

Original Research Article

Assessment of Adenosine Deaminase and Total Antioxidant of Rheumatoid Arthritis Patients in Hilla City

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Abstract

Rheumatoid arthritis is an inflammatory, autoimmune disease that causes pain, joint stiffness and loss of function. It can occur at any age but is more common in persons over the age of 30 years and affects women more often than men. The Aims of the study is Compare changes in Adenosine deaminase activity among patients with rheumatoid arthritis and control group, Compare total anti-oxidant for patients with RA and control group. The study was conducted in rheumatology unit in Marjan teaching hospital in Hilla city / Babil / Iraq from 1st December 2014 to 1st February 2015.

The present study was conducted on (60) patients with rheumatoid arthritis and (53) apparently healthy subjects were taken as control group and the ages between (30–79) years. The sera obtained from the blood of patients and healthy subjects were used to measure the concentrations of Adenosine deaminase and Total antioxidant capacity.

ADA is an important enzyme of purine metabolism catalyzing the irreversible deamination of adenosine to form inosine and is considered as a marker of cell mediated immunity.

RA patients have lower levels of serum antioxidants comparison to healthy person.

In comparison with the control group, the patients with RA showed a significant increase in of Adenosine deaminase ($P \leq 0.05$) concentrations ($120.91 \text{ ng/ml} \pm 7.171$ vs. $50.717 \text{ ng/mL} \pm 5.613$), and a significant decrease in Total antioxidant capacity ($P \leq 0.05$) concentration (2.8214 ± 1.118 vs. 9.413 ± 1.48).

Key words : ADA, T-AOC, RA, Seurm

الخلاصة

التهاب المفاصل الروثوي هو مرض المناعة الذاتية والالتهابات التي تسبب الالم وتيبس المفاصل (خصوصا في الصباح) وفقدان الوظيفة , على الرغم من ان هناك العديد من اشكال التهاب المفاصل والتي تعرف بشكل شاسع لكن التهاب المفاصل الروثوي اكثر شيوعا والثاني (بعد هشاشة العظام). المرض يمكن ان يحدث في أي سن لكن اكثر شيوعا في الاشخاص الذين تزيد اعمارهم عن 30 سنة. يزداد المرض بشكل ملحوظ عند النساء اكثر من الرجال. تهدف الدراسة الى مقارنة التغيرات في نشاط الادينوسين دي امينيز بين المرضى الذين يعانون من التهاب المفاصل و مجموعة الاصحاء و كذلك مقارنة مضادات الاكسدة الكلية لمرضى التهاب المفاصل و مجموعة الاصحاء

أجريت هذه الدراسة في وحدة امراض الروماتيزم في مستشفى مرجان التعليمي في مدينة الحلة من 1 كانون الاول 2014 الى 1 شباط 2015 حيث تضمنت الدراسة (60) مريضاً مصاباً بالتهاب المفاصل الروثوي و (53) شخصاً معافى ظاهرياً لمجموعة الاصحاء. تم استخدام الامصال التي تم الحصول عليها من دم المرضى والاصحاء لقياس تركيز ادينوسين دي امينيز ومضادات الاكسدة.

و بالمقارنة مع مجموعة الاصحاء فان مرضى التهاب المفاصل الروثوي اظهروا زيادة معنوية في تركيز ادينوسين دي امينيز ($120.91 \text{ ng/ml} \pm 7.171$) و بالمقارنة مع مجموعة الاصحاء فان مرضى التهاب المفاصل الروثوي اظهروا انخفاضاً معنوياً في الجهد الكلي المضاد للاكسدة (2.8214 ± 1.118 vs. 9.413 ± 1.48) ($P \leq 0.05$) و انخفاضاً معنوياً في الجهد الكلي المضاد للاكسدة (2.8214 ± 1.118 vs. 9.413 ± 1.48) ($P \leq 0.05$).

Introduction

Rheumatoid arthritis is an inflammatory, autoimmune disease that produces pain, joint stiffness - particularly in the morning - and loss of function. While there are many types of arthritis, of those commonly known, rheumatoid arthritis is the most serious and the second most common (after osteoarthritis). 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 affects the whole body, including several organs, and so is described as a systemic disease[1].

Progressive and irreversible joint damage is caused by the immune system attacking its own body tissues, particularly those lining the joints. Joint pain and swelling lead to structural deformities and disability, causing a reduction in joint movement and muscle use. In turn, muscle size and strength decreases and the resulting abnormal forces on tendons cause deformity. The disease can also lead to problems with the heart, respiratory system, nerves and eyes.

The disease primarily affects the synovial joints, resulting in pain, deformity and eventual functional limitation, causing substantial morbidity and accelerated mortality [2].

The incidence of RA is typically two to three times higher in women than men and the onset, in both women and men, is highest among those in their sixties [3].

The epidemiology of RA is quite well characterized. RA is the most common chronic inflammatory joint disease, affecting 0.5-1 % of the populations in the industrialized world and women more frequently than men (3:1)[4-6].

The causes of the disease are unknown; however, several cases of indirect evidence suggest that environmental factors play an important role: RA has already at the time of its description been regarded as a disease of the poor and lower levels of education and upbringing under adverse socioeconomic conditions are afflicted with a more severe course of RA [7], smoking may increase the risk and possibly also the severity of RA and is associated with increased tumor necrosis

factor (TNF) and autoantibody production which in turn is related to genetic factors characteristic of RA [8]Over time, rheumatoid arthritis can cause joints to deform and shift out of place [9].

Diagnosis is generally based on clinical assessment, laboratory tests and X-rays. The initial clinical assessment will be based on the symptoms, the pattern of joints involved and the person's medical history. The doctor will also check for the presence of rheumatoid nodules-lumps under the skin that occur near affected joints [10].

- Laboratory tests include measuring the level of an antibody called rheumatoid factor (RF) in the blood. However the presence of RF does not establish a firm diagnosis, as only about 80% of people with rheumatoid arthritis test positive, while about 5% of people without the disease test positive. More recently, the anti-CCP (anti-cyclic citrullinated peptide antibody) test has been added. The two tests (RF and anti-CCP) when combined are better able to diagnose rheumatoid arthritis in its early stages [11].

This study include two parameters total anti-oxidant and Adenosine deaminase

Oxidative stress is thought to contribute to the development of a wide range of diseases including rheumatoid arthritis[12].

Adenosine deaminase is an important enzyme of purine metabolism catalyzing the irreversible deamination of adenosine to form inosine[13]and is considered as a marker of cell mediated immunity[14].Serum ADA was found to reflect monocyte/macrophage activity in inflammatory conditions such as RA and has also been suggested as a marker of inflammatory processes in RA [15].It is well-known that continued disease activity results in joint damage, decreased physical activity or even irreversible disability [16].Hence, early diagnosis and intervention help in reducing the morbidity associated with RA. Besides clinical indices such as Disease activity score (DAS), evaluation of inflammatory biomarkers provides a means of objectively estimating the degree of inflammation, thereby allowing optimised treatment plans.

The aims of this study was to compare changes in adenosine deaminase activity among patients with rheumatoid arthritis and control group and to compare total anti-oxidant for patients with rheumatoid arthritis and control group

Materials and Methods

The study was conducted in rheumatology unit in Marjan teaching hospital in Hilla city / Babil/Iraq from 1st December 2014 to 1st February 2015.

The present study was conducted on (60) patients with rheumatoid arthritis and (53) apparently healthy subjects were taken as control group , the ages between (30 – 79).

The sera obtained from the blood of patients and healthy subjects were used to measure the concentrations of adenosine deaminase and total antioxidant capacity

Biochemical test

- ❖ Adenosine Deaminase ADA
Concentration was measured by Enzyme linked immunosorbent assay kit (Elabscience, China).

The ELISA kit uses sandwich–ELISA as the method.

- ❖ Determination the concentration of T-AOC (Total Anti - Oxidant Capacity) in serum (Elabscience, China).

Statistical Analysis

SPSS program (20 version) was used in this study. All values were expressed as mean $\pm$ standard deviation (SD). Unpaired T-test and Chi-square was used to estimate differences between groups. The differences were considered significant when the probability (P) was less than 0.05 ($P < 0.05$) highly significant when the probability (P) was less than 0.01 ($P < 0.01$).

Results

Measurement of Adenosine deaminase (ADA)

1- Effect of Age on ADA level

The current study revealed that the mean level of serum ADA in patients was significantly higher than that in healthy control (120.91 ng/ml $\pm$ 7.171 vs. 50.717 ng/mL $\pm$ 5.613) as shown in figure (1).

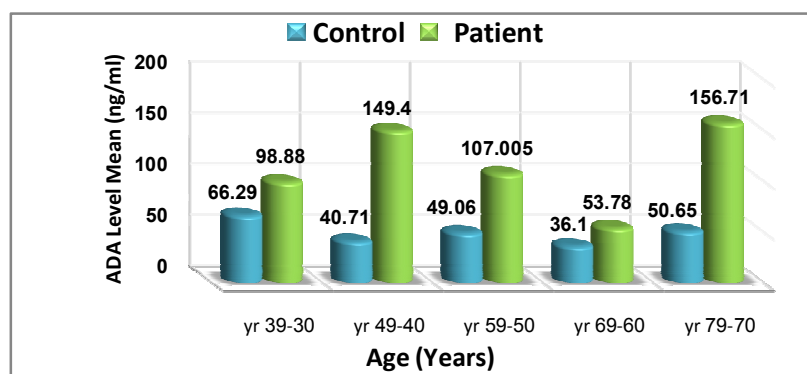


Figure 1:Concentration mean of ADA (ng/mL) in patients with RA compared with control group

2- Effect of gender on ADA level

The current study revealed that the mean level of serum ADA in patients females group was significantly higher than males patients group 126.186 ng/ml $\pm$ 8.556 vs. 78.611 ng/mL $\pm$ 8.242).

The mean level of serum ADA in males control group was more than females control group (106.51 ng/ml $\pm$ 8.91 vs. 63.72 ng/mL $\pm$ 4.995) as shown in figure (2).

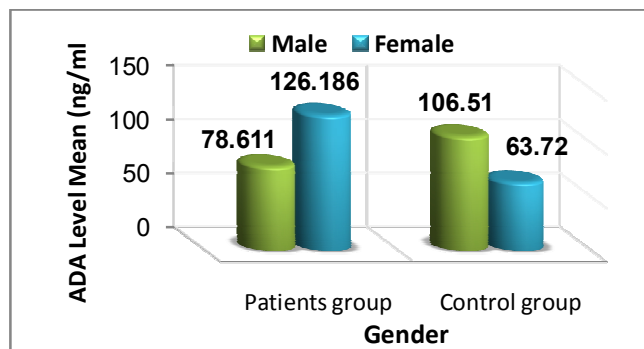


Figure 2: Concentration mean of ADA (ng/mL) according to gender in patients with RA compared with control group.

3- Effect of Residence on ADA level

The current study revealed that the mean level of serum ADA in patients rural area group was higher than patients urban area group ($125.10 \text{ ng/ml} \pm 8.788$ vs. $121.59 \text{ ng/mL} \pm 9.684$), and the control rural area

group was higher than control urban area group ($59.30 \text{ ng/ml} \pm 4.407$ vs. $54.38 \text{ ng/mL} \pm 4.188$) as shown in figure (3).

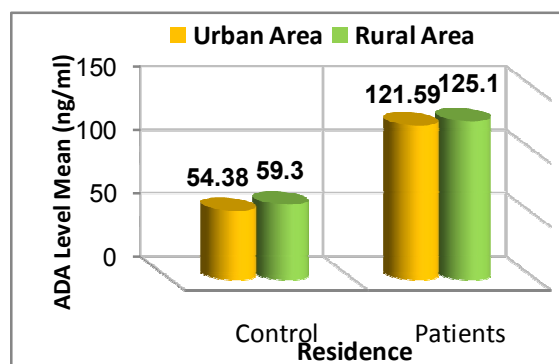


Figure3: Concentration mean of ADA (ng/mL) according to residence in patients with RA compared with control group.

Measurement of Total antioxidant capacity (T-AOC)

The concentration of (T-AOC) was decreased significantly in patients with

rheumatoid arthritis compared with control group as shown in Figure (4).

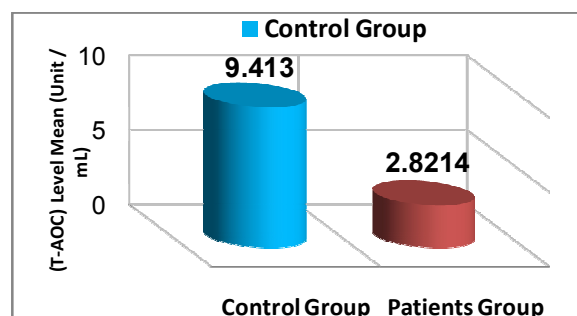


Figure 4: Total anti-oxidant level (Unit/mL) in patients with rheumatoid arthritis compared with control group

Discussion

Adenosine deaminase (ADA) is introduced as helpful marker in diagnosis, prognosis, and monitoring of treatment in rheumatoid arthritis [17-18], Serum ADA levels were found to be significantly higher in RA patients compared to controls (figure 1). Although the exact cause of increase in ADA levels is not known, the activity may be increased due to its release from damaged cells and increased cellular proliferation in RA [19].

ADA catalyzes the irreversible hydrolysis of adenosine to inosine. Adenosine has been shown to be a potent endogenous anti-inflammatory agent [20]. The enzyme ADA represents a checkpoint in the regulation of extra cellular Adenosine levels [21] and thus is likely to modulate the inflammatory processes. Hence, although determination of serum adenosine levels is an appropriate way to assess disease activity in RA [21], ADA also seems to be a prediction marker of the inflammatory process in RA [22]. ADA has been suggested as a helpful biochemical marker of inflammatory process in the patients with RA [23-24].

Rheumatoid arthritis patients have lower levels of serum antioxidants, including vitamin E, vitamin C, β -carotene, selenium and zinc in comparison to healthy person [25].

The Total Antioxidant Activity in patients Group was found to be significantly lower ($p < 0.05$) than normal subjects shown (figure 4). This can be attributed to the oxidative burden generated due to increased reactive oxygen species and body's attempt to circumvent this oxidative insult. Lastly, the level of Uric acid which was considered for the patients of Rheumatoid Arthritis were found to be significantly elevated than that of normal subjects [26-27]. Unstable free radical species attack cellular components causing damage to lipids, proteins, and DNA [28].

Living organisms have developed complex antioxidant system to counteract (ROS) and to reduce their damage. The sum of endogenous and food-derived antioxidants represents the total antioxidant capacity (i.e. TAC) of the system [29].

Significant decrease in (TAC) in patients with Rheumatoid Arthritis compared to control group observed in the present study may be attributed to oxidative stress, which causing free radical formation resulting in tissue damage, and imbalance between the production and detoxification of (ROS) results in oxidative stress [30].

Conclusion

- 1- Total anti-oxidant capacity was decreased significantly in patients with Rheumatoid Arthritis compared with control.
- 2- Acute Rheumatoid Arthritis is associated with elevated oxidative stress as indicated by decreased total anti-oxidant capacity.
- 3- Adenosine deaminase levels was significantly higher in patients with RA compared control
- 4- Increase in ADA levels due to release from damaged cells and increased cellular proliferation in Rheumatoid Arthritis
- 5- Adenosine deaminase has been suggested as a prediction marker or a useful biochemical marker of inflammatory process in patients with Rheumatoid Arthritis

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