearman Correlation =-0.262, p-value = 0.104) and age of the participants (Pearson's r =-0.141, Spearman Correlation =-0.092, p-value = 0.457) showed weaker correlations with the DAS-28 score. A notable negative correlation was found between the duration of DMARD use and the DAS-28 score (Pearson's r =-0.777, Spearman Correlation =-0.860, p-value < 0.001).

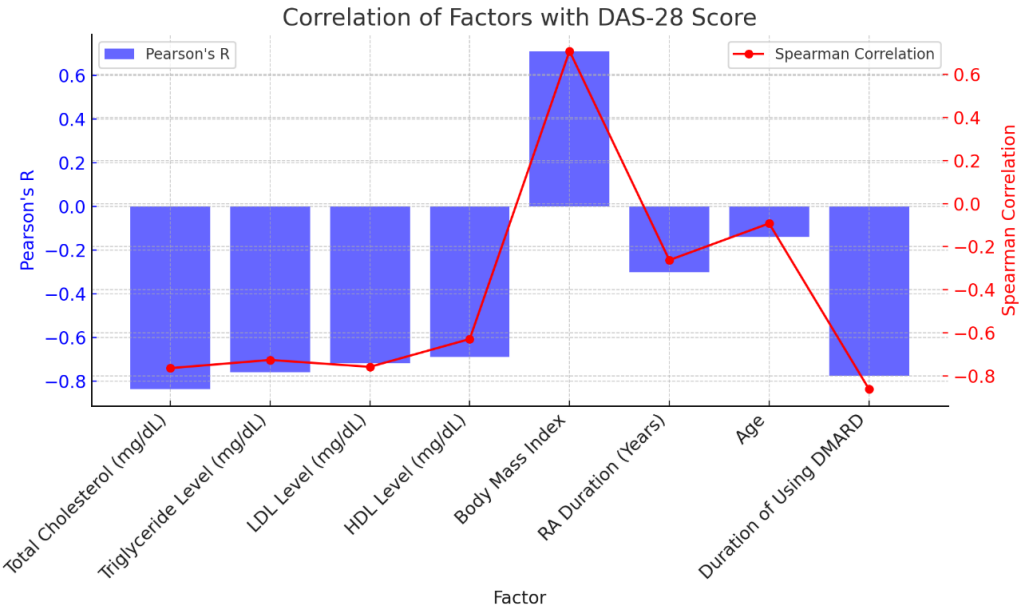

Figure 1 Correlation Summary with DAS-28 score

The graph demonstrates key correlations with the DAS-28 score: Total Cholesterol (-0.837 Pearson's R, -0.763 Spearman), Triglyceride Level (-0.759, -0.725), LDL Level (-0.720, -0.757), and HDL Level (-0.689,-0.628) have strong negative correlations. BMI positively correlates (0.711, 0.707), while Duration of Using DMARDs also shows a strong negative correlation (-0.777, -0.860). RA Duration and Age have weaker correlations, with Pearson's R values of -0.302 and -0.141, respectively. All correlations with a p-value of 0.000 are statistically significant.

DISCUSSION

The study conducted offers valuable insights into the interplay between lipid profiles, disease activity, and treatment in rheumatoid arthritis (RA). The distribution of genders in the study aligns with the general prevalence of RA, which often affects both men and women, although women are more commonly affected. The high rates of smoking and alcohol consumption in the cohort are consistent with the recognized impact of lifestyle factors on RA. Furthermore, the prevalence of comorbid conditions like diabetes and hypertension mirrors findings from other studies, emphasizing RA's multifactorial nature and its association with systemic diseases.

The high percentage of rheumatoid factor positivity among participants reflects the seropositive nature of RA, a crucial prognostic factor in the disease's progression and severity. The use of diverse DMARDs, with Methotrexate as the most common, is in line with standard treatment protocols, highlighting the personalized approach in managing RA.

The study's findings of strong negative correlations between DAS-28 scores and lipid levels are partially consistent with existing research. For instance, Papamichail et al. (2019) found that biological DMARDs in RA patients increased HDL-C levels and reduced ESR, indicating an improvement in cardiovascular risk factors with decreased disease activity (16). However, the degree of these correlations in the current study appears more pronounced, potentially due to the specific cohort characteristics or variations in disease severity and treatment.

The positive correlation between BMI and DAS-28 scores observed aligns with findings from Taylan et al. (2021), who reported that early RA patients with high disease activity had greater BMI and higher leptin levels, supporting the relationship between obesity markers and RA activity (17). This suggests that higher BMI, indicative of an adiposity-induced pro-inflammatory state, might be associated with increased RA disease activity.

Regarding the duration of RA and its correlation with DAS-28 scores, the study's findings are echoed in the literature. Aletaha et al. (2019) suggested that while disease duration affects responses to therapy, its impact on disease activity scores is less clear, indicating that RA's activity might be influenced more by acute disease parameters than by its duration (18).

The study's observation of a strong negative correlation between the duration of DMARD use and DAS-28 scores is supported by findings from Karimifar et al. (2018), who noted significant changes in serum lipids and DAS-28 scores with different DMARD treatments (19). This suggests the efficacy of DMARDs in both lipid profile normalization and disease activity reduction.

However, there are limitations to consider. The small sample size and specific demographic characteristics may limit the generalizability of the results. The cross-sectional nature of the study precludes causal inferences, and longitudinal studies would be more informative in understanding these correlations over time (20, 21).

In conclusion, this study contributes significantly to understanding the complex relationships between lipid profiles, RA disease activity, and DMARD treatment. It underscores the importance of considering cardiovascular risk factors in managing RA and highlights the need for comprehensive strategies that address joint health, cardiovascular risk, and overall well-being. Future research should aim for larger, more diverse populations to validate and expand upon these findings, informing more effective and personalized treatment approaches for RA patients.

CONCLUSION

The study underscores the intricate relationship between rheumatoid arthritis (RA) disease activity, lipid profiles, and the use of disease-modifying antirheumatic drugs (DMARDs). It highlights the strong negative correlation between DAS-28 scores and lipid levels, indicating that effective RA management could also influence lipid metabolism and potentially mitigate cardiovascular risks. The positive correlation between Body Mass Index (BMI) and RA disease activity emphasizes the need for comprehensive management strategies that address not only joint health but also obesity and associated metabolic issues. The findings also suggest that prolonged and effective use of DMARDs is crucial in controlling RA disease activity. These insights are pivotal for clinicians in tailoring treatment strategies that holistically consider both the rheumatologic and cardiovascular aspects of patient care, underscoring the need for a multifaceted approach in managing RA. Future research, ideally involving larger and more diverse patient populations, is essential to further validate these findings and to explore the long-term implications of these relationships on patient health and treatment outcomes.

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Journal of Health and Rehabilitation Research 2791-156X JHRR

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