

Prevalence of celiac disease in children with Down syndrome screened by anti-tissue transglutaminase antibodies

To the Editor

I have 3 comments on the interesting study by Saadah et al¹ on the prevalence of celiac disease (CD) in children with Down syndrome (DS) screened by anti-tissue transglutaminase antibodies (anti-tTG).

First, Saadah et al¹ adopted in their study the protocol of performing upper gastrointestinal endoscopy and histopathological examination of distal duodenum specimen in patients who had an elevated level of anti-tTG beyond the cutoff (20 unit/ml). I presume that protocol will miss substantial cases of CD as it was noticed that a subgroup of patients with DS could present with subtotal villous atrophy but without characteristic for CD immunological and genetic markers.²

Second, I disagree with Saadah et al¹ in their recommendation that routine screening for CD in patients with DS is indicated in order to avoid associated complications, in particular lymphoma. This is based on the following points: 1) DS does not represent a major chromosomal disorder in Saudi Arabia where it has an incidence of 1 in 554 live births (1.8 per 1,000).³ 2) Patients with CD are generally known to be at increased risk of malignancy. However, the overall risk of malignancy in CD patients declines with time after diagnosis and is not significantly increased after 15 years. Most of the increased risk could be attributed to the development of hematological malignancies, despite their very low absolute rate of occurrence.⁴ 3) The frequency of CD in the Saadah et al's studied population with DS¹ was low where only 4% were seropositive using anti-tTG and total immunoglobulin A and 2% prevalence of biopsy proven CD which is considered among the lowest prevalence rates reported.³ It is of no doubt that increased prevalence of CD in persons with DS has led some organizations and authors to recommend universal screening of children with DS. However, many children with DS are asymptomatic, and the long-term implications of screening are unknown. The complication of CD that leads to mortality in the general population is non-Hodgkin's lymphomas. The available evidence does not support the cost-effectiveness of screening for CD in patients with DS. Screening not only costs more but also results in fewer quality-adjusted life-years. A screening strategy costs more than \$500,000 per life-year gained. Screening

of all asymptomatic children with DS for CD costs almost \$5 million in order to prevent a single case of lymphoma.⁵

Third, interestingly, thyroid disorder was reported in 31.4% of patients with DS in Saadah et al's study¹ which is higher than 15% reported worldwide.⁶ According to the American Academy of Pediatrics guidelines on screening for thyroid dysfunction in patients with DS,⁶ screening program to achieve that goal seems justifiable to be applied in Saudi Arabia.

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Reply from the Author

Thank you for your interest in our study on the prevalence of celiac disease (CD) in children with Down syndrome (DS) screened by anti-tissue transglutaminase antibodies (anti-tTG).¹

Screening for CD using enzyme-linked immunosorbent assay (ELISA), based anti-tissue transglutaminase antibody (IgA) is now widely used for identifying patients who might require small bowel biopsy. The test has a sensitivity of more than 95% and specificity of almost 100%.⁷ Supplementing the test with total IgA estimation may lessen the chance of missing cases with CD. Routine screening of children with DS for CD although recommended by professional organizations and in DS health care guidelines,^{8,9} some authors have been more cautious in recommending routine screening for asymptomatic DS patients since the long term implications of screening are unknown.^{10,11} Others doubt the costeffectiveness of screening asymptomatic children to prevent lymphoma that was considered the main complication that leads to mortality in CD patients¹⁰ as indicated in the comment by Dr. Al-Mendalawi.

The higher association with thyroid dysfunction with DS prompted us to adopt regular screening of thyroid function in DS population attending our Down's syndrome clinic at King Abdulaziz University Hospital, Riyadh, Saudi Arabia.

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Ethical Consent

All manuscripts reporting the results of experimental investigations involving human subjects should include a statement confirming that informed consent was obtained from each subject or subject's guardian, after receiving approval of the experimental protocol by a local human ethics committee, or institutional review board. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed.