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Original Research Article

ASSOCIATION OF CELIAC DISEASES WITH SEVERE ACUTE MALNUTRITION CHILDREN, AT TERTIARY CARE CENTRE: - A PROSPECTIVE STUDY

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Abstract

Introduction: Celiac disease (CD) may be an underlying cause of malnutrition.

Aim: The objective of this study was to find out the seroprevalence of CD in children suffering from severe acute malnutrition (SAM) in age group of 1–5 years.

Materials and Methods: This was a prospective, observational, hospital-based study carried out at Malnutrition Treatment Centre attached with the ananta institute of medical science & research center Rajsamand, Rajasthan, from February 2019 to January 2020. A total of 220 children with SAM were enrolled and screened for CD on the basis of celiac serology (tissue transglutaminase [tTg]-immunoglobulin A/G [IgA/IgG]).

Results: Celiac serology was positivity in 60 (27.28%) cases; out of total 60 seropositive cases, 28 (46.66%) cases were seropositive for both tTg-IgA and IgG, while only tTg-IgA and only tTg-IgG were positive in 18 (30%) and 14 (23.33%) cases, respectively. Mean serotiter of serum tTg-IgA and IgG in seropositive cases was 134.01±198.74 and 49.05±25.74 unit/ml.

Conclusions: High seroprevalence of CD in SAM should be taken as alert as CD may be an underlying cause and responsible for malnutrition. These children should be screened by celiac serology (tTg-IgA/IgG) to rule out CD.

Key words: *Celiac disease, Seroprevalence, Severe acute malnutrition*

Introduction

Celiac disease (CD) is defined as a permanent intolerance to ingested gluten (the protein components of wheat, barley, and rye). The intolerance to gluten results in immune-mediated damage to the mucosa of the small intestine characteristically inducing villous atrophy and crypt hyperplasia that resolves with the removal of gluten from the diet [1]. CD is one of the most common lifelong disorders in countries populated by individuals of European origin, affecting approximately 1% of the general population worldwide [2].The exact incidence of CD in India is not known, but the disease is estimated to constitute 26% of all cases of malabsorption syndrome or 4–5% of all chronic diarrheas. In PGI, Chandigarh, 20–40 new patients are seen every year and CD constitutes 7% of indoor admissions and about 5% of the patients attending pediatric gastroenterology clinic [3]. Indian Council of Medical Research task force commissioned community- based study completed recently at three sites in India, the pooled prevalence of CD and potential CD, respectively, were 8.53/1000 and 3.70/1000 in northern (Haryana), 4.66/1000 and 3.92/1000 in northeastern (Assam), and 0.11/1000 and 1.22/1000 in the southern (Tamil Nadu) study sites [4]. This is clearly an area for further inquiry and evidence generation.Diagnosis of CD is based on the combination of clinical features with a high index of suspicion, celiac serology, duodenal biopsy, and/or human leukocyte antigen (HLA)-DQ2/DQ8 typing [5]. The clinical features of severe acute malnutrition (SAM) often overlap with the common manifestations of CD such as diarrhea, failure to thrive, vomiting, abdominal distension, anemia, and weight loss [6,7]. As per the National Family Health Survey-4 (2015–2016), SAM affects nearly 7.5% of children

<60 months of age in India [8]. Several studies had reported a high prevalence of CD in North India particularly, Punjab and Rajasthan, in general population and children [9-12].Considering the high prevalence of CD among the children, it could be a major contributor or comorbid condition in children with SAM. There is very little information currently available regarding the prevalence of CD among children with SAM. The treatment of SAM in the rehabilitation phase involves cereal- based diet, which may have high gluten content. If SAM child has an underlying undetected CD, then the response to cereal based diet will be poor due to gluten content. This study was planned to find out the seroprevalence of CD in children with SAM. The objective of the study was to make the early

screening of CD in SAM children so that gluten-free diet may be started early.

Materials and Methods

The present study was an observational hospital-based prospective study, carried out at Malnutrition Treatment Center (MTC) attached with the ananta institute of medical science & research center Rajsamand, Rajasthan, from February 2019 to January 2020. Written approval from the Institutional Ethical Committee was obtained before the study. After written and informed consent from the parents, total 220 children of either gender who were admitted in MTC and fulfilling the inclusion criteria, were enrolled for the study. Inclusion criteria of this study were all the SAM children(meeting the WHO criteria for SAM) of age 1–5 years admitted in MTC and exposed to gluten containing diet and whom parents willing to enroll their child in the study. Exclusion criteria were: seriously sick SAM, children admitted in pediatric intensive units. Patients with secondary malnutrition – known c/o chronic medical or surgical disorders leading to malnutrition – congenital heart diseases with congestive heart failure, chronic renal failure, hepatic cholestasis, thyrotoxicosis, isolated childhood diabetes mellitus, HIV, childhood tuberculosis, cerebral palsy, genetic/chromosomal syndromes, inborn errors of metabolism, malignancies, surgical resection of intestine, etc., and the patients, who were not exposed to gluten-containing diet. CD seropositivity was accessed by screening for tissue transglutaminase-immunoglobulin IgA (tTg-IgA) and IgG (tTg-IgG) antibodies by enzyme-linked immunosorbent assay method(Aeskulisa tTg-A/tTg-g new generation antigen-based kit). As per manufacturer manual of the kit cutoff value for seropositivity for tTg-IgA/IgG was >18 U/ml (normal range for tTg-IgA and tTg-IgG: 12-18 unit/ml as per manufacturer manual of thekit)(13). All the collected data regarding positivity or negativity of celiac serology were entered and managed in an Excel sheet and analyzed with standard software (SPSS Version 20). P<0.05 was considered significant.

Results:

A total of 220 enrolled cases of SAM, serology for CD (either tTg-IgA or IgG or both IgA and IgG) was positive in 60 (27.28%) cases.A total of 60 seropositive cases, 28 (46.66%) cases were seropositive for both tTg-IgA and IgG, while only tTg-IgA and only tTg-IgG were positive in 18 (30%) and 14 (23.33%) cases, respectively (Table 1).

Table 1: Seropositivity status of cases

Seropositivity Status*	No (%)
Seronegative (Serum tTg-IgA and IgG negative)	160 (72.72)
tTg-IgA Positive	18 (30)
tTg-IgG Positive	14 (23.33)
Both tTg-IgG and IgA positive	28 (46.66)
Total seropositive	60 (100)
Total cases	220 (100)

***Cutoff values: tTg-IgA/tTg-IgG>18 U/ml (as per manufacturer manual of the kit) [13], tTg: Tissue transglutaminase, IgG: Immunoglobulin G, IgA: Immunoglobulin A**

Mean serotiter of serum tTg-IgA and IgG in seropositive cases was 134.01±198.74 (range – 21.04–800) and 49.05±25.74 (range – 22.20–109) unit/ml. Out of 46 tTg-IgA celiac seropositive cases, tTg-IgA titer of <10 times of upper limit of normal (ULN) was present in 34 (73.91%) cases while titer of>10 times of ULN was present in 12 (26.08%) cases (Table 2).

Table 2: CD seropositivity according to tTg-IgA titer (n=23)

tTg-IgA seropositivity	Titer (unit/ml)	No (%)
<10 times of ULN	>18 upto 180	34 (73.91)
>10 times of ULN)	>180	12 (26.08)

***Cutoff value for tTg-IgA: >18 U/ml (as per manufacturer manual for the kit) [13]; ULN-Upper limit of normal, CD: Celiac disease, Tg: Tissue transglutaminase, IgA: Immunoglobulin A**

CD seropositivity was more in males (60%, 36 in 60) as compared to females (40%, 24 in 60), and this difference in seropositivity was statistically insignificant (p>0.05). Celiac seropositivity was maximum (24/60, 40%) in age group of 4–5 years followed by 1–2 years age group (18/60, 30%) (Table 3).

Table 3: Gender and age-wise distribution of seropositivity

Anthropometric measures	Seronegative (n=80) (%)	Seropositive (n=30) (%)
Gender		
Male	94 (58.75)	36 (60)
Female	66 (41.25)	24 (40)
Age		
1–2	98 (61.25)	18 (30)
2–3	30 (18.75)	12 (20)
3–4	10 (6.25)	6 (10)
4–5	22 (13.75)	24 (40)
Total	160 (100)	60 (100)

Discussion:

CD is a common disorder in children with variable presentation wherein, underweight or malnutrition is a common presentation. Clinical manifestation of CD and SAM, in children, overlaps each other. CD may be an underlying cause responsible for malnutrition in these children. Till date, very few studies were conducted to find out the prevalence of CD in children suffering from SAM in the age group of 1–5 years age group [6,7]. We planned and conducted this study to find out and evaluate the seroprevalence of CD in children suffering from SAM. The status of seropositivity in enrolled cases according to the positivity of serology (tTg–IgA/tTg-IgG) was evaluated. Out of total 220 enrolled cases, 60 (27.28%) were seropositive (tTg-IgA/IgG/both IgA and IgG positive) for CD. Out of these 60 seropositive cases, only Ttg -IgA was positive in 18 (8.18%) cases and only Ttg-IgG was positive in 14 (6.63%) cases while both tTg-IgA and IgG were positive in 28 (12.70%) cases. Overall, the seroprevalence of CD was 27.28%. The cases in whom only tTg-IgG were positive (14 cases) may have underlying IgA deficiency, and these case may be missed if accessed for tTg-IgA only.The prevalence reported by Kumar *et al.* [6] was 13.1% (seropositive and biopsy confirmed) among the SAM children. Seroprevalence for CD reported by Beniwal *et al.* [7] was 15.38% while, the prevalence of biopsy-confirmed CD was 14.42% among the SAM children. The

prevalence of CD was more in our study as compared to other reported studies. The reason for this may be that our study is based on celiac serology only as we were not able to perform a duodenal biopsy or HLA typing for confirmation either due non-availability or feasibility at our institute. Other reason may be a high prevalence of SAM in our region having underlying CD presenting as SAM in children. This needs further research.In our study, the mean serotiter of serum tTg-IgA and IgG in seropositive cases was 134.01±198.74 and 43±24.43 unit/ml. We evaluated the CD seropositivity status according to serum tTg-IgA titers. In our study, serum tTg-IgA titer <10 times of ULN was present in 34 (73.91%) cases and serum tTg-IgA titer >10 times of ULN was present in 12 (26.08%) cases. More cases were having tTg-IgA titers of <10 times of ULN due to a low titer of tTg-IgA in these cases. It is well known fact that titer of tTg antibodies depends on the quantity and duration of gluten in the ingested diet.We compared various parameters in CD seronegative and seropositive cases. Seropositivity was more in males as compared to females. Similarly, male preponderance in seropositivity was reported by Kumar *et al*. [6] and Sharma *et al*. [14]. This suggests gender biases in society as more male children are brought for admission as compared to females. CD seropositivity was maximum in the 4–5 years age groups, suggesting the cumulative effect of gluten in the ingested diet with age. In our study, we observed high seroprevalence of CD in children suffering from SAM.The study has a few limitations, for example, only hospitalized SAM patients were included in this study. Children suffering with SAM at the community level also should be included for true seroprevalence of CD in SAM. We were not able to estimate serum IgA level to rule out serum IgA deficiency and presumed all tTg-IgA negative but tTg-IgG positive cases as IgA deficient. Our study was purely based on celiac serology for the prevalence of CD. We were not able to do upper gastrointestinal endoscopy for duodenal biopsy or HLA typing due to non-availability/feasibility at our center or expanse involved in these investigations.

Conclusions

We found high seroprevalence of CD in children of 1–5 years age, suffering from SAM which is much higher than the prevalence reported in the general population. We should have a high index of suspicion in children suffering from SAM. It is recommended that early screening and diagnosis of CD in these children by celiac serology should be done where the facility of duodenal biopsy/HLA typing not available/possible followed by gluten-free diet challenge in celiac seropositive cases.

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