

# Anemia in Patients with Ulcerative Colitis in Remission: A Cross-Sectional Study from Pakistan

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## ABSTRACT

**Background and Aim:** Anemia is an extra intestinal manifestation of inflammatory bowel disease that frequently causes complications. In inflammatory bowel disease (IBD) such as ulcerative colitis and Crohn's disease, anemia is mostly caused by iron deficiency which impacts the patient's quality of life [1, 2]. The present study aimed to assess the anemia in ulcerative colitis patients in remission.

**Methodology:** A cross-sectional study was conducted on 82 ulcerative colitis patients at the Department of Medicine and Gastroenterology, Jinnah hospital, Lahore from February 2021 to January 2022. All the patients were assessed for anemia based on Mayo clinical score <3 for at least three months. Hemogram tests such as CBC, vitamin B12 serum levels, ferritin, folic acid levels, concentration of C - reactive protein (CRP), and transferrin were performed for the initial screening. Further, patients were evaluated for the determination of different causes of anemia. Patients were categorized into mild, moderate, and severe anemia cases. Oral iron, intravenous iron, and blood transfusion were given to mild, moderate, and severe anemia patients respectively. SPSS version 25 was used for data analysis.

**Results:** Of the total 82 ulcerative colitis patients, there were 48 (58.5%) male and 34 (41.5%) females. The prevalence of anemia in ulcerative colitis patients and control was 51.2% (n=42) and 11.9% (n=5) respectively. The hemoglobin mean values in UC patients and control was 11.95 g/dL and 13.21 g/dL respectively. Out of 42 ulcerative colitis patients, the prevalence of mild, moderate, and severe anemia was 52.4% (n=22), 35.7% (n=15), and 11.9% (n=5) respectively. Iron deficiency was the prevalent etiology of anemia found in 22 (52.4%) patients followed by chronic anemia disease with iron deficiency found in 8 (21.9%). Hemoglobin level has no association with ferritin level. Hemoglobin level has no association with ferritin level. The hemoglobin level was increased with oral iron and intravenous iron by 1.6 g/dL and 2.3 g/dL respectively.

**Conclusion:** The present study concluded that prevalence of anemia was higher in ulcerative colitis patients. The most common etiology of anemia was iron deficiency in both groups. Increased CRP and moderate activity associated to anemia disease was significantly related with comorbid anemia. Oral iron and intravenous iron could increase hemoglobin levels in ulcerative colitis associated anemia patients.

**Keywords:** Anemia, Ulcerative Colitis, Iron deficiency

## INTRODUCTION

Anemia is an extra intestinal manifestation of inflammatory bowel disease that frequently causes complications. In inflammatory bowel disease (IBD) such as ulcerative colitis and Crohn's disease, anemia is mostly caused by iron deficiency which impacts the patient's quality of life [1, 2]. A previous systematic review reported 27% prevalence of anemia in Crohn's disease patients whereas 21% in ulcerative colitis patients with 95% confidence interval [3]. Iron deficiency was the prevalent etiology for anemia which comprised more than a half patients. Another study reported incidence of anemia to vary from 6.2% to 73.3% in inflammatory bowel disease patients [4, 5]. Morbidity caused by anemia in ulcerative colitis patients triggered different symptoms such as restless leg syndrome, easy fatigability, female infertility, sleeping disorders, and attention deficit impairing quality of life [6]. Other causes for anemia in ulcerative colitis patients are blood loss, nutritional deficiency, and medication used by the general population [7].

Comparing the prevalence of anemia in inflammatory bowel disease, it has been observed that hospitalized patients are more susceptible to anemia than others [8]. The incidence of anemia in IBD hospitalized patients was reported to range from 44% by Gonzalez et al [9] to 74% by Herrera [10]. However, advanced studies found lower prevalence of anemia in IBD patients due to improving anemia treatment and outcome. Anemia successful therapy could improve life's quality in a better way than anti-inflammatory therapy [11]. Additionally, the most prevalent comorbid conditions related to IBD patient's mortality was anemia [12]. However, in such patients, IBD severity was simply a factor that contributed to acute morbidity cases. The present study involved all the ulcerative colitis patients with at least 3 months

remission and had normal limits of C-reactive protein level. Therefore, the aim of the current study was to assess the anemia in ulcerative colitis patients.

## METHODOLOGY

A cross-sectional study was conducted on 82 ulcerative colitis patients at the Department of Medicine and Gastroenterology, Jinnah hospital, Lahore from February 2021 to January 2022. All the patients were assessed for anemia based on Mayo clinical score <3 for at least three months. Hemogram tests such as CBC, vitamin B12 serum levels, ferritin, folic acid levels, concentration of C - reactive protein (CRP), and transferrin were performed for the initial screening. Further, patients were evaluated for the determination of different causes of anemia. Patients were categorized into mild, moderate, and severe anemia cases. Oral iron, intravenous iron, and blood transfusion were given to mild, moderate, and severe anemia patients respectively.

Prior to study conduction, ethical approval was taken from the institutional ethical committee. Written informed consent was taken from each individual. All those patients with history of ulcerative colitis, had clinical remission, normal C-reactive protein level, and no rectal bleeding were enrolled. Besides 82 ulcerative colitis patients that satisfied the inclusion criteria, 40 patients were in the control group as a functional dyspepsia. A detailed history regarding drug usage was taken. Hematinic user patients were excluded from the study. Based on WHO classification for anemia patients, hemoglobin cut off value was set 12 g/dL and 13 g/dL for females and males respectively. Ulcerative colitis patients with anemia were further investigated. The range for counting red cell distribution width (RDW) and corrected reticulocyte count were 11.5% to 14.5% and 0.5% to 1.5% respectively. Patients were

assessed for anemia which had low/normal mean corpuscular volume (MCV), higher RDW, and low/normal reticulocyte count. Ferritin normal level and transferrin saturation were 30–300 microgram per litre (mcg/L) and 15% to 50%. Anemia was considered to be present in patients having transferrin saturation <20% and ferritin levels <30%. SPSS version 25 was used for data analysis. Anemia prevalence was compared between two groups using Chi-square test. Student's t-test was used for comparing hemoglobin values between study and control groups. P<0.05 was considered of statistical significance.

**RESULTS**

Of the total 82 ulcerative colitis patients, there were 48 (58.5%) male and 34 (41.5%) females. The prevalence of anemia in ulcerative colitis patients and control was 51.2% (n=42) and 11.9% (n=5) respectively. The hemoglobin mean values in UC patients and control was 11.95 g/dL and 13.21 g/dL respectively. Out of 42 ulcerative colitis patients, the prevalence of mild, moderate, and severe anemia was 52.4% (n=22), 35.7% (n=15), and 11.9% (n=5) respectively. Iron deficiency was the prevalent etiology of anemia found in 22 (52.4%) patients followed by chronic anemia disease with iron deficiency found in 8 (19.04%). Hemoglobin level has no association with ferritin level. The hemoglobin level was increased with oral iron and intravenous iron by 1.6 g/dL and 2.3 g/dL respectively. Figure-1 shows the gender's distribution. Baseline characteristics are shown in Table-I. Anemia prevalence and severity in ulcerative colitis patients are illustrated in Figure-2. Table-II represents the association of iron deficiency and ferritin levels. Figure-3 depicts the different causes of anemia in ulcerative colitis patients.

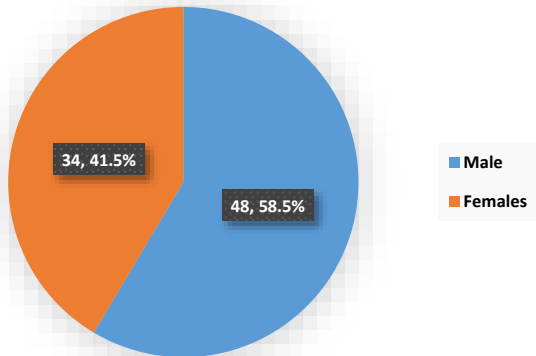


Figure-1: Gender's distribution (n=82)

Table-1: Baseline characterization

Parameters	Male (n=48)	Females (n=34)	Overall (n=82)
Mean Hb (g/dL)	12.31	11.1	11.71
Mean MCV (fl)	83.62	76.92	80.27
Mean RDW (%)	16.9	22.9	19.9

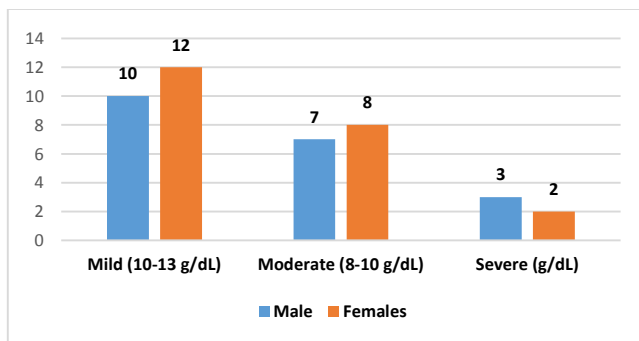


Figure-2: association of anemia severity and gender's distribution

Table-2: Association of iron deficiency and ferritin levels

Mgc/L	Male n (%)	Females' n (%)	Overall n (%)
<30	15 (48.4)	16 (51.6)	31 (73.8)
30-100	6 (66.7)	3 (33.4)	9 (21.4)
>100	1 (50%)	1 (50%)	2 (4.8)

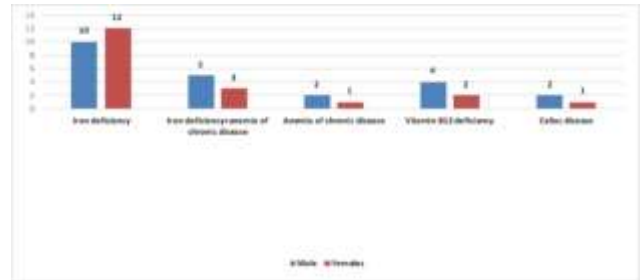


Figure-3: Different causes of anemia in ulcerative colitis patients

**DISCUSSION**

The present study demonstrated the prevalence of anemia in ulcerative colitis patients. The results show that higher CRP and moderate disease activity has significant association with anemia. Till now, it has been observed for the first time that an important risk factor for anemia is moderate disease activity in ulcerative colitis patients. Additionally, iron deficiency anemia was the prevalent etiology of anemia in inflammatory bowel disease patients. Oral iron and intravenous iron could increase hemoglobin levels in ulcerative colitis associated anemia patients. The prevalence of anemia in ulcerative colitis patients and control was 51.2% found in the current study. A recent study conducted in Europe reported the overall prevalence of anemia in IBD patients was 24% (95% CI, 18-31) which is lower than our findings [13]. The prevalence of anemia range from 17% to 20% as reported by various studies [14, 15] which is quite lower than the anemia prevalence found in the current study.

The present study reported 5 cases of severe anemia. It, however, due to the inclusion of severe IBD and anemia patients which needed high probability of hospitalization. Additionally, the IBD patients were followed for continuous monitoring and achieving the target of intestinal inflammation tight control. The underlying activity of disease was correlated with inflammatory bowel disease patients who had anemia [16]. The anemia of chronic disease, terminal ileitis due to vitamin B12 deficiency, induced azathioprine, chronic blood loss, and folate deficiency were attributable factors for anemia in ulcerative colitis patients [17]. Chronic fatigue could results from anemia that blight the life's quality [18].

Ulcerative colitis patients with remission were chosen for the current study because certain anemia patients might go unrecognized until tested specifically for anemia. Anemia was defined based on world health organization criteria set for hemoglobin level cut off value that is 12 g/dL and 13 g/dL for females and male respectively. According to the study conducted by Peyrin-Biroulet et al [19] the incidence of anemia range from 16% to 74% in inflammatory bowel disease patients [20].

The current study found the prevalence of mild, moderate, severe anemia cases were 52 %, 35.7%, and 11.9% respectively. A previous study reported that almost one third patients of ulcerative colitis with anemia were not tested for anemia symptoms like iron deficiency [21]. Nutritional deficiency was reported based on indications such as high RWD and low reticulocyte count. Microcytosis, macrocytosis, and normocytosis generally suggests deficiency of iron, vitamin B12, and mix picture like disease of chronic anemia. All the patients underwent flexible sigmoidoscopy for the detection of endoscopic inflammation. In anemia patients. Iron deficiency was the common etiology present in 52.4%. Chronic anemia disease with iron deficiency was present in 19.04% ulcerative colitis patients. These findings almost resemble another study results according to which ulcerative colitis patients

required iron supplementation, had blood loss, treatment modification, and nutritional deficiency [22].

The association of hemoglobin levels and ferritin levels were investigated for the gender's difference in the present study. The acceptable limit for increasing the level of hemoglobin to be 2 g/dl within four weeks were considered appropriate [23]. Another study compared the oral iron to intravenous iron and found that the later one provides higher efficacy and better tolerability [24]. In our study, we used ferric carboxymaltose. However, iron isomaltoside, iron sucrose, ferric carboxymaltose, and even advanced ferumoxytol has been used for preparation of intravenous iron. We observed that the increase in hemoglobin level was higher in intravenous iron users compared to oral iron. However, mostly patients tolerated the oral iron compared to lower willingness for injectable iron. As a result, we conclude that ulcerative colitis patients treated for iron deficiency are only the tip of the iceberg, and the majority of patients with quiescent disease have underlying iron deficiency. These patients should be identified and screened using a simple test, such as a hemogram, so that their iron deficiency can be treated in a cost-effective manner.

Vitamin B12 deficiency was discovered in six patients, three of whom were vegetarians and three of whom had pernicious anemia. Three patients were discovered to have celiac disease. Iron deficiency anemia persists in a significant proportion of ulcerative colitis patients in remission and must be treated appropriately. In IBD patients, intestinal inflammation plays a critical role in the development of anemia. Particularly in the presence of active disease and/or an elevated CRP level, the suspicion of underlying anemia should be raised, and it should be carefully investigated.

## CONCLUSION

The present study concluded that prevalence of anemia was higher in ulcerative colitis patients. The most common etiology of anemia was iron deficiency in both groups. Increased CRP and moderate activity associated to anemia disease was significantly related with comorbid anemia. Oral iron and intravenous iron could increase hemoglobin levels in ulcerative colitis associated anemia patients.

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