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Prevalence and Risk Factors for Anemia in Inflammatory Bowel Disease: A Hospital Based Study from Saudi Arabia

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Abstract

Background: Anemia is a common extra-intestinal manifestation of inflammatory bowel disease. The magnitude of anemia in Inflammatory Bowel Disease (IBD) patients and the risk factors were not previously studied from Saudi Arabia.

Objectives: Objectives of the study were to find prevalence of anemia, etiology and its risk factors.

Design: Retrospective cohort study

Setting: Hospitalized patients at King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia

Patients and methods: The data pertaining to anemia was collected from IBD patients between 2000 to 2018, at the time of first presentation to the hospital, and the lowest hemoglobin during the follow up. Anemia was diagnosed if hemoglobin (Hb) level was below 13 g/dl in males and below 12 g/dl in females. Severe anemia was defined as Hb <10 g/dl for both genders. Patients were further classified into iron deficiency anemia, Anemia of Chronic Disease (ACD), based on c-reactive protein and serum ferritin levels. Vitamin B12 deficiency was diagnosed if the vitamin B12 level was <150 pg /ml.

Main outcome measures: Prevalence of anemia, etiology and its risk factors in IBD patients

Results: From 190 patients IBD screened, 109 patients were included, 56% were males. Crohn's disease was in 77 (70.6%) and ulcerative colitis in 32 patients (29.4%) At the time of first presentation to the hospital, 51.4% of patients had anemia, and during the median follow-up of 759 days, 62.4% of our cohort were diagnosed with severe anemia. Iron deficiency anemia was diagnosed in 13.8%, ACD was diagnosed in 3.7%, and iron deficiency plus ACD was diagnosed in 2.8%. From 101 patients, 26 of them (23.9%) had vitamin B-12 deficiency. No identifiable risk factors were found at the time of presentation for anemia in IBD population. Binary logistic regression analysis showed female gender (p-value 0.001) and anemia at presentation (p-value 0.0001) were risks for subsequent development of severe anemia.

Conclusion: Anemia in IBD population is highly prevalent. Female gender and anemia at presentation are risks for the development of severe anemia in IBD population.

Limitations: Hospital based retrospective study.

Keywords

Inflammatory Bowel Diseases (IBD) • Extra-intestinal manifestations• Anemia

Abbreviations

IBD: Inflammatory Bowel Diseases; CRP: C-Reactive Protein; Hb: Haemoglobin; UC: Ulcerative Colitis; CD: Crohn's Disease; ACD: Anemia of Chronic Disease

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Introduction

Inflammatory Bowel Diseases (IBD) include Cohn's disease and Ulcerative colitis. Crohn's disease is characterized by transmural inflammation of the bowel wall and it may affect any part of the gastrointestinal tract while ulcerative colitis is characterized by inflammation limited to the colonic mucosa [1,2]. IBD is characterized by frequent relapses and remissions, and associated morbidities.

Anemia is most common extra-intestinal manifestations in IBD. Prevalence of anemia in IBD in the outpatient setting has been reported in the range of 9% to 73%, and it is 32% to 74% in the inpatient settings [3,4]. Patients with anemia have poor quality of life, decreased physical performance, changes in emotional and cognitive functions, the ability to work, and they are at risk of increased hospitalization and added healthcare costs [1].

Iron deficiency anemia and anemia of chronic illnesses are the two most common types of anemia in IBD. Other causes of anemia include vitamin B12 (cobalamin Cbl) deficiency, folate deficiency, and drug induced anemia [1].

Disease burden and incidence of IBD has been steadily increasing

in Saudi Arabia [5,6]. Accordingly, an increase in the prevalence and the incidence of morbidities and mortalities related to systemic complications and extra-intestinal manifestations of IBD are expected to increase among IBD patients. In general, systemic complications and extra-intestinal manifestations of IBD are underdiagnosed, underreported or undertreated.

There have been studies from Europe, North and South America of anemia in IBD [3,4,7]. Patient characterization and disease behavior might be different in our population and the facts found from studies from Europe and America may not be applicable to our patients. Therefore, we conducted a cross-sectional cohort study in hospitalized patients with IBD to assess the etiology, prevalence, and risk factors of anemia in IBD in Saudi Arabia.

Methods

Study design

A retrospective cohort study was conducted.

Settings

We reviewed IBD (Crohn's and UC) patients' data from 2000 to 2018. Study was conducted in King Faisal specialist hospital and Research Centre, Riyadh, Saudi Arabia. Most of the patient's data were selected while they were inpatient in the hospital.

Patients and methods

Patients with confirmed diagnosis of CD or UC based on accepted diagnostic criteria were included. Most of the patients had a diagnosis of CD or UC for more than a year before the recruitment. We included those above the age of 18 years. Pregnant and lactating women, patients with other significant medical or surgical illnesses were excluded.

Outcome measures

The parameters for anemia work up included complete blood count, ferritin, serum iron, total iron binding capacity, transferrin saturation, CRP, vitamin B12 levels, red cell folate levels, etc. These results were collected at the time of the first presentation of the patient to our hospital and the lowest hemoglobin during the follow up.

Anemia was diagnosed if hemoglobin (Hb) level was below 13 g/dl in males and below 12 g/dl in females. Severe anemia was defined as Hb <10 g/dl for both genders. Patients were classified into iron deficiency anemia if the serum ferritin was below 30 microgram/L and CRP below 6 mg/L or CRP above 6 mg/L and serum ferritin below 100 microgram/L. Anemia of Chronic Disease (ACD) was diagnosed if CRP >6 mg/L and ferritin >100 microgram/L. Vitamin B12 deficiency was diagnosed if the vitamin B12 level was <150 pg /ml [1,8].

Data collection

Patients with IBD were initially identified from the medical records by searching with ICD code. Data base included both electronic and physical charts; they were reviewed for necessary information. In addition to demographic data, data pertaining to anemia work up was collected.

Statistics

Statistical analysis was done for Crohn's disease and ulcerative colitis together. Analyses for baseline characteristics of the patients were done by grouping them into those with anemia at the time of initial presentation to the hospital and those without anemia. In addition, depending on relevance, separate analysis of CD and UC was done.

Prevalence of anemia was calculated by dividing patients with anemia at the time of initial presentation and total number of patients. Prevalence of severe anemia was calculated by dividing number of patients with hemoglobin less than 10 gm/dl irrespective of gender during the follow up. We also did binary logistic regression analysis to find risk factors for developing severe anemia.

Categorical variables were expressed as proportions, while continuous variables were expressed as means with standard deviations. The Pearson's Chi-square test was used to compare categorical variables, and t-test for comparing continuous variables. The data was analyzed by statistical software SPSS, Chicago, Illinois. A two-tailed p-value of <0.05 was considered statistically significant. Statistical analysis was done by using, by IBM SPSS statistics, Version 25.0. Armonk, NY: IBM Corp.

Results

From 190 patients IBD screened, 109 patients were included; remaining 81 patients did not meet inclusion criteria. Males were 56%. Crohn's disease was 77 (70.6%) and ulcerative colitis in 32 patients (29.4%). The onsets of IBD in the cohort studied were from 1989 until 2017. Baseline characteristics of the patients who developed anemia and did not develop anemia are given in the Table 1.

	Anemia	No anemia	p-value
Male n (%) Female n (%)	28 (58.3%) 28 (58.3%)	33 (54.1%) 20 (41.7%)	0.25
Age (mean and SD)	30.04 (12.4)	29.75 (11.3)	0.76
Crohns disease	41 (53.20	36 (46.8)	0.54
Ulcerative colitis	15 (46.9)	17 (53.1)	0.54
CD location			
I. Small intestine	21 (50)	21 (50)	0.56
II. Colon and small intestine	19 (55.9)	15 (44.1)	
III. Colon	1	0	
CD phenotype			
I. Fistulizing	26 (57.8)	19 (42.2)	0.59
II. Inflammatory	9 (50)	9(50)	
III. Stricture	6 (42.9%)	8 (57.1)	
UC location			
I. Left sided	9 (50)	9 (50)	0.9
II. Pan colitis	3 (42.9)	4 (57.1)	
III. Rectum	2 (40)	3 (60)	
CD phenotype			
I. Fistulizing	26 (57.8)	19 (42.2)	0.59
II. Inflammatory	9 (50)	9(50)	
III. Stricture	6 (42.9%)	8 (57.1)	
CRP			
I. <6mg/L	18 (52.9)	16 (47.1)	0.25
II. >6mg/L	31 (67.4)	15 (32.6)	
Ferritin			
I. 0-30	10 (71.4)	4 (28.6)	0.98
II. 31-99	3 (75)	1 (25)	
III. 100 and above	3 (75)	1 (25)	
Vitamin B12			
I. Mean (SD)	278 (145)	350 (225)	0.2
II. Vitamin B12 deficiency (<150 pg/ml)	18 (69.2)	8 (30.8)	0.047
Mean MCV	75 (9.5)	85 (9.99)	0.72
Median MCV	74.95	85.1	
Anemia at presentation	56 (51.4)	53 (48.6)	
Severe anemia	68 (62.4)	40 (36.7)	0.0001

Table 1. Baseline characteristics of the IBD patients who developed anemia and not.

Prevalence of anemia

At the time of first presentation to the hospital, 51.4% of patients (56 out of 109) had anemia. Prevalence of anemia at the time of presentation was not statistically different between CD, UC, males, females, location of the disease, phenotype of the disease (Table 1).

Incidence of severe anemia and etiology of anemia

During the median follow-up of 759 days, 62.4% of our cohorts were diagnosed with severe anemia. Serum ferritin, C-reactive protein and hemoglobin results were available only in 22 (20%) patients to calculate the type of anemia. Iron deficiency anemia was diagnosed in 13.8%, ACD was diagnosed in 3.7%, and iron deficiency plus ACD was diagnosed in 2.8%.

Vitamin B12 deficiency

From 101 patients, 26 of them (23.9%) had vitamin B12 deficiency. The diagnostic criteria for the diagnosis of vitamin B12 deficiency was the vitamin B12 level of less than 150 pg /ml.(9)

Risk factors for anemia

No identifiable risk factors were found at the time of presentation for anemia in IBD population. However, the female gender (p-value 0.001) and anemia at presentation (p-value 0.0001) were risks for subsequent development of severe anemia and the results of binary logistic regression analysis are given in the Table 2. Figure 1 shows mean hemoglobin at the time of presentation in relation to the disease location in IBD.

	p-value	Odds ratio	95% C.I. (lower)	95% C.I. (upper)
Males	0.009	0.094	0.016	0.559
Fistula	0.999	0	0	.
Disease in the left side of the colon	0.141	43.303	0.285	6570.
Inflammatory phenotype of IBD	0.999	0	0	.
Pancolitis	0.999	0	0	.
Disease involving the colon and small bowel	0.657	0.646	0.094	4.446
Disease involving the colon	0.999	0	0	.
CRP at the presentation	0.326	0.986	0.959	1.014
CRP at the time of severe anemia	0.41	0.986	0.954	1.019
Patients with anemia at first presentation	0.002	15.384	2.692	87.929
Crohn's disease or Ulcerative colitis	1	0.013	0	.

Table 2. Binary logistic regression analysis of IBD patients for the risk of development of severe anemia.

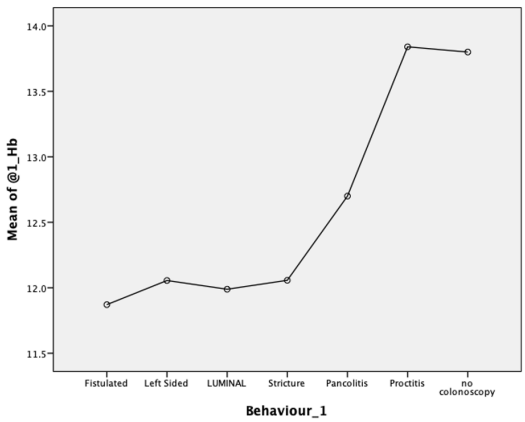

Figure 1. Means plot showing mean hemoglobin at the time of first presentation in IBD patients in relation to behavior/phenotype of the disease (p-value 0.55).

Discussion

Our study demonstrated anemia is very common among IBD patients in Saudi Arabia. Prevalence of anemia at the time of first presentation to the hospital was 51.4%. Patients' characteristics with anemia at presentation did not differ much from those without anemia. Severe anemia was observed in 62.4% of patients during their follow-up. In addition, our study suggested most common etiology of anemia was iron deficiency anemia. The study also highlighted the fact that work up of the anemia was not carried out in most patients. To the best of our knowledge, this is the first study from Saudi Arabia studying anemia, a major systemic complication of IBD.

Most of our findings are in agreement with results from other studies. The prevalence of anemia in IBD has been reported in the range of 21% to 65%. The reported prevalence varied in the inpatient settings compared to the outpatient settings. Most published studies have assessed anemia in outpatient settings [4].

A study from the USA that collected information from a database of outpatient encounters has reported prevalence of anemia in CD 32.4% and 27.6% in UC [3]. The prevalence of anemia in Brazil in outpatients with IBD was 21% [7]. Another study from 29 European and one Australian Centre in an outpatient setting reported an overall prevalence of anemia of 49% in CD and 39% in UC [4]. In a meta-analysis form Europe, the overall prevalence of anemia in patients with Crohn's disease was found at 27% (95% confidence interval, 19-35) and 21% (95% confidence interval, 15-27) in patients with ulcerative colitis [10]. Higher prevalence of anemia in our study is related to the fact that our patients were mostly of inpatient setting.

The most common type of anemia in our study was iron deficient anemia (13.8%). In the European meta-analysis, 57% of the anemic patients were iron deficient [10]. Brazilian study reported 10% of iron deficiency anemia in CD and 6% in UC [7]. Prevalence of iron deficiency anemia from the USA has been reported in 79.2% in CD and 85.1% in UC [3].

Most of our patients did not have full work up for classifying their anemia, except in 20%. This observation from our study is similar to others. The study from the USA, only 19.8% had associated ferritin and CRP measurements [3]. Similar findings were reported from Germany, only in one-third of patients with proven anemia had undergone further diagnostic workup. In addition, patients with diagnosed iron-deficiency anemia were infrequently and inconsequently treated with iron preparations [11].

At any point of time from our study, 101 patients had tested for Vitamin B12 deficiency (cobalamin (Cbl) deficiency), and 26 of them (23.9%) had vitamin B12 deficiency. We used the diagnostic criteria by the Vitamin B12 deficiency recommended by NHANES [9]. From a systematic review, the reported prevalence of Vitamin B12 deficiency in CD patients ranged from 5.6% to 38%. The prevalence of Vitamin B12 deficiency in UC was not different to the general population [12].

Limitations of the study include weaknesses of a retrospective cohort study; these include missing information and incomplete data for many patients. The study did not focus on treatment or complications of anemia. Advantages of the study include for best of our knowledge; this is the first study from Saudi Arabia addressing an important extra-intestinal/systematic complication of IBD. We also have enrolled a good number of patients. The study assessed the magnitude of anemia, etiologies of anemia, including cobalamin deficiency, and risk factors for severe anemia.

Conclusion

In conclusion, Anemia in IBD population is highly prevalent. Irrespective of the disease location, phenotype, gender, CRP level, approximately one in two patients have anemia in our IBD patients at the time of their hospital presentation. Female gender and anemia at presentation are risks for the development of severe anemia in IBD population. Complete work up to classify anemia was available in 20% of the IBD population.

Ethics Statement

The study design was approved by the institute's ethics committee with a RAC number 2181218, and by the research promotion group under the department of medicine. Study was conducted by following rules and regulations of the institutes research committee and declaration of Helsinki for medical search.

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