The Role of Oxidative Stress in the Pathogenesis of Systemic Lupus Erythmatosus (SLE) Among Some Iraqi Patients

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ABSTRACT:

BACKGROUND AND OBJECTIVE:

Systemic Lupus Erythematosus (SLE) is a chronic progressive autoimmune disorder with a wide spectrum of clinical and immunological abnormalities, predominantly developed in women of childbearing age, oxidative stress has been postulated in many pathological conditions including atherosclerosis , inflammatory conditions and some autoimmune disease such as multiple sclerosis , rheumatoid arthritis and Systemic Lupus Erythematosus (SLE).

The present study was conducted to support the idea of oxidative stress during the pathogenesis of (SLE) among some Iraqi patients, comparing it with healthy controls group matched for the same sex and age .

PATIENTS AND METHODS:

Twenty-three Iraqi Arab patients (21 females and 2 males) with Systemic Lupus Erythmatosus (SLE) admitted to Baghdad Teaching Hospital were included in the present study ,and have been compared with 13 healthy controls .

The patients group were diagnosed as having SLE according to the basis of the revised criteria of the American College of Rheumatology ,

Analysis of the parameters of oxidative stress , serum malondialdehyde (MDA) and glutathion (GSH) was performed in all patients before starting any type of drug treatment and their levels were compared with those belong to healthy controls.

RESULTS:

The results presented in this study showed elevated serum MDA concentration in the SLE patients group compared to healthy control ; however , this elevation failed to reach the statistically significant ($P<0.05$).

Significant variation was also demonstrated in serum levels of glutathione between both patients group , in which serum GSH level was significantly lower in the diseased group compared to healthy controls ($P<0.05$).

CONCLUSION:

Oxidative stress mechanism can be proposed as a cause and / or consequence in the pathogenesis of SLE , supporting the theory of free radical –induced tissue damage in this respect.

*KEY WORDS :*systemic lupus Erythematosis , oxidative stress ,malonbialdehide , glutathion.

INTRODUCTION :

The role of oxidative stress has been postulated in many pathological conditions including atherosclerosis , inflammatory conditions and some autoimmune disease such as multiple sclerosis , rheumatoid arthritis and SLE[1]. Systemic lupus erythematosus (SLE) is a chronic progressive auto-immune disorder with a wide spectrum of clinical auto-immunological abnormalities [2] , although the pathogenesis of SLE is multi factorial , the inflammatory nature implies that a state of oxidative stress may exist in this disease which may contribute to immune cell dysfunction , auto-antigen production and auto antibody reactivity [3].

In many cases, oxidative stress leads to production of increased amount of free radical damaging products , especially malondialdehide (MDA), the end product of lipid peroxidation , or decrease in the level of antioxidant defense molecules such as glutathione (GSH) [4].

Glutathione (g-Glutamylcysteinylglycine, GSH) is a sulfhydryl (-SH) antioxidant, antitoxin, and enzyme cofactor. it is ubiquitous in animals, plants and microorganisms, and being water soluble, it is found mainly in the cell cytosol and other aqueous phases of the living system.[5,6]

Experimental depletion of GSH is found to inhibit immune cell functions, markedly,[7] Both T and B lymphocytes require adequate levels of intracellular GSH for normal differentiation [8],these and other findings indicated that intracellular GSH status plays a central role in the functioning of immune cells.

In many disorders including the SLE ,rheumatoid arthritis (RA), and aging, T lymphocytes demonstrate depressed responsiveness to the effect of many antigens and mitogens, perhaps because of insufficient IL-2 production and patients with RA were found to have low blood sulfhydryl (-SH) status [9].

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PATIENTS AND METHODS:

Twenty-three patients with SLE (21 females, 2 males of age range 16-66 years) and 13 healthy controle subjects of same age range , were included in this study. SLE patients were diagnosed according the basis of the revised criteria of the American College of Rheumatology [10] , the patients received no medication and their disease were in the active state .

Venous blood was collected from all subjects in plain non heparinzed tubes , allowed to clot for 30 minutes at room temperature and centrifuged for 15 minutes to obtain the serum.

Malondialdehyde (MDA) level in the serum was determined utilizing the thiobarbituric acid (TBA) method , to (0.25 ml) serum(2 ml) of TCA-Na-arsenite 28% was added , then after vortex , incubation at room temperature then centrifuged and the supernatant was analyzed by adding 0.5 ml of (TBA) (prepared by dissolving 0.05gm of TBA in 5ml NaOH, the mixture was heated for 15 minutes in a boiling water bath . After cooling , absorbance of the resultant mixture was determined at 532nm and 453nm respectively .

Serum Glutathion (GSH) levels were determined , using the slandered methode of colorimetric analysis [11] , where 0.5ml of TCA-Na2-EDTA was added to 0.5 ml of serum then vortexed and centrifuged for 8 minutes To the resulted supernatant , 0.1 ml of Dithionitrobenzen DTNB (prepared by dissolving 0.006 gm of DTNB in 5ml of phosphate buffer) was added ;

absorbance of the resulted colored complex was measured spectrophotometrically at 412 nm within 2 min.

Statistical evaluation of data was performed utilizing Student's (t- test) , P-values <0.05 was considered significant.

RESULTS:

Lipid peroxidation measured as serum MDA level was higher in patients with SLE compared with healthy control subjects (table1) While there is significant reduction (P<0.05) in serum GSH in patients group as compared to healthy control.

Table (1): Serum level of gsh ,mda in patient and control groups

Parameter	Control	Patients
	n= 13	n= 23
MDA µmol /l	1.157 ± 0.381	1.614 ± 0.821
GSH µmol /l	0.718 ± 0.297	0.099* ± 0.077

- Each value represents mean ± SD.
- MDA : malondialdehyde .
- GSH : Glutathione .

n : number of patients .

* Significantly different (P<0.05) .

DISCUSSION :

From the beginning of researches on oxidative stress , scientists have been obsessed with discovering a biomarker that would be a sure sign of oxidative stress in various experimental and clinical situation , the measurements of malondialdehyde (MDA) was long viewed as a reference test , elevation of MDA level (both in plasma and RBCs) during oxidative stress was observed in several previous studies [12].

The results of the present study come in agreement with these studies in which the MDA serum level of SLE patients were higher than that of healthy control ; yet , it failed to reach the statistical level of significance , these observations could be rationalized on the suggestion that increased lipid peroxidation was obviously found in SLE patients .

Lipid peroxidation results from the attack of the active oxygen species (ROS) to polyunsaturated fatty acids of the cell membrane [13].

This mechanism clarify the role of free radical generation and oxidative stress in the pathogenesis of SLE, and since MDA is one of the lipid peroxidation products , it can be measured in the whole blood or plasma in order to evaluate the presence of lipid peroxidation [14].

On the other hand , several studies suggest that anti-oxidant supplementation may improve the disease status in SLE patients , in one study, the effect of vitamin E supplementation on the state of oxidative stress in SLE patients was evaluated and shown to effectively reduce the oxidative stress, and increase anti-oxidant enzymes in the blood. [15]

Additionally, it has been reported that low serum levels of

GSH were detected in patients with many types of diseases compared to healthy controls[16] . Glutathione represents an important cellular defense molecule capable to scavenge directly most of the generated radicals in the biological system [17] . During the pathogenesis of SLE , many types of free radicals were excessively produced , and consequently will lead to depletion of GSH [18] , the state which already reported in this study . Moreover , the activities of many antioxidant enzymes are found to be depressed during the course of SLE [19] , this may give another chance for damaging radicals to be available in high concentrations in many biological fluids including blood .

CONCLUSION:

The present study suggest the idea that oxidative stress mechanism can be proposed as a cause and / or consequence in the pathogenesis of SLE , supporting the theory of free radical –induced tissue damage in this respect.

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