

Serologically (tTG) Detected Celiac Disease Cases in Children with Down's Syndrome

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Abstract

Background : Down's syndrome (DS) is the most common chromosomal abnormality. Some autoimmune diseases are over represented in children with DS like insulin dependent diabetes mellitus, autoimmune thyroiditis and celiac disease (CD). Classical presentations of CD may be absent in children with Down's syndrome. Worldwide different tests are available for the diagnosis of CD. Among these, tissue transglutaminase (tTG) is cost effective, sensitive and the only test available in Bangladesh.

Objective : To ascertain the frequency of celiac disease and their clinical presentations in children with Down's syndrome by doing serum tTG (IgA) level.

Methods : A cross sectional study was carried out in the department of Paediatric Gastroenterology and Nutrition and Paediatric Neurology of Bangabandhu Sheikh Mujib Medical university (BSMMU) Dhaka, Bangladesh. Blood samples of 30 consecutive cases of DS were taken for estimation of tissue transglutaminase (IgA) level and clinical features of all positive cases were also recorded.

Result : Tissue transglutaminase (tTG) was detected in 10% cases of studied Down's syndrome children. One third of patients, who had CD, had growth failure. Common features of associated CD cases were diarrhoea, vomiting and abdominal pain.

Conclusion : Celiac disease was found in 10% of the studied cases of Down's syndrome in the present study. Serological tests for celiac disease could be performed in all cases of Down's syndrome whether it would be symptomatic or asymptomatic .

Key words : Downs syndrome, celiac disease, tissue transglutaminase (tTG)

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Introduction

Down's syndrome is the most common chromosomal abnormality affecting 1 in 733 new born.¹ The disease is characterized by the presence of an extra chromosome that alters motor, physical and intellectual development.² Patients with Down's syndrome have an impaired immune system due to altered T cell activity. Some autoimmune diseases, like insulin dependent diabetes mellitus, autoimmune thyroiditis and celiac disease are over represented in children with DS.³ Celiac disease (CD) is a gluten dependent immune mediated enteropathy strongly associated with the human leukocyte antigens (HLA) DQ2 and DQ8.⁴

In its classic form, CD appears with symptoms and signs of intestinal malabsorption. However, the disease may occur in a silent or latent form.⁵ Malabsorption will continue to cause under nourishment producing anemia, osteoporosis

and peripheral neuropathy if associated CD is not treated properly. Classic and symptomatic features of CD are seen in a minority of cases. On the other hand, most of the patients present with nonspecific symptoms like dyspepsia, abdominal pain, flatulence and alteration of the intestinal rhythm. CD usually presents with chronic diarrhoea, recurrent abdominal pain, growth failure, iron deficiency anaemia and the incidence of CD is more among the children with DS.⁶ However one study suggested 43 times and another study showed 20 times increased the prevalence of celiac disease in Down's syndrome.^{6,7}

For the diagnosis of CD tissue transglutaminase tTG (IgA) offers advantages in terms of sensitivity and simplicity. Although anti-endomyseal antibodies (EMA), anti-gliadin antibody (IgA) and anti-reticulon antibody (IgG) are also valuable tests in the diagnosis of CD but

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the methods are laborious, investigator dependant, inoperable, expensive and not available in our country. In contrast to this tissue transglutaminase is simple, investigator independent, operable, less expensive. Therefore measurement of tTG (IgA) antibodies can be used as a sensitive and specific marker for the diagnosis of CD.³

A small bowel biopsy is still the gold standard for the confirmation of CD, but this is neither easy, nor cheap and it's not in the best interest of the child or family to do an endoscopic biopsy. Therefore the best thing would be to have an easy blood test. TG is an intracellular enzyme that binds gliadin and starts to process it in a way that starts the autoimmune sequence in CD.

Tissue transglutaminase antibodies (TG) have been widely used in the last few years as a screening test for the diagnosis of celiac disease in the general population and in patients with Down's syndrome.⁸ It is the only test available in our country.

Therefore the present study was undertaken to ascertain the frequency of celiac disease in children with Down's syndrome with this test.

Methods

This cross sectional study was conducted at the out patient department of Paediatric Gastroenterology and Nutrition and Paediatric Neurology, BSMMU, Dhaka from January 2010 to December 2010 on 30 consecutive children with Down's syndrome aged between 6 months to 15 years. Down's syndrome children with severe respiratory distress or not willing to participate were excluded from the study.

Detail clinical history was taken with special attention for symptoms of CD and a thorough physical examination including anthropometry was done by the researchers. All children with Down's syndrome who attended the OPD during the study period were included. Laboratory investigations included Karyotyping, tTG (IgA) and Hb% were done. All data were recorded with frequency and percentage. *p*-value were statistically significant with < 0.05 .

Results

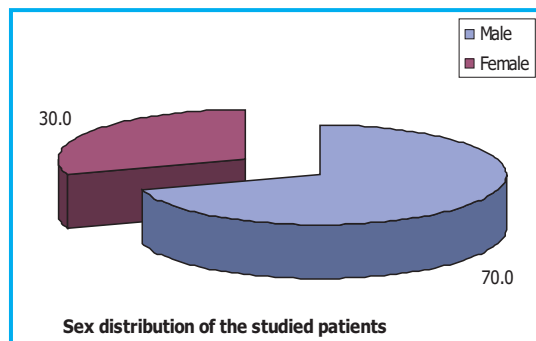
In the present study a total of 30 DS patients were evaluated. The maximum number i.e. 14 (46.7%) children were found in the age group of <3 years followed by 11 (36.7%) in the age group of 3-6 years. The mean \pm SD was 3.5 ± 2.9 years, ranged from 6 months to 15 years. (Table I).

Table I : Distribution of studied subjects (DS) according to age group (n=30)

Age group (years)	No of patients	Percentage
<3	14	46.7
3-6	11	36.7
6-9	3	10.0
9-12	1	3.3
12-15	1	3.3
Mean \pm SD (years)	3.5 \pm 2.9	
Range	(6 months -15 years)	

Regarding sex distribution of the studied children we found that 21 (70.0%) were male and 9 (30.0%) were female. Male female ratio was 2.3:1(fig-1).

Figure I: the sex distribution of the studied patients



Among the studied 30 subjects, 19 (63%) children presented with weakness, 13 (43%) with diarrhea, 6 (20%) with vomiting and 7 (23.3%) with abdominal pain. (Table II).

Table II: Distribution of features of Celiac disease in studied DS subjects (n=30)

Variable	Number	Percent (%)
Weakness	19	63
Diarrhea	13	43
Vomiting	6	20
Abdominal pain	7	23.3

For screening of the celiac disease, serum tTG (IgA) was done in all DS patients and it was found positive in 3 (10%) cases.

Regarding the distribution of presenting features between DS with CD and DS without CD, it was observed that diarrhea, vomiting and abdominal pain were found in all (100%) and weakness in 2 (66.7%) DS children with CD.

On the other hand in DS without CD cases weakness was found in 17 (63.0%), diarrhea in 10 (37.0%), vomiting in 3 (11.1%), abdominal pain in 4 (14.8%) and anemia in 9 (33.3%) children (Table III).

Table III : Distribution of presenting features between DS with CD and DS without CD (n=30).

Clinical feature	DS with CD (n=3)		DS without CD (n=27)		p value
	n	%	n	%	
Weakness (n=19)	2	66.7	17	63.0	0.899 ^{NS}
Diarrhea (n=13)	3	100.0	10	37.0	0.036 ^S
Vomiting (n=6)	3	100.0	3	11.1	0.001 ^S
Abdominal pain (n=7)	3	100.0	4	14.8	0.001 ^S
Pallor	0	0.0	9	33.3	0.231 ^{NS}

S=Significant, NS=Not significant

p value reached from chi square test.

More than 50% studied children had moderate stunting (HAZ <-2) at presentation (Table-IV) and 40% had anaemia (Hb% 8-42 gm/dl). Overall study population 11 (32%) were anaemic. (Table-V)

Table IV: Important physical & laboratory features of studied subjects (n=30)

Variable/ Parameter	DS with CD (n=3)	DS without CD (n=27)
* HAZ (<-2)	3(100%)	20(74%)
* WAZ (<-2)	1(33%)	12(44.4%)
Anaemia (Hb 8-<12gm/dl)	2(66%)	9(33.3%)
No Anaemia (Hb >12 gm/dl)	1(33.3%)	18(66.6%)

In some cases stunted and wasted present in the same child.

Discussion

Different studies have shown that patients with Down's syndrome presented with several immune dysfunctions, which lead to increased frequency of recurrent infections as well as autoimmune diseases.⁹ A high association between Down's syndrome and autoimmune diseases has been already reported by several authors with the most significant association with celiac disease.¹⁰⁻¹¹ Hilhorst et al. reported celiac disease were found 43 times higher in children with Down's syndrome.⁶ As the TG test has turned out to be a very sensitive and specific screening test for CD, it has become the favored screening test, especially for children who have no symptoms suggestive of CD.¹²

In this study it was observed that the mean (\pm SD) age was 3.5 \pm 2.9 years ranged from 6 months to 15 years. Almost a half (46.7%) of the children were found in below 3 year age group and more than one third (36.7%) belonged to 3-6 year age group. It was observed in this study that weakness (63.3%), diarrhea (43.3%) pallor were the most common clinical features. In a study diarrhea was the main mode of presentation (62%), with the remainder classified as silent (38%).¹³ Diarrhea, vomiting and abdominal pain were found in all (100%) and weakness in 2 (66.7%) children with Down's syndrome associated with CD. On the other hand, in DS without CD, weakness was observed in 17 (63.0%), diarrhea in 10 (37.0%), vomiting in 3 (11.1%), abdominal pain in 4 (14.8%) and anemia in 9 (33.3%) patients.

In the present study out of 30 DS children tTG was found in 3 (10.0%) cases. Study conducted by Shamaly et al. tTG level was found positive in 9.6% (5/52) cases of DS which is similar to the present study. Similar results were also observed in several other studies.^{11,14,15}

In this study among DS children with CD, 3(100%) was moderately stunted and 1(33%) were found moderately wasted. However, in DS without CD, 20(74%) were found moderately stunted and 12(44.4%) were found normal. These findings may be due to not using special growth chart for Down syndrome¹⁶ for measuring anthropometry in this study. Malnutrition in these cases may be due to repeated infection or diarrhoea.

In this current study in DS children with CD it was found that 2(66%) had anemia and 1(33.3%) had no anaemia. Shalitin et al. observed that 9.6% patients were anaemic in their study.¹⁷ Causes of anaemia in these cases may be due to less intake and/or impaired absorption.

Conclusion

Celiac disease may be associated in children with Down's syndrome. Serological tests tTG could be performed for detection of symptomatic and asymptomatic cases of Celiac disease in children with Down's syndrome.

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