Screening Children with Severe Short Stature for Celiac Disease using Tissue Transglutaminase

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ABSTRACT

Objective. To determine the prevalence of anti-tissue transglutaminase in children and adolescents with severe short stature (<-3 SD).

Methods. All children in age group of 1-18 years having height less than -3 SD for their age and sex, were included. For each child age and sex matched healthy control (height more than -2 SD) was taken. The included subjects (study & control group) were subjected to anti tissue transglutaminase (tTG) (IgA) antibody assay estimation.

Results. Of the 112 cases, 23 were tTG positive, giving a prevalence of 20.5% for seropositivity among cases of short stature while all the controls were seronegative for tTG. All the 23 had tTG values above 40 U/ml and 11 had values above 100 U/ml. On univariate analysis we found that the presence of chronic diarrhea (OR = 2.55, 95%CI - 1.08-5.98), bulky stools (OR = 3.03, 95%CI - 1.52-6.05), hemoglobin < 7 gm/dl (OR = 3.12, 95%CI - 1.55 - 6.29) and more severe short stature (<-4 SD) (OR = 0.41, 95%CI - 0.17- 0.95) had significant association with the tTG positivity. On logistic regression analysis in all cases, hemoglobin < 7gm/dl (OR = 0.090, 95%CI = 0.024-0.342) and bulky stools (OR=0.212, 95%CI = 0.069-0.649) were significantly associated with tTG positivity.

Conclusion. More than one fifth of all severe short stature are seropositive for tTG and the chances of seropositivity increases if severe anemia and bulky stool are also associated.

Key words: Short stature; Celiac; Anti-tissue transglutaminase

There were 130 celiac disease (CD) cases reported from India in 1966-2000 compared to 517 in 2001-2005. At our center, in Aligarh, we found a frequency of CD to be 37.1% among children with chronic diarrhea. Sood et al. carried out the first CD field study in India in Ludhiana district of the state of Punjab. They found disease frequency of 1 in 310 and a prevalence rate of 0.3% that is comparable to the average worldwide prevalence of 0.37% based on screening. Various other Indian studies have shown that the major difference in clinical features of CD when compared to the west are the higher incidence of stunted growth and anemia. Short stature is well described as the only symptom of CD in older children and adolescents. It is believed that as many as 9%-10% of these with “idiopathic” short stature have CD. Except for a work on atypical CD where 25 cases of short stature were included, there are no other Indian data available. We planned this work with the aim to determine the prevalence of anti-tissue transglutaminase among severe short stature (<-3 SD) children and adolescents between 1-18 years of age.

MATERIAL AND METHODS

This prospective study was conducted, in the Departments of Pediatrics, Microbiology and Pathology, between the months of February 2006 to October 2007. All children in age group of 1-18 years presenting to Pediatric outpatient, inpatient and Gastroenterology clinic, having height less than -3 SD for their age and sex, were included irrespective of whether or not they had any other symptom suggestive of celiac disease. One age and sex matched healthy control (height more than -2 SD) was taken for every case within a week of enrolling the case. Those who have been previously diagnosed as celiac disease and those who were short stature but had height not less than -3 SD for their age and sex were excluded.
Detailed history and examination along with demographic data were recorded on a predesigned proforma. Detailed anthropometric evaluation was done. All the subjects underwent routine investigations like hemoglobin, hematocrit, general blood picture, urine routine and microscopy, X-ray wrist joint and other investigations, wherever required. The included subjects (study and control group) were then subjected to anti tissue transglutaminase (tTG) (IgA) antibody assay estimation in the Department of Microbiology, of our Institution. Total IgA estimation was not done. Upper gastrointestinal endoscopy for duodenal biopsy was done for the study group subjects who had positive values on anti tissue transglutaminase (IgA) antibody estimation.

Anti-tissue transglutaminase antibody assay was done by using Bindazyme™ Human Anti Tissue Transglutaminase IgA EIA KIT manufactured by The Binding Site Limited, Birmingham, United Kingdom. Blood (5 ml) was collected in a sterile plain vial and left as such to clot at room temperature. The serum was separated by centrifugation and stored at -20 °C to be tested later for IgA anti tTG antibody. Quality control was ensured by manually plotting of the calibration curve of the anti-tTG IgA autoantibody concentration on the log scale against the optical density (OD) on the linear scale for each calibrator. The levels of the anti-tTG IgA autoantibody in the diluted samples were read directly from the calibration curve. The assay was calibrated in U/ml against an arbitrary reference calibrator as no internationally recognized reference preparation is currently available. Result interpretation was done by using the values given by the kit manufactures (Negative was < 4 U/ml, Weak Positive was 4-10 U/ml and Positive was >10 U/ml). Small intestinal histological features in the present study were graded according to the Marsh Classification.12

Sample size calculation and statistical plan: The sample size of 138 cases and controls was calculated by taking the anticipated prevalence of 8.3%13, keeping estimate to be within 5% points of true proportion with 95% confidence interval and 80% power of the study. SPSS (Version 10) was used to analyse the data. Continuous variables were compared with the help of student t test for independent groups. Fisher’s exact test was used to compare the proportions. Logistic regression analysis was done to the association of risk factors with CD in severely short stature children.

RESULTS

One hundred and twelve cases of severe short stature were included in the present study. Their age group ranged from 12 to 185 months (Mean 79.13 ± 44.44 months). The majority of cases were in the age group of 1 to 5 years (43.8%). Only fifty-two controls could be taken due to logistic constraints. There were 33 (63.46%) males and 19 (36.53%) females in the control group with the mean age of 83.04 ± 40.05 months and age range of 17 to 170 months. Of the 52 controls 30.8% were in the age group of 1 to 5 years. Forty-eight of 112 cases had weight z-score <–3 SD, of which 28 had weight z-score <–4 SD. Fifty nine cases had height z-score <–4 SD. The median weight and height z scores of the cases were – 3.24 and – 4.16 respectively. Only 3 out of 52 (5.8%) controls had weight z-score <–2 SD with none <–3 SD for their age and sex. The median value of weight z score and height z score of the controls were -0.80 and -0.65 respectively (Table 1).

Of the 112 cases 23 were IgA tTG positive, giving a prevalence of 20.5% for seropositivity among short stature cases for tTG, while all the controls were seronegative for tTG. All the 23 had tTG values above 40 U/ml (mean ± SD being 84.2 ± 20.8) 11 had values above 100 U/ml.

On univariate analysis it was found that the presence of chronic diarrhea, bulky stools, and hemoglobin < 7 gm% had significant association with the tTG (IgA) positivity (Table 2). However, on logistic regression analysis it was noted that, out of the above mentioned risk