Celiac disease in adult patients with type 1 diabetes mellitus in Tunisia

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SUMMARY

Objective: Type1 diabetes mellitus may be associated with celiac disease. The prevalence of celiac disease as determined by screening among adult patients with type 1 diabetes is high with rates of 1.0-7.8% in Europe and U.S.A.

The aims of the study are to determine the prevalence of celiac disease in adults with type 1 diabetes in Tunisia.

Methods: 348 consecutive adult patients with type1 diabetes were investigated prospectively and screened for celiac disease. The mean age was 28.45 ± 10.74 years old. There were 176 females and 172 males. For the screening of celiac disease, we used immunoglobulin A (IgA) anti-endomysium (EMA) antibodies determined by an indirect immunofluorescence method. Anti-transglutaminase (tTG) antibodies were determined by an ELISA method. Those patients with positive results for anti EMA and or tTG were proposed for duodenal biopsy.

Results: 14 patients were positive for anti EMA and had high or a weak positive level of tTG antibodies. One patient from this group was already known to have celiac disease. Only 8 patients consented to biopsy and morphological changes were consistent with celiac disease in all cases. Prevalence of biopsy-proven celiac disease was 2.3% (95% CI = 1.0-4.5%).

Conclusion: The present study confirms that celiac disease of adults is prevalent in type 1 diabetic patients in Tunisia. Serological screening for celiac disease in type 1 diabetes is important because many patients are asymptomatic and most are detected by the screening.

Key-words: Celiac disease · Adult type1 diabetes mellitus · Prevalence · Screening.

RÉSUMÉ

Maladie coeliaque chez les diabétiques de type 1 adultes en Tunisie

Objectif : La prévalence de la maladie coeliaque de l’adulte chez le diabétique de type 1 déterminée par le dépistage sérologique systématique est de 1.0 %-7.8 % en Europe et aux États-Unis.

Le but de ce travail est de déterminer la prévalence de la maladie coeliaque chez les diabétiques de type 1 adultes.

Méthode : Nous avons réalisé une étude transversale avec un recrutement consistatif de 348 (172 hommes et 176 femmes) diabétiques de type1 adultes qui s’est déroulée de 2000 à 2003. La moyenne d’âge était de 28 ± 10,7 ans. La durée moyenne du diabète était de 7,99 ± 7,57 ans. Nous avons recherché les anticorps anti-transglutamínase (tTG) de classe IgG et IgA et les anticorps anti-endomysiums (EMA). La biopsie duodénale a été pratiquée chez les patients ayant des tTG et/ou des anti EMA positifs.

Résultats : 14 patients avaient les anticorps anti-tTG et anti-EMA de classe IgA positifs. 8 patients seulement ont réalisé la biopsie duodénale qui était pathologique dans tous les cas. Une patiente avait une maladie coeliaque déjà connue. La prévalence de la maladie coeliaque avec preuve histologique est de 2,3 % (8/347) (IC 95 % : 1.0-4.5 %).

Conclusion : La fréquence élevée de l’association diabète type 1-maladie coeliaque dans notre série justifie le dépistage sérologique systématique de la maladie coeliaque chez l’adulte diabétique tunisien.

Mots-clés : Maladie coeliaque · Diabète de type 1 adulte · Prévalence · Dépistage.
Celiac disease is a permanent intolerance to ingested gluten that results in immunologically mediated inflammatory damage to the small intestinal mucosa. Serological screening studies have shown the worrildi prevalence to be 1 in 266 [1, 2]. Silent celiac disease has been reported in first and second degree relatives of patients with biopsy proven celiac disease and in type 1 diabetes, thyroid related auto-immune disease. Down syndrome and anemia [1, 2, 3, 4]. Children and adults with type 1 diabetes are at increased risk of celiac disease and the prevalence of celiac disease as determined by screening among adult patients with type 1 diabetes is high, with rates ranging from 1.0 to 7.8% in Europe and United States of America [5]. The prevalence of celiac disease in diabetic children was found to be high in Libya and Algeria: 10.3% and 16.3% respectively [6, 7]. But the prevalence of celiac disease in adults with type 1 diabetes is unknown in Arab countries and in North Africa.

The objective of our study was to determine the prevalence of celiac disease in unselected hospital based adult type 1 diabetic patients using the anti-endomysial antibodies and anti-transglutaminase antibodies test as a screening test.

 Patients and methods

Our study was carried out prospectively in the National Nutrition Institute in Tunis between January 2000 and June 2003. The cohort consisted of 348 consecutive adults with type 1 diabetes (176 females, 172 males), attending the outpatient and the inpatient clinics. The mean age of the patients was 28.45 ± 10.74 years (range: 16-60 years), and median diabetes duration was 7.57 years. The mean age at diagnosis of diabetes was 20.3 ± 5 years.

Inclusion criteria included the diagnosis of type 1 diabetes mellitus based on insulin requirement at diagnosis and ketosis pronoens. The age at diagnosis of diabetes was over 15 years old and before age 40.

Three hundred and forty-eight consecutive adults with type 1 diabetes mellitus were prospectively screened for celiac disease. Samples were taken during the consultation and serum was tested for IgG and IgA immunoglobulin for the four antibodies. We had considered gastro-intestinal symptoms as diarrhoea and/or constipation and abdominal pain.

Anti-endomysium and anti-reticulin antibodies were determined by indirect immunofluorescence antibody. Anti-transglutaminase and anti-gliadin were determined by ELISA method. Determination of IgA tissue transglutaminase antibodies (tTG) were carried out with Bindazyme Human Anti Transglutaminase Enzyme Immunoassay Kit (The Binding Site, Birmingham, U.K) in accordance with the manufacturer’s instructions. We defined the cut off point for positivity at 5 U/ml and a weak positive as a level of 4 to 10 U/ml and high when it exceeds 10 U/ml. IgA anti-endomysium (EMA) antibodies were determined using an indirect immunofluorescence technique on sections of monkey esophagus (The Binding Site, Birmingham, U.K) and human umbilical cord.

Duodenal biopsy sampling: patients positive for anti-endomysial and or anti-transglutaminase antibodies were informed of their antibody positivity and proposed for gastro-intestinal endoscopy with biopsies of distal duodenum. Four biopsies of the distal duodenum were taken at endoscopy. Standard criteria for the diagnosis of celiac disease were used. Mucosal tissue was graded according to predefined criteria. Intra-epithelial lymphocytes were counted after immunohistochemical staining for CD8 cells. An elevated intra-epithelial lymphocyte count was defined as more than 60 intra-epithelial lymphocytes per 100 enterocytes [8].

Results

Of the three hundred and forty-eight patients who underwent testing, fourteen were positive for IgA anti-EMA antibodies and IgA anti-tTG antibodies. One patient from this group had already been known to have biopsy-proven celiac disease. Only eight patients agreed to undergo endoscopy and distal duodenal biopsy. Morphologic changes were consistent with coeliac disease in all of them. Prevalence of biopsy-proven celiac disease detected by screening was 2.3% (8/347) (95% CI: 1.0-4.5%). Prevalence rates were estimated considering already known cases 0.02% (1/348) and newly detected ones together 2.6% (9/348). The group detected by screening was not statistically different regarding gastro-intestinal symptoms or anaemia from patients with both negative antibodies but had a significantly longer duration of diabetes (p < 0.04) (Tab I).

Seven patients had isolated weak positivity of IgA anti-tTG antibodies and were negative for anti-EMA antibodies. Duodenal biopsies were performed in 6 cases of them and all were normal.

Discussion

The number of patients detected by screening in our study was much greater than that those who had previously been known to have celiac disease. Thus, among the 348 patients included in this study, eight had biopsy-proven celiac disease detected by screening [2.3% (95% CI: 1.0-4.5 %)]. So the total prevalence of biopsy-proven celiac disease was 2.6% (9/348), while five patients who were positive for both IgA anti-EMA and IgA anti-tTG antibodies refused to undergo biopsy and remained with sus-

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expected celiac disease [1.1% (5/348)]. However, all subjects positive for both IgA anti-EMA and IgA anti-tTG antibodies and who underwent duodenal biopsy had a lesion consistent with celiac disease in our study in agreement with other studies [9]. We can safely presume that the overall prevalence of coeliac disease is about 4.0% (14/348) in our study. We found that the prevalence of celiac disease in adults with type 1 diabetes has not been estimated yet in Arab countries and in North Africa. Previous studies in neighbouring countries have noted a high rate of celiac disease in children. Celiac disease is common in the Saharawi paediatric population and reported mean prevalence is of 5.6% [10, 11]. Prevalence in paediatric population with diabetes in Libya and Algeria was found to range between 10 and 16% [6, 7].

Adults with celiac disease may be asymptomatic and have the silent or subclinical forms of the illness. Gastrointestinal complaints may be few and when present may be misinterpreted as due to autonomic neuropathy [12, 13, 14]. The prevalence of gastro-intestinal symptoms and hypochromic microcytic anaemia was not statistically different when we consider patients with biopsy-proven celiac disease and patients without celiac disease in our study.

Patients with type 1 diabetes found to have symptomatic celiac disease will potentially benefit from improved control of diabetes with reduction in hypoglycaemic episodes and reduction in complications associated with celiac disease when they are treated with gluten free diet [4, 5, 14, 15]. The risk of gastrointestinal malignancy is increased in patients with symptomatic disease; whether patients with silent or subclinical celiac disease are at increased risk for gastro-intestinal malignances is still unclear [2, 14]. Undetected celiac disease increases the risk of reduction in bone mineral density, osteoporosis and fractures in adults [2, 4, 14].

The potential benefit of systematic screening of CD in patients with type 1 diabetes is still a matter of debate [14]. Other studies suggested regular testing at regular intervals, but were uncertain about the length of these intervals or the duration of the testing period [5, 14].

**Conclusion**

The present study confirms that celiac disease of adults is common in type 1 diabetic patients in Tunisia. The benefits of diagnosis and treatment in adults are such that this disorder should be screened in all adult type 1 diabetic patients by preferably tests for IgA anti-endomysial and anti-transglutaminase antibodies.

**References**


**Table I**

Characteristics of patients with and without celiac disease.

<table>
<thead>
<tr>
<th>N</th>
<th>Sex ratio</th>
<th>Age (years)</th>
<th>D.D (years)</th>
<th>Prevalence of Anaemia (%)</th>
<th>Prevalence of GIS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with both negative antibodies</td>
<td>327</td>
<td>1</td>
<td>28.5 ± 10.8</td>
<td>7.9 ± 7.5</td>
<td>12.2</td>
</tr>
<tr>
<td>Patients with both positive antibodies and biopsy proven C.D</td>
<td>8</td>
<td>1</td>
<td>30.1 ± 8.3</td>
<td>13.4 ± 11.3*</td>
<td>25.0</td>
</tr>
<tr>
<td>Patients with both positive antibodies but no biopsy</td>
<td>5</td>
<td>0.25</td>
<td>28.3 ± 9.2</td>
<td>10.1 ± 11.6</td>
<td>20.0</td>
</tr>
<tr>
<td>Patients with isolated weak positive tTG antibodies</td>
<td>7</td>
<td>0.50</td>
<td>27.0 ± 9.9</td>
<td>6.8 ± 4.8</td>
<td>14.3</td>
</tr>
</tbody>
</table>

*p = 0.04

N: number of patients
D.D: duration of diabetes
GIS: gastro-intestinal symptoms
C.D: celiac disease

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