**PREVALENCE OF DYSLIPIDEMIA AND ITS ASSOCIATION WITH DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SULAIMANI GOVERNORATE**

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**ABSTRACT**

**Objectives:** Rheumatoid arthritis is a systemic inflammatory disease characterized by chronic and erosive polyarthritis, affecting from 0.5-1% of the general population. Dyslipidemia is a quite important problem in Rheumatoid arthritis (RA) patient, which causes morbidity and mortality. Objectives are to measure prevalence of dyslipidemia in patients with Rheumatoid Arthritis compared with healthy control peoples and to find out correlations between dyslipidemia and disease activity in patients with Rheumatoid Arthritis.

**Methods:** A total of one hundred patients with RA (80 female and 20 male) were included in the study, they were attending consultation clinic and division of rheumatology in the General Medical Teaching Hospital in Slemani city from (October 2015 to September 2016) who fulfilling the 2010 American College of Rheumatology/European league against Rheumatism classification criteria for RA and one hundred healthy age and sex-matched controls. Fasting lipid profiles of cases and control were estimated after an overnight fast of 12 hours.

**Results:** RA patients showed a higher prevalence of associated dyslipidemia (48%) in comparison to control (4%) p < 0.01. Results showed a significant reduction in serum high density lipoproteins (HDL) p-value less than 0.001, with significant elevation of serum total cholesterol, triglyceride, low density lipoprotein and very low density lipoprotein p-value 0.001, 0.007, 0.01 and 0.5 respectively in comparison to controls. There is a significant association between dyslipidemia and high DAS 28 score (p=0.02).

**Conclusion:** There is a significant association between high ESR of RA patients and dyslipidemia (p=0.001). A significant association was observed between high CRP level and RA patients with no dyslipidemia (p<0.001). Dyslipidemia are frequent among the patients with rheumatoid arthritis and highly associated with active RA. Serum HDL significantly reduced while other parameters of lipid profiles significantly increased in comparisons to control.

**Keywords:** Activity, disease, dyslipidemia, rheumatoid arthritis.

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**INTRODUCTION**

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease characterized by chronic and erosive polyarthritis, associated with persistent inflammatory synovitis, progressive joint destruction, and an excess mortality when compared to the general population. It is characterized by symmetric erosive synovitis. Female are 2.5 times more likely to be affected than male. The onset of disease can occur at any age but peak incidence occurs within fourth and fifth decade of life. Its clinical diagnosis made on the basis of symptoms, physical examinations, X-ray and laboratory investigations. Patients with RA have an increased mortality when compared with age-matched controls, primarily due to cardiovascular disease. This is most marked in those with severe disease, with reduction in expected life span by 8-15 years. Dyslipidemia are being increasingly recognized as an important contributory factor toward the development of cardiovascular disease. Premature cardiovascular disease (CVD) is very common in RA patients. RA is associated with 50% increase in incidence of myocardial infarction (MI) and cardiovascular diseases as compared to general population. It has been observed that increased inflammation and active disease has an impact on lipid patterns in blood. Atherosclerosis is now considered as an inflammatory disease as it is a result of inflammation and...
inflammatory cytokines are prevalent in atherosclerotic plaques\textsuperscript{2,13}. Although dyslipidemia in RA may be partially governed by a genetic predisposition, it is also influenced by an array of other factors including disease activity\textsuperscript{14}, reduced physical activity secondary to pain, disability\textsuperscript{14}, and drug therapy\textsuperscript{15-17}. Dyslipidemia is highly prevalent in RA affecting between 55-65\% of patients\textsuperscript{18,19} and can manifest in RA patients with both early\textsuperscript{20} and advanced disease\textsuperscript{21}. The Disease Activity Score 28 (DAS28) is a major scoring system for evaluating disease activity of RA. In clinical practice CRP and ESR are used in monitoring disease activity and response to the treatment CRP\textsuperscript{22}.

\section*{PATIENTS AND METHODS}

\subsection*{Study design and setting:} A prospective case control was done. This study was conducted at Rheumatology Unit, outpatient clinic in Sulaimani Teaching Hospital, Sulaimani city. The study was carried out over 12 months from October 2015 to September 2016.

\subsection*{Sampling}
This study included one hundred patients with RA (80 female and 20 male) fulfilling the 2010 American College of Rheumatology/European league against Rheumatism classification criteria for RA and one hundred healthy sex and age-matched controls patients and controls age were between 20-70 years old.

\subsection*{Exclusion criteria}
History of smoking or patients suffering from condition that affect the lipid profile such as diabetes mellitus, hypertension, ischemic heart disease, renal impairment, liver and thyroid functional abnormalities, cushing syndrome and obesity (BMI >30) were excluded. Also any patients received medications affecting lipid metabolism such as beta blocker, diuretics, cyclosporine, oral contraceptive pills (OCP), patients who received oral or intra-articular steroid till one month before study and pregnant women were excluded.

\subsection*{The study protocol}
The study protocol includes :- (Questionnaire, clinical examination of RA patients, disease Activity Score (DAS 28), Laboratory investigations) -Laboratory investigations include: (ESR),(RFT), (LFT), (TSH), (FBS or RBS), (ECG), lipid profile, immunological tests, (CRP), (ACCP). The Body Mass Index (BMI) was also measured for all patients

\subsection*{Questionnaire}
A protocol was designed to obtain data about the name, age, occupation, residence of the patients, weight, height, and drug history, duration of the disease, history of chronic disease, and history of smoking, number of tender and swollen joints. The results of investigations (RF, ESR, CRP, lipid profile, RFT, LFT, TFT, and ACCP) were recorded on the same questionnaire.

\subsection*{Statistical analyses:}
All patients’ data entered using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 17 was used. Descriptive statistics presented as (mean\pm standard deviation) and frequencies as percentages. Kolmogorov Smirnov analysis verified the normality of the data set. Multiple contingency tables conducted and appropriate statistical tests performed, Chi-square used for categorical variables and Fishers exact test was used when more than 20\% of the cells less than 5. In all statistical analysis, level of significance (p value) set at \textless{}0.05 and the result presented as tables and/or graphs. Statistical analysis of the study was done by the community medicine specialist.

\begin{table}
\centering
\caption{Distribution of RA patients’ lipid profile according to gender.}
\begin{tabular}{|c|c|c|c|}
\hline
Variable & Male & Female & \chi^2 & P \\
\hline
Dyslipidemia & 0.04 & 0.8 \\
Yes & 10 & 50 & 38 & 47.5 \\
No & 10 & 50 & 42 & 52.5 \\
\hline
\end{tabular}
\end{table}

\section*{RESULTS}
A total 100 rheumatoid arthritis (RA) patients were included in present study with mean age of as 57\±8.6 years, 36\% of them were 50-59 years age. Females were more than males with female to male ratio as 4:1. Disease duration distribution of RA patients RA disease duration of studied patients, 52\% of them had disease duration of more than 5 years.

\begin{figure}
\centering
\caption{Age distribution of RA patients.}
\end{figure}

Mean cholesterol level of RA patients was 174.5\±42.8 mg/dl, 27\% of them had high cholesterol level. Mean triglycerides level of RA patients was 132.1\±56.4 mg/dl, 37\% of RA patients had high Tg level. Mean LDL level of RA patients was 101.9\±39.5 mg/dl, 18\% of RA patients had high LDL level. Mean VLDL level of RA patients was 29.8\±14.8 mg/dl, 38\% of RA patients had high VLDL level. Mean HDL level of RA patients was 55\±18.6 mg/dl, 38\% of RA patients had low HDL level.

\begin{figure}
\centering
\caption{Gender distribution of RA patients}
\end{figure}

Dyslipidemia was detected among 48\% of RA patients. Mean DAS 28 score of RA patients was 5.3\±1.9, 46\% of RA patients had moderate score and 35\% of RA patients had high score. There was a significant association between high cholesterol level and RA...
cases (p=0.001). High triglycerides level was significantly higher among RA patients (p=0.007). A significant association was observed between high LDL level and RA cases (p=0.01). A significant differences were observed between RA cases and controls regarding VLDL level (p=0.5). Low HDL level was significantly higher among RA cases (p<0.001). Generally, Dyslipidemia was significantly higher among RA patients (p<0.001). No significant differences were observed between male and female RA cases regarding lipid profile. There was a significant association between dyslipidemia and high DAS 28 score (p=0.02). There was a significant association between high ESR of RA patients and dyslipidemia (p=0.001). A significant association was observed between high CRP level and RA patients with no dyslipidemia (p<0.001).

Table 2: Distribution of RA patients' ESR and CRP according to dyslipidemia of RA patients.

| Variables | Dyslipidemia | No Dyslipidemia | X² | P  |
|-----------|--------------|-----------------|----|----|
| ESR       | No. %        | No. %           |    |    |
| Normal    | 5 10.4       | 20 38.5         | 10.4| 0.001|
| High      | 43 89.6      | 32 61.5         |    |    |
| CRP       |              |                 |    |    |
| Positive  | 15 47.9      | 48 77.0         | 39.9| <0.001|
| Negative  | 33 52.1      | 4 23.0          |    |    |

DISCUSSION

Several pieces of evidence indicate that rheumatoid arthritis (RA) is a proatherogenic disease associated with increased cardiovascular (CV) mortality, which account for about half of all deaths in these patients.

Patients with rheumatoid arthritis (RA) have higher rates of morbidity and mortality than the general population, which is highly attributed to an increased risk of cardiovascular disease (CVD) among RA patients. The increased risk of CVD appears to be linked to coronary atherosclerosis and may be directly caused by chronic inflammation or secondarily caused by physical inactivity and drugs used to treat RA. In this study, we found that patients diagnosed with RA had significantly reduced levels of HDL-cholesterol in comparison to control groups and this was matched with many other studies done in all of Pakistan by Nisar A et al., Tunisia by Zour SH et al., Malaysia by Manjunatha Goud BK et al., South India by Vinapamula KS et al., Saudi Arabia
Figure 6: Dyslipidemia distribution of RA patients.

Current study revealed a significantly higher cholesterol level of RA patients in comparison to controls (p=0.001). This is consistent with Attar study in Saudi Arabia. In present study, blood levels of triglycerides and LDL cholesterol of RA patients were significantly higher than healthy controls with significantly lower HDL cholesterol level. These findings are similar to results of previous Spanish study done by Gonzalez Gay MA et al. Regarding HDL-cholesterol, it has been reported that patients with active RA consistently demonstrate reduced levels. Also in current study Serum VLDL level of RA patients was significantly higher than healthy controls. This finding coincides with Al-Kaisi et al., study in Jordan, reported high VLDL prevalence among RA patients but inconsistently with our results, Al-Chetachi and Shaher study in Iraq reported no significant difference in VLDL and Tg levels between RA and healthy controls.

| Variables       | RA Cases | Control | χ²   | P     |
|-----------------|----------|---------|------|-------|
| Cholesterol level |          |         |      |       |
| Normal          | 73       | 90      |      | 9.5   | 0.001 |
| High            | 27       | 10      |      |       |       |
| Tg level        |          |         |      |       |
| Normal          | 63       | 80      | 7.1  | 0.007 |
| High            | 37       | 20      |      |       |       |
| LDL level       |          |         |      |       |
| Normal          | 82       | 93      | 5.3  | 0.01  |
| High            | 18       | 7       |      |       |       |
| VLDL level      |          |         |      |       |
| Normal          | 67       | 73      | 0.2  | 0.05  |
| High            | 33       | 27      |      |       |       |
| HDL level       |          |         |      |       |
| Normal          | 62       | 86      | 14.9 | <0.001|
| Low             | 38       | 14      |      |       |       |
| Dyslipidemia    |          |         |      |       |
| Yes             | 48       | 4       |      | <0.001|
| No              | 52       | 96      |      |       |

In general, dyslipidemia was significantly noted in RA patients in present study (p<0.001). This is consistent with results of Mahdi et al., study in Iraq and Curtis et al., study in USA. In current study, the RA activity (DAS) was significantly high among RA patients with dyslipidemia (p=0.02). This is consistent with results of Georgiadis et al., study in Greece.

Figure 7: Dyslipidemia in RA cases and controls

Current results showed that ESR and CRP levels were significantly higher among RA patients with dyslipidemia. These findings are significant to results of Curtis et al., study in USA. Inflammation is a common denominator in both RA and atherosclerosis. A growing body of evidence supports the involvement of common pro inflammatory cytokines such as macrophage migration inhibitory factor (MIF), interleukin (IL)-1, IL-6, and tumor necrosis factor-alpha (TNF-α)-in the development and progression of both RA and atherosclerosis.

Figure 8: Dyslipidemia distribution in RA disease activity.

CONCLUSION

The prevalence of dyslipidemia among rheumatoid arthritis patients in Sulaimani is high. The blood levels of total cholesterol, triglycerides and LDL cholesterol were higher among RA patients. HDL cholesterol level was lower among RA patients. Dyslipidemia may be a risk factor for rheumatoid arthritis severity and cardiovascular diseases. Obesity is a risk factor for rheumatoid arthritis incidence.

RECOMMENDATIONS

Dyslipidemia among RA patients are common and this increase risk of cardiovascular disease and mortality among RA patients, lipid management including greater use of statin therapy may be appropriate to reduce this. Screening programs for RA patients on lipid profile to predict activity and severity of disease. Cardiovascular screening should be recommended every 6 months to once yearly in Sulaimani city. Encouraging the diet restriction programs and physical activities in schools to prevent the obesity. Further national large sized studies on prevalence and effect of hyperlipidemia on RA patients must be supported.
Additional prospective, long-term studies are needed to comprehensively determine the role of inflammation and the impact of biologics on lipid levels and cardiovascular outcomes in patients with RA.

**CONFLICT OF INTEREST**

No conflict of interest was associated with this work.

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