


# Biological Abnormalities Associated with Crohn's Disease

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**How to cite this paper:** El Jim, R., El Kirami, Y., Lamine, A., Lahlali, M., Abid, H., El Mekkaoui, A., El Yousfi, M., Benajah, D.-A., El Abkari, M., Ibrahim, S.A. and Lahmidani, N. (2025) Biological Abnormalities Associated with Crohn's Disease. *Open Journal of Gastroenterology*, **15**, 490-501.  
<https://doi.org/10.4236/ojgas.2025.159044>

**Received:** August 1, 2025

**Accepted:** September 1, 2025

**Published:** September 4, 2025

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## Abstract

**Background:** Crohn's disease is a chronic inflammatory bowel disorder with complex and multifactorial pathogenesis and presentations. This retrospective study aims to analyze the biological abnormalities observed at the initial diagnosis of Crohn's disease in a cohort of 231 patients. **Methods:** We performed a five-year retrospective study at the Hepato-Gastroenterology Department of University Hospital Hassan II in Fez, Morocco, involving 231 patients diagnosed with Crohn's disease. A standardized form was used to extract data from medical charts and the Hosix electronic medical system. With an emphasis on hematologic, inflammatory, and nutritional parameters, as well as superinfections at presentation, demographic, clinical, and paraclinical variables were gathered. **Results:** The cohort's mean age was  $37.8 \pm 12.2$  years, and the majority of participants (66.7%) were female. Seventy-seven percent of patients had a chronic disease onset when they first arrived, and the average diagnostic delay was 16.7 months. 1) Inflammatory markers: Of the 196 patients tested, 91.8% had elevated fecal calprotectin (74.8% had  $>250 \mu\text{g/g}$ ), and 83% had elevated C-reactive protein. 2) Anemia: Found in 61 percent of patients ( $n = 139$ ), primarily microcytic hypochromic; 20 percent had iron deficiency, 44.6 percent had inflammation, and 35.4 percent had mixed. 3) Nutritional deficiencies were prevalent and included hypoalbuminemia (59%), vitamin D deficiency (90%), and hypocalcemia (39%), as well as hypomagnesemia (17%). 4) 24.8 percent of patients experienced superinfections, primarily from *Entamoeba histolytica* (14 percent) and *Clostridium difficile* (9.2 percent). **Conclusion:** These results highlight how Crohn's disease affects more than just the gastrointestinal tract. To improve patient outcomes and optimize management strategies, routine evaluation of inflammatory markers, hematological parameters, and nutritional status are essential.

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## Keywords

Crohn's Disease, Initial Diagnosis, Biomarkers, Anemia, CRP, Fecal Calprotectin, Nutritional Deficiencies, Superinfections

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## 1. Introduction

Crohn's disease is a chronic autoimmune inflammatory disorder affecting the gastrointestinal tract. It is characterized by a multifactorial etiology and a heterogeneous presentation involving clinical, biological, endoscopic, and radiological features.

Chronic inflammation, intestinal malabsorption, nutritional deficiencies, and possible superinfections are the main causes of the biological abnormalities seen in Crohn's disease. Elevated inflammatory markers that reflect disease activity, such as fecal calprotectin and C-reactive protein (CRP), are among the primary biological markers found. Systemic inflammation, iron, vitamin B12, or folic acid malabsorption, or chronic blood loss can all contribute to hematological abnormalities, especially anemia. While abnormalities in liver function tests may be linked to hepatobiliary complications like primary sclerosing cholangitis, hypoalbuminemia is frequently an indication of severe inflammation and protein-losing enteropathy. Because of malabsorption, decreased dietary intake, or protracted diarrhea, deficiencies in fat-soluble vitamins (A, D, E, and K) and trace elements like zinc and magnesium are common.

The severity and extent of these biological abnormalities are often correlated with disease activity, influencing therapeutic choices and prognosis. Identifying these abnormalities at the time of diagnosis is crucial for optimizing patient management, guiding therapeutic decisions, and preventing long-term complications.

The objective of this study is to analyze the biological abnormalities observed at the initial diagnosis of Crohn's disease in a cohort of 231 patients, in order to better understand the systemic impact of the disease and identify potential severity markers.

## 2. Materials and Methods

Over a period of five years, 231 patients with Crohn's disease who were treated and diagnosed at the Hepatogastroenterology Department of University Hospital Hassan II in Fez, Morocco, were included in this retrospective, descriptive study. The study was conducted from January 2013 to December 2018 and included all patients with a confirmed diagnosis according to internationally recognized clinical, endoscopic, radiologic, and histopathologic criteria.

A standardized extraction form created especially for this study was used to gather patient data from both paper and electronic medical records.

Among the variables examined were:

- Sociodemographic data: sex, age at diagnosis, and place of origin (rural or ur-

ban).

- Clinical features include the disease's location and behavior based on the Montreal classification, extra-digestive manifestations, and initial digestive symptoms.
- Paraclinical findings: laboratory test results, endoscopic examinations, imaging studies, and histopathology.
- Biological data: Hematologic and biochemical profiles, inflammatory markers (C-reactive protein, erythrocyte sedimentation rate), and, if available, fecal calprotectin levels. Anemia subtypes were classified according to standard laboratory criteria: iron deficiency anemia was defined by low ferritin (<30 ng/mL) and/or low transferrin saturation (<16%) with normal or low CRP; anemia of chronic disease (inflammatory anemia) by normal or elevated ferritin with low transferrin saturation in the presence of elevated CRP (>5 mg/L); and mixed-type anemia by the simultaneous presence of low ferritin and elevated CRP.
- Screening for superinfections (*E. histolytica*, *C. difficile*, cytomegalovirus) was not performed routinely for all patients; rather, it was carried out only in cases with specific clinical or endoscopic suspicion, in accordance with local practice protocols.
- Evolutionary data include early outcomes during the first year of follow-up, therapeutic management, and complications noted at diagnosis.

The "Hosix" computerized hospital management system was used to retrieve all data, and medical files were manually reviewed to guarantee accuracy and completeness. The analysis did not include cases with missing or insufficient core data.

Ethical Considerations: Strict measures were taken to protect patient privacy. During data processing, all personally identifiable information was eliminated. The study was carried out in compliance with the Declaration of Helsinki's tenets, and University Hospital Hassan II's local ethics committee gave its consent for the use of anonymized patient data.

### 3. Results

#### Population characteristics:

231 people with active Crohn's disease were included in the study. The patients ranged in age from 18 to 69 years, with an average age of  $37.76 \pm 12.2$  years. On average, 16.7 months passed between the onset of symptoms and the diagnosis. There were 77 men (33.3%) and 154 women (66.7%) in the study population. In terms of health insurance, 1% of patients lacked coverage, 3% had private insurance, and 96% had public insurance. While 23.7% of patients were from rural areas, the majority (76.3%) lived in urban areas.

Regarding medical history, 2.86% of patients had been in contact with a tuberculosis case, 7.6% had a history of tuberculosis, and 89.5% reported no tuberculosis history. Autoimmune diseases were present in a minority of patients, including ankylosing spondylitis (6%), celiac disease (1%), psoriasis (1%), and lupus (1%), while 91% of patients had no history of autoimmune disease.

From a surgical perspective, 72% of patients had never undergone surgery. Among those with prior surgery, 10.7% had undergone an appendectomy, 5.7% anal abscess drainage, 3.6% anal fistula surgery, and 2.8% segmental digestive resection. Regarding toxic habits, 13% of patients were active smokers, 7.7% used cannabis, and 2% consumed alcohol.

Clinically, the illness manifested acutely in 23% of cases and chronically in 77% of cases. Chronic diarrhea (80.95%), abdominal pain (81.90%), rectal syndrome (24.7%), obstructive syndrome (3.8%), and fever (13.3%) were the primary symptoms.

According to the Montreal classification, the phenotypic distribution of Crohn's disease showed pure ileal involvement (L1) in 30% of cases, colonic involvement (L2) in 15%, ileocolic involvement (L3) in 55%, and perianal lesions in 20% of cases.

Anti-TNF drugs and immunosuppressants were the mainstays of medical treatment; azathioprine was administered to 67% of patients, corticosteroids to 30%, infliximab to 69%, adalimumab to 11%, and ustekinumab to 1.7%.

**Table 1** summarizes the different characteristics of Crohn's disease in our patients, including epidemiological, clinical, and endoscopic features, as well as treatment approaches.

**Table 1.** Epidemiological, clinical, endoscopic, and therapeutic characteristics of patients with Crohn's disease.

		Category	Overall count	%
Epidemiological characteristics	Average Age		37.76 ± 12.2 (18 - 69 years)	
	Symptom Onset to Diagnosis		16.7 months	
	Sex	Female	154	66.7%
		Male	77	33.3%
	health coverage	Public coverage	222	96%
		Private Coverage	7	3%
		No coverage	2	1%
	Origin	Urban	176	76.3%
		Rural	55	23.7%
	past medical	Tuberculosis and the concept of contact	History of Contact	10
Tuberculosis Disease			18	7.6%
None			206	89.5%
History of Autoimmune Disease		Celiac Disease	3	1%
		SPA	14	6%
		Psoriasis	3	1%
		Lupus	3	1%
		NONE	208	91%

**Continued**

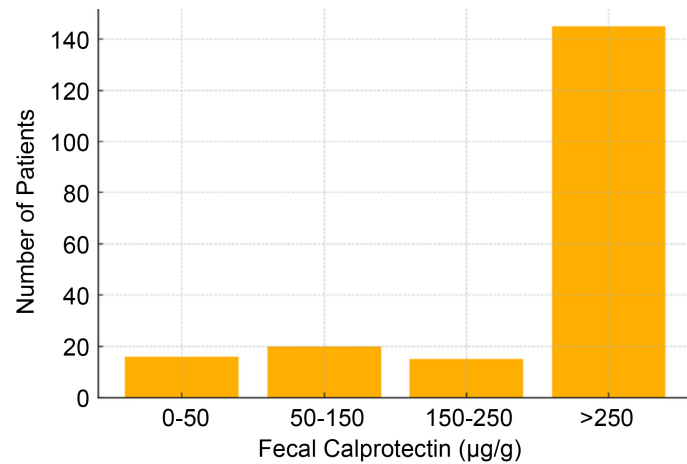
		None	167	72%
		Appendectomy	24	10.7%
	Surgical History	Anal Abscess Drainage	13	5.7%
		Anal Fistula Surgery	8	3.6%
		Digestive Segmental Resection	6	2.8%
	Lifestyle risk factors	Active Smokers	30	13%
		Cannabis Use	18	7.7%
		Alcohol Consumption	4	2%
<b>Clinical Characteristics</b>	Presentation Mode	Chronic Onset	177	77%
		Acute Onset	53%	23%
	Clinical Symptoms	Chronic Diarrhea	186	80.95%
		Abdominal Pain	189	81.90%
		Rectal Syndrome	57	24.7%
		Obstructive syndrome	<b>8</b>	<b>3.8%</b>
	Fever	34	13.3%	
<b>phenotype of disease</b>	The Montreal classification of Crohn's disease	Pure Ileal (L1)	69	30%
		colinic(L2)	34	15%
		Ileocolic (L3)	128	55%
		perianal lesions	46	20%
<b>treatment</b>	medical treatment	Azathioprine	155	67%
		Corticosteroids	69	30%
		Infliximab ± in combotherapy	159	69%
		Adalimumab	25	11%
		Usekitinumab	4	1.7%

**Biomarkers of Inflammation in Crohn's Disease****Fecal Calprotectin**

Fecal calprotectin (FC) testing was performed in 196 patients, representing 84.8% of the study population. The results were positive in 91.84% of cases, reinforcing its strong association with intestinal inflammation. The distribution of FC levels is illustrated in the graph (**Figure 1**), showing that the majority of patients (74%) exhibited values exceeding 250 µg/g, indicating a significant intestinal inflammatory burden. Conversely, lower levels were observed in a much smaller proportion of patients: 8.2% had values between 0 - 50 µg/g, 10.2% between 50 - 150 µg/g, and 7.7% between 150 - 250 µg/g.

**C-reactive protein (CRP)**

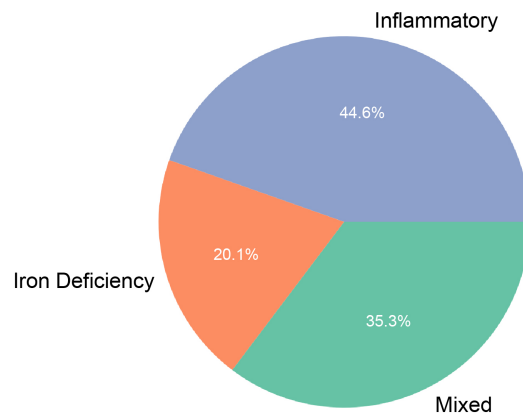
Reactive protein (CRP) testing was performed in all patients, revealing that 83% had elevated CRP levels exceeding 5 mg/L, with an average value of 76.7 mg/L.



**Figure 1.** Distribution of patients according to fecal calprotectin levels at the Time of Diagnosis.

### Anemia/Ferritin

Iron metabolism disorders were found to be a major factor in the diagnosis of anemia in 61% (N = 139) of the patients, with 80% presenting with hypochromic microcytic anemia. In 20% of cases, iron deficiency anemia was found, most likely as a result of intestinal malabsorption and chronic blood loss. Furthermore, inflammatory anemia, which is caused by chronic systemic inflammation that impairs iron utilization, was present in 44.6% of patients. Lastly, the complicated pathophysiology of anemia in Crohn's disease was highlighted by the fact that 35.4% of patients had mixed-type anemia, which combined both iron deficiency and inflammatory mechanisms, as illustrated in **Figure 2**.

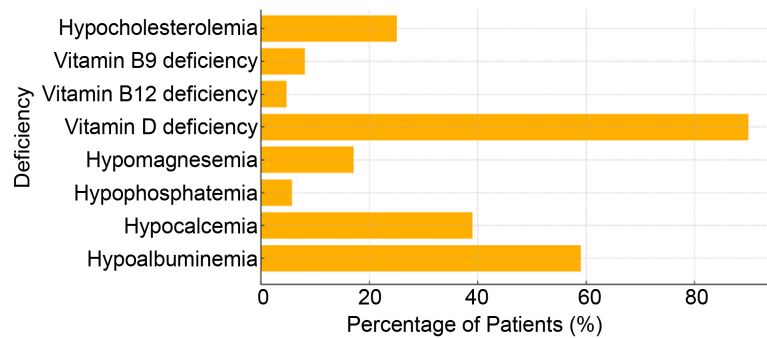


**Figure 2.** Types of Anemia in Our Patients at the Time of Diagnosis.

### Nutritional Deficiencies

Crohn's disease frequently results in nutritional deficiencies because of reduced dietary intake, chronic inflammation, and malabsorption. With an average albumin level of  $22.11 \pm 7.0$  g/L, hypoalbuminemia was found in 59% of patients (N =

136) in our study, indicating systemic inflammation and protein loss. Significantly, patients with severe complications had albumin levels below 16 g/L, indicating a link between severe hypoalbuminemia and unfavorable outcomes, such as a higher risk of malnourishment, infectious complications, and worsening inflammation, as shown in **Figure 3**.



**Figure 3.** Nutritional Deficiencies in Our Patients at the Time of Diagnosis.

Hypocalcemia was present in 39% of patients ( $N = 90$ ), while hypophosphatemia and hypomagnesemia were reported in 5.7% ( $N = 13$ ) and 17% ( $N = 39$ ) of cases, respectively, indicating deficiencies related to intestinal malabsorption and prolonged diarrhea.

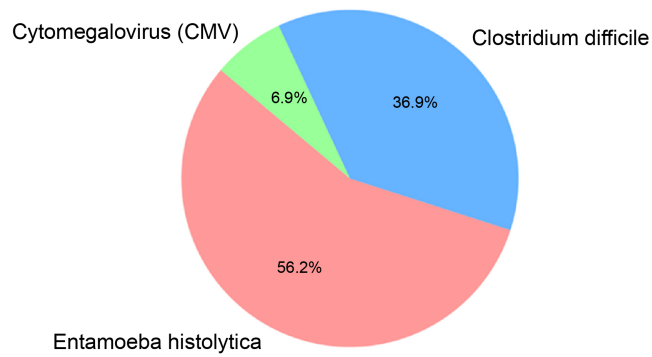
Vitamin D deficiency, which was particularly prevalent and suggested a high risk of metabolic diseases and bone demineralization, was present in 90% of patients ( $N = 208$ ). Additionally, it was discovered that 4.7% ( $N = 11$ ) and 8% ( $N = 19$ ) of the patients had vitamin B12 and B9 deficiencies, respectively. Finally, hypocholesterolemia was present in 25% of patients ( $N = 58$ ), which may indicate malnourishment, chronic inflammation, or metabolic dysfunction. In order to maximize supplementation and avoid complications related to micronutrient deficiencies, these findings highlight the necessity of routine nutritional assessment in patients with Crohn's disease. Since severe hypoalbuminemia may be a predictor of complications and slow disease progression, it should be closely watched.

#### **Superinfections**

In patients with Crohn's disease, superinfections are a serious complication, especially for those on immunosuppressive medication or with compromised immune systems. As illustrated in **Figure 4**, the most commonly found pathogens in our study were *Entamoeba histolytica*, *Clostridium difficile*, and Cytomegalovirus (CMV), with 57 patients (24.8%) presenting with a superinfection.

## **4. Discussion**

Crohn's disease (CD) is becoming more commonplace worldwide in both incidence and prevalence [1] [2]. This condition is characterized by a chronic and recurrent course, leading to progressive intestinal lesions responsible for the gradual destruction of the gastrointestinal tract wall [3].



**Figure 4.** Assessment of superinfection in our patients at the time of diagnosis.

Guidelines for practitioners regarding the use of serum and fecal biomarkers in the evaluation and follow-up of patients with Crohn's disease were recently released by the American Gastroenterological Association (AGA) [4], as well as exploring the overall diagnostic performance of biomarkers in detecting postoperative recurrences. Fecal calprotectin is a protein primarily derived from neutrophils, but also from monocytes to a lesser extent, which is measured in stool samples [5]. It constitutes 60% of the cytosolic content of neutrophils. Fecal calprotectin is a simple and non-invasive tool for the evaluation and risk stratification of patients with digestive symptoms. It is mainly elevated in gastrointestinal conditions associated with mucosal lesions, particularly in the presence of ulcers [6]. The measurement of fecal calprotectin (FC) is recommended for the initial diagnosis of inflammatory bowel diseases (IBD) [7]. It is the most sensitive biological marker of intestinal inflammation in IBD with a good correlation with endoscopic activity indices. The initial FC test both strengthens the diagnosis, although it is not specific to IBD and can be increased in differential diagnoses, especially infections [7].

C-reactive protein (CRP) is an acute-phase protein synthesized by the liver in response to systemic inflammation. Its level is strongly correlated with disease activity, although it can be negative in 25% of cases of active Crohn's disease [8]. Neither CRP nor fecal calprotectin is specific to Crohn's disease activity. CRP can indeed be elevated in various systemic inflammatory processes [9]. Twenty studies reported the diagnostic performance of CRP, most using a threshold of 5 mg/L. The sensitivity of CRP > 5 mg/L for detecting endoscopically active disease was 67%, and the specificity was 73%. Similarly, the sensitivity of fecal calprotectin > 150 µg/g ± 50 for detecting endoscopically active disease was 81%, with a specificity of 72% [9].

A frequent negative consequence of Crohn's disease is anemia, which can be caused by a number of factors such as iron deficiency, chronic inflammation, and poor intestinal absorption. 61.4% of the 231 patients in our study at Hassan II University Hospital had anemia, with hypochromic microcytic anemia being the most common type. These findings align with a number of earlier investigations,

such as Gracie *et al.* (2018) [10], who reported an anemia prevalence ranging from 36% to 76% in patients with IBD, depending on disease activity. Similarly, Cohen *et al.* (2018) [11] observed a prevalence of 50% in European patients with Crohn's disease, with microcytic anemia primarily due to chronic inflammation. In a systematic review, Khan *et al.* (2020) [12] confirmed the high prevalence of anemia in up to 76% of IBD patients, reinforcing the importance of anemia as a major complication of the disease.

The average diagnostic delay of 16.7 months may have played a substantial role in the severity of the biological abnormalities observed in our cohort. Prolonged untreated inflammation and malabsorption during this period likely contributed to the high prevalence of anemia and nutritional deficiencies, as ongoing mucosal damage and chronic blood loss exacerbate micronutrient depletion. Early diagnosis and intervention are therefore essential to prevent the progression of these systemic complications.

Due to malabsorption, dietary restrictions, and symptoms like diarrhea, Crohn's disease can result in deficiencies in vital nutrients. Deficits in iron, calcium, and vitamin D may be present in patients with this illness [13]. According to the Crohn's & Colitis Foundation (CCF), malnutrition is common in inflammatory bowel diseases (IBD), particularly in Crohn's disease, affecting between 20% and 85% of patients with IBD [13]. In addition to being connected to intestinal inflammation and Crohn's disease activity, vitamin D is essential for immune system regulation. The high frequency of vitamin D deficiency in patients with Crohn's disease was highlighted by our study, which revealed that 95% of patients (102 out of 108 tested) had the condition. These findings align with a study conducted in Tunisia [14] that found a high prevalence of vitamin D deficiency in Crohn's disease patients (98.1%). Low vitamin D levels [15] have been associated with more active disease, more severe endoscopic lesions, and an increased frequency of hospitalizations and surgeries.

Vitamin B12 is essential for DNA synthesis, red blood cell production, and neurological function. Patients are more susceptible to deficiency because it is mainly absorbed in the terminal ileum, an area that is commonly impacted in Crohn's disease. Nonetheless, 87% of patients (out of 92 tested) had normal vitamin B12 levels, according to our study, indicating that the majority of patients had sufficient stores. The low prevalence of vitamin B12 deficiency in our cohort (4.7%), despite a high rate of ileal involvement, is noteworthy. This finding may be partly explained by the relatively short average diagnostic delay of 16.7 months, which may not have allowed sufficient time for hepatic vitamin B12 stores to become significantly depleted. Moreover, some patients may have had subclinical depletion without meeting the biochemical threshold for deficiency at the time of diagnosis. These factors could account for the apparent discrepancy between disease location and laboratory evidence of deficiency. The European Society for Clinical Nutrition and Metabolism (ESPEN) has published practical recommendations on vitamin B12 in chronic inflammatory bowel diseases (IBD) [16]: The prevalence

of deficiency varies between 5.6% and 38% in Crohn's disease and is associated with resection of more than 30 cm of the ileum, whether or not the ileocecal valve has been resected, but apparently not with a resection of 20 cm of ileum. It is advised that patients with ileal involvement and/or those who have had ileal resection undergo annual screening for vitamin B12 deficiency by measuring their vitamin B12 concentrations.

In Crohn's disease, albumin and prealbumin are biomarkers of inflammation and nutritional status. Prealbumin is a more dynamic and early indicator of malnutrition, whereas albumin is a major plasma protein involved in nutrient transport and the control of oncotic pressure. According to our research, hypoalbuminemia affected 59% of patients, with severely ill patients having much lower albumin levels. Significantly, patients with albumin levels less than 16 g/L were more likely to experience infections, delayed wound healing, and extended hospital stays.

The results of a Canadian study (Squirell *et al.*, 2020) [17] complement these findings, showing that hypoalbuminemia was independently associated with malnutrition and inflammation in Crohn's disease patients, with the lowest levels observed in those with both malnutrition and active inflammation. While albumin levels may be a marker of malnutrition or active disease, the lowest levels are found in patients with both conditions. These results highlight the importance of a thorough evaluation of inflammation and malnutrition in Crohn's disease patients.

In our cohort, *Entamoeba histolytica* was the most frequent superinfection, affecting 14% of patients. This is of particular clinical importance, as amebic colitis can mimic an IBD flare both clinically and endoscopically, leading to potential misdiagnosis and inappropriate escalation of immunosuppressive therapy. In endemic settings such as Morocco, this underscores the need for systematic screening for *E. histolytica* in patients presenting with suspected IBD exacerbations. Early identification and treatment not only improve patient outcomes but also help avoid confounding the assessment of disease activity.

## 5. Conclusions

The biological abnormalities linked to Crohn's disease at the time of initial diagnosis are highlighted in this study, underscoring the disease's substantial systemic impact beyond its digestive manifestations. In order to maximize patient care, these results highlight the significance of biomarker assessment, nutritional evaluation, and early problem detection.

Our findings demonstrate that CRP and fecal calprotectin are important inflammatory markers that have a strong correlation with disease activity. Their combined use in clinical practice can facilitate early diagnosis, reduce reliance on invasive procedures, and improve disease monitoring. Anemia was present in 61% of patients, with a predominance of hypochromic microcytic anemia. Differentiating between iron deficiency anemia and inflammatory anemia is crucial for guiding therapeutic strategies.

The effects of malabsorption and chronic inflammation were reflected in the high prevalence of nutritional deficiencies, particularly hypoalbuminemia, vitamin D deficiency, and vitamin B12 deficiency. Severe hypoalbuminemia (<16 g/L) is a significant prognostic indicator because it has been linked to an increased risk of complications.

These results emphasize the value of a multidisciplinary strategy that incorporates infection screening, hematological and nutritional evaluation, and inflammatory markers into the treatment of Crohn's disease. Future research should examine the prognostic significance of these abnormalities as well as their long-term effects on treatment response and disease progression.

### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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