

Celiac disease in patients with chronic psychiatric disorders

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ABSTRACT

Aim: The aim of this study was to determine the prevalence of celiac disease in Iranian patients suffering from chronic depression or schizophrenia.

Background: Psychiatric disorders are common in untreated celiac disease.

Patients and methods: Two hundred Iranian inpatient men with in chronic phase of depressive disorders or schizophrenia, and 200 age-matched healthy male subjects were screened for celiac disease by anti-tissue transglutaminase IgA antibodies. The mean age of the study patients was 37 years.

Results: One (1 %) schizophrenic and two (2%) depressive patients were positive for anti-tissue transglutaminase IgA antibodies; duodenal biopsy was not possible in these subjects. In the control group one (0.5%) individual was positive for anti-tissue transglutaminase IgA antibodies, but had normal duodenal histology. The difference between patients and controls was not statistically significant.

Conclusion: The frequency of celiac disease serology in schizophrenic and depressive inpatients was not significantly higher than that in the general population. We would therefore not advocate systematic serologic screening in these patients, but alertness to celiac disease should be kept in mind.

Keywords: Celiac disease, Depression, Schizophrenia, Serologic screening, Tissue transglutaminase antibodies.

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Introduction

Celiac disease is an under diagnosed condition in which gluten ingestion in genetically

susceptible individuals results in small-bowel mucosal inflammation and villous atrophy. Most patients are asymptomatic or suffer from mild symptoms only, (1) and many present with extraintestinal manifestations such as neurologic disorders (2). The anti-tissue transglutaminase antibody (TTGA) test is a sensitive and specific tool in disclosing celiac disease with overt villous

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atrophy (3) With a specificity of approximately 95%, false positive tests are uncommon, and TTGA may appear in serum at an early stage in the disease, in other words before the clinical manifestations and even before the development of villous atrophy (4). Psychiatric disorders are also common in untreated celiac disease, especially depressive symptoms (5-8). Hallert & Derefeldt reported that nine out of 42 studied subjects had attended a psychiatric clinic because of neurotic problems and most of them are involved with depressive disorders (7).

Celiac disease was considered relatively uncommon in Iran, until recently an estimated population prevalence of 1:166 was reported (9). Greater awareness of its varying presentation and the availability of new serologic tests have shown celiac disease to be relatively common (10). These observations prompted us now to assess the association between celiac disease and severe chronic depression and schizophrenia.

Patients and Methods

This cross-sectional study was carried out in 2006-2007. By random sampling, 200 inpatient men comprising 100 with chronic depression and 100 with schizophrenia (mean age 37 years, range 18-68 years) were enrolled in Razi Hospital, Tabriz, Iran. Chronic depression was defined according to DSM-IV criteria, (11) diagnosed and treated by semi-structural clinical interview by two psychiatric experts. The duration of the diseases was more than two years, and the diseases were unbearable without antipsychotic drugs. Patients with schizophrenia suffered from different types of the disease such as paranoid, phrenetic or undistinguished. Two hundred healthy males were selected as controls, matched for age and birthplace (mean age 32, range 4-77 years).

A written informed consent was obtained from patients (or from next of kin if necessary) and the

study was approved by the Institutional Ethics Committees of the Research center for gastroenterology and liver disease, Tabriz Medical University. Blood samples were collected and the sera stored at 20°C until analysis. IgA class TTGA antibody was measured by enzyme-linked immunosorbent assay using a commercially available kit (Eu-tTG IgA, Eurospital, Trieste, Italy). A titer of > 7 U/mL was considered positive as recommended by the manufacturer. Serum IgA was measured in each subject.

Statistical analysis

A frequency of 0.6% celiac disease has been reported in Iran (9). Assuming this frequency in 200 controls and a tenfold frequency in psychiatric patients (6%, as has been reported in many autoimmune conditions) the statistical power of 0.80 at a significance level of 0.05 would then be achieved. Percentages were compared by rates and proportion; 95% confidence intervals (CI) were reported.

Results

None of the 200 patients had a history of chronic diarrhea and all were taking antipsychiatric drugs (antipsychotic such as risperidone, haloperidol or perphenazine and anticholinergic for schizophrenic patients, and fluoxetine and tricyclic antidepressants for depressive patients). Three patients with chronic psychiatric disorders were TTGA positive, in which one (age 52 years) with schizophrenia and two (both 30 years of age) with chronic depression. Of these three patients, two refused duodenal biopsy and one died during the study period. In the control group, one (age 25 years) out of 200 individuals was positive, but duodenal histology proved normal. The prevalence of positive celiac disease serology in patients with chronic psychiatric disorders was thus slightly but not significantly higher than in controls; 1.5%, (95% CI: 0.38-4.03) and 0.5 % (95% CI: 0.00025-

2.44), respectively ($P=0.06$). Clinical features and laboratory findings among the patients with schizophrenia and depression are shown in Table 1. Five in the study group and none in the control group had selective IgA deficiency.

Table 1. Clinical and laboratory features of male patients with schizophrenia and depression

	Schizophrenia	Depression	Healthy controls
Number	100	100	200
Age (years)	37±11 [†]	37±8	32±14
TTGA [*]	1	2	1
Constipation	12	12	---
Heartburn	7	10	---

^{*}TTGA IgA-class anti-tissue transglutaminase antibody;

[†] mean±standard deviation

Discussion

In our reports, the frequency of positive celiac disease serology in Iranian inpatients suffering from depression or schizophrenia was 1.5%. By comparison, Pynnönen et al. have shown the prevalence of celiac disease in patients with depression to be 0.7% (5). The same authors have reported that in adolescent celiac disease patients the frequency of depression and disruptive behavioral disorders was higher than in controls, 31% and 7%, respectively (6).

The present observations support earlier findings that celiac disease is not increased in patients with schizophrenia. Eaton et al. (12) studied 7754 schizophrenia patients in Denmark and found a frequency of untreated celiac disease of 0.05%. In UK, West et al. showed that in subjects with celiac disease the prevalence of schizophrenia was 0.25%, the adjusted odds ratios showing no association between the two conditions (celiac disease vs. controls 0.76, 95% CI: 0.41-1.4) (13).

By contrast, a study in the UK revealed that patients with celiac disease developed schizophrenia 3 times more frequently than non-celiac controls (14). Some studies have suggested

that schizophrenia and celiac disease may be associated with similar or adjacent genes (15, 16). It has indeed been reported that genetic susceptibility in schizophrenia lies in human leukocyte antigen (HLA) DQ, similarly to autoimmune disorders such as celiac disease (17). By contrast, a recent study showed no such HLA association in schizophrenia (18).

In a case report, the symptoms of schizophrenia were improved in a celiac patient aged 33 years after the introduction of gluten free diet (19). Here we had no opportunity to investigate the effect of gluten-free diet, since two patients refused and one died during the study.

In this present study, the frequency of positive celiac disease serology in patients with chronic depressive (2%) and schizophrenia (1%) was in fact similar to that found in healthy blood donors in Iran (0.6%) (9). In the latter study, the frequency of celiac disease in males (1.8%) was higher than in females (0.5%), although usually 60%-70% of celiac disease patients are female. We could not investigate females with psychiatric disorders, which may be considered as a limitation to the current study. On the other hand, all our patients were inpatients, indicating that they suffered from severe manifestations of chronic psychiatric disorders. Patients with selective IgA deficiency remain negative by TTGA IgA class screening, and we had no opportunity to test our 5 such subjects by IgG class TTGA. In blood donors positive IgG class TTGA was found in 9.8% (19). There may thus be additional celiac case in our study group, but we consider that this would not change our conclusions.

To conclude, mass screening for celiac disease in patients with depression or schizophrenia is not advocated. Despite this, alertness to celiac disease should be high, since early diagnosis and treatment by gluten-free diet may ameliorate the symptoms and quality of life of these patients.

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