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The Prevalence of Positivity of Anti Tissue Transglutaminase in Patients with Short Stature in Pediatric Endocrinology Clinic of Tishreen Hospital in Lattakia

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Abstract: Background: Short stature is a public health problem that, by definition, affects 2.5% of the population around the world, and higher rates in some areas. Celiac disease is one of the causes of short stature, it occurs with multiple mechanisms. And it is one of the causes that can be treated and thus the final length improvement, especially with the early start of treatment. Detection of celiac disease serologically is easy and cost-effective. Aims: To determine the prevalence of antiTTG-IGA antibody positivity in patients who meet the standard definition of short stature. Methods: A cross-sectional study that included 132 short children over two years of age attending the Pediatric endocrinology Clinic at Tishreen University Hospital from the beginning of 2016 until the end of 2019. The data of the patients attending the clinic with complaints of short stature was reviewed and the patients with antiTTG-IGA antibodies were identified and their data related to anemia and clinical symptoms were analyzed. Results: The number of short children included in the study was 132 children (69 males and 63 females), 10 of whom had positive antiTTG-IGA antibodies that were 7.6%. Digestive symptoms or anemia were not statistically significant in predicting the presence of celiac disease. It was found that the near-normal BMI and the absence of severe weight growth failure do not exclude the presence of celiac disease. Conclusion: Celiac disease is an important cause of short stature that is difficult to predict through clinical symptoms, which requires for titration of antiTTG-IGA antibodies in all children with short stature.

Keywords: Celiac Disease, Short Stature, Failure to Thrive, Body Mass Index, Anti Tissue Transglutaminase

1. Introduction

Celiac disease is an immune-mediated systemic disease that affects the small intestine as a result of eating foods containing gluten in genetically predisposed patients [1]. Short stature is defined as a height more than two standard deviations below the mean for age and gender. Celiac disease is one of the most common genetic diseases, with a prevalence rate of 0.5-1% of the total population in many countries. Where the highest prevalence rates were in Western Europe, North America and Australia [2]. Cataldo and Montalto review of the prevalence of celiac disease in developing countries found that rates in the Middle East are similar to global rates [3]. The prevalence of celiac disease in patients with short stature varies widely from 4.7%to 15.2% in various countries [4-8]. Jansen et al demonstrated in 2015 in a cohort study that positivity of antiTTG-IGA antibodies alone is associated with decreased height gain [9]. Suggested mechanisms of celiac disease's effect on height gain include: Lack of absorption of nutrients, not only protein and caloric intake, but also calcium and vitamin D [10] and micronutrients deficiencies [11], increased resistance to growth hormone leading to decreased levels of insulin-like growth factor 1 [12], hypogonadism and consequently weak growth spurt [13], associated hypothyroidism [14], presence of antibodies against the pituitary gland in some patients [15].

The most positive point in the relationship of celiac disease with short stature is that starting treatment with a gluten-free diet leads to an improvement in final height unless there are comorbidities, and this improvement is the

best when the treatment is started as earlier as possible [16]. In the past, most patients were thin children, but screening tests showed that a significant portion of patients had normal or increased BMI [17].

This study aims to determine the prevalence of anti-TTG-IGA positivity in patients who meet the standard definition of short stature. In addition to studying the clinical characteristics (diarrhea, constipation, flatulence, abdominal pain) and laboratory (anaemia) for patients who are positive for AntiTTG-IGA antibodies.

2. Materials and Methods

This study is Observational Descriptive Cross-Sectional study included a continuous series of consecutive patients older than 2 years attending the pediatric endocrinology clinic in Tishreen University Hospital who met the standard definition of short stature. All the patients were tested for anti TTG antibodies. Patients' files were reviewed from the beginning of 2016 until the end of 2019. The study was limited to the positivity of AntiTTG-IGA antibodies in the analysis of the data without referring to the biopsies results, noting that all the positive patients were directed to undergo a gastroenterology consultation. The French M. Sempe growth charts used by the clinic were adopted for the classification of short stature in this study [18]. IBM SPSS statisticsVersion15 software was used to calculate the statistical parameters and analyze the results. Patients' total Iga is not titrated in the clinic because it is not available in hospital laboratories due to the war conditions in Syria.

3. Results

The number of children who visited the pediatric endocrinology clinic at Tishreen University Hospital in Lattakia reached 777 during the period from 1-1-2016 to 31-12-2019, including 306 children with a short stature complaint. Those who achieved the standard definition of short stature based on the French M. Sempe growth charts used by the clinic were 132 children (69 males, 63 females) made up the research sample. AntiTTG-IGA antibodies were investigated in all of these children. All children who tested positive for AntiTTG-IGA were referred to the pediatric gastroenterology clinic.

The ages of the research sample patients ranged between 28 and 160 months, with an average age of 78 months. 53% of the total patients of the research sample were in the age group of 6-10 years. The number of patients positive for Anti-TTG IgA was 10 (7.6%); 6 males and 4 females.

As shown in Table 1: no statistical significance was observed for gender, age group, anemia, or digestive symptoms.

Table 1. *The distribution of the study sample according to the result of anti-TTG IgA antibodies.*

	Anti TTG IgA		**statistical significance**
	Positive n:10 (%)	**Negative n:122 (%)**	
Gender			0.6
Male	6 (60%)	63 (51.6%)	
Female	4 (40%)	59 (48.4%)	
Age group by years			0.4
[2-6]	5 (50%)	45 (36.9%)	
[6-10]	3 (30%)	67 (54.9%)	
[10-14]	2 (20%)	10 (8.2%)	
Anemia	7 (70%)	79 (64.8%)	0.7
Gastrointestinal symptoms	4 (40%)	78 (63.9%)	0.1

The weight deviation was less than -2 in 30% of the antibody-positive patients. While 80% of the antibody -positive patients had a body mass index deviation of less than -2.

As shown in Table 2, there was no statistically significant difference between the height of the positive and negative antibodies groups. While there was a difference in weight between the two groups, and a very important difference in BMI.

Table 2. *Relationship of the presence of anti TTG IgA antibodies with deviations in height, weight and body mass index.*

	Anti TTG IgA	**Mean ± SD**	**U-Value**	**P-value**
Height	Pos	- 2.47±0.4	489	0.2
	Neg	- 2.65±0.5		
Weight	Pos	- 2.85±1.05	462	0.02
	Neg	- 2.36±1.1		
BMI	Pos	- 1.04±1.1	285	0.005
	Neg	- 0.02±0.8		

4. Discussion

The number of anti-TTG IgA-positive patients reached 10, with a rate of 7.6%, and this percentage falls within the global range of celiac disease prevalence rates in children of short stature. With difficulty in evaluating accurate differences between this study and global studies for several reasons, including that this study relied on the positivity of antibodies without knowing the results of the gastrointestinal endoscopy and histological results. In addition to the absence of a local study showing the prevalence of celiac disease among healthy children.

The results showed that about two-thirds of patients with short stature in the research sample suffer from anemia and digestive complaints. This may primarily be due to the prevalence of high rates of poverty due to the war and its impact on the nutritional status of children [19].

This study showed that 30% of patients of short stature who were positive for anti-TTG IgA antibodies had a weight deviation of less than -2. And 80% had a body mass index deviation of less than -2. This indicates that a BMI that is close to normal and the absence of severe failure to thrive do not rule out the presence of celiac disease. This is consistent with other studies in this field [7].

The current study gives statistically significant results because it includes a continuous sample of patients for 4 years.

While the results of gastrointestinal endoscopy and histological study of antibody-positive patients were absent from the study. In addition, total IgA was not titrated.

5. Conclusion

This study showed that celiac disease constitutes a significant proportion of patients of short stature, even in a society where the prevalence of celiac disease among the general population is not known, such as Syria. The absence of typical signs of malabsorption syndrome (digestive symptoms, anemia) does not rule out the presence of celiac disease. Also a normal or slightly decreased BMI does not rule out the presence of celiac disease, but its severe drooping in a child with short stature increases the likelihood of diagnosis. The study also showed a very high prevalence of anemia and digestive complaints among children of short stature, even those who do not suffer from celiac disease. This problem is an important issue that deserves further study and is often due to the consequences of the war in Syria.

Abbreviations

TTG: Tissue transglutaminase. IgA: Immunoglobulin A

Author Contributions

Both authors developed and carried out sample collection. Literature review was done by Dr. Mohammad Daaboul, and both authors did data analysis and read through the final data.

Competing Interests

All the authors do not have any possible conflicts of interest.

Ethics Approval

Ethical clearance for this study was obtained from the Ethical Committee of Tishreen University Hospital.

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