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The prevalence of celiac disease among children with short stature

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Abstract

Background and objectives: The most important characters of children are growth and development. There are many causes of short stature. Among causes of short stature celiac disease is the important reversible cause. Celiac disease can be diagnosed serologically or/and duodenal biopsy according to the level of serological tests or/and symptoms. The main objective of the study was to find the relation between having high tissue transglutaminase antibody and short stature

Methods: This is a cross sectional study. From March 2021 to March 2022, consecutive sampling from of 79 children who presented to Helina center in Erbil city and Hawler teaching hospital (department of endocrinology) complaining to have short stature and recorded as short child. Tissue transglutaminase antibody were sent for all patients, and duodenal biopsy for selected cases were done.

Result: Seventy-nine children with short stature were included in the study. Their mean age (SD) was 8.3 (3.3) years. The median was 8 years, and the age range was 1.1-16 years. More than half (54.4%) of the sample were aged 5-9 years, and 42 patients (53.2%) were females

The prevalence of celiac disease among children with short stature in our study was 13.9%, which is statistically is significant.
The majority (69.6%) of the children had severe short stature (less than -2 Z score), and the rest had acceptable Z score.

Conclusion: In conclusion, celiac disease should be considered in the differential diagnosis of patient who presents with short stature as it is not uncommon in our community. Sending for non-invasive investigations for diagnosing celiac disease is easier and simpler than other invasive procedures.

Keywords: Celiac, Tissue transglutaminase antibody, Short stature

Introduction

Celiac disease (CD) is regarded as a most common disorder of worldwide relating to food sensitivity.[1] It triggered by eating some food that contains sensitive protein such as gluten. It causes flattening of small intestinal mucosa which is the primary site of its affect.[1]

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Types of celiac disease includes silent, potential, or latent celiac disease.[2] In patient with silent celiac disease, has no any symptoms of celiac disease, but they have biochemical and endoscopical features of celiac disease. This diagnosed is made in a symptomatic patient who has suspicion or has risk to have celiac disease. In potential celiac disease patients have positive serum autoantibodies and may or may not have symptoms consistent with celiac disease, but the endoscopy is negative for celiac disease. latent celiac disease: individuals with normal mucosal morphology (like the potential) but known to have had a gluten-dependent enteropathy at some point in their life.

New guidelines of diagnoses of celiac disease had been made by the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition ESPGHAN in 2012,[2] North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition NASPGHAN in 2005,[3] American Gastroenterological Association AGA in 2006 [4] this new guidelines recommend not to do duodenal biopsy if the patient has symptoms of celiac disease, positive HLA for celiac disease, more than 10 folds increase of TTG and positive anti endomyseal antibody.[4]

The most fundamental characteristics of a child are growth and development. Growth pattern of children is usually predicted if the child has normal pathway of growth. If the child has deviation from normal pattern of growth, there may be a wide variety of processes of both endocrine and non-endocrine that can involve any organ system of the body.[5]

Normal growth pattern of a child is a good indicator for a good general health. The pediatrician should know that the child has normal or abnormal growth. pediatricians have to recognize a normal variation from a pathological condition based on medical history, growth chart, and physical examination, including body proportions and dysmorphic features. Every 6 months, a thorough height measurements are performed and plotted on the reference growth curve is the simplest and low-cost tool to recognize an abnormal growth pattern. Measuring height with comparing to target height is the most important factor in evaluating growth of a child.[6]

Patient and methods

This cross-sectional study was conducted in Hawler city/Iraq. Sample collection started from March 2021 to March 2022.The study has been approved by Hawler medical university. Permission and ethical approval have been given from the Hawler medical university, then we started to collect patients. Seventy-nine children were enrolled in this study. All patients were evaluated in Helina center and endocrinological department in Hawler teaching hospital and the purpose of referral was the short stature. All included candidates were complaining of short stature (height below 3rd centile for his/her age). For all candidates, tissue transglutaminase antibody (TTG) IgA & IgG, total IgA, and anti-endomyseal antibody were measured. Cutoff of TTG is 10 U/ml, value more than 10 is regarded abnormal, while more than 100 regraded to have celiac disease. For those whose TTG revealed high, we offered for OGD and duodenal biopsy (if the parent agrees). The TTG higher than 10 folds of normal with positive anti-endomyseal antibody is diagnosed to have celiac disease. If the number is more than normal but less than 10 folds high, we proceed to duodenal biopsy for confirmation of the diagnoses. All patients were evaluated for excluding other causes of short stature.

Results

Seventy-nine children with short stature were included in the study. Their mean age (SD) was 8.3 +_ 3.3 years. The median was 8 years, and the age range was 1.1-16 years. More than half (54.4%) of the sample were aged 5-9 years, and more than half (53.2%) were females (Table 1).

Table (1): Age and gender distribution.

	No.	(%)
Age (years)		
< 5	12	(15.2)
5-9	43	(54.4)
≥ 10	24	(30.4)
Mean (SD)	8.3	(3.3)
Gender		
Male	37	(46.8)
Female	42	(53.2)
Total	79	(100.0)

The prevalence of celiac disease among children with short stature was 13.9% Fig (1).

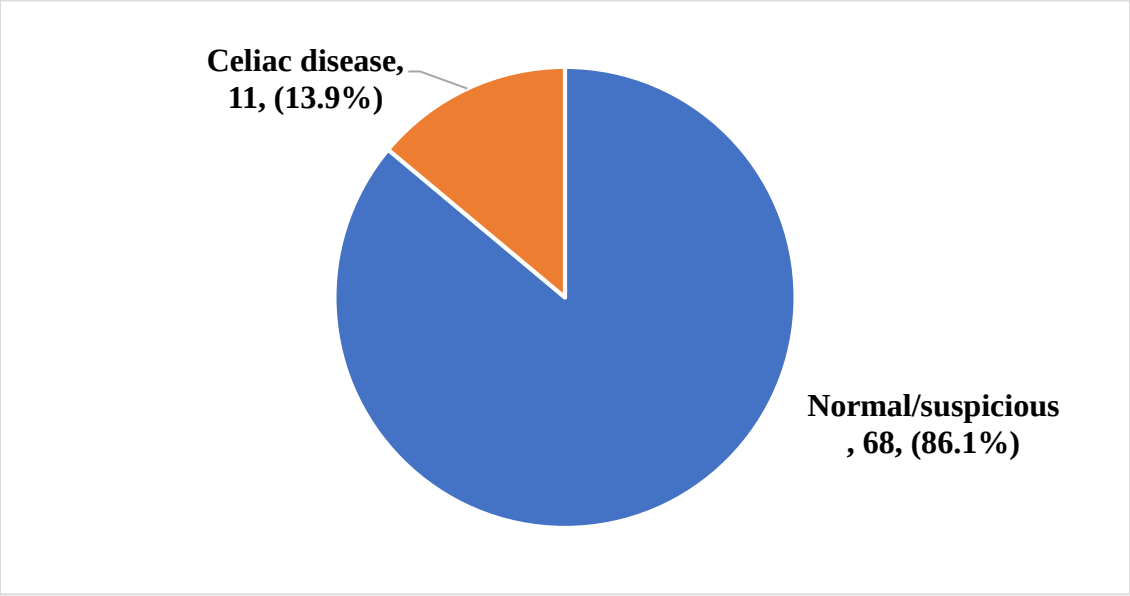

Figure (1): Prevalence of celiac disease according to TTG IgA (or TTG IgG) test results

The majority (69.6%) of the all included children in our study had severe short stature (less than -2 Z score), and the rest had acceptable Z score (Figure 2).

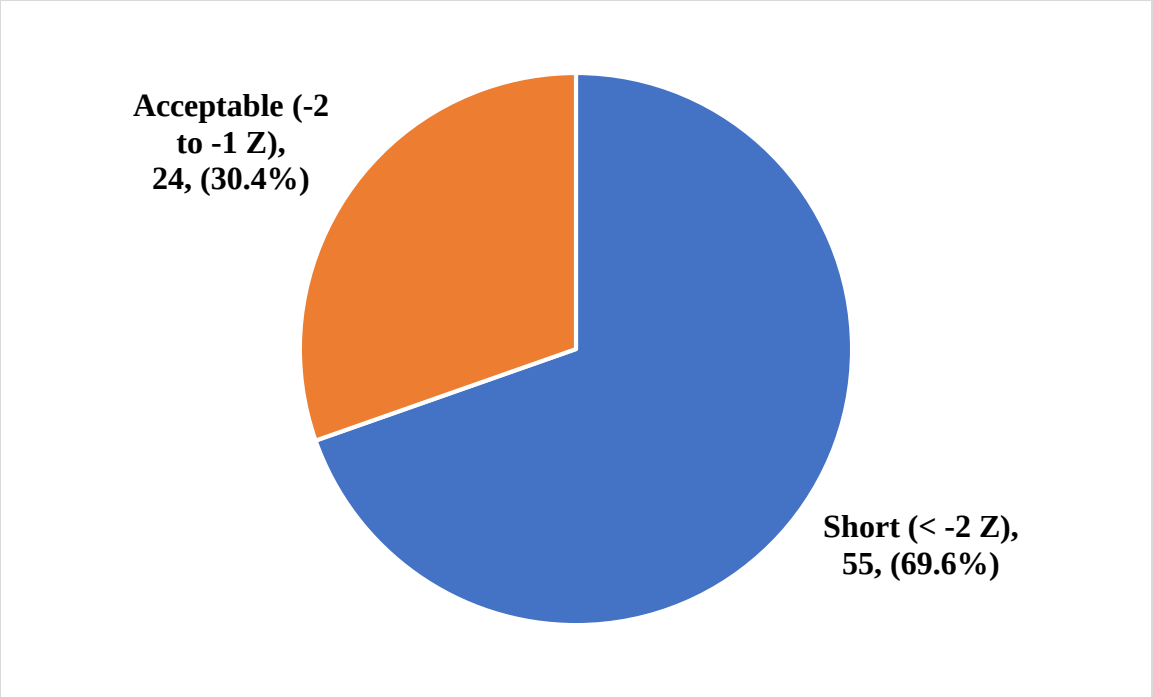

Figure (2): Degree of short stature as assessed by Z scores

According to the results of TTG IgA and IgG, 12.7% of children with HAZ (height for age Z score) of less than 2 Z score are having celiac disease, compared with 16.7% of children with acceptable height for age (p = 0.629 and p = 0.287 respectively) as presented in Table 2.

Table (2): Transglutaminase (TTG) IgA and Transglutaminase (TTG) IgG tests results by degree of short stature.

	Degree of short stature (HAZ)			
	Short (< -2 Z)	Acceptable (-2 to -1 Z)	Total	
TTG IgA				
Normal < 10	46 (83.6)	18 (75.0)	64 (81.0)	
Suspicious 10-100	2 (3.6)	2 (8.3)	4 (5.1)	
Celiac disease (> 100)	7 (12.7)	4 (16.7)	11 (13.9)	0.629*
TTG IgG				
Normal < 10	47 (85.5)	18 (75.0)	65 (82.3)	
Suspicious 10-100	1 (1.8)	2 (8.3)	3 (3.8)	
Celiac disease (> 100)	7 (12.7)	4 (16.7)	11 (13.9)	0.287*
Total	55 (100.0)	24 (100.0)	79 (100.0)	

*By Fisher's exact test.

No significant correlation was detected between the HAZ with the following variables: Father's height (r = 0.092, p = 0.418), mother's height (r = 0.170, p = 0.134), TTG IgA (rho = -0.016, p = 0.885), TTG IgG (rho = -0.041, p = 0.720).

Table (3): Correlation between HAZ with some variables.

	Correlation coefficient	p
Father's height	0.092*	0.418
Mother's height	0.170*	0.134
Transglutaminase IgA	-0.016**	0.885
Transglutaminase IgG	-0.041**	0.720

*By Pearson correlation coefficient (r). **By Spearman (rho) correlation coefficient.

It is clear in Table 4 that the highest prevalence of celiac disease was in Tanner stage 1 (15.8%) , Tanner stage 5 (14.3%), and Tanner stage 2 (10%), while none of the children of Tanner stage 3 and 4 had celiac disease. No significant association was detected between Tanner stage and results of TTG IgA (p = 0.269), and TTG IgG (p = 0.515) (Table 4).

Table (4): Transglutaminase (TTG) IgA and Transglutaminase (TTG) IgG tests results by puberty Tanner scale.

	Puberty Tanner scale					
	1	2	3	4	5	
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	
TTG IgA						
Normal	47 (82.5)	7 (70.0)	4 (100.0)	1 (100.0)	5 (71.4)	
Suspicious	1 (1.8)	2 (20.0)	0 (0.0)	0 (0.0)	1 (14.3)	
Celiac	9 (15.8)	1 (10.0)	0 (0.0)	0 (0.0)	1 (14.3)	0.269*
TTG IgG						
Normal	47 (82.5)	8 (80.0)	4 (100.0)	1 (100.0)	5 (71.4)	
Suspicious	1 (1.8)	1 (10.0)	0 (0.0)	0 (0.0)	1 (14.3)	
Celiac	9 (15.8)	1 (10.0)	0 (0.0)	0 (0.0)	1 (14.3)	0.515*
Total	57 (100.0)	10 (100.0)	4 (100.0)	1 (100.0)	7 (100.0)	

*By Fisher's exact test.

Discussion

The height measurement of children and plotting on the growth chart is an important element for linear growth observation. Because of early detection of the abnormal height and early diagnosis of the disorders beyond their short stature can affect the final height, frequent assessment of children is regarded as the important heath issue.

There are many causes that make the child to be short as compared to his/her peers. Celiac disease is regarded as one of the causes that may be detected early to put the affected child on gluten free diet and improving the final height.[7]

Diagnosis of celiac disease is based on the positive serological test (tissue transglutaminase antibody) and endoscopically (histological) finding.[4]

Although all the included candidates in our study were free of gastro-intestinal symptoms, they all tested for celiac disease and 11 patients (13.9%) diagnosed to have celiac disease and put of gluten free diet.

Among 11 patients who had suspicion to have celiac disease, only 5 patients accepted to do OGD and 4 OGD returned positive by the biopsy. While just in one patient the jejunal biopsy returned normal.

Many previous studies have been done for short children with no GI symptoms, showing different results regarding prevalence of celiac disease (0-59%) depending on the region that the study performed.[7,9]

High prevalence of celiac disease showed (%59) with cataldo et al.[7]

While Bonamico et al. showed the prevalence was 4.7%.[9]

Assiri et al. although has limited studies, showed a prevalence of approximately 10%.[8-10]

The cause of being short in patients having celiac disease is not well-known. Nutritional deficiencies that result in low level of IGF1[8] and poor growth hormone response [11,12] is thought to be the cause of being short in celiac disease. Eichler et al.[14] concluded that prolonged exposure to gluten diet causes reduction in IGF1 level.

The most likely cause of short stature in celiac disease refers to villous atrophy that result in malabsorption. However, presence of high inflammatory process like elevation of pro-inflammatory cytokines like IL-6, TNF-α, and IL-1 results in the dysregulation of growth hormone secretion.[14–16]

The prevalence of celiac disease in short stature patients among studies is highly variable, it depends on the way of diagnosing celiac disease. If duodenal biopsies done for all included patients rather than sequential strategy result in higher prevalence of celiac disease. [8,17,18,20,21] Furthermore, underestimation of celiac disease appears in studies where single serological test has been used to diagnose celiac disease. A new study showed that 24% of the IgA TTG-ab is false negative.[22] If just single measure of IgA TTG ab sends for diagnosing celiac disease, the prevalence will be falsely low. Also, around 2% patients with celiac disease may have seronegative Celiac Disease in the presence of normal IgA levels, which can be diagnosed by duodenal biopsies.[23,24] Because of the above controversy, duodenal biopsy is the best way for diagnosis of celiac disease in idiopathic short stature. Otherwise, more than one reading of TTG antibody will eliminate the false negative results.

Higher prevalence of celiac disease appears in studies that included small number of patients compares with larger sample size studies (17.2% vs 3.9%, p value 0.006). The study with the smallest number of patients (n = 49) showed the prevalence of Celiac Disease to be as high as 59.2% 20 as compared with the study that included the largest number of subjects (n = 1066), which showed a prevalence of 1.1% [28]. This because of the case selection among referral doctors in small studies. [22]

The new update in the diagnosis of Celiac Disease by just serology made the diagnosis of celiac disease easier [27]. Recent European Society for Pediatric Gastroenterology, Hepatology and Nutrition guidelines, demonstrate that more than 10 folds increase of tissue transglutaminase antibody plus positive anti-endomyseal antibody is the diagnostic criteria for celiac disease. This suggests without doing duodenal biopsy we can diagnose celiac disease. However, it is important to proceed to duodenal biopsy if the patient does not fulfill the above criterias for diagnoses of celiac disease. Also, the

diagnosed of celiac disease improves if duodenal biopsy done for suspicion patients who have anemia and short stature or in patients with idiopathic short stature even if the serological tests yield negative.

We have some weak points in our study. For example, in order to detect the prevalence of celiac disease we must collect larger sample size and compare to prevalence in general population.

Because of time limitation we could not collect larger sample size.

Hormonal analyses and OGD are cost burden as patients who visit public hospitals have poor economic status so we could not oblige them to send for blood tests or for more investigations to detect the causes of short stature.

The strength of our study is the prevalence of celiac disease is high despite limited number of cases.

Conclusion

The prevalence of Celiac Disease is not rare in our community among children with short stature. This condition should be in the differential diagnosis in patient with short stature especially those who has idiopathic short stature. Because the diagnoses of celiac disease by serology is simpler than doing growth hormone, excluding celiac disease as a cause of short stature is crucial.

Conflict of interest: None**.**

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