**Brief Report**

**When to Screen Children with Down Syndrome for Celiac Disease?**

*by Momcilo Pavlovic,1 Nedeljko Radlovic,2 Zoran Lekovic,2 Zorica Stojic,3 Katja Puleva,1 and Karolina Berenji4*

1Department of Pediatrics, General Hospital Subotica, Izvorska 3, 24000 Subotica, Serbia
2Department of Gastroenterology, Tirsova 10, University Children Hospital, 11000 Belgrade, Serbia
3Institute of Pathology, Dr Subotica 1, 11000 Belgrade, Serbia
4Public Health Institute, Zmaj Jovina 30, 24000 Subotica, Serbia

**Correspondence:** Momcilo Pavlovic, Department of Pediatrics, General Hospital Subotica, Izvorska 3, 24000 Subotica, Serbia.
Tel: +381 24 559 637; Fax: +381 63 823 3331. E-mail <momodec@tipnet.rs>.

**Summary**

The coexistence of Down syndrome (DS) and celiac disease (CD) has been reported in many studies. In our study, we examined 82 children with DS aged 8 months to 8.6 years for the existence of CD using serological markers immunoglobulin A (IgA) and immunoglobulin G (IgG) transglutaminase antibodies, followed by follow-up determination of total IgA levels. In four children who were positive for one of the above-mentioned antibodies, enteric biopsy has been performed that showed absence of CD. Our findings raise doubt about the need for obligatory serological screening of children with DS aged <8 years.

**Key words:** celiac disease, Down syndrome, tissue transglutaminase.

**Introduction**

High prevalence rates of celiac disease (CD) in patients with Down syndrome (DS) have been reported in several countries and they are estimated to be from 2.5% to 16.7% [1]. Due to this increased prevalence, recommendations for universal screening of children with DS have been made in the literature [1, 2] and by professional organizations [3]. However, some authors do not support the cost-effectiveness of screening asymptomatic children with DS [4].

This study was undertaken in order to estimate the prevalence of CD in children <8 years old who have DS to help determine whether screening for CD should be part of the routine work-up in this age group.

**Materials and Methods**

A total of 82 asymptomatic children with DS from the city of Subotica, Vojvodina, Serbia, were screened during the period of 2007–09 using immunoglobulin A (IgA) tissue transglutaminase (TTG) and total IgA levels. The study has been performed among protéges of Facility for Children with Developmental Disorders ‘Kolevka’ in Subotica. All the children who were exposed to a gluten-containing diet during at least 2 months were eligible to enter the study. There were no cases of translocation or mosaicism, and all children had accessible genetic reports of trisomy 21. The age of the children with DS ranged from 8 months to 8.6 years. The mean age was 4.6 ± 1.44 years. Male to female ratio was 1.3 (46 boys/36 girls). DS-specific mean weight percentile was 9.4 ± 3.35% (range <5–75%). Thirty-five (42.6%) of them had constipation.

All patients were screened using TTG IgA and total IgA levels. In cases where total IgA level was low, we estimated immunoglobulin G (IgG) TTG levels. TTG IgA and TTG IgG were measured using commercial enzyme-linked immunosorbent assay (Orgentec Diagnostika, Mainz, Germany) based on recombinant human TTG as an antigen. Values ≥ 10 U ml⁻¹ were considered positive as recommended by the manufacturer. Quantitative determinations of serum IgA levels were performed using routine method.

When either TTG IgA or TTG IgG yielded positive results, patients underwent upper endoscopy with small bowel biopsy with at least four mucosal specimens of descendent duodenum.

**Results**

A total of 82 children with DS were screened using TTG IgA and total IgA levels. One child with DS had...
TTG IgA serum levels $>10 \text{ U ml}^{-1}$ (17.7 U ml$^{-1}$). Low IgA levels (0.05–0.1 g l$^{-1}$) were detected in 5 (6%) patients. Because of the low levels of IgA in those six children, we also determined TTG IgG level. Three of them had TTG IgG serum levels slightly $>10 \text{ U ml}^{-1}$ (11.1, 12.6 and 10.4). In one child with increased level of TTG IgA and three children with increased level of TTG IgG, we performed upper endoscopy with small bowel biopsy. In all four children, small bowel mucosa was normal (Fig. 1).

**Discussion**

DS is a genetic condition characterized by trisomy or other aberrations of chromosome 21. Subjects with DS have the impairment of the immunologic system, which is associated with increased risk of infection; DS may also be associated with the increased frequency of autoimmune diseases such as hypothyroidism, Hashimoto thyroiditis, type 1 diabetes and CD [1].

An isolated absence or near absence ($\leq 0.1 \text{ g l}^{-1}$) of serum and secretory IgA is the most common well-defined immunodeficiency disorder with a disease frequency of 0.33% among the population [5]. CD is 10 times more common in patients with IgA deficiency [6]. In our children with DS, IgA deficiency was detected in 5 (6%) patients, which represents high prevalence of this immunologic disorder.

Considering increased prevalence of CD in DS and high prevalence of IgA immunodeficiency in our group of patients, it has been expected that there was a certain number of children with CD.

However, histopathological examination of mucosa in selected cases showed no single clear intestinal mucosal damage. There is little doubt that these patients represent a challenge to diagnosis. In fact, positive autoantibodies in patients having normal small bowel mucosal villous morphology do not necessarily constitute a false positive finding, because they may be a predictive sign of forthcoming mucosal villous atrophy (latent CD) [7].
In a multicentric study performed on 1202 children with DS aged 6.5 years on the average, Bonamico et al. [8] found CD prevalence of 4.6%, explaining this finding with the fact that CD usually occurs in children with DS during the adolescence period. This explanation could be applied to our sample too, as the mean age of our subjects was 4.6 years.

Based on our observations, the universal screening of children with DS for CD before their 8th year should be considered. Besides, the follow-up of these patients and other investigations will contribute in final conclusions.

References