

# Association between autoimmune thyroiditis with gluten sensitive enteropathy patients in Baghdad

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## Abstract

Gluten sensitive enteropathy (GSE) is an inflammatory disease with autoimmune features was triggered and maintained by ingestion of protein named gluten found in wheat and barley. The incidence of thyroid disorders is likely elevated among persons that suffering from coeliac disease. The results were done show highly significant differences between laboratory investigations of patients with autoimmune thyroiditis (Hb% ,iron, ferritin, free T4,TSH,Ca<sup>++</sup> ,alk.ph & vit.B<sub>12</sub>) compared with healthy control group as well as the results of anti-tissue glutaminase & endomysial antibodies (IgA & IgG) were highly significant in patients with coeliac disease. The prevalence of gluten sensitive enteropathy among patients with thyroiditis 12.7% among risk population with autoimmune thyroiditis patients ,the presence of deficiency in calcium , haemoglobin , free T4 and TSH ,for indicating celiac disease investigations .This must be done for all autoimmune thyroiditis patients because of its high percentage.

**Key words** :Autoimmune thyroiditis , gluten-sensitive enteropathy

## INTRODUCTION

Gluten sensitive enteropathy (GSE) is small bowel enteropathy as a result from immunological hypersensitivity against protein of wheat or barley (gluten) with susceptible genetic patients;initiate the disease because the overlap of HLA-DQ<sub>2</sub> binding and T-cell stimulating epitopes that are resist against intestinal proteinase (1).

The gluten sensitive enteropathy patients responses to gliadins promote an inflammatory reactions in the upper parts of small intestine ,followed by infiltration in the lamina propria and epithelial layer with chronic and inflammatory cells (2).

The interaction of gliadin in wheat and barley products with the inner layer of small intestine is crucial to the pathogenesis of sprue disease , endogenous tissue transglutaminase deaminates glutamine in gliadin, negative charged gliadin has been shown to induce interleukin-15 in enteric epithelial cells stimulating the proliferation of NK cells and intraepithelial lymphocytes to express NK-G2D as a marker of lymphocytes (3).

The genetics play an crucial role in sprue disease in relatives of patients ,the concordance for the disease in monozygote twins about 75% and about 30% for the first degree relatives ,this disease does not develop unless the individual has alleles that encode for HLA genes (4).

The strong association of heredity exists between celiac and two human leucocyte antigen hepatocytes DQ2 & DQ8, damage to the inner mucosa is presentation of gluten – derived peptide gliadin, consisting of 33 amino acids ,by the HLA molecules helper T-cells, helper T-cells mediates the inflammatory response ,the absence of villi and elongation of crypts characterize the mucosal lesions in un- treated sprue disease ,more lymphocytes were infiltrate the epithelial cells(5).

The gluten sensitive enteropathy formed about 1% in the western countries (6,7). The correlation of celiac disease with Crohn's disease ,ulcerative colitis and autoimmune liver diseases and several other immune and non immune based disease in digestive

system are well distinguished by other diseases outside of digestive system such as thyroid disease .Sjogren's syndrome ,diabetes mellitus and Adison's disease ,are correlated with coeliac disease (8).

Thyroid disorders may be related with celiac disease, this correlation in Sweden was 10.8%(9) .Present study was aimed to evaluate the risk of thyroid disorders in patients that suffering from coeliac disease .

## MATERIALS AND METHODS

Forty seven outpatients both sexes (20 males and 27 female) were investigate as autoimmune thyroiditis , and thirty healthy individuals as control group .The diagnostic parameters comprised positive for anti-thyroglobulin(ATG)antibodies free thyroxin (free T4) and thyroid stimulating hormone (TSH), also the patients were analysed according to gender , age, haemoglobin concentration ,iron,ferritin ,calcium,alkaline phosphatase and vitamin –B<sub>12</sub>. The immunoglobulins IgA & IgG were estimated as tissue- transglutaminase antibodies (tTG) and endomysial antibodies (EMA).These tests were detected by enzyme –linkaged immunosorbent assay (ELISA) with rabbit polyclonal antisera . Some investigations (vit.B<sub>12</sub>, Ca<sup>++</sup> , iron ,ferritin, alk.phosphatase ) were measured by spectrophotometer .Patients with tTG and EMA reactive antibodies are considered serologically positive coeliac disease.

## RESULTS

Table (1) show the characteristics of 47 patients suffering from autoimmune thyroiditis ,their mean age was 17 years ; 57% were women and 43% were men . The titer or concentration of haemoglobin ,iron,ferritin,calcium, alk.phosphatase and vitamin B<sub>12</sub> as well as free thyroxine (free T4) and thyroid stimulating hormone TSH in the autoimmune thyroiditis patients were decreased significantly compared with healthy control.

Table (1):Laboratory investigations of 47 patients suffering from autoimmune thyroiditis according to presence of coeliac disease antibodies.

	Patients		Healthy control		Normal value	P-value
	Male	Female	Male	female		
Gender	20	27	14	16	–	0.04
Age	18	16	17	15	–	0.07
Hb.	12.72	11.82	14.1	12.3	12-16 g/L	0.023
Iron	13.4	12.7	21.9	16.2	14-29 μmol /L	0.21
Ferritin	61.4	63.2	103	98	80-120 μg /L	0.21
Free T4	1.2	1.2	1.1	1.1	0.8-2.0 ng/L	0.04
Ca <sup>++</sup>	8.2	8.0	9.4	9.1	8.2-10.5g/L	0.33
TSH	2.6	2.7	3.2	3.4	0.5-5.2 mU/L	0.31
Alk.ph.	77.6	83.4	99.7	92.3	80-145mmol/L	0.13
Vit.B <sub>12</sub>	181	173	296	203	160-900ng/L	0.11
Coeliac disease patients	2	4	0	0		

Table (2) show investigations of six patients with autoimmune thyroiditis who were positive coeliac disease.

Parameter	Male No.(2)	Female No.(4)	Normal value	P-value
Anti-tTG IgA	3.1	4.2	0.8-5 g/L	0.002
Anti-tTG IgG	8.2	7.5	7.2-19 g/L	0.031
Anti-EMA IgA	1.6	1.9	≥1.0+ve	0.047
Anti-EMA IgG	23.9	26.3	≥20+ve	0.039

Table (2) show investigations of six patients who were positive for coeliac disease were with autoimmune thyroid disease and negative coeliac disease antibodies.

All six patients (4 females & 2 males) gives a positive result for anti-tissue transglutaminase antibodies (IgA & IgG) and endomysial antibodies (IgA & IgG)

#### DISCUSSION

Thyroid hormones (thyronine ,thyroxine &thyroid stimulating hormone) have crucial role on the gastro-intestinal tract at all levels of organization and the physciations have prolonged extinguished the relations that exist between gastro-intestinal symptoms and thyroid disorders (10).

The relation between gluten-sensitive enteropathy and autoimmune thyroid disease has been discussed worldwide,particularly in European states.Elevated prevalence of thyroid disorder has been recorded in patients with gluten sensitive enteropathy and vice versa, Volta *et al.* ,1997(11)recorded a hypothyroidism rate of 5.7% among 70 coeliac patients , also to Midhagen *et al.*,1988(12) who recorded of 5.8%,Velluzzi *et al.*,1998 (13) estimated of 47 patients with gluten sensitive enteropathy and 91 healthy control group and recorded incidence of ATPO was higher in GSE patients (29.7%). Gluten sensitive enteropathy and autoimmune thyroid diseases are common among women more than men (14,15,16).

Ferritin reflects an a person iron reserves , hypothyroidism found in cases of iron deficiency through decreased inventories of this element and also in cases of scurvy & hypothyroidism,the serum levels of ferritin were lower, but haemoglobin slightly low,possibly because the men have higher levels than women (17).

Some studies are currently performed in children with an elevated risk for some diseases,however, abeneficial effect of an gluten free diet may be expected in general both in adults & children , intestinal inflammation and the correlated with dysbiosis,with or without underlying coeliac disease are known to initiate extra-intestinal autoimmune disorders(18,19,20).

Mechanism of correlation of gluten sensitive enteropathy and autoimmune thyroid disease are not complete understood. At least partly , be explained genetic factor ,play a crucial role ,human leucocyte antigen (HLA-DQ2)& (DQ8)haplotypes are over – expressed in gluten sensitive enteropathy disease ,and inheritance of these haplotypes and correlated immunological phenotypes may clear this correlation ,HLA-DQ2 and DQ8 as well as exhibit a weak correlation with Hashimoto's thyroid disease , however the correlation between the HLA-DQ2 and haplotype and Grave's disease is disclear (21,22,23). Furthermore ,the gene of T-lymphocyte-associated antigen -4 (CTLA-4) is related with coeliac and autoimmune thyroiditis , CTLA-4 is a candidate gene outside HLA region that is correlated with thyroid autoimmunity and exhibits a good correlation with coeliac disease (24,25).

In present study reported 12.76% presence of coeliac disease among patients with autoimmune thyroid disease ,all six patients (12.76%) were positive for IgA &IgG for both for both for both tissue transglutaminase antibodies and endomysial antibodies .Many studies have been done in Italy, and the prevalence of coeliac disease among patients with autoimmune thyroiditis recorded 27.4% among 113 patients with autoimmune thyroiditis (26),while Ravaglia *et al.*,2003(27 ),reported of coeliac disease

antibodies was 1.5% of (EMA IgA & IgG and tTG IgA & IgG) among 737 patients with autoimmune thyroid disease (27).

In Finland, tested for EMA IgA & IgG and found three a symptomatic coeliac patients and one patient with previously diagnosed coeliac disease over all recorded of 4.2%(28), while in northern Brazil recorded within 457 anti-thyroid antibodies 2.2% were reactive for EMA IgA and 3.1% for tTG (29).

The prevalence of gluten sensitive enteropathy was 12.76% among patients with autoimmune thyroid disorders complained of decreased level of calcium haemoglobin ,ferritin, alk.phos.,vit.B12,iron and free T4. Further studies should be compare between (GSE) and autoimmune thyroid disorders because of it's high prevalence.

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