

**Prevalence of celiac disease in Diyala
children and adolescents with short stature**

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Abstract

The aim of the present study was to determine the prevalence of celiac disease (CD) in children and adolescences of short stature in diyala governorate. A total of 80 short stature patients (65% males) their ages were between 4-17 years of with or without gastrointestinal symptoms were studied over three years (2003-2006). Routine physical and laboratory examinations performed to exclude other causes of short stature and those with negative workup were studied with endoscopic intestinal biopsy. Seventeen 17 (21.25%) of them showed histological abnormalities compatible with CD, 70.58% of them were males. There was no statistically significant difference in anthropometric characters between patients with CD and short stature and those with short stature of undetermined cause. 82% of patients with CD showed abnormal duodenal mucosa endoscopically and 82.35% of them they have marsh's grade three histopathological changes. Those with normal histopathological results are referred for endocrinological studies.

Conclusions: There was high prevalence of celiac disease among short stature children and adolescents in diyala governorate.

الخلاصة

ان هدف الدراسة الحالية هو لتبيان شيوع مرض سيلياك في الاطفال واليافعين المصابين بقصر القامة في محافظه ديالى. من مجموع 80 حالة مرضية بقصر القامة تم دراستها (65% ذكور) تراوحت اعمارهم بين 4-17 عاما مع او بدون اعراض هضمية للفترة من 2003-2006، اجري الفحص السريري والمختبري الروتيني لاستبعاد الاسباب الاخرى لقصر القامة اولئك الذين كانت نتائجهم سلبية قد درسوا بواسطة خزعة ناظور المعدة والاثنى عشري، 17 حالة (21,25%) منهم وجدت تغيرات نسيجية متوافقة مع مرض سيلياك 70,58% منهم كانوا ذكورا. لم تكن هنالك اختلاف احصائي ملحوظ في الصفات الانسانية بين مرضى قصر القامة مع مرض سيلياك و اولئك المصابين بقصر القامة غير محدد السبب. 82% من مرضى قصر القامة مع مرض سيلياك لديهم تغيرات ناظورية في بطانة الاثنى عشري و 82,35% لديهم الدرجة الثالثة تغيرات نسيجية مرضية حسب تصنيف مارش .

الاستنتاج: كان هنالك نسبة شيوع عالية لمرض سيلياك بين الاطفال واليافعين المصابين بقصر القامة في محافظة ديالى.

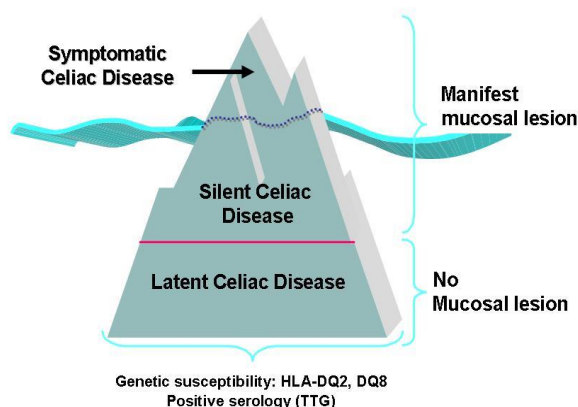
Introduction

People are considered to be of short stature if they're among the shortest 3 to 5% of the population. Short stature can sometimes be normal, but sometimes it can be related to a medical problem and it's increasingly being recognized that short stature can be a symptom of celiac disease. In fact, it can sometimes be the *only* symptom of celiac disease.

Celiac disease is a common disorder induced by gluten present in wheat, barley, and rye, and affects up to 1% of the population of several developed countries.^{(1),(2),(3),(4)} The disease can be overt, with the classic features of diarrhea, abdominal distension, generalized malnutrition and failure to thrive, or subclinical, with isolated nutrient deficiencies such as anemia, aphthous ulcer, bone pain, etc., without gastrointestinal symptoms, particularly at a later age. Incidence of gastrointestinal carcinoma or lymphoma increases among patients with untreated CD⁽⁵⁾

CD symptoms and signs may be absent or very subtle.^{(6),(7)} As a result celiac disease shows
An iceberg phenomenon.

The Celiac Iceberg



Accordingly, only a minority have the clinically recognized disease while the majority of patients have silent CD, which remains undiagnosed because the condition has no symptoms or has symptoms which are unrelated to intestinal manifestation.

CD is an inflammatory disorder of the upper small intestines, caused by an abnormal immune reaction to wheat gliadin. The striking association between HLA class II molecules, DQ2 and DQ8 and celiac disease, implicates a role for immune response in and it is not uncommon for patients with CD to have associated other autoimmune disease (table below)

Prevalence of Celiac Disease in other autoimmune conditions

Type 1 Diabetes Mellitus:	3.5 - 10%
Thyroiditis:	4 - 8%
Arthritis:	1.5 - 7.5%
Autoimmune liver diseases:	6 - 8%
Sjögren's syndrome:	2 - 15%
Idiopathic dilated cardiomyopathy:	5.7%
IgA nephropathy:	3.6%

CD is systemic disease, has a wide spectrum of gastrointestinal and extraintestinal manifestations (table below) atypical symptoms or none at all. Classically, infants with celiac disease present impaired growth, diarrhea and abdominal distention between the ages of 4 and 24 months. Atypical disease is usually seen in older children or adolescents, who often have no overt features of malabsorption. In addition to recurrent abdominal pain, aphthous stomatitis, arthralgia, defects in dental enamel, short stature, and delayed puberty, affected children may show behavioral disturbances such as depression and irritability, and may perform poorly in school (8).

Extra-Intestinal manifestations of celiac disease

- Dermatitis Herpetiformis and other skin disorders
- Dental enamel hypoplasia
- Osteopenia/Osteoporosis
- Short Stature
- Delayed Puberty
- Iron-deficient anemia resistant to oral Fe
- Liver and biliary tract disease
- Arthritis
- Neurological problems
 - Ataxia
 - Peripheral neuropathy
 - Epilepsy
- Psychiatric Disorders
- Women Sub-In-fertility
 - Miscarriages
 - Low birth weight babies

CD is familial disease and the table below shows the relative risk of developing CD among different patients populations

1 in 56	People who have gastrointestinal symptoms yet undiagnosed as celiac
1 in 22	People who have a first-degree relative (sibling, child, or parent) with celiac
1 in 39	People who have a second-degree relative (grandparent, aunt, uncle, or cousin) with celiac
1 in 133	Not at risk individuals

Histological evidence of celiac disease among patients consuming a regular (gluten-containing) diet includes small-bowel mucosal villous atrophy, crypt hyperplasia and increased numbers of intraepithelial lymphocytes. Although celiac disease is a known cause of short stature in children, its diagnosis is often difficult because of the presence of few symptoms and of biochemical parameters that fall within the normal range. Sometimes short stature could be the principal or only finding (9)) and the rate of diagnosis depends on the level of suspicion for the disease. The diagnosis is based on clinical symptoms, positive antibodies, and an intestinal biopsy, which is considered to be the Gold Standard (10,11).

The purpose of the present study was to determine the prevalence of CD among diyala children and adolescences with short stature with or without gastrointestinal symptoms

Patients and methods

A total of 80 children and adolescents, 28 girls (35%) and 52 boys (65%) with Short stature were enrolled in this prospective cross-sectional, analytical study which carried out between January 2003- to January 2006. Age ranged from 4 to 17years (mean = 10.6 years, SD = 4.3 years). Inclusion criteria for the study included: Children and adolescents between 4 and 17 years of age, height less than the 3rd percentile adjusted for age and sex, not on gluten free diet and with other etiologic factors known to produce growth failure had also been excluded, like :congenital heart disease, chronic respiratory disorder, diabetes mellitus, hematological and liver disease, renal failure, fetal growth failure, disease of bone metabolism, and chromosomal abnormalities.

Clinical features and examination ,height (Ht) .weight, body mass index (BMI), Laboratory workup including: haemoglobin, blood urea, serum creatinine, blood sugar, serum albumin, bilirubin, liver enzymes, chest radiographs, abdominal ultrasonography and echocardiography all performed to all participants to assess their general and systemic condition and to exclude other potential causes of short stature.

When no cause of the short stature was found, patients were selected for an Upper oesophageogastroduodenal endoscopy (OGD) which carried out in baquba general hospital and in private clinic. During the procedure the general appearance was observed for scalloping, attenuated folds and cobblestoning.

The grasp biopsy forceps was used to take 2-3 biopsy specimens from the second or more distal part of the duodenum and send for histopathological examination .

The Marsh classification was used to grade the mucosal changes as follow:

- 0 - normal histology
- 1 - mild increase in intraepithelial lymphocytes (IEL), crypt-villous ratio 1:1
- 2 - moderate villous atrophy with CV ratio more than 1
- 3 - flat mucosa with no recognizable villi. (12), (13).

The slides were examined and reported by a pathologists experienced in celiac disease.

Chi-square test was used for statistical analysis as applicable with P-value less than 0.05 being significant.(14)

RESULTS

The Physical examination of a total of 80 patients with short stature revealed no obvious abnormality and they were studied.

The overall characteristics of all patients are described in table 1 .

Their anthropometric assessment shows means $\pm$ SD of body weight, height and BMI, The mean ($\pm$ SD) age, height, weight and BMI were: 11.1 ± 5.3 years (range, 4-17 years), 89.0 ± 37.7 cm (41–130 cm), 16.04 ± 9.5 kg (13-45 kg) and 14.12 ± 10.58 kg/cm² respectively

Table 1: Characteristics of patients with short stature

Patients No.	(n = 80)
Age (years), mean $\pm$ SD	11.1 ± 5.3 years (range, 4-17 years)
Sex n (%)	
Male	52 (65%)
Female	28 (35%)
Weight (kg)	16.04 ± 9.5 kg (13-45 kg)
Height (cm)	89.0 ± 37.7 cm (41–130 cm)
BMI (kg/ m ²)	14.12 ± 10.58 kg/cm ²

Among 80 patients with short stature studied, the histopathological examination reports of the biopsies revealed that 17(21.25%) participant's biopsies showed abnormal histopathological abnormalities compatible with CD. While the rest 63 (78.75%) participants having normal results.

The differences between anthropometric means of the two groups were statistically not significant, $P > 0.05$, table 2.

Table 2: Characteristics of patients with short stature stratified according to CD diagnosis

Variables	Patients with CD	Patients without CD	p-value
No. (total 80)	n = 17 (21.25%)	n = 63(78.75%)	
Age (years)	10 (4 - 17)	9 (4- 17)	0.763
Gender (male/female)	12/5	44/19	0.629
Weight (kg)	16 (11.50 - 29.25)	17 (7.5 - 34.0)	0.870
Height (cms)	94 (81.5 - 131)	101 (85- 125)	0.916
Body mass index (kg/m ²)	12.1 (10.19 - 12.30)	13.23 (12.50- 15.19)	0.924

The OGD shows that 3 patients (17%) with CD had normal looking mucosa with 6 patients (35%) had attenuated duodenal mucosal folds and 8 (47%) had scalloped folds (table3)

Table 3: The macroscopic endoscopic features of patients with CD

Endoscopic feature	No. (%)
Normal folds	3 (17%)
Attenuated folds	6 (35%)
Scalloped folds	8 (47%)

The severity of histopathological changes of patients with CD according to marsh's criteria is given in table 4 .The majority i.e. 14/17 had Marsh type 3

Table 4: classifications of patients with CD (n = 17) according to Marsh' criteria

Marsh's grade	No. (%)
1	2 (11.7%)
2	1(5.8%)
3	14(82.35%)

DISCUSSION

Short stature is important and not uncommon medical problem, the frequency with which it is associated with CD has not been defined in our governorate. To address this issue, the patient population endoscopically obtained histopathological diagnosis was used to assess this association.

CD was diagnosed in 17 patients(21.25%) from 80 patients screened. The present data show an expressive number of celiac disease in children with short stature, thereby justifying the search for this disease in all children with short stature. Previous studies on children with short stature have shown a variable incidence of celiac disease (0 to 59.0%) depending on the region where the study was performed (15-22). A review of the literature (23-27) led us to conclude that there is no single parameter suggesting the presence of celiac disease in children of short stature. Our data support the view that there is no single test or measurement that can identify all subjects with celiac disease nor did they differ significantly between patients diagnosed as having celiac disease and others of short stature of unknown etiology The children affected by celiac disease did not differ from those without celiac disease in any of the parameters tested. Hence, it is important to *search for celiac disease in all children with short stature.*

In the December 2007 issue of the Journal of Gastroenterology and Hepatology, doctors in India who studied children with short stature

reported that 15% of the children had celiac disease. Indeed, the doctors discovered that celiac disease was the single most common cause of short stature in the children in this particular study (28).

In the 1990s, Italian researchers who studied a group of children with short stature found that 59% of them had celiac disease(29). Celiac disease had already been linked to short stature in Brazil (30).None of the children with celiac disease and short stature in any of these studies had any gastrointestinal symptoms of celiac disease.

The Magazzù G,et al analyze the prevalence (30,8%) of short stature in 39 coeliac patients at variable age. Height defect was especially remarkable in the subjects diagnosed after the fourth year of life. In 8 out of the studied coeliac patients, short stature was the only clinical sign at the time of diagnosis(31).

American Academy of Pediatrics studied this topic in Thirty-four patients aged 2^{1/2}to 17 years with short stature of undetermined cause and no gastrointestinal symptoms underwent jejunal biopsy for exclusion of CD. The conclusion was that short stature by itself, in the complete absence of gastrointestinal symptoms, is an indication for jejunal biopsy. In this study 21% of children with short stature, in whom dysmorphic or primary endocrinopathy had been ruled out, proved to have coeliac disease(32).

In our study the endoscopic intestinal mucosal folds were scalloped in 31 (69%), attenuated in 34 (76%) and normal looking in 11 (24%) of them. Makharia GK,et al found that Intestinal mucosal folds were scalloped in 31 (69%), attenuated in 34 (76%) and normal looking in 11 (24%) of them. Mild, moderate and severe villous abnormalities on intestinal mucosal biopsies were present in 10 (22.2%), 15 (33.3%) and 19 (42.2%) patients, respectively(33).

CONCLUSIONS

Short stature can sometimes be the only symptom of celiac disease in children. Short children should be tested for celiac disease, even if they have no gastrointestinal symptoms.

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