Detection of autoimmune thyroid diseases in patients with celiac disease

Rana S.Aboud* ***Haidar J.Mohammad**** ***Nawal M.Jawad*****

Date of acceptance 6 /3 / 2009

Abstract

Celiac disease is an autoimmune disorder induced by gluten intake in genetically susceptible individuals. The incidence of celiac disease in various autoimmune disorders is increased 10-30 fold in comparison to the general population and the prevalence of celiac disease was noted to be 2-5% in autoimmune thyroid disease. To detect the autoimmune thyroid disease in patients with celiac disease, we investigated 22 patients suspected with celiac disease of age 1-13 years old and 20 healthy controls. IgA and IgG antigliadin antibodies were measured in serum with celiac disease sample. The patients which were positive to gliadin antibody were carried out to T3, T4 and TSH by ELISA tests. There was no significant differences ($P>0.05$) in age group and gender of patients afflicted with celiac disease and there was highly significant deferances ($P<0.01$) with increased mean level of IgG antibody in sera of hyperthyroidism patients afflicted with celiac disease than normal group. We found a relationship between celiac disease and hyperthyroidism in patients. The aim of this study was to detect the autoimmune thyroid disease in patients with celiac disease.

Key words: Celiac disease, IgA and IgG antigliadin Abs and T3, T4, TSH hormones.

Introduction

Celiac disease (CD) or gluten sensitive enteropathy is a permanent intolerance of dietary gluten leading to mucosal damage in the proximal small bowel in genetically susceptible individuals characterized by inflammation, crypt hyperplasia and villous atrophy which regress on withdrawal of gluten from the diet [1].The principal environmental factor in celiac disease is dietary gluten, which is essential for the development of the disease. A part from gliadin (wheat gluten), secalin (rye) and hordein (barley) are consider harmful, whereas oat protein avenin appears to lack a toxic effect in celiac disease [2].

Some studies have shown an inverse relationship between cigarette smoking and celiac disease, smoking may influence on T or B cells response and also decrease the intestinal permeability that is a common feature in celiac disease [3].Endocrinologists should consider celiac disease in different autoimmune condition is distinctly higher than in the general population [4].Recent population screening studies have shown the prevalence of CD in western countries approaches 1% but the condition is greatly under diagnosed, partly because many cases are sub clinical , but also because of its previously

*Dr.University of Baghdad /college of sciences Dept. Biology.
** Assistant lecture University of Al-Mustansiriya /college of sciences Dept. Biology.
***Dr. University of Baghdad /college of Ibn Haitham Dept.Chemistry.

perceived variety [5,6,7]. The association between primary hyperthyroidism and celiac disease is disputable ,there are no series activity screening for celiac disease in these patients ,more ever compared with other endocrinological disease, primary hyperparathyroidism seems to be a rare finding in celiac disease ,detected for instance, in only 0.3% of 1026 patients with celiac disease in Italy whereas secondary hyperparathyroidism may of course occur in celiac disease as a consequence of hypocalcaemia[8].Resent evidence suggests that the association between autoimmune thyroid disease and celiac disease is quite similar to that between auto immune disease Diabetes mellitus (AIDDM) and celiac disease, whereas in earlier study approximately 5% of patients with celiac disease have been found to suffer from hyper or hypothyroidism, even though the percentage are highly variable[4].Thyroid autoimmunity due to an apparent immune reaction directed against self antigen of the thyroid ,three thyroid diseases are considered to have autoimmune etiology: Hashimotos thyroiditis,idiopathic myxedima and Graves disease, so the antigen against which the autoimmune reactions are directed to produced thyroid autoimmune disease include thymoglobulin (T3) thyroid peroxides (TPO) and TSH receptor, and these auto antibodies cause direct thyroid dysfunction as in Grave's disease caused by antibodies to the TSH receptor or destructive process as in Hashimotos thyroiditis and idiopathic myxedema [9].

Material and methods

The study include 22 patients which was suspected with celiac disease of age (1-13) years and 20 healthy blood donors taken as a healthy control group.IgA and IgG antigliadin antibodies* were measured in both serum samples by using Enzyme-Linked Immuno Sorbent Assay (ELISA).The patients which were positive to antigliadin antibodies are carried out to T3, T4 and TSH test by using ELISA method**. This was performed as in the leaflet of the kit.

Statistical analysis

Comparison of paired data from the groups of subjects was done using T-test (t), while correlations between groups were analyzed using person correlation coefficient (r) formula. The computer programmer SPSS and Microsoft excel were used for T-test and correlation coefficient calculations respectively [10].

Results and discussion

The demographic study showed that there were a non-significant differences ($P>0.05$) in age group and gender of patients afflicted with celiac disease, 1-13 years and male predominant. A hyperthyroidism cases consist of a half number of patients (11, 50%) and the other patients were normal thyroids, further more the immunological specific antibody for gliadin noted a positive IgA observed with high frequency (18, 81.8%) with highly significant differences ($P<0.01$), while the negative IgG antibody result represented with increased percent (14, 63.6%), with non-significant differences ($P>0.05$).The above data documented in table and figure (1).

***The results of the antigliadin antibodies (IgA & IgG) assay are expressed in arbitrary units (AU).

****The result of the T3, T4, and TSH test are expressed in (ng/ml), (Mg/dl) and (mIu/I) respectively.

Table (1): Demographic study for patients with celiac disease.

Parameters		No.	%	Comparison of significant	
				P-value	Sig.
Age groups /Years	1-5	8	47.1	0.465	Non Sig. (P>0.05)
	6-10	4	23.5		
	>10	5	29.4		
	Total	17	100		
Gender	Male	15	68.2	0.088	Non Sig. (P>0.05)
	Female	7	31.8		
	Total	22	100		
Thyroids	Normal	11	50	1.00	Non Sig. (P>0.05)
	hyperthyroidism	11	50		
	Total	22	100		
IgA results	Positive	18	81.8	0.003	Highly Sig. (P<0.01)
	Negative	4	18.2		
	Total	22	100		
IgG results	Positive	8	36.4	0.201	Non Sig. (P>0.05)
	Negative	14	63.6		
	Total	22	100		

The table (2) proved that a highly significant differences (P<0.01) with increased mean level of IgG antibody in sera of hyperthyroidism patients afflicted with celiac disease (237.8 ± 178.9) than normal groups (60.85±40.512).

Table (2): Mean distribution of antibodies (IgA &IgG) among Thyroids.

Ab.	Thyroids hormones	N	Mean	SD	Std. Error	Mini.	Maxi.	Student test (t-test)	
								P-value	Sig.
IgA (AU)	Normal	11	60.85	40.512	12.81	8.8	129.9	0.00	Highly Sig. (P<0.01)
	hyper	11	237.8	178.9	71.71	41.6	830.3		
	Total	22							
IgG (AU)	Normal	11	47.31	50.881	16.09	1.3	136.8	0.982	Non Sig. (P>0.05)
	hyper	11	46.83	44.243	13.34	2.4	152.9		
	Total	22							

The IgG antibody gliadin levels showed similar in sera of normal (47.31 ± 50.881) and hyperthyroidism (46.83 ± 44.243), with non-significant differences (P>0.05).The thyroid hormone levels when evaluated in specific antibodies IgA and /or IgG gliadin gives a semi equal levels in sera of patients positive and /or negative IgA for three hormones (T3, T4 and TSH), with non-significant differences (P>0.05) in table (3) and (4).

Table (3): Mean distribution of thyroids hormones level among IgA antibody in sera of celiac disease patients.

Thyroids hormones	IgA	N	Mean	SD	Std. Error	Mini.	Maxi.	Student test(t-test)	
								P-value	Sig.
T3 (ng/ml)	Positive	8	1.906	0.723	0.170	0.02	3	0.418	Non Sig. (P>0.05)
	Negative	14	1.575	0.718	0.359	0.8	2.5		
	Total	22							
T4 (Mg/dl)	Positive	8	11.650	3.006	0.708	1	16	0.847	Non Sig. (P>0.05)
	Negative	14	11.325	3.015	1.507	7	14		
	Total	22							
TSH (mIu/I)	Positive	8	2.222	1.035	.244	0.5	4.5	0.812	Non Sig. (P>0.05)
	Negative	14	2.350	0.173	0.086	2.1	2.5		
	Total	22							

Table (4): Mean distribution of thyroids hormones level among IgG antibody in sera of celiac disease patients.

Thyroids hormones	IgG	N	Mean	SD	Std. Error	Mini.	Maxi.	Student test (t-test)	
								P-value	Sig.
T3 ng/ml)	Positive	8	2.063	0.678	0.240	1.1	3	0.294	Non Sig. (P>0.05)
	Negative	14	1.721	0.733	0.196	0.2	2.7		
	Total	22							
T4 (Mg/dl)	Positive	8	11.975	2.116	0.748	7	14	0.564	Non Sig. (P>0.05)
	Negative	14	11.371	3.374	0.902	1	16		
	Total	22							
TSH (mIu/I)	Positive	8	1.850	0.602	0.213	1.1	2.4	0.137	Non Sig. (P>0.05)
	Negative	14	2.471	1.032	0.276	0.5	4.5		
	Total	22							

In this study we have tried to analyze the association between autoimmune thyroid disease in patients with celiac disease .An increased prevalence of thyroid dysfunction has been reported in patients with CD [1].The result of this study agreement with other studies. So in a study from Sweden where the prevalence of CD was 95.5 per 10.000 and found that thyrotoxicosis occurred in 5.0% and spontaneous hypothyroidism in 5.8% of the celiac patients [11]. In another report a small-intestine mucosal biopsy findings in 32 patients with hyperthyroidism, but non showed villous atrophy [12].At present, it is widely accepted that immunological mechanisms are implicated in the development of the mucosal damage in celiac disease. In untreated patients there are signs of activation of both mucosal cellular and humoral immune systems[13,14].The major single environment trigger is ingested gluten (gliadin) which is essential for the development of the disease [2].So that serum antiendomysial antibody, a specific indicator of activate celiac disease, recognizes enzyme tissue transglutaminase, of which activated endothelial, fibroblast and mononuclear cells are a rich source this enzyme seems to play a critical role in controlling cell homeostasis, regulating the cell cycle through its involvement in proliferation, differentiation and apoptosis [15].Gliadin is an excellent substrate for tissue transglutaminase, which has now been shown to be the predominant auto antigen for celiac disease [16].Celiac disease could be explained by which gliadin or tissue transglutaminase activates T cells that are cross-reactive with various self-antigens, so that of such inflammatory responses may have the capacity to persist in genetically susceptible hosts and lead to chronic organ-specific autoimmune disease [17].It is also possible that a part from gliadin ,transglutaminase can modify other external or self-antigens by cross-linking or deamidation and thus generate different new antigens [18]. These antigens and antibody production can further induce various autoimmune phenomena outside the intestine. On the other hand, apart from antiendomysial antibodies, celiac patients have an increased frequency of other auto antibodies. [19, 20, 21].Furthermore, oxidative stress and inflammation may cause aberrant activation of transglutaminases in different tissues, which leads to the formation of inappropriate protinaceous aggregates that may be

cytotoxic and contribute to a variety of disease [22]. The coexistence of celiac disease and endocrinology autoimmune disease appears to be at least partly due to a common genetic predisposition [23].Susceptibility to these disease has localized to the HLA region of chromosome 6 approximately 90% of celiac disease patients have the HLA DR3-HLA DR2 configuration (encoded by alleles DQA1 0501 and DQB1 0201) and most of the remainder express the DR4-DQ8 haplotype encoded by DQA1 0301, DQB1 0302 alleles [23, 24, 25]. Genome-wide screening studies have resulted in a number of proposals for candidate non HLA regions. In Irish CD patients, five other chromosome locations have been identified 6p23, 7q31, 11p11, 15q26 [23]. Outside the HLA region both CD and autoimmune thyroid disease are reported to be associated with the gene encode cytotoxic T-lymphocyte associated with antigen-4 (CTLA-4) a candidate gene for conferring susceptibility to thyroid autoimmunity [26, 27, 28].A recurrent study indicated that is many as 43% of patients with Hashimotos thyroiditis showed an increased density of T-cell receptor bearing intra epithelial lymphocytes signs of mucosal T-cell activation both typical for CD [29].The results of this study showed a close association between various autoimmune endocrinologyical disorders and CD patients.

References

1-Ching, C.L., Jones, K.J.and Jermy, G.C. 2007.Celiac disease and autoimmune thyroid disease.Clin. Med and Res.5 (3):184-192.

2-Jnatuinen, E.K., Pikkarainnen, P.H., kmppainen, T. A., Kosm, V.M., Jarvinen, R.M.K.,Uusitupa, M.I.J., and Julkunen,R.J.K. 1995.A comparison of diet with and without oats in adult with celiac . N.E.ngl.J.Med.333:1033-1037.

3-Vazque, H., Samecol, E., Bai, J.C. 2001.Relation between cigarette smoking and celiac disease: evidence fro a case control study. Am.J.Gastroenttero.96:798-802

4-Collin, P., Kaukinen, K., Valimaki, M.and Salmi, J. 2002. Endocrinological disorders and celiac disease .Endo. Rev.23 (4): 464-483.

5-Kolho, K.L., Farkkila, M.A, and Savilahli, E. 1998.Undiagnosed celiac disease is common in finish adults. Scand .J.Gastroenteral. 33:1280-1283.

6-West,J., Logan, F.F., Hill,P., Holmes, G.K. ,and Khaw,K.T. 2003 .Seroprevalence, correlates and characteristics of undetected celiac disease. England.Gut.52:960-965.

7-Tommasini, A.Not, T., Kiren, V.Baldes, V., Santon, D., Trevisiol, C. 2004.Mass screening for celiac disease usinantihuman transglutaminas antibodyassay. Arch. Dis.Child.89:512- 515.

8-Bttaro, G.,Calado,F.,Rotolo,N.,Spina,M.,and Corazza,G.R.. 1999. The clinical pattern of sub clinical/silent celiac disease: an analysis on 1026 consecutive cases.Am.J. Gastroenterol. 94:691-696.

9-Kumer, V., RaJadhyaksha, M., and Wortsman, J. 2001.Celiac disease associated autoimmune endocrinopathes. Clin and Diac. Lab. Immun.8 (9):678-685.

10-Sorlie, .D.E. 1995.Medical biostatics and epidemiology: Examination and board review first ed.Norwalk, Connecticut, Appleton and Lange 47-88.

11-Meiddhagen, G., Jamerot, G. and Kraaz, w. 1988.Adult celiac disease within a defined geographic area in Sweden. Study of prevalence and

associated disease J.Scand. Gastro.23:1000-1004.

12-Siurala, M., Varis, K.Lamberg, B.A. 1966.Gastrointestinal tract in hyperthyroidism before and after treatment .J.Scand. Gastro. 1:79-85.

13-Tredjosiewics L.K., Howdle P.D. 1995. T-cell responses and cellular immunity in celiac disease. Baillieres Clin. Gastroenterol.9:251-272.

14-Sollid L.M.,Molberg O.,McAdam S.,Lundin K.E.A.1997. Autoantibodies in celiac disease :tissue transglutaminase-guilt by association. Gut. 41:851-852.

15-Piacentini M., Colizzi V.1999. Tissue transglutaminase as the auto antigen of celiac disease. Nat Med.3:797-801.

16-DietrerichW., EhnisT, Bauer M., Donner P.1977. Identificationof tissuetransglutaminase as the autoantigen of celiac disease.Nat. Med 3:797-801.

17-Schuppan D.2000.Current concepts of celiac disease pathogenesis .Gastroenterology 119:234-242.

18-Lerner A., Blank M., Lahat N., Shoenfeld Y.1998.Encreased prevalence of autoantibodies in celiac disease. Dig.Dis.Sci.43:723-726.

19-Lancaster-Smith M.J., Perrin J., Swarbrick E.T., Wright J.T.1974. Celiac disease and autoimmunity. Postgrad.Med. J.50:45-48.

20-DA Rosa Uyiyama S.R.,Da Silva kortze L.M.,deMessias Reason I. J. 2001.spectrumof autoantibodies in celiac patients and relatives. Dig.Dis.Sci. 46:2624-2630.

21-Kim S.Y., Jeitner T.M., Steinert P.M.2002.Transglutaminase in disease .Neurochem. Int.20:85-103.

22-Sollid, L.M., Markusses, G.E.K.J., Gjerde, H., Vtdal, F. and Throsby. 1989. Evidence for a primary association of celiac disease to a particular HLA_DQ, B heterodimer. J.Exp.Med.169:345-350.

23-Michalaski, J.P., McCombs, C.C., Aria, T., Elston, R. C., Cao, T.McCarlly, C.F., and Steveens, F.M. 1996.HLA_DR, DQ genotypes of celiac disease patients and healthy subjects from the west of Irlend.Tissue.Antigenes.47:127-133.

24-Polvi, A, .Eland, C., Koskimies, S.Maki, M., and Partanen, J. 1966.HLADQ and DP in Finnish families with celiac disease .Eur.J.Immunogen.23:221-234

25-Balas,A.,Vicario,J.L.,Zambrano, A.,acuna,D., and Garcia-Novo,D. 1997.Absolute linkage of celiac disease and dermatitis herpetiforis. Tissue Antigens.50:52-56.

26- Hunt, K.A., McGovern, D.P., Kumar ,P.J.Ghsh, S.,Tavis, S.P., Walters, J.R., Jewell, D.P., Play ford, R.J., and Vanlteel,D.A. 2005.CTLA4 haplotype associated with celiac disease.J.Eur. Hum. Genet.13:440-444.

27-Chiskatiakov, D.A., and Turakulov, R.I. 2003.CTLA_4and its role in autoimmune thyroid disease.J. Mol. Endorinolo.31:21-36.

28-King,A.L.,Moodie,S.J.,Fraser,J.S., Curtis,D.,Reid,E.,Dearlove,A.M., and Ciclitira, P.J. 2003. Coeliac disease: Investigation of proposed causal variants in the CTLA4 gene region.J.Eur.Immungenet.30:427-432.

29-Valentino,R.,Savostano,S., Maglio, M.,Paparo,F.,Ferrora,F.,Doralo,M., Lombardi, G. and Troncon,R. 2002. Markers of potential co iliac disease in patients with hashimotos thyroiditis.J.Eur. Endocrinol.146: 479-483.

التحري عن أمراض الغدة الدرقية الذاتية في مرضى حساسية الحنطة

رنا سعدي عبود* ***حيدر جاسم محمد**** ***نوال محمد جواد*****

*جامعة بغداد / كلية العلوم / قسم علوم الحياة
** الجامعة المستنصرية / كلية العلوم / قسم علوم الحياة
***جامعة بغداد /كلية التربية ابن الهيثم/ قسم الكيمياء.

الكلمات المفتاحية : مرض حساسية الحنطة ، ضد الكليادين IgA و IgG ، هرمونات T3 , T4 , TSH

الخلاصة

يعتبر مرض حساسية الحنطة من أمراض المناعة الذاتية والذي يحفز من خلال امتصاص مادة الكلوتين من الغذاء في الأشخاص الذين يتحسسون من هذه المادة ويعتبر هذا المرض وراثي و.إن التعرض لهذا المرض يزداد(10-30) مرة مقارنة مع باقي أمراض المناعة الذاتية في عموم الأفراد . وقد لوحظ أن انتشار مرض حساسية الحنطة كان بمعدل (2-5%) من بين أمراض الغدة الدرقية الناتج من أمراض المناعة الذاتية . لأجل التحري عن الغدة الدرقية الذاتية في المرضى المصابين بحساسية الحنطة فقد تم اخذ (22) عينة مصل من المرضى المصابين بحساسية الحنطة بأعمار تتراوح بين (1-13) سنة مع (20) عينة مصل من الأصحاء الذين يعتبرون عينات سيطرة. تم قياس كل من نسبة وجود الأجسام المضادة من نوع IgA و IgG ضد مادة الكليادين في عينات الأشخاص قيد الدراسة من خلال تقنية الاليزا. وقد خضع المرضى الموجبين لاختبار مادة الكليادين لقياس مستوى هورمونات T3وT4وTSH من خلال نفس التقنية باستخدام أمصال المرضى المصابين بحساسية الحنطة ضد هورمونات T3وT4وTSH . لم تكن هناك فروق معنوية ($P>0.0.5$) في مجموعة الدراسة لدى المرضى الذين يعانون من حساسية الحنطة بينما كانت هناك فروق معنوية عالية ($P<0.01$) مع زيادة مستوى متوسط الجسم المضاد IgG في أمصال المرضى المصابين بفرط إفراز الغدة الدرقية و الذين يعانون أساسا من مرض حساسية الحنطة مقارنة مع مجموعة السيطرة الطبيعية. إن الهدف الرئيسي من هذه الدراسة هو الكشف عن العلاقة بين أمراض الغدة الدرقية التي تعتبر من أمراض المناعة الذاتية لدى مرضى حساسية الحنطة.