Celiac disease is a member of oxidative stress syndrome

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Abstract:

Background: celiac disease is an intestinal disorder with multifactorial etiology. Little is known about its relation with oxidative stress.

Objective: This study was designed to show that celiac disease is a member of oxidative stress syndrome through measuring some of its markers.

Design: sixteen adult patients with celiac disease were studied with 20 healthy control subjects matched by age. All were attending for upper gastrointestinal endoscopy and they underwent a small intestinal biopsy to confirm or overrule suspicion of celiac disease. Celiac patients were graded according to the marsh score. Fasting serum malonldialdehyde (MDA), uric acid, total albumin and creatinine were measured as a marker of oxidative stress.

Results: serum levels of MDA were significantly higher in celiac patients in comparison to that of controls (5.363±0.737 V.S 4.335±0.511 respectively) ($p < 0.05$). The results showed that celiac patients with high MDA level had more marked histological changes. Serum levels of total albumin and creatinine were low while serum uric acid was little bit higher than that of controls without reaching significant levels.

Conclusion: The results indicated that celiac disease is a member of oxidative stress syndrome, and the result may open a new line of treatment of celiac patients with antioxidants.

Key wards: celiac disease, oxidative stress, MDA, free radicals, total albumin.

Introduction:

Celiac disease (CD) is a multifactorial disorder characterized by morphological and functional aberrations of the small intestinal mucosa, i.e. crypt hyperplastic, villous atrophy, infiltration of intraepithelial lymphocytes and alteration of permeability. [1, 2] In addition, some of inflamatory consequences occur in the intestinal wall of celiac patients which may include activation of mast cells, eosinophils and neutrophils, elaboration of different cytokines and other products of inflammation. [3,4] Moreover, it has been found that patients with CD express significantly inducible nitric oxide synthase in the intestinal wall that results in significantly increased levels of nitric oxide. [5, 6] All these facts about CD are important as it may give hints about its relation with oxidative stress.

To the best of our knowledge, and from the literature review, no study concerned with the relation of oxidative stress and CD has been conducted. Thus, the aim of the present study was to investigate markers of oxidative stress in adults with CD, in order to confirm that CD is a member of oxidative stress syndrome.

Patients & Methods:

This study was conducted at Al-Rashid teaching hospital during 6 months period (June– December 2002). Sixteen adult patients with CD were enrolled in the current study. The diagnosis of CD was based on clinical, upper gastrointestinal endoscopy and histopathological ground. In addition, distal duodenal biopsies for celiac patients were graded according to the Marsh score. Twenty healthy control subjects matched by age were used as a control group.

A blood sample was collected after an overnight fast from both patient and control subjects, immediately centrifuged at 1500 xg for 15 min at 25°c and stored until biochemical measurements done.

Total serum albumin, uric acid and creatinine were measured by using standard laboratory technique. The byproduct of lipid peroxidation malondialdehyde (MDA) levels was determined from the same blood samples by using a modified procedure of Shah and Walker. (7)

The results were presented as number and mean ± SD whenever possible. The data was analyzed by using Students t-test taking $p < 0.05$ as the lowest limit of significant.

Results:

A total number of 16 adult patients with celiac disease and 20 healthy individuals served as controls were enrolled in the present study.

Assessment of activity lipid peroxidation: The byproduct of lipid peroxidation malondialdehyde was determined in the serum tended to be significantly higher in celiac patients in comparison to that of controls **(table- 1).**

In addition, the results showed that celiac patients with high MDA levels had more marked histopathological changes **(Table- 2).**

Table- 1: Serum MDA levels in patients and controls.

Items	Serum MDA nmol/ml
Patients	5.363 ± 0.737
Controls	4.335 ± 0.511

(P< 0.05)

Table- 2: Serum MDA level related with Marsh score in celiac disease.

Marsh score	Serum MDA nmol/ml
Score 1	5.317 ± 0.635
Score 2 and 3	5.409 ± 0.841

(P< 0.05)

Assessment of Antioxidant status:

1-Serum total albumin and creatinine:

The results showed that levels of total albumin and creatinine in celiac patients were within normal range; however, these levels were not significantly lower than those of controls **(table3).**

2-Serum uric acid:

Serum uric acid level in celiac patients tended to be little bit higher than that of controls but do not reach to the level of significance (table 3).

Table 3: Serum antioxidant level in celiac patients and controls.

Biochemical parameters	Controls (n= 20)	Celiac patients (n= 16)	P value
Serum total albumin (g/l)	7.720 ± 0.752	7.575 ± 0.475	> 0.05
Serum creatinine (mg/dl)	0.795 ± 0.170	0.718 ± 0.175	> 0.05
Serum uric acid (mg/dl)	5.045 ± 0.976	5.443 ± 1.382	> 0.05

Discussion:

Our data showed that the byproduct of lipid peroxidation malondialdehyde levels were significantly higher in celiac patients than that of controls ($p < 0.05$). Serum MDA levels were also increased with increasing Marsh score of celiac patients but were not significantly.

The byproduct of lipid peroxidation malondialdehyde is considered as a marker of free radical production inside the body. [8]) Thus, results were indicated that celiac patients are in state of high free radical production result in oxidative stress. Theoretically, oxidative stress can be caused by an increase in the generation of free radicals (i.e., reactive oxygen species (ROS) and reactive nitrogen species (RNS) or it can be caused by decline in the efficiency of antioxidant system (i.e. enzymatic and non-enzymatic antioxidants). [9]

In general, there are many potential sources for ROS/RNS that may be involved in inflamatory cell signaling. These include the following pathways; NADPH oxidase, [10, 11] nitric oxide synthase, [12, 13] xanthenes oxidase [14, 15] mitochondrial respiratory chain, [16] and cymdoxygenase and lipoxygenase pathway. [17] Celiac disease is characterized by a state of chronic inflammation of small intestine, the source of free radical production may include, activated neutrophil as macrophage, presence of various pro inflammatory agents such as TNF-a, interleukins and interferon gama, in addition to activation of nitric oxide synthase. [4, 5, 6, 7, 8] It has been found that activated inflammatory cells can produce ROS via respiratory burst as well as by prostaglandins and leukotriens metabolism. [17, 19]

In addition conversion of xanthine dehydrogenase to xanthine oxidase occurs in the presence of various pro inflammatory agents like TNF-a as well as by activated neutrophils. [20, 21] Moreover, it has been found that celiac patients express significantly inducible nitric oxide synthase in the intestinal wall that results in significantly increased levels of nitric oxide [18] which reacts with super oxide free radical to produce oxidant peroxy nitric an important oxidizing agent. [22] Additionally, sustained production of ROS during state of chronic inflammation of celiac intestinal wall can overwhelm the antioxidant defense system resulting in more damage to tissue. This situation is not surprising, as it has been found that intestinal mucosa contains much smaller amount of antioxidant enzyme than does other part of the body like the liver. [23]

On the other hand, the results showed that in celiac patients the levels of total albumin and creatinine, which act as an antioxidants [24, 25] were low in comparison to that of controls; but without reaching significant levels. Serum uric acid levels, which is considered as the strongest antioxidant agent, [26] not differ significantly from that of control. In general, we can say that there was a decline in antioxidant activity of celiac patients.

So, celiac patients were in a state of high free radical production with low in antioxidant capacity, but whether oxidative stress is a cause or a result of celiac disease is uncertain and need further studies.

Conclusion:

The results indicated that celiac disease is a member of oxidative stress syndrome, and the result may open a new line of treatment of celiac patients with antioxidants.

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