



Gastroenterology in Arab Countries

Seroprevalence of coeliac disease in at-risk subjects at the main tertiary hospital, southwest of Saudi Arabia



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ABSTRACT

Background and study aims: Coeliac disease (CD) is a gluten-induced autoimmune inflammation of small bowel villi, leading to atrophy and malabsorption. The current study aims to assess the prevalence of CD in high-risk subjects in the Aseer region, southwest of Saudi Arabia and to investigate the associated presentations.

Patients and methods: This is a retrospective case-finding study of the laboratory records for a 3-year period (2009–2012) at the main tertiary hospital (Aseer Central Hospital). Serum anti-tissue transglutaminase (atTG) and endomysial antibody (EmA) levels were determined along with small intestinal histopathological examination.

Results: The proportion of cases that tested positive for at least one coeliac antibody marker was 18.4% (58/315). Forty cases underwent endoscopic examination during the analysis, among which 22 were confirmed to have CD. The individual antibody positivity for atTG and EmA was 17.5% and 15.6%, respectively. The most common clinical condition (47%) associated with these markers was type 1 diabetes mellitus (T1DM). Interestingly, gastrointestinal presentations constituted only 11.5%.

Conclusions: The rate of CD among hospital requests, including non-gastrointestinal symptomatic patients, at the Aseer main tertiary hospital seems to be high. Determining the prevalence of CD and also investigating the high-risk group commonly affected by CD warrant more screening studies.

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Introduction

Coeliac disease (CD) is an autoimmune disorder triggered by ingestion of the gluten protein that causes damage to the small intestinal mucosa, thereby leading to malabsorption and gastrointestinal complications [1]. This disease is often underdiagnosed as several cases are missed in clinical settings [2], as typical presentation of symptomatic diarrhoea and abdominal pain. However, unusual presentations such as short stature, failure to thrive (FTT), anaemia, and calcium and vitamin deficiency were counted in high percentages of disease presentations [3]. Furthermore, autoimmune diseases such as type 1 diabetes and autoimmune thyroiditis are associated with an increased incidence of CD [4–6]. Recent categorisation of this disease presentation by the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHN) divides them into gastrointestinal and extra-intestinal symptoms and signs – silent, latent, and potential – conveying how common diseases exist in the absence of apparent symptoms [7,8].

With the advent of various serological screening antibodies such as anti-human tissue transglutaminase (atTG) and endomysial antibody (EmA), diagnosis of CD has improved, but duodenal

biopsy still remains a cornerstone in the diagnosis of CD [9]. The European society of CD has approved positive serological markers for both atTG and EmAs in addition to HLA DQ2 or DQ8 as a diagnostic for CD [10,11]. In general, CD antibody detection is the less invasive and most suitable method for primary investigation of CD in suspected subjects and for assessing disease prevalence.

In contrast to that previously assumed about the prevalence of CD (0.03%) [3], the more recent studies showed a high prevalence of this disease (1%) in some European countries and the United States [12–14]. CD prevalence varies from one area to another according to the genetic and environmental factors. For example, the prevalence of CD in Saharawi children was confirmed by intestinal biopsies with serological markers to be 5.6% [15]. Studies in Saudi Arabia showed some degree of variation, with prevalence in school-age children and healthy adults shown as much as 1.5–2.2% [16,17]. Conversely, the percentage of symptomatic or high-risk patients varies from 4% in symptomatic to 11% in type 1 diabetes mellitus (T1DM) individuals [18,19]. However, such variations can be attributed to difference in the methodology and the targeted age groups, and both genetic and environmental factors cannot be excluded.

The aim of this study is to investigate the prevalence of CD and to describe the associated presentations among at-risk individuals attending the main tertiary hospital in Aseer region, a southwestern area of Saudi Arabia.

Patients and methods

This is a hospital-based retrospective study conducted at Aseer Central Hospital, a tertiary and the main reference hospital for Aseer region, a southwestern area of Saudi Arabia. A total of 313 patient files were obtained from the medical records department, where requests of CD markers were ordered. The data obtained during the period from July 2009 to September 2012 were analysed for patient demographics, symptoms, coeliac antibodies, atTG, EmAs, and intestinal histopathological findings.

The main presentations such as chronic diarrhoea or abdominal pain or/and the reason of requests such as T1DM, thyroid disease, FTT, short stature, anaemia, and associated neurological diseases constituted the inclusion criteria. Coeliac profile was requested routinely for most of T1DM, thyroid diseases, short stature, and FTT as well as chronic abdominal symptomatic patients.

The diagnosis of CD is based on the specific antibody detection and histopathological findings of intestinal biopsy. Antibodies used were anti-tissue transglutaminase A antibody test (atTG-A; Immco diagnostics, Buffalo, NY, USA) with a cutoff value of 50 EU/ml, anti-tissue transglutaminase G antibody test (atTG-G; Immco diagnostic, Buffalo, NY, USA) and endomysial antibodies (EmA; Immco diagnostic, Buffalo, NY, USA).

Histopathological examination was conducted to visualise the typical characteristic features of crypts, atrophy of villi, and intraepithelial lymphocytosis. Changes were reported by pathologists according to Marsh classification [8,10]. Histopathological data were missing for some patients due to an incomplete follow-up. Some patients might visit alternative private or abroad hospitals.

Data were analysed using the Statistical Package for Social Sciences programme (SPSS; Version 16). All p -values < 0.05 were considered statistically significant.

Results

Out of 315 (139 male and 176 female) individuals, 58 (18.4%; 18 (13%) men and 40 (22.7%) women) tested positive for at least one antibody marker; a significantly increased positivity was observed in female patients ($p < 0.05$). The median age of the study population was 10 years (range: 1–79 years; SD \pm 10.6). Antibody markers used for CD diagnosis during the study periods were atTG and EmA. Among 268 atTG tests performed in the study period 47 (17.5%) cases tested positive, whilst 17 (15.6%) tests showed a positive result for 109 cases of anti-EmA (Table 1). Further assessment of atTG-IgG (immunoglobulin G) levels was performed concomitant with IgA levels. Eleven atTG-IgG-positive patients

Table 1

The frequencies of coeliac disease among high-risk subjects. Serology results (in the first row) are recorded for any coeliac markers used in the time period (atTG-A and EmA). Lower rows show different coeliac markers used for coeliac disease diagnosis. The columns in the right side indicate the number of positive cases for each test out of the tested cases. More than one antibody test was used in some of the cases.

	Parameters	Number of cases	Positive	
General results	Serology	315 (139 m/176 f)	58	18.4%
	Histopathology		22	6.9%
Specific antibodies and histopathology results	atTG-A	268	47	17.5%
	EmA	109	17	15.6%
	V. Atrophy	40	22	55%

tested negative for atTG-IgA; nine showed low positive atTG-IgA titre whilst one was moderate. Only one patient was found to be strong atTG-IgG positive and tested negative for atTG-IgA levels. Both moderate and strong IgG-positive samples tested negative for EmA. The duodenal histopathological results of only 40 cases could be derived within the study time period. Out of these 40 cases, 22 cases were confirmed for CD and six showed intestinal abnormalities with no confirmatory changes of CD, whilst 12 showed normal intestinal mucosa. The results of the six suspicious cases showed that two of them showed low positive atTG-IgA titre with intestinal abnormalities (March-II). Only one sample tested positive for atTG-IgA and EmA with normal intestinal mucosa (Table 1).

Clinical presentations of patients varied from classical gastrointestinal symptoms such as chronic diarrhoea and abdominal pain to nonclassical symptoms such as endocrine and neurological diseases. During the study period, T1DM was the most prevalent clinical condition in about half (46.5%) of the requested cases. About 4.5% of the patients with T1DM had hypothyroidism, whilst 3.7% had only hypothyroidism. The other clinical diagnostic data for CD markers included FTT (11.9%) and short stature (6.6%). Gastrointestinal presentations such as abdominal pain and chronic diarrhoea were observed only in 11.5% of the requested cases. Other non-categorised conditions included anaemia, neurological symptoms, Down syndrome, and rickets which accounted for the rest of the cases (Table 2).

T1DM was the most common clinical condition among CD-positive patients. In general, about 30 (22.9%) of 131 cases of T1DM were positive for any single antibody test. Specifically,

Table 2

Reason for coeliac disease requests in Aseer Central Hospital for a three 3-year period. Total number of the files reviewed was 315; only in 243 files the reason for the request was stated. Others (in row number 9) include epilepsy, Ricket's, anorexia nervosa, Bartter's syndrome, Down syndrome, Turner syndrome, and SLE with lupus nephritis.

S/No	Reason for request	n	%
1	T1DM	113	46.5
2	T1DM + Hypothyroidism	11	4.5
3	Hypothyroidism	9	3.7
4	Short stature	16	6.6
5	Failure to thrive	29	11.9
6	Abdominal pain	16	6.6
7	Chronic diarrhoea	12	4.9
8	Anaemia	8	3.3
9	Others	29	11.9
Total		243	100

Table 3

Positives among the reasons for request. The most common positive cases are type 1 diabetes (T1DM).

Positives among the reasons for request									
Reason for request	Number of cases and %	Any Pos.		AtTG-A		EMA		V. atrophy	
		n	%	n	%	n	%	n	%
1	T1DM	30	51.7	24	51	12	70.5	5	22.7
2	T1DM + hypothy.	2	3.5	2	4.3	1	5.8	1	4.5
3	Hypothyroidism	1	1.7	0	0	1	5.8	0	0
4	Short stature	2	3.5	2	4.3	0	0	1	4.5
5	Failure to thrive	3	5.2	3	6.4	1	5.8	2	9
6	Abdominal pain	4	6.9	4	8.5	0	0	2	9
7	Chronic diarrhoea	1	1.7	1	1.7	0	0	3	13.6
8	Anaemia	2	3.5	2	4.3	0	0	2	9
9	Others	6	10.3	5	10.6	1	5.9	5	22.7
Total*	51			43		15		22	

* All positive cases for any antibody marker as shown are 58, but in some positive; data of the main presentations are missing in the reviewed records.

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