Assessment of dyslipidemia in patients of rheumatoid arthritis attending a tertiary care centre in kumaon region of Uttrakhand

[1]Dr Makrand Singh, Associate Professor, Department of General Medicine , Government Medical College, Haldwani, Nainital

[2]Dr Tara Singh, Post Graduate, Department of General Medicine , Government Medical College, Haldwani, Nainital

Corresponding Author: Dr Makrand Singh, Associate professor, Department of General Medicine , Government Medical College, Haldwani, Nainital

Abstract

Introduction: Rheumatoid arthritis (RA) is a chronic inflammatory disorder of autoimmune origin that may affect many tissues and organs but principally attacks the joints, producing a non-suppurative proliferative and inflammatory synovitis. 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.

Aims and objectives: To assess dyslipidemia in Rheumatoid Arthritis, to assess the frequency of dyslipidemia in Rheumatoid Arthritis, to correlate dyslipidemia with disease activity in Rheumatoid Arthritis

Materials and methods: This study was hospital based descriptive cross-sectional observational study conducted in the Department of Medicine at Government Medical College and associated Dr. Susheela Tiwari Government Hospital, Haldwani. The total study duration was of two years, from January 2019 to September 2020. The study population of 186 was drawn from patients who presented with rheumatoid arthritis.

Results: Dyslipidemia was present amongst 72.6% of the patients and out of these, majority (89.6%) were females. The difference of dyslipidemia in males and females was found to be significant as p-value was <0.05. Regarding lipid profile, mean TC of the patients was 172.68 with SD of 29.94, LDL (90.24±25.14), TG (106.49±33.91) and HDL (38.69±7.73). Dyslipidemia, TC>200 was present in 14.0%, LDL>130 (5.9%), TG>150 (14.0%), HDL<40 (73.7%), and TC/HDL >6 was in 10.2% of the patients. Regarding disease activity, majority (34.9%) of the patients were in remission phase, moderate (26.3%), low and active phase was seen in 19.4% of the patients. Disease activity score (DAS28) and TC, LDL, TG and HDL, all were positively correlated but it was not significant (p-value>0.05).

Conclusion: Dyslipidemia is common among RA patients. This may be considered as a secondary impact of the chronic inflammatory state seen in RA.

Keywords: dyslipidemia, rheumatoid arthritis

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disorder of autoimmune origin that may affect many tissues and organs but principally attacks the joints, producing a non-suppurative proliferative and inflammatory synovitis.

Dyslipidemia is being increasingly recognized as an important contributory factor towards the development of cardiovascular disease.[1] Premature cardiovascular disease (CVD) is very common in RA patients. [2,3] RA is associated with 50% increase in the incidence of myocardial infarction (MI) and cardiovascular diseases as compared to the general population.[1] It has been observed that increased inflammation and active disease have an impact on the lipid patterns in blood.[4] 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[5], reduced physical activity secondary to pain, disability [4], and drug therapy.[4,5] Dyslipidemia is highly prevalent in RA affecting between 55-65% of patients[1,2] and can manifest in RA patients with both early and advanced disease.[2,3]

Materials and methods

This study was hospital based descriptive cross-sectional observational study conducted in the Department of Medicine at Government Medical College[GMC] and associated Dr. Susheela Tiwari Government Hospital, Haldwani. The total study duration was of two years, from January 2019 to September 2020. The study population of 186 was drawn from patients who presented with rheumatoid arthritis in the above mentioned institute. All patients of ≥ 15 years had rheumatoid arthritis according to the ACR criteria and given consent for the study were included. Patients with non-inflammatory conditions, patients already on drugs that affect lipid parameters like statins, fibrates, ezetimibe, colesevelam, obese patients with BMI more than 30, patients with DM, hypertension, thyroid disorders, cardiovascular diseases, family history of dyslipidemia were excluded from the study.

An interview was conducted for detailed history from patients and their attendants, demographic characteristic of patient such as age, gender and area were assessed along with full clinical examination and detail laboratory investigations. RA was diagnosed according to set ACR criteria. Lipid profile including high density lipoproteins (HDL), low density lipoproteins (LDL), total cholesterol (TC) and triglycerides (TG) was estimated after an overnight fasting of 12 hours in a fully automated Roche Diagnostics Cobas c501 analyzer using enzymatic assays. Disease activity was classified according to clinical assessment, laboratory tests and disease activity scores.

Hematological evaluation to assess haemoglobin, total leucocyte count, differential leucocyte count, packed cell volume, platelets count, reticulocyte count, and ESR. biochemical examination for serum creatinine, blood urea, serum bilirubin, serum liver enzymes, serum uric acid, total cholesterol, triglycerides, HDL, LDL, VLDL, LP(a), Apo B, T3, T4, TSH, Fasting blood sugar, Rheumatoid Factor, ANA, dsDNA, Anti-CCP, CRP, urine –routine/microscopy, X –ray chest, X-ray bilateral hands and wrists, electrocardiography, ultrasound abdomen (kidney ureter bladder) as per requirement of the case. Statistical analysis: Collected data were coded appropriately, entered in Microsoft

Excel (MS Excel) spreadsheet, and later cleaned for any possible errors in SPSS (Statistical Package for Social Studies) for Windows version.16.0. Analysis was also carried out using SPSS. Categorical data is presented as percentage (%). Pearson's chi square test and Fisher's exact test has been used to evaluate differences between groups for categorized variables. The descriptive analysis of data is presented in graphs, percentages etc. All tests were performed at a 5% level of significance; thus, an association was significant if the p value was less than 0.05.

Results:

The study population of 186 was drawn from patients who presented with RA in Department of Medicine at Government Medical College and associated Dr. S.T.M.Govt Hospital, Haldwani. Majority of the patients 54(29%) were from age range 46-55, followed by 47 (25.3%) in 36-45, 45 (24%) in 56-65, 24 (12.9%) in 26-35 and 11 >= 66 yrs.

Out of total 160 (86%) were female and 26 (14%) were male. Majority i.e. 148 were hindu. 182 (97.8%) were married. 66 were each Illiterate and educated till middle school. 30 were each graduated and above and educated till primary school. Most of the patients were privately employed. 19(10.2%) were involved in smoking and 16(8.6%) were involved in alcohol.

As per compliance to DMARDs 46.2% had complaint. 56, were naïve, 23 were irregular, 18 were defaulter and 3 were refractory.

Distribution of patients according to limb deformities Ulnar drift in 67 (36.0%), Boutonniere's deformity in 24 (12.9%), Swan Neck deformity in 23(12.4%), Z-thumb deformity in 16(8.6%), Bunion in 18 (9.7), Spondylolisthesis in 1(0.5%), Secondary Osteo-arthritis Knee 22(11.8%) and Others in 1(0.5%).

Majority of the patients had anaemia as extraarticular manifestations 50(30.6%). Most of the female patients were infected with RA. Out of those majority had dyslipidemia 89.6%.

Table 1: Distribution of patients according to lipid profile

Lipid Profile	Mean	Standard Deviation(SD)
Total Cholesterol (TC)	172.683	29.9461
LDL	90.2391	25.13601
Triglycerides (TG)	106.49	33.914
HDL	38.694	7.7311

Mean ± Standard Deviation (SD) of Total Cholesterol (TC) was 172.683±29.9461, LDL 90.2391±25.13601, Triglycerides (TG) in 106.49±33.914, HDL in 38.694±7.7311.

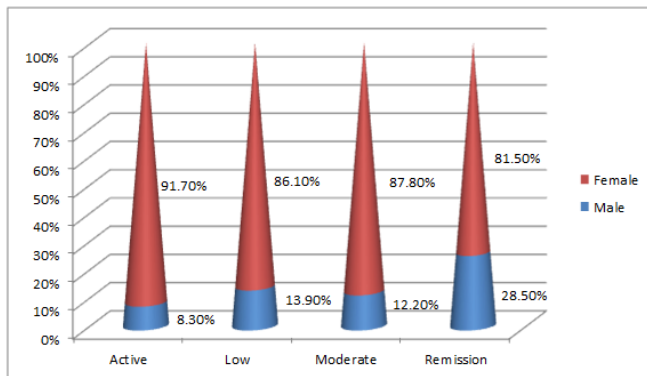Table 2: Distribution of patients according to type of lipid disorder (N=186)

Type of Lipid disorder		Number (n)	Percent
Total Cholesterol (TC)	>200	26	14.0
LDL	>130	11	5.9
Triglycerides (TG)	>150	26	14.0
HDL	<40	137	73.7
TC/HDL	>6	19	10.2

In majority of cases HDL was <40 in 137 (73.7%), Total cholesterol (TC) was more than >200 in 26(14%) patients, LDL was more than 130 in 11(5.9%), TG >150 in 26(14%), and TC/HDL was >6 in 19(10.2%)

Table 3: Distribution of patients according to disease activity (N=186)

Disease activity	Male	Female	Total N (%)
Active	3(8.3%)	33(91.7%)	36(19.4)
Low	5(13.9%)	31(86.1%)	36(19.4)
Moderate	6(12.2%)	43(87.8%)	49(26.3)
Remission	12(18.5%)	53(81.5%)	65(34.9)

Disease activity was more in female than male patients, in most of the patients remission was observed i.e. 65(34.9%).

Distribution of patients according to disease activity

Table 4: Distribution of patients according to Haematological profile (N=186)

Haematological profile	Mean	Standard Deviation (SD)	Minimum	Maximum
Hb (gm/dl)	11.4	1.7390	6.0	15.1
ESR(mm/hr)	27.7	17.0010	4.0	124.0
TLC	8846.075	3254.3566	790.0	30600.0
C-reactive Protein	29.71	35.659	Negative	320.0

Mean ± sd of TLC was 8846.075±3254.3566 with range (790-30600)

Table 5: Distribution of patients according to Serological profile (N=186)

Serological profile		Number (n)	%
Rheumatoid Factor (n=186)	Positive	157	84.4
Anti-citrullinated peptide Antigen(n=20)	Positive	19	95.0

Table 6: Correlation of various lipid disorders with disease activity score (DAS28)
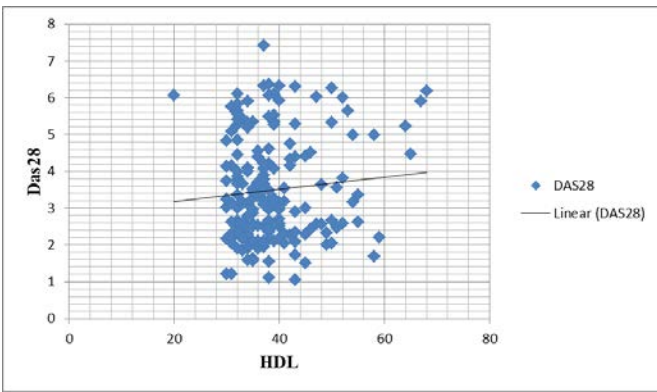
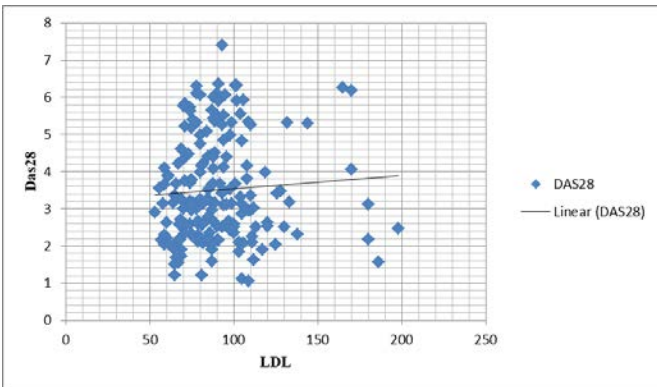|	r**	p-value
TC	0.153	0.037*
LDL	0.063	0.392
HDL	0.091	0.215
TG	0.018	0.813
TC/HDL	0.068	0.355
r** = Karl Pearson correlation coefficient *= significant		
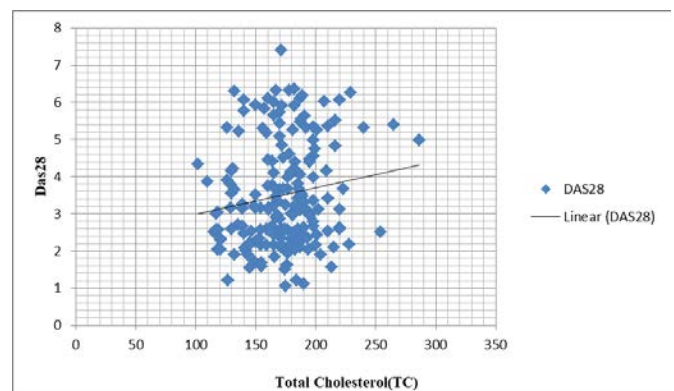
P - Value was significant for total cholesterol.
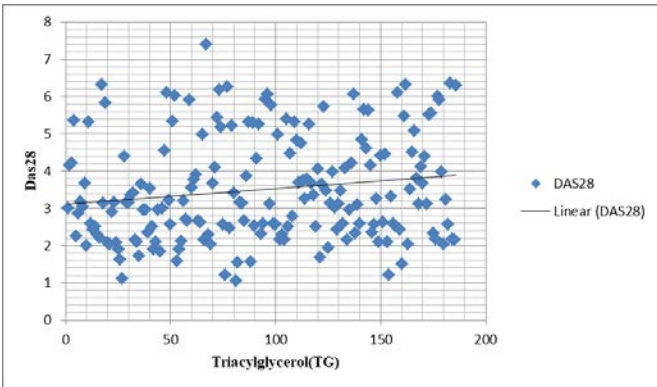
Correlation of total cholesterol with DAS28

Correlation of HDL with DAS28

Correlation of LDL with DAS28

Correlation of Triacylglycerol (TG) with DAS28

Table 7: Association of various lipid disorders with disease activity

Type of Lipid Disorder	Disease activity		P - value*
	Active (n=36)	Others (n= 150)	
TC>=200	8(30.8%)	18(69.2%)	0.112
LDL>=130	4(33.3%)	8(66.7%)	0.251
HDL<40	24(18.9%)	103(81.1%)	0.817
TG>=150	6(23.1%)	20(76.9%)	0.604
TC/HDL	5(20.8%)	19(79.2%)	0.844
*Chi square test, Fisher's exact test			

P - value was not significant between active and others.

Discussion

Lipid metabolism is a complex process, especially when associated with chronic inflammatory states; therefore, in many autoimmune diseases, lipid abnormalities are frequently seen. This study was designed to observe the pattern of abnormal lipid profile in relation to the chronic inflammatory state seen in RA patients and to correlate it with disease activity.

Of all patients in our study 135 (72.6%) had dyslipidemia. The mean total cholesterol in our study was 172.683±29.95, 14% of them had high cholesterol (>200mg/dl), mean LDL was 90.23±25.14, 5.9% had high LDL (>130mg/dl), mean triglyceride level was 106.49, 26% had high TG (>150mg/dl) and mean HDL among RA patients was 38.69, 73.7% had low HDL (40mg/dl). High TC/HDL ratio was seen amongst 10.2% patients.

According to Gharib et al [6], Dyslipidemia was detected among 48% of RA patients which is less in comparison to our findings. 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 HDL level of RA patients was 55±18.6 mg/dl, 38% of RA patients had low HDL level.

In a study conducted by Uzma erum et al [7], 107 (53.5%) patients had dyslipidemia. The mean values for total cholesterol, HDL and LDL were 169.68±36.68

mg/dL, 40.02±10.23 mg/ dL, and 93.29±26.17 mg/dL respectively. Of all patients, 83 patients (41.5%) had low HDL; 16 (8%) had high TC, whereas, 8 (4%) patients had combination of low HDL with high LDL and high TC.

According to Yadav et al [8], the serum total cholesterol (TC) in cases was 150.86± 12.18 mg/dl, HDL cholesterol in cases was 41.7±7.20 mg/dl, LDL cholesterol was 82.00 ± 13.36 and Triglycerides were 133.01 ± 27.33. According to Toosi et al [9], mean serum HDL, LDL, Total Cholesterol, and TG were 52.76±13.8, 96.65±21.6, 177.26±38.9, and 128.04±33.9, respectively.

In our study mean Disease Activity Score (DAS 28) was 3.49± 1.40, 19.4% of RA patients had high disease activity, 26.3% had moderate activity and 34.9% patients were in remission phase. According to Gharib et al [6] 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. Yadav et al [8] found, of the 50 cases of rheumatoid arthritis, 13 cases were in remission and 37 cases had active disease according to the disease activity score (DAS 28 ESR). According to Toosi et al [9] prevalence of patients in remission phase, low, moderate, and high disease activity were 48 (32%), 24 (16%), 74 (49.3%), and 4 (2.7%), respectively.

In our study a positive correlation was found between disease activity and TC, LDL cholesterol, HDL, TG and TC/HDL ratio with Karl Pearsons's Correlation coefficient of 0.153, 0.063, 0.091, 0.018 and 0.068 respectively but the correlation was significant only with TC (p value<0.037). A study conducted by Joshi et al found positive correlation of DAS-28 (ESR) with total cholesterol and LDL levels in female patients only

[10]. No correlation of HDL, LDL and triglyceride were observed with DAS- 28 (ESR) in both male and female patients. Yadav et al [8] observed a significant negative correlation is seen between HDL and DAS28 in patients with rheumatoid arthritis. For total cholesterol, negative correlation is seen, though not significant which is in contrast to our findings. Mullick et al (2014) [11] found a significant inverse correlation between HDL-C and DAS28 (r = -0.35, p<0.01).

In our study, the mean serum level of Total Cholesterol amongst active (DAS28>2.6) and remission phase was 176.29±30.16 and 167.83±29.16 respectively but the t test for independent samples did not reveal it to be significant (p value>0.05). Similarly mean LDL, HDL, TG, TC/HDL ratio were almost similar in both active and remission phase patients and the difference was also not significant. According to Yadav et al [8] the mean serum level of total cholesterol in active cases was 148.70 ± 11.42 mg/dl and in remission was 157.0± 12.61 mg/dl. T-test revealed significant difference in between the two groups showing that the total cholesterol in active cases was lower in comparison to cases in remission (p<0.05). HDL level in cases in remission was 46.73±7.48 mg/dl and 39.92±6.28 mg/dl in active cases, thus signifying that HDL in active cases was low compared to those in remission. The difference was highly significant (p<0.01).

Conclusion

In our study of dyslipidemic patients with RA.. Disease activity score (DAS28) and TC, LDL, TG and HDL, all were positively correlated but it was not significant (p-value>0.05). Further, the mean serum level of total cholesterol was slightly greater in active cases than in cases in remission but the difference was not

significant. So to conclude, dyslipidemia is common among RA patients. This may be considered as a secondary impact of the chronic inflammatory state seen in RA and further detailed studies are required for assessments and therapeutic strategies regarding the same.

References

1. Avina-Zubieta JA, Thomas J, Sadatsafavi M, Lehman AJ, Lacaille D. Risk of incident cardiovascular events in patients with rheumatoid arthritis: a meta-analysis of observational studies. Ann Rheum Dis. 2012;71(9):1524-1529.

2. Haye-Salinas MJ, Bertoli AM, Lema L, Saucedo C, Rosa J, Quintana R, et al. Prevalence of dyslipidemia and elevated cardiovascular risk in patients with rheumatoid arthritis. Medicina (B Aires). 2013;73(1):26-30.

3. Choy E, Ganeshalingam K, Semb AG, Szekanecz Z, Nurmohamed M. Cardiovascular risk in rheumatoid arthritis: recent advances in the understanding of the pivotal role of inflammation, risk predictors and the impact of treatment. J Rheumatol 2014; 53(12): 2143-2154.

4. Gabriel SE, Crowson CS. Risk factors for cardiovascular disease in rheumatoid arthritis. Curr Opin Rheumatol.2012;24(2):171-176.

5. Boyer JF, Gourraud PA, Cantagrel A, Davignon JL,Constantin A. Traditional cardiovascular risk factors in rheumatoid arthritis: a meta-analysis. Joint Bone Spine. 2011;78(2):179-183.

6. Gharib SM. Prevalence of dyslipidemia and its association with disease activity in patients with rheumatoid arthritis in Sulaimani Governorate, Universal Journal of Pharmaceutical Research 2016; 1(2): 19-24.

7. Erum U, Ahsan T, Khowaja D. Lipid abnormalities in patients with Rheumatoid Arthritis. Pak J Med Sci. 2017;33(1):227-230.

8. Sushma Yadav, R. K. Goswami and Girindra Kumar Bora. (2018); Correlative Study Between Lipid Profile And Disease Activity In Patients With Rheumatoid Arthritis- A Hospital Based Study. Int. J. of Adv. Res. 6 (Apr). 625-632.

9. Toosi TD, Rostamiyan A, Moharrami K, Movassaghi S, Nakhjavani M, Norooznezhad AH. Lipid Profile Changes in Rheumatoid Arthritis Patients: Investigation of Different Affecting Factors Acta Medica Iranica, Vol. 56, No. 10 (2018).

10. Joshi P, Prakhar K, Jha RK. Dyslipidemia Pattern in Rheumatoid Arthritis Patients with Correlation of Disease Activity. J Contemp Med 2017; 7(2): 132-137.

11. Mullick OS,Bhattacharya R, Bhattacharyya K, Das A. Lipid profile and its relationship with endothelial dysfunction and disease activity in patients of early Rheumatoid Arthritis March 2014Indian Journal of Rheumatology 9(1)