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DYSLIPIDEMIA IN RHEUMATOID ARTHRITIS

Medicine

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ABSTRACT

Introduction:
There is a significantly higher mortality in Rheumatoid arthritis (RA) patients compared to general population, mostly due to cardiovascular diseases (CVD) like myocardial infarction and stroke. Persistent chronic inflammation due to high disease activity taking its toll on the vascular endothelium along with the higher prevalence of traditional cardiovascular risk factors like dyslipidemia is thought to be responsible for the higher CVD-related morbidity. Another contributing factor could be the widespread use of glucocorticoids, which increase carotid intimal thickening. There are only very few studies in Asian population on the prevalence of dyslipidemia in RA and the effect of corticosteroids on the lipid profile in RA patients. Here we describe the lipid abnormalities in RA patients compared to general population and the effect of corticosteroids on their lipid profile.

Methods:
The study was conducted at a Government Medical College in North Kerala, India. RA Patients aged between 16 and 80 years who satisfied the ACR-EULAR 2010 criteria attending the Rheumatology clinic during a period of 1 year were studied in comparison with age and sex matched controls.

Results:
There is statistically significant difference (p value 0.001) in mean total cholesterol level (TC) in the RA group (204.7+42.9 mg/dl) and controls (181.1+40.3 mg/dl). Similar statistically significant difference in the mean LDL cholesterol levels were noted between the RA cases and controls (133.1+39.8 vs 116.7+32 (p value 0.006). However there was no statistically significant alteration in lipid profile that could be attributed to steroid use.

Conclusions:
This study highlights the importance of management of lipid abnormalities in RA patients to improve CVD outcome.

KEYWORDS

Dyslipidemia, Rheumatoid Arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, progressive, inflammatory autoimmune disease with articular, extra-articular and systemic effects. Most of the extra-articular manifestations are due to persistent uncontrolled inflammation. Mortality rates in RA is about twice that of the general population, and is mostly due to premature atherosclerosis-related cardiovascular disease (CVD). Identification and tackling of CVD risk factors will help to reduce mortality in RA. Traditional CVD risk factors (hypertension, smoking, and dyslipidemia) account for about 50% of all coronary heart disease (CHD) events in the general population. Effect of persistent chronic active inflammation on vascular endothelium due to poor disease control as well as the increased burden of traditional CVD risk factors has been attributed to cause higher CVD-related death in RA. Another contributing factor could be glucocorticoids, commonly used in RA which increase the carotid intimal thickening, which is an independent predictor of cardiovascular mortality in RA.

The CV risk factor profile of RA patients has not been studied thoroughly. RA patients have an increased mortality (standardized mortality rate 1.4–3.0) and die on average 2.5 year earlier in community based studies and up to 18 year earlier in hospital based cohorts than the general population. A meta-analysis by Avina-Zubieta and colleagues, which included 14 studies and 41,490 patients with RA, showed a 48% increased risk of CVD compared to general population. Patients with RA in these multiple studies were also noted to have a 68%, 41%, and 87% increase risk of myocardial infarction (MI), cerebrovascular accident (CVA), and CHF, respectively. Patients with RA are more prone to recurrent cardiac events and have higher mortality after acute cardiovascular events[1].

Glucocorticoids are associated with an increase in traditional CV risk factors. Cardiovascular risk (CR) with steroid use in RA is dose dependent as shown in a study by Greenberg *et al*[2] in which prednisone dosages of 1 - 7 mg daily had an CR of 1.78 (95% CI 1.06– 2.96) versus a CR of 2.62 (95% CI 1.29–2.96) for dosages above 7.5 mg/day. Separate multivariable models showed that current daily dose, cumulative duration of use, and total cumulative dose were all associated with a significant increased risk of MI.[3]

Dyslipidemia is an important risk factor for atherosclerotic CHD in the general population. In particular, decreased levels of high density lipoprotein (HDL) cholesterol, elevated levels of low-density lipoprotein (LDL) cholesterol, and/or an elevated total cholesterol (TC) or an elevated LDL: HDL ratio predict increased coronary risk, both in established CHD and patients who were initially free of CHD.[4] Several studies have examined serum lipid levels in RA patients compared to controls.[5] A consistent finding is decreased HDL level in active or untreated RA, which increases cardiovascular risk.[6] HDL levels increase in RA patients after treatment. There is also a favorable shift in the TC/ HDL ratio in treated RA. Statin therapy in RA has efficacy in primary prevention of CVD and improves all-cause mortality as well.[7]

The impact of traditional risk factors on the development of CVD in RA patients is an area of active research. Very few data is available from India regarding conventional cardiovascular risk factors like dyslipidemia in RA. Here we studied the lipid profile abnormalities of RA patients who are under our treatment in relation to age and sex matched controls to determine the CV risk in RA.

Materials and methods

The study was conducted at Government Medical College, Calicut which is the largest tertiary referral hospital in North Kerala, India. RA patients (16 to 80 years) who satisfied the ACR-EULAR 2010 criteria[1] attending the Rheumatology clinic during a 1 year period were studied. Patients with pre-existing CHD were excluded. The study was approved by the Institutional Ethics Committee, and signed informed consent was taken from all patients. There were 75 patients in the study group and 75 age and sex matched controls.

Baseline values of serum lipids including TC, LDL, HDL and serum triglyceride levels (TG) were recorded. The tests were performed using

standard laboratory procedures. Details of the medications including steroids and their dose were recorded.

Patient was considered to have dyslipidemia if TC > 200 mg/dl or HDL-C <40 mg/dl or LDL-C >70 mg/dl. The lower-than-usual cut-off value was used as the revised National Cholesterol Education Program-3 Guidelines recommends an LDL-C ≤70 mg/dl as the cut-off level that should be considered a treatment option for patients at very high-risk for CVD like RA patients.[8]

Results

80% of the 75 patients in the study group and 77% of age and sex matched controls were females. This reflects the female preponderance of the disease in our population.

Table 1 Age distribution of RA patients and controls

Age group (Years)	Controls n(%)	Cases n(%)
<40 years	13 (17.3)	13 (17.3)
40 to 49	25 (33.3)	24 (32.0)
50 to 59	26 (34.7)	25 (33.3)
60 and above	11 (14.7)	13 (17.3)

35% of the RA patients had a disease duration of less than 2 years, while in 33% patients, the duration was between 2-4 years, and in 25% 5-9 years. Only 7% had more than 10 year disease duration.

RA disease activity was assessed using a composite DAS28 score (Disease Activity Score), which included tender joint count, swollen joint count, ESR and patient global assessment of pain.[8] DAS 28 score less than 2.4 indicates clinical remission, 2.4-3.2 indicate mild disease activity, 3.3-5.1 moderate disease activity and more than 5.1 severe disease activity.

56% of our RA patients had mild disease activity while 16% had moderate and 9.3% had severe disease activity. 18.6% patients were in clinical remission.

22.6% of RA patients were not using steroids while 46.6% of the patients were using very low dose steroids <5mg/day (prednisolone or equivalent) and 25.3% were using low dose steroids (5-10 mg/day). Only 5.3% were using more than 10 mg/day.

The mean total cholesterol level (TC) in the RA group was 204.7+42.9 mg/dl and in the control group was 181.1+40.3 mg/dl and the difference is statistically significant with p value 0.001 (Table 2). There is statistically significant difference in the mean LDL cholesterol level between the cases and controls (133.1+39.8 vs 116.7+32 (p value 0.006). The mean values of TG, HDL, VLDL and TC/HDL ratio did not show any significant difference between cases and controls. However there was no statistically significant difference in dyslipidemia in those who took steroids and who did not (Table 3). Also there was no statistically significant relation between DAS28 and elevated TC or LDL (p value 0.092 and 0.819 respectively) (Table 4).

Table 2 Prevalence of dyslipidemia

Lipid profile(mg/dl)	Control		Cases		p value
	Mean	SD	Mean	SD	
Total cholesterol	181.1	40.3	204.7	42.9	0.001
TG	113.3	33.7	118.3	48.3	0.460
HDL	46.8	9.4	45.8	8.5	0.511
LDL	116.7	32.0	133.1	39.8	0.006
VLDL	23.9	9.0	25.5	10.6	0.307
TC/HDL	4.2	0.8	5.5	5.9	0.068

Table 3 Effect of steroid on dyslipidemia

	Steroid	N	Mean	SD	p value
Total cholesterol	Present	49	201.98	46.18	0.447
	Absent	26	209.96	36.17	
LDL	Present	49	129.51	41.00	0.288
	Absent	26	139.85	37.32	

Table 4 Relation between DAS score and Lipid Abnormalities

DAS 28 SCORE	Total Cholesterol < 200mg/dl	Tot Cholesterol > 200mg/dl	LDL Cholesterol >70mg/dl	Tot Cholesterol < 70mg/dl
< 2.4	6	12	17	1
2.4 – 3.2	30	14	41	3
3.2- 5.1	6	5	11	0
> 5.1	1	1	2	0
Total	43	32	71	4
Pearsons Chi-Square	p value 0.092 ; df 3	p value 0.819 ; df 3		

Discussion

In our observational case control study to assess prevalence of dyslipidemia in RA, 75 RA patients were compared with age and sex matched controls. 80% of our patients were female which is consistent with the results of several studies on RA.8

Majority of RA patients (65.3%) were between 40-60 years. The duration of the disease was less than 2 years in 35% and between 2-5 years in 33%. Majority patients (56%) had low disease activity as evidenced by DAS28 score of 2.4-3.2 and 18.6% were in clinical remission while 9.3% had severe disease.

Regarding prevalence of dyslipidemia, it was found that serum TC and LDL cholesterol were significantly higher in RA patients than controls, which might be related to poor life-style and eating habits of RA patients . Two previous studies from India have shown increased prevalence of dyslipidemia in RA similar to our study.[5,6,8] There was no statistically significant difference in dyslipidemia in those who took steroids and who did not. Also there was no statistically significant relation between DAS28 and elevated TC or LDL indicating that dyslipidemia is risk factor independent of disease activity.

Conclusion

1. There is a higher prevalence of dyslipidemia in RA patients compared to normal population which could be contributing to their higher mortality.
2. Neither medications for RA like corticosteroids nor disease activity influenced the prevalence of CV risk factors such as dyslipidemia.

Identification and correction of the traditional CVD risk factors like dyslipidemia in RA is of paramount importance to reduce the excess cardiovascular mortality in RA which is compounded by accelerated atherosclerosis due to chronic inflammation.

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