Dyslipidemia in Rheumatoid Arthritis

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ABSTRACT

Background: Mortality in patients with rheumatoid arthritis (RA) is higher than in the general population, which is due mainly to premature cardiovascular disease. There is growing evidence that the-more or less persistent-high-grade inflammation present in RA is the main driver of the development of premature atherosclerosis and its complications. Dyslipidemia is highly prevalent in rheumatoid arthritis and appears to be present very early in the RA disease process. Lipid abnormalities have been shown to contribute to accelerated atherosclerosis, leading to an increased risk for cardiovascular diseases (CVD). For decades, increased low-density lipoprotein (LDL) levels have been recognized as strong predictors of CVD, and it is also known that high-density lipoproteins (HDL) usually protect from atherosclerosis. The objective of this study was to investigate the lipid profile in rheumatoid arthritis patients.

Methods: LDL, HDL, total cholesterol and serum triglycerides levels were determined in 25 clinically diagnosed adult rheumatoid arthritis female patients (as per 1987 ACR criteria) and an equal number of age and sex matched healthy subjects.

Results: In established RA, 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.

Conclusions: Our findings emphasize the need to raise awareness among healthcare professionals regarding the development of hyperlipidemia in RA patients. Screening for hyperlipidemia may be particularly important in patients with active RA to prevent cardiovascular related morbidity and mortality.

Keywords: Cardiovascular disease, Lipids, Lipoproteins, Rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic multisystem disease of unknown etiology characterized by persistent inflammatory synovitis, usually involving peripheral joints in a symmetric distribution. RA is a systemic disease often associated with cutaneous and organ-specific extra-articular manifestations. Epidemiological studies have disclosed an increased risk of premature atherosclerosis and an increased mortality due to CV events in patients with RA. [1-3]

Cardiovascular disease in RA may result from accelerated atherosclerosis caused by clinical or subclinical vasculitis. The main determinants of cardiovascular risk are concentrations of serum low density lipoproteins (LDL), high density lipoproteins (HDL) and triglycerides. RA-related inflammation that is responsible for synovial lesions may be implicated in the...
development of accelerated atherosclerosis, leading to increased risk of CVD. \[4,5\] Furthermore, the magnitude and chronicity of inflammation strongly correlated with the emergence of premature atherosclerosis in RA. \[6,7\] The positivity of rheumatoid factor (RF) or anti-cyclic citrullinated peptide (anti-CCP) antibodies or both appears to be associated with high prevalence of subclinical atherosclerosis in RA. \[8\] In addition, the presence of HLA-DRB1*04 shared epitope alleles and tumor necrosis factor (TNF)A-308 (rs1800629) gene polymorphism is associated with a higher risk of CVD in patients with RA. \[9,10\] Data regarding TC and LDL levels in RA patients have been conflicting, with reports indicating increased \[11\] decreased \[12\] or similar \[13\] levels compared with controls. Regarding HDL-cholesterol, it has been reported that patients with active RA consistently demonstrate reduced levels. \[14\]

Recent clinical studies identified elevated levels of pro-inflammatory cytokines, including TNF-\(\alpha\) and interleukin-6 (IL-6), as independent variables in association with artherosclerosis in rheumatic patients and the general population. TNF-\(\alpha\) cause deterioration of the lipid profile and promotes insulin resistance (IR), both of which are traditional risk factors for atherosclerosis. \[15\]

Aims and Objectives
To determine dyslipidemia in rheumatoid arthritis patients

Materials and Methods
The study was conducted in the Department of Physiology in collaboration with department of Medicine, Pt. B.D. Sharma PGIMS, Rohtak in 50 females of age group 30-50 years. Proven cases of rheumatoid arthritis (as per 1987 ACR criteria) on the basis of detailed history, clinical examination, routine laboratory investigations including baseline radiographic and biochemical evaluation from Rheumatology OPD were included in the study.

Control group comprised of 25 healthy female subjects of age 30 to 50 years while study group comprised of 25 female patients with Rheumatoid arthritis (RA) of more than 5 years. Low density lipoproteins (LDL), High density lipoproteins (HDL) and serum triglycerides levels were determined in established cases of RA (as per 1987 ACR criteria). Abnormal lipid levels were defined according to the Adult Treatment Panel III (ATPIII) guidelines as Total cholesterol \(\geq 240\) mg/dL, LDL \(\geq 160\) mg/dL, Triglycerides \(\geq 200\) mg/dL or HDL <40 mg/dL.

Inclusion criteria: Patients of rheumatoid arthritis with disease duration of more than five years as per 1987 ACR criteria were included in the study.

Exclusion Criteria: Patients with the following characteristics were excluded: diabetes mellitus, hypertension, hypothyroidism, hyperlipidemia treated with a lipid lowering therapy.

An informed consent was taken from the patients to participate in the study and the study was well within the ethical norms.

Statistical Analysis
The data in the study was expressed as mean±SD and was analyzed by using paired students’ ‘t’ test.

Observations

<table>
<thead>
<tr>
<th>Parameters</th>
<th>CONTROL GROUP (Mean ± SD)</th>
<th>RA PATIENTS (Mean ± SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SERUM LDL</td>
<td>116.48±11.09</td>
<td>155.96±36.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SERUM HDL</td>
<td>58.76±9.39</td>
<td>28.36±5.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SERUM TOTAL CHOLESTEROL</td>
<td>168.28±20.01</td>
<td>224.45±38.86</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SERUM TRIGLYCERIDES</td>
<td>150.84±24.09</td>
<td>147.16±37.61</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>
RESULTS

RA subjects had atherogenic lipid profile characterized by elevated total cholesterol, LDL cholesterol and decreased HDL cholesterol.

In established RA, LDL levels and total cholesterol levels were highly raised in RA patients and it was statistically very highly significant (p<0.001) when compared with control group whereas HDL levels were significantly lowered in RA patients and it was also statistically very highly significant (p<0.001) when compared with control group but triglycerides were slightly raised in RA patients although it was statistically insignificant (p>0.05).

DISCUSSION & CONCLUSION

In the present study we observed an increase in lipids and lipoproteins in rheumatoid arthritis patients as compared to healthy subjects. The lipid pattern observed in RA in our study is atherogenic lipid profile or dyslipidemia. Similar atherogenic lipid profile was observed by Mullick et al. [16] in early cases of RA. Rheumatoid arthritis is a multifactorial disease which affects the immune system and ultimately various tissues in the body. RA is characterized by local and systemic inflammation and wide range of biochemical markers contribute directly or indirectly to pathogenesis of RA. [17] Hypotheses exist that connect the inflammation found in RA to the accelerated atherosclerotic process: the synovitis, which appears at the joints, is associated with the release of a number of proinflammatory mediators. [18] These cytokines not only lead to local inflammation and joint destruction, but also gain access to the vascular system. Thus, they circulate and potentially affect distant organs such as the liver, as well as adipose tissue or the endothelium. [19] As a consequence, an unfavorable; ‘proatherogenic’ state may evolve.

One of the results of inflammation is insulin resistance. [20,21] Anti-rheumatic treatment with corticosteroids and sulfasalazine seems to improve insulin resistance. [22,23] Inflammation is further related to dyslipidemia. Endothelial dysfunction precedes manifest atherosclerosis, and the endothelium of RA patients shows signs of dysfunction. It has been shown with the use of flow-mediated dilatation that endothelium-dependent dilatation is impaired in RA patients when compared with control patients. This is already present early in the course and improves with anti-inflammatory treatment. The impairment of the endothelium is also evident at the cellular level. Endothelial progenitor cells (EPCs) derived from the hematopoietic system participates in the development and maintenance of the endothelial cell layer and has a potentially reparative role, protecting against ischemia and atherosclerosis. It has been demonstrated that in RA patients there is a reduced number and an impaired function of EPCs, which is associated with endothelial dysfunction. All these changes in the cardiovascular system are in line with increased cardiovascular morbidity and mortality in RA patients. [24]

Our findings emphasize the need to raise awareness among healthcare professionals regarding the development of hyperlipidemia in RA patients. Screening for hyperlipidemia may be
particularly important in patients with active RA to prevent cardiovascular related morbidity and mortality.

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1. Symmons DP, Gabriel SE. Epidemiology of CVD in rheumatic disease, with a focus on RA and SLE. Nat Rev Rheumatol. 2011; 31: 399-408.


