Original Article

Hematological Manifestations of Celiac Disease in Children

Celiac Disease in Children

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ABSTRACT

Objective: The frequency of different hematological manifestations of celiac disease in children.
Study Design: A case series study.
Place and Duration of Study: This study was conducted at the Pediatrics Department of Shalamar Medical and Dental College, Lahore from January 2015 to December 2018.
Materials and Methods: A total of 120 children, aged 1 to 12 years, diagnosed with CD. Diagnosis of CD was confirmed as small intestine biopsy showing intestinal mucosal changes as per Modified Marsh criteria, were included Frequency and percentages were calculated for qualitative variables like gender, thrombocytosis, leucopenia, anemia, coagulopathy, iron deficiency and vitamin B12 deficiency whereas mean and standard deviations were calculated for quantitative variables like age.
Results: Out of a total of 120 children, there were 68 (56.7%) male and 52 (43.3%) female, representing a male to female ratio of 1.31:1. Mean age was noted to be 9.21 years with a standard deviation of 2.6 years. Anemia was found in 113 (94.2%) children, thrombocytosis 93 (77.5%), leucopenia 12 (10.0%) and coagulopathy in 10 (8.3%). As per modified marsh scoring, 37 (30.8%) were type 3a, 36 (30.0%) type 3b, 28 (23.3%) type 3c, 17 (14.2%) type 2 and 2 (1.7%) type 1.
Conclusion: In children, hematological abnormalities related celiac disease is quite common. Anemia is the commonest hematological finding that is mostly found accompanying thrombocytosis.
Key Words: Celiac disease, anemia, thrombocytosis, coagulopathy.

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INTRODUCTION

Celiac disease (CD) is characterized as immune mediated enteropathy due to eternal sensitivity related to gluten in those individuals who are susceptible genetically.[1,2] It exhibits once exposure related to dietary gluten in wheat rye or barley. Diarrhea of recurrent nature, weight loss and inability to thrive are some of the most common presentations among children.[3,4] In some children, hypoalbuminemia casing edema is also found. In the recent years, CD has become more known regarding its non gastrointestinal (GI) symptoms like anemia, osteoporosis, short statue, coagulopathy or peripheral neuropathy.[5] Biopsy of the small intestine depicting characteristic mucosal alterations as per Modified Marsh criteria[6] confirms the diagnosis of CD, whereas a full clinical remission is witnessed following a diet that is gluten free. Further confirmatory findings include detection of anti-endomysial (Anti-EM) and anti-tissue transglutaminase (Anti-tTGA).[7]

The prevalence of CD is thought to be around 1% in general population around the world while Europe shows that to be 1-3%. Amongst children, the prevalence of CD is estimated to be 0.5-1% while it has also been shared that about 90% children with are undiagnosed that goes on to interpret that these undiagnosed children are not getting a timely diagnosis or treatment.[8-11] Actual burden of CD in Pakistan is unknown but, it was noted in a study that 61% of the children were found to be positive for CD who presented having persistent diarrhea and poor growth.[12]

Anemia, coagulopathy, thrombocytosis and leucopenia are some of the most common hematological findings in CD.[13,14] Anemia has been noted to be the commonest, found in about 86% of the CD cases.[14] Malabsorption related to iron, folic acid and vitamin B12 are some of the key factors contributing to anemia while local studies from Pakistan has shown that anemia was found in about 90% of CD cases.

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Coagulopathy is found in around 19% of CD cases and is thought to be related with vitamin K and vitamin D malabsorption.[15] Thrombocytosis is noted to be present in 60% of CD cases while leucopenia is recorded to be affecting about 9% of CD cases.[14]

In Pakistan, not much work has been done evaluating hematological spectrum of CD amongst children as very few studies have recorded these entities. The hematological findings in CD are also thought to play an important role for the timely diagnosis and management of CD that can minimize the morbidity and mortality associated with CD. This study was planned to find out the frequency of different haematological manifestations of CD in children.

MATERIALS AND METHODS

This study was conducted from 1st January 2015 to 31st December 2018 at Pediatrics Department of Shalamar Medical and Dental College was the venue for this case series study. A total of 120 children, aged 1 to 12 years, diagnosed with CD. Diagnosis of CD was confirmed as small intestine biopsy showing intestinal mucosal changes as per Modified Marsh criteria that includes partial to total villous atrophy, crypt elongation and / or increased intraepithelial lymphocytes. Children with liver disease (ALT more than 40 IU/L) or intestinal tuberculosis were not included.[6,16]

Approval from the institution's ethical committee was granted and informed consent was taken from parents or guardians of all the study participants. As per hospital criteria, all essential investigations like complete blood count, platelet count,rothrombin time (PT) and activated partial thromboplastin Time (APTT)to decide coagulopathy were ordered. In children with anemia (hemoglobin < 10 g/dl), serum iron, serum ferritin, serum & red cell folate and serum vitamin B12 were asked. All the investigations were done from institute's central laboratory.

All the data was recorded on a predesigned proforma. SPSS version 21.0 was used or data handling and analysis. Frequency and percentages were calculated for qualitative variables like gender, thrombocytosis, leucopenia, anemia, coagulopathy, iron deficiency and vitamin B12 deficiency whereas mean and standard deviations were calculated for quantitative variables like age.

RESULTS

Out of a total of 120 children, there were 68 (56.7%) male and 52 (43.3%) female, representing a male to female ratio of 1.31:1. Mean age was noted to be 9.21 years with a standard deviation of 2.6 years. There were 52 (43.3%) children between the age of 1 to 4 years, 38 (31.7%) above 4 and up to 8 years of age and 30 (25.0%) above 8 and up to 12 years of age.

In terms of overall hematological manifestations, anemia was found in 113 (94.2%) children, thrombocytosis 93 (77.5%), leucopenia 12 (10.0%) and coagulopathy in 10 (8.3%).

Anemia only was noted in 23 (19.2%) children, thrombocytosis only 2 (1.7%), leucopenia only 3 (2.5%), coagulopathy only 2 (1.7%), anemia plus thromobocytosis 73 (60.8%), anemia plus leucopenia 9 (7.5%) and anemia plus thromocytosis plus coagulopathy in 8 (6.7%). When children with anemia (n=113) were further evaluated for etiology, iron deficiency anemia was observed in 83 (73.5%), vitamin B12 and folate deficiency anemia 12 (10.6%) and double deficiency anemia in 18 (15.9%).

When patients were distributed in terms of modified marsh scoring, 37 (30.8%) were type 3a, 36 (30.0%) type 3b, 28 (23.3%) type 3c, 17 (14.2%) type 2 and 2 (1.7%) type 1.

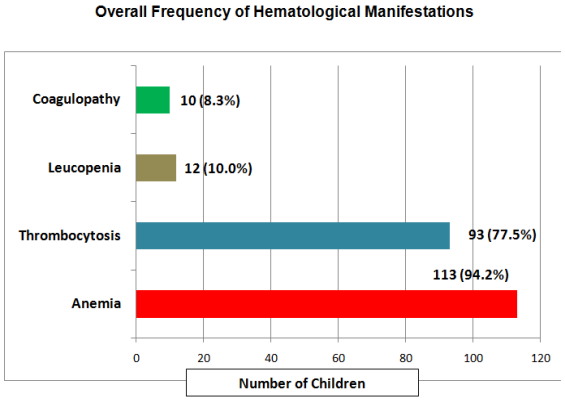

Figure No.1: Overall Frequency of Hematological Manifestations

Table No.1: Hematological Manifestations Amongst Children with CD

Hematological Manifestations	Number (%)
Anemia only	23 (19.2%)
Thrombocytosis only	2 (1.7%)
Leucopenia only	3 (2.5%)
Coagulopathy only	2 (1.7%)
Anemia + thrombocytosis	73 (60.8%)
Anemia + leucopenia	9 (7.5%)
Anemia + thrombocytosis + coagulopathy	8 (6.7%)

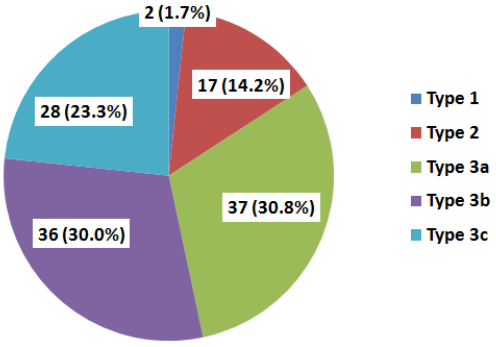

Figure No.2: Distribution of Children According to Modified Marsh Score

DISCUSSION

CD is known to be a systemic disorder that has several hematological manifestations.[14]In Pakistan, not many studies have evaluated the hematological aspects of CD and this study stands one of the very few done in this regard.

Over the years, many hematological features of CD have been described by researchers but anemia due to iron, folic acid and / or vitamin B12 malabsorptionhas been noted to be the most frequent complication associated with CD and most of the patients have anemia at the time of CD diagnosis.[16]We studied the most frequent hematological findings associated with CD, like anemia, thrombocytosis, leucopenia as well as coagulopathy.

Lots of difference persists in terms of presence of anemia in CD.[14] In the current study, we noted anemia to be present in 94.2% children. Our results are very consistent with another local study conducted by Saqlain N et al[16] where they found anemia to be present in 93% of children with CD. Mansoor A et al[15] noted that 90% of the CD children had anemia at the time of diagnosis. Another local study conducted by Ayesha H and colleagues[17] showed that 95% of the children had iron deficiency anemia. Most of the children with CD in our study, 73 (60.8%) had thrombocytosis along with anemia that could possibly be because of iron deficiency. Another study local study from Lahore[16] recorded that 64% of the children with CD had thrombocytosis that is very close to what we found in the current study. Only 2 (1.7%) children in our study had thrombocytosis only and this pattern has also been found in an earlier study where it was noted that only 2.9% children with CD had thrombocytosis alone while most others had thrombocytosis along with anemia.[16] Iron deficiency along with chronic inflammation can possibly be the reasons of thrombocytosis in children with CD but the precise etiology is still unknown. The previous work done has also noted thrombocytosis to be present in as much as 60% of the CD cases and it has been found more frequent than thrombocytopenia.[14,17]

Leucopenia has been shown to be a rare disorder[18] in some of the studies evaluating CD cases but in the current study, we got leucopenia to be present in 12 (10.0%) of the cases. Our results are similar to what has been found by Saqlain N et al[16] where they found that 105 of children with CD had leucopenia. Another study done by Halfdanarson TR and coworkers[14] noted 9% of children with CD had leucopenia. Leucopenia has been found to be accompanied with anemia in most of the cases with CD.

Coagulopathy was another hematological disorder found in our study and we noted 10 (8.3%) children with CD to have it. None of the children presented to us with any kind of active bleeding. Coagulopathy only was reported in 2 (1.7%) children in our study while all others had anemia as well thrombocytosis as well. The probable mechanism behind all this could be decreased vitamin K synthesis because of malabsorption as well as chronic diarrhea. Deficiency in the levels of vitamin K could lead in to decrease in vitamin k dependent factors that may go on to prolong PR as well as APTT.[16] Intramuscular hemorrhage has also been noted in one of the findings.[5]

As per Modified Marsh Score, we found that most of the CD children had type 3 disease. These results are aligned with those found earlier in other local studies.[14,16]

In our setting, CD is not a likely diagnosis when children present having chronic diarrhea along with mild to moderate villi blunting. Traditionally, enteric etiology of tropical sure are thought to be the usual causes in these cases.[16]As the diagnosis of CD is not always in time and with advancement in the disease, hematological manifestations are found to be more pronounced[19] as was found in the present study. CD can also present with hematological abnormalities as has been advocated in the past[20] so children presenting with these common hematological abnormalities should always be assessed thoroughly to rule out any possible diagnosis of CD.

CONCLUSION

In children, hematological abnormalities related celiac disease are quite common. Anemia is the commonest hematological finding that is mostly found accompanying thrombocytosis. In children with anemia, iron deficiency anemia is noted to be the most common etiology which should be managed with iron supplementation coupled with gluten free diet.

Author's Contribution:

Concept & Design of Study:	Bushra Madni
Drafting:	Kaleem Akhtar Malhi, Fazal ur Rehman
Data Analysis:	Khurram Shahnawaz, Farhan Zahoor, Beenish Bashir Mughal
Revisiting Critically:	Bushra Madni, Kaleem Akhtar Malhi
Final Approval of version:	Bushra Madni

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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