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Serum prevalence of celiac disease in children and adolescents with type 1 diabetes mellitus

Dear Editor,

We would like to make some comments about the article entitled "Serum prevalence of celiac disease in children and adolescents with type 1 diabetes mellitus."[1]

In most diabetic patients, celiac disease (CD) is insidious and asymptomatic; therefore, serological screening for CD is crucial for an early diagnosis and introduction of appropriate treatment.[2] In a cross-sectional study, Araújo et al.[1] found a prevalence of 10.5% for CD among children and adolescents with type 1 diabetes mellitus (DM-1) using the anti-tissue transglutaminase (anti-tTG) antibody assay, recommended as the test of choice for the initial screening of CD in diabetic patients.[3]

Serological tests for the detection of anti-tTG and anti-endomysial antibodies should be reserved for IgA isotypes; therefore, it is necessary to identify patients with IgA deficiency (IgAD) beforehand in order to rule out false-negative results.

Of 361 diabetic patients selected by Araújo et al.[1], seven (1.9%) had IgAD.

In a previous study carried out at Hospital de Clínicas of Universidade Federal do Paraná, Brazil, eight out of 149 diabetic children and adolescents screened for CD had IgAD (IgA < 5 mg/dL), which corresponds to a prevalence of 5.3%. Serum IgA levels were measured by the enzyme-linked immunosorbent assay (ELISA), standardized to determine serum IgA titers below the radial immunodiffusion sensitivity level in the low-concentration plate and turbidimetry. In this same group of diabetic patients, the diagnosis of CD was confirmed in 8.7% (13/149) by anti-endomysial antibody testing and intestinal biopsy.[4]

Liblau et al.[5] reported that one out of 261 diabetic patients in France had IgAD, a higher prevalence rate than that for the normal French population, which corresponds to 1:1,400. In Italy, IgAD was detected in seven of 191 diabetic patients, i.e., a prevalence of 1:27, higher than that for the normal Italian pediatric population (1:500).[6]

The prevalence of CD in DM-1 patients, recently assessed by anti-endomysial antibody testing and intestinal biopsy in the state of São Paulo, Brazil, amounted to 4.8%, comparable to the prevalence rate described in U.S. and European studies.[7]

Tanure et al. found a prevalence of 2.6% for CD in diabetic patients from the Brazilian state of Minas Gerais.[8] The patients were identified based on the positive results for antigliadin antibodies (AGA), anti-endomysial antibodies and intestinal biopsy.[7] However, only diabetic patients with positive IgG-AGA and negative IgA-AGA results had their IgA level measured by nephelometry. The 12 patients who were positive only for IgG-AGA had normal serum IgA levels.

We agree that multicenter studies should be conducted in Brazil on the association of CD and DM-1 and that diabetics should be screened for CD on a routine basis. However, due to the higher prevalence of IgAD among diabetic patients, the serum IgA level should be determined before the serological tests for the detection of anti-tTG and anti-endomysial antibodies of the IgA isotype class for the screening of CD. This eliminates false-negative results, by the use of criteria established for IgAD, and by more sensitive methods for IgA measurement, such as ELISA (Table 1).

Table 1 - Prevalence of IgAD and CD in DM-1 patients, according to different studies

	DM-1	IgAD	CD
Curitiba, Brazil[4]	149	8 (5.3%) *	13 (8.7%)
Belo Horizonte, Brazil[8]	234	?	6 (2.6%)
São Paulo, Brazil[7]	104	3 (2.9%)	5 (4.8%)
Recife, Brazil[1]	354	7 (2.0%)	37 (10.5%)
France[5]	261	1 (0.4%)	NP
Italy[6]	191	7 (3.6%)	NP

CD = celiac disease; IgAD = IgA deficiency; DM-1 = type 1 diabetes mellitus; NP = not performed.
* Criteria for IgAD: serum IgA < 5 mg/dL.

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Authors' reply

To the Editor,

It was with great interest that we read the letter to the editor of Jornal de Pediatria sent by Dr. Loraine Farias Landgraf and Dr. Nelson Rosário, from the Department of Pediatrics of Universidade Federal do Paraná, Brazil, regarding the article "Serum prevalence of celiac disease in children and adolescents with type 1 diabetes mellitus."[1]

The comments made by our colleagues are extremely relevant and confirm the findings of our study by pointing out the necessity to measure serum IgA in type 1 diabetes mellitus (DM-1) patients under investigation for celiac disease (CD). This is due to the fact that serological screening using tissue anti-transglutaminase and anti-endomysial antibodies is not appropriate for patients with IgA deficiency.

This is an important concern in population-based studies (of seroprevalence) and in clinical trials, in order to guarantee that the prevalence of CD is not underestimated and that patients with false-negative serological results are further investigated.

In the table where the four Brazilian studies are cited, we observed that the results regarding the frequency of IgA deficiency and of CD among DM-1 patients are similar, since numerical differences are likely to result from methodological factors rather than from actual differences in frequency itself.

We reinforce the final recommendations made by our colleagues: multicenter studies should be conducted in Brazil on the association of CD and DM-1 and diabetics should be screened for CD on a routine basis.

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Pediatrics - research and publications

Dear Editor,

We were satisfied with the article written by Blank et al.,[1] and with the editorial by Marcovitch[2] in Jornal de Pediatria, which address the growing publication and citation of Brazilian articles in the child and adolescent health field. Between 1990 and 2004, the number of indexed Brazilian articles grew 404%, a figure that exceeds that for the rest of the world (61%), and should be a matter for pride and incentive for Brazilian Pediatrics.

However, attention should be paid to the remark by the editor of the *BMJ Group*, according to whom "Brazilian research in Pediatrics *seems* healthy," followed by the information that research in clinical pediatrics has recently decreased in the United Kingdom, which might also happen to us.[2] Some data obtained by Blank et al. also seem to warn against this fact: there was a decrease in the participation of pediatric scientific articles in indexed publications on child and adolescent health. Figure 3 in that article shows a decrease in the percentage of publications regarded by the