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Oxidative Stress in Patients with Rheumatoid Arthritis

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Abstract

Background: There is a relationship between oxidative stress and rheumatoid arthritis.

Objective: To assess oxidative stress parameters represented by total antioxidant status and malondialdehyde, in patients with rheumatoid arthritis.

Design: case -control study.

Setting*:* Referred patients from private clinics .

Methodology: The study was conducted on patients with rheumatoid arthritis, referred from private clinics of rheumatology**.** The study period from Nov.1st 2017 and Jun. 1st 2018. Thirty-four female with rheumatoid arthritis, and thirty, sex and age-matched healthy volunteers as control group were participated in the study. Total antioxidants status and malondialdehyde were measured in both groups.

Results: Rheumatoid Arthritis patients have lower total antioxidants status values than that of the control group (0.94±0.24 and 1.95±0.20 respectively) (P value <0.0001). The malondialdehyde values was higher in patients group than control group (1.34±0.42 and 0.88±0.26 respectively) (P value <0.0001).

Conclusion: Rheumatoid Arthritis patients have decreased level of total antioxidants status and increased level of malondialdehyde than the control group .

Key words: Antioxidant status, Oxidative stress, Rheumatoid Arthritis

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Introduction

Rheumatoid arthritis (RA) is multisystem chronic autoimmune disease of unknown aetiology with prevalence up to 1-2% of the total world population (Mclnnes and Georg, 2017, p2328), causing destruction of joint, ligaments, and tendons, which lead to physical disability (Kumar *et al.,* 2016, p 510). Women are affected more than men (Phaniendra *et al.,* 2015, p11).

Although the onset is more frequent in 40's or 50's, RA can affect individuals of any age (Gibofsky, 2012, p295).

There is no single etiologic factor and it is a multifactorial, affect the susceptible host that trigger reactions leading to RA (Desai *et al.,* 2010, p959).

Oxidative stress has been defined as the imbalance of oxidant/antioxidant forces in favor of the oxidant (Ibrahim *et al.,* 2008, p195). In the lack of adequate antioxidant protections, oxygen radicals can cause oxidation of macromolecules resulting in oxidative damage of lipids, proteins and DNA (Griffiths *et al.,* 2002, p875).

Researchers are interested to determine the cause of RA. It is thought that certain environmental factors such as infection could stimulate the immune system in susceptible individuals to cause inflammation in multiple tissues (Chandankhede and Gupta, 2013, p3088). In the same time during the inflammatory processes, and during the activation of neutrophil granulocytes, macrophages and lymphocytes, the oxygen and nitrogen species produced . The generation of free radicals (FR), especially oxygen species and nitrogen species (OS/NS) induce cartilage damage through either degradation of matrix or activation of matrixmetalloproteinases (MMPs) (Zheng *et al.,* 2017, p1923).

Although RA is an autoimmune inflammatory disease whose pathogenic mechanisms remain to be elucidated, it is clear that oxidative stress contribute in the disease process; therefore, this study was aimed to:

1. Evaluate the antioxidant status of RA patients.
2. Evaluate the oxidative stress in patients with RA.

Subjects and methods

The study had approval from Mosul College of Medicine. Thirty-four female patients whose ages range between (35-50) years, known to have Rheumatoid Arthritis (RA) according to the American College of Rheumatology (ACR), receiving conventional treatment, enrolled in this study. Another thirty healthy subjects , were considered as a control group.

Individuals receiving trace element, antioxidants or vitamin B complex, smokers and alcohol users, patients with acute or chronic illness other than RA, were excluded from study.

Total antioxidants status was measured using Randox TAS kit (London – UK) (Miller et al., 1993, p704)

Serum MDA level, measured using thiobarbiturc acid (TBA) assay. (Buege, and Aust, 1978, p302) .

Statistical analysis

Unpaired T-Test was used to identify the variation in these variables. All values expressed as Mean ± SD and P value of <0.05 was considered to be statistically significant (Kirkwood , 1988, p43).

Results:

The individuals in the RA and control groups were comparable in terms of age , as shown by non statistically significant differences between the groups ($p > 0.5$) as shown in table (1). Table (2) Shows the results of comparisons of TAS and MDA between studied groups.

Table (1): The age of the studied groups.

Parameters	Patients (n=34)	Control (n=30)	P value
Age (years)	42.79±10.30	40.10±8.17	0.256

There are very significant differences between patients group and control (p-value = 0.000), regarding TAS and MDA value as shown in table (2)

Table (2): TAS and MDA serum level of the studied groups.

Parameters	Patients (n=34)	Control (n=30)	P value
TAS (mmol/L)	0.94±0.24	1.95±0.20	0.000
MDA(µmol/L)	1.34±0.42	0.88±0.26	0.000

Discussion

The present study was performed to assess the antioxidant status in a sample of RA patients by measuring total antioxidant status (TAS), in a parallel way; oxidative status was evaluated, by measurement plasma levels of a byproduct of lipid peroxidation, *i.e.* malondialdehyde (MDA).

The current study involved 64 individuals divided into 2 groups of 34, and 30 for RA patients and control subjects respectively. Both groups were matched concerning their ages as confirmed statistically by the absence of significant differences between the studied groups. This matching of individual groups may exclude any effect of this factor on the results of the study. The removal of this factor interference with results of clinical trials were done in the majority of other trials concerning antioxidant field (Jimenez-Jimenez *et al.,* 1998, p75; Besler *et al.,* 2003, p78; Besler and Comoglu 2003, p189; Miller *et al.,* 2011,p1012) .

The present study demonstrated that TAS level was lower in RA patients (0.94±0.24 mmol/l), when compared with the control group (1.95±0.20 mmol/l), (P= 0.001). These results are in accordance with studies done by (Shah *et al*., 2011, p1010; Mohammed *et al*.,2016, p2591)

Jaswal *et al*., (2003) assessed total oxidant status (TOS), and total antioxidant status (TAS) in 40 RA patients; they found RA patients have low level of antioxidants and high plasma level of MDA.

Zhou *et al.*, (2017) found in their study that patients with RA have low level of TAS compared to control.

Gansu, (2018) compared TAS, oxidants index level between 35 RA women patients, and 35 control, and found patients have low level of TAS and higher level of oxidants stress index than control.

In this study, oxidative stress was assessed in terms of MDA, and it was found that serum MDA levels were higher in patients with RA (1.34±0.42 µmol/l) than the healthy control subjects (0.88±0.26 µmol/l) p <0.001. Our findings are in agreement with the results obtained by Shaabani *et al*.,(2009) (Similar results of increased MDA levels have been reported in patients with rheumatoid arthritis (Gambhiri *et al*., 1997, p351; Karatas *et al*., 2003, p178; Walwadkar *et al*., 2006, p134; Ansari *et al*., 2008, p429; El-barbary *et al*., 2011, p179; Marie *et al*., 2017, p47).

Increased MDA level is an evidence of exaggerated oxidative stress in these patients.

Recent evidence suggests that articular chondrocytes can actively produce OS, which are produced during inflammation of the synovial membrane. These OS with oxidative activity participate in the chondrocyte catabolism, being the mediators and effecters of cartilage damage (Vyas *et al*., 2016, p58)

Our question arises whether oxidative stress in RA, play a role in pathology or it is a non-specific process. Evidence for an important contribution of oxidative stress in the development RA, should be based on clinical trials that combine antioxidant drugs with conventional antirheumatic drugs. However, clinical trials of antioxidant treatments in RA are lacking.

Conclusion: TAS levels were lower in RA patients , and higher level of MDA than the control group . Therapy with antioxidants vitamins such as E and C can be used as adjunct to other therapies of RA.

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