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EDITORIAL

Celiac Disease and the Forgotten 10 %: The "Silent Minority"

Benjamin Lebwohl

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We have known for more than a decade that celiac disease (CD) is present in nearly 1 % of individuals in the USA, but we know less about the prevalence of CD among racial and ethnic minorities in this country. In a landmark multicenter screening study published in 2003, Fasano et al. [1] calculated a US prevalence of 0.75 % in average-risk individuals. In that study, in addition to an overall population estimate, Fasano et al. reported that the prevalence of CD in non-Caucasians as an aggregate was 1:236 (0.4 %), but estimates for each racial and ethnic group were not provided. While precise data were lacking, the impression has long been that CD is less common among non-Caucasian individuals. African-Americans comprised only 1 % of the population of CD patients attending a referral center in New York [2]. In a recent prevalence study, Rubio-Tapia et al. [3] analyzed CD serologic data collected in 2009–2010 as part of the National Health and Nutrition Examination Survey (NHANES), reporting an overall prevalence of 0.71 %. Though the vast majority of patients identified were Caucasian (whose prevalence of CD was calculated as 1.01 %), the low number of identified patients with CD precluded prevalence estimates in other groups.

In this issue of *Digestive Diseases and Sciences*, Mardini et al. [4] now report on the updated response data from NHANES, incorporating 4 years of data collection, 2009–2012. The most compelling reason to reexamine this updated survey data is that the sample size is now sufficient to provide prevalence estimates on non-Caucasian populations. As was the case in the initial analysis by Rubio-Tapia et al. [3], the definition of CD was based on serologic, and not histologic, criteria. Therefore, the diagnostic criteria cannot be said to be using the current "gold standard" and may have missed some patients with seronegative CD, particularly those with selective IgA deficiency. Nevertheless, for comparative purposes, this serologic approach [tissue transglutaminase (TTG) screening, followed by endomysial antibody (EMA) testing in weakly positive or fully positive cases] is valuable. CD autoimmunity was defined as a fully positive TTG and/or EMA, or dual weakly positive serologies.

The investigators explained that the overall prevalence of CD autoimmunity was 0.79 %, similar to those reported previously in NHANES and other US populations [1, 5]. The prevalence was the highest in non-Hispanic whites (1.08 %) and was much lower in Mexican-Americans (0.23 %), other Hispanics (0.38 %), and non-Hispanic blacks (0.22 %). This first racially and ethnically stratified national CD prevalence study in the USA confirms that CD is significantly less common in non-Caucasian populations. The low prevalence of CD in Hispanics is in contrast to studies in Mexico [6] and Argentina [7] that found CD prevalence equal to or greater than that of the US population. Explanations for this discrepancy may be genetic (such as different admixtures of the studied groups) or environmental (i.e., different exposures among immigrants) and requires further investigation. Also novel is the finding that the concordance of TTG and EMA positivity appears to differ between racial and ethnic groups. Specifically, Caucasians have much higher rates of TTG/EMA concordance (72 %) than non-Caucasians (32 %), and non-Caucasians are more likely than Caucasians to

B. Lebwohl (✉)
Department of Medicine, Celiac Disease Center, Columbia University College of Physicians and Surgeons, 180 Fort Washington Avenue, Suite 936, New York, NY 10032, USA
e-mail: BL114@columbia.edu

B. Lebwohl
Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA

have a positive EMA in the setting of a weakly positive TTG level. This raises the possibility that the threshold (or cutoff value) for an abnormal TTG might be lower in non-Caucasians. If confirmed, the definition of an abnormally elevated TTG, triggering a diagnostic endoscopy, might vary depending on whether the subject being tested is Caucasian.

What proportion of patients with CD in the USA is non-Caucasian? This study provides the answer: 10 % of the CD patients identified had a race or ethnicity other than non-Hispanic Caucasian. Mardini et al. convincingly show that CD is less common in non-Caucasian groups. At the same time, the nonzero prevalence found in these groups indicates that CD can and does occur in non-Caucasians; in fact, the prevalence of CD in non-Caucasians, while lower than that of Caucasians, is still greater than previously published low estimates of overall CD prevalence in the USA that had been based on symptom-triggered testing [8].

Under-diagnosis of CD in other groups can occur if CD is assumed to only affect Caucasians. Indeed, there is evidence that this erroneous assumption occurs in clinical practice, with resultant under-diagnosis of CD among non-Caucasian individuals. An analysis of the Clinical Outcomes Research Initiative National Endoscopic Database found that among patients undergoing upper endoscopy for iron deficiency, anemia, diarrhea, and weight loss (all potential manifestations of CD), only 43 % underwent duodenal biopsy and that biopsy was less likely to be performed in black or Hispanic patients [9]. Much has been made of the phenomenon of seronegative CD, a difficult-to-diagnose group that comprises approximately 5–10 % of CD patients [10]; a similar proportion of CD patients is comprised of non-Caucasians, and we should dedicate our efforts to diagnosing and treating these individuals.

Mardini et al. also noted that 0.9 % of the study group responded that they adhere to a gluten-free diet, a rise from 0.63 % in the 2009–2010 data reported by Rubio-Tapia et al. [3], even though 85 % of this group was not diagnosed with CD. This result is certainly in accord with the increasing global focus on gluten in the lay press and concerns about the health effects in gluten in the population at large. It is concerning, however, that some patients consuming a self-prescribed gluten-free diet may have CD and have not been fully evaluated. One recent questionnaire study in Australia found that among 147 patients with self-reported non-celiac gluten sensitivity, 62 % had an inadequate exclusion of CD due to a lack of serologic testing, or a serologic or endoscopic evaluation that was performed after the individual had already adopted a gluten-free diet [11]. This is alarming since more than a quarter of the respondents reported that they were not strictly following this diet. Given the attendant morbidity associated with untreated CD, it behooves us to send a clear message: CD is common, potentially serious, and is present in Caucasians as well as non-Caucasians. Testing for CD should be performed prior to commencing a gluten-free diet.

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Conflict of interest None.

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