International Journal of Contemporary Pediatrics
*Tulsi N et al. Int J Contemp Pediatr. 2025 Aug;12(8):1378-1381*
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20252220

**Original Research Article**

# Anti-tissue transglutaminase IgA levels in severe acute malnutrition in children up to 60 months of age-a cross-sectional study from North-West India

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**Received:** 17 May 2025
**Revised:** 02 July 2025
**Accepted:** 09 July 2025

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## ABSTRACT

**Background:** To evaluate anti-tissue transglutaminase IgA (anti-tTG IgA) levels among children suffering from severe acute malnutrition (SAM) aged up to 60 months.
**Methods:** This observational study was conducted at Dr. Rajendra Prasad Government Medical College, Kangra at Tanda, Himachal Pradesh. A total of 100 children diagnosed with SAM, meeting the inclusion criteria, were enrolled. Following thorough clinical assessment and management as per standard protocols, their anti-tTG IgA levels were measured.
**Results:** Elevated anti-tTG IgA levels (>4 U/ml) were observed in 37% of participants. Among them, 21% showed weakly positive results while 16% had strongly positive levels.
**Conclusion:** Screening for celiac disease using anti-tTG IgA levels in SAM patients with persistent gastrointestinal symptoms is crucial. For children with levels exceeding 10 U/ml, further diagnostic procedures like intestinal biopsy are recommended to facilitate timely diagnosis and intervention.

**Keywords:** Anti-tissue transglutaminase, Severe acute malnutrition, Celiac disease

## INTRODUCTION

Childhood malnutrition continues to be a major health issue in India. Severe acute malnutrition (SAM) is diagnosed by one or more of the following: weight-for-height below-3 standard deviations (SD), a mid-upper arm circumference (MUAC) ≤11.5 cm, or the presence of bilateral pedal edema.[1] Globally, millions of children under five succumb to preventable conditions such as diarrhea, pneumonia, and malnutrition.[2]

Celiac disease (CD) is an autoimmune disorder triggered by gluten ingestion in genetically predisposed individuals. It causes damage to the small intestinal lining and is often characterized by gastrointestinal symptoms.[3] Many children with SAM present with recurrent or chronic diarrhea, similar to those seen in CD, making differential diagnosis challenging and potentially delaying appropriate treatment.[4] Several blood-based tests are commonly used to screen for CD including that those detect anti-tissue transglutaminase antibodies (a-tTG), anti-endomysial antibodies (EMA) and anti-gliadin antibodies (AGA). Among these, the IgA a-tTG is considered the most reliable due to its high sensitivity (up to 98%) and consistency across results.[5] The EMA test is highly specific (~100%), but less sensitive than IgA a-tTG (93–96%). Therefore, EMA testing should be used preferably in a-tTG-positive cases as a confirmatory test prior to an intestinal biopsy.[6] The IgG anti-tTG antibodies can only be used as a specific marker in patients with an IgA deficiency.[7] According to the 2012 diagnostic criteria established by European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN), celiac disease can be diagnosed based on

clinical symptoms, positive serology and intestinal biopsy findings. In symptomatic children, a diagnosis may be confirmed without biopsy, if IgA-TG2 titres are more than ten times the normal upper limit and specific conditions are met.[8] Early recognition of nutritional deficiencies and CD in SAM can be difficult because symptoms are often vague and nonspecific. There is little information currently available regarding the prevalence of CD among children with SAM. Several studies have reported the high prevalence of CD in north India particularly Punjab and Rajasthan.[9] Considering the increasing reports of high prevalence of CD and high prevalence of SAM in North India, CD could also be one of the major cause or co- morbid condition of SAM.

Given the overlapping symptoms between SAM and CD and limited data on their co-occurrence in India, particularly in the northwestern regions, our study explores the potential role of celiac disease as a contributing factor in SAM cases. Thus, we evaluated anti-tissue transglutaminase IgA (anti-tTG IgA) levels among children suffering from severe acute malnutrition (SAM) aged up to 60 months.

## METHODS

This prospective study was conducted in the Department of Pediatrics, Dr. Rajendra Prasad medical college Kangra at Tanda, Himachal Pradesh in India, for one year i.e. from August 2018 to July 2019.

### *Selection criteria*

All the children aged up to 60 months getting admitted in the department of Pediatrics and fulfilling any one out of the four criteria for SAM as per World Health Organization (WHO) 10 guidelines with regard to growth parameters were included in study. Patients with other causes of edema for example nephrotic syndrome and/or associated systemic diseases, congenital heart disease and cerebral palsy were excluded.

A total of 138 children were screened, 38 were excluded based on our exclusion criteria and finally 100 children were enrolled. Detailed history regarding the risk factors and examination of all patients was done. Along with standard set of investigations, anti-tTG IgA levels were done in all patients.

Enrolled children were managed as per SAM protocol guidelines and their course of stay was monitored periodically (biweekly) on prescribed pre coded performa till the time of discharge. All children were discharged according to WHO guidelines (discharge criteria).[10] Anti-tTG IgA levels <4.0 U/ml were taken as negative, 4.0-10.0 U/ml were taken as weakly positive and >10.0 U/ml were taken as positive.[11] Data was compiled using Microsoft Excel and analyzed using Stata software. Statistical significance was evaluated using ANOVA and t-tests with a p value <0.05 considered significant.

## RESULTS

Out of a total of 3278 children admitted who were less than 5 years of age, 138(3.4%) children were SAM. On the basis of study participant selection criteria, 100(3.1%) SAM children were enrolled in the study. Forty seven percent of studied children were less than 12 months of age, followed by 27.0% who were in 13-36 months age group and 26.0% were in >36 months age group; while mean age of studied children was 25.31±20.09 months. Sixty six percent of children were males, with male: female ratio of 2:1 (Table 1).

**Table 1: demographic distribution of studied children.**

| Age (in months) | Frequency (n=100) | % |
|---|---|---|
| **≤12** | 47 | 47.00 |
| **13-36** | 27 | 27.00 |
| **>36** | 26 | 26.00 |
| **Males** | 66 | 66 |
| **Females** | 34 | 34 |

Table 2: Distribution of studied children on the **basis of symptoms mimicking celiac disease.**

| S. No. | Symptoms mimicking celiac disease | Frequency (n=100) | % |
|---|---|---|---|
| **1** | Failure to thrive | 100 | 100.00 |
| **2** | Diarrhoea | 15 | 15.00 |
| **3** | Vomiting | 14 | 14.00 |
| **4** | Anemia | 5 | 5.00 |
| **5** | Weight loss | 2 | 2.00 |

**Table 3: Distribution of studied children on the basis of anti-tTG IgA profile.**

| Anti-tTg IgA | | Frequency (n=100) | % |
|---|---|---|---|
| **<4.0 U/ml** | Negative | 63 | 63.00 |
| **4.0-10.0 U/ml** | Weak positive | 21 | 21.00 |
| **>10.0 U/ml** | Positive | 16 | 16.00 |

Chief complaints were failure to gain weight in 100%, fever in 74.0%, followed by cough in 42.0%, diarrhea in 15.0%, convulsion in 14.0%, lethargy in 10.0%, pallor in 7%, bleeding manifestations in 2 %, generalized body swelling and weight loss in 1.0% each. Symptoms mimicking celiac disease were failure to thrive in 100.0%, while diarrhoea was in 15.0%, vomiting in 14.0%, anemia in 5.0% and weight loss in 2.0%. (Table 2). In our study, 55.0% of studied children were on mixed (breast+ top) feeding, 40% were on breast feeding and 5.0% were on top feeding in first 6 months of life. Out of all children who were not on exclusive breast feeding in first 6 months of life, cow's milk (51.6%) was the most common type of milk used, bottle feeding (36.0%) was the most common method of feeding with improper sterilization technique and 100% cases used diluted milk.

In 8% cases complimentary feeding was started before 6 months while 92.0% cases were started on complimentary feeding after 6 months, out of which only 12% were fed as per IYCF guidelines. Ninety percent children belonged to upper lower class, followed by lower middle (8.0%) and upper middle (2.0%). Fifty four percent of children had more than 6 members in family and 49% were having more than 2 children in their family. Anti-tTg IgA levels were >4 U/ml in 37% of all studied children, out of which 21.0% children were weak positive and 16.0% children were positive (Table 3).

## DISCUSSION

Good nutrition plays a pivotal role in ensuring optimal growth and overall health. In this study, the proportion of hospitalized children diagnosed with severe acute malnutrition (SAM) was identified as 3.1%, which is higher than the 2.2% prevalence reported by Bhadoria et al.[12] However, it remains lower than the national average of 7.9%. This variation could be attributed to factors such as family size, lower parental education levels, and socioeconomic disparities. Comparable findings were observed in studies from Puducherry by Shewade et al and Nepal by Pravana et al, who reported SAM prevalence rates of 3.6% and 4.14%, respectively.[13,14]

Almost half of the children in this study (47%) were under 12 months of age, followed by 27% between 13 to 36 months, and 26% older than 36 months. The average age of participants was approximately 25 months. These results align with previous research by Bhadoria et al and Prashanth et al, who similarly documented higher rates of SAM among younger children.[15] The male-to-female ratio in our study was 2:1, indicating a higher incidence of SAM among boys. Similar gender disparities were reported by Sahoo et al and Mehta et al, suggesting that boys may be more vulnerable to malnutrition or that there may be gender-based healthcare-seeking differences.[16,17] All enrolled children presented with failure to gain weight, accompanied by other symptoms such as fever (74%), cough (42%), diarrhea (18%), convulsions (14%), lethargy (10%), pallor (7%), and a smaller percentage experiencing bleeding, generalized swelling, or weight loss. These findings are consistent with previous research by Sharma M and others.

Symptoms resembling celiac disease, including growth failure, diarrhea (15%), vomiting (14%), anemia (5%), and weight loss (2%), were frequently observed. Such clinical presentations, as described by Ludvigsson et al and Thapa et al, underscore the need for screening for celiac disease in children with SAM exhibiting gastrointestinal or growth-related concerns.[19,20] Feeding practices in early infancy were suboptimal among the study population. Only 40% of children were exclusively breastfed during the first six months. Among those who were not, cow's milk was the predominant alternative, and bottle-feeding was common, often with inadequate sterilization and milk dilution. These practices likely contributed to nutritional deficiencies and underline the need for promoting exclusive breastfeeding and proper infant feeding guidelines, as emphasized in studies by Pravana et al and Prashanth et al.

Complementary feeding was delayed in the majority of cases, with only 8% introduced to complementary foods before six months, and merely 12% adhering to infant and young child feeding (IYCF) recommendations. This gap in appropriate nutritional practices during the weaning period likely exacerbates the risk of malnutrition. Nearly all children were calorie-deficient, and 95% had protein deficiencies, echoing findings by Prashanth et al and Kulkarni et al.[21] The overwhelming majority (90%) of families belonged to lower socioeconomic classes, consistent with studies by Dwivedi et al and Avachat et al, highlighting the strong association between poverty and malnutrition.[22,23] This study also identified that larger family sizes correlated with higher SAM prevalence, a trend supported by Pravana et al., suggesting that limited resources in bigger households can compromise child nutrition.

Importantly, elevated anti-tTG IgA levels were observed in 37% of participants, with 21% showing weakly positive results and 16% classified as positive. These results align with the findings of Sharma M et al. and Beniwal et al who reported similar rates of positive celiac serology among malnourished children. Beniwal et al, also highlighted an association between celiac disease and specific clinical presentations, underscoring the need for heightened vigilance for celiac disease in children with SAM, even when symptoms are atypical.[24]

This study was limited to a single center and involved a relatively small sample size. Regional baseline anti-tTG IgA levels were unavailable, and biopsy facilities were not accessible during the study period. Larger, multicenter studies with biopsy confirmation are needed.

## CONCLUSION

A substantial proportion of SAM children had elevated anti-Ttg IgA levels, suggesting possible celiac disease. Screening with anti-tTG IgA should be considered for SAM patients, especially those with ongoing gastrointestinal symptoms. Positive cases (>10 U/ml) warrant further evaluation, including biopsy where available.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Tulsi N, Sharma S, Rehalia N. Anti-tissue transglutaminase IgA levels in severe acute malnutrition in children up to 60 months of age- a cross-sectional study from North-West India. Int J Contemp Pediatr 2025;12:1378-81.