Association of Malabsorption and Anaemia in Adults in Tertiary Care Hospital

Altaf Hussain, Muhammad Hafeez, Muhammad Naveed, Syed Umer Shah, Muhammad Shahid Khan*, Ahmed Ammar Cheema

Pak Emirates Military Hospital/National University of Medical Science (NUMS) Rawalpindi Pakistan, *HITEC Institute of Medical Sciences, Taxila/
National University of Medical Science (NUMS) Pakistan

ABSTRACT

Objective: To determine the association of malabsorption in celiac disease with anaemia and other sociodemographic factors at a tertiary care hospital in Pakistan.

Study Design: Cross sectional study

Place and Duration of Study: Department of General Medicine, Pak Emirates Military Hospital Rawalpindi-Pakistan, from Jul to Dec 2019.

Methodology: A total of 300 adults were included in the study, 150 cases were patients with the diagnosis of celiac disease, and the other 150 were controls without celiac disease. Celiac disease was diagnosed based on biopsy findings by a consultant gastroenterologist. Defined was defined based on haemoglobin levels. In addition, the relationship between age, gender, anaemia, and the presence of comorbidities was assessed with the presence of celiac disease among the adults included in the study.

Results: Out of 300 cases and controls, 116 (38.7%) patients were males, and 184 (61.3%) were females. One hundred and forty-eight (49.3%) did not show the presence of anaemia, while 152 one hundred and fifty-two (50.7%) showed the presence of anaemia. we found a statistically significant difference in cases and controls regarding the presence of comorbidities and the presence of anaemia ($p<0.05$).

Conclusion: Patients with celiac disease showed a greater frequency of anaemia as compared to those who were not having celiac disease. Therefore, patients with celiac disease are at high risk for developing anaemia, or patients with anaemia should be screened for malabsorption problems. In addition, patients with celiac disease were also at high risk for acquiring other systemic disorders.

Keywords: Anemia, Celiac disease, Malabsorption.

INTRODUCTION

Anaemia has been a problem faced by patients in all parts of the world, especially in the population of developing countries with limited resources due to nutritional problems or underdiagnosed medical conditions leading to various kinds of anaemias.[1] A number of medical, gastroenterological and neurological illnesses affect the blood counts and may lead to anaemia. Chronic renal disease, endocrinopathies, liver disease, autoimmune diseases and migraine are some of the diseases linked in the past with the presence of anaemia among the patients.[2-5]

Diseases linked to the GI tract are notorious for predisposing the individual to develop iron deficiency anemias.[6,7] A huge number of patients who have Crohn's disease or ulcerative colitis also suffer from the extra-intestinal manifestations, including the anemias.[8] Sometimes it is the lesion in GI tract itself which cause malabsorption of the nutrients and lead to anaemias or sometimes it is the immune-based phenomenon which may lead to both GI symptoms and different GI manifestations including the reduction in blood counts.[9]

Celiac disease has been studied from an anaemia perspective in many studies done in the recent past all around the world. Berry *et al*. concluded that anaemia was detected in 96 out of 103, meaning 93.2% of patients' haemoglobin was less than normal. Iron deficiency was the commonest type, followed by the B 12 deficiency and folate deficiency.[10]

As we belong to an underdeveloped country where health care facilities are not within reach of every citizen and gastroenterologists are limited in number working in major cities only, laboratory or histological diagnosis is not possible early on for all patients of celiac disease. However, if anaemia turns out to be closely related to celiac disease, then high-risk patients could be picked up early and screened for this multi-system disease. Therefore, we planned this study to examine the association of malabsorption in

Correspondence: Dr Altaf Hussain, Department of Medicine, Pak Emirates Military Hospital Rawalpindi Pakistan
Received: 17 Jun 2020; revision received: 23 Jul 2020; accepted: 28 Jul 2020

celiac disease with anaemia and other sociodemographic factors at a tertiary care hospital in Pakistan.

METHODOLOGY

This cross sectional study was conducted at the Department of General Medicine, Pak Emirates Military Hospital Rawalpindi in collaboration with the Medicine Department, Combined Military Hospital Rawalpindi, from July to December 2019. The sample size was calculated by WHO Sample Size Calculator using the population prevalence of anaemia as 4.8%.[11] Nonprobability consecutive sampling technique was used to gather the cases of celiac disease from both departments. The Ethical Review Board Committee of the hospital gave the ethical approval for this study (via IREB letter number A/123/EC 130).

Inclusion Criteria: All patients between 18 and 60 years with celiac disease diagnosed by a consultant medical specialist or gastroenterologist based on the clinical picture, radiological findings, colonoscopy findings and histopathology report were included in the study. Controls were selected from the community. They were healthy adults matched for age and gender with the cases.

Exclusion Criteria: Patients with anaemias prior to the diagnosis of celiac disease, malignancies (solid or haematological), inflammatory bowel diseases, severe infection or any organ failure in the past six months were excluded from the study. Patients who were pregnant or breastfeeding, had B-12 or folate deficiency or replacement therapy, had recent surgery, had NSAIDs abuse or had any autoimmune disorder in which follow-up was not possible were also not included in our study. Exclusion criteria for cases were also valid for the exclusion of controls.

Written informed consent was taken from all the potential participants of this study, whether cases or controls, before the start after a complete description of the study. Patients of celiac disease fulfilling the inclusion mentioned earlier and exclusion criteria coming to medical or gastroenterology OPD at Military Hospital Rawalpindi were included in the study after all the ethical formalities. Venous blood was taken from the participants between 9-11am after 12 hours of fasting. Complete blood count (CBC) was measured. CBC was measured using a flow cytometer and an automated analyzer. Variables in the study included age, gender, presence of anaemia and presence of comorbid diseases other than those mentioned in the exclusion criteria. Common comorbid diseases included in analysis were diabetes mellites, asthma hypertension.

Iron deficiency anaemia was defined as blood haemoglobin values of <12 g/dl found in the routine complete blood count performed at the laboratory of our hospital.[1,12] All the cases and control underwent this investigation from the same laboratory and machine.

Characteristics of participants and the distribution of the cases and controls were described by using descriptive statistics. Participants were resulted by categorical compared as cases and controls. Chi square test was performed to evaluate the relationship between age, gender, presence of anaemia and presence of comorbid illnesses with celiac disease (cases). All statistical analysis was performed using Statistics Package for Social Sciences (SPSS) version 24.00. Differences between groups were considered significant if p-values were less than or equal to 0.05.

RESULTS

A total of 300 participants were recruited, having an equal number of cases of celiac disease and healthy controls without the diagnosis of celiac disease. Out of 300 cases and controls, 116 (38.70%) patients were males, and 184 (61.30%) were females. One hundred and forty-eight (49.30%) did not show the presence of anaemia, while one hundred and 52 (50.70%) showed the presence of anaemia (Table).

Table: Characteristics of the Cases and Control Included in the Study (n=300)

Characteristics	Frequency (%)
Age (years)	
Mean±SD	40.15±6.45
Range (min-max)	18 years-64 years
Gender	
Male	116 (38.70)
Female	184 (61.30)
Presence of Anemia	
No	148 (49.30)
Yes	152 (50.70)
Mean Duration of Celiac Disease	4.27±2.35 years
Comorbid Medical Illness	
No	217 (72.30)
Yes	83 (27.70)
Comorbid Illnesses	
Diabetes mellitus	39 (46.90)
Hypertension	26 (31.30)
Asthma	11 (13.20)
Others	07 (8.40)

Diabetes mellitus (46.90%) was the commonest comorbid illness among the study participants, followed by hypertension (31.30%). After applying the chi-square test, we found a statistically significant difference in cases and controls regarding the presence of comorbidities and the presence of anaemia. At the same time, age and gender had no relationship with

the diagnosis of celiac disease among the study participants (*p*-value 0.208 and 0.118, respectively).

DISCUSSION

Nutrition and nutritional parameters have been a neglected area in the health sector of our country. However, some diseases directly affect an individual's nutritional status and lead to undesirable consequences.[13] Celiac disease is one of those diseases directly linked with nutrition-related problems due to its pathophysiology and management plan. With the revolution in gastroenterology and immunology and the availability of the latest noninvasive and invasive investigations, celiac disease is not an uncommon diagnosis.[14-16] The prevalence of celiac disease in our part of the world is around 0.6%.[17] Anemia could be a consequence of celiac disease or may be comorbidity complicating the celiac disease. For more precise results and to establish the risk factors, we adopted a cross-sectional study design to determine the association of malabsorption in celiac disease with anaemia and other sociodemographic factors at a tertiary care hospital in Pakistan.

Spencer *et al*. in their survey on primary care physicians regarding screening of anaemia patients for celiac disease, concluded that primary care physicians are under-testing for celiac disease in patients with anaemia, regardless of age, gender, race, or post-menopausal status. In addition, most primary health care doctors surveyed reported they do not strictly adhere to established guidelines regarding a confirmatory duodenal biopsy in a patient with positive serology for celiac disease.[18] This shows a big lapse in the health care system of the west. Our study from the developing country concluded that anaemia had been strongly associated with celiac disease, so anaemic patients must be screened for this disease, especially the resistant cases or cases with more than one risk factor.

Rodrigues *et al*. conducted a very interesting study regarding anaemia and gastroenterology referrals. Usually, it is presumed that patients referred for invasive investigations and specialist review would have undergone all the baseline tests, especially those referred to gastroenterology, the speciality linked closely to nutritional deficiency. Nevertheless, the reality was different from the assumption.[19] Most patients had incomplete investigations, and those later diagnosed with various GI diseases, including celiac disease, were not screened for anaemia. Therefore, our study also highlights that anaemia and celiac disease should be considered together, and if you find one, do consider the possibility of the other.

Freeman in 2015 published a comprehensive review highlighting all the possible links between anaemia and celiac disease. He mentioned that anaemia could cause or consequence autoimmune bowel diseases. Celiac disease may impair the bowels' ability to absorb iron, resulting in low haemoglobin levels inside the body. Such patients should also be screened for all the other comorbid gut conditions.[20] Our study also supported this fact and emphasized the holistic approach of the physician so that he should not miss the association between anaemia and celiac disease.

LIMITATIONS OF STUDY

A cross-sectional study design could ascertain the association, and a logical conclusion could be drawn, but still, a prospective cohort study could answer the question more precisely and accurately. Only two military setups were targeted for data collection, which becomes another limitation in generalizing the results of this study. Large multi-center studies involving public hospitals and following up on the patients for a long time may generate results which could be generalized to the population.

CONCLUSION

Patients with celiac disease showed a greater frequency of anaemia as compared to those who were not having celiac disease. Therefore, patients with celiac disease are at high risk for developing anaemia, or patients with anaemia should be screened for malabsorption problems. In addition, patients with celiac disease were also at high risk for acquiring other systemic disorders.

Conflict of Intrest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

AH: Conception, study design, drafting the manuscript, approval of the final version to be published.

MH & MN: Critical review, drafting the manuscript, approval of the final version to be published.

SUS & MSK: Data analysis, data interpretation, approval of the final version to be published.

AAC: Data acquisition, Critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Soofi S, Khan GN, Sadiq K, Atif S, Habib A. Prevalence and possible factors associated with anaemia, and vitamin B12 and folate deficiencies in women of reproductive age in Pakistan: analysis of national-level secondary survey data. BMJ Open 2017; 7(12): e018007. doi:10.1136/bmjopen-2017-018007.

2. Zahra K, Mahmoud M, Mahdi M. Shahram E, Maji A, The Relationship between Migraine Headache and Iron Deficiency Anemia in Patients Referred To Neurology Clinic of Shahrekord University of Medical Sciences. Iran J Nurs 2010; 23 (64): 37-43.

3. Wimbley TD, Graham DY. Diagnosis and management of iron deficiency anemia in the 21st century. Therap Adv Gastroenterol 2011; 4(3): 177-184. doi: 10.1177/1756283X11398736.

4. Gkamprela E, Deutsch M, Pectasides D. Iron deficiency anemia in chronic liver disease: etiopathogenesis, diagnosis and treatment. Ann Gastroenterol 2017; 30(4): 405-413.

5. Aoun M, Karam R, Sleilaty G, Antoun L, Ammar W. Iron deficiency across chronic kidney disease stages: Is there a reverse gender pattern? PLoS One 2018; 13(1): e0191541. doi: 10.1371/journal.pone.0191541.

6. Cui G, Yuan A. A Systematic Review of Epidemiology and Risk Factors Associated With Chinese Inflammatory Bowel Disease. Front Med (Lausanne) 2018; 5(1): 183-186.

7. Misra R, Faiz O, Munkholm P, Burisch J, Arebi N. Epidemiology of inflammatory bowel disease in racial and ethnic migrant groups. World J Gastroenterol 2018; 24(3): 424-437. doi: 10.3748/wjg.v24.i3.424.

8. Vavricka SR, Schoepfer A, Scharl M, Lakatos PL, Navarini A, Rogler G. Extraintestinal manifestations of inflammatory bowel disease. Inflamm Bowel Dis 2015; 21(8): 1982-1992. doi: 10.1097/MIB.0000000000000392.

9. Yang BR, Choi NK, Kim MS, Chun J, Joo SH, Kim H, et al. Prevalence of extraintestinal manifestations in Korean inflammatory bowel disease patients. PLoS One 2018; 13(7): e0200363. doi:10.1371/journal.pone.0200363

10. Berry N, Basha J, Varma N, Varma S, Prasad KK, Vaiphei K, et al. Anemia in celiac disease is multifactorial in etiology: A prospective study from India. JGH Open 2018; 2(5): 196–200. doi:10.1002/jgh3.12073.

11. Mahadev S, Laszkowska M, Sundström J, Björkholm M, Lebwohl B, Green PHR, et al. Prevalence of celiac disease in patients with iron deficiency anemia - a systematic review with meta-analysis. Gastroenterol 2018; 155(2): 374-382. doi: 10.1053/j.gastro.2018.04.016.

12. Abdalla A, Saifullah SM, Osman M, Baniya R, Sidahmed S, LaChance J, et al. Prevalence of occult celiac disease in females with iron deficiency in the United States: an NHANES analysis. J Community Hosp Intern Med Perspect 2017; 7(6): 347–350. doi:10.1080/20009666.2017.1396169.

13. Rajalahti T, Repo M, Kivelä L, Huhtala H, Mäki M, Kaukinen K, et al. Anemia in Pediatric Celiac Disease: Association With Clinical and Histological Features and Response to Gluten-free Diet. J Pediatr Gastroenterol Nutr 2017; 64(1): e1-e6. doi: 10.1097/MPG.0000000000001221.

14. Khatoon S, Ahmed A, Yousaf S. Iron Deficiency Anaemia in Pakistan: Celiac Disease An Underlying Cause. J Ayub Med Coll Abbottabad 2018; 30(3): 372-376.

15. US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, Curry SJ, Barry MJ, Davidson KW, et al. Screening for Celiac Disease: US Preventive Services Task Force Recommendation Statement. JAMA 2017; 317(12): 1252-1257. doi: 10.1001/jama.2017.1462.

16. Kaitha S, Bashir M, Ali T. Iron deficiency anemia in inflammatory bowel disease. World J Gastrointest Pathophysiol 2015; 6(3): 62-72. doi: 10.4291/wjgp.v6.i3.62.

17. Singh P, Arora A, Strand TA, Leffler DA, Catassi C, Green PH et al. Global prevalence of celiac disease: systematic review and meta-analysis. Clin Gastroenterol Hepatol 2018; 16(6): 823-836.e2. doi: 10.1016/j.cgh.2017.06.037

18. Spencer M, Lenhart A, Baker J, Dickens J, Wissman J, Read AJ, et al. Primary care physicians are under-testing for celiac disease in patients with iron deficiency anemia: Results of a national survey. PLoS One 2017; 12(9): e0184754. doi:10.1371/journal.pone.0184754

19. Rodrigues JP, Pinho R, Silva J, Ponte A, Sousa M, Silva JC, et al. Appropriateness of the study of iron deficiency anemia prior to referral for small bowel evaluation at a tertiary center. World J Gastroenterol 2017; 23(24): 4444–4453. doi:10.3748/wjg.v23.i24.4444

20. Freeman HJ. Iron deficiency anemia in celiac disease. World J Gastroenterol 2015; 21(31): 9233–9238. doi:10.3748/wjg.v21.i31.9233.

....