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RESEARCH ARTICLE

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 it is the most common inflammatory arthritis, 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 RA.
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- value less than 0.001. 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, 0.01and 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.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease characterized by chronic and erosive polyarthritis[1], associated with persistent inflammatory synovitis, progressive joint destruction, and an excess mortality when compared to the general population[2,3]. It is characterized by symmetric erosive synovitis[3]. Female are 2.5 times more likely to be affected than male[4]. The onset of disease can occur at any age but peak incidence occurs within fourth and fifth decade of life[5]. Its clinical diagnosis made on the basis of symptoms, physical examinations, X-ray and laboratory investigations[6]. 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[7]. Dyslipidemia are being increasingly recognized as an important contributory factor toward the development of cardiovascular disease[8]. Premature cardiovascular disease (CVD) is very common in RA patients[9,10]. RA is associated with 50% increase in incidence of myocardial infarction (MI) and cardiovascular diseases as compared to general population[10]. It has been observed that increased inflammation and active disease has an impact on lipid patterns in blood[11].

Atherosclerosis is now considered as an inflammatory disease as it is a result of inflammation and inflammatory cytokines are prevalent in atherosclerotic plaques[12,13]. 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[14], reduced physical activity secondary to pain, disability[14], and drug therapy[15-17]. Dyslipidemia is highly prevalent in RA affecting between 55-65% of patients[18,19] and can manifest in RA patients with both early[20] and advanced disease [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[22].

PATIENTS AND METHODS

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.

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.

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.

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

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.

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±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 ≤0.05 and the result presented as tables and/or graphs. Statistical analysis of the study was done by the community medicine specialist.

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.

Table 1: Distribution of RA patients' lipid profile according to gender.

Variable	Male		Female		X^2	P
	No.	%	No.	%		
Dyslipidemia					0.04	0.8
Yes	10	50	38	47.5		
No	10	50	42	52.5		

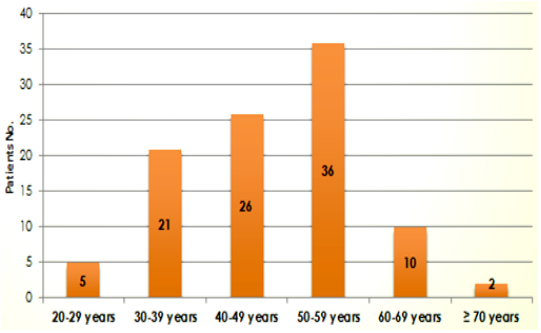

Figure 1: Age distribution of RA patients.

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.

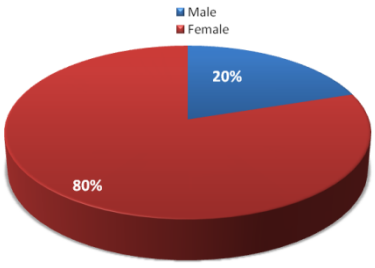

Figure 2: Gender distribution of RA patients.

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		X^2	P
	No.	%	No.	%		
ESR					10.4	0.001
Normal	5	10.4	20	38.5		
High	43	89.6	32	61.5		
CRP					39.9	<0.001
Positive	15	47.9	48	77.0		
Negative	33	52.1	4	23.0		

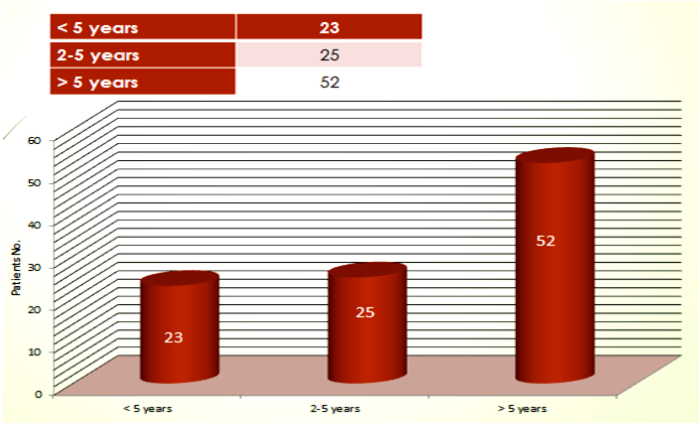

Figure 3: Lipid profile of RA patients.

DISCUSSION

Several pieces of evidence indicate that rheumatoid arthritis (RA) is a proatherogenic disease associated with increased cardiovascular (CV) mortality[23] which account for about half of all deaths in these patients[24].

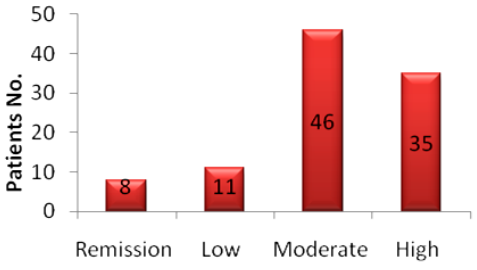

Figure 4: DAS 28 scores distribution of RA patients.

Besides genetic and traditional CV risk factors chronic[25] inflammation has effect in the development of this process[26]. Results showed that RA occurs in all age groups between 20-70 years, which showed that 36% of them between 50 to 59 years and 26% were between 40 to 49 years of age; this is in accordance with other study which mentioned that RA affects usually people above 40 years old[27] and also matched with the study done by Abdul Qahar ZH *et al.*, in Baghdad, Iraq[28]. The prevalence of dyslipidemia among RA patients in present study was 48%. This prevalence is close to results of Haye Salinas MJ *et al.*, in Argentin[29] that reported dyslipidemia prevalence in RA patients as 43%, on other hand, Akiyama *et al.*, study in Japan[30] showed that 56.5% of RA patients had dyslipidemia[31].

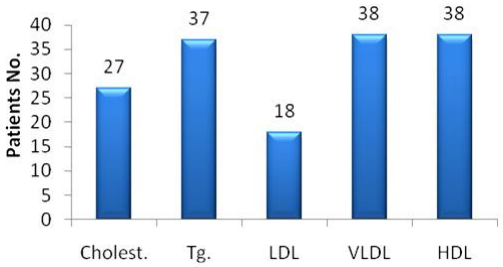

Figure 5: Lipid profile of RA patients.

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[32]. The increased risk of CVD appears to be linked to coronary atherosclerosis[33] and may be directly caused by chronic inflammation or secondarily caused by physical inactivity and drugs used to treat RA[34]. 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 study done in all of Pakistan by Nisar A *et al.*,[35] Tunisia by Zrour SH *et al.*,[36] Malaysia by Manjunatha Goud BK *et al.*,[37] South India by Vinapamula KS *et al.*,[38] Saudi Arabia by Bahlas S *et al.*,[39] Bagdad, Iraq by Ameer KH *et al.*, by Georgiadis AN *et al.*,[40] and United Kingdom[41] which is un favorable profile with regard to cardiovascular risks[42] and there was no study against it.

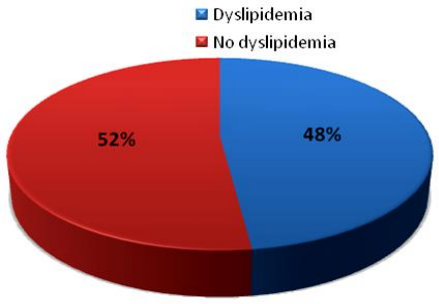

Figure 6: Dyslipidemia distribution of RA patients.

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[43]. In present study, blood levels of triglycerides and LDL cholesterols 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.*,[44]. Regarding HDL-cholesterol, it has been reported that patients with active RA consistently demonstrate reduced levels[45]. Also in current study Serum VLDL level of RA patients was significantly higher than healthy controls. This finding coincides with Al-Kaissi *et al.*, study in Jordan[46] reported high VLDL prevalence among RA patients but inconsistently with our results, Al-Chetachi and Shaher study[47] in Iraq reported no significant difference in VLDL and Tg levels between RA and healthy controls.

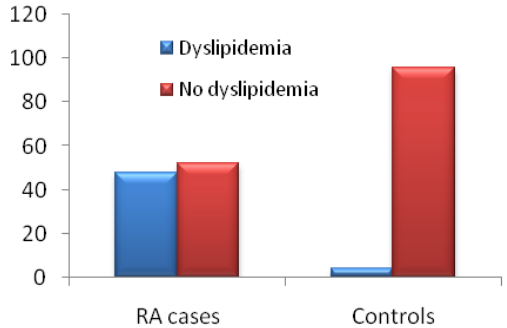

Figure 7: Dyslipidemia in RA cases and controls.

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[48,49]. 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[50].

Table 3: Distribution of lipid profile according to RA cases and controls.

Variables	RA Cases		Control		x^2	P
	No.	%	No.	%		
Cholesterol level					9.5	0.001
Normal	73	73	90	90		
High	27	27	10	10		
Tg level					7.1	0.007
Normal	63	63	80	80		
High	37	37	20	20		
LDL level					5.3	0.01
Normal	82	82	93	93		
High	18	18	7	7		
VLDL level					0.2	0.05
Normal	67	62	73	70		
High	33	38	27	30		
HDL level					14.9	<0.001
Normal	62	62	86	86		
Low	38	38	14	14		
Dyslipidemia						<0.001
Yes	48	62	4	4		
No	52	38	96	96		

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[49]. 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[51].

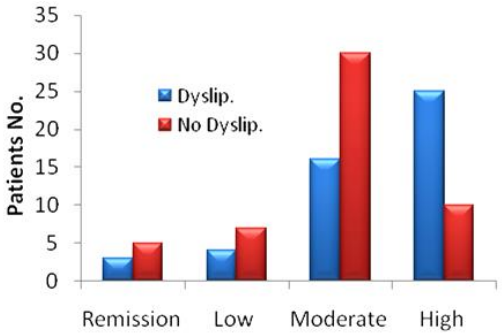

Figure 8: Dyslipidemia distribution in RA disease activity.

CONCLUSIONS AND RECOMMENDATIONS

The prevalence of dyslipidemia among rheumatoid arthritis patients in Sulaimani is high. The blood levels of total cholesterol, triglycerides and LDL cholesterols 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. 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.

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AUTHOR'S CONTRIBUTION

Gharib SM: Writing original draft, review, methodology, data curation, literature survey, editing.

DATA AVAILABILITY

The data supporting the findings of this study are not currently available in a public repository but can be made available upon request to the corresponding author.

CONFLICT OF INTEREST

No conflict of interest was associated with this work.

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