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THE OCCURRENCE OF CELIAC DISEASE IN NUTRITIONAL ANEMIA PATIENTS; A CROSS SECTIONAL STUDY

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Abstract:
Objectives: *The aim of our study was to find out the occurrence of celiac disease in nutritional anemia patients.*
Study design*: A cross sectional study.*
Time and duration: *This study was conducted in Medical department, Ayub Teaching Hospital Abbottabad for the duration of eight months starting from 1st January, 2020 to 31st August, 2020.*
Methodology: *In this study we included a total number of 100 patients who were diagnosed with nutritional anemia. Hematologic work completed such as peripheral smear, blood complete picture (Blood CP), folate, iron and B12 levels. By gender distribution, Anemia defined in male is Hb <13 g/dL and Anemia defined in females is <12 g/dL. In this study nutritional cases like folate, iron or shortage of B12 in minor anemia cases were included and then the Anti-tissue transglutaminase antibody (anti tTG) antibody testing was carried out. The Anti-tissue transglutaminase antibody (anti tTG) antibody had taken for those cases which tested positive by Jejunal biopsy. We established a Celiac disease (CD) for the diagnosis of histopathology in the behalf of positive findings. A pre- designed proforma was used for the collection of data. SPSS v.20 was used for the analysis of collected data.*
Results*: According to the study the frequency of celiac disease was in 12 patients. According to the findings of our study there were 10 positive cases of Iron Deficiency Anemia (IDA) out of 12 celiac disease patients. From the remaining two patients, one patient presented concomitant B12 + folate deficiency and one patient showed dimorphic anemia.*
Conclusion*: In our study we concluded that in Pakistan 12% of Pakistani may be found in Celiac disease who present nutritional anemia. Consequently, those patients should be tested for celiac disease who do not respond for standard anemia.*
Keywords: *Celiac Disease (CD), Iron Deficiency Anemia (IDA), Anti-Tissue Transglutaminase Antibody (Anti-tTG).*

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INTRODUCTION:

Celiac disease (CD) is a gluten sensitive enteropathy characterized by villous atrophy of the small intestine in genetically susceptible individuals. Its worldwide prevalence is estimated to be somewhere between 0.5-1% [1]. The exact prevalence of celiac disease in Pakistan is unknown. HLA DQ2 and DQ8 subtypes genetically predispose the individual to celiac disease [2]. The pathophysiology behind celiac disease involves abnormal interaction between gluten, immune system and the gut leading to destruction of villi. Villous atrophy in celiac disease renders absorption of various nutrients ineffective. Iron, B12, folic acid and fat-soluble vitamin deficiencies are particularly noticeable [3]. Patients with classical celiac disease present with gastrointestinal symptoms of malabsorption i.e., diarrhea, abdominal pain and weight loss. However, majority of the cases are asymptomatic. Estimates show that up to 90% of the cases remain undiagnosed and the classic cases just represent the tip of iceberg [4]. Diagnosis of celiac disease involves antibody testing and histopathology. Anti-Tissue-transglutaminase antibody is the best initial test. A positive test has to be confirmed with jejunal biopsy which is the gold standard investigation for diagnosis of celiac disease [5]. Anemia is frequently seen in celiac disease owing to greatly reduced iron, folic acid and B12 absorption. It has been estimated that iron deficiency anemia is present in up to 80 to 90% of patients with celiac disease [6]. What is important to recognize is the fact that sometimes the sole presentation of celiac disease is that of anemia without any diarrheal symptoms [7]. This Iron Deficiency Anemia (IDA) is unique in a way that it does not respond to iron supplementation therapy as the absorptive surface areas has been greatly reduced. Its management involves gluten free diet and can take up to 1 year for complete recovery. Celiac disease (CD) is a gluten sensitive enteropathy characterized by villous atrophy of the small intestine in genetically susceptible individuals. Anemia is frequently seen in celiac disease owing to greatly reduced iron, folic acid and B12 absorption. Presence of a dimorphic picture on blood smear is highly suggestive of concomitant iron and folate / B12 deficiency [8]. As vitamin B12 is absorbed in the terminal ileum, it is hard to explain its deficiency in celiac disease. Dahele et al [9]. reported that 56% of the anemic patients 30% of the nonanemic patients with Celiac disease (CD) were vitamin B12-deficient.

A recent study by Shahzad et al [10]. reported a prevalence of 12.99% in Iron Deficiency Anemia (IDA) patients. An Iranian study by Baghbanian et al [6]. reported a prevalence of 10.4% amongst Iron Deficiency Anemia (IDA) patients. Kavimandan et al [11] found out Celiac disease (CD) was prevalent 10.42% of the patients with nutritional anemia. Local studies are lacking in this area so we decided to conduct this study with the principal aim of determining the prevalence of Celiac disease (CD) in patients with nutritional anemia.

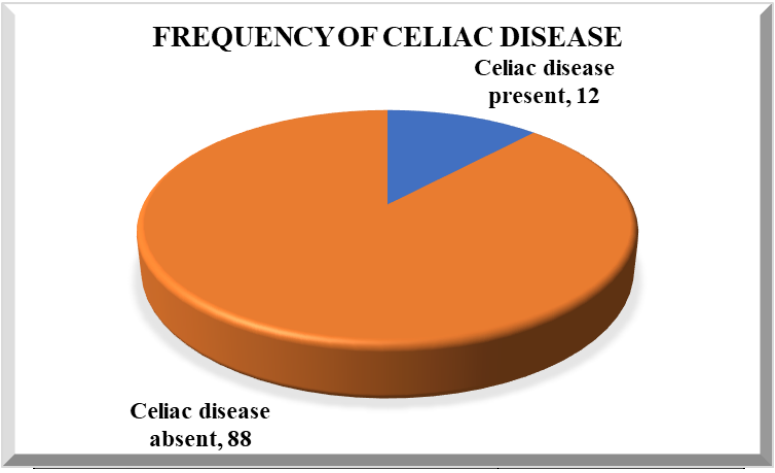
METHODOLOGY:

This cross-sectional study was conducted in Medical department, Ayub Teaching Hospital Abbottabad for the duration of eight months starting from 1st January, 2020 to 31st August, 2020. The sample size was calculated using Open Epi calculator with the statistical assumptions of 6% alpha error and 95 % confidence interval taking prevalence of celiac disease to be 10.42%6 amongst patients with nutritional anemia and comes out to be at least 100 patients for this study. Non probability purposive sampling. After getting ethical approval from IRB, 100 consecutive patients presenting with nutritional anemia were enrolled. Patients having malignancy, chronic diseases (IBD, tuberculosis, autoimmune diseases), pregnancy or any primary hematological disorder were excluded from the study. Informed consent was taken in each case. Anemia was defined as Hb <13 g/dL in males and <12 g/dL in females. Only cases with anemia secondary to iron, folate or B12 deficiency i.e., nutritional causes were included in the study. Detailed clinical history was taken from each patient. Complete hematologic workup was done including blood CP, peripheral smear, iron, folate and B12 levels. Patients were then subjected to certain screening and diagnostic tests. Blood sample was withdrawn from a peripheral vein followed by testing for Anti-tissue transglutaminase antibodies (tTG) antibody. Jejunal biopsy was taken in all those cases which tested positive for Anti-tissue transglutaminase antibodies (anti tTG) antibody. The specimens were inspected by a histopathologist having experience of at least 5 years. A diagnosis of Celiac disease (CD) was established upon positive histopathology findings of crypt hyperplasia and villous atrophy. A pre- designed proforma was used for the collection of data. SPSS v.20 was used for the analysis of collected data.

Mean and standard deviation was calculated for all quantitative variables like age and Hb level etc. Frequency and percentage were calculated for all qualitative variables like gender, cause of nutritional anemia, prevalence of celiac disease etc. Data was represented as pie charts and bar graphs.

RESULTS:

100 patients took part in the study comprising of 45 males and 55 females. Mean age of the patients was 34.12 ±11.23 years. A mean Hb of 8.71 ±1.23g/dL was observed (Table 1).



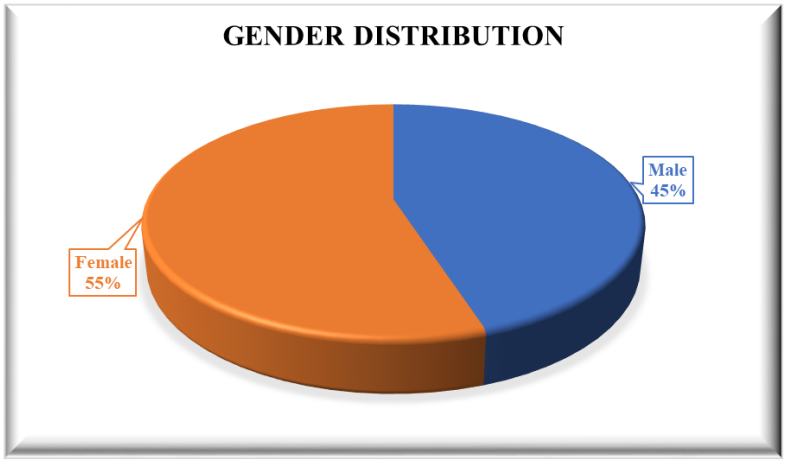


Table No 02: Frequency of Celiac Disease in Patients with Nutritional Anemia

Nomenclature	Frequency
Celiac disease present	12
Celiac disease absent	88
Total	100

The prevalence of Celiac disease (CD) was found to be 12% (table 02). Initially 14 patients tested positive for anti-tTG antibody. Upon further testing only 12 of them showed the characteristic biopsy findings necessary to qualify for diagnosis of celiac disease. IDA was the most frequent cause of anemia present in 85% of the cases. 5 patients had folate deficiency; 3 had B12 deficiency whereas 6 patients showed concomitant B12 and folate deficiency. One patient showed dimorphic blood picture. 10 out of 12 celiac disease cases were having Iron Deficiency Anemia (IDA); 1 each showed dimorphic picture and concomitant B12 + folate deficiency respectively with none of the Celiac disease (CD) patients having folate or B12 deficiency alone (table 03).

Table No 03: Distribution of Celiac Disease among Various Nutritional Anemias

Nutritional anemias	Celiac disease	
	Present	Absent
Iron deficiency anemia	10	75
Folate deficiency anemia	0	5
B12 deficiency anemia	0	3
Concomitant B12 + folate deficiency	1	5
Dimorphic anemia	1	0

DISCUSSION:

Anemia is one of the common extraintestinal manifestation of celiac disease. Often, the only symptoms present are those of anemia without any characteristic features of celiac disease like diarrhea etc. This anemia is resistant to standard treatment because the problem lies in the absorptive surface leading to reduced absorption of vital nutrients. The only possible cure is gluten free diet. Therefore, it is important to screen all those patients with anemia who do not seem to respond to routine management. Hence, we conducted this study to determine the prevalence of Celiac disease (CD) in anemia patients in our local population. Our study reported a prevalence of 12% for Celiac disease (CD) amongst nutritional anemia patients. This was comparable to the findings of Kavimandan et al [11] who reported a prevalence of 10,42%? Some other studies conducted on Iron Deficiency Anemia (IDA) patients reported an overall prevalence of 12.99% and 10.4% respectively [9-10]. Our study showed that 10 out 0f 85 Iron Deficiency Anemia (IDA) patients (11.76%) were having celiac disease. Mean age of patients in our study was 34.12±11.23 years which was quite close to that reported by Kavimandan et al [11] i.e., 32.1±13.1 years. In our study, 85% of the subjects had Iron Deficiency Anemia (IDA). This was consistent with the findings of Kavimandan et al [11] who showed that 83.3% of patients were having Iron Deficiency Anemia (IDA)? Megaloblastic anemia was seen in 14% (5%: Folate; 3%: B12; 6%: concomitant B12+Folate deficiency) patients which was comparable to the findings of Kavimandan et al [11] who reported a frequency of 11.46%. Mean Hb observed in our study was 8.71±1.03 g/dL. This was quite similar to the value reported by Shahzad et al [9] who reported a mean Hb of 8.81±1.23 g/dL [11]. We relied upon jejunal biopsy findings in order to diagnose the patient with celiac disease. However, we did not take biopsy of all the 100 patients as it was not feasible. Instead, we screened the patients using serologic testing for Anti-Tissue Transglutaminase Antibody (anti-tTG) antibody and only performed jejunal biopsy on patients who tested positive on serology. 14 of the patients screened positive for celiac disease initially however the diagnosis could be validated in only 12 of those 14 cases.

A similar trend was noticed by Kavimandan et al [11]. There were certain limitations to our study. Effect modifiers and confounders (gender, cause of nutritional anemia) were not controlled through stratification. The sample size was small and future large-scale surveys are warranted to estimate the true prevalence of Celiac disease (CD) amongst anemia patients and screening guidelines updated accordingly.

CONCLUSION:

Celiac disease may be found in up to 12% of Pakistanis presenting with nutritional anemia. Hence, all those patients not responding to standard anemia treatment should be screened for celiac disease.

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