

## The hidden danger: Silent celiac disease

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Celiac disease (CD) is a permanent immune-mediated inflammatory disease of the small intestine, which is induced by gluten. It was considered to be highly prevalent primarily in populations of European descent; however, currently, it is known that CD is a global disease, and the overall frequency of incidence is increasing throughout the world. It is estimated that 1% of the world population has this disease (1,2). The pathogenic mechanism of CD involves both genetic and environmental factors. It is known that genetic predisposition, observed as human leukocyte antigen (HLA) DQ2 or DQ8 positivity, for the disease is the most important, and almost all patients with CD exhibit these molecules (3). In fact, the absence of either of these two molecules has a negative predictive value in terms of excluding the diagnosis of CD. Therefore, these two HLA haplotypes are considered to be necessary but not sufficient. Serological tests are important to screen for and diagnose CD. Over the years, serological tests have improved with better availability. Currently, the determination of serum anti-tissue transglutaminase immunoglobulin A antibodies seems to be the most sensitive and specific test for the primary diagnosis of CD. Because recent tests are more sensitive than those in the past, the current prevalence of CD may be higher. However, when the current screening methods are applied to stored sera, the prevalence is still observed to have increased during the course of time. In two serological studies from US and Europe, the prevalence of CD has been shown to increase four and two times, respectively, over the years (1,4). Although there are still some geographic differences, currently, the frequency of CD is increasing in Asia and Africa also (2). This increase is attributed to available and improved serological tests or increased awareness of the physicians. There are also some environmental factors that influence the prevalence of CD, the most important being the consumption of gluten. One reason for the increased prevalence of CD may also be the increased amounts of gluten in the

diet worldwide. Especially in developing countries, wheat consumption has increased at a faster rate than all other regional cereals. This can be attributed to changes in global dietary habits, westernization of diet to contain a large amount of wheat (including gluten), and changes in the processing of cereals (5). Currently, wheat-containing foods comprise as much as up to 50% of energy intake worldwide. In addition, the wheat available now is not the same as the wheat available thousands of years ago that contained smaller amounts of the highly toxic peptide 33-mer gliadin (6,7).

In this issue, Comba et al. (8) reported the prevalence of CD in Çorum, a central Anatolia city, to be 0.46 % among school-age children. They screened 1730 students of primary, secondary, and high schools. Students were initially screened by rapid celiac test kits (tissue transglutaminase IgA and total IgA), and then, small-bowel biopsy was performed for screening positive cases. It is important to keep in mind that intestinal biopsy is still an essential criterion for the final diagnosis of CD. According to other screening studies from Turkey, the frequency of biopsy-proven CD was found to be 0.4%-0.9% (9-11). These frequencies are similar to those reported from other parts of the world (12). The clinical picture of CD varies from overt malabsorption to the silent form, and it is believed that there may be more than five undiagnosed patients for each diagnosed patient. This has led to the concept of "celiac iceberg," wherein majority of the patients have silent or latent CD. Screening studies in children have revealed that the silent form is more frequent (12). Comba et al. (8) found 8 patients with CD; 3 of them presented with atypical CD and 5 with silent CD. Patients with untreated CD are at risk of some diverse manifestations that include osteoporosis, infertility, lymphoma, and other autoimmune disorders, such as diabetes mellitus and thyroiditis (13). Treatment with gluten-free diet precludes most of these complications. This raises the importance of early diagnosis and treatment of the disease, especially in subjects with silent CD. It is impossible to identify asymptomatic patients without screening. This study indicates that despite improved recognition rate of

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diagnosis there are still asymptomatic patients who are undiagnosed. Awareness should be increased, especially for individuals who are at a high risk for disease development.

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