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# The Prevalence of Celiac Disease in Children with Unexplained Failure to Thrive in South West of Iran

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***Abstract***

***Background***

Celiac disease (CD), considered as a common chronic and genetic diseases that caused by hypersensitivity to gluten. Failure to thrive (FTT), is one of three major clinical features of CD during childhood. The current study aimed to determine the prevalence of celiac disease in children with unexplained FTT in South West of Iran.

***Materials and Methods***

This cross-sectional study was conducted on 433 children 9-month to 6 years old that diagnosed as unexplained FTT referred to Abuzar Children's Hospital, Ahvaz, South West of Iran, in 2014. In this study, we examined the serum levels of anti-transglutaminase antibody (anti-tTG) in children with unexplained FTT. Data were analyzed using SPSS version 16.0 software.

***Results***

The results showed that the prevalence of CD in children with unexplained FTT in was 8.8%. The mean scores of children's anti-tTG serum levels in both gender and age groups, showed no significant difference (P> 0.05).

***Conclusion***

At current study, the prevalence of CD in children with FTT was 8.8%. Since the CD is an important cause of unexplained FTT in children, the early screening and diagnosis and dietary management can be decrease the risk for long-term complications in these children.

***Key Words:*** Celiac disease, Children, Iran, Failure to Thrive, Prevalence.

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## 1-INTRODUCTION

CD as one of the most common genetic disorders is lifelong immunoreactions of small-bowel mucosal to gluten that cause damage and various symptoms in genetically susceptible individuals. Detection of the affected patients is low (less than 10%), and most of them being asymptotic (1-3). It is estimated that the overall prevalence of CD is 1% in the pediatric population in Iran and the world, although only 10-15% of these affected children have been diagnosed and treated. Because of the wheat is a major staple food in Iran, and Iranian people have 160 kg of wheat per capita annual consumption, this disease can be considered as an important health problem in our country (1, 3-7).

So, screening can be considered as an important tool in detecting patients (up two thirds of patients are clinically asymptomatic). It is estimated that the genetic, environmental, and immunological factors has a role in pathogenesis of this disease (1, 8). The prevalence of CD as common chronic diseases is five times higher in children than adults, and it was originally considered as a pediatric disorder. The CD has wide spectrum of clinical manifestation of intestinal and/or extra intestinal symptoms with varying severity and responds to gluten withdrawal. Chronic diarrhea (84%), FTT (91%), and anemia (84%), are typical and three major clinical features of CD during the first 2 years of life (2, 8-13).

Presentation of CD in children has varied and affected by age and duration of disease. "Classical" celiac disease that marked by diarrhea, abdominal distension, and FTT, is more common in young children. Also, in older children and adolescents, atypical gastrointestinal complaints such as pain, vomiting, or constipation; extra intestinal symptoms such as arthritis, neurologic symptoms, and anemia or even silent disease without any apparent symptoms, is common (4, 13, 14). Early diagnosis of silent patient due to increased risk for long-term complications such as osteoporosis, lymphoma, osteopenia, infertility, intestinal malignancies, and autoimmune disorders such as diabetes mellitus type 1, is important (1, 5). Search for case finding for CD is recommended in a wide range of clinical situations ranging from the presence of gastrointestinal symptoms (diarrhea, abdominal pain and distension), FTT in children, prolonged fatigue, unexpected weight loss, recurrent aphthous stomatitis, anemia, increased liver transaminases, and also in conditions that associate with CD such as autoimmune thyroid disease, dermatitis herpeticformis (DH), type 1 diabetes, and in patients with irritable bowel syndrome associated with diarrhea and first-degree relatives of celiac (11). FTT in the youngest children or short stature among older children considered as one of three major presentations of CD in the of children (13).

A overall accepted definition about the FTT is not available, but the subnormal growth or weight gain was considered as an essential element for FTT (15). In Iran was done the studies about the prevalence of CD in healthy school children (1, 5), down syndrome children with and without congenital heart defects (16), children with idiopathic short stature (17), type 1 diabetes mellitus (18), diarrhea (19), and recurrent abdominal pain (20), the prevalence was varied from 1.3 to 33.6%. The worldwide prevalence of CD has been shown in **Figure.1**.

In this study we aimed to evaluate the prevalence of CD among children with unexplained FTT in South West of Iran.

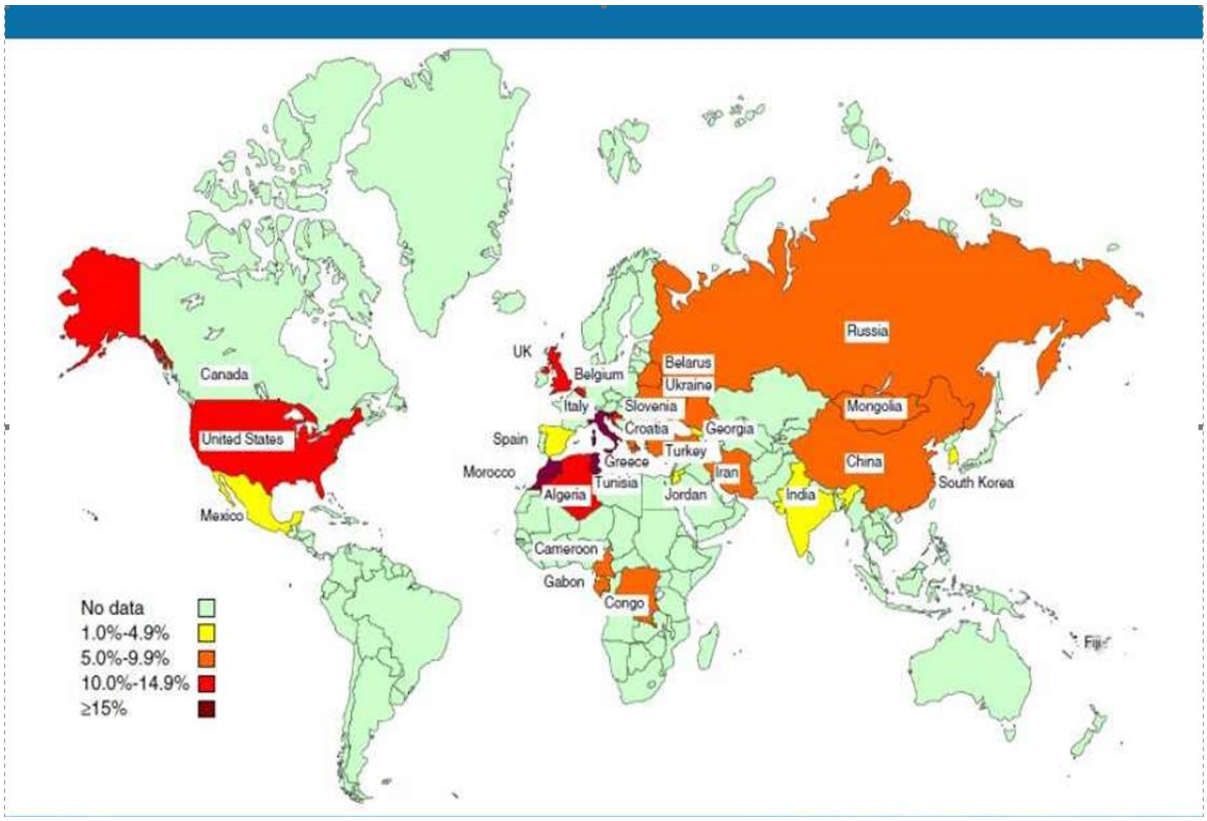


**Fig.1**: Worldwide prevalence of Celiac disease, expressed as percentage prevalence of elevated tissue transglutaminase antibody levels in unselected adult and pediatric populations (21).

## 2-MATERIALS AND METHODS

### 2-1. Study design and population

This cross-sectional study was conducted on 433 children aged 9 months to 6 years old that diagnosed as unexplained FTT admitted in Abuzar Children's Hospital (a referral teaching hospital in Ahvaz Jundishapur University of Medical Sciences, South West of Iran) in 2014.

Inclusion criteria were children aged 9 months to 6 years old that diagnosed as FTT. A consensus definition not available for FTT, including duration of concern about growth (22). We used the term FTT to describe children whose weight was below the 3th percentile or have weight loss of as much as 2% of previous weight, or have weigh less than 80% of their ideal weight based on standard growth curves (23).

Exclusion criteria were children with chronic infections, chronic systemic diseases and immunoglobulin A (IgA), serum level below normal (8 mg/dl) (24). Non-probabilistic consecutive method was used for sampling, so that way with beginning of the study, all children who met the inclusion criteria were enrolled and this continued until to achieve the final samples size. The sample size was calculated according to the data from a previous study (10), using the following formula:

$$n=\frac{(Z_{1-\alpha/2})^2 \times P(1-P)}{d^2}=\frac{(1.96)^2 \times 0.24 \times 0.76}{(0.04)^2}=437$$

In this formula, the level of error (α), the prevalence of CD children with unexplained FTT of previous study (10)

(p), and the optimal accuracy (d), was 5%, 0.24 and 0.04, respectively.

### 2-2. Measurement tool and methods

At the first, careful history was taken in order to rollout chronic infections, chronic systemic diseases, and also to rollout other FTT causes. Routine physical examination including measurement weight, and height of children were done for evaluating malnutrition. The height and weight of children were measured by the expert using a digital scale (Emjoi, made in Japan), and a tape, with regard to correct principles (in a standing position with minimum clothes and no shoes), and compare with standard growth curves.

Then, the anti-tTG test with sensitivity and specificity of over 95%, was used for detection CD in children with unexplained FTT in this study (7, 24-26). Although it is recommended that the final diagnosis confirmed with a biopsy of the small intestine (23, 25, 27). Because of the anti-tTG is a kind of IgA, the diagnosis can be difficult in cases, who have concurrent IgA deficiency. In order to avoid of false negative results, serum levels of IgA was also assessed in all children (immune turbid metric method was used for evaluation of serum levels of IgA). To measure anti-tTG, immunometric enzyme immunoassay (ELISA) method, the blood samples (5 ml of venous blood that impregnated with anticoagulant) was taken from children by a lab technician. Then the serum samples were separated by a centrifuge machine that serum should be clear and without hemolysis. Serum samples can be kept for 5 days at 2 to 8 °C and for 6 months at a temperature of minus 20 °C. The minimum amount of IgA was considered 8 mg/dl, and 10 unit/cc as the maximum amount of normal anti-tTG (24). The used kit was the German ORGENEC Diagnostic. GmbH for identifies tTG-IgA (with sensitivity of average 87% for identifying the individuals who may have CD).

### 2-3.Ethical considerations

This study was approved by the Institutional Ethics Committee of the Ahvaz Jundishapur University of Medical Sciences (ID number: 93171). Informed consent was taken from the parents prior to enrollment in the study and they were informed on the research purpose and ensured that their information will be kept confidential

### 2-4. Data Analyses

Collected data were analyzed using the statistical software SPSS version 16.0, and $P < 0.05$ was considered significant. In addition Chi-square test was used to compare the mean scores between two sexes and one way ANOVA was used to compare the mean scores of the groups based on ages.

## 3-RESULTS

A total of 437 children with unexplained FTT, were screened during the study period. Of these, four (9%) children exclude from study (because of IgA serum levels below normal [8 mg/dl]). The mean value of children's age was 2.5 ± 1.49 years, and 222 (51.3%) of participants were girls. Of these, were 277 (64%) less than 2 years, 114 (26.3%) two to five years and 42 (9.7%) more than five years old.

Results showed that children less than 2 years had the highest frequency (64%). The test results of anti-tTG serum levels showed that 38 (8.8%) children, had anti-tTG higher than normal (10 u/cc). Also, in the positive group, there was 21 child (7.7%) less than 2 years, 10 child (8.4%) 2-5 years, and 7 child (17.4%) more than 5 years (**Table.1**). In this study, the test results of 21 girls (55.3%), and 17 boys (44.7%), were positive. It was not observed a statistically significant difference in the mean scores of children's anti-tTG serum levels in both gender and three age groups (P> 0.05) (**Table.2)**

**Table- 1:** The age distribution of anti- tTG test results in studied children

| Age Category | Less than 2 years n (%) | 2-5 years n (%) | More than 5 years n (%) |
|---|---|---|---|
| Test result | | | |
| Positive | 21 (7.7) | 10 (8.4) | 7 (17.4) |
| Negative | 256 (92.3) | 104 (91.6) | 35 (82.6) |

**Table-2**: The mean of anti-tTGserum levels in children with positive anti-tTG based on age and gender

| **Variable** | Mean (SD) of anti-tTG serum levels (u/cc) | | P- value |
|---|---|---|---|
| Age of child | | | |
| Less than 2 years | 6.5 | (20.4) | 0.75 |
| 2-5 years | 8.3 | (28) | (one way ANOVA) |
| More than 5 years | 13.7 | (13.7) | |
| Gender | | | |
| Girl (n=21) | 80.8 | (69.1) | 0.45 |
| Boy (n=17) | 64.9 | (57.7) | (Chi-square) |

## 4- DISCUSSION

The results of this study reavealed that the prevalence of CD in children with unexplained FTT in Ahvaz, South West of Iran was 8.8% (at least one out of 12). In Iran, there are different statistics about the prevalence of CD in children. In the different studies reported the prevalence 1.3% for children with recurrent abdominal pain (20), 33.6% for children with the idiopathic short stature (17), 0.5% among healthy school age children (1), 2% (0.6% through biopsy) in healthy school children (5), 6.2% in diabetic children (18) and 6.5% for children with chronic diarrhea (19). The overall prevalence of CD is 1% in the pediatric population in Iran and the world (1, 6, 13, 28), and reported the incidence of its is a three to fourteen cases per thousand in children (1), and three to thirteen cases per thousand, with a higher prevalence among first-degree relatives of patients with CD (29). In a study in India, the CD prevalence reported 24% in children one to twelve years of either gender with unexplained FTT (10). Despite there was more number of girls with positive test results in our study, this difference was not significant. In India, in a study by Rana et al. the number of boys was predominance, may be due to the importance and attention that given to the boys in this country (10).

In our study, the prevalence of CD in children less than 2 years old with unexplained FTT was higher. A significant decrease happens in the CD prevalence in pediaterics with increasing age, especially after three years old, although the its reason is not cleared (9). Since the CD prevalence in the normal population is 1:300 to 1:100 in other countries, and 50% of affected children are asymptomatic, and due to complications arising from lack of

early diagnosis of this disease for children, screening is recommended for all adults and children (1). Given that wheat is the staple food of Iranians, attempts to the correct and early screening for diagnosis of children with CD, and dietary management, can be decreased the risk for long-term complications in them.

### 4-1. Limitations of this study

One of the limitations of this study was the low number of subjects, also, this study was done in South West of Iran. Therefore, it is recommended to conduct further studies with larger sample sizes and in other areas of Iran, which would be useful for confirming the results of this study.

## 5- CONCLUSSION

Although the prevalence of CD (8.8%) and population (children with unexplained FTT in South West of Iran) of our sutudy, is not representive of the prevalence of CD in Iranian children with unexplained FTT as a whole, but the children as one of vulnerable population requires enough attention and care to have normal growth and development. Given the importance of screening and early diagnosis of CD diease as one of the most common genetic disorders in children, especially in children with unexplained FTT, seem to be necessary that planning and implementation of screening strategies in order to identify the affected children in the early stages, initiation of gluten free diets for them and reduce the risk of further complications.

## 6-CONFLICT OF INTEREST: None.

## 7- ACKNOWLEDGMENT

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