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Original Article

Serum adiponectin and its impact on disease activity and radiographic joint damage in early rheumatoid arthritis – A cross-sectional study



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ABSTRACT

Objective: To study the level of serum adiponectin in steroid and DMARD naïve early rheumatoid arthritis patients and its correlation with disease activity and radiographic damage.

Materials and methods: Forty-three patients fulfilling ACR 2010 criteria for rheumatoid arthritis, with disease duration less than 2 years and 25 age, sex and BMI matched controls were recruited for the study between July 2012 to January 2013. Demographic data, tender joint count, swollen joint count, erythrocyte sedimentation rate, and rheumatoid factor status were recorded. Radiographs of hands and feet were obtained. BMI, DAS28-ESR and HAQ-DI were calculated. Serum concentration of adiponectin was measured by ELISA.

Results: Among 43 early rheumatoid patients (38 females), 18 had erosive disease. There were 25 controls (21 females). Median serum adiponectin levels (14 µg/ml), range (8.5–19) were significantly higher in early RA patients compared to controls (10.2 µg/ml), range (7.9–13.5) ($p = 0.02$). No difference in the adiponectin levels between erosive and nonerosive disease was noted. No correlation to duration of disease, BMI, waist hip ratio and disease activity was noted.

Conclusion: In this study, while exploring the levels of adiponectin in a cohort of early RA, we observed increased serum adiponectin concentration in steroid and DMARD naïve early rheumatoid arthritis patients.

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1. Introduction

Adipose tissue is a major source of several mediators, termed adipocytokines that include leptin, resistin, adiponectin, and

visfatin and also inflammatory cytokines, such as tumor necrosis factor alpha and interleukin-6 (IL-6).¹ Adipocytokines such as leptin, resistin, and visfatin are proinflammatory, whereas adiponectin is anti-inflammatory. Studies have shown that obesity was associated with reduced joint damage,

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but the underlying mechanisms are not known.¹ Obesity is associated with a chronic inflammatory response. Therefore, the association between obesity and reduced radiographic joint damage appears to be paradoxical.

Most studies on serum adiponectin in rheumatoid arthritis (RA) were done on patients who were on DMARDS and steroids and report higher concentration in patients. Serum adiponectin is altered by inflammation-modulating treatment including biologic and nonbiological agents such as TNF inhibitors, steroids and methotrexate as reported previously.² Most studies did not exclude conditions, including diabetes, hypothyroidism, hypertension chronic kidney disease, etc. which affect serum adiponectin concentration. This study determined the relation between adiponectin and early rheumatoid steroid and DMARD naïve RA patients with exclusion of confounding factors.

2. Materials and methods

Forty-three patients fulfilling American College of Rheumatology (ACR) criteria 2010 for a diagnosis of RA attending the Nizam's Institute of Medical Sciences, Hyderabad were recruited for the study. 25 healthy age, sex and BMI matched controls were enrolled.

Clinical information and laboratory data were obtained through a structured interview, self-reported questionnaires, physical examination, and blood tests. The degree of obesity was measured using the body mass index (BMI; in kg/m²) and also by waist hip ratio. Serum concentration of adiponectin was measured by singleplex ELISA (BioVendor, Czech Republic).

Disease activity was measured using the Disease Activity Score in 28 joints (DAS28). Functional capacity was measured using the modified Health Assessment Questionnaire (MHAQ), a standard 8-question instrument addressing activities of daily living (Pune version).³ X-rays of hands and feet were assessed for erosions. Erosive disease was labeled, if 2 rheumatologists and 2 radiologists opined that at least one erosion was noted on radiograph.

Inclusion criteria included patients with early RA (<2 years disease duration), DMARD naïve patients diagnosed by the ACR 2010 criteria for RA. Exclusion criteria included patients with RA on steroids, and having comorbidities such as diabetes, hypertension, hypothyroidism, not satisfying 2010 criteria and negative for both rheumatoid factor and anti cyclic citrullinated peptide.

All participants gave written consent. The study was approved by the Ethics Committee Board of the Nizam's Institute of Medical Sciences, Hyderabad, India.

2.1. Statistical analysis

This was a prospective observational study. In this study, descriptive statistics were reported as the mean and standard deviation. Concentrations of adiponectin were compared in RA patients and control subjects using Mann-Whitney *U* test. The relationship among serum adiponectin level and obesity (as indicated by the BMI), disease activity (DAS28), function (MHAQ) and inflammation (ESR) was assessed by using Spearman's rank correlation test.

Table 1 – Clinical and demographic characteristics of healthy controls and patients with early RA.

	RA (both erosive and nonerosive)	Controls	p value
Number of patients	43	25	
Sex (F:M)	38:5	21:4	
Age distribution (years)	35.0 ± 9.3	31.6 ± 8.3	0.10
Body mass index, kg/m ²	23.1 (19.8–25.3)	21.91 (19.31–24.29)	0.32
Median (IQR)			
Waist hip ratio	0.86 (0.82–0.93)	0.85 (0.82–0.88)	0.40
Median (IQR)			
Adiponectin (µg/ml)	14 (8.5–19)	10.2 (7.9–13.5)	0.02
Median (IQR)			

3. Results

The characteristics of patients with RA and controls and the concentrations of adiponectin in the 2 groups were shown in [Table 1](#). Median body mass index and waist hip ratio were comparable between RA patients and controls. Concentration of adiponectin is significantly higher in patients with RA than in control subjects ($p = 0.02$). Two were smokers in our RA patients, none in controls.

Out of 43 early RA patients, 18 had erosive disease. Clinical and demographic characteristics of erosive and nonerosive early rheumatoid arthritis patients are shown in [Table 2](#). Disease was more severe in patients with erosive disease as shown by significantly higher tender joint count, swollen joint count, DAS-28 ESR and duration of early morning stiffness compared to nonerosive disease. There was no statistically significant difference in BMI, waist hip ratio, and rheumatoid factor titers. Serum adiponectin levels were higher in erosive disease than in nonerosive disease, but it was not statistically significant ($p = 0.18$).

The Spearman correlations between adiponectin, BMI, and measures of inflammation and disease activities are shown in [Table 3](#). Serum adiponectin did not correlate with age, duration of disease, HAQ, DAS-28, tender joint count, swollen joint count, BMI, and waist hip ratio.

4. Discussion

Adiponectin is an adipocytokine, synthesized by mature adipocytes. Its concentration in serum is higher compared to other adipocytokines. Studies have also shown that low adiponectin plasma levels are associated with type 2 diabetes mellitus, dyslipidemia, and hypertension.^{1,4} Thus adiponectin is decreased in metabolic syndrome, which is considered an inflammatory state. However, classic inflammatory and immune-mediated diseases such as rheumatoid arthritis and systemic lupus erythematosus showed elevated levels of serum adiponectin.⁴

Studies in rheumatoid arthritis patients have demonstrated elevated serum adiponectin in the serum⁵ and synovial

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