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A STUDY FOR THE LEVEL OF ADENOSINE DEAMINASE CRP AND URIC ACID IN RHEUMATOID ARTHRITIS PATIENTS

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Abstract:
Introduction: Rheumatoid arthritis (RA) is characterized by inflammation of synovial membrane and oxidative stress has been implicated as mediators of tissue damage. Adenosine deaminase plays an important role in inflammation and uric acid, an endogenous antioxidant has free radical scavenging capacity.
Aims and Objectives: To estimate the level of ADA, CRP and uric acid in Rheumatoid arthritis patients and compare with controls.
Materials and Methods: The study group included a total of 102 subjects of which 52 were RA patients and 50 were healthy controls. Serum ADA, CRP, Uric acid and Rheumatoid factor levels were analyzed. Statistical analysis was performed using SPSS and student t test.
Results: Serum ADA, CRP and Rheumatoid factor levels were found to be significantly high in RA patients when compared to controls. No significant difference was observed in Uric acid ($p<0.02$) level in RA patients compared with controls.
Conclusion: There was a significant difference in the levels of ADA activity between the RA patients and healthy controls, which may indicate its usefulness in diagnosing the disease.
Keywords: Rheumatoid Arthritis, Adenosine Deaminase, Uric Acid

Introduction

Rheumatoid Arthritis (RA) is a chronic inflammatory multisystem disorder that affects primarily cartilage and joints. It is an autoimmune disease that produces pain, morning stiffness and loss of function. The synovial inflammation and destruction of joints is often progressive and leads to joint destruction (1-3). The prevalence of the disease is 1-2% in general population. In India alone there are some 10 million people with RA. It is associated with reduced life expectancy and is a major cause of chronic disability and handicap. It can occur at any age but is more common in people over the age of 30 years and affects female more often than male Rheumatoid arthritis (2, 4). It is still not clear what are the exact cause and factor that support the destructive inflammatory process in RA. Adenosine deaminase, is an enzyme, which is present in red cells and the vessel wall, it catalyses the irreversible hydrolytic deamination of adenosine to inosine and 2'-deoxyadenosine to 2'-deoxyinosine. Inosine and 2'-deoxyinosine are converted to hypoxanthine, xanthine and finally to uric acid (5). ADA is considered as a good marker of cell mediated immunity (6). During inflammatory process, this enzyme is released in extra cellular and serosal fluids and produces different levels of ADA. The levels depend on the numbers of nuclear cells, especially T cells and macrophages (7). High lymphocyte ADA activities were found to be elevated in those diseases in which there is cell mediated immune response (8).

Uric acid is a ubiquitous by-product of purine metabolism and was thought to have a beneficial role by acting as an endogenous antioxidant with 10 fold higher concentration in plasma, than vitamin C and vitamin E. It contributes 2/3rd of free radical scavenging capacity in plasma (9, 10). Some studies reported that ADA level rise but Uric acid level is no change in RA and some studies reported a rise in the level of serum ADA and uric acid in patients in RA patients. Hence this study was undertaken the changes in serum levels of ADA and Uric Acid level in RA patients.

MATERIALS AND METHODS:

The present case control study was carried out in the department of Biochemistry and orthopedics in Chirayu medical College, Bhopal, Madhya Pradesh, India. Patients were selected from the Ortho department. 52 patients of Rheumatoid arthritis were taken as cases and 50 healthy age matched women were taken as controls. The patients with age around 30 - 60 years were selected for this study. They all are from rural area of Bhopal. Patients of Rheumatoid arthritis were diagnosed according to the revised criteria formulated by the American college of Rheumatology. The written consent and all ethical measures were taken prior and during the study. Patients with positive RA factor were included in the study. Patients with osteoarthritis, inflammatory diseases, SCID, coronary artery disease, diabetes mellitus, infectious diseases and smokers were excluded from the study. Demographic characteristics including age, sex, body mass index (BMI), BP in all subjects, and drug intake and disease duration of RA patients were recorded.5 ml venous blood was drawn from antecubital vein in a plain tube. Serum was separated by centrifugation. The ADA activity was immediately estimated by spectrophotometric method (Tulip diagnostics-ADAMTB Kit). Uric acid was estimated by Uricase colorimetric method (ERBA Kit). RA factor and C reactive protein were estimated by Turbilatex method (Agappe diagnostic kit). Data are presented as mean ± standard deviation values. The statistical differences between cases and controls were determined by student independent sample *t*-test using SPSS version 16. Statically significance was defined at $p<0.001$.

RESULTS:

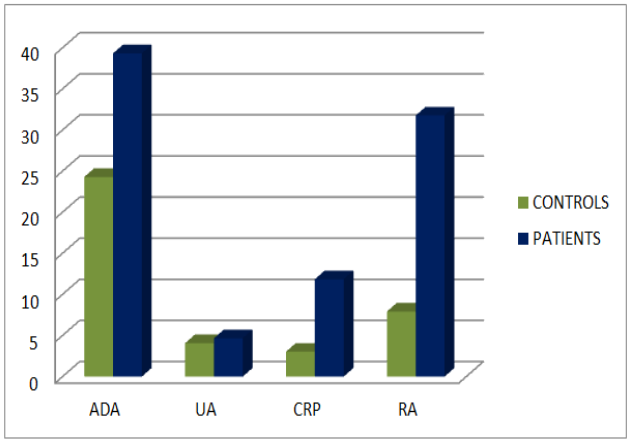
The study group comprised total 102 age and sex matched subjects among them, 52 (group 1) were RA patients and 50 (group 2) were healthy control subjects. The demographic characteristics of the subjects are shown in Table 1. There is no statistical difference was observed between the controls and RA patients in age, sex and BMI. Table 2 is showing the different parameters like RA, CRP, ADA, Uric Acid in controls and RA patients group. All rheumatoid arthritis patients included in the present study had positive RF. serum CRP levels were significantly raised (11.8±7.9 mg/L) in Rheumatoid arthritis patients ($p<0.001$) when compared with normal healthy control individual. Serum ADA levels were significantly elevated in RA patients (31.7±14.6 U/L) compared to that of the healthy controls ($p<0.0001$). There is no significant change of uric acid in RA patients and controls.

Table 1: Table is showing the demographic characteristics of the controls and RA patients.

	CONTROLS (n=50)	PATIENTS (n=52)
Age (mean±SD) years	33±9	41±10
Sex (F/M)	22/28	17/35
Body mass index (kg/m2)	24.6±5.0	26.8±4.2

Table 2: Table is showing the Mean and standard deviation for the parameters among controls and RA patients

Parameters	Normal range	Mean±SD (in Controls)	Mean±SD (in Patients)
RF (IU/ml)	0-18	7.9±3.8	31.7±14.6**
CRP (mg/L)	0-6	3.0±1.5	11.8±7.9**
ADA (U/L)	0-30	24.2±4.0	39.3±7.7**
Uric Acid (mg/dl)	3.5-7.2	4.0±1.1	4.2±1.4



DISCUSSION:

Rheumatoid Arthritis is most common inflammatory arthritis, affecting about 1% of the general population worldwide. RA is likely to affects female appropriately two times more than male and 80% of people with RA develop signs and symptoms of disease between 30-50 years of age. In our study female were more than 2 times higher compare with male and the means age was 41±52. T -cells play a key role in initiating and perpetuating the inflammation. The prominence of T-cells and monocyte/macrophages in rheumatoid synovium suggests that T cells may localize and amplify the effector functions of monocyte/macrophages in rheumatoid disease. T cells activated by dendritic cells or inflammatory cytokines, in turn activate monocytes/ macrophages, endothelial cells, smooth muscle cells and fibroblasts to produce pro inflammatory cytokines (tumor

necrosis factor alpha, interleukin-6), chemokines, tissue factor, the main inhibitor of the coagulation cascade in vivo and finally matrix metalo-proteinases responsible for tissue destruction (20-21). ADA is considered as a good marker of cell mediated immunity. During inflammatory process, this enzyme is released in extra cellular and serosal fluids and produces different levels of ADA. The levels depend on the numbers of nuclear cells, especially T cells and macrophages. High lymphocyte ADA activities were found to be elevated in those diseases in which there is cell mediated immune response (6-8). Most of the previous studies had shown a significant relation between the mean serum ADA level and disease activity markers (11-14). Zamani *et al.* found that a relationship between ADA and disease activity and reported that 'serum ADA may help to predict disease activity in RA Patients (14). Nalesnik *et al.* have indicated that ADA activity is directly related with inflammation and ADA could be a useful biochemical marker of inflammatory process in RA patients (13). The results of present study of serum ADA concentration was similar to results obtained by previous studies which suggested that serum ADA level in RA patients increases significantly as reported by Sari et al, Surekha Rani et al, Milada et al, Zahra et al, Gautam et al, Vyas Shalini et al (11,15-19). CRP is one of the most responsive acute phase serum reactants produced by liver. CRP produces various proinflammatory cytokines derived either from monocyte and macrophages and it reflects more short term changes in disease activity associated with joint destruction. In addition CRP determination is widely available, easy to perform and of low cost, making it the preferred biomarker of disease activity and play a pivotal role in pathogenesis of RA. In the present study the levels of CRP were significantly high in patients compared to controls and high values of CRP indicates of active inflammation in RA patients (11, 15, 23).

We have also estimated the levels of uric acid which is a protective antioxidant, particularly effective in quenching hydroxyl, superoxide and peroxinitrite radical, thereby preventing lipid peroxidation. We have not found any significant change in the uric acid level in the rheumatoid arthritis patients compared to the healthy individuals. Though we expect that an increase in uric acid levels due to increase in adenosine deaminase levels in rheumatoid arthritis patients, our study showed normal uric acid levels but the reason may be due to increased utilization of uric acid in trapping the free radicals produced and its conversion to allantoin (9,14, 22).

CONCLUSION:

Serum ADA level has been found to be increased in RA patients, which indicate its usefulness in diagnosis the disease. During inflammations of RA ADA is released in extra cellular location, resulting in the considerable increase of its activity by cell mediate immunity. It indicates that this may be evaluated as a diagnostic marker of the RA patients but uric acid is not a significant marker in RA patients.

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