The association of gluten-free diet with pentraxin-3 and lipid profile in Iraqi patients with celiac disease

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Abstract

Aim: Estimated serum Pentraxine-3(PTX3) levels, Lipid profile, and BMI in Iraqi patients with celiac disease with and without GFD in order to validate their role in the exacerbation of celiac disease symptoms.
Method: One hundred Iraqi patients with celiac disease (aged from 20-55 years) were sign up in the current study. The Patients group were divided according to the period of the disease forP (n=48) (male=16, female=32) with a period less than one year and G (N=52) (male=24, female=28) with a period from (1-10 years) The G group was further subdivided in the form of G1 (gluten-free diet (GFD)=29) and G2 (non-gluten free diet (Non-GFD=23). Diagnosis is based on clinical examination. The Patients' group matched with a control group (C, n=51) (male=25, female=26). Serum PTX3 and Lipid profile levels were resolute for each participant.
Results: The outcomes obtained from our study indicate a highly significant increase (p=0.000) in serum anti-TtG and PTX3 as compared with a control group. A significant increase was found in LDL, VLDL, and TG levels in G1 as compared with G2 and control groups while a significant decrease in BMI was found in G1 and G2 as compared to the control group.
Conclusion: High serum PTX3 are associated with CD with and without gluten free diet (GFD), while high serum LDL, TG and VLDL are associated with long life gluten free diet.
Keywords: *Celiac disease, GFD, PTX3, Lipid profile, BMI, CD.*

1. INTRODUCTION

Celiac disease or (CD) is a persistent illness characterized via a lifelong sensitivity to gluten, culminating in immunologically induced inflammatory injury to the small intestinal mucosa [1], Individuals who are genetically prone and have a adjustable mix of gluten-reliant on clinical symptoms, CD-specific antibodies, HLA-DQ2 or HLA-DQ8 haplotypes, and correspondingly enteropathy. CD has a worldwide prevalence of 1.4% as well as is more prevalent in children than in adults[2].The immune system of celiac patients reacts to gluten, which has an influence on nutrient absorption and utilization, resulting in a variety of issues[3].

The Gastrointestinal symptom is a list of gastrointestinal and extraintestinal symptoms connected with a number scale (score range from 0 to 10), which depicts the intensity reported by patients during a given eating regimen[4]. Abdominal discomfort, stomachache, acid regurgitation, bloating, vomiting, borborygmus, swelling, burping, flatulence, reduced, increased removals, loose or hard stools, burning need for defecation, and oral ulcers are some gastrointestinal symptoms. Dermatitis, headache, hazy thought, weariness, numbness of the limbs,

joint/muscle discomfort, and fainting are examples of extra intestinal symptoms[5].

Until recently, celiac disease (CD) was believed to be an uncommon infant dietary intolerance marked by severe malabsorption and flattened intestinal mucosa [6]

Pentraxine-3 (PTX3) is a pivotal component of humoral innate immunity, embroiled in the regulation of the inflammation condition and pathogen resistance [7]. In contrast to its related, C-reactive protein (CRP) the short pentraxin, which is mostly createdin the liver in answer to(IL)-6 interleukin throughan acute-phase reaction [8]. Variety of cell types such as endothelial cells, myeloid cells, and breathing epithelial cells, synthesized PTX3 in response to the IL-1, tumor necrosis issue, microbial compounds, and tissue injury[9]. The resemblance to CRP stimulated research into the efficacy of PTX3 as anindicator in a variety of human illnesses of an inflammatory origin. The quickness of PTX3 rise in these situations is attributed to local creation by distinct cell kinds at sites of injury and the released of the produced protein by the neutrophils in responses to main pro-inflammatory cytokines or a pathogen identification. Increased PTX3 plasma concentrations have been reported in fungal, bacterial, and viral infections[10], Sepsis, severe inflammatory reaction syndrome [11] and, cardiovascular diseases[7]. High PTX3 serum concentrations were linked to disease activity and mortality in many clinical situations [11]. It was proved that PTX3 served as a biomarker in inflammatory vascular diseases[11].

Several studies support the idea that PTX3 acts as a regulator of inflammatory processes in individuals with autoimmune illnesses such as systemic lupus erythematosus (SLE), rheumatoid arthritis, and systemic vasculitis, and that PTX3 level rises in association with disease activity[13].

PTX serum levels were shown to be high in individuals with active CD illness, particularly in those with AGA IgA abnormal levels. Previous research found that active-CD patients who had normal AGA IgA levels showed serum PTX3 levels equivalent to healthy controls or inactive-CD patients[9].

Gluten-free diet (GFD), considered its only available treatment of CD, affected lipid profile due to lower carbohydrate and fiber intake combined by higher saturated fat intake[14]. A recent study found a link between celiac patients on a GFD and an increased frequency of weight gain, elevated blood glucose levels, and a poorer lipid profile[15]. the lipid status is a risk factor of age even in healthy adults[16].

It is well recognized that many adult celiac disease patients have a normal or high BMI at the time of diagnosis[17].According to multiple studies, people who strictly adhere toward a GFD have a greater BMI [16]. Other research evaluating BMI in celiac disease patients at diagnosis and/or following a gluten-free diet have shown inconsistent results. Few research on BMI and other growth metrics in children have been conducted, and the results of those studies have been ambiguous[17].So, the current study aims to investigate the effect of GFD on the lipid profile of celiac disease patients and the relationship of pantraxin-3 with these parameters.

2. Materials and Methods:

The collection of patients went off at the medical city (The digestive system and liver department) in Baghdad-Iraq from October 2021 to March 2022. Patients with formal history of celiac disease (n=100) and healthy individuals (C, n=51) (male=25, female=26) were included in the present study. Each patient was conforming by either biopsy or clinical tests. The Patients Group (n=100) wasdivided into 2 groups the first is celiac

patients with a Duration of less than one year (P=48) (male=16, female=32), and the second is patients duration of 1-10 years (G=52) (male=24, female=28). In addition, a second division was applied on G group to G1 group(n=29) which containsPatients with gluten-free diet and, G2 (n=23) which contains patients with non- gluten-free diet.

2.1. Excluded from this Study:

Patients and control with obesity, cancer, hepatitis, and who have liver diseases, active inflammatory conditions, Irritable Bowel Disease, and alcohol drinking that may interfere with this study were excluded.

2.2. Blood Samples Collection:

Five ml of blood gained venepuncture from each participant in our study (aged range 20-55 y) after fasting forabout8-10hours. And the sample of the blood was distributed in a gel tube after thatleft to accumulate atroom temperature. All gel tubes were centrifugated at (3000 r.p.m) for ten min. togather serum to be used for an estimate ofPentraxin3, lipid profile.

2.3. Laboratory Tests:

Pentraxin3 (PTX3) was assessed by(ELISA) an enzyme-linked immunosorbent assay utilizing a widely available ELISA kit (U.S.A.).Cholesterol, High-density lipoprotein (HDL), Triglyceride (TG), Low-density lipoprotein (LDL), and finally Very low-density lipoprotein (VLDL) were determined using HUMAN, Germany kit. The procedures listed in the manufacturer's instructions were carried out in this study.

2.4.Statistical Analysis

The data was quantitatively examined by (SPSS) software version 22. The variable staris reported as (m±SD) means ± standard deviation. One-way ANOVA and hoc Tukey test were used to compare between groups. A statistically significant difference was considered when P value of <0.05.

3. Results

In our study, 151 Iraqi participants (aged range 20 -55) were separated into three groups: control group (n=51, C), patients with a historical disease less than one year (n=48, G1), and patients with historical disease period between 1-10 years (n=52, G2). The results of this study arelisted in (Table 1). The results obtained from Table (1) showed that no significant differences were found in age between all the studied groups(P>0.05).

Table (1): Information of celiac patients with a period less than 1 year, and patients with a period more than 1 year to 10 years compared to apparently healthy control.

Parameters	Control (n=51)	P(n=48) <1 year	G (n= 52) 1-10 years	P-value	
Age(Year)	37.43±9.72	35.37±10.75	36.01±9.48	C&P	0.563
				C&G	0.754
				P&G	0.944
Anti-TtG(U/l)	1.90±0.95	10.42±5.45	11.06±6.27	C&P	0.000
				C&G	0.000
				P&G	0.785
PTX-3(ng/ml)	1.74±0.33	3.31±0.80	3.47±0.97	C&P	0.000
				C&G	0.000
				P&G	0.556
HDL(mg/dl)	37.36±15.50	36.53±7.75	35.42±7.87	C&P	0.925
				C&G	0.644
				P&G	0.870
VLDL(mg/dl)	25.40±3.86	26.11±7.04	27.68±6.53	C&P	0.826

				C&G	**0.132**
				P&G	**0.389**
LDL(mg/dl)	**65.46±16.77**	**78.19±35.96**	**92.84±40.20**	**C&P**	**0.131**
				C&G	**0.000**
				P&G	**0.067**
Cholesterol(mg/dl)	**127.66±15.75**	**136.10±37.14**	**130.34±18.00**	**C&P**	**0.221**
				C&G	**0.852**
				P&G	**0.489**
TG(mg/dl)	**126.66±21.17**	**130.56±35.23**	**138.21±24.63**	**C&P**	**0.761**
				C&G	**0.087**
				P&G	**0.348**
BMI(Kg/m^2)	**22.45±2.36**	**19.92±2.76**	**19.89±2.81**	**C&P**	**0.000**
				C&G	**0.000**
				P&G	**0.998**

C: Control group, GFD: gluten free diet group, NGFD: non-gluten free diet group *P>0.05; **P>0.001; no significant P<0.05

Anti-tissue transglutaminase levels showed anextremely significant increase (P=0.000) in P(10.42±5.45 U/l) and G (11.06±6.27 U/l) as compared with a control group (1.90±0.95 U/l), but there is no significant difference (P=0.785) between P and G groups. Serum PTX-3 levels showed a highly significant (P=0.000) in P (3.31±0.80 ng/ml) and G (3.47±0.97 ng/ml) as compared with a control group (1.74±0.33 ng/ml), but there is no significant difference (P=0.556) between P and G groups. Serum HDL levels showed no significant difference (P=0.925) in P (36.53±7.75 mg/dl) and G (35.42±7.87 mg/dl) as compared with a control group (37.36±15.50 mg/dl), in addition, no significant difference (p=0.870) between P and G groups. Serum LDL showed no significant difference (P=0.131) in P (78.19±35.96 mg/dl) as compared with a control group (65.46±16.77 mg/dl), while showed a highly significant increase (P=0.000) in G (92.84±40.20 mg/dl) as compared with a control group, in addition, there is no significant difference(p=0.067) between P and G groups. Serum VLDL showed no significant difference (P=0.826) in P(26.11±7.04 mg/dl) and G (27.68±6.53 mg/dl) as compared with a control group (25.40±3.86 mg/dl), also there is no significant (P=0.389) between P and G groups. Serum cholesterol levels showed no significant difference (P=0.221) in P (136.10±37.14 mg/dl) and G (130.34±18.00 mg/dl) as compared with a control group (127.66±15.75 mg/dl), also there is no significant (P=0.489) between P and G groups. Serum triglyceride levels showed no significant difference (P=0.761) in P (130.56±35.23 mg/dl) and G (138.21±24.63 mg/dl) as compared with a control group (126.66±21.17 mg/dl), also there is no significant decrease (P=0.348) between Pand G. Highly significant decrease (p=0.000) of BMI in P (19.92±2.76 Kg/m2) and G (19.89±2.81 Kg/m2) as compared with a control group (22.45±2.36 Kg/m2), but there is no significant decrease (P=0.998) between P and G groups.

In our study, we further divided the G group (n=52, period of celiac disease 1-10 years) into the G1 group which consists of 29 patients of celiac disease with the gluten-free diet and,the G2 group which consists of 23 patients of celiac disease not committed to a gluten-free diet. The results are listed in Table (2) showed that no significant differences were found in age between all the studied groups(P>0.05).

Anti-TtG levels showed a highly significant increase (P=0.000) in G1 (11.12±6.45 U/l) and G2 (10.99±6.16 U/l) as compared with a control group (1.90±0.95 U/l), but there is no significant difference (P=0.995) between G1

and G2 groups. Serum PTX-3 levels showed a highly significant increase (P=0.000) in G1 (3.52±1.01 ng/ml) and G2 (3.40±0.94ng/ml) as compared with a control group (1.74±0.33 ng/ml), but there is no significant difference (P=0.826) between G1 and G2. Serum HDL and cholesterol levels showed no significant difference in G1 and G2 (P<0.05) as compared with a control group, which also showed no significant difference (P<0.05) between G1 and G2. Serum LDL levels showed a highly significant increase (P=0.000) in G1 (104.32±43.02 mg/dl) as compared with a control group (65.46±16.77 mg/dl), while no significant difference (P=0.198) was found as compared G2 with a control group. In addition, it was found a highly significant increase (P=0.006) in G1 (104.32±43.02 mg/dl) as compared with G2 (78.37±31.59 mg/dl). Serum triglyceride levels showed a highly significant increase (P=0.002) in G1 (145.10±25.13 mg/dl) as compared with a control group (126.66±21.17 mg/dl), but there is no significant difference in G2 (P=0.868) (129.52±21.47 mg/dl) as compared with a control group (126.66±21.17 mg/dl).While a significant increase (P=0.038) was found between G1 and G2. Serum VLDL levels showed a significant increase (P=0.010) in G1 (29.08±7.65 mg/dl) as compared with a control group (25.40±3.86 mg/dl), but there is no significant difference in G2 (P=0.925) as compared with a control group (25.90±4.29 mg/dl), also between G1 and G2 groups (p=0.084). BMI showed a highly significant decrease (P=0.000) in G1 (20.00±2.98 Kg/m2) and G2 (19.74±2.63 Kg/m2) as compared with a control group (22.45±2.36 Kg/m2), but there is no significant (P=0.925) between G1 and G2 groups.

Table (2): Information of celiac patients with a period of more than one to 10 years with and without gluten-free diet compared to apparently healthy control.

Parameters	Control (n=51)	G (n=52) 1-10 years		P-value	
		G1(n=29) with GFD	G2 (n=23) without GFD		
Age(Year)	37.43±9.72	37.65±10.06	33.95±8.47	C&G1	0.994
				C&G2	0.321
				G1&G2	0.353
PTX-3(ng/ml)	1.74±0.33	3.52±1.01	3.40±0.94	C&G1	0.000
				C&G2	0.000
				G1&G2	0.826
Anti-TtG(U/l)	1.90±0.95	11.12±6.45	10.99±6.16	C&G1	0.000
				C&G2	0.000
				G1&G2	0.995
HDL(mg/dl)	37.36±15.50	36.69±7.76	33.81±7.89	C&G1	0.970
				C&G2	0.485
				G1&G2	0.680
VLDL(mg/dl)	25.40±3.86	29.08±7.65	25.90±4.29	C&G1	0.010
				C&G2	0.925
				G1&G2	0.084
LDL(mg/dl)	65.46±16.77	104.32±43.02	78.37±31.59	C&G1	0.000
				C&G2	0.198
				G1&G2	0.006
Cholesterol (mg/dl)	127.66±15.75	133.89±13.21	125.86±22.17	C&G1	0.251
				C&G2	0.905
				G1&G2	0.205
TG (mg/dl)	126.66±21.17	145.10±25.13	129.52±21.47	C&G1	0.002
				C&G2	0.868

				G1&G2	**0.038**
BMI(Kg/m^2)	**22.45±2.36**	**20.00±2.98**	**19.74±2.63**	**C&G1**	**0.000**
				C&G2	**0.000**
				G1&G2	**0.929**

C: Control group, GFD: gluten-free diet group, NGFD: non-gluten-free diet group *P>0.05; **P>0.001; no significant P<0.05.

The correlations relationships between biochemical parameters were studied and the results revealed that in the G1 group only anti-TtG have a positive correlation with PTX-3(r=0.835, P=0.000) while it was negatively correlated with HDL(r=-0.413, P=0.026). In addition, no significant correlations were found between other parameters, Table (3).

Table (3): Correlation between different parameters in the G1group (n=29) with GFD (period of disease =1-10 years).

Parameters	Person correlation	P
PTX-3&Anti	**0.835****	**0.000**
HDL &Anti	**-0.413***	**0.026**

4. Discussion:

Celiac disease is a chronic inflammatory disorder that can lead to consequences such as nutritional deficiencies, osteoarthritis, and an increase in risk of positive types of cancer[18]. There are no Celiac disease monitoring protocols or metrics to check on a regular basis during CD follow-up. Anti-TtGtiters, on the other hand, are presently used to assess observance and compliance to the GFD and are often tested yearly in everyday clinical training. It is well understood that adhering to a GFD will result in disease control in the vast majority of CD patients, lowering the risk of difficulties and mortality[19].

In celiac disease, the immune response involves the development of antibodies against the intestine enzyme Tissue Transglutaminase. These autoantibodies are immunoglobulin G (IgG) or immunoglobulin A (IgA) (IgA). Because it is created in the small intestine, where gluten causes inflammation in gluten-sensitive people, the level of anti-TtG IgA in the blood is more trustworthy for illness identification[20].

It is recommended that anti-TtGtiters be measured on a regular basis in children after GFD implementation to demonstrate a decrease in antibody titers as an indirect sign of dietary adherence and disease control[21]. If serology remains aberrant after one year of GFD, some experts advise further study[22].

Several investigations have found that after starting a GFD, serum CD antibodies such as anti-transglutaminase and/or anti-endomysium (t- TG/EMA) are more frequently related with intestinal injury[23][24]. Furthermore, antibody negativity is not always correlated with histological healing and may be associated with incorrect results[25][26].

In the present study,we found that TTG has high levels in the P and G groupsas compared to a control group. In addition, when we compared G1and G2 we found no difference in TTG levels between the two groups which means GFD has no effect on the level of TtG.

Pentraxin-3 is released in situ by local monocytes and macrophage lineage cells in vascular inflammation sites and is rarely altered by systemic inflammation[27][28]Previous research suggested that PTX-3 could increase local inflammation by boosting complement deposition and enhancing endothelial and monocyte tissue factor secretion[27].

The results found from our study showed significance increase in PTX-3 levels in P,G,G1 (GFD), and G2 (non-GFD) groups as compared with a control group. That means GFD has no role in decreasing the

inflammation innate by PTX-3.Many studies have been conducted to determine whether PTX-3 plays numerous regulatory roles in innate immunity[9]. It is now understood that PTX3 influences opsonization[8] complement activation[9], in addition to leukocyte recruitment and activation [29], All processes that have an impact on autoimmune tissue damage. According to one study, GFD patients have lower PTX3 serum levels than active patients[30].

Our results in the present study revealed that serum LDL had a highly significant increase as compared to C group, while no significant difference were found in other parameters.Depending on GFD, we found a significant increase in serum LDL, VLDL,and TG in G1 as compared with a control group. According to certain research, a GFDmight be related with an increase levels in total cholesterol, triglycerides,LDL, and a decrease in HDL segment concentration[31]. Other studies, however, show important changes in TG levels after a year of gluten-free eating[32][13].

In our study,the results of BMI revealed a highlyimperativedecrease in all groups with and without GFD as compared with the control group. The majority of research in the works have found that CD patients consume a minor BMI than the overallpopulace (at diagnosis)[34],[35]. However, it has been clearly proven that at the time of diagnosis, a growing number of Celiac disease patients have a regular or higher BMI [36],[37].In contrast to our findings, prior studies found an increase in average BMI in CD patients on a GFD. A rise in the BMI is likely due to increased consumption of calories, lipids, and simple carbs, but also to decreased physical motion[38].

5. Conclusion:

The results obtained from the present study showed that gluten-free diet did not aid to decrease anti-TtG andPTX-3 levels, and this could be due to non-compliance with the dietary standards that patients are supposed to refrain from eating, or it may be due to the commercial gluten-free diet products in the local markets, most of which are not subject to health control, in addition to that, the results indicate a high level of lipoprotein in patients, which indicates the possibility of exposure to increase the risk for high blood pressure, fatty liver, or heart disease.

6. Acknowledgement:

The authors would like to express their gratitude to all staff of the Hydrogen Medical lab., Calcium Medical lab and Baghdad teaching Hospital. Sincere thanks to the patients and healthy people who supplied us with blood samples.

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