CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
http://doi.org/10.5281/zenodo.4362178

Avalable online at: http://www.iajps.com *Research Article*

STUDY TO DETERMINE THE INCIDENCE OF CELIAC DISEASE AMONG SHORT STATURED CHILDREN

[1]Dr Mah Rukh Tanveer, [2]Dr Asma Riaz, [3]Dr Zainab Khalid
[1]Shalamar Medical and Dental College, Lahore
[2]Shalamar Medical and Dental College, Lahore
[3]Shalamar Medical and Dental College, Lahore

Article Received: October 2020 **Accepted:** November 2020 **Published:** December 2020

Abstract:

Aim: *To determine the incidence of celiac disease (CD) in short-stature children reported to the Services Hospital, Lahore.*

Study design: *A Descriptive cross-sectional study.*

Place and Duration: *In the Pediatric Unit-II of Services Hospital, Lahore for one-year duration from November 2019 to November 2020.*

Methods: *Children of short stature (height ≤ - 2 SD for mean or below the 3rd percentile due to age and gender) attending the Pediatric department were included after obtaining informed consent. A detailed interview and physical examination have been recorded. Appropriate studies were performed, including an antibody against tissue transglutaminase (IgA and IgG) by ELISA as a CD marker. The reasons for the short stature were recorded on the previously prepared proforma for the final analysis.*

Results: *Of the 288 short stature patients, 151 (52.43%) were male with a male to female ratio of 1.1: 1. Nineteen (6.6%) patients had CD, 43 (14.9%) had hypothyroidism. and 28 (9.72%) with growth hormone deficiency (GHD). One of the GHD patients also suffered from CD. Similarly, among diagnosed cases of hypothyroidism, one was related to coexisting CD and diabetes. Of the 19 patients with CD, 11 were male and 8 were female, all were anemic (Hb <9Gm%), and bone age was delayed in 18 (94.7%) cases. Anti-tTG levels were increased in all CD patients.*

Conclusion: *CD should be considered in a child with short stature, especially if height is ≤ -2 SD below the mean for age and gender, even in the absence of gastrointestinal symptoms. In conclusion, the measurement of anti-tTG antibodies should be included in the diagnostic evaluation of a child with short stature.*

Key words: *short stature, celiac disease (CD), anti-tissue transglutaminase (anti-tTG)*

Corresponding author:
Dr. Mah Rukh Tanveer,
Shalamar Medical and Dental College, Lahore

QR code

Please cite this article in press Mah Rukh Tanveer et al., ***Study To Determine The Incidence Of Celiac Disease Among Short Statured Children.,*** *Indo Am. J. P. Sci, 2020; 07(12).*

INTRODUCTION:

Growth retardation in childhood may be one of the earliest symptoms of an underlying disease such as celiac disease, which is a genetically determined autoimmune, chronic inflammation caused by gluten and related proteins, causing nutritional deficiencies. The clinical spectrum includes symptomatic, silent, latent and potential forms of the disease. Patients usually present with the classic symptoms of malabsorption in early childhood, while older children with CD often have atypical forms, including short stature and maturation delay. Short stature is one of the most common parenteral symptoms of CD, so all children with short stature should be assessed for CD. The cause of short stature in CD is still unclear, growth retardation in children with CD is usually attributed to nutrient malabsorption caused by gluten, as its withdrawal from the diet is often associated with marked improvement in linear growth, but many reports suggest an abnormal growth hormone-insulin-like axis growth factor in children with CD. The possibility of autoimmune pituitary involvement in CD patients has been suggested, some studies have shown positive anti-pituitary antibodies and growth hormone deficiency (GHD) in these patients, so growth hormone (GH) replacement therapy may be considered. total catching up growth. Final height in adulthood may be influenced by age at diagnosis of CD, children diagnosed early achieve greater growth gain than children diagnosed late. Turner syndrome (TS) is another important cause of short stature in girls and is often associated with CD (6–18% of patients). Therefore, early diagnosis of CD in these TS patients would be beneficial when treated with a gluten-free diet and GH10 replacement. CD is a multi-system autoimmune disorder, sometimes short stature is the main or only symptom of CD, and the diagnosis rate depends on the degree of suspicion of the disease. The aim of this study was to determine the prevalence of celiac disease (CD) in short-statured children.

METHODOLOGY:

The study was conducted at the Pediatric Unit-II of Services Hospital, Lahore for one-year duration from November 2019 to November 2020 to determine the prevalence of celiac disease in a group of children with the primary ailment: short stature. Children of both sexes, 2-15 years of age, with short stature (height ≤ -2 SD for mean, or less than the 3rd percentile for age and gender) were recruited after informed consent. The study excluded patients with contractures and kyphoscoliosis, whose height could not be accurately measured, and patients with chronic diseases such as (chronic kidney disease, bronchial asthma, chronic liver disease) who had a clinical profile and appropriate tests. All children have had a detailed history including; gastrointestinal symptoms; and a thorough physical examination, including anthropometric measurements. Patients were divided into groups to see the disease occurring at different ages and genders. Age was divided into three groups; 2-5 years old,> 5-11 and> 11-15 years old. Height was measured with a Harpenden Stadiometer. The lower segment was calculated by subtracting the seat height from the standing height, on the basis of these measurements the ratio of the upper and lower segments (US / LS) was calculated. Patient weight was measured on an exact scale. Maturation was assessed in the 11-15 age group according to Tanner's classification. Parents were asked for any previous records available. Appropriate research has been carried out to find the cause of their short stature. The serum was tested for the presence of anti-tissue transglutaminase antibodies (IgA and IgG) by ELISA as a serological marker for CD. Serum anti-tTG antibody levels (IgA and IgG) between 0-15 units per milliliter were considered normal. Upper gastrointestinal endoscopy was performed in all patients with high anti-tTG levels (> 15 units / ml) and four biopsy samples were collected from different parts of the duodenum and sent for histopathological examination (mucosal lesions according to modified Marsh criteria). Other laboratory tests included (complete blood count, ESR, urinalysis, liver and kidney function, random blood sugar, bone profile, and serum free T4 and TSH levels (free T4 less than 0.93 ng / dL and TSH greater than 6.4 u IU / ml was considered a case of hypothyroidism.) Karyotyping was performed in all selected patients to exclude TS.GH was assessed in patients with strong clinical suspicion of growth hormone deficiency (GHD) whose baseline test results were within normal ml in a stress test Insulin levels were considered GHD.) Left hand and wrist radiographs were performed in all patients to assess rickets and bone age using the published standards of Greulich and Pyle's Atlas of Skeletal Development. Genetic Syndromes; like (, Noonan syndrome) based on clinical profile and relevant studies. Data entered in SPSS version (19.0). Descriptive statistics used. Incidence of celiac disease in short adult patients.

RESULTS:

Of the 288 cases, 151 (52.43%) were men with a male to female ratio of 1.1: 1. 19 (6.6%) patients with CD were identified based on elevated anti-tTG levels and changes in the duodenal mucosa. Anti-tTG levels were increased in all 19 patients, gender distribution in CD patients is presented in Table 1.

TABLE I: Gender distribution of CD in short statured patients (n=288)

Celiac Disease	Gender		Total
	Male	Female	
Present	11(57.9%)	8(42.1%)	19
Not Present	140(52.0%)	129(48.0%)	269
Total	**151(52.4%)**	**137(47.6%)**	**288**

All CD patients were anemic (Hb <9Gm%), and bone age was delayed in 18 (94.7%). Family history of CD occurred in 2 (10.5%) children. All recruited patients were divided into three age groups, 74 (25.7%) were aged 2 to 5 years, 143 (49.65%) were> 5-11 years old, while the rest of 71 (24.65 %) of the children were> 11 to 15 years of age. years. CD patients in different age groups are listed in Table 2.

TABLE 2: CD in different age groups of short statured patients(n=288)

Celiac Disease	Age groups			Total
	2-5 year	>5-11 years	>11-15	
Present	2 (10.52%)	5 (26.31%)	12 (63.15%)	19 (6.6%)
Not Present	72 (26.76%)	138 (51.30%)	59 (21.93%)	269 (93.4%)
Total	**74 (25.7%)**	**143(49.65%)**	**71 (24.65)**	**288 (100%**

GHD was found in 28 (9.72%) cases of all subjects; one of the 19 celiac patients also suffered from GHD. Similarly, hypothyroidism was diagnosed in 43 (14.9%) cases, one of them had diabetes and CD.

DISCUSSION:

Celiac disease is an immune-mediated enteropathy resulting from persistent gluten intolerance in genetically susceptible individuals. It is now considered to be a multi-system autoimmune disorder in which many patients are asymptomatic, oligosymptomatic, or with parenteral symptoms. Lack of stature is one of the well-known symptoms of overt CD in young children, and short stature may be the only obvious symptom in older children with atypical CD. In the current series of 288 cases of CD, 19 (6.6%) patients were affected. GHD was found in 28 (9.72%) cases, and one of the 19 celiac patients also suffered from GHD. Hypothyroidism was diagnosed in 43 (14.9%) cases, one of them had diabetes and CD. Short stature may be the only finding in CD patients. The diagnosis depends on the high rate of suspicion and the region in which the study is conducted. In this study, the CD diagnosis rate among short-statured patients was 6.6%, while Giovenale et al. Showed 0.63%, Queiroz et al .17 4.7%, and Dehghani et al. 2.8%. Bhadada et al. Reported a 15.3% rate indicating CD as the most common cause of short stature, which is strikingly different from previous reports from India. Currently, the number of publications in which the only manifestation of CD is low growth is growing. Previous reports probably overlooked CD as a cause of short stature due to low suspicion, monosymptomatic presentation, lack of widespread availability of diagnostic tests, and lack of access to duodenal biopsy. Common expressions of children's CDs include; chronic diarrhea, abdominal pain, anemia, weight loss and linear lack of growth. Common symptoms in our patients were short stature, anemia, gastrointestinal symptoms, weight loss, and endocrine problems; because these patients presented to our endocrinology clinic with the main complaint of short stature. The anti-tTG antibody has been reported to have a sensitivity close to 100% in the diagnosis of CD, which is consistent with the results of this study. Duodenal biopsy of all our patients showed signs of celiac disease according to the modified Marsh criteria. Hypothyroidism may be associated with CD due to a similar autoimmune predisposition and may contribute to growth retardation. In the presented study, hypothyroidism was diagnosed in 43 (14.9%) cases, and one patient had coexisting CD. GHD was found in 28 (9.72%) cases, and one of the 19 celiac patients also suffered from GHD. Endocrine causes of short stature as a group were the most common in this study, possibly due to the fact that it is the only endocrine reference center for children in the region. A similar observation was made by Colaco et al. In their studies with Indian children, where the dominance of the normal short stature variety was consistent with other international studies. The disadvantages of this study include that it was a hospital study for which patients with specific diseases are referred. Second, there is an increased incidence of serum IgA deficiency in CD patients compared to healthy

subjects28. We did not measure serum IgA levels in this study. Reporting of celiac disease has increased sharply, possibly due to targeted screening and better available serological tests. It is very important to know the exact frequency of the different causes of short stature in a given population to distinguish between individual short stature cases that require early diagnosis and treatment, such as celiac disease. Close cooperation between pediatric endocrinology clinics and gastroenterology clinics can be fruitful in identifying patients with CD, especially in older children with short stature, bone age delay, and microcytic anemia. This study could help establish the baseline data in the region, so finding treatable causes early would help to get a better long-term prognosis.

CONCLUSION:

We conclude that celiac disease is an important cause of short stature. We propose that anti-tTG antibody levels be part of the routine treatment of short stature regardless of the presence or absence of gastrointestinal symptoms.

REFERENCES:

1. Shull, Mary H., Tracy R. Ediger, Ivor D. Hill, and Rose L. Schroedl. "Health-related Quality of Life in Newly Diagnosed Pediatric Patients With Celiac Disease." *Journal of pediatric gastroenterology and nutrition* 69, no. 6 (2019): 690-695.
2. Singh, Achintya D., Prashant Singh, Naba Farooqui, Tor Strand, Vineet Ahuja, and Govind K. Makharia. "Prevalence of celiac disease in patients with short stature: A systematic review and meta-analysis." *Journal of Gastroenterology and Hepatology* (2020).
3. Saadah, Omar I., and Nouf M. ALNosani. "Celiac disease in Saudi children with isolated short stature: is it rare or are we not screening rigorously enough?." *Journal of Pediatric Endocrinology and Metabolism* 33, no. 1 (2020): 89-93.
4. Nardecchia, Silvia, Renata Auricchio, Valentina Discepolo, and Riccardo Troncone. "Extra-Intestinal manifestations of coeliac disease in children: clinical features and mechanisms." *Frontiers in Pediatrics* 7 (2019): 56.
5. Yılmaz, Songül, Ceyda Tuna Kırsaçlıoğlu, and Tülin Revide Şaylı. "Celiac disease and hematological abnormalities in children with recurrent aphthous stomatitis." *Pediatrics International* (2020).
6. Kreutz, Johanna M., Marlou PM Adriaanse, Elisabeth van der Ploeg, and Anita CE Vreugdenhil. "Narrative Review: Nutrient Deficiencies in Adults and Children with Treated and Untreated Celiac Disease." *Nutrients* 12, no. 2 (2020): 500.
7. Qutub, Lujain M., and Omar I. Saadah. "Prevalence of combined growth hormone deficiency and celiac disease among Saudi Arabian children with short stature: a tertiary care center experience." *Chinese Medical Journal* 6 (2020): 729-731.
8. Walia, Rama, Amandeep Singh, Anshita Aggarwal, Baburam Thapa, Manni Luthra Guptasarma, Anil Bhansali, and Niranjan Khandelwal. "Look Beyond Gluten in Short Stature with Celiac Disease–A Prospective, Interventional Study." *The Indian Journal of Pediatrics* (2020): 1-5.
9. Masood, Jaweria, Hooria Rehman, Zahid Mahmood Anjum, Irum Iqbal, Sadia Zafar, and Hina Ayesha. "Prevalence of Celiac Disease in Idiopathic Short Stature Children Presenting in OPD of Children Hospital, Faisalabad." *Annals of Punjab Medical College* 14, no. 1 (2020): 9-12.
10. Liu, Edwin, Kristine Wolter-Warmerdam, Juana Marmolejo, Dee Daniels, Garrett Prince, and Fran Hickey. "Routine Screening for Celiac Disease in Children With Down Syndrome Improves Case Finding." *Journal of pediatric gastroenterology and nutrition* 71, no. 2 (2020): 252-256.
11. Bayrak, Nevzat Aykut, Engin Tutar, Burcu Volkan, Bilge Sahin Akkelle, Esra Polat, Gunsel Kutluk, and Deniz Ertem. "Helicobacter pylori infection in children with celiac disease: Multi-center, cross-sectional study." *Helicobacter* 25, no. 3 (2020): e12691.
12. Al-Ani, Rafi Khaleel, Mushtaq Talib Abed, Buthainah Bahjet Al-Ani, and Muntaha Qasim Hendi. "Diagnosis of Celiac Disease in Short Stature Children in Anbar Growth Center in Ramadi Pediatric Teaching Hospital." *International Medical Journal* 27, no. 3 (2020).
13. Ramosaj-Morina, Atifete, Alije Keka-Sylaj, Arbana B. Zejnullahu, Lidvana Spahiu, Virgjina Hasbahta, Vlora Jaha, Vjosa Kotori et al. "Celiac Disease in Kosovar Albanian Children: Evaluation of Clinical Features and Diagnosis." *Current pediatric reviews* 16, no. 3 (2020): 241-247.
14. Gupta, Vipin, Alka Singh, Rajesh Khadgawat, Ashish Agarwal, Asif Iqbal, Wajiha Mehtab, P. K. Chaturvedi, Vineet Ahuja, and Govind K. Makharia. "The spectrum of clinical and subclinical endocrinopathies in treatment-naïve

patients with celiac disease." *Indian Journal of Gastroenterology* (2019): 1-9.

15. Yerushalmi, Baruch, Sergei Vosko, Galina Ling, Ronit Raanan, Daniel L. Cohen, Haim Shirin, Tzipora Shalem, Shay Matalon, and Efrat Broide. "Bedouin Children With Celiac Disease: Less Symptoms but More Severe Histological Features at Presentation." *Frontiers in pediatrics* 8 (2020).