Original Research Article

Lipid profile in arthritides

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A B S T R A C T

Aim and Objectives: The present study was undertaken to evaluate the relation between various type of arthritis and lipid profile. This was a comparative study in which lipid profile of arthritis patients were statistically compared with age and sex matched controls.

Materials and Methods: During one year of study period, a total of 150 clinically diagnosed cases of arthritis and 75 ages and sex matched controls were studied, regarding demographic characteristics, clinical characteristics and biochemical changes with special reference to lipid profile in relation to the type of arthritis and severity of arthritis.

Results: There was no relation found between age/gender and lipid profile. Rheumatoid arthritis (RA) was the most common type of arthritis and knee joint was commonest involved joint. RA factor was negative in majority of cases (63%) and mean ESR of cases was 40.2 mm. Peri-articular osteopenia was the commonest radiological finding. The frequency of cases with hypercholesterolemia, hyper triglyceridemia and low HDL value was 13.33%, 16.67% and 70.67% respectively. There was no significant difference found between cases and controls in regards to serum total cholesterol (TC), triglycerides, HDL, LDL, VLDL levels, TC/HDL and LDL/HDL ratio. In different types of arthritis, there was a statistically significant difference was found in the mean HDL levels while no significant difference in the mean of TC, LDL, VLDL, and triglyceride levels.

Conclusion: Study reveals that the lipid profile is altered in RA characterized by low TC and LDL with lower RA factor titres. However, the mean triglycerides, HDL, LDL, VLDL, TC/HDL and mean LDL/HDL did not show a significant difference between subgroups of the patients having different titres of RA factor.

1. Introduction

Rheumatoid arthritis (RA) is a chronic systemic disease affecting primarily the synovium, leading to joint damage, bone destruction and its affecting around 0.5%-1% of the adult population worldwide.[1] Epidemiological studies have shown an increased premature mortality in patients with RA compared with the general population.[2] RA is associated with increased cardiovascular morbidity and mortality that is largely attributed to accelerated atherosclerosis. Both traditional and novel risk factors have been invoked to explain the accelerated atherogenesis in

RA.[3] However the risk factors for atherosclerotic events and cardiovascular disease include male sex, increased age, elevated plasma total cholesterol (TC) and lowdensity lipoprotein cholesterol (LDL-C), decreased high-density lipoprotein cholesterol (HDL-C), high blood pressure, smoking and diabetes mellitus.[4] Approximately 50% of atherosclerotic coronary artery disease (CAD) in the community occurs in the absence of traditional risk factors.

Studies have shown that patients with untreated RA have dyslipidemia that contributes to atherosclerosis and that this atherogenic lipid profile can be positively influenced by the use of disease-modifying antirhumatic drugs (DMARD) therapy. Some studies have also shown ethni c differences in this respect.[4–6] Majority of the reports of the prevalence of

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dyslipidemia in RA have been from Western countries with only an occasional small study from India. Further there is a paucity of studies that have compared the lipid profiles across different types of arthritides. Thus there is a need for an in-depth study of lipid profiles in a spectrum of patients with arthritides in our endemic setting.

The current study was carried out with an objective to investigate the lipid profile in patients with various types of arthritides, also to assess whether there is a correlation between disease activity and treatment given with the levels of different lipid fractions in these patients and compared with age and sex matched controls.

2. Materials and Methods

This study was carried out in the Department of Pathology at Tertiary Care Hospital, Mumbai for the period of one year. The data for this study was collected from patients who presented to Rheumatology Department on outpatient basis. A total 150 patients of age between 21 to 50 years, suffering from various types of arthritides were included in the study. 75 apparently healthy, non-smoking volunteers, proportionally matched for age and sex were studied as a control group. These subjects were selected from blood donors and the general population. An informed written consent was taken from case and healthy controls. Known case of Diabetes Mellitus or RBS > 200mg/dl or FBS.> 126 mg/dl or PPB S> 200 mg/dl, hypertension, alcoholics, smokers, known case of kidney diseases, ischaemic heart disease/cerebrovascular accident, endocrine disorders like hypothyroidism, cushing's syndrome, history of use of steroids, oral contraceptives, diuretics beta-blockers, thyroxine and those having history of familial dyslipidemia were excluded from the study.

All the selected cases were referred to the pathology laboratory for RA factor estimation. A clinical history, all relevant examination, radiological examination (if any) and other investigations (ESR, HLA B- 27, CRP, and ANA etc) were done for all the patients and treatment history was noted in case record forms.

The blood samples were drawn from all the patients after a minimum of 12 hour of complete fasting. About 3 ml of blood was drawn using perfectly dry and sterile syringes. Serum was separated within two hours of collection to prevent artifactua I changes in concentration of HDL. The serum was transferred to centrifuge tube and centrifuged at 5000 rpm for 10 minutes. The supernatant clear serum was then pipetted out using dry piston pipettes with disposable tips and stored in dry thin walled vials at 4°C. The samples were analyzed the same day or within 48 hours. Care was taken to exclude the hemolysed serum.

RA factor test was done in all of 150 cases. Normal RF test results are indicated by rheumatoid factor levels that are less than 10 u/mL or by a ratio of less than 1:8 titre (i.e. the concentration of RF antibodies). Estimation of total cholesterol, HDL-cholesterol, and triglycerides (TG) were done enzymatically with commercially available kit on Randox Daytona system. Concentration of VLDL was calculated using the formula, VLDL=Triglyceride/5 and LDL-c holesterol was calculated by using the Friedewald's equation, LDL=Total cholesterol-[(Triglycerides/5) +HDL] mg/dl.[7] The normal values of the lipid parameters used in current study were based on NCEP guidelines.

2.1. Statistical analysis[8,9]

Student t test has been used to test the homogeneity of age and Chi-square test used to find the homogeneity of sex between case and control. Student t test has been used to find the significance of lipid profiles between case and controls. Analysis of variance (ANOVA) has been used to find the significance of mean lipid profiles when there are more than 2 groups. Mann Whitney U test has been carried out to find the significance between case and control for TC/HDL and LDL/HDL ratio. Statistical significance was taken when p value < 0.05. The statistical software used for the analysis was SPSS 17.0.

3. Observations and Results

During the one year of study period, a total of 150 clinically diagnosed cases of arthritis and 75 age and sex matched controls were studied. The cases were mostly clustered in the age group of 41-50 years (47.55 %). The mean age of cases was 38.65±8.56 years and the mean duration of disease was 1.8±1.03 years. The cases consisted of 31 males (20.66%) and 119 females (79.33 %), thus the female preponderance observed in the study, (Table 1).

Table 1: Age and sex distribution in cases and Control

Age in yrs	Cases (n=150)	Controls (n=75)
21-30	35 (23.3%)	17 (22.67%)
31-40	44 (29.55%)	23 (30.67%)
41-50	71 (47.55%)	35 (46.67%)
Sex	**Cases (n=150)**	**Controls (n=75)**
Male	31 (20.66%)	15 (20%)
Female	119 (79.33%)	60 (80%)

Figure 1 shows the case distribution and the types of arthritis. Rheumatoid arthritis (RA) was the most common type of arthritis. 140 out of 150 cases complained of multiple joint pains. The most common presenting symptom was knee joint pain (75 cases). The next common involved joints were wrist joint (51 cases), ankle joint (43 cases), PIP joint (39 cases), MCP joint (38 cases), shoulder and elbow joint (31 cases each). Other joints involved were the DIP joint (6 cases), hip (3 cases) and MTP joint (2 cases). 79 cases (52.67%) complained of early morning stiffness lasting for more than a hour. 90 cases (60%) complained of swelling of joints.
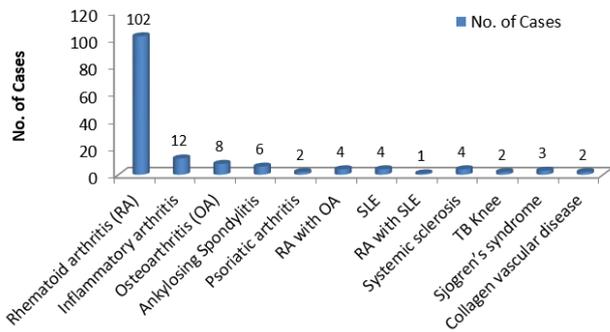
Fig. 1: Case distribution and the types of arthritis

RA factor was negative in majority of cases (63%). Cases with higher titres of RA factor were found to have affection of multiple joints. The mean ESR of cases was 40.2 mm. Peri-articular osteopenia was the commonest radiological finding seen in 22 cases. There was no significant difference found between two groups with respect to total cholesterol (TC), triglycerides, HDL, LDL, VLDL levels, TC/HDL and LDL/HDL ratio as shown in Table 2.

The frequency of cases with hypercholesterolemia and hypertriglyceridemia was 13.33% and 16.67% respectively. 106 cases (70.67%) had HDL values less than the normal value of 40 mg/dl. Also 26 cases (17.33%) had high LDL levels (> 100 mg/dl) and 25 cases (16.67%) had high VLDL levels (> 20 mg/dl) in blood. There was a statistically significant difference was found in the mean HDL levels while no significant difference in the mean of TC, LDL, VLDL, and triglyceride levels in different types of arthritis, (Table 3).

The total cholesterol (TC) and LDL was found to be significantly lower in rheumatoid arthritis patients with lower RA factor titre. However, the mean triglycerides, HDL, LDL, VLDL, TC/HDL and mean LDL/HDL did not show a significant difference between subgroups of the patients having different titres of RA factor antibody, (Table 4).

4. Discussion

As shown by several studies,[5,10,11] in current study majority of cases were in the age group of 41-50 years. The female predominance observed in the study which was compared with the study done by Yadav et al[3] and Erum et al[12] and We did not observed significant correlation between the age/sex and total cholesterol or any of the lipid parameters studied. The lipid profile of patients with RA has been evaluated in several studies. Some of these studies have reported lower levels of HDL-C and TC, higher serum concentrations of lipoprotein (a) and higher TC/HDL-C and LDL-C/HDL-C ratios in active and/or untreated disease than in the general population.[13–15] However, other studies have not shown

significantly different lipid levels from those observed in the healthy population[16] while some others refer to an overall reduction in all lipid sub-fractions in cases of active disease.[17–20] These contrasting results could be attributed to the size of the samples, the type of study (prospective or cross-sectional), differences in the disease type (established or early), or to differences in the disease activity. Patients in remission or with controlled disease show an increase in HDL-C levels and a reduction in the atherogenic index compared to patients with active disease.[17]

In present study, the mean total cholesterol was found to be almost equal in patients when compared to controls. Also it was found that there was no statistically significant difference in level of sub-fractions of serum lipoprotein i.e. HDL, LDL, VLDL. This finding was correlated with various studies done on arthritis patients.[20,21] Unlike, Vijaykumar et al[21] study we did not find that the serum lipids were lower in our patients than in controls. This may be due to differences in the lipid profile of their control population. There was a significant difference of HDL levels between the different types of arthritis. However, no significant difference was found in the total cholesterol, triglycerides, LDL as well as VLDL levels between the various sub-groups of patients. This was accordance with the study done by Swenson et al[22] and Lazarevic et al.[23]

Dyslipidemia (DL) is frequently observed in patients with active RA. Systemic inflammation has a general effect in lowering circulating lipid levels [PJMS]. The etiology of dyslipidemia in RA is not clear. The correlation of disease activity pattern and hypolipidemia imply that the degree of inflammation may play a role in the development of dyslipoproteinemia in RA patients.[22,23] Supporting these points, hypocholesterolemia has also been described in other rheumatic inflammatory diseases like SLE and Reiter.[23,24] The liver is a key organ in lipoprotein metabolism. The results of experimental studies indicate that in the course of inflammation, the liver preferentially uses aminoacids for the production of inflammatory mediators rather than for manufacturing the enzymes important in lipid metabolism, resulting with a reduction in production of the lipoproteins.[23,25] Based on the results of these in vivo and in vitro studies, altered lipoprotein metabolism was suggested to be a systemic sequel partly due to the host's response to inflammation.

The mean total cholesterol (TC) and LDL was found to be significantly lower in rheumatoid arthritis patients with lower RA factor titre. However, no significant difference was found for triglycerides, HDL and VLDL among the subgroups. Very few studies have studied the relationship between RA factor titre and change in lipid profile. However, in present study as DAS-28 score and other rheumatoid disease activity parameters were not available. The value of RA factor titre was considered as a marker of disease activity. Hadda et al[26] found that

Table 2: Comparison of Lipid profile in cases and controls

Lipid Profile	Cases (n=150)	Control (n=150)	p-value
Total Cholesterol	161.7±31.7	160.5±31.5	0.78
Triglycerides	116.8±37.5	117.3±32.0	0.79
HDL	35.3±10.8	36.5±7.3	0.33
LDL	103.3±27.5	100.6±29.3	0.47
VLDL	23.3±7.5	23.5±6.4	0.79
TC/HDL ratio	5.0±1.8	4.6±1.3	0.08
LDL/HDL ratio	3.3±1.6	2.9±1.2	0.08

Table 3: Type of arthritis and lipid profile

| Lipid Profile | Type of Arthritis | | | | | | p-value |
	RA	OA	Inflammatory Arthritis	Ankylosing Spondylitis	Lupus Arthritis	Others	
TC (mg/dl)	164.9±31.8	173.4±34.5	159.1±19.08	133.7±28.9	145.8±35.4	150.9±32.1	0.07
TG (mg/dl)	115.4±34.2	124.8±31.8	121.2±48.4	113±38.6	106.3±27.4	114.1±34.3	0.91
HDL (mg/dl)	36.2±11	43.3±11.7	33.9±6.4	30.4±5.0	31.7±5.2	30.0±11.8	0.04
LDL (mg/dl)	106±28.9	105.6±22.8	103.4±16.3	80.7±20.3	92.9±26.6	98.1±26.9	0.27
VLDL (mg/dl)	23.1±6.8	25.0±6.4	24.8±8.8	22.6±7.7	21.3±5.5	22.8±6.9	0.91
TC/HDL ratio	5.0±1.8	4.2±0.9	4.9±0.9	4.4±0.6	4.6±0.7	5.8±2.8	0.31
LDL/HDL ratio	3.3±1.6	2.6±0.6	3.1±0.8	2.6±0.4	2.9±0.5	3.9±2.5	0.161

Table 4: Comparison of RA factor titres and lipid profile

| Lipid Profile | RA factor titres | | | | | | p-value |
	< 1:8 (n=48)	1:8 (n=3)	1:32 (n=6)	1:64 (n=21)	1:128 (n=10)	> 1:256 (n=14)	
TC (mg/dl)	156.1±27.8	180.3±41.7	136.0±33.5	177±28.2	176.7±34.2	177.2±32.9	0.005
TG (mg/dl)	111.5±33.7	108.7±27.7	96.3±30.9	126.4±33.9	121.9±36.3	117.2±36.5	0.40
HDL (mg/dl)	35.6±10.2	44.4±3.1	37.8±9.1	35.3±9.9	36.8±9.9	36.5±16.8	0.98
LDL (mg/dl)	99.1±26.1	114.2±40.3	78.9±26.5	116.5±28.6	115.5±29.5	117.3±26.9	0.01
VLDL (mg/dl)	22.3±6.7	21.7±5.5	19.3±6.2	25.3±6.8	24.4±7.3	23.4±7.3	0.40
TC/HDL ratio	4.7±1.6	4.1±1.2	3.7±0.8	5.5±2.3	5.1±1.5	5.7±2.2	0.11
LDL/HDL ratio	3.0±1.4	2.6±1.1	2.1±0.7	3.7±2.0	3.4±1.4	3.9±1.9	0.13

DAS-28 showed a significant negative correlation with total cholesterol and LDL.

Since, the patients were on multiple therapeutic modalities it was not statistically possible to analyze the effect of treatment on lipid profile.

5. Conclusion

The current study reveals that the lipid profile is altered in Rheumatoid arthritis characterized by low TC and LD L with lower RA factor titres. However, the mean triglycerides, HDL, LDL, VLDL, TC/HDL and mean LDL/HDL did not show a significant difference between subgroups of the patients having different titres of RA factor.

The study suggested that- 1. A study of more number of cases in each of the disease groups would provide a clear picture of the abnormality of the lipid profile in different type of arthritis. 2. Availability of other parameters of disease activity could also have enhanced the study. 3. Estimation of Apo-lipoproteins would be a useful extension of this study. 4. More sensitive test of RA factor like ELISA and nephelometry could also clarify the association of RA factor with lipid profile. 5. A study that includes more number of cases of each disease group with more uniform therapeutic protocols would help to analyze the influence of therapy on the lipid profile.

6. Source of funding

None.

7. Conflict of interest

None.

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