Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2014; 2(5C):1711-1714 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com **DOI:** 10.36347/sjams.2014.v02i05.044

Research Article

Relationship between Uric Acid and Ascorbic Acid in Rheumatoid Arthritis Patients

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Abstract: It has been well accepted that oxidative stress plays a crucial role in the pathogenesis of various chronic diseases including rheumatoid arthritis (RA). Although some studies suggest that uric acid as an important factor in precipitation of disease process by inducing inflammation, there is no satisfactory explanation for its role in disease complexity. Uric acid also acts as an antioxidant in vivo. The objective of present study was to determine the level of serum urate and plasma ascorbate in RA patients and to determine their role in disease process. Serum uric acid and plasma ascorbic acid levels were estimated by using standard methods in 30 patients of RA and in 30 age matched healthy volunteers, served as control. The values were expressed as Mean ± SD and data from patients and controls were compared using students't' test. Serum urate levels were significantly high ($p<0.05$) and plasma ascorbate levels were significantly low in patients as compared to control. These finding suggest that elevated serum urate level is associated with enhanced protective mechanism against oxidative stress and decreased ascorbate level is due to its free radical scavenging and urate radical repairing action in RA. Therefore, serum uric acid and ascorbic acid are efficient marker of oxidative stress status in rheumatoid arthritis patients. In addition, ascorbate supplementation in drug/diet regime in these patients can prove to be protective.
Keywords: Oxidative stress, Uric Acid, Ascorbic Acid, Rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis, a major inflammatory joint disease, is characterized by destruction of cartilage, bones and joints. Free radicals mediated oxidative stress plays a significant role in the etio-pathogenesis of certain chronic diseases including rheumatoid arthritis [1]. To combat with oxidant mediated injury, the most important biological antioxidants would appear to be vitamin C, uric Acid, vitamin E, glutathione peroxidase, catalase and superoxide dismutase etc. Vitamin C, an exogenous water soluble antioxidant functions as primary defense against free radicals in plasma and disappeared more quickly. It has a significant role in protecting plasma lipids against peroxidation (i.e. anti atherosclerotic effect) and positive correlation with HDL-cholestrerol [2]. Moreover, ascorbate concentration in blood has been found to be protective in various chronic inflammatory disease and age related complications as well [3].

Uric Acid, an end product of purine metabolism and is thought to act as an endogenous antioxidant in vivo. It is an endogenous, preventive and chain breaking antioxidant which contributes about 65% of free radical scavenging action, stabilizes ascorbate, protects DNA and erythrocytes from oxidative damage [4]. Agerter and Kirkpatrick reported that uric acid is responsible for the attack of arthritis [5]. Indeed, it is even not clear at this stage whether uric acid has damaging or protective effect in rheumatoid arthritis patients. Therefore, the objectives of present study was to estimate serum uric acid and plasma ascorbic acid levels in rheumatoid arthritis patients and to determine the relationship of these two parameters with disease complexity which may confer us more rational approach to the treatments of such degenerative joint diseases.

MATERIALS AND METHODS

In the present study 30 patients of both sex with Arthritis and 30 age matched healthy individuals, served as control, were taken. A general information or pre-experimental questionnaire regarding demographic information, family history and limited physical examination including blood pressure measurement was completed from all the subjects after taking their informed consent and approval of protocol by ethics committee of college. Patients with diabetes mellitus, hepatic disease, hypertension, those taking antioxidant vitamin supplements or non-steroidal anti–inflammatory drugs and with other connective tissue disease like systemic sclerosis and osteoarthritis were excluded. Fasting blood samples were collected in EDTA vials from the anticubital vein of the study group subjects and processed immediately. Serum uric acid was estimated by Caraway's method and plasma ascorbate by Mc Cormick and Greene method spectrophotometrically [6, 7]. Values were expressed as Mean ± SD. The significance of mean difference between groups was compared by using Student's t-test and distribution of probability (P).

RESULTS

In the present study, serum uric acid levels were significantly high in patients with rheumatoid arthritis as compared to healthy controls (Table 1, $p<0.001$) whereas plasma ascorbic acid levels were significantly low in patients as compared to controls ($p<0.05$), as represented in Table 1 and Fig. 1. A statistically significant negative correlation was observed between rise in serum urate level and fall in plasma ascorbate level in R.A. patients. ($r = - 0.74$).

Table 1: Serum uric acid and plasma ascorbic acid level in control and patient group (Mean ± SD)

Sl. No.	Parameter	Control group	Patient group	Level of Significance	% Increase	% Decrease
1.	No. of samples	30	30	-	-	-
2.	Male: Female ratio	1:1	1:1	-	-	-
3.	Uric acid (mg %)	4.27 ±0.63	6.91 ±1.89	p<0.001	62%	-
4.	Ascorbic acid (mg %)	0.78 ± 0.12	0.35 ± 0.03	p<0.05	-	57.2%

Where, * p<0.05 : Significant; ** p<0.001 : Highly Significant

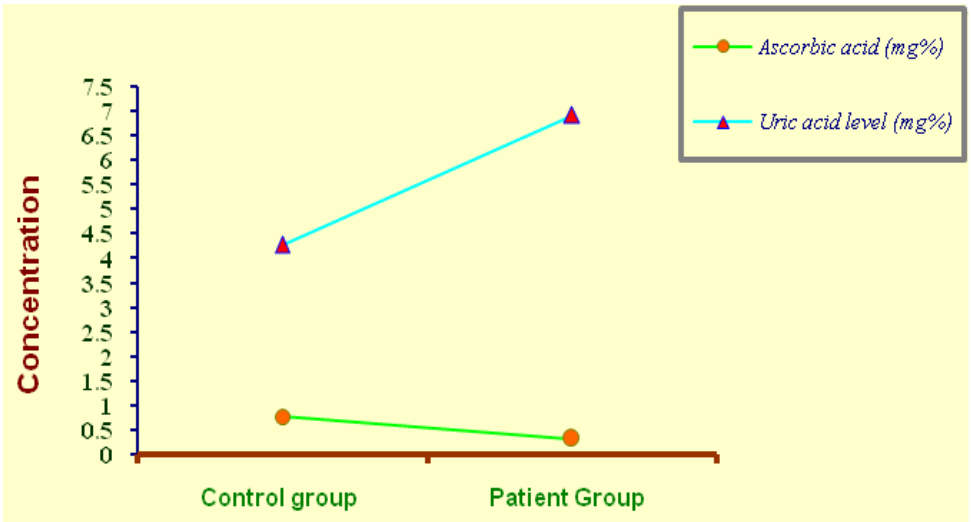


Fig. 1: Plasma ascorbic acid and serum uric acid levels in study group subjects

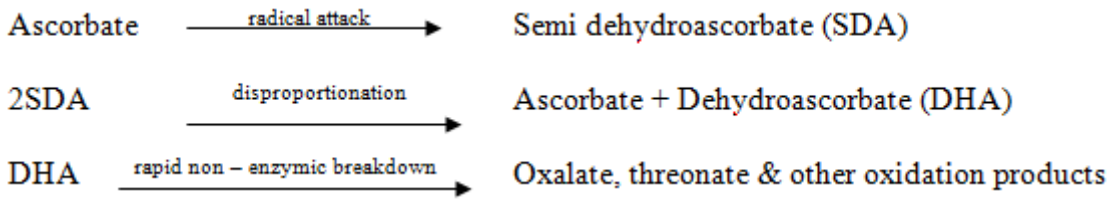
DISCUSSION

Reactive oxygen species have been implicated in a number of chronic diseases such as rheumatoid arthritis, osteoarthritis etc. [8]. In rheumatoid arthritis patients, neutrophils migrate into the synovium and release large amount of free radicals eg. Superoxide radical ($O_2^{\cdot}$), hydrogen peroxide and highly reactive hydroxyl radical ($OH^{\cdot}$). These free radicals attack and damage the hyaluronic acid and cartilage of synovial fluid, and at confluence, contributing to the destruction of joints [9].

To combat with oxidant mediated injury, there are various sorts of antioxidants present in the body. Amongst these, uric acid and ascorbic acid are important biological antioxidant present in extra cellular fraction. Ames et al. pointed out the fact that urate provides antioxidant defense against radicals causing cancer and aging in humans which in turn direct the researchers towards the antioxidant role of uric acid in rheumatoid arthritis. In the present study, serum urate concentration was found to be significantly high ($p<0.001$) in the patients as compared to healthy controls. Our findings were in agreement with the

previous findings of Allen *et al*. [10]. According to him, hyperuricemia in RA patients may be due to increase concentration of xanthine oxidase which catalyse oxidation of hypoxanthine and xanthine to uric acid. Increased concentration of xanthine oxidase also produces superoxide anion in synovium that attack and damage the hyaluronic acid and cartilage of synovial fluid leading to destruction of joint and aggravation of hypoxic – reperfusion injury. Urate has been found to be an excellent scavenger of superoxide anion and thus inhibit the oxidative degradation of hyaluronic acid, as reported by Liu [11].

Another most important antioxidant in human extracellular fluid is ascorbic acid which disappears rapidly under condition of oxidative stress [12]. In the present study, plasma ascorbate concentration was found to be significantly low in rheumatoid arthritis patients ($p<0.01$) as compared to control and negative correlated ($r = – 0.74$) with that of serum urate levles. Our findings were quite similar to the findings of Lunec *et al*. [13]. The main reason behind the depletion of ascorbate level in rheumatoid arthritis patient is due to its reaction with free radical in order to scavenge them.



Thus, ascorbic acid get oxidised to dehydroascorbate, followed by non–enzymic breakdown into a number of oxidation products in synovial fluid in the knee joint of rheumatoid arthritis patients [14]. Maple and Mason documented the fact that the ascorbic acid not only scavenges reactive oxygen species but also repairs the urate radical generated by attack of free radicals on uric acid. As a consequence, uric acid level increases with simultaneous decrease in ascorbate level, under condition of oxidative stress [15]. These studies ensure us that another reason of decreased ascorbate level in rheumatoid arthritis, as observed in the present study, is due to urate radical repairing action of ascorbate as well.

CONCLUSION

On the basis of present study and the findings of previous studies, we conclude that both uric acid and ascorbic acid are important biological antioxidant in rheumatoid arthritis patients, and alteration in their level is not only the risk factor for rheumatoid arthritis but also a useful tool in the assessment of oxidative stress status in arthritic patients. High level of uric acid provide antioxidant defense against free radicals and low level of ascorbate is due to its urate radical repairing & free radical scavenging action in rheumatoid arthritis patients. Thus, the changes occur during rheumatoid arthritis cannot be avoided but can be delayed and controlled to some extent by antioxidants supplementation. Therefore, ascorbate supplementation in diet/drug regime can prove to be protective against oxidative stress induced free radical damage in rheumatoid arthritis.

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