CORRELATION OF LIPID PARAMETERS AND CARDIOVASCULAR MANIFESTATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS ATTENDING A TERTIARY CARE CENTRE OF NORTH EAST INDIA

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ABSTRACT

BACKGROUND

Rheumatoid Arthritis (RA) is a chronic inflammatory disease of unknown aetiology marked by a symmetric and peripheral polyarthritis, which often results in joint damage and physical disability. Rheumatoid arthritis is not just only a disease affecting joints, but it goes well beyond the barricade of arthritis into systemic inflammatory manifestations. Various factors play an important role in the morbidity and mortality of the disease.

The aim of this study was to investigate the clinical spectrum of rheumatoid arthritis with special reference to dyslipidaemia and cardiovascular manifestations.

MATERIALS AND METHODS

We conducted a hospital-based observational study comprising of 72 patients of rheumatoid arthritis who had been diagnosed, based on criteria laid down by 2010 ACR/EULAR classification criteria, admitted in Gauhati Medical College and Hospital, Guwahati, Assam (India) and fulfilled the inclusion and exclusion criteria. Statistical analysis was performed using GraphPad InStat version 3.00 for Windows 7, GraphPad Software, San Diego, California, USA (www.graphpad.com). P value <0.05 was taken as statistically significant.

RESULTS

In this study, out of 72 patients, 16 patients were male and 56 patients were female, 31.94% cases were in the 5th decade of life followed by the 4th decade (30.56%) with a mean age of 43.63 years. Our study found that the most common derangement of lipid parameter was being attributed to low HDL level (31%) followed by a high triglyceride level (20.83%). The prevalence of dyslipidaemia was 41.67%. Atherogenic index was high in 23.6% of the cases with a mean of 4.52 of borderline range. In this study, ECG abnormalities were present in 12.5% of study subjects, abnormal echocardiography findings were present in 11.11% of patients and abnormal carotid Doppler findings were present in 18%. The most common ECG abnormality was nonspecific ST-T changes, most common echocardiographic abnormality was pericardial effusion, most common abnormal carotid Doppler finding was increased IMT. As a whole, 27.78% patients of the study population was having cardiovascular manifestations. Statistical analysis shows a significant association between dyslipidaemia and disease activity (P<0.05) and with cardiovascular manifestations (P<0.0001).

CONCLUSION

From this study, it was concluded that, Dyslipidaemia is common in RA patients with low HDL-Cholesterol being the commonest abnormality in this part of the country. Overt cardiovascular manifestations in the form of advanced atherosclerosis, Ischaemic Heart Disease, Pericarditis are also commonly encountered in patients with RA.

KEYWORDS

Rheumatoid Arthritis, Dyslipidaemia, Cardiovascular manifestations, DAS 28 score.

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BACKGROUND: Rheumatoid Arthritis (RA) is a chronic inflammatory disease of unknown aetiology marked by a symmetric and peripheral polyarthritis which often results in joint damage and physical disability. The prevalence of Rheumatoid Arthritis (RA) in most populations is around 1%, with an incidence in women twice than that in men. The prevalence in Indian rural population is said to be 0.75% (Malviaya et al 1993).[(1)]

The name "Rheumatoid Arthritis" (Rheuma-Greek for Flowing as a River, Arthron-Greek for Joint) was coined in

1859 by British rheumatologist Dr. Alfred Baring Garrod (Storey GD et al 2009).[2]

The exact cause of rheumatoid arthritis is yet to be ascertained, but the pathological mechanism of synovial inflammation is hypothesised to result from a complex interplay of genetic, immunologic and environmental factors (Mackenzie AR et al 2005).[3]

The diagnosis of rheumatoid arthritis is essentially clinical. The newer classification criteria (ACR/EULAR, 2010) attempts to capture early rheumatoid arthritis. RA being a systemic inflammatory disease may result in a variety of extra-articular manifestations including fatigue, subcutaneous nodules, lung involvement, peripheral neuropathy, pericarditis, vasculitis, haematological abnormalities and dyslipidaemia.

Several investigators have demonstrated dyslipidaemia in RA. The National Cholesterol Education Programme (NCEP) criteria define dyslipidaemia as one or more of the lipid parameter derangement in the form of high Total Cholesterol, high LDL Cholesterol, high Triglyceride or low HDL Cholesterol or taking lipid-lowering therapy (NCEP:ATPIII).

Nurmohamed et al (2003)[4] proposed that dyslipidaemia. In RA appears to be as a consequence of systemic release of inflammatory cytokines such as TNF-α, IL-1, IL-6 leading to a proatherogenic state with insulin resistance, endothelial cell activation and hypercoagulation. Dyslipidaemia in RA is dependent on disease activity, e.g. higher disease activity leads to decreased HDL with increased atherogenic index (Nurmohamed et al 2003).[5]

RA patients have an increased mortality primarily due to cardiovascular diseases, which is most marked in those with severe disease with a reduction in expected lifespan by 8-15 years (Doherty M. Ralston S. H. 2010).[6] A.N. Georgiadis et al (2008)[7] found a significant association of dyslipidaemia with cardiovascular manifestations including association for individual lipid parameters.

This study was conducted at Gauhati Medical College and Hospital with the following Aims and Objectives:

1. To find the prevalence of dyslipidaemia in RA and its correlation with the disease activity.
2. To study the cardiovascular manifestations in patients of RA and to correlate it with dyslipidaemia in this part of the country.

MATERIALS AND METHODS

Study Design: This is a hospital-based observational study.

Study Venue: The study was conducted in the Department of Medicine, Gauhati Medical College and Hospital, Guwahati, Assam, who attended Rheumatology and General Medicine OPD/Ward.

Ethical Clearance: Ethical clearance was obtained from ethical committee of Gauhati Medical College.

Period of Study: The period of study extended from 1st June 2013-31st September 2014.

Study Group: The study sample comprised of 72 adult rheumatoid arthritis patients selected randomly who had attended medicine OPD/Ward and fulfilled the inclusion and exclusion criteria.

Inclusion Criteria:

1. Rheumatoid arthritis patients (Diagnosed as per 2010 ACR:EULAR Classification Criteria).
2. Patients at the age of 18 yrs. or above.
3. Both male and female patients.

Exclusion Criteria:

1. Patients less than 18 yrs. of age.
2. Those subjects taking lipid lowering agents.
3. Patient with Overlap Syndrome or MCTD.
4. Chronic liver disease.
5. Chronic renal failure.
6. Patients who are not willing to give an informed consent.

METHODOLOGY: Detailed clinical history, thorough clinical examination and relevant laboratory investigations were done. The diagnosis of rheumatoid arthritis was made according to the 2010 ACR:EULAR Classification Criteria.

Clinical data comprised of symptom analysis, history of past medical illness (Comorbidities), history of drug intake, thorough examination to identify signs. Disease activity was assessed by using DAS28 Score.

Laboratory data consisted of CBC, FBS, serum creatinine, BUN, AST, ALT, serum uric acid, ESR, CRP, fasting lipid profile, Urine R\E, rheumatoid factor were tested in all patients. Anti-CCP was advised in patients with a negative RF. All patients underwent chest x-ray, joint x-ray of hands and ECG. Ultrasound whole abdomen, Serum ANA, Echocardiography, Carotid Doppler study, HRCT lung were done in selected patients, whenever indicated.

Procedure: Assessment of Disease Activity and Damage: Disease activity of the study subjects was assessed by using DAS28 (Disease Activity Score in 28 joints) severity index.

The DAS28 includes;

- 28 tender joint count.
- 28 swollen joint count.
- Patient's global health assessment.
- Erythrocyte Sedimentation Rate.

1. **Tender Joint Count:** Done by passive joint movement.

2. **Swollen Joint Count:** Swollen Joint Count was assessed by the judgement of fluctuation of joints. ACR tender joint count includes an assessment of 28 joints mentioned above.

3. **Patient's Global Health Assessment:** The patient's overall assessment of how the arthritis is doing. It was assessed according to an acceptable method for determination by asking question from the AIMS (arthritis impact management scale) instrument.
"Considering all the ways your arthritis affects you, mark 'x' on the scale for how well you are doing". From this, patients had given a horizontal visual analogue scale (usually 10).

4. **Acute Phase Reactant Value:** ESR in mm/hr by Westergren's method.

Quantification of Current Disease Activity:
Method of Scoring: The DAS28 score was calculated using a programmed calculator.

Formula for calculating DAS28:
"DAS28 = 0.56 * sqrt (tender28) + 0.28 * sqrt (swollen28) + 0.70 * ln (ESR) + 0.014 * GH"

Score: The range of the DAS28 is 0-9.4.

Interpretation of Scores: The level of RA disease activity was interpreted as scoring of DAS28.

- DAS28 >5.1 = High disease activity.
- DAS28 3.2-5.1 = Moderate disease activity.
- DAS28 <3.2 = Low disease activity.
- DAS28 <2.6 = Remission.

Subjective Assessment of Disease Disability: It was assessed with the help of MHAQ-DI questionnaire. (Modified Health Assessment Questionnaire).

Estimation of Fasting Lipid Profiles: Blood sample was drawn from the patients at least after 9 hours of overnight fasting.

The VITROS CHOL slide method used to estimate lipid levels.

STATISTICAL ANALYSIS: All the statistical graphs were prepared using Microsoft Excel 2007 and Microsoft Word 2007. Statistical analysis was performed using GraphPad InStat version 3.00 for Windows 7, GraphPad Software, San Diego, California, USA (www.graphpad.com). P value <0.05 was taken as statistically significant.

RESULTS AND OBSERVATIONS:

Age group (in years)	18-30	31-40	41 -50	51-60	>60	Total	Mean±SD
No. of patients (N=72) (%age)	10 (13.89%)	22 (30.56%)	23 (31.94%)	12 (16.67%)	5 (8.33%)	72 (100%)	43.63±10.88

Table 1: Age Distribution of the Study Subjects

Table 1 shows that age of the male patients ranged from 35-70 years with a mean age of 48.56 years and a standard deviation of 9.52; in female, the age ranged from 22-65 years with a mean age of 42.48 and a standard deviation of 10.42.

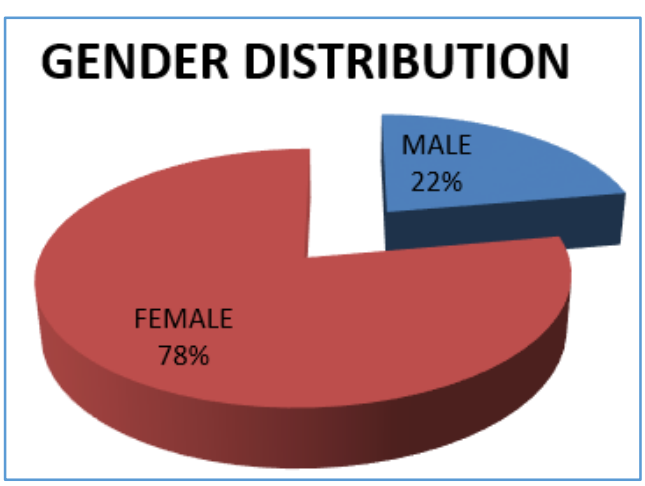

Fig. 1: Sex Distribution of Study Subjects

From figure 1, it is shown that out of total study subjects, 78% patients were female and 22% patients were male with a male-to-female ratio 1:3.5.

Duration of Symptoms (in months)	Male (% age) (N=16)	Female (% age) (N=56)	Total Number (N=72)
<6	2 (12.5%)	12 (21.43%)	14 (19.44%)
6-12	5 (31.25%)	17 (30.36%)	22 (39.28%)
13-24	0 (0%)	4 (7.14%)	4 (5.56%)
25-60	3 (18.75%)	11 (19.64%)	14 (19.44%)
>60	6 (37.5%)	12 (21.42%)	18 (25%)
Mean	40.32 months		72

Table 2: Distribution of Study Subjects as per Duration of Symptoms at Presentation

Table 2 denotes that the mean duration of disease was 40.32 months with a range of 2 to 396 months. Maximum number of patients were in the range of 6-12 months 21 (29.17%) patients and least number of cases 4 (5.56%) were with a duration of symptoms of 13-24 months.

DAS28 Score	Number of Patients (N=72) (% age)	Mean±SD
High Disease activity (>5.1)	32 (44.44%)	5.11±1.57
Moderate Disease Activity (3.2-5.1)	27 (37.5%)	
Low Disease Activity (<3.2)	13 (18.06%)	
Total	**72**	

Table 3: Distribution of DAS28 Scoring amongst Study Subjects

The Table 3 denote DAS28 Scoring. The maximum number of patients 32 (44.44%) were with high disease activity followed by moderate disease activity (37.5%) and (18.06%) were with low disease activity. The mean DAS28 scoring was 5.11 with a standard deviation of 1.57.

Name of Lipid Parameters	Total Cholesterol (mg/dL)		LDL-C (mg/dL)		HDL-C (mg/dL)		TG (mg/dL)	
	Normal (<200)	High (≥200)	Normal (<130)	High (≥130)	Normal (≥40)	Low (<40)	Normal (<150)	High (≥150)
Number	64	8	62	10	50	22	57	15
Percentage (N=72)	88.89%	11.11%	86.12%	13.88%	69.44%	30.56%	79.17%	20.83%
Mean±SD	172.17±37.9		102.48±35.41		43±13.47		135.25±58.34%	

Table 4: Patterns of Dyslipidaemia in Study Subjects

Table 4 show the patterns of dyslipidaemia in the study subjects. The most common was being attributed to a low HDL-C level 22 (31%) followed by a high triglyceride level 15 (21%), then high LDL-C in 10 (14%) and high total cholesterol in 8 (11%) cases. The mean total cholesterol was 172 mg/dL, LDL cholesterol was 102 mg/dL, HDL cholesterol was 43 mg/dL and triglyceride was 135 mg/dL.

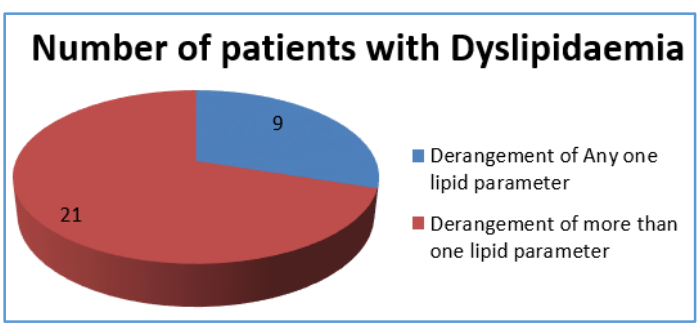

Fig. 2: Pie Chart showing the Number of Study Subjects with Dyslipidaemia

Figure 2 shows that there were 30 patients (41.67%) with dyslipidaemia. Out of them, 9 patients were having derangement of any one lipid parameter and 21 patients were having derangement of more than one lipid parameters.

Atherogenic Index (TC/HDL)	Number of Patients (N=72)	Mean±SD
Normal (<4)	39 (54.17%)	4.52±2.14
Borderline (4-5)	16 (22.22%)	
High (>5)	17 (23.6%)	

Table 5: Analysis of Atherogenic Index in the Study Population

Table 5 show the atherogenic index in the study population. Majority of the patients 39 (54%) were with a normal atherogenic index. Atherogenic index was high in 17 (24%) patients. Mean atherogenic index was 4.52 in the borderline range with a standard deviation of 2.14.

Status of Disease (DAS28)	Dyslipidaemia		Total (N=72)	P Value
	Present (N=30)	Absent (N=42)		
High Disease Activity (>5.1)	21 (70%)	11 (26.2%)	32	0.0011 (Statistically Significant)
Moderate Disease Activity (3.2-5.1)	6 (20%)	21 (50%)	27	
Low Disease Activity (<3.2)	3 (10%)	10 (23.8%)	13	
Total	**30 (100%)**	**42 (100%)**	**72**	

Table 6: Association of Dyslipidaemia with Disease Activity

Table 6 show that maximum no. of patients, 21 (70%) patients with dyslipidaemia were with high disease activity, 6 (20%) patients were with moderate disease activity and least number of dyslipidaemic patients were with low disease activity.

Status of Treatment		Dyslipidaemia	
		Present (N=30)	Absent (N=42)
Naive Patients		13 (43.3%)	10 (23.8%)
Already on Treatment	DMARDs Only (N=13)	3 (10%)	10 (23.8%)
	DMARDs plus Steroids (N=33)	13 (43.3%)	20 (47.6%)
	DMARDs plus Biologics (N=3)	1 (3.33%)	2 (4.8%)

Table 7: Proportion of Dyslipidaemia as per Status of Treatment

Table 7 shows the proportion of dyslipidaemia as per status of treatment. Out of total 30 patients with dyslipidaemia, 17 (56.7%) patients were already on treatment for RA with DMARDs, biologics, steroids either as monotherapy or in combination. 33 patients were on steroid therapy, out of which 13 (39%) patients were with dyslipidaemia.

Name of Comorbidities		Dyslipidaemia		Total (n=72)	P Value
		Present (N=30)	Absent (N=42)		
Diabetes Mellitus	Overt	4	5	9 (12.5%)	1.000 (Statistically not significant)
	IGT (FBS-100-125 mg/dL)	13	12	25 (34.72%)	0.2183 (Statistically not significant)
Hypothyroidism		4	2	6 (8.33%)	0.2267 (Statistically not significant)
Hypertension		14	7	21 (29.16%)	0.0084 (Statistically significant)
Heart Disease		18	2	20 (27.78%)	0.0001 (Statistically significant)
Smoking		5	2	7 (9.72%)	0.1199 (Statistically not significant)
Body Mass Index	Overweight (25-29.99 kg/m2)	15	18	33 (45.83%)	0.6341 (Statistically not significant)
	Obesity (≥30 Kg/m2)	0	0	0	-
Isolated RA (None of the above comorbidities)		3	13	16 (22.22%)	0.0455 (Statistically significant)

Table 8: Dyslipidaemia with Associated Comorbidities

Table 8 show the prevalence of dyslipidaemia in relation to associated comorbidities. Hypertension was the most common comorbidities accounting for 29.16% followed by in order heart disease (27.78%), diabetes (12.5%), smoking (9.72%) and hypothyroidism (8.33%). Statistical analysis shows significant association for hypertension and heart disease. 25 (34.72%) patients were having Impaired Glucose Tolerance (IGT) and 33 (45.83%) were having BMI in the category of overweight. Out of total 16 patients without the comorbidities as mentioned 3 (18.75%) patients were having dyslipidaemia.

Extra-Articular Manifestations	Dyslipidaemia		Total Number	P Value
	Present (N=30)	Absent (N=42)		
Anaemia (Hb <12 g/dL)	22 (73%)	5 (12%)	27	<0.0001
Cardiovascular	17 (56.7%)	3 (7.14%)	20	<0.0001
Pulmonary	9 (30%)	4 (9.5%)	13	0.0332
Subcutaneous nodule	3 (10%)	3 (7.14%)	6	1.000
Vasculitis	2 (6.7%)	2 (4.8%)	4	1.000
Renal	2 (6.7%)	3 (7.14%)	5	1.000

Table 9: Association of Dyslipidaemia with Extra-Articular Manifestations

Table 9 shows the association of dyslipidaemia with extra-articular manifestations in RA. Dyslipidaemia was present in around 70 % cases of anaemia, 90% cases of cardiovascular manifestations, 69% cases with pulmonary manifestations, 66.67%

cases with subcutaneous nodules, 50% of cases with vasculitis, 60% of cases with renal involvement. Statistical analysis shows significant association of dyslipidaemia with cardiovascular manifestations, pulmonary manifestations and anaemia.

CVS Manifestations		No. of Patients	Total No. Patients (N=72)
ECG Abnormalities	Ischaemic Changes	2	9 (12.5%)
	Non-specific ST-T Changes	3	
	AV Block(1st degree)	1	
	Sinus Bradycardia	2	
	LVH	1	
Echocardiography	Pericardial effusion	4	9 (11.11%)
	LVDD	3	
	LVSD	1	
	LVH	1	
Carotid Doppler	IMT ≥0.6 mm	7	13 (18.1%)
	Plaque	6	

Table 10: Different Cardiovascular Manifestations

Table 10 shows different cardiovascular manifestations in RA patients. ECG abnormalities were present in 12.5% of study subjects, abnormal echocardiography findings were present in 11.11% of patients and abnormal carotid Doppler findings were present in 18.1%. The most common echocardiographic abnormality was pericardial effusion, most common abnormal carotid Doppler finding was increased IMT (≥0.6 mm).

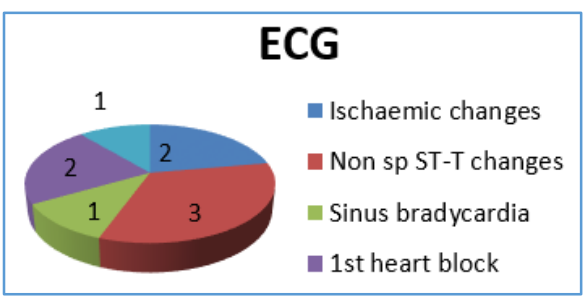

Fig. 3: Pie Chart showing ECG Findings in Study Subjects

The most common ECG abnormality was non-specific ST-T changes.

CVS Manifestations	Dyslipidaemia		Total	P Value
	Present (N=30)	Absent (N=42)		
Present	17 (56.6%)	3 (7.1%)	20	<0.0001 (Extremely Significant)
Absent	13 (43.4%)	39 (92.9%)	52	

Table 11: Proportion of Dyslipidaemia as per Cardiovascular Manifestations

Presence of CVS Manifestations Means: ECG or echocardiography or carotid Doppler abnormalities.

Absence of CVS Manifestations Means:

i. Asymptomatic and normal ECG.
ii. Normal echocardiography and carotid Doppler findings in selected patients.

Table 11 shows association of dyslipidaemia as per cardiovascular manifestations. Out of total 30 dyslipidaemic patients, 17 (56.6%) were having CVS manifestations. Statistical analysis shows significant association of dyslipidaemia with cardiovascular manifestations.

DISCUSSION: Rheumatoid arthritis being a systemic inflammatory disease affects various body organs. The disease process of rheumatoid arthritis itself is proatherogenic. This is evident from the fact that inflammation has been shown to be fundamental to all stages of atherosclerotic plaque development thereby resulting in premature atherosclerosis in rheumatoid arthritis. Cardiovascular events account for more than half of excess mortality in rheumatoid arthritis.

There is paucity of the literature on the correlation of the dyslipidaemia with rheumatoid arthritis in India including this part of the country.

A. Age and Gender Distribution: In our study, maximum number of cases were in the 5th decade of life (31.94%) followed by 4th decade of life (30.56%) with a mean age of 43.63 years. In the study conducted by Dasgupta S et al (2007)[8] found that the maximum age incidence was 40-49 years. The finding is similar to that of the present study.

Maoine et al (1993),[9] Dasgupta S et al (2007)[8] and Parida P et al (2011)[10] found the mean age of the study group were 46.4 years, 43.6 years and 42.8 years, respectively. These findings are comparable with the present study.

In this study, out of 72 study subjects, 16 patients (22.2%) were male and 56 patients (77.8%) were female with a female-to-male ratio of 3.5:1. This finding is in

accordance with the Dasgupta S et al (2007)[8] found a female-to-male ratio of 3:1. Turesson C et al (2003)[11] showed a female-to-male ratio of 2.7:1 in their study.

B. Duration of the Disease: In this study, it is found that the mean duration of the disease was 3.36 years. 29.17% patients were in the range of 6-12 months followed by 25% patients with a disease duration of more than 5 years. Fleming et al (1976)[12] found a mean disease duration of 4.5 years. Arun Gupta (2011)[13] at Nepal found a mean disease duration of 2.34 years.

C. Prevalence of Dyslipidaemia in Rheumatoid Arthritis: In this study, it is found that the most common derangement of lipid parameter was being attributed to a low HDL level 22 (31%) followed by a high triglyceride level 15 (20.83%). The prevalence of dyslipidaemia was 41.67%.

Hadda et al (2007)[14] found dyslipidaemia in 38.5% patients in the study carried out in a tertiary Hospital in North India. V. Mahajan et al (2008)[15] in a cross-sectional study conducted at AIIMS encountered dyslipidaemia in 33% patients of RA.

In this study, mean value of lipid parameters were for total cholesterol 172 mg/dL, for LDL cholesterol 103 mg/dL, HDL cholesterol 43 mg/dL and for triglycerides 135 mg/dL. Agarwal et al (2013)[16] had shown in their study demonstrated a mean total cholesterol level of 179 mg/dL, mean LDL cholesterol 111 mg/dL, HDL cholesterol 45 mg/dL and for triglyceride 114 mg/dL, which was comparable with the present study. Varunkumar D et al (2011)[17] had reported a mean total cholesterol of 174 mg/dL, mean LDL cholesterol 114 mg/dL, HDL cholesterol 36.33 mg/dL and mean triglyceride of 173 mg/dL.

In our study, atherogenic index was high (>5) in 17 (23.6%) of the cases with a mean of 4.52. Nurmohamed M.T et al (2003) observed that atherogenic index greater than five have an increased chance of developing myocardial infarction.

Low HDL-C was the commonest abnormality seen in 34% in this study. Ghosh et al (2008) reported that TC/HDL-C ratio was more than 5 in approximately 25% of cases.

D. Correlation of Dyslipidaemia with Various Rheumatoid Arthritis Disease Related Factors:

1. **Association of Dyslipidaemia with Disease Activity:** Maximum number of patients 21 (70%) patients with dyslipidaemia were with high disease activity, 6 (20%) patients were with moderate disease activity and least number of dyslipidaemic patients were with low disease activity.

Statistical analysis shows a significant association between dyslipidaemia and disease activity. (P<0.05). Arts et al (2012)[18] found a significant association of dyslipidaemia and disease activity especially with decrease of HDL cholesterol concentration, there was increase in DAS28 score (P=0.05). Hadda et al (2007) demonstrated that with a decline in disease activity, there was a rising trend for HDL.

2. **Dyslipidaemia in Association with Treatment Modalities and Comorbidities:** This study revealed that out of total 30 patients with dyslipidaemia, 17 (56.7%) patients were already on treatment for RA with DMARDs, biologics, steroids either as monotherapy or in combination. Thirty-three patients were on steroid therapy, out of which 13 (39%) patients were with dyslipidaemia. Eighty five percent of the patients on steroid therapy were having a favourable atherogenic index (≤5). Amongst the overt diseases, hypertension was the most common comorbidity accounting for 29.16% followed by in order, heart disease (27.78%), overt diabetes (12.5%) and hypothyroidism (8.33%). There was significant statistical association for hypertension and heart disease with dyslipidaemia (p<0.05). Overweight accounted for 46% of the patients and impaired glucose tolerance was present in 35% of the patients. Al-Bishri et al[19] found that the most common comorbidity in RA was hypertension followed by diabetes mellitus. Agarwal et al found that most common comorbidity being hypertension (26.8%), followed by diabetes (17.9%), smoking (5.4%) and hypothyroidism (12.2%).

3. **Dyslipidaemia in association with extra-articular manifestations:** The present study depicted that the 31 patients (43%) had one or more extra-articular manifestation. Anaemia 27 (37.5%) was found to be the most common followed by cardiovascular manifestations 20 (27.8%), constitutional symptoms 19 (26.39%), pulmonary manifestations 13 (18%) and rheumatoid nodules 6 (8%).

Association of dyslipidaemia with cardiovascular manifestations, pulmonary manifestations and anaemia were found to be statistically significant. Grover S et al (2006)[20] and Parida P et al (2011) observed 36.44% and 36.8% prevalence of extra-articular manifestations in rheumatoid arthritis respectively, which are similar to the observation made by the present study. The most common manifestations in these studies were also anaemia, constitutional and pulmonary manifestations.

E. Cardiovascular Manifestations in RA:

1. **Prevalence of Cardiovascular Manifestations in RA:** In this study, ECG abnormalities were present in 12.5% of study subjects, abnormal echocardiography findings were present in 11.11% of patients and abnormal carotid Doppler findings were present in 18%. The most common ECG abnormality was non-specific ST-T changes, most common

echocardiographic abnormality was pericardial effusion and most common abnormal carotid Doppler finding was increased IMT. In the carotid Doppler study, 6 (8.3%) patients were having plaque suggesting advanced atherosclerosis, 7 (9.7%) of patients were having increased intimomedial thickness (IMT ≥0.6 mm) suggesting subclinical atherosclerosis. As a whole, 31 (43.1%) patients of the study population was having cardiovascular manifestations. In the study done by Kaushal et al (1988),[21] cardiac manifestations were seen in 20% of the study population. Hochberg et al (2008)[22] demonstrated that 27% of RA patients developed cardiovascular complications in their 7 year long period study between 1999-2006. Dessein PH et al (2005)[23] had found that 72% patients had atherosclerosis, 31% had plaque and 28% were free of plaque. Mahajan V et al (2008) had demonstrated RA patients had higher prevalence of carotid plaques (21%) compared to controls (1%).

2. **Association of Dyslipidaemia with Cardiovascular Manifestations:** Out of total 30 dyslipidaemic patients 17 (56.6%) were having CVS manifestations. Association of dyslipidaemia with cardiovascular manifestations was statistically significant. A. N. Georgiadis et al (2008) found a significant association of dyslipidaemia with cardiovascular manifestations including association for individual lipid parameters ($p < 0.001$).

CONCLUSION: Unlike as was thought previously, rheumatoid arthritis is not just only a disease affecting joints, but it goes well beyond the barricade of arthritis into systemic inflammatory manifestations. From this study, it was concluded that dyslipidaemia is common in RA in this part of the country with HDL-cholesterol being the commonest abnormality. Comorbidities like hypertension, diabetes mellitus, hypothyroidism, smoking, heart disease do exist with RA and accelerate the risk of dyslipidaemia. The dose and duration of glucocorticoid treatment greatly influence atherogenic index and dyslipidaemic status. Overt cardiovascular manifestations in the form of advanced atherosclerosis, ischaemic heart disease and pericarditis are more common in RA patients.

This study being a small observational study, the role of pharmacological intervention on dyslipidaemia in RA cannot be assessed. Large prospective analytical studies are required to extrapolate our findings in the community to address the effect of pharmacological intervention for reducing the burden of dyslipidaemia and cardiovascular risk in patients with rheumatoid arthritis.

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