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Celiac Disease in Children With Short Stature

KEYWORDS: Short stature,Celiac disease,ChildrenAnti tissue transglutaminase Antibody.

DR.SATISH KUMAR
ASSISTANT PROFESSOR,PG DEPTT. OF PAEDIATRICS,JLNMCH,BHAGALPUR.

DR.SIDDHARTHA NANDI
2ND YEAR POST GRADUATE STUDENT, PG DEPTT. OF PAEDIATRICS,JLNMCH,BHAGALPUR

ABSTRACT *Objective. The aim of the present study was to determine the prevalence of celiac disease in children with short stature.*

Methods. In all children with short stature (height more than 2 SD below the mean for age and sex) and normal physical examination, attending deptt.of paediatrics jlnmch BHAGALPUR, from 2014 till 2015, work-ups were made to find a cause for their short stature and of course their serum was assayed for IgG anti-tissue transglutaminase (TTG) antibody by ELISA test, as a marker for CD.

Results. There were 26 girls and 46 boys with mean age of 9.8 years, Routine work-up showed microcytic hypochromic anemia in four children (5.6%) and giardiasis in five (6.9%). GH stimulation test revealed GH deficiency in five children (6.9%) Elevated IgG anti-TTG antibody level was detected in two children (2.8%). Duodenal biopsies of these children were in favour of celiac disease.

Conclusion. Although, the prevalence of CD in this study was not significantly different (P value=0.14) from the prevalence rate in healthy blood donors in INDIA, the findings emphasize the fact that CD must be considered in a child with short stature, especially if the height is more than 3 SD below the mean for sex and age, even in the absence of gastrointestinal symptoms,. In conclusion, the measurement of anti-TTG antibody should be included in the diagnostic avaluation of children with short stature

Introduction:Although in the past celiac disease (CD) was primarily considered to be a gluten enteropathy, during the last two decades, its clinical concept has been expanded, and it is now considered a multisystem autoimmune disorder, 1 with many patients being asymptomatic, oligosymptomatic, or with extraintestinal manifestations.2 Among these extraintestinal manifestations, there is a growing body of publications that report short stature as the sole manifestation of CD and without gastrointestinal symptoms. 3-9 Sometimes, short stature is the principal or only finding of CD and the rate of diagnosis depends on the level of suspicion for the disease.10

Until recently, CD was considered uncommon in INDIA despite the fact that there were no studies to assess its prevalence; however, the availability of new accurate serologic tests has led to the realization that CD could be relatively common. A recent study pointed out a prevalence of undiagnosed CD of 1:133 among apparently healthy blood donors.11

Although small intestinal biopsy is the gold standard for the diagnosis of CD, for patients with mild or atypical symptoms a less-invasive screening test should be used.[12] In recent years, antibody to tissue transglutaminase (TTG) has proved useful as a reliable marker of CD and a useful means of selecting subjects for small intestinal biopsy.[8]

The purpose of the present study was to determine the prevalence of CD among INDIAN children with short stature.

MATERIALS AND METHODS

All children with short stature [height more than 2 standard deviation (DS) below the mean for age and sex] attending Deptt of paediatrics, jlnmch, bhagalpur were enrolled in this prospective study. The patients and their parents answered a structured questionnaire after signing an informed consent. Gastrointestinal symptoms were not a major complaint in these children. Short stature was their chief complaint. All children had undergone a thorough physical examination (anthropometric measurements were taken by a paediatrician) and an extensive work-up which included: concentration of serum electrolytes, calcium, phosphorus, glucose, total protein and albumin, assessment of liver and renal functions, and hormonal evaluation through the measurement of thyroid stimulating hormone, T4 and growth hormone (GH). Routine GH stimulation testing using L.dopa-induced hyponglycemia as secretagogue was performed (dose 500 mg/1.73 m2 with propranolol 0.75 mg/kg).

Patients were considered not to be GH deficient when the peak GH value during the stimulation test was equal to or higher then 7 ng/ml. Enzyme-linked immunosorbent assay for IgG anti-TTG antibody was used as the serologic marker of the CD. Serum level of IgG anti-TTG antibody between 0-15 unit per millilitre was considered normal. All patients with high IgG anti TTG antibody level (above 15unit/ml) underwent upper endoscopy and multiple biopsies were taken from different parts of duodenum and sent for histopathological examination.

The data were kept confidential through codes and analyzed by Fisher's exact test. P value ≤0.05 was considered as significant.

RESULTS

There were 26 girls and 46 boys with height more than 2 SD below the mean for their age and sex. The mean age of the patients was 9.8± 4.5 years SD (range 1.5-17.3 years). Among these 72 patients, 47 (65.3%) from rural areas.

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All children had normal physical examination except for four patients (5.6%) with microcephaly. Among these children, 28 (38.9%) had heights more then 3 SD below the mean for their sex and age. The remaining children had heights between 2 to 3 SD below the mean for their sex and age.

Routine work-up showed microcytic hypochromic anemia in four patients (5.6A%) and giardiasis in five (6.9%). GH stimulation test using L.dopa revealed GH deficiency in five patients (6.9%). All of them had heights more than 3 SD below the mean for their sex and age. Elevated IgG anti-TTG antibody level (greater than 15 unit/ml) was detected in two children (2.8%). Duodenal biopsies for these children were in favour of celiac disease (in one of them, Marsh II and in another one, Marsh III classification). Both of these children had heights more than 3 SD below the mean for their sex and age.

DISCUSSION

In 1950 Dicke first noticed the association between celiac disease and dietary protein(gluten in wheat,rye,barley). There is association with HLADQ2 AND HLADQ8.screening tests should be confirmed by intestinal biopsy in all cases.Celiac disease may be associated with autoimmune disease,DOWN SYNDROME,TURNER SYNDROME.Intestinal biopsy revealed villous atrophy with Although an intestinal biopsy is still considered necessary to confirm the diagnosis of CD, serological tests are frequently used to identify individuals for whom the procedure is indicated. Commercially available tests include anti-gliadin IgA and IgG (AGA IgA and AGA IgG), anti-reticulin, anti-endomysium, and anti-TTG antibodies. [13] These tests are particularly helpful in individuals without gastrointestinal symptoms, those with conditions associated with CD. And for screening asymptomatic first=degree relatives of known cases. These have also been widely used in epidemiological studies to determine the prevalence of CD. [13] The sensitivity and specificity of TTG in both children and adults range from 92-100%, respectively. [14.16] There is evidence that TTG assays using human recombinant protein and human derived red cell TTG, have a higher sensitivity (96-100% vs. 89-94%) and specificity (84-100%) vs. 74-98%) when compared to assays using guinea pig protein. [17-19] Based on the current evidence and practical considered, including accuracy, reliability and cost, measurement of antibody to human recombinant TTG is recommended for initial testing for CD. [13] Although as accurate as TTG, measurement of antibody to endomysium is observer dependent and is therefore more subject to interpretation error and added cost. Because of the inferior accuracy of the AGA, the use of AGA IgA and AGA IgG tests is no longer recommended for detecting CD. After withdrawl of gluten from diet level of anti ttg and anti endomyseal antibody reaches normal within 6-12 months.

Sometimes, short stature could be the principal or only finding of CD and the rate of diagnosis depends on the level of suspicion for the disease.[10] Results of this study showed that 2.8 percent of short stature children had CD. Previous studies on children with growth failure but without gastrointestinal symptoms have shown a variable incidence of CD (0-59%) depending on the region where the study was performed. [3-5,7-9,20-24.] The results of the present study were similar to the dindings by Knudtzon J et al in Norway. [5] Rossi TM et al un USA [21] and Stenhammer L et al in Sweden.[22] In contrast, the prevalence of CD in children with short stature in this study i lower than the findings by Bonamico et al (Italy), [4] Groll et al (UK), [7] Rosenbach et al (Israel),[19] and Altuntas et al (Turkey).[9] This defference may be due to the differences in methodology (eg. Endospic biopsy for determination of CD in some series) and the population studied.

Although the prevalence of CD in the present study was not significantly different (P value=0.14) from the Prevalence rate in healthy blood donors in Iran,[11] the findings emphasizes the fact that CD must be considered in a child with short stature, especially if the height is more than 3SD below the mean for sex and age, even in the absence of gastrointestinal symptoms. I conclusion: the measurement of anti-TTG antibody should be included i the diagnostic evaluation of children with short stature.

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