ORIGINAL ARTICLE

Hematological & Clinico-Endoscopic Profile of Celiac Disease

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ABSTRACT

Introduction : Celiac disease is a chronic small intestinal immune-mediated enteropathy that is precipitated by dietary gluten in genetically predisposed individuals. This study was conducted to study of hematological & clinico-endoscopic profile of celiac disease.

Methods : A total 41 patients, suspected of celiac disease on serological evaluation (IgA anti-tTG antibody titre >100) included in study. History, physical examination, multiple small bowel biopsy, IgA anti-tTG along with iron studies (s. iron, ferritin, TIBC), vitamin B12 levels, INR & other routine investigations was done. Endoscopic findings that considered suggestive for diagnosis of celiac disease were scalloping of the folds, flattening of the duodenal folds, nodularity, multiple fissures & mosaic pattern & classified according to Marsh classification. Diagnosis of celiac disease was made based on clinical probability of celiac disease (typical GI symptoms, family history, steatorrhea, unexplained iron deficiency or signs of malabsorption), with IgA anti-tTG titre>100 & biopsy proven histological evidence.

Results : Of the total 41 subjects with IgA anti-tTG antibody titre >100; 16 (36.02%) had partial villous atrophy, whereas 4 (9.76%) has subtotal or total villous atrophy. Most common findings were anemia (100%) out of that 87.8% were IDA & 12.2% were megaloblastic anemia. After anemia, the other common features in subjects were diarrhea (53.66%), abdominal distention (29.26%), vomiting (14.63%), pain abdomen (9.76%) & edema (7.3%). In subjects with IDA (n= 36), 47.22% had stage 1, whereas 34.15% had stage 3a dystrophy. In subjects with megaloblastic anemia (n=5), 4 out of 5 had Marsh stage IIIa & IIIb, suggesting that more extensive & severe celiac disease only affects the vitamin B12 & folate absorption.

Conclusion : Celiac disease has clinically significant hematological manifestations, which should be evaluated & treated.

INTRODUCTION

Celiac disease (CD) is a chronic small intestinal immune-mediated enteropathy that is precipitated by dietary gluten in genetically predisposed individuals[1]. It affects approximately 1% of the population worldwide[2]. Clinical presentation includes signs and symptoms of malabsorption such as diarrhea, steatorrhea, weight loss, and nutritional deficiencies

The iron deficiency in celiac disease primarily results from impaired absorption of iron but there may also be occult blood loss in the gastrointestinal (GI) tract[3,4]. The clinical picture has changed considerably

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since the advent of serologic screening, with an increase in the frequency of individuals presenting with more atypical (i.e. non-gastrointestinal) manifestations.

MATERIAL & METHOD

In an retrospective analysis, 41 patients, suspected of celiac disease on serological (IgA anti tTG antibody titre >100) evaluation, presenting in Department of Gastroenterology & General Medicine, Mahatma Gandhi Medical College & Hospital, Rajasthan from 1st October 2018 to 1stNovember 2019 were evaluated. UGI Endoscopy &biopsy was taken from all subjects.

Subjects socio-demographic profile, history, physical examination, multiple small bowel biopsy, IgA anti-tTG along with Iron studies (S. Iron, Ferritin, TIBC), Vitamin B12 levels, complete blood counts, peripheral blood films, prothrombin time, INR & other routine investigations were considered for evaluation.

Following Endoscopic findings were considered suggestive for diagnosis of celiac disease, scalloping of the folds, flattening of the duodenal folds, nodularity, multiple fissures & mosaic pattern.

All biopsy samples were interpreted using Marsh Classification, stage 0-normal, pre-infiltrative, increased IEL; stage 1-infiltration of the lamina propria with lymphocytes; stage 2- crypt hyperplasia; stage 3- villus atrophy, lamina propria lymphocytosis to complete loss of villi and crypt hyperplasia[5,6]. Oberhuber classified the Marsh III into three sub-categories (IIIa, IIIb, IIIc)[7].

Diagnosis of celiac disease was made based on, moderate to high clinical probability of celiac disease (typical GI symptoms, family history, statorrhea, unexplained iron deficiency or signs of malabsorbtion), with a Ig A anti tTG titre >100 &biopsy proven histological evidence[8-12]. Statistical analysis was performed with Statistical Package for the Social Sciences software (SPSS version 26.0, Chicago, Illinois, USA). In total study group, for continuous data mean, standard deviation and range were calculated. For categorical data, number and percentages were calculated. The study protocol was approved by the ethics committee.

Table 1 : Demographic Characteristics of subjects with Celiac disease

Variable	Subjects N=41
Age (mean ± SD)	42.5 ±16.4
Sex	
Male	26 (63.41%)
Female	15 (36.59%)
Urban	23 (56.1%)
Rural	18 (43.9%)
Degree of Villous Atrophy	
PVA*	16 (39.02%)
S/TVA**	4 (9.76%)

* PVA = partial villous atrophy, ** S/TVA = subtotal/ total villous atrophy

Table 2 : Comparison of clinical features at presentation (%)

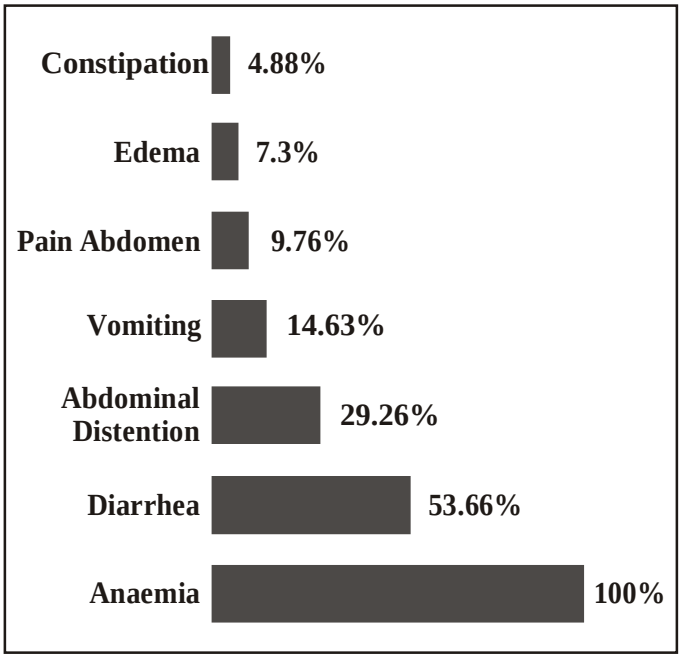

Table 3: Haematological Manifestation of Celiac Disease (%)

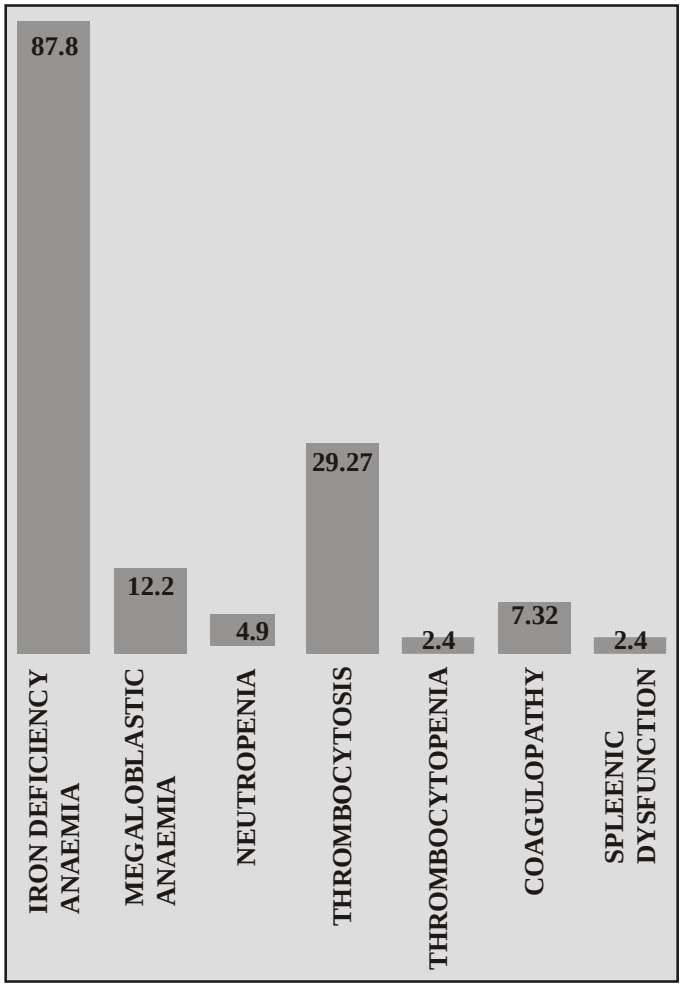

Figure 1: IgA anti-tTG antibodies titre of subjects with endoscopic evidence of Celiac Disease (n=68)

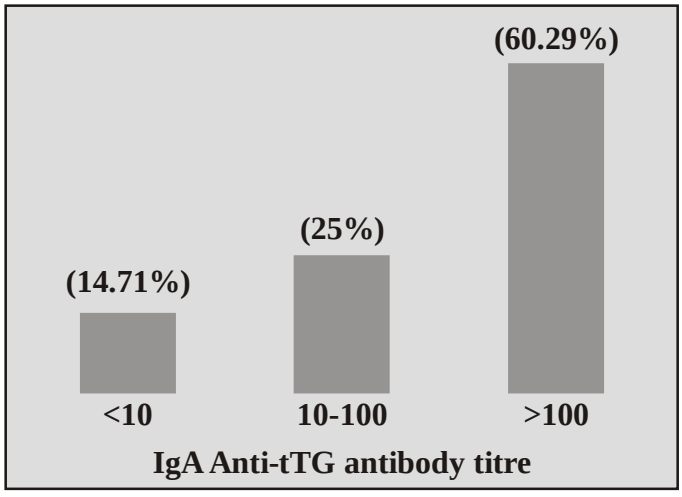

Table 4 : Histological Severity & Its correlation with type of Anemia

MARSH CLASSIFI-CATION	N=41 (%)	Iron deficiency anemia	Megaloblastic anemia
I	15 (36.59)	17	0
II	4 (9.75)	3	1
III A	16 (39.02)	14	0
III B	3 (7.32)	1	2
III C	3 (7.32)	1	2
Total	**41**	**36**	**5**

RESULT

The mean age of the subjects was 42.5 ±16.4 years. Most of the subjects were males (63.41%)& were from an urban background (56.1%). Of the total 41 subjects with Ig A anti-tTG antibody titre >100; 16 (36.02%) had partial villous atrophy, whereas4 (9.76%) has subtotal or total villous atrophy. After anemia, the most common clinical feature in subjects were diarrhea (53.66%), abdominal distention (29.26%), vomiting (14.63%), pain abdomen (9.76%) and edema (7.3%). On evaluation of biopsy, most 39.02 % subjects had partial villous atrophy (Marsh stage 3a), followed by (36.59%) with infiltration of the lamina propria with lymphocytes (Marsh stage 1) followed by36 (87.8%) had iron deficiency anemia (IDA). In subjects with IDA, 47.22% had stage 1, whereas 34.15% had stage 3a dystrophy. 4 out of 5 subjects developing megaloblastic anemia were from Marsh stage III a & III b suggesting that more extensive & severe celiac disease only affects the vitamin B12 & folate absorption.

DISCUSSION

Western (Walker Smith 13.5%)[13] vs Indian literature(Thapa et al 100%, Patwari et al 100%, Poddar et al 84%)[14-16] suggest higher incidence of anemia at time of diagnosis of CD in India. Thapa et al has reported that all patient (n=150) have anemia at the time of presentation (100%). Anemia has been reported in 38-89% newly diagnosed CD subjects worldwide, whereas late diagnosis & more severe ileal involvement can be attributed to more incidence of anemia (IDA & megaloblastic) in developing countries like India at time of diagnosis. The delay in diagnosis is attributed to infection as a cause of chronic

diarrhea and lack of awareness in developing countries like India. On other hand, the prevalence of CD in patients with refractory IDA may be as high as 20%[17]. Clinicians should consider CD as a possible cause of anemia in all subjects with unexplained IDA, including menstruating women, in Indian setup. Typical GI symptoms like Chronic Diarrhea, vomiting & abdominal distention, followed by anemia as common presentations in adulthood presentation CD. Early diagnosis in urban patients may have probably led to their higher distribution in our study sample. In the present study, the major symptoms at presentation were diarrhea, failure to thrive, abdominal distension, while pain abdomen, 63.41% male subjects, coincide with literature suggesting a higher male predominance of disease. In our study, 12.2 % subjects presented with Megaloblastic anemia. 8-41 % incidence has been reported in literature[18,19]. Thrombocytosis is more common in CD than thrombocytopenia (29.27 vs 2.4%) as also suggested by Croese J et al & Nelson EW et al[20,21]. Neutropenia has been reported in literature, is mainly attributed to copper &folate deficiency (Fisgin T et al)[22]. Our study found that 7.32% of untreated CD patients had prolongation of PT and these patients were also more likely to present with anemia and abnormal iron proteins. Similar results were shown by Cavallaro R et al[23] (2004). A low incidence of splenic dysfunction in our study (2.4%), when compared to literature (19-21%)[20] can be attributed to the more precise use of scintigraphy and measurements of the clearance of labeled heat damaged red cells by most studies compared to use of PBF findings (Howell-Jolly bodies, acanthocytes and target cells), which may not detect milder forms of hyposplenism. 80% of subjects diagnosed with megaloblastic anemia were of class III histological severity (Marsh criteria), compared to 44.44% IDA, suggesting presentation of megaloblastic anemia in more severe, late disease.

CONCLUSION

Celiac disease has clinically significant hematological manifestations, which should be evaluated & treated.

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