Original Article

A Comparative Study on Different Fraction of Lipid and Das28 Score In Patients of Early Arthritis

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ABSTRACT

BACKGROUND: Dyslipidaemia is a major Cardiovascular disease (CVD) risk factor in the general population. Evidence suggests that lipid metabolism is altered in rheumatoid arthritis due to inflammation. The aim of this study is to find out the prevalence of different fraction of lipid abnormality in early rheumatoid arthritis in a tertiary care centre so as to take necessary steps for intervention and early detection, and thereby reducing the chance of cardiovascular morbidity and mortality.

METHODS: Fifty patients who met the 2010 American College of Rheumatology/ European league Against Rheumatism(ACR/ EULAR) criteria for early rheumatoid arthritis, with disease duration of less than 1 year and no prior treatment were included in the study. Thirty healthy volunteers were included as control.

RESULTS: The mean Disease Activity Score-28 (DAS-28) at disease onset was 5.8 ± 0.9. Early rheumatoid arthritis (ERA) patients exhibited higher serum levels of total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) levels compared to controls. The atherogenic indices: TC/HDL-C as well as LDLC/HDL-C were significantly higher in ERA patients compared to controls. Difference of mean LDL vs. DAS 28 (p=0.0073) and mean ESR vs. DAS 28 (p=0.0499) were statistically significant in this study.

CONCLUSION: Early rheumatoid arthritis patients are characterized by an atherogenic lipid profile, which is major cardiovascular risk factor.

Keywords: Rheumatoid arthritis, Low density lipoprotein cholesterol, Total Cholesterol/High density lipoprotein cholesterol, Cardiovascular risk, Disease activity score-28 (DAS 28).

Introduction:

Rheumatoid arthritis (RA) is a long-term autoimmune disorder that primarily affects joints.[1] It typically results in warm, swollen, and painful joints.[2] Pain and stiffness often worsen following rest.[3] Most commonly, the wrist, hands and feet are involved, with the same joints typically involved on both sides of the body.[4] The disease may also affect other parts of the body.[5] This may result in a low red blood cell count, inflammation

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around the lungs, and inflammation around the heart.[6] Fever and poor energy may also be present.[7] Often, symptoms come on gradually over weeks to months.[8]

The cut-offs between 'early' and 'established 'RA have progressive decreased over the past decades. Previously, a cut off of < 5 years after symptom onset was used to define early disease. By the 1990s, symptom duration of <12-24 months was considered early.[9] This length of time was chosen because by 2 years up to 70% of patients treated conventionally may have erosive. Currently 'early RA' is defined as disease duration of less than 1 year. It is suggested that very early RA, i.e. within the first 12 weeks of symptom onset-may present an immune pathologically distinct disease phase compared with later RA disease.[10] Thus, the early RA period is divided into 'very early RA' with disease duration of < 3 months and 'late early RA' with duration of symptoms of 3-12 months.[9]

The classification of RA is based on criteria introduced in 1987—the American College of Rheumatology criteria.[3] Unfortunately, these criteria do not perform well in early RA.[4] We currently use 2010 American College of Rheumatology/ European league Against Rheumatism (ACR/EULAR) Classification Criteria for recognizing early RA.

RA is known to reduce the lifespan of patients as they suffer a double risk of heart disease, [11] independent of other risk factors such as diabetes, alcohol abuse and elevated cholesterol, blood pressure and body mass index. The mechanism by which RA causes this increased risk remains unknown, while high levels of systemic inflammation have been identified as an independent risk factor for plaque development.[12] Estimated standardized mortality ratios (SMR) associated with RA range from 1.3 to 3.0 and this increased mortality is largely attributed to cardiovascular disease (CVD) particularly coronary atherosclerosis.

Dyslipidaemia appears to manifest in RA patients in both early[13] and advanced disease.[14] Atherogenic lipoprotein phenotype, characterized by decreased high density lipoprotein-cholesterol (HDL-C), moderately raised triglycerides (TG) and increased levels of small dense LDL (sdLDL) is linked to increased cardiovascular risk, much more than low density lipoprotein-cholesterol (LDL-C) levels alone. In fact, not only the quantity of LDL-C, but the composition exerts a direct influence on cardiovascular risk and the predominance of small dense LDL (sdLDL) has been accepted as an emerging cardiovascular risk factor by the National Cholesterol Education Program Adult Treatment Panel III.[15]

Aim and Objective: To find the prevalence of different fraction of lipid abnormality in early rheumatoid arthritis.

Materials & Methodology

Fifty patients between 18-60 years age irrespective of sex with early RA who attended the Rheumatology clinic of Midnapore Medical College between July 2017 and June 2018 were included in this study. Patients who fulfil ACR/EULAR 2010 Rheumatoid Arthritis criteria and with duration of disease of more than 12 weeks and less than 1 year without prior use of Disease modifying anti rheumatoid drugs (DMARDs) and systemic steroids or use of DMARDs less than 12 weeks were included in the study. Thirty (30) age and sex matched healthy subjects were recruited as control.

Smokers and patients suffering from conditions that affect lipid levels such as Diabetes Mellitus, Hypothyroidism, Hypertension, Coronary artery disease, Liver and Kidney Disease, Cerebrovascular accident, family history of dyslipidemia, Obesity (BMI > 30) and drugs such as lipid lowering drugs and oral contraceptive pills were excluded from the study. The study was approved by the hospital Institutional

Ethical Committee. All patients gave written informed consent for the study.

Disease activity score-28 (DAS-28) was measured in all ERA patients and lipid profile was measured in both case and control subjects.

Data were analyzed using software packages SPSS 24.0 and Graph Pad Prism Version 5.

Results:

Among the 50 patients, 30 were females and 20 were males. In the control group of 30 healthy subjects, there were 19 females and 11 males. The percentage positivity of IgM RF in cases is 100 % and the percentage positivity of Anti Citrullinated protein antibody in cases is 90 %. Demographic, hematological and lipid profile of patients are presented in Table 1.

Table 2 shows comparison of lipid parameters in cases and controls. TC, LDL-C was significantly higher in cases than controls. TG and HDL-C were similar in cases and controls. Our results indicate that compared to the general population patients with early active RA before therapy had an atherogenic lipid profile characterized by significantly higher TC-25 %, LDL-C-31 %, at base line compared to controls. The HDL-C was higher by 9 % and the TG by 8 %.

The atherogenic ratios: TC/HDL-C and also LDL-C/HDL-C were higher in cases than in controls and statistically significant.

17(34.0%) patients had ≤40 years of age, 13(26.0%) patients had 41-50 years of age, 17(34.0%) patients had 51-60 years of age and 3(6.0%) patients had >60 years of age.

Table 1: Baseline characteristics of patients with early arthritis:

Parameters	**Mean ± SD**	**95% CI**
Age (yrs)	45.86 ± 11.96	42.54-49.17
BMI (Kg/m²)	25.42 ±4.67	24.21-26.88
Leukocytes (per cc)	7020± 2193	6412.-7628
Haemoglobin (g/ dl)	10.7±1.4	10.35-11.16
Platelet (lakh/ cc)	3.31±2.34	2.66-3.95
Total Cholesterol (mg/ dl)	207.4±55.1	192.08-222.67
Triglycerides (mg/ dl)	144. 7±64.5	126.79-162.54
HDL-cholesterol (mg/ dl)	44.8±17.8	39.84-49.71
LDL-cholesterol (mg/ dl)	124.5±47.9	111.23-137.82
C-reactive protein (mg/ L)	25.4±29.8	17.17-33.68
ESR (mm/ h)	42.2±18.5	37.07-47.34
DAS 28	5.3±1.5	4.88-5.73
Rheumatoid factor (IU/ ml)	64±165.8	18.09-109.82
Serum creatinine (mg/ dl)	1.37±0.6l	1.18-1.55
ALT (IU/ L)	30.2±8.8	27.77-32.66
AST (IU/L)	30±8. l	27.84-32.31
TSH (mIU/L)	2.59±0.96	2.32-2.85

Table 2: Comparison of Lipid profile among cases and controls

Parameter	Case (50)	Control (30)
TC (mg/dL)	207.4±55.1	155.9±44.3*
TG(mg/dL)	144.6±64.5	132.5±36.8
HDL-C(mg/dL)	44.8±17.8	40.5±12.3
LDL-C(mg/dL)	124.5±47.9	85.3±34.2*
TC/HDL-C	4.63	3.84*
LDL-C/ HDL-C	2.78	1.99*

Values are mean±SD of number of observations; *indicates significant at p<0.05

Table 3: Distribution of Anti CCP

Anti CCP	Frequency	Percent
Negative	5	10.0%
Positive	45	90.0%
Total	50	100.0%

45(90.0%) patients had positive anti CCP.

According to DAS 28 score, 5(10%) patients had <3.5, 22(44%) patients had 3.5 to 5 and 23(46%) patients had >5.0. In DAS 28 <3.5, the average platelet (mean± s.d.) of patients was 5.88 ±6.81. In DAS 28 3.5 to 5, the mean platelet of patients was 3.2 ±1.. In DAS 28 >5.0, the mean platelet of patients was 2.8322 ±1.0044. Difference of mean platelet vs. DAS 28 was statistically significant (p=0.0271).

In DAS 28 <3.5, the mean LDL (mean± s.d.) of patients was 82.1 ±36.6. In DAS 28 (3.5 to 5), the average LDL of patients was 145.4 ±48. In DAS 28 >5.0, the average LDL of patients was 113.7304 ±41.2908. Difference of mean LDL vs. DAS 28 was statistically significant (p<0.01)

In DAS 28 <3.5, the mean TC/HDL (mean± s.d.) of patients was 4.2876 ±.8756. In DAS 28 3.5 to 5, the mean TC/ HDL (mean± s.d.) of patients was 5.7189 ±2.4038. In DAS 28 >5.0, the mean TC/ HDL (mean± s.d.) of patients was 4.5516 ±1.8519. Difference of mean TC/HDL vs. DAS 28 was not statistically significant (p=0.1254).

Discussion:

Cardiovascular risk in RA is enhanced through several factors such as hypertension, insulin resistance and obesity which occur more frequently in RA. Disease specific factors such as systemic inflammation, activation of the coagulation pathway and hyper-homocysteinaemia also confer additional cardiovascular risk. High levels of systemic inflammation have been identified as an independent risk factor for plaque development and may exert this effect by increasing levels of oxidative stress, activation of coagulation and secondary dyslipidaemia.

In one study having 203 patients, that included 180 female and 23 males, man duration of disease was 2.55 ± 2.09 years and mean age was 47 ± 10.9 years.[16] The mean total cholesterol, HDL-C, LDL-C and triglycerides were 198.6 ± 43.6 mg/ dl, 41 ± 8.2 mg/dl, 109 ± 28 mg/dl and 224.8 ± 89 mg/dl respectively. Mean ESR was 37mm/ h and mean CRP was 9.6 mg/ dl. A statistically significant negative correlation was found between CRP and total cholesterol (p<0.001), CRP and HDL-cholesterol (P<0.001), CRP and LDL-cholesterol (P<0.001).[16] In our study mean ESR and CRP were 42 and 25 respectively,

which was slightly higher than this study. One study found that lipid profiles, disease activity for the 28 joint indices score (DAS-28) as well as ACR 50% response criteria were determined for all patients[17]. The mean DAS-28 at disease onset was 5.8 ± 0.9. ERA patients are characterized by an atherogenic lipid profile, which improves after therapy. Thus, early immuno-intervention to control disease activity may reduce the risk of the atherosclerotic process and cardiovascular events in ERA patients. Studies reported that the early Rheumatoid Arthritis (ERA) patients exhibited higher serum levels of total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) and lower serum high-density lipoprotein cholesterol (HDL-C) levels compared to controls[18-19]. As a consequence, the atherogenic index of plasma [log (TG/HDL-C)], and the atherogenic indices: TC/HDL-C as well as LDLC/HDL-C was significantly higher in ERA patients compared to controls. We found that in positive anti CCP, the mean RA factor (mean± s.d.) of patients was 70.56 ± 173.73. Difference of mean RA factor in anti-CCP was not statistically significant (p=0.4082). In positive anti-CCP, the average CRP of patients was 25.42 ± 30.33. Difference of mean CRP in anti CCP was not statistically significant (p=0.99).We found that in positive anti CCP, the mean DAS 28 (mean± s.d.) of patients was 5.22 ± 1.51. Difference of mean DAS 28 in anti CCP was not statistically significant (p=0.18). In DAS 28 <3.5, the mean WBC of patients was 6610 ± 1235. In DAS 28 3.5 to 5, the mean WBC of patients was 7124 ± 1950. In DAS 28 >5.0, the mean WBC (mean± s.d.) of patients was 7010 ± 2599. Difference of mean WBC vs. DAS 28 was not statistically significant (p=0.8974).Deswal S et al [20] found that LDL levels and total cholesterol levels were highly raised in RA patients but triglycerides were slightly raised in RA patients whereas HDL levels were significantly lowered in RA patients. In our study we found that HDL-C level did not shows significant changes in ERA patient.

Conclusion:

The study demonstrates that in early RA patients, the levels of TC, LDL-C are higher and levels of HDL-C , TG, are not different from the controls. This study also demonstrates that level of LDL-C is higher in the ERA patients with disease activity. Hence ERA patients have higher atherogenic nature. The management of dyslipidaemia in RA should be a part of the general cardiovascular risk management. Therefore, a good control of the disease activity should be the priority, given that both the quality of life and the long-term outcomes can be improved.

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Conflict of interest:

There is no conflict of interest.

Reference:

1. Emery P. The Roche Rheumatology Prize Lecture. The optimal management of early rheumatoid disease: the key to preventing disability. Br J Rheumatol 1994; 3:765–68.
2. Aletaha D, Eberl G, Nell VP, Machold KP, Smolen JS. Attitudes to early rheumatoid arthritis: changing patterns. Results of a survey. Ann Rheumatol Dis 2004; 63:1269–75.
3. Arnett FC, Edworthy SM, Bloch DA et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988; 31:315–24.
4. Saraux A, Berthelot JM, Chales G et al. Ability of the American College of

Rheumatology 1987 criteria to predict rheumatoid arthritis in patients with early arthritis and classification of these patients two years later. Arthritis Rheum 2001; 44:2485–91.

5. Symmons DP. Classification criteria for rheumatoid arthritis: time to abandon rheumatoid factor? Rheumatology 2007; 46:725–26.
6. Dixon WG, Symmons DP. Does early rheumatoid arthritis exist? Best Pract Res Clin Rheumatol 2005; 19:37–53.
7. van Aken J, van Bilsen JHM, Allaart CF, Huizinga TWJ, Breedveld FC. The Leiden Early Arthritis Clinic. Clin Exp Rheumatol 200; 21(Suppl 31):S100–S105.
8. Emery P. Treatment of rheumatoid arthritis. BMJ 2006; 332:152–55.
9. Ajeganova S, Catrina AI. Early arthritis- diagnosis and management. In: Bijlsma JWJ, Hachulla E(eds) *Eular textbook on rheumatic diseases,*3rd edn. London:BMJ group, 2018; 211.
10. Raza K, Falciani F, Curnow SJ et al. Early rheumatoid arthritis is characterized by a distinct and transient synovial fluid cytokine profile of T cell and stromal cell origin. Arthritis Res Ther 2005; 7(4): R784-95.
11. Wiles N, Dunn G, Barrett E, Silman A, Symmons D. Associations between demographic and disease-related variables and disability over the first five years of inflammatory polyarthritis: a longitudinal analysis using generalized estimating equations. J Clin Epidemiol 2000; 53:988–96.
12. Kobelt G, Jonsson L, Lindgren P, Young A, Eberhardt K. Modeling the progression of rheumatoid arthritis: a two-country model to estimate costs and consequences of rheumatoid arthritis. Arthritis Rheumatol 2002; 46:2310–19.
13. West E, Jonsson SW. Health-related quality of life in rheumatoid arthritis in Northern Sweden: a comparison between patients with early RA, patients with medium-term disease and controls, using SF-36. Clin Rheumatol 2005; 24:117–22.
14. Bukhari MA, Wiles NJ, Lunt M et al. Influence of disease-modifying therapy on radiographic outcome in inflammatory polyarthritis at five years: results from a large observational inception study. Arthritis Rheumatol 2003; 48:46–53.
15. Choy EH, Scott DL, Kingsley GH et al. Treating rheumatoid arthritis early with disease modifying drugs reduces joint damage: a randomised double blind trial of sulphasalazine vs diclofenac sodium. Clin Exp Rheumatol 2002; 20:351–58.
16. Shah SJ. Lipid profile in rheumatoid arthritis and its relation with inflammatory markers. Archivos de Medicina 2017; 2(1):6.
17. Georgiadis AN, Papavasiliou EC, Lourida ES et al. Atherogenic lipid profile is a feature characteristic of patients with early rheumatoid arthritis: effect of early treatment–a prospective, controlled study. Arthritis Res Ther 2006; 8(3):R82.
18. Parveen S, Jacob R, Rajasekhar L, Srinivasa C, Mohan IK. Serum lipid alterations in early rheumatoid arthritis patients on disease modifying anti rheumatoid therapy. Indian J Clin Biochem 2017; 32(1):26-32.
19. 19.Anoze A, Jasim ZM, Ewadh RS, Nassir SF. Serum Lipid Profile in Early Rheumatoid Arthritis. Med J Babylon 2007; 4(3-4):275-82.
20. Deswal S, Deswal M, Goel V, Singh H. Dyslipidemia in Rheumatoid Arthritis. Int J Health Sci Res 2016; 6(1):180-4.