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Original Research Article

Assessment of Clinical and Lab Profile of Seropositive Celiac Diseases in 1-5 Years Old Children Suffering from Severe Acute Malnutrition

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Abstract

Aim: The objective of this study was to study clinico-laboratory profile of seropositive Celiac Diseases in Severe Acute Malnutrition.

Methods: The present study was single centric hospital based observational prospective study was conducted at Department of Pediatrics, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar for one year. Total 110 children with Severe Acute Malnutrition in age group 1-5 years, admitted in MTC were enrolled and screened for celiac serology. Out of these 100 cases celiac serology was positive in 30 cases with sero-positivity of 30%.

Results: Out of total 30 seropositive cases, 14 (46.66%) cases were seropositive for both tTg and only tTg-IgG were positive in 9 (30%) and 7 (23.33%) cases, respectively. Seropositivity of only Serum tTg IgA and only tTg IgG was maximum (4/9, 44.44%; 3/7, 42.86%) in age group 1 while sero-positivity of both tTg-IgA and IgG was maximum (7/14, 50%) in age group 4-5 years. The mean age, mean weight and mean height in seronegative v/s seropositive was1.69±1.24 v/s 2.65±1.54,6.81±1.88 v/s 7.24±2.24 and 74.95±10.20 v/s 81.23±12.49. The difference among the all three parameters was statistical significant (P-value<0.5). While mean MUAC was 11.10±1.41 v/s 11.26±1.17. The difference in MUAC in seronegative and seropositive cases was statistically insignificant (p-value>0.5). The mean age of starting gluten containing diet in seronegative and seropositive group was 8.47(±2.98) and 8.35 (±2.15) respectively. This difference was statistically insignificant (P-value>0.05).

Conclusion: Recurrent diarrhoea and blood in stool was common presenting feature on admission in celiac seropositive patients suffering from severe acute malnutrition. Vit. B12 and Folic acid deficiency were also observed as a common finding in seropositive patients.

Keywords: Celiac Disease, Sero-positive, Severe Acute Malnutrition (SAM).

Introduction

Celiac disease, known as gluten-sensitivity enteropathy, is a chronic autoimmune inflammatory disease in the small intestine. It is characterized by permanent gluten intolerance and malabsorption syndrome. The etiology of CD could be

environmental factors such as the ingestion of gluten and genetic factors such as HLA and tTG auto-antigen. Therefore, CD affects genetically susceptible individuals. Gluten is recognized as a protein found in prolamine fragments of barley (hordein), wheat (glutenin and gliadin), or rye (secalin). [1-5]

Nutrition in Celiac Disease is an important issue. When someone who has Celiac Disease consumes food containing gluten, it reacts by attacking the intestinal villi. Eventually, those tiny tentacles can be completely flattened, leaving them unable to do their job of absorbing nutrients. It doesn't matter how well a person eat if villi are destroyed by untreated celiac disease he is almost certain to be malnourished. [6-8] The clinical features of Severe Acute Malnutrition (SAM) often overlap with the common manifestations of Celiac Disease such as recurrent diarrhea, failure to thrive, vomiting, abdominal distension, anemia and weight loss. [9-10] As per NFHS-4 (2015-16) Severe Acute Malnutrition afflicts nearly 7.5% of children below 60 months of age in India. [11]

The clinical presentation of Celiac Disease can vary from a classical mal-absorption syndrome to more subtle atypical gastrointestinal manifestations (similar to irritable bowel syndrome) or extra intestinal presentations (for example- infertility, malnutrition, osteoporosis, anemia, short stature, neurological & psychiatric manifestations). Celiac disease (CD) is one of the most common lifelong disorders in countries populated by individuals of European origin, affecting approximately 1% of the general population in worldwide. [12] Exact incidence of disease in India is not known. CD 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. [13] Nutrition in Celiac Disease is an important issue. When someone who has Celiac Disease consumes food containing gluten, it reacts by attacking the intestinal villi.

Celiac disease could be major contributor or co-morbid condition in children with Severe Acute Malnutrition. The objective of this study was to study clinico-laboratory profile of seropositive Celiac Diseases in Severe Acute Malnutrition.

Materials and Methods

The present study was single centric hospital based observational prospective study was conducted at Department of Pediatrics, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar for one year. Total 110 children with Severe Acute Malnutrition in age group 1-5 years, admitted in MTC were enrolled and screened for celiac serology. Out of these 100 cases celiac serology was positive in 30 cases with sero-positivity of 30%. The study was conducted for the period of one year. All the children of 1-5 years age group suffering from Severe Acute Malnutrition (SAM) admitted in Jawaharlal Nehru Medical College and Hospital.

Inclusion Criteria

1. All the children admitted with Severe Acute Malnutrition (meeting the WHO criteria for SAM) of age 1 to 5 years, exposed to gluten containing diet and
2. Parents willing for informed and written consent to enroll in the study.

Exclusion Criteria

1. Seriously sick children with SAM admitted in PICU.
2. Patients with secondary malnutrition– known case of chronic medical or surgical disorders leading to malnutrition- Congenital Heart Diseases with CHF, Chronic renal failure, Hepatic Cholestas is, Thyrotoxicosis, Isolated Childhood

Diabetes Mellitus, HIV, Childhood Tuberculosis, Cerebral Palsy, Genetic/ Chromosomal Syndromes, Inborn errors of Metabolism (IEM), Malignancies, Surgical resection of intestine etc.

3. Patients with known celiac serology.

Intervention: Prior approval for ethical clearance was sought from Institutional Ethical Committee. After obtaining informed written consent from both the parents, patients were enrolled for the study. Detailed clinical and dietary history followed by anthropometric measurements and examination was done.

Blood sample was collected for relevant investigations. Celiac serology was accessed by screening for tissue trans-glutaminase IgA/IgG by ELISA method (Aeskulisat tTg-IgA/ tTG-IgG new generation antigen based kit by Aesku. Diagnostics. Gmbh & Co. Kg). As per manufacturer manual of the kit cut off value for seropositivity for tTg-IgA/IgG was >18 U/ml (As per manufacturer manual of the kit -normal range for tTg-IgA & tTg-IgG: 12-18 unit/ml). [14]

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

Results

Table 1: Sero-positivity pattern according to tTg -IgA/IgG and gender distribution

Sero-positivity	**N**	**%**
Only tTg-IgA Positive	9	30
Only tTg-IgG Positive	7	23.34
Both tTg-IgG &IgA Positive	14	46.66
Gender (Seropositive)		
Male	18	60
Female	12	40
Gender (Seronegative)		
Male	42	60
Female	28	40

Out of total 30 seropositive cases, 14 (46.66%) cases were seropositive for both tTg and only tTg-IgG were positive in 9 (30%) and 7 (23.33%) cases, respectively. Celiac Disease sero-positivity was more in males (60%, 18 in 30) as compared to females (40%, 12 in 30), and this difference in sero-positivity was statistically insignificant.

Table 2: Distribution of Seropositivity According to Age group

Age group (yrs)	**Seronegative (70)**	**Seropositive (30)**			
		Only tTg IgA Positive	**Only tTg IgG Positive**	**tTg IgA + IgG both Positive**	**Total**
1-2	45 (64.2)	4 (44.44)	3 (42.86)	2 (14.29)	9 (30)
2-3	10 (14.28)	1 (11.11)	1 (14.29)	4 (28.57)	6 (20)
3-4	5 (7.14)	1 (11.11)	1 (14.29)	1 (7.14)	3 (10)
4-5	10 (14.28)	3 (33.33)	2 (28.57)	7 (50)	12 (40)
Total	70	9	7	14	30

Seropositivity of only Serum tTg IgA and only tTg IgG was maximum (4/9, 44.44%; 3/7, 42.86%) in age group 1 while sero-positivity of both tTg-IgA and IgG was maximum (7/14, 50%) in age group 4-5 years.

Table 3: Mean Age and anthropometric measurements in cases

Parameters	Seronegative	Seropositive	P Value
	Mean±SD	Mean±SD	
Age (years)	1.69 ±1.24	2.65 ±1.54	0.02
Anthropometric Measurements			
Weight (Kg)	6.81 ±1.88	7.24 ±2.24	0.04
Height (cm)	74.95 ±10.20	81.23 ±12.49	0.01
MUAC (cm)	11.10 ±1.41	11.26 ±1.17	0.54

The mean age, mean weight and mean height in seronegative v/s seropositive was1.69±1.24 v/s 2.65±1.54,6.81±1.88 v/s 7.24±2.24 and 74.95±10.20 v/s 81.23±12.49. The difference among the all three parameters was statistical significant (P- value<0.5). While mean MUAC was 11.10±1.41 v/s 11.26±1.17. The difference in MUAC in seronegative and seropositive cases was statistically insignificant (p-value>0.5).

Table 4: Weight/Height Z-score in cases

Weight/ Height	Seronegative		Seropositive	
	No.	%	No.	%
< 2SD	5	7.15	0	0
<-3SD	65	92.85	30	100
Total	**70**	**100**	**30**	**100**

Total no. of cases in form of Z-score (<-2SD, <-3SD) in seronegative group and seropositive group were 5, 65 and 0,30 respectively. This difference in sero-negative and sero-positive cases was statistically insignificant (P-value= >0.05).

Table 5: Mean Age of Gluten Sensitization in Seropositive and Seronegative Cases

Age group (Months)	Sero-negativity		Sero-positivity		P value
	No.	%	No	%	
<6	10	76.92	3	23.08	>0.05
6-12	63	73.26	23	26.74	
12-18	7	63.64	4	36.36	
Mean Age (Months) of starting Gluten containing diet	8.47±2.98		8.35±2.15		

The mean age of starting gluten containing diet in seronegative and seropositive group was 8.47(±2.98) and 8.35 (±2.15) respectively. This difference was statistically insignificant (P-value>0.05).

Table 6: Distribution of Clinical Sign & Symptoms

Clinical Features	Seronegative (n=70)		Seropositive (n=30)								Total	P value
			Only tTg IgA Positive (n=9)		Only tTg IgG Positive(n=7)		Both tTg IgA & IgG Positive (n=14)		Total			
	N	%	N	%	N	%	N	%	N	%		
Rec. Diarrhea	24	47.06	9	17.65	5	9.80	13	25.49	27	52.94	51	**<0.001**
Rec. Blood in stool	5	45.45	0	0.00	3	21.43	3	21.43	6	54.45	11	**<0.03**
Rec. Vomiting	21	61.76	2	5.88	3	8.82	8	23.53	13	38.23	34	0.10
Rec. Abd. Pain	19	61.29	3	9.68	2	6.45	7	22.58	12	38.70	31	0.24
Abd. Distension	35	66 .04	3	5.66	4	7.55	11	20.75	18	33.96	53	0.07
Anorexia	26	76.47	2	5.88	3	8.82	3	8.82	8	36.00	34	0.69
Wt. loss	16	64.00	2	8.00	2	8.00	5	20.00	9	36.00	25	0.61
Irritability	28	80.00	3	8.57	2	5.71	2	5.71	7	20.00	35	0.49
Clinical Sign												
Pallor	62	72.94	5	5.88	6	7.06	12	14.12	23	27.05	85	0.35
Oedema	10	76.92	1	7.69	1	7.69	1	7.69	3	23.0	13	0.95
Skin change	18	78.26	3	13.04	1	4.35	1	4.35	5	21.73	23	0.43
Nails change	8	61.54	1	7.69	1	7.69	2	15.38	4	30.76	12	0.96
Tongue Chelosis	1	50.00	1	50.00	0	0.00	0	0.00	1	50	2	0.18
Hairs hypo-pig.	48	73.85	4	6.15	4	6.15	9	13.85	17	26.15	65	0.81

The mean sero-titre of tTg-IgA and IgG increases with the duration of gluten containing diet consumption (Figure-2). Irritability (80%) and anorexia (76.47%) were common clinical features in seronegative cases while in seropositive cases recurrent blood in stool (54.45%) and recurrent diarrhoea (52.94%) were common clinical features at the time of admission (P value <0.05). In only tTg-IgA seropositive cases common clinical feature was recurrent diarrhea (17.65%) while in tTg-IgG seropositive cases recurrent blood in stool (21.43%) was common (P value <0.05).

In seropositive cases chelosis of tongue was common sign (50%) followed by nail changes (30.76%) and pallor (27.05%) but there was no statistically significant difference (P value >0.05) among the clinical signs between seropositive and seronegative groups.

Table 7: Hematological profile in cases

Hematologicalindices	Seronegative (n=80)		Seropositive (n=30)		P value
	Mean	SD	Mean	SD	
Hb	7.81	±2.45	8.21	±2.58	0.464
Hct	26.12	±7.64	26.16	±8.12	0.981
MCV	69.47	±15.14	71.48	±15.04	0.284
MCH	23.55	±17.35	23.66	±6.27	0.142
MCHC	29.71	±4.08	30.91	±3.18	0.589
TLC	11911.99	±7235.11	10810.77	±7550.19	0.492

In Seronegative v/s Seropositive cases mean haemoglobin (7.81±2.45 v/s8.21±2.58 gm%), mean Hct (26.12±7.64 v/s 26.16±8.12 %), mean MCV (69.47±15.14v/s 71.48±15.04 fl), mean MCH (23.55±17.35 v/s 23.66 ±6.27 pg), mean MCHC (29.17±4.08 v/s 30.91±3.18 g/dl) were lower in Seronegative group. while mean TLC (11911.99±7235 v/s.110810.77±7550.19 cells/mm3) were lower in seropositive cases but there was no statistical significant (P-value >0.05).

Table 8: Vit.-B12, Folic Acid levels and Thyroid status in cases

	Seropositive	Seronegative
Vit. B12	20	10
Folic acid deficiency	9	5
Hypothyroidism	15	10

In seropositive cases folic acid deficiency was present in 30% (9 out of 30) children while in seronegative cases it was present in 6.25% (5 out of 80) children. The difference observed in folic acid deficiency between seropositive and seronegative cases was statistically significant (P value<0.05).

Discussion

The word “Celiac” came from Greek word “Koilia”, which means belly or abdomen. Celiac Disease is also known as celiac sprue, non-tropical sprue, gluten intolerance, gluten sensitive enteropathy. [15] Celiac Disease is a common cause of mal-absorption 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. [16] Overall sero-prevalence of Celiac Disease in our study among the children suffering from severe acute malnutrition was 30% (30 out of 100). Out of these seropositive cases 7 patients (23.33%) showed only tTg-IgG positive serology and these patients may have underlying IgA deficiency and may be missed if accessed for tTg-IgA only.

Prevalence reported by Kumar P et al was 13.1% (sero positive and biopsy confirmed) among the SAM children. [17] Sero-prevalence for Celiac Disease reported by Beniwal N et al was 15.38% while prevalence of biopsy confirmed Celiac disease was 14.42% among the SAM children.10 We compared various parameters in Celiac Disease seronegative and seropositive cases. Sero-positivity was more in males as compared to females. Similarly male preponderance in sero-positivity was reported by Sharma M et al. [18] This suggests gender biasness in society as more male children brought for admission as compared to females. [19]

Anthropometric measurements were comparable in sero-nergative and sero-positive cases without statistical significant difference. Anthropometric measurements were consistent with Severe Acute Malnutrition. There was no

significant difference in mean age of starting gluten containing diet in sero-negative and sero-positive cases. The mean age of starting gluten containing diet in seropositive cases was 8.35±2.15 months. Beniwal N et al[10] reported mean age of starting gluten containing diet in Celiac Disease children of 10.33±5.20 months. In our study mean age of starting gluten containing diet in sero-positive cases was less because most of the enrolled cases were between 1-2 years of age. We also observed that mean titre of tTg-IgA and IgG increased with duration of gluten containing diet consumption which is suggestive of cumulative effect of gluten with duration of gluten ingestion.

We observed that recurrent diarrhea was more common clinical features at the time of admission in seropositive cases in comparison to seronegative cases (P value <0.001). In only tTg –IgA sero-positive cases common clinical feature was recurrent diarrhea while in tTg-IgG sero-positive cases recurrent blood in stool was common clinical feature. Only tTg-IgG seropositive cases may have underlying IgA deficiency leading to recurrent invasive GI infection causing recurrent blood in stool. In these patients serum IgA estimation needed to rule out IgA deficiency. Kumar P et al[17] and Beniwal N et al[10] reported chronic diarrhea as a common clinical feature of Celiac Disease in children suffering from Severe Acute Malnutrition. We observed that in sero-positive cases chelosis of tongue was common (50%) clinical sign followed by nail changes (30.76%), pallor (27.05%), hair hypopigmentation (26.15%) and skin change (21.72%), but there was no statistical significant difference (P-value >0.05) among the clinical signs between sero-positive and sero-negative cases. All the clinical signs were consistent with signs of Severe Acute Malnutrition. We analyzed hematological parameters (Hb, Hct, MCV, MCH, MCHC) and observed that the microcytic hypochromic anemia was common in all the malnourished children.

In this study we assessed for Vit.-B12 and Folic Acid deficiency status by estimation of S.Vit.-B12 and Folic acid levels. Both seropositive and seronegative cases were Vit-B12 and Folic acid deficient (S. Vit.-B12 levels <200 pg/dl and Folic Acid <3ng/dl) but difference of Vit. B-12 in between two groups was statistically insignificant but difference of Folic Acid deficiency was statistically significant (P-value <0.05) between two groups. Macrocytic anemia in PBF was found in 10% of seropositive cases and only in 3.75% of seronegative cases. This is suggestive that S.Vit.-B12 and Folic Acid deficiency was more in seropositive cases. Subclinical hypothyroidism was reported in both seronegative (5%) and seropositive (13.33%). Although subclinical hypothyroidism was reported more in seropositive cases than seronegative but this difference was statistically insignificant (P value >0.05). So in our study we observed that Celiac Diseases should be suspected and may be diagnosed in children suffering with Severe Acute Malnutrition on the basis of clinical features and Celiac Disease serology (tTg-IgA/IgG).

Conclusion

Sero-positivity of Celiac Disease observed in children of 1-5 years age, suffering from Severe Acute Malnutrition was 27.28% in our study. Recurrent diarrhea was found to be common clinical features at the time of admission in sero-positive patients. In tTg – IgA sero-positive cases recurrent diarrhea was common clinical feature while in tTg-IgG sero-positive cases recurrent blood in stool was common. Macrocytic anemia in peripheral blood film associated with S. Vit. B12 & Folic acid deficiency was more common in celiac seropositive children with severe acute malnutrition.

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