

Frequency of Celiac Disease In Children With Chronic Functional Constipation in Shiraz-Iran

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ABSTRACT

BACKGROUND

Celiac disease is an autoimmune mediated small intestine inflammation which occurs due to hypersensitivity reaction to gluten and related proteins in diet in genetically predisposed individuals. Prevalence of celiac among the population is about 0.5 – 1 % in most countries. Frequency of celiac disease in children is the subject of a few research. In this study, we aim to determine the frequency of celiac disease in patients presenting with functional constipation.

METHODS

This cross-sectional study was conducted on children referring to Imam Reza Clinic, affiliated to Shiraz University of Medical Sciences during one year starting from 2011, March 20. One hundred and one children 2-18 years of age with constipation for more than 2 months according to ROME III criteria. The entire participants underwent serologic studies of Total IgA and IgA TTG. Serum IgG TTG was measured in cases with reported values of Total IgA below the lowest normal limits. Moreover, endoscopic biopsy of the small intestine was also performed for patients with positive serology.

RESULTS

Of all the 101 studied participants, only four individuals (3.96 %) had positive test results for IgA TTG (potential celiac disease). One of these patients refused to do endoscopy and endoscopic small intestine biopsy was performed for 3 patients. Two of them had normal pathology and one of them (0.99 %) was confirmed for celiac disease.

CONCLUSION

The frequency of celiac disease in children with chronic constipation is slightly higher than general population but without significant difference (0.99% VS 0.6% ; $p=0.64$). So the screening serologic test for celiac disease is not recommended in children with chronic constipation.

KEYWORDS

Celiac disease; Constipation; IgA anti-tissue transglutaminase

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INTRODUCTION

Constipation is explained as difficulty in defecation or delay in that; this delay is modified specifically by child's age and stage of its maturation. It is mostly common among children especially those in preschool age; 1-30 percent of pediatrician visits are estimated to include such patients.¹ Their most chief complaints are infrequent bowel evacuation, painful evacuation, hard stool, large diameter stool, and fecal incontinence.^{2,3} However, small proportion of children has organic causes of constipation which should be identified by clinicians. The most common cause of chronic constipation in children is functional one. In this group of patients, early treatment causes better outcome while delay in adequate treatment may cause fecal incontinence and psychological consequences.

Celiac disease, known as gluten sensitive enteropathy, is an immune mediated small intestine inflammation due to sensitivity to gluten and related proteins in diet in genetically sensitive individuals. Prevalence of celiac disease is 0.5 – 1 % of population in most countries.⁴ Celiac disease occurs primarily in Caucasians. In Europe and the United States, this prevalence ranges from 1:80 to 1:300 children (3 to 13 per 1000 children).⁴ Women are affected approximately two times more than men, yet, this ratio may change depending on the strategy used to find cases.⁵ The prevalence of celiac disease in normal population is 0.6 % in Shiraz, Iran.⁶ In another study the prevalence rate of celiac disease in healthy population has been 1:104-1:180.⁷ Prevalence of occult celiac disease was reported to be about 0.5% in the study from Tehran-IRAN.⁸ Specific proteins which can trigger symptoms of celiac disease are mostly present in wheat, barley and rye.

Although Celiac disease is recognized mainly as an infantile disease, symptoms can mostly be found at the age of 10 – 40 years. It often presents itself classically at the age of 6 to 24 month in infants (after gluten including into the infant's diet).⁹ Symptoms include diarrhea, anorexia, abdominal distention accompanied by pain, vomiting, failure

to thrive and weight loss. Serologic tests (IgA antibody to human recombinant tissue transglutaminase or anti TTG) may be used as an additional evidence of diagnosis and mostly valued in individuals with minimal symptoms. Such tests for celiac disease are useful for screening; in other words they are associated as first key step in the diagnosis of the disease. Currently, the most valuable test is detecting antibodies against tissue transglutaminase (anti-TTG), which is highly sensitive, specific, and more cost-effective than other antibody tests.¹⁰

Some studies were conducted in patients with functional constipation to find prevalence of celiac. Pelleboer et al conducted a study on 370 children with functional constipation.¹¹ They found 1.89% of cases had biopsy proven celiac disease.¹¹ In the study by Chogle and Sap, biopsy proven celiac disease was detected in 1.67% of cases.¹²

There are a few published researches on the frequency of celiac among children with chronic constipation according to Pubmed and Scopus databases using celiac, coeliac, and constipation. The present study was therefore designed with the primary aim of finding the frequency of Celiac disease among children with constipation.

MATERIALS AND METHODS

Study participants

This cross-sectional study was conducted on children referring to Imam Reza Clinic, affiliated to Shiraz University of Medical Sciences for one year starting from 2011, March 20. Written informed consent was taken from all of the participants' parents after giving all the necessary information about the study. Its protocol was approved by the ethical committee of the Shiraz University of Medical Sciences. The study was conducted on 101 children aged 2-18 years.

ROME III criteria was used for definition of constipation.¹³ Criteria are as the following:

“Symptoms must occur at least once per week for at least 2 months and include 2 or more of the following in a child with a developmental age of > 4 years with insufficient criteria of irritable bowel

syndrome:

- Two or fewer defecations in the toilet per week
- At least 1 episode of fecal incontinence per week
- History of retentive posturing or excessive voluntary stool retention
- History of painful or hard bowel movements
- Presence of a large fecal mass in the rectum
- History of large diameter stools that may obstruct the toilet⁷

Measurements

The entire participants underwent serologic studies of total IgA and IgA TTG. In cases where the reported values of total IgA were under the normal limit, serum IgG TTG was then measured. Normal range of Total IgA is 0.22 – 1.18 g/l and of IgA TTG is 0 -18 U/ml . In addition, endoscopic biopsy of the small intestine was also performed for patients with positive IgA TTG. At the end, all of the specimens were examined by one expert pathologist who addressed the definite diagnosis of celiac disease. The definite diagnosis was based on the pathology report and finally, the prevalence of celiac disease among children with functional constipation would be estimated.

Statistical analysis

Based on α coefficient 0.05 to detect significant differences between corresponding variables ($p=0.05$, 2-sided), 107 patients were required for study. The statistical software package SPSS for Windows, version 16.0 (SPSS, Chicago, IL, USA) was used for data analysis. For evaluation of P value, the Fisher's exact test was used. Data were reported as mean \pm SD. A p -value less than 0.05 was considered significant.

RESULTS

Overall, there were 101 studied patients, aged 24 – 144 months(2 – 12 years) with the mean (SD) of 57.68 (29.96) month. All of whom were diagnosed with functional constipation. Of the participants

Table 1: Age, IgA anti TTG, and Total IgA among boys and girls.

	Sex	Mean \pm SD	p -value
Age (months)	Male(n=54)	59.96 \pm 30.33	0.548
	Female(n=47)	55.06 \pm 29.64	
IgA-Anti TTG (U/ml)	Male(n=54)	3.11 \pm 4.95	0.752
	Female(n=47)	2.82 \pm 4.24	
Total IgA (g/l)	Male(n=54)	1.07 \pm 0.59	0.616
	Female(n=47)	1.05 \pm 0.63	

Table 2: Feature of patients with abnormal IgA-anti TTG.

Sex	Age(months)	IgA anti TTG(NL=0-18U/ml)	Total gA (NL=0.27-1.18 g/L)	Duodenal Bx.
F	54	19	1.88	NL
M	24	26.1	0.84	NL
M	96	26.5	1.89	Marsh 3B
F	84	22	1.58	Not done

54(53.5%) were male and 47(46.5%) were female. In this study, the range of IgA tTG was 0.01 – 26.5 U/ml with the mean (SD) of 2.97 \pm 4.61 U/ml. Range of Total IgA was 0.17 – 4 g/L with the mean 1.06 \pm 0.61 g/L among all participants. Age, IgA-Anti TTG, and total IgA among boys and girls were shown in Table-1.

Of all the 101 study participants, only four individuals (3.96%) had positive test for IgA TTG test. One patient refused endoscopic biopsy; therefore, endoscopic evaluation of the small intestine was performed for three of the four seropositive patients. Two of them had normal pathology and Celiac disease was confirmed in one of them (0.99% of all children)(Table-2).

DISCUSSION

In our study, 0.99 of cases had biopsy proven celiac disease. In the study by Pelleboer et al., of 370 children with constipation, 7 (1.89%)cases had biopsy- proven celiac disease.¹¹ In the study by Chogle and Saps on 7472 children with functional constipation, 1731 patients were tested for celiac antibodies; and 55(3.17%) had elevated tissue transglutaminase IgA levels and 29(1.67%) had biopsy-positive celiac disease. The results of studies by Pelleboer et al.¹¹ and Chogle and Saps¹² were

similar and were slightly higher than our study.

Among all cases, 3.96% had elevated IgA TTG levels. In the study by Chogle and Saps¹², 3.2% had elevated IgG TTG level which was lower than our study.

Prevalence of celiac disease in healthy school aged children in Shiraz was 0.6%⁶ But this study shows the prevalence of celiac disease in children with functional constipation is 0.99% (1/101) that is also not statistically significant.

Chogle and Saps in their study didn't recommend screening celiac in patients who have constipation alone.¹² Since the prevalence of celiac disease in children presenting chronic constipation is not statistically significantly higher than general population in our study, TTG test is not recommended for them as routine check up in our population. Further studies with more participants is recommended.

Limitation: Low sample size has been the main limitation of the current study

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CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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