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Original Research Paper

Investigation of Serum Interleukin-10 & Tumor Necrosis Factor (TNF-a) Levels in Celiac Disease Patients

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Abstract: In genetically predisposed subjects, gluten can trigger (celiac disease), an autoimmune syndrome affecting the small intestine, leading to immune reactions that damage the colon and cause various symptoms. The investigation was aimed at measuring serum levels of tissue transglutaminase both (Immunoglobulin IgG, IgA), Interleukin-10 with Tumor Necrosis Factor-alpha in patients confirmed with celiac disease (CD). The research utilized a case-control methodology at AL-Sadder Medical Center, involving a sample of 158 specimens. It included 79 individuals with coeliac disease and 79 normal controls of the identical ages (18-50) along with gender. Blood serum for tissue-transglutaminase (t.TG) immunoglobulins (IgG, IgA) levels were measured using ChLIA, while interleukin-10 (IL-10), and tumor necrosis factor-alpha were assessed using an ELISA kit. The current investigation revealed that patients exhibited significantly elevated levels of IL-10 nearly 2.5-fold higher (46.875 ± 24.533) compared to the control group (18.597 ± 8.324), with a p-value of less than 0.001, indicating a statistically significant difference. Furthermore, the findings demonstrated that Tumor Necrosis Factor-alpha (TNF-α) levels were substantially higher in patients with celiac disease (43.985 ± 21.782), nearly triple the levels observed in the control group (15.510 ± 12.294), also with a p-value of less than 0.001. There was a significant increase in the levels of Tumor Necrosis Factor-Alpha (TNF-α) and Interleukin-10 in patients confirmed with celiac disease. Additionally, the investigation identified a positive correlations significantly among TNF-α and tissue transglutaminase (t.TG) IgG, as well as between t.TG IgA and Interleukin-10.

Keywords: Celiac Disease, IL-10, TNF-alpha, Anti-t.TG antibody

1. Introduction

Celiac disease (CD) is a long-term, immune-associated enteropathy that exhibits complaints induced by gluten-containing food consumption in naturally susceptible individuals [1]. The average rate of (CD) in the whole population is around 1%, despite of geographic factors. The fundamental reasons are still mysterious [2]. It may manifest at any age contingent upon the presence of glutens in the diet. However, the evolution of CD is particularly predicted in my earliest years with extending into older ones [3]. Various clinical experiments and studies of CD illustrated the fact that ambiguous manifestations or nonexistent symptoms are prominent in the eastern part of the world [4]. This condition primarily affects the upper portion of the gut in order to

cause irritation and harm to the mucosal barrier. In contrast, there is a rising occurrence of extra-digestive manifestations of those with celiac disease (CD), such as dwarfism, precocious puberty, neuronal dysfunction, oral ulceration, and gluten-sensitive dermatitis. Identifying celiac disease in these patients requires increased awareness of hallmarks that could point to what underlies CD [5-6]. The best approach to distinguish or monitor for celiac illness, irrespective of their ages, includes the tests of anti- percent for confirming asymptomatic CD, and its specificity is equally 95% or much above. The check's accuracy for recognizing celiac disease (CD) is best with t.TG, and the potential of attaining a truly positive result boosts as the assessment level raises [7]. Additionally, Cytokines and CD4+ lymphocytes (T lymphocytes) perform a vital part in the immune disorder pathways of coeliac condition. IL-10 is an important anti-inflammatory cytokine that helps regulate the immune system in the gastrointestinal tract by reducing immune responses, particularly by affecting antigen presentation and lowering the reactivity of gliadin-specific T lymphocytes [8-9]. Consequently, fibroblasts get excited to create cell-damaging proteases once cells from the immune system become attracted to the inflamed region. Furthermore, the above process promotes Effector CD4+. T cells tend to be less exposed to regulatory T cells' immune-suppressive actions [10]. Moreover, some cytokines, especially tumor necrosis factor (TNF-α), have been implicated in mucosal damage by raising the generation of specifically identified metalloproteinases, culminating in the deterioration of the extracellular matrix's (ECM) constituents [11]. In vitro conditions, the gliadin peptide has been illustrated to stimulate TNF-α expression by peripheral blood monocytes in individuals with efficacious CD. The cytokines might suppress or boost immune system responses via modulating T lymphocytes and other immune-mediated effectors of TNF-α, prompting Th-1 lymphocytes, whilst IL-10 triggers Th-2 cells [12-13].

2. Methodology

Study design and setting

The research used a case-control strategy and was done in Najaf governorate (AL-Sadder Medical Center Hospital). The data was compiled from participants who were enrolled from October 2024 to January 2025.

The research groups

An efficient selection of 158 samples was divided into two groups: 79 individuals with coeliac disorder (CD) and 79 normal volunteers. Participants with CD were diagnosed by specialized physicians and confirmed by a gastrointestinal doctor, while both groups were differentiated using serological diagnostics for t.TG autoantibody.

Selective criteria

All participants in this research are at least 18 years old and not older than 50 years. However, the investigation excluded those who suffered from microbiological illnesses or other immune conditions, were undergoing pregnancy, had hypertension, or were heavy smokers.

Biomarker assays

Sun-Long Bioassay, a Chinese manufacturer, utilized an ELISA kit to investigate both IL-10 as well as TNF-Alpha levels in human serum. Furthermore, t.TG autoantibodies were quantified utilizing a ChLIA kits via the immunodiagnostic multifunctional system provided by EUROIMMUN, United Kingdom.

Statistical analysis

The study used IBM-SPSS version 26 and MS Office Excel Professional 2018 for data analysis and display. The Shapiro-Wilk test assessed variable normality, with the mean and standard deviation calculated. For non-normally distributed data, the Mann-Whitney test was used. The t-test evaluated mean differences between two independent groups with normally distributed variables, while the chi-square test examined correlations between categorical variables. Levels of significance were set at $P \leq 0.05$, highly significant results represented by $P \leq 0.01$.

3. Results

Sociodemographic characteristics concerning CD patients

Figure (1) reveals that there were no significant differences in the percentages of those with celiac disorders as compared with the normal set ($p = 0.920$). Consequently, absences of a statistically significant difference ($p = 0.437$) when considering sex across the patient and control categories can be observed in Figure (2). Figure (3) demonstrates that there are statistically significant differences between the patients group and the control group concerning familial history ($p = 0.000$).

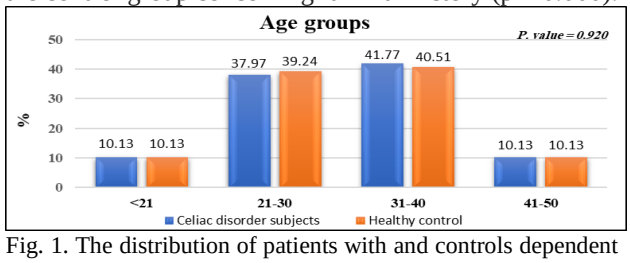

Fig. 1. The distribution of patients with and controls dependent on age groups

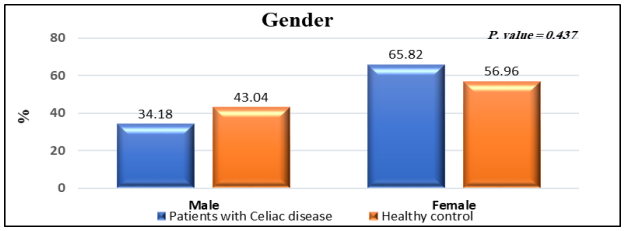

Fig. 2. The sexual distribution for celiac disorder and control subjects

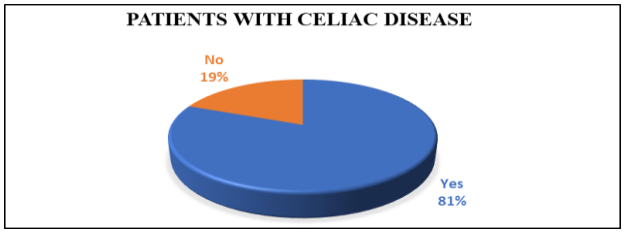

Fig. 3. The distribution of familial history for participants with celiac disease.

Evaluation of anti-t.TG antibodies among patients and control subjects.

Results demonstrated that patients had considerably increased TTG IgA antibody levels (78.523 ± 43.185) compared to the control group (2.296 ± 1.884), p < 0.001. Patients sustained substantially greater averages in TTG IgG levels (76.146 ± 51.483) above those of controls (1.622 ± 1.781), with the same strong statistical significance (p < 0.001). As represented in **Table (1)**.

Table (1): The differences between patients' compared to healthy individuals in diagnostic marker (t.TG)

Immunoassay	Categories	Mean± SD (AU/ml)	Median	P. value
Anti-t.TG (IgA)	Patients	78.523 ± 43.185	68.150	**<0.0001**
	Control	2.296 ± 1.884	2.0000	
Anti-t.TG (IgG)	Patients	76.146 ± 51.483	49.700	**<0.0001**
	Control	1.622 ± 1.781	1.4000	

** The Mann-Whitney test was utilized to compare data not distributed normally*

Comparing serum IL-10 and TNF-alpha concentrations in CD patients and healthy groups

Table (2) presents interleukin-10 (IL-10) and tumor necrosis factor-alpha (TNF-α) levels within celiac disorder problem patients as well as control persons. It was observed that those with celiac disease had substantially higher IL-10 levels (46.875 ± 24.533) when compared with controls (18.597 ± 8.324), having a p-value of less than 0.001. Furthermore, TNF-α levels were additionally considerably higher in those with coeliac disorder (43.985 ± 21.782) in contrast to controls (15.510 ± 12.294), and a p-value of less than 0.001.

Cytokines	Categories	Mean± SD (Pg/ml)	Median	P. value
IL-10	Patients	46.875 ± 24.533	47.000	<0.001
	Control	18.597 ± 8.324	17.199	
TNF-α	Patients	43.985 ± 21.782	44.789	<0.001
	Control	15.510 ± 12.294	11.728	

Table (2): The comparison of celiac disorder patients' in contrast to control participants' levels of certain cytokines
** The Mann-Whitney test was utilized to compare data not distributed normally*

The association among the examined factors in celiac disorder

Table (3) indicates that t.TG IgA shows a strong positive correlation with IL-10 (r = 0.573, p = 0.001) as well as a weak positive correlation with TNF-Alpha (r = 0.168, p = 0.043), both statistically significant. In contrast, t.TG IgG has no significant correlation with IL-10 (r = 0.110, p = 0.371) but shows a moderate positive correlation with TNF-Alpha (r = 0.285, p = 0.010), which is statistically significant.

		r	P. value
Tissue transglutaminase (IgA)	**IL-10**	0.573	0.001**
	TNF-Alpha	0.168	0.043*
Tissue transglutaminase (IgG)	**IL-10**	0.110	0.371
	TNF-Alpha	0.285	0.010*

Table (3): The correlation between the investigated variables within celiac disease patients
***Means significant correlation at the 0.001 level (one-tailed) while * at the 0.05 level (two-tailed)*

	Genders		T-test	P. value
	Male (N=27)	Female (N=52)		
	(Mean ± S.D)	(Mean ± S.D)		
Anti-t.TG IgG	75.042±69.622	77.518±79.730	0.142	0.887
Anti-t.TG IgA	74.553±43.866	89.489±40.769	1.470	0.147
IL-10	34.686±17.573	37.130±14.257	0.623	0.535
TNF-Alpha	38.956±11.405	41.434±10.633	0.937	0.353

Gender distribution of study variables in CD patients

In the current study, the results disclosed in **Table (4)** were aimed at demonstrating a negative association between the quantities of the indicator in the serum blood sample and genders.

Table (4): The distribution of studied variables linked to gender in celiac disorder participants

4. Discussion

This research observed no gender or age differences between the control and patient groups (p. value > 0.05), confirming [14]. Research subjects should match age and genders in order to prevent biases. By establishing an equitable gendered ratio, investigators could minimize the influence of ages on gender features, which led to greater precision in case-control contrasting and improved research credibility.

Concerning familial histories, those results correspond with previous investigations that proved a connection between relatives with a history of celiac illness and a higher probability of having the disease in the future. More specifically, clinical experiences concerning relatives from the first degree [15-16].

Subjects with coeliac disorder (CD) had considerably greater amounts of t.TG antibody IgA (78.523 ± 43.185 AU/ml) in contrast to normal (2.296 ± 1.884 AU/ml), p. value less than 0.001. The findings line up with past studies exposing higher t.TG levels of IgA in those with disorder [17]. Additionally, investigations has revealed that t.TG IgA affinity is much more intense in those suffering from CD [18-19]. A research study conducted within Iraq analogously concluded that celiac disease in particular subjects had far greater average t.TG antibody amounts of IgA compared to those in good health [4]. These increases can be ascribed to the existence of enhanced tissue transglutaminase (TTG) IgA antibodies in individuals with celiac disease, which suggests an immunological response in the small intestine to glutenen. The system of immunity erroneously targets t.TG, an enzyme tasked with altering gluten proteins, triggering the inflammation and tissue damage linked to coeliac illness. This response leads to the formation of IgA antibodies against TTG, which may be identified by blood testing. The identification of celiac disease needs to have evidence of increased t.TG IgA autoantibodies [20-21].

The patients had considerably higher mean TTG IgG levels (76.146 ± 51.483 AU/ml) than controls (1.622 ± 1.781 AU/ml), with a P. value < 0.001. The results correspond with those of other investigation [22], which revealed that isolated t.TG antibody IgG presented around 97 percent efficacy in finding cases of celiac disorders (172 among 178 participants). Coeliac disease sufferers' systems of immunity are assaulting the small gut since gluten is a danger. T.TG IgG autoantibodies rise owing to this immunological response affecting intestine t.TG. Gluten manifestations originate from autoimmune damage to gut villi that inhibits enterocyte function [23].

Regarding IL-10, the present investigation indicated that IL-10 expression was greater in celiac condition patients who had significantly greater mean blood levels. In prior investigations, the anti-inflammatory mediator IL-10, which was initially recognized as an integral immunomodulatory in the digestive tract, appeared both augmented and unaltered in those with celiac disorder in comparison with control subjects [4]. The reaction of the adaptive immune system initiates when antigen-presenting cell types (APCs) identify deamidated gliadin particles, break them down, and then deliver them to activated CD4+ T lymphocytes utilizing the second class of major histocompatibility complex (MHC) molecules. CD4-Th2 cells subsequently generate a humoral immune reaction by excreting a substance called IL-10, facilitating the acceleration and specialization of B-cell lymphocytes in the body [24-25-26], indicating the post-stimulus maturations of IL-10 might be an element of a regular celiac manifestation [27].

The investigation revealed that levels of TNF-α are significantly elevated in individuals diagnosed with coeliac disease in comparison to healthy individuals. Peripheral blood monocytes are stimulated to produce more TNF-α by gliadin peptides. Cytokine levels, specifically TNF-α, IL-6, and IL-2, increased significantly in celiac disease patients after exposure to gliadin peptides [28]. TNF-alpha and INF-gamma initiate the nonspecific immune system reaction by activating cells such as neutrophils and macrophages. In the gut, the ejection of Immunoglobulin-E leads to degradation of mast cells and an extensive histamine response. Grain includes no less than three chemicals, particularly gluten, that can seriously harm the body's defenses [29]. Additionally, gluten stimulation led to elevated mRNA levels of TNF-α in biopsies [30]; those who are gluten-free (GFD) have lower levels of tumor necrosis factor-alpha (TNF-α) than those who have active celiac disorders (A.C.D) [12]; while Th-1 response boosts pro-inflammatory reactions and cell-mediated immunity, impacting the humoral immune response, which is seen in individuals with coeliac sprue [31].

Investigations have linked the condition to higher serum immunoglobulins, specifically IgA classes including

E.M.A. and T.TG antibodies. Mucosal cytokines, except INF-gamma, enhance IgA plasma cells synthesis, although many time-dependent monitoring must be performed to determine inflammatory or systemic implications [32-33]

In this investigation, the indicators considered didn't differ significantly based on the patients' sex, and there was not a significant relationship among the blood levels of the indicators and gender, pursuant to the statistical analysis. Research back up the levels in the blood of t.TG in male as well as female individuals suffering from CD are not affected significantly, according to a reports [15-34].

Conclusion

There was a significant elevation in levels of tumor necrosis factor-alpha and interleukin-10 among subjects with celiac disease. Moreover, this research has shown that t.TG IgA and IgG have a significant positive correlation between them. On the other hand, there were positive correlations between TNF-alpha with tTG (IgG) and IL-10 with tTG and both (IgG, IgA). The findings suggest that inflammation-related cytokines play a role in the pathophysiology of celiac disease.

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Ethics

The study was conducted in accordance with the protocols' approval from the Najaf Health Directorate's department with the University of Kufa/Medical College's Medical Ethics Committee.

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