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Original Article

Lipid profile and its relationship with endothelial dysfunction and disease activity in patients of early Rheumatoid Arthritis

Omar Sharif Mullick [a], *Raja Bhattacharya* [a], *Kuntal Bhattacharyya* [a], *Rathindra Nath Sarkar* [a,*], *Adwitiya Das* [b], *Debajyoti Chakraborty* [a], *Arijit Sarkar* [c], *Abhisekh Das* [a]

[a]*Department of Medicine, Rheumatology Division, Calcutta Medical College, Kolkata,* [b]*Department of Preventive and Social Medicine, All India Institute of Hygiene and Public Health, Kolkata,* [c]*Department of Microbiology, GSL Medical College, Rajahmundry, AP, India*

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ABSTRACT

Background: Lipid profile derangements in patients with early rheumatoid arthritis (RA) have been described. These may predispose to premature atherosclerosis and early cardiovascular events. However data from India is sparse.

Objective: To evaluate the serum lipid profiles in patients of early RA, and assess the interrelationship between serum lipid profile, endothelial dysfunction, disease activity and inflammatory markers.

Materials and methods: 50 patients of early RA and 50 age and sex matched healthy controls were included in the study. Fasting lipid profiles and brachial artery flow mediated vasodilatation (FMV%) were estimated, along with other disease activity parameters in the RA group.

Result: Early RA patients showed an atherogenic lipid profile characterized by an increase in the Total Cholesterol (TC) (180.12 ± 16.50 versus 141.30 ± 9.57; p value < 0.0001) and Low Density Lipoprotein-Cholesterol (LDL-C) (126.82 ± 17.49 versus 79.36 ± 10.04; p value < 0.0001) and a reduction in the High Density Lipoprotein-Cholesterol (HDL-C) (37.92 ± 3.85 versus 44.42 ± 4.38; p value < 0.0001) as compared with their age and sex matched healthy controls. Mean FMV% in early RA patients (3.87 ± 1.70) was less than the controls (8.7 ± 1.58). Patients of early RA showed an atherogenic lipid profile with high atherogenic ratios of TC/HDL and LDL/HDL thus suggesting that these patients are at higher risk of developing atherosclerosis. There was significant correlation between lipoprotein levels, disease activity, endothelial dysfunction and inflammation.

Conclusion: Patients of early rheumatoid arthritis have an atherogenic lipid profile and impaired FMV%, which correlates with disease activity and inflammation.

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* *Corresponding author*. 43 GD, Sector-3, Salt Lake City, Kolkata, West Bengal 700106, India.
E-mail address: drrnsarkar09@gmail.com (R.N. Sarkar).

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1. Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory, multi system disease of unknown aetiology with a female preponderance characterized by significant morbidity, joint destruction and associated disability due to synovial inflammation.[1] Recent data suggests that various diseases associated with systemic inflammation including RA are associated with increased risk of premature atherosclerosis.[2] Atherosclerotic cardiovascular disease is the major cause of mortality and morbidity in RA patients and is thought to be due to production of different cytokines, pro inflammatory markers and activation of leucocytes.[3]

Various studies have shown that the lipid profile of untreated patients of early RA have low levels of High Density Lipoprotein Cholesterol (HDL-C).[4] However, the findings regarding the serum levels of Total Cholesterol (TC) and Low Density Lipoprotein Cholesterol (LDL-C) in early RA are not conclusive, though most studies suggest a lower level of TC, HDL-C and LDL-C compared to general population.[4–6] The reduction in HDL-C causes an increase in the TC/HDL-C ratio which represents the atherogenic index and serves as an important prognostic marker for cardiovascular disease.[4]

Endothelial dysfunction is an important sign of early atherosclerosis and a trigger of cardiovascular events. It may be detected as an impaired ability of the artery to dilate in response to a variety of physical and chemical stimuli, as a consequence of reduced nitric oxide bioavailability. The endothelial dysfunction can reliably be measured by a novel non-invasive method using ultrasonography, by assessing flow mediated vasodilatation (FMV) of brachial artery.

The present study was undertaken to assess serum lipid profile in patients of early RA, and to determine, if there is any inter-relationship between serum lipid profile, endothelial dysfunction, disease activity and inflammatory markers.

2. Materials and methods

This cross-sectional study was conducted among patients attending the outpatient or in patient clinic of the Department of Medicine and Rheumatology in Medical College Kolkata from 1st February 2012 to 31st July 2012. Patients with age between 18 and 55 years, newly diagnosed as rheumatoid arthritis as per the American College of Rheumatology and European League Against Rheumatism 2010 classification criteria for RA,[7] having disease duration of less than one year and without history of prior use of disease modifying anti-rheumatic drugs (DMARDs) and/or systemic glucocorticoids were included in the study. The exclusion criteria were: smoking, diabetes mellitus, hypothyroidism, liver disease, renal disease, Cushing's syndrome, history of familial dyslipidemia, body mass index >30, receiving medications affecting lipid metabolism, such as lipid-lowering drugs, beta-blockers, oral contraceptives, oestrogen, progestin, thyroxin and vitamin, pregnancy, active infection or neoplasm. Fifty patients of early rheumatoid arthritis and 50 age and sex matched healthy controls (comprising medical and paramedical staff of the institution who volunteered to participate, and were screened clinically and by laboratory tests) were included in the study.

After obtaining written informed consent the individuals were subjected to detailed history and clinical assessment. Laboratory assessment included fasting lipid profile, fasting blood sugar (FBS), urea, creatinine, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Liver function test (LFT), complete haemogram, Rheumatoid factor (RF). Chest X-ray (PA view), X-ray of both hand & wrist (AP). DAS-28 ESR and visual analogue scale (VAS) for pain and global health assessment was done to assess disease activity

$$\text{DAS28 ESR} = 0.56 \times \sqrt{(\text{t28})} + 0.28 \times \sqrt{(\text{sw28})} + 0.70 \times \text{Ln}\,(\text{ESR}) + 0.014 \times \text{GH}$$

where t28 is tender joints out of 28 counted, sw28 is swollen joints out of 28 counted, GH is global health status assessment by patient, 100-mm visual analogue scale. It was calculated using programmed calculator "Rheumatology Calculator LN-28", pharma-cal, china or URL: http://das-score.nl/www.das-score.nl/index.html.

Visual analogue scale for pain (VAS-pain) was measured on a double-anchored VAS (a horizontal line where each end represents opposite ends of a continuum) that is standardized to 15 cm in length. It is labelled 0 = no pain at left anchor point and 100 = severe pain at the right anchor point. Patients are instructed to place a vertical mark on the line to indicate the severity of their pain.

Visual analogue scale for global health assessment by patient (VAS-GH patient) is a 15 cm, double-anchored horizontal VAS that starts at 0 = very well to 100 = very poor. Handling patient responses and scoring are similar to the pain scale.

CRP levels were analyzed with a Cobas Integra system (Roche diagnostics, Switzerland). Serum lipid levels were measured using Hitachi 912 analyser (Roche Diagnostics, Germany). Rheumatoid factor was estimated using standard nephelometric assay.

Flow mediated vasodilatation (FMV) was assessed on the brachial artery by ultrasonography. The measurements were performed in supine position on the right arm after 10–20 min resting in a quite room. The brachial artery was scanned longitudinally just above the antecubital crease using a 10 MHz transducer probe in *hp*Agilant machine (Netherlands), by experienced radiologist in the department of radiology. The diameter of the brachial artery was measured at the time of systolic flow of blood observed by Doppler, on the interface between the media and adventitia of the anterior and posterior wall. Hyperaemia was induced by inflation of a pneumatic cuff (12.5 cm wide) [blood pressure measuring instrument sphygmomanometer was used] at 250 mm of Hg for 4 min on the most proximal portion of the upper arm. The arterial diameter measurement was repeated 45–60 s after sudden deflation of the cuff. The average of the three measurements of basal (before occlusion by pneumatic cuff) and post-hyperaemia (after occlusion by pneumatic cuff) diameter was used for the analysis. FMV was expressed as the relative increase in Brachial Artery Diameter during hyperaemia, and defined as [(post-hyperaemia diameter − basal diameter)/basal diameter]. It is expressed as percentage value.

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