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BRIEF ARTICLE

Seroprevalence of celiac disease among healthy adolescents in Saudi Arabia

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Abstract

AIM: To identify the seroprevalence of celiac disease among healthy Saudi adolescents.

METHODS: Between December 2007 and January 2008, healthy students from the 10th to 12th grades were randomly selected from three regions in Saudi Arabia. These regions included the following: (1) Aseer region, with a student population of 25512; (2) Madinah, with a student population of 23852; and (3) Al-Qaseem, with a student population of 16067. Demographic data were recorded, and a venous blood sample (5-10 mL) was taken from each student. The blood samples were tested for immunoglobulin A and immunoglobulin G endomysial antibodies (EMA) by indirect immunofluorescence.

RESULTS: In total, 1167 students (614 males and 553 females) from these three regions were randomly selected. The majority of the study population was classified as lower middle class (82.7%). There were 26 (2.2%) students who had a positive anti-EMA test, including 17 females (3.1%) and 9 males (1.5%). Al-Qaseem region had the highest celiac disease prevalence among the three studied regions in Saudi Arabia (3.1%). The prevalence by region was as follows: Aseer 2.1% (10/479), Madinah 1.8% (8/436), and Al-Qaseem 3.2% (8/252). The prevalence in Madinah was significantly lower than the prevalence in Aseer and Al-Qaseem (P = 0.02).

CONCLUSION: Our data suggest celiac disease prevalence might be one of the highest in the world. Further studies are needed to determine the real prevalence.

Key words: Celiac disease; Saudi Arabia; Prevalence; Antiendomysial antibody; Epidemiology

Core tip: The celiac disease (CD) prevalence has progressively increased and, recently, it was proposed that it might be higher than 1 in 100. Until the 1990s, the prevalence of CD in Middle Eastern and North African countries was considered low. In this cohort of 1167 healthy young Saudi students who had anti-endomysial antibodies (EMA) test, the seroprevalence of celiac disease was 2.2% (1 in 45) and as high as 3.1% among females. Although intestinal biopsies were not available in our study, the high specificity of immunoglobulin A anti-EMA might indicate the celiac disease prevalence in Saudi Arabia might be one of the highest celiac disease prevalence rates in the world.

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INTRODUCTION

Celiac disease (CD) is a chronic systemic autoimmune disorder induced by gluten proteins present in wheat, barley, and rye. Genetically susceptible individuals develop autoimmune injury to the gut, skin, liver, joints, uterus, brain, heart, and other organs. The classical definition of CD includes gastrointestinal manifestations (chronic diarrhea, failure to thrive, weight loss, vomiting, abdominal pain, bloating, distention, and constipation) confirmed by a small bowel biopsy, with findings of villous atrophy, crypt hyperplasia, and normalization of the villous architecture in response to a gluten-free diet[1]. Celiac disease has been classified into 4 phenotypes: classic, atypical, silent and latent. "Latent" celiac disease describes asymptomatic individuals with currently normal histological findings on a gluten-sufficient diet who subsequently develop celiac disease or those with a prior diagnosis of celiac disease who responded to a gluten free diet and retained normal mucosal histological findings despite the long-term ingestion of gluten[2]. Until the 1980s, CD was considered to be a rare disease, but in the 1990s, it became clear that CD was a frequent condition. In 1995, it was suggested that the prevalence of CD in the general population could be approximately 1 in 250 individuals[3]. This prevalence has progressively increased and, recently, it was proposed that it might be higher than 1 in 100. This increase is mainly due to the increased use of assays that detect celiac antibodies to identify affected individuals[4,5]. Until the 1990s, the prevalence of CD in Middle Eastern and North African countries was considered low. However, with the introduction of antigliadin antibodies, anti-endomysial antibody (EMA), and tissue transglutaminase antibodies testing, CD has been more readily reported from these regions[6], and its prevalence appears similar to that of North American and European countries[6-9]. There are scarce data regarding the prevalence of celiac disease in Saudi Arabia[10]. A recent study has shown a seroprevalence of 1.5% among 204 healthy blood donors[11].

The aim of this study was to identify the seroprevalence of celiac disease among a healthy adolescent population in three regions of Saudi Arabia.

MATERIALS AND METHODS

Study population

Saudi Arabia is comprised of 13 regions. The first region in our study, Aseer, is located in the southwestern part of Saudi Arabia and is a mountainous area with mild weather throughout the year. The population of this region is estimated to be 1.75 million people. Madinah, where the second holy city is located, is in the western part of Saudi Arabia and has a population of 1.61 million people. The third region, Al-Qaseem, is located in central Saudi Arabia, with a total population of approximately 1.07 million people. Al-Qaseem is considered an agricultural region. The three regions comprise approximately 18.5% of the Saudi population. These data were taken from the last population census in Saudi Arabia conducted in 2007.

To test for the prevalence rate of celiac disease using anti-EMA, we used blood samples that had been collected for a previous study[12]. The samples had been collected from a population of students in the 10th to 12th grades (corresponding to the ages of 16 to 18 years) in three regions of Saudi Arabia. The composition of the student population was as follows: Aseer region, with a total school population of 25512 (13996 males and 11516 females); Madinah region, with a total school population of 23852 (12133 males and 11719 females); and Al-Qaseem region, with a total school population of 16067 (7974 males and 8093 females).

The sample was selected using a stratified random sampling technique, where the Kingdom was stratified into three strata. A proportional allocation method was used to determine the recruited number of students in each stratum.

Within each stratum, the sample was proportionally allocated according to sex. In every region, the schools served as the sampling units. It is worth noting that the schooling system in Saudi Arabia depends on segregating males and females in different schools, and this situation was taken in consideration for sampling. From the list of schools in the region, one or more male schools and one or more female schools that satisfied the required sample size were randomly selected. A total of 1358 students (679 males and 679 females) from these regions were randomly selected. The socioeconomic status (SES) of this population was stratified as lower, middle, and upper class. The SES of a student was taken to be representative of that of the father and/or mother and was classified from the socioeconomic score derived from the type of house, the number of rooms per house, the number of cohabiting family members, parents' educational levels, and parents' occupations. The SES of students was measured using a point scale of 1-21 as follows: housing, 3 points; education of parents, 6 points; type of work of parents, 6 points; number of family members, 3 points; and number of rooms in the house, 3 points. Students who scored 17-21 points were classified as upper class, 15-16 as upper middle class, 11-14 as lower middle class, and 10 or less as lower class[12].

The protocol of this study has been approved previously by King Abdulaziz City for Science and Technology, and informed consent was obtained from the parents and the participating students. All participants were offered further medical evaluation by a gastroenterologist in case of a positive EMA test.

Data collection, blood sampling and testing

The fieldwork for this study was undertaken in December

2007 and January 2008. Demographic data were recorded, and a venous blood sample (5-10 mL) was taken from each student. The serum was separated by centrifugation, coded, and stored at -70°C. The blood samples were tested for immunoglobulin A (IgA) and immunoglobulin G anti-EMA by indirect immunofluorescence (IMMCO Diagnostics, Inc., Buffalo, NY, United States).

Statistical analysis

Data were entered into electronic databases and analyzed using Stata Version 10 (Stata Corporation, College Station, TX, United States). Descriptive statistics (proportional) were used to summarize categorical variables. The chi-square test, followed by an analysis of residuals, was used to calculate the statistical association between two categorical variables. The chi-square test for trends was used to calculate the significance of proportions of variables with three or more categories. A P value of < 0.05 was considered statistically significant. Based on a general prevalence of 1% in various populations and an estimated prevalence of 3% in the Saudi population, we determined the sample size at P value (alpha) = 0.05 and power = 0.70 and a standard deviation of 0.25, the estimated sample size would be 965 individuals.

RESULTS

Blood samples of 1167 students (614 males and 553 females) were available for testing, while 191 samples were either missing or insufficient for analysis. The mean age for the study population was 16.6 ± 0.6 years. There were no differences in the sex distribution among the three regions ($P = 0.08$). The majority of the study population was classified as lower middle class (82%).

There were 26 (2.2%) students who had a positive anti-EMA test, including 17 females (3.1%) and 9 males (1.5%). Al-Qaseem region had the highest CD prevalence among the three studied regions in Saudi Arabia (3.1%) (Table 1).

The prevalence by region was as follows: Aseer 2.1% (10/479), Madinah 1.8% (8/436), and Al-Qaseem 3.2% (8/252). The prevalence in Madinah was significantly lower than the prevalence in Aseer and Al-Qaseem ($P = 0.02$). There was no statistically significant difference in prevalence between Aseer and Al-Qaseem.

Table 1 Seroprevalence according to regions and sex *n* (%)

	Aseer (479)	Madinah (436)	Al-Qaseem (252)	Total (1167)
Male (614)	4/250 (1.6)	1/244 (0.4)	4/120 (3.4)	9/614 (1.5)
Female (553)	6/229 (2.6)	7/192 (3.6)	4/132 (3.0)	17/553 (3.1)
Total (1167)	10/479 (2.1)	8/436 (1.8)	8/252 (3.2)	26/1167 (2.2)

DISCUSSION

Two decades ago, celiac disease was considered a comparatively uncommon disorder, with prevalence rates of 1 in 1000 or lower[13,14]. CD was even thought to be rare or nonexistent among native Africans, Japanese or Chinese populations[14]. Several recent population based studies, however, have shown a much higher prevalence, and it is now estimated that celiac disease may affect between 1 in 100 to 200 individuals[4,15].

The seroprevalence rate of 2.2% (1 in 45) found in our study might be one of the highest seroprevalence rates of celiac disease in the world. Although the prevalence of diagnosed CD varied widely, the estimates of combined undiagnosed and diagnosed (or silent and active) CD were remarkably similar at 0.7%-2.0% in most other populations, including the United States. The prevalence of childhood CD has been reported to be between 1:285 and 1:77 in Sweden[16] and 1:230 and 1:106 in Italian school aged children[17]. Generally, similar rates have been reported for non-European white populations, such as New Zealand[18], Australia[19], Brazil[20] and Argentina[21]. Recent epidemiological studies of CD prevalence rates for North Africa (reported as 0.53% in Egypt, 0.79% in Libya, and 0.6% in Tunisia), the Middle East (0.88% in Iran and 0.6% in Turkey), and India (0.7%) show prevalence rates that overlap with the European data[22]. A recent study among 204 healthy Saudi blood donors showed a celiac seroprevalence of 1.5%[11].

A recently published large international, multicenter study investigated a large population sample in four different European countries; on average, the overall prevalence of CD was 1%, with large variations among the studied countries (2.0% in Finland, 1.2% in Italy, 0.9% in Northern Ireland, and 0.3% in Germany). This study confirmed that many CD cases would remain undetected without active serological screening[23].

Of 3654 students (age range, 7 to 16 years) from Finland who had been screened for anti-endomysial and tissue transglutaminase antibodies, Mäki *et al*[15] found that 1 in 66 students (1.5%) had positive antibody tests. Of the 36 students from that study with positive antibody assays who agreed to undergo biopsy, 27 had evidence of celiac disease on biopsy. Thus, the estimated biopsy proved prevalence was 1 case in 99 (1%) children. In our study, we have only used a single serological marker (EMA) without duodenal biopsy. The diagnostic standard in celiac serologies remains the anti-endomysial IgA antibodies. These markers are highly specific for celiac disease, with nearly 100% accuracy, which is a crucial point when we use them to study populations at low risk of CD[24]. Of 20190 Turkish students, Dalgic *et al*[25] found 489 (2.4%) patients with positive antibodies (IgA-tTG and IgA-EMA). Among 215 patients who underwent an intestinal biopsy, there were only 95 children who were consistent with CD, with an estimated biopsy proven prevalence of 1:212 (0.47%) children. Hogen Esch *et al*[26] demonstrated that mass screening unavoidably reveals some false-positive and/or false-negative test results, regardless of the type of celiac antibody test. The predictive value of a diagnostic test depends on the prevalence of the disease and the sensitivity and specificity of the test[27]. In low-risk populations (such

as groups undergoing mass screening), the positive predictive value of the serological tests is always lower than in symptomatic patients or at-risk groups[28]. However, IgA EMA has an approximately 100% specificity and is the best among all celiac serologies.

Another important finding of our study is the higher prevalence of celiac disease among female compared to male students, which is a finding that was observed in most of the celiac disease epidemiological studies. In addition, there was a significant variation of celiac disease seroprevalence from region to region in Saudi Arabia.

The high prevalence of celiac disease found in our study might be attributed to the high levels of consanguinity and the heavy gluten ingestion in our population. The Saharawi population of Arab-Berber origin living in Algeria has the highest prevalence of CD (5.6%) among all world populations[29]. The reason for such a frequency of the "celiac trait" in this population is not clear but is likely to be related to their genetic background.

In conclusion, our study provides evidence of a high seroprevalence of CD in a group of school-aged children in 3 regions of Saudi Arabia. Although intestinal biopsies were not available in our study, the high specificity of IgA anti-EMA might indicate one of the highest celiac disease prevalence rates in the world. Further seroprevalence studies with larger samples combined with multiple duodenal biopsies are highly recommended to determine the true celiac disease prevalence in our country.

COMMENTS

Background

The celiac disease (CD) prevalence has progressively increased and, recently, it was proposed that it might be higher than 1 in 100. This increase is mainly due to the increased use of assays that detect celiac antibodies to identify affected individuals. Until the 1990s, the prevalence of CD in Middle Eastern and North African countries was considered low. However, with the introduction of celiac antibodies, CD has been more readily reported from these regions, and its prevalence appears similar to that of North American and European countries. A recent study has shown a seroprevalence of 1.5% among 204 healthy Saudi blood donors. The aim of this study was to identify the seroprevalence of celiac disease among a healthy adolescent population in three regions of Saudi Arabia.

Research frontiers

There are scarce data regarding the prevalence of celiac disease in Saudi Arabia. A recent study has shown a seroprevalence of 1.5% among 204 healthy blood donors.

Innovations and breakthroughs

The results suggest a very high seroprevalence of celiac disease among healthy young Saudi students. Although intestinal biopsies were not available in this study, the high specificity of immunoglobulin A anti-endomysial antibody might indicate one of the highest celiac disease prevalence rates in the world.

Applications

Further seroprevalence studies with larger samples combined with multiple duodenal biopsies are highly recommended to determine the true celiac disease prevalence in Saudi Arabia.

Peer review

The manuscript underlines the seroprevalence of the celiac disease in Saudi Arabia.

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