Detection of some auto antibodies of Celiac disease in Sera of patients with Chronic Hepatitis B virus

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Abstract
To determine the relationship between chronic hepatitis B virus and autoimmune celiac disease, seventy five patients with chronic hepatitis B virus of ages (8-70) years have been investigated and compared to 50 healthy individuals. All the studied groups were carried out to measure anti-tissue transglutaminase antibodies IgA and IgG by ELISA test and anti-endomysial antibodies IgA and IgG by IIFT. There was a significant elevation in the concentration of anti-tissue transglutaminase antibodies IgA and IgG compared to control groups (P< 0.01) .The prevalence of antiTtG IgA and IgG was 14.67% and 12.0% respectively.There was a highly significant difference (P<0.01) when compared between studied groups .While the prevalence of anti-endomysial antibodies IgA and IgG was 9.33% and 4.0% respectively. There was a highly significant difference(P< 0.01) when compared between studied groups. These results indicated that infection with chronic hepatitis B virus may play an important role in pathogenesis of celiac disease.

Keywords: Hepatitis B virus, chronic infection, celiac disease, auto antibodies.

التحري عن بعض الأضداد الذاتية لداء الزلاقي في مصول المرضى المصابين بالتهاب الكبد الفيروسي المزمن النمط – ب–

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الخلاصة:
لغرض تعيين العلاقه بين التهاب الكبد الفيروسي المزمن النمط – ب– والداءالزلاقي الذاتي المناعة ، تم التحري عن (75) شخص مصاب بالتهاب الكبد الفيروسي المزمن النمط – ب– باعمار تتراوح من (70-8) سنة وتمت المقارنة مع (50) شخص سليم . خضعت جميع عينات الدراسة لقياس مستوى اضدادAbs anti–tissuetransglutaminase الصنف (IgA,IgG)باستخدام تقنية الامتزازالمناعي المرتبط بالانظيم و anti–endomysial Abs (IgA,IgG) باستخدام تقنية التالق المناعي غيرالمباشر. اظهرت نتائج الدراسة ارتفاعا معنويا (P< 0.01) في تركيزاضداد anti–tissue transglutaminase Abs الصنف (IgA,IgG) مقارنة بمجاميع السيطرة.كانت نسب اضداد anti–tissuetransglutaminase Abs الصنف

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(gA,IgG) 12.0% (9/75),14.70% (11/75)على التوالي وقد كانت هنالك فروق معنوية عاليه
(P < 0.01) بين مجاميع الدراسة بينما كانت نسب اضداد anti−endomysial Abs 9.33% (7/75)
(IgA,IgG)، 4.0%(3/75) على التوالي وهنالك فروق معنوية عاليه (P< 0.01) بين مجاميع
الدراسة.تشير الدراسة بان الخمج بالتهاب الكبد الفيروسي المزمن النمط – ب– يمكن أن يلعب دورا مهما في
أمراضية حساسية الحنطة.

Introduction:

Celiac disease (CD) is an intolerance to gluten, a protein found in wheat, rye and barley, it is recognized as a chronic autoimmune disorder that occurs in genetically predisposed individuals, both children and adults and it affects approximately 1% of the world population [1, 2].Abnormal immune response to gliadin , genetic factors, and environmental factors play a role in the pathogenesis of CD[3].Infectious agents have been implicated in the pathogenesis of CD via various pathogenic mechanisms, such as molecular mimicry, resulting in modulation of the host s immune tolerance. Transient infections or increased permeability of the mucosa may facilitate disease onset induced by the uptake of gluten peptide into a microenviromental milieu in the small intestinal mucosal [4].Recently, it has been hypo-
thesized that non intestinal inflammatory disease may trigger immunologic gluten intolerance in susceptible individuals, and hepatitis B virus (HBV) as far as Hepatitis C virus (HCV) were thought to be suitable candidates[5].Hepatitis B virus infection leads to the activation of several immune system components that has been suggested to culminate in the production and release of interferon and interleukins that disrupt the intestinal mucosal barrier, allowing the penetration of immunogenic peptides and activation of CD4 T lymphocytes.There appears to be an increase in the production of HLA-DQ8, which links gluten peptide molecules and facilitates activation of other immune cells.It is suggested that HBV can trigger the pathophysiological processes that lead to mucosal inflammation induced by gluten [4].The association between CD and several liver disorders has long been documented, about 40% of adult CD patients have been reported to have a mild to moderate hyper transaminasemia (up to five times the upper normal limit) at the time of diagnosis of CD [6,7]. Several isolated cases of infection with HBV and other viruses, which probably only reflect a fortuitous associated with CD [8].

Because the relationship between HBV and celiac disease has yet be established, this study aimed to estimate the seroprevalenve of some autoantibodies of CD in patients with chronic hepatitis B virus.

Materials and methods

The study was carried out on seventy five patients infected with chronic hepatitis B virus who attended to hepatic and gastrointestinal tract hospital in capital of Baghdad during the
Period from first of November 2013 until February 2014.The ages of the total patients were ranged from (8-70) years,27(36%) female and 48(64%)male .Fifty samples of healthy individuals; 23 female and 27 male were studied as a control groups of same ages and sex. Blood samples (5ml) were collected by disposable syringe into gel tubes and stand at room temperature until the coagulant was form. Then the samples are centrifuged at 3000 rpm for 5 minutes .Serum samples were dispended on a seven Ependroff tubes. All samples were marked by the name, day and numbering and stored at (-20˚C) until carried out to immunological examinations.

Immunological examination

All the studied groups were carried out to measure anti-tissue transglutaminase antibodies IgA and IgG by ELISA test(Aeskulisa, Germany) and anti-endomysial antibodies IgA and IgG by IFAT test (Uroimmune, Germany) according to the leaflet of kit.[9].

Statistical analysis

The statistical analysis system-SAS [10] was used to effect of different factors in study parameters .Chi-square test was used to significant comparison between percentage and least significant difference. LSD test was used to significant compression between means in this study.

Results and Discussion:

A total of seventy five CHB patients were classified into three groups,group 1 with age less than 30 years,which included twenty five patients (33.3%). The highest number of CHB patients were located within group 2 in which range of age (30-50) years (54.7%),and the last group which was greater than 50 years and was included only 9 CHB patients (12%) .The results of the present study showed that there was a significant elevation($P< 0.05$) in the concentration of anti-tissue trsansglutaminase antibodies IgA and IgG (9.62 ± 0.35), (5.62 ± 0.12) U/ml compared to control groups (3.12 ± 0.16), (1.67 ± 0.06)U/ml as shown in fig(1).The prevalence of anti-tissue trsansglutaminase antibodies IgA and IgG was(11/75) 14.67% and (9/75)12.0% respectively. There was a highly significant differences ($P< 0.01$) when compared between studied groups as shown in table (1).The prevalence of anti-endomysial antibodies IgA and IgG was (7/75)9.33% and (3/75) 4.0% respectively. There was a highly significant differences ($P< 0.01$) when compared between studied groups as shown in table- 2 and figure-2-a,2b.

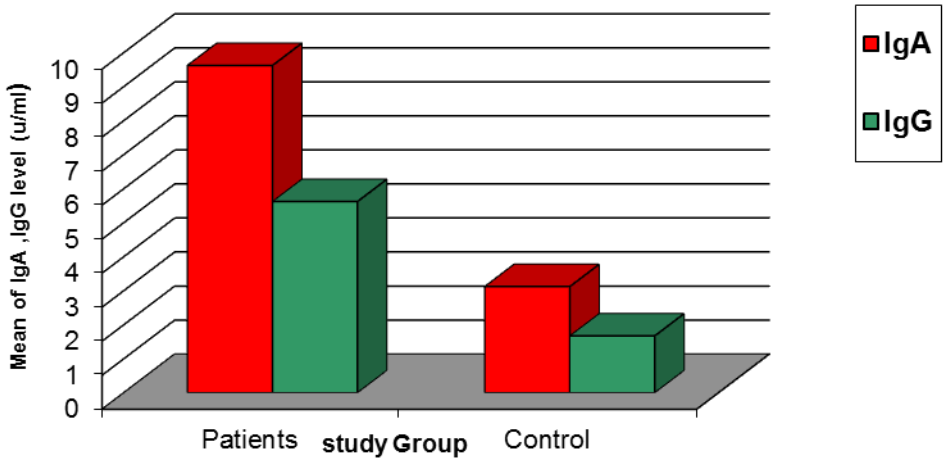

Figure 1- Mean level of anti- tissue transglutaminase IgA and IgG(U/ml)in the sera of patient with chronic hepatitis B virus and control groups.

Table 1- The percentage distribution of TtG Abs in sera of CHB patients.

Test	IgA (TtG)		IgG(TtG)	
	No.	%	No.	%
Positive	11	14.67	9	12.00
Negative	64	85.33	67	88.00
Total	75	100 %	75	100 %
Chi-square value	---	13.294 **	---	14.983 **
** (P<0.01).				

Table 2- The percentage distribution of EMA Abs in sera of CHB patients.

Test	IgA (EMA)		IgG(EMA)	
	No.	%	No.	%
Positive	7	9.33	3	4.00
Negative	68	90.67	72	96.00
Total	75	100 %	75	100 %
Chi-square value	---	15.063 **	---	16.295 **
** (P<0.01).				

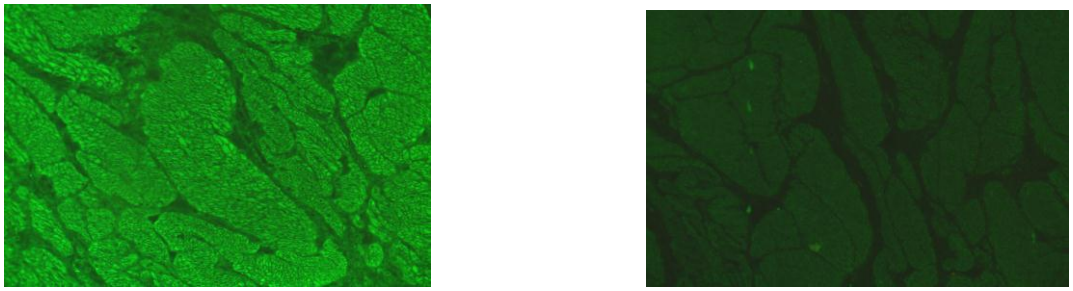

Figure 2-a- Posaitive anti-endomysial Abs IgA, IgG and (2b): Negative anti-endomysial Abs by IFAT test for sera of patients with chronic hepatitis B virus .

In this study we have tried to analyze the association between autoimmune celiac disease in patients with chronic hepatitis B virus. The results of the present study were agreed with other studies. Several studies which examined the possibility of hepatitis B virus and its linkage with celiac disease [11].One study showed that the prevalence of anti-TtG antibodies 8.8%[12].

Another study demonstration a prevalence of 3% for anti-endomysial antibodies and 9% for anti-tissue transglutaminase antibodies in CHB patients.[13].While [4] reported two patients who received the diagnosis of CD following an acute hepatitis B infection. Other research revealed that six of fifty patients had positive serology for CD (four were anti-endomysial antibodies positive and five were anti-tissue transglutaminase antibodies positive [14].

Our results show anti-tissue transglutaminase antibodies and anti-endomysial antibodies of both IgM and IgG type with increased prevalence in patients with chronic hepatitis B virus and differences in patients with controls group.

Anti-tissue transglutaminase antibodies has been showed closely to correlate with the acute phase of the disease, both IgA antiendomysial antibodies and IgA tissue transglutaminase antibodies serves as a specific and sensitive marker of celiac disease, and is highly useful in diagnosis and follow up[15,16]. Polyclonal lymphocyte activation, molecular antigen mimicry, epitope spreading, bystander activation, and activation by a super-antigen, have all been proposed as possible mechanistic links between the development of autoimmunity and exposure to infectious agents.[17].Some hepatotropic virus is capable of triggering autoimmune phenomena in the course of the disease [18].

It had been hypothesized that chronic HBV could trigger immunological gluten intolerance in susceptible individuals [5].This hypothesis, however, has not yet been supported by sufficient scientific evidence and data. Similarly, hepatitis B and hepatitis C, which may have amino acid sequences homologous to the toxic epitopes in gliadin, could trigger immunological gluten intolerance in susceptible subject [19]. Some authors suggested that the development of immune

response for hepatitis B virus clearance triggers the intestinal tissue damage that observed in celiac disease in genetically predisposed individuals [4].Also, celiac disease may be one of the immune disease associated with a high rate of HBV vaccine non-responsiveness due to a very high incidence of a particular extended HLA haplotype in no responders to HBV vaccine. [20, 21].

Conclusion:

These results indicated that infection with chronic hepatitis B virus may play an important role in pathogenesis of celiac disease.

Recommendation:

Patients with chronic hepatitis B infection should be carried out the laboratory examination of celiac disease especially anti-tissue transglutaminase Abs.

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