

Original Research Article

Response to gluten free diet in sero-positive celiac disease children suffering from severe acute malnutrition in age group 1-5 years

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ABSTRACT

Background: Diagnosis of celiac disease in children suffering from severe acute malnutrition without duodenal biopsy or HLA typing is a dilemma. The objective of this study was to study the response to gluten free diet in sero-positive Celiac Disease children suffering from severe acute malnutrition in age group 1-5 years.

Methods: This prospective, observational, hospital-based study was conducted at MTC of tertiary care medical college hospital of southern Rajasthan from Dec. 2017 to Nov. 2018. Total 110 children with SAM were enrolled and screened for celiac disease on the basis of tissue tTg-IgA/IgG serology. Seropositive cases were kept on gluten free diet for short period of time and observed for the resolution of symptoms and improvement in growth, monitored by anthropometry on discharge and follow up visit.

Results: Mean weight gain (gm/kg/day) on follow up was 3.87 ± 3.49 in seropositive and 1.88 ± 3.79 in seronegative cases (P -value < 0.05). Mean weight gain was 6.43 ± 3.28 gm/kg/day in only tTg-IgA positive and 3.04 ± 2.95 gm/kg/day in only tTg-IgG positive cases (P -value < 0.05). The mean weight gain in strictly gluten free adherent sero-positive cases was 4.89 ± 2.97 gm/kg/day while in gluten free non-adherent patients it was -0.49 ± 1.70 (P -value < 0.001). Mean weight gain in probable (tTg-Ig-A < 10 times ULN) and presumptive (tTg-IgA > 10 times ULN) Celiac disease were 3.44 ± 3.73 and 5.44 ± 3.78 , respectively without statically significant difference (P -value > 0.05).

Conclusions: In situations where facility of duodenal biopsy and or HLA DQ2/DQ8 typing is not available, resolution of symptoms and improvement in growth on gluten free diet confirms the diagnosis of celiac disease.

Keywords: Celiac disease, Gluten free diet, Tissue trans-glutaminase, Severe acute malnutrition

INTRODUCTION

Celiac disease is emerging as a public health problem in India. Almost 6-8 million Indians are estimated to have celiac disease.¹ A massive increase in the number of patients with celiac disease is expected now and in the subsequent decade in India because of increasing awareness and availability of diagnostic facilities. Celiac disease is a common cause of malabsorption in the children and adults. It is characterized by an enteropathy and lifelong intolerance to gluten initiated by ingestion of gliadin related prolamines from cereals such as wheat,

barley and rye in genetically susceptible individual.² As per NFHS-4 (2015-16) severe acute malnutrition afflicts nearly 7.5% of children below 60 months of age in India.³ Several studies had reported high prevalence of celiac disease in north India particularly Punjab and Rajasthan in general population and children.⁴⁻⁷ The clinical features of severe acute malnutrition (SAM) often overlap with the common manifestations of celiac disease such as diarrhea, failure to thrive, vomiting, abdominal distension, anemia, weight loss and irritability.^{8,9} The diagnosis of celiac disease is based on clinical features, celiac serology followed by confirmation by duodenal

biopsy and or HLA DQ2/DQ8 typing.¹⁰ Facility of upper GI endoscopy and duodenal biopsy or HLA typing is available at very few centres and are expensive and most of the time not possible.

This study was designed to diagnose the celiac disease in SAM children of 1-5 years of age group on the basis of celiac serology and observe the response to gluten free diet in celiac seropositive patients.

METHODS

The present study was an observational hospital based prospective study, carried out at malnutrition treatment center (MTC) of tertiary care center Pediatric hospital associated with medical college of Southern Rajasthan. The study was conducted from December 2017 to November 2018. Prior approval was sought from institutional ethical committee of medical college. After written informed consent from both the parents total 110 children of either gender admitted in MTC, fulfilling the inclusion criteria, were enrolled for the study. Diagnosis of severe acute malnutrition was based on WHO criteria for severe acute malnutrition.

Inclusion criteria

- All the SAM children (meeting the WHO criteria for SAM) of age 1 to 5 years admitted in MTC and who are exposed to gluten containing diet
- Parents given informed and written consent to enrol in the study.

Exclusion criteria

- Seriously sick SAM children admitted in PICU.

- Patients with secondary malnutrition-known c/o chronic medical or surgical disorders leading to malnutrition-congenital heart diseases with CHF, chronic renal failure, hepatic cholestasis, thyrotoxicosis, isolated childhood diabetes mellitus, HIV, childhood tuberculosis, cerebral palsy, genetic/chromosomal syndromes, inborn errors of metabolism (IEM), malignancies, surgical resection of intestine etc
- Patients with known celiac serology
- Patients who were not exposed to gluten containing diet
- Parents not given for consent.

Celiac disease sero-positivity was accessed by screening for tissue transglutaminase IgA (tTg-IgA) and IgG (tTg-IgG) antibodies by enzyme linked immuno-sorbent assay (ELISA) method (Aeskuliat tTg-A/tTg-G new generation antigen-based kit by Aesku. Diagnostics Gmbh and Co. Kg). As per manufacturer manual of the kit, cut off value for sero-positivity for tTg-IgA/IgG was >18U/ml. Celiac Disease status was labeled according to titer of tTg-IgA and tTg-IgG as shown in Table 1.

All the celiac disease seropositive patients were kept on strict gluten free diet after proper counselling. After admission anthropometric measurements and symptomatic improvement were recorded on discharge and on follow up visit.

Statistical analysis

All the collected data were managed and analysed with standard software (SPSS version 20). P-value of <0.05 was considered significant.

Table 1: Celiac disease status according to titer of tTg-IgA and tTg-IgG.

Celiac disease status	t Tg-IgA Titre (Unit/ml)*	tTg-IgG Titre (Unit/ml)*
No celiac disease	≤18	≤18
Probable celiac disease (<10 times of ULN)	>18 - up to 180	>18
Presumptive celiac disease (10 times of ULN)	>180	

* Normal Range for tTg-IgA and tTg-IgG: 12-18 unit/ml (as per manufacturer manual of the kit); ULN- Upper limit of normal.¹¹

RESULTS

Out of total 110 enrolled cases 65 (59.09%) were male and 45 (40.91%) were female. The male to female ratio was 1.44:1 (Table 2).

Table 2: Gender wise distribution of cases.

Gender	No.	Percentage
Male	65	59.09
Female	45	40.91
Total	110	100.00

Table 3: Mean weight gain at follow-up.

Sero-positivity status	Weight gain (gm/kg/day) at follow-up	
	Mean	SD
Seronegative	1.88	±3.79
Seropositive	3.87	±3.49

P-value >0.05

Seropositive celiac disease (either tTg-IgA or IgG or both IgA and IgG) was positive in 30 (27.28%) cases out of

110 enrolled cases of severe acute malnutrition. Mean weight gain (gm/kg/day) on follow up was (3.87±3.49) in seropositive group and in seronegative was 1.88±3.79. This difference was statistically significant (P-value<0.05) (Table 3).

Table 4: Mean weight gain at follow-up according to tTg-IgA titre levels.

Levels of tTg-IgA titre (U/ml)	Mean weight gain (gm/kg/day) at follow-up	
	Mean	SD
>18 up to 180	3.44	3.73
>180	5.79	3.78

P-value >0.05

Mean weight gain (gm/kg/day) on follow up in both tTg-IgA positive cases was statically insignificant (P-value >0.05) (Table 4).

Mean weight gain (6.43±3.28) was more in only tTg-IgA positive compared to tTg-IgG positive group (3.04±2.95). This difference was statically significance (P-value<0.05) (Table 5).

Table 5: Mean weight gain at follow-up in only tTg-IgA v/s only tTg -IgG seropositive cases.

Seropositivity status	Mean weight gain(gm/kg/day)	
	Mean	SD
Only tTg-IgA positive (n=8)	6.43	3.28
Only tTg-IgG positive (n=7)	3.04	2.95

P-value <0.05

After discharge follow-up was 70% (21 out of 30) in seropositive group and 37.5% (30 out of 80) in seronegative group (Table 6).

Table 6: Follow up status in cases.

Follow-up status	Seronegative group (n=80)	%	Seropositive group (n=30)	%
Follow-up	30	37.50	21	70
Follow-up failure	50	42.50	9	30

Table 7: Gluten free diet adherence status and mean weight gain in seropositive cases on follow-up.

Gluten free diet adherence status	No.	%	Mean weight gain (gm/kg/d)	SD	P- value
Strictly Followed Gluten free diet	17	80.95	4.89	±2.97	<0.001 (HS)
Not Followed Gluten free diet	4	19.05	-0.49	±1.70	

Most of the seropositive patients 17 (80.95%) were adhered to gluten free diet as per counselling at discharge. while 4 (19.05%) were not adhered to gluten free diet (Table 7).



Figure 1: Mean weight gain (gm/kg/day) in gluten free diet adherent and non-adherent cases.

Mean weight gain (gm/kg/day) in strictly gluten free adherent sero-positive cases was 4.89±2.97 while in

gluten free non-adherent patients it was -0.49±1.70. This difference of mean weight gain in gluten free adherent and non-adherent was statistically highly significant (P-value <0.001) (Table 6 and Figure1).

DISCUSSION

Celiac disease and severe acute malnutrition in children share common clinical features. Confirmatory diagnosis of celiac disease is based on serology followed by duodenal biopsy or HLA DQ2/DQ8 typing.

In situations where availability of Pediatric Gastroenterologist and facility of upper GI endoscopy for duodenal biopsy in small sick children (less than 5 years) is not possible or available and HLA typing is also not available/feasible then gluten free diet may be tried in celiac positive serology patients and observed for improvement in anthropometry and resolution of symptoms.

In present study, authors kept the celiac seropositive patients suffering from SAM on gluten free diet and observed the response.

On follow up the mean weight gain (gm/kg/day) in seropositive cases was more in comparison to seronegative cases (P-value <0.05). This shows good response to gluten free diet in sero-positive cases and confirms the diagnosis of celiac disease in these cases.

The mean weight gain on follow up was more in presumptive celiac disease sero-positive cases (5.79 ± 3.78 gm/kg/day) in comparison to probable celiac disease sero-positive cases (3.44 ± 3.73 gm/kg/day). Although the mean weight gain was more in presumptive celiac Disease sero-positive cases but the difference of weight gain between probable and presumptive celiac sero-positive cases was statistically not significant (P-value >0.05). This suggests that response to gluten free diet is similar in tTg-IgA titre <10 and >10 times of ULN cases.

So, we should not wait for to rise the tTg antibody titres >10 times of ULN and start the gluten free diet at lower level if clinical features are also suggestive of celiac disease and observe the response to gluten free diet.

Mean weight gain in only tTg-IgA seropositive cases was more (6.43 ± 3.28 gm/kg/day) in comparison to only tTg-IgG sero-positive cases which was statistically significant (P-value <0.05). Comparatively lower weight gain in only tTg-IgG sero-positive cases may be because of underlying IgA deficiency leading to recurrent gastrointestinal infections and another reason may be more damage to intestinal epithelium requiring more time to regenerate and slow response to gluten free diet.

In present study most of patients (93%) discharged successfully but follow-up was 70% (21 out of 30) in seropositive group and rest 30 % of seropositive cases could not be followed and follow up failure was reported for these cases. This showed that more emphasis should be given on follow up counseling in addition to dietary counseling at the time of discharge.

On follow up visit after discharge authors observed that most of the sero-positive patients were well adhered to gluten free diet as per dietary counselling at the time of discharge.

The mean weight gain was more in strictly adhered to gluten free diet as compared to non-adhered to gluten free diet (P-value <0.001). This is suggestive of importance of adherence to gluten free diet in Celiac disease.

Other study conducted by Bhadada S et al, in short stature children age 10-15 years were screened for Celiac disease and observed that all patients showed good response in growth velocity (cm/year) to a gluten-free diet, but no other study was conducted so far to see the response to gluten free diet in celiac disease in children suffering from severe acute malnourished children in age group 1-5 years.¹³

CONCLUSION

Gluten free diet may be started empirically in seropositive patients for short period of time assuming presumptive celiac disease and observed for resolution of signs/symptoms and improvement in growth.

If there is rapid resolution of signs/symptoms and significant improvement in growth, confirmed celiac disease may be considered and gluten free diet continued for life long. There is no need for duodenal biopsy or HLA DQ2/DQ8 typing in these patients.

If sero-positive patients with good adherence to gluten free diet do not show neither resolution of symptoms nor improvement in growth, then gluten free diet may be stopped and evaluated further to find the etiology.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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