

Prevalence of Celiac Disease in Developing Countries

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Abstract

Celiac disease (CD) is an autoimmune disorder, which affects genetically predisposed individuals upon the ingestion of gluten. So, it is the result of both environmental (gluten) and genetic factors (carriers of HLA-DQ2 and DQ8 haplotypes). A duodenal biopsy with positive serology is the gold standard for the diagnosis of CD. Celiac disease world geographical distribution seems to have followed the spread of wheat consumption in addition to the migratory flows of mankind. Following the application of simple serological tests for the diagnosis of CD in the 1980s, it gradually became clear that the prevalence of CD in different countries in the Middle East, North Africa and India is almost the same as that in Western countries. A high index of suspicion for CD should be maintained in all developing countries for patients who present with chronic diarrhea or iron deficiency anemia. The prevalence of CD varies with sex, age, and geographic location. The global prevalence of CD has increased over time from 0.6% in 1991 to 2000 to 0.8% between 2001 and 2016. According to that, there is a need for population-based prevalence studies in many developing countries especially middle east to estimate the burden of CD properly.

Keywords Celiac disease, gluten, HLA, prevalence, meta-analysis, Middle East, developing countries.

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List of abbreviation: CD = Celiac disease, HLA-DQ2 and DQ8 = Human leukocyte antigen serotype group/ cell surface receptor proteins

Celiac disease (CD) is an autoimmune disorder which affects genetically predisposed individuals upon the ingestion of gluten ⁽¹⁾. So it is the result of both environmental (gluten) and genetic factors (carriers of HLA-DQ2 and DQ8 haplotypes). It is characterized by inflammation of the small-intestinal mucosa and numerous gastrointestinal and systemic manifestations. A duodenal biopsy with positive serology is the gold standard for the diagnosis of CD, communication of pathologist and gastroenterologists is essential for appropriate interpretation of duodenal biopsy ⁽²⁾. The distribution of these two constituents can be

used to identify the areas of the world at risk for gluten intolerance.

Celiac disease world geographical distribution seems to have followed the spread of wheat consumption in addition to the migratory flows of mankind. The classic clinical picture of pediatric celiac disease, which includes malnutrition, diarrhea, bloating, and abdominal pain, should be replaced with the more typical presentation of CD. The patient with CD is an asymptomatic school-aged child who belongs to a high-risk group. Despite improved awareness and screening protocols, many patients with CD may remain undiagnosed. It was recommended for the primary care physicians to implement screening programs in all high-risk populations, including first-degree family members of known patients with CD and patients with Down syndrome, Turner

syndrome, type 1 diabetes, thyroiditis, Addison disease, short stature, iron deficiency anemia, and unexplained elevation of aminotransferase levels. A high level of suspicion for CD should be entertained in other autoimmune disorders even if there are no apparent gastrointestinal symptoms ⁽³⁾. Also, there has been some work looking to evaluate if other factors, such as gastrointestinal infection, surgery, or certain drugs, may be the trigger for development of CD ⁽⁴⁾.

Following the application of simple serological tests for the diagnosis of CD in the 1980s, it gradually became clear that the prevalence of CD in different countries in the Middle East, North Africa and India is almost the same as that in Western countries ⁽⁵⁾.

A significant change in diet habits, particularly in gluten consumption as well as in infant feeding patterns are probably the main factors that can account for these new trends in celiac disease epidemiology ⁽⁶⁾.

Europe historically was considered a geographical area at high frequency, with a prevalence of 1-2%, although it has been recently shown a similar prevalence in United States. It has been shown that CD is not exclusive of industrialized countries, but includes North Africa, Middle East and India with an incidence overlapping those of European countries. It has been shown that the Saharawi, an Algerian population has the highest prevalence of CD (nearly 6%) among all of the worldwide populations ⁽⁷⁾. However, the diagnostic rate is mostly low in these countries due to low availability of diagnostic facilities and poor disease awareness. In the classical Anderson's textbook of Pediatric Gastroenterology first published in 1975, it was reported that 'The typical child with celiac disease, usually fair-haired, blue-eyed...'. The subsequent developments of CD epidemiology proved that this statement was incorrect as the highest prevalence of celiac disease in the world has been described in a black-eyed, black-haired mostly African population originally living in Western Sahara, the

Saharawi, of Arab-Berber origin. Besides in a sample of 990 Saharawi children screened by anti-endomysium testing and intestinal biopsy, it was found a celiac disease prevalence of 5.6%, which is almost 5-fold higher than in most European countries.

The reasons behind such spiking frequency of CD are still unclear but could be primarily related to genetic factors given the high level of consanguinity of this population. The main susceptibility genotypes, HLA-DQ2 and -DQ8, exhibit one of the highest frequencies among them ⁽⁸⁾. Also, it was found that the amount of gluten as well as gluten consumption patterns in early life have no impact on CD development before 6 years of age ⁽⁹⁾. Other study on ethnic variations in duodenal villous atrophy consistent with CD in the United States mentioned that there were no significant differences in CD prevalence between Middle Eastern descent patients when compared with other Americans ⁽¹⁰⁾. An Iranian study mentioned that CD in countries of Eastern Mediterranean Region Organization (EMRO) including North Africa and the Middle East are increasingly on the rise. In some studies, this disease has been diagnosed two to three times more in women than in men, besides the prevalence of celiac disease in Iran was similar or even higher than world-wide reported ⁽¹¹⁾. And in a systematic review and meta-analysis, it was found that celiac disease to be reported worldwide. The prevalence of celiac disease based on serologic test results was 1.4% and based on biopsy results was 0.7%. The prevalence values for celiac disease were 0.4% in South America, 0.5% in Africa and North America, 0.6% in Asia, and 0.8% in Europe and Oceania; the prevalence was higher in female vs male individuals (0.6% vs 0.4%; $P < 0.001$). The prevalence of celiac disease was significantly greater in children than adults (0.9% vs 0.5%; $P < 0.001$) and concluded that CD is a global disease and the global seroprevalence and prevalence of CD varies with sex, age, and geographic location. The prevalence of CD has increased over time from

0.6% in 1991 to 2000 to 0.8% between 2001 and 2016 ⁽¹²⁾.

So, CD clinical manifestations may vary with age, the duration and the extent of disease and multiple clinical studies showed that presentation with non-specific symptoms or no symptoms is as common in the Middle East as it is in Europe. The consumption of wheat has been the major primary food in these regions for many centuries and that the continuous and high level of exposure to its proteins induced some degree of immune tolerance, leading to milder symptoms, which are misdiagnosed as irritable bowel syndrome or unexplained gastrointestinal disorders. A high index of suspicion for CD should be maintained in all developing countries for patients who present with chronic diarrhea or iron deficiency anemia.

According to that, there is a need for population-based prevalence studies in many developing countries especially middle east to estimate the burden of CD properly.

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