

# Frequency of Dyslipidemia in Patients with Rheumatoid Arthritis

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## ABSTRACT

**Objective:** To determine frequency of dyslipidemia in rheumatoid arthritis patients.

**Study Design:** Descriptive / cross sectional study

**Place and Duration of Study:** This study was conducted at the Department of Medical OPD, Lahore General Hospital, Lahore from 30<sup>th</sup> September 2014 to 30<sup>th</sup> March 2015.

**Materials and Methods:** One hundred and fifty patients with rheumatoid arthritis, of both gender, age 18-80 years, disease duration  $\geq 6$  months, BMI 19-25 were included in the study. Fasting lipid profile was measured.

**Results:** Mean age of study sample was  $54.51 \pm 3.052$  years (age range 44 to 60 years of age). There were 60 (40%) male patients and 90 (60%) female patients. 48 (32%) patients had dyslipidemia. Dyslipidemia was associated with duration of disease but not with age, gender or treatment

**Conclusion:** Frequency of dyslipidemia is quite high (32%) in our patients of rheumatoid arthritis.

**Key Words:** Rheumatoid arthritis, dyslipidemia, cholesterol, lipoproteins, diabetes mellitus.

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## INTRODUCTION

Rheumatoid arthritis (RA) is the most common form of polyarticular inflammatory arthropathy characterized by persistent synovitis, bony erosions and progressive articular destruction leading to varying degree of physical disability.<sup>1</sup> Long-term complications of the disease are hospitalization, work disability, medical costs, poor quality of life, and cardiovascular disease (CVD) etc.<sup>2,3</sup>

Rheumatoid arthritis is considered as an independent risk factor of cardiovascular disease ischemic heart disease (IHD) or congestive heart failure which cause up to 40% of deaths in these patients.<sup>3-5</sup> In the general population, dyslipidemia, especially elevated levels of low-density lipoproteins (LDL), has been shown to be one of the strongest predictors of CVD and it constitutes the primary treatment target according to national guidelines.<sup>6</sup>

Dyslipidemia in RA mainly presents as low concentrations of high-density lipoprotein (HDL), which is associated with an unfavourable cardiovascular risk.

Total cholesterol and HDL levels in RA are inversely associated with the acute phase response, regardless of antirheumatic therapy.<sup>5</sup> It is also recommended that lipid levels should be monitored and managed in patients with RA to minimize the long-term risk of cardiovascular disease. A study reported prevalence of dyslipidemia in 48% patients of RA.<sup>7</sup> A local study also quoted various types of dyslipidemia in 54% of patients.<sup>8</sup> However, this study included patients with < 6 months duration of disease and other CVD risk factors like smoking, obesity, hypertension were not recorded. The present study was undertaken to know the frequency of dyslipidemia in patients of rheumatoid arthritis who did not have any other risk factor for CVD. As cardiovascular disease is the leading cause of death in RA patients,<sup>9</sup> disease-modifying therapies can be added to minimize the risk of mortality.

## MATERIALS AND METHODS

It was a cross-sectional study, carried out in Department of Medical OPD, Lahore General Hospital, Lahore, over a six-month period from 30<sup>th</sup> September 2014 to 30<sup>th</sup> March 2015. The study was approved by the Institutional Ethical Committee. Non-probability, purposive sampling technique was used and estimated sample size was 150 patients at 95% confidence level, 8% margin of error taking an expected percentage of patients of dyslipidemia in RA patients 54%.<sup>8</sup> Patients of both genders, 18-80 year of age, diagnosed as rheumatoid arthritis on the basis of American College of Rheumatism-(ACR-ELUR) criteria, with duration of RA  $\geq$  six months, and having BMI 19-25 (with normal weight) were enrolled in the study. Exclusion criteria included smoking, diabetes (previous medical record or blood sugar fasting >126 mg/dl, blood sugar random

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>200mg/dl), lipid-lowering drugs, history of CAD or cerebrovascular accident (CVA), or any chronic systemic or metabolic disorder. Informed consent was obtained from each patient. Demographic profile (name, age, sex, contact no.) was taken. Complete medical history and physical examination including body mass index (BMI) and blood pressure measurement were done on patient's presentation. Patients' fasting (12-15 hour) blood sample (5cc) were taken and sent to hospital laboratory for analysis of lipid profile including high density lipoproteins (HDL), low density lipoproteins (LDL), total cholesterol (TC) and triglycerides (TG). Patients were labelled as dyslipidemic if there were  $\geq 1$  abnormal serum lipid abnormalities i.e. cholesterol ( $>150$  mg/l), triglycerides ( $>150$  mg/dl), HDL ( $<40$  mg/dl), LDL ( $>100$  mg/dl) and VLDL ( $>32$  mg/dl).

All data were analyzed by SPSS-20. Quantitative variables like age, cholesterol, triglyceride, HDL, LDL and VLDL were presented as mean $\pm$ SD. Qualitative variables like, gender and pattern of dyslipidemia were calculated as frequency and percentage. Data were stratified for age  $<$  or  $\geq 55$  year, gender, duration of disease (6-12 months, 12-24 months and  $> 24$  months). Chi-square test was applied for comparison of stratified variables for dyslipidemia.  $P$  value  $< 0.05$  was considered as significant.

## RESULTS

One hundred and fifty patients were included in our study sample with mean age of  $54.51 \pm 3.052$  years and age range from 44 to 60 years (Table 1). 85 (56.7%) patients were less than 55 years of age while rest (43.3%)  $\geq 55$  years of age. 60(40%) patients were male and 90 (60%) were females, with M:F of 1:1.5. 48 patients (32%) had dyslipidemia (Table 2). In 102 (68%) patients, duration of dyslipidemia was 6 to 12 months, in 28 (18.7%) it was 13 to 24 months and in remaining 20 (13.3%) patients it was above 24 months (Table 1). 114 patients (76%) were currently on treatment (Table 2). To determine the frequency of dyslipidemia among gender (20 male and 28 female patients), we stratified data, but there was insignificant difference ( $p=0.775$ ). Among 48 dyslipidemia patients 43 were treated and 5 were not treated. Results were again non-significant [ $p=0.008$ ] (Table 2). When we cross tabulated age groups with dyslipidemia, results were insignificant ( $p=0.332$ ). Out of 48 dyslipidemia patients, 25 were less than 55 year while 23 were more than 55 years of age. When we cross tabulated duration of disease with dyslipidemia, results were significant ( $p=0.001$ ). Among 48 dyslipidemia patients 28 had duration of 13 to 24 month and 20 had 24 month duration. However no patient of dyslipidemia had duration of 6 to 12 months.

**Table No.1: Demographic and clinical data of patients (n=150).**

| Variable                            | No. | %age |
|-------------------------------------|-----|------|
| <b>Age (years)</b>                  |     |      |
| < 55                                | 85  | 56.7 |
| $\geq 55$                           | 65  | 43.3 |
| <b>Sex</b>                          |     |      |
| Male                                | 60  | 40.0 |
| Female                              | 90  | 60.0 |
| <b>Duration of disease (months)</b> |     |      |
| 6-12                                | 102 | 68.0 |
| 13-24                               | 28  | 18.7 |
| > 24                                | 20  | 13.3 |
| <b>Treatment</b>                    |     |      |
| Under treatment                     | 114 | 76.0 |
| No treatment                        | 36  | 24.0 |
| <b>Dyslipidemia</b>                 |     |      |
| Present                             | 48  | 32.0 |
| Absent                              | 102 | 68.0 |

**Table No.2: Stratification of dyslipidemia, according to age, sex, treatment and duration of disease (n=150).**

| Variable                     | Dyslipidemia |     | P value* |
|------------------------------|--------------|-----|----------|
|                              | Yes          | No  |          |
| Age (year)                   |              |     |          |
| < 55                         | 25           | 60  | 0.43     |
| ≥ 55                         | 23           | 42  |          |
| Gender                       |              |     |          |
| Male                         | 20           | 40  | 0.77     |
| Female                       | 28           | 62  |          |
| Treatment                    |              |     |          |
| Under treatment              | 5            | 31  | 0.008    |
| No treatment                 | 43           | 71  |          |
| Duration of disease (months) |              |     |          |
| 6-12                         | 0            | 102 | 0.001    |
| 13-24                        | 28           | 0   |          |
| > 24                         | 20           | 0   |          |

\* determined by  $X^2$  test.

## DISCUSSION

Patients with rheumatoid arthritis (RA) have an increased risk of cardiovascular disease that may not always be related to the presence of traditional cardiovascular risk factors. In the general population, dyslipidemia has been found to be one of the strongest predictors of CVD, with elevated levels of low-density lipoproteins (LDL) constituting the primary treatment target according to various guidelines.

In our study, 48 (32%) patients had dyslipidemia. This figure is lower than the previously reported data. A study from Spain by Batun-Garrido et al<sup>9</sup> reported

dyslipidemia in 54.9% of patients. Dyslipidemia was frequent in 51-60 year age group, type 1 obesity, positive cyclic citrullinated antipeptide antibodies and positive rheumatoid factor, ESR >13mm/hr and CRP >2mg/l. A negative correlation was seen with lower rate of disease activity and treatment with hydroxychloroquine. Chavan et al<sup>10</sup> also reported increased serum cholesterol and decreased HDL along with reduced serum magnesium level and raised uric acid levels. In the study by Nisar et al<sup>8</sup> 54% of patients of RA had dyslipidemia in the form of deranged total cholesterol levels and low HDL levels. Another study from Tunis by Hassen Zrour et al<sup>11</sup> studied 92 patients with active RA and 82 healthy subjects for lipid profile analysis. They reported a higher prevalence of associated dyslipidaemia 95.7% in RA patients versus 65.9% in control,  $p < 0.001$ ).

Reported pattern of lipids in RA patients has been quite conflicting in different studies. Some studies described similar,<sup>12</sup> higher<sup>13</sup> or lower<sup>14</sup> levels of total cholesterol (TC) while others reported increased levels of TC and LDL-C in patients with RA.<sup>11</sup> Liao et al.<sup>15</sup> compared 16,085 RA patients with 48,499 non-RA controls. They found that the relationship between LDL cholesterol levels, HDL cholesterol levels and risk of cardiovascular events was nonlinear and similar between RA patients and non-RA control.

When we cross tabulated age groups with dyslipidemia. Out of 48 dyslipidemia patients, 25 were less than 55 year while 23 were more than 55 years of age i.e. results were non-significant ( $p = 0.332$ ). It shows that age of the patients in RA has no bearing on the presence of dyslipidemia. In our study sample 60 patients (40%) were male and remaining 90 patients (60%) were females. It implies that females are at more risk of developing this disease. Stratification of the data revealed that there is no effect of gender on the presence of dyslipidemia.

When we cross tabulated duration of disease with dyslipidemia, results were significant ( $p = 0.001$ ). Among 48 dyslipidemia patients 28 were having duration 13 to 24 month and 20 were above 24 month duration however no patient of dyslipidemia was in duration of 6 to 12 months. This implies that longer the duration of disease, higher the chances of dyslipidemia and risk of cardiovascular diseases. Another parameter which we assessed in our study was treatment of the disease. Our results showed that patients under treatment had less chances of dyslipidemia. Similar findings have been reported previously.<sup>16,17</sup> Disease modifying agents used in the treatment of RA like hydroxychloroquine and methotrexate have anti-atherogenic effect whereas the impact of biologicals on lipid levels is variable.<sup>16,17</sup>

Limitations of the present study were that we did not use healthy controls and did not measure the effect of lipid levels in relation to different treatments. We

suggest analysis of lipid profile should be stratified by the presence of the use of corticosteroids, nonsteroidal antiinflammatory drugs, selective cyclo-oxygenase 2 inhibitors etc. in some prospective studies.

## CONCLUSION

It is concluded that frequency of dyslipidemia is quite high (32%) in our population presenting with rheumatoid arthritis. It is not associated with gender, younger age and being on treatment. It is associated with duration of disease.

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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