

Clinical Characteristics of Crohn's Disease in a Cohort from a Tertiary Care Center

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Abstract

Objective: Crohn's disease is a chronic inflammatory gastrointestinal condition characterized by periods of relapse and remission. The incidence and prevalence of Crohn's disease (CD) are increasing both globally and locally. This study aims to contribute to the literature by providing a retrospective analysis of patients diagnosed with CD in our hospital, thereby enhancing the Turkish data on the rising incidence of this condition.

Methods: This study included 247 patients diagnosed with Crohn's disease (CD) who were at least 18 years old. These patients were monitored by the Department of Gastroenterology at Eskişehir Osmangazi University. The study covered the period from January 1, 2016, to September 1, 2020. Data were collected across various categories, including clinical, laboratory, radiological, and histological characteristics at the time of presentation, as well as disease-related complications.

Results: The mean age at diagnosis was 38.84 years, with a mean disease duration of 76.56 months. Terminal ileal involvement was observed in 40.9% of cases, colonic involvement in 19%, and ileocolonic involvement in 32.4%. An inflammatory phenotype was identified in 80% of cases. Complications occurred in 30% of patients, and 23.5% underwent surgery.

Conclusion: In our study, isolated terminal ileum involvement was the most common presentation. The older age at diagnosis and longer disease duration in this patient group suggest an increased risk of complications due to diagnostic delays. These findings highlight the need for future research to identify factors contributing to such delays in diagnosis.

Keywords: Crohn's disease, inflammatory bowel disease, terminal ileum

INTRODUCTION

Inflammatory bowel diseases (IBD) are a group of inflammatory disorders characterized by cycles of remission and exacerbation, including ulcerative colitis (UC), Crohn's disease (CD), and indeterminate colitis (IC).¹ CD can affect any part of the gastrointestinal tract, from the mouth to the anus, as well as various segments of the colon. It often presents in a non-symmetrical and transmural pattern.^{2,3} The clinical manifestations vary significantly depending on the extent, location, and severity of the inflammation.⁴

The disease is most commonly diagnosed between the ages of 20 and 30, making it a condition that primarily affects younger individuals⁵. This study aims to evaluate the clinical and laboratory characteristics, time to diagnosis, phenotypic behavior, site of involvement, extraintestinal manifestations, surgical treatment requirements, and complications observed during follow-up in patients diagnosed with CD. For this purpose, the data of all patients diagnosed with CD and treated in our clinic over the past five years were retrospectively analyzed.

MATERIALS AND METHODS

A total of 247 adult patients (≥ 18 years of age) diagnosed with Crohn's disease (CD) were admitted to and followed up by the gastroenterology department at Eskişehir Osmangazi University Faculty of Medicine between January 1, 2016, and September 9, 2020. Patient information was collected from gastroenterology outpatient clinic follow-up notes and epicrisis using the ENLIL electronic record system.

Following approval granted by the Eskişehir Osmangazi University Faculty of Medicine Clinical Research Ethics Committee on November 3, 2020, under decision number 20, patient information was retrospectively analyzed. The study did not utilize artificial intelligence (AI)-assisted technologies, such as Large Language Models (LLMs), chatbots, or picture generators.

The following data were obtained from the follow-up records of patients with clinical, endoscopic, radiological, and histopathological diagnoses of Crohn's disease who were hospitalized or followed up as outpatients in the Department of Gastroenterology at a tertiary care center: gender, age at diagnosis, initial gastrointestinal symptoms, initial extraintestinal symptoms, initial extraintestinal findings, localization of disease involvement,

disease phenotype at diagnosis, and disease phenotype at the time of diagnosis.

A comprehensive review of the patients' medical histories was conducted, including the following variables: disease phenotype throughout the disease course, laboratory values prior to initiating treatment (complete blood count, C-reactive protein, fecal calprotectin test, erythrocyte sedimentation rate, and albumin), the presence of extraintestinal involvement, the localization of fistulas, and the type of medical treatments received (5-aminosalicylic acid, immunosuppressive agents, anti-TNF agents, and anti-integrin agents). Additionally, the patients' surgical histories were examined.

The results of colonoscopy, endoscopy, MR enterography, and biopsy obtained during endoscopy were retrospectively analyzed to determine the localization of the disease. The study was conducted in compliance with the Declaration of Helsinki.

Statistical Analyses

The suitability of the data for normal distribution was assessed using the Shapiro-Wilk test. Parametric tests were used for data conforming to a normal distribution, while nonparametric tests were applied to data that did not follow a normal distribution. Chi-square tests (Pearson, Pearson exact, Yates', and Fisher's exact tests) were used to analyze cross-tabulations. Data were summarized as mean±SD and median (Q1; Q3). A significance level of $P<0.05$ was considered. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA).

RESULTS

The demographic, clinical characteristics, and laboratory data of 247 patients diagnosed with Crohn's disease (CD) who were admitted to our hospital between January 1, 2016, and January 9, 2020, are summarized in Tables 1 and 2. The majority of patients were male (50.2%), with females accounting for 49.8%. Regarding age distribution, 34.8% of patients were under 30 years old, while 65.2% were over 30. The mean age at CD diagnosis was 38.84±14.2 years.

A total of 118 patients had relevant data available, with 48.3% reporting a history of smoking. Additionally, 15.7% of 115 patients had a family history of inflammatory bowel disease (IBD), and 18.5% of 243 patients ($n=45$) had a history of appendectomy.

The mean disease duration was 76.56±63.37 months, while the mean follow-up period was 38.3±31.10 months. For 117 patients with available data, the mean time to diagnosis was 18.4±25.8 months.

Isolated terminal ileal involvement was observed in 40.9% of cases, isolated colonic involvement in 19%, ileocolonic involvement in

Table 1. Demographic Characteristics of Study Population

| | Patients Whose Data Can Be Accessed | |
|-----------------------------|-------------------------------------|-----|
| Sex-male (n %) | 124 (50,2) | - |
| Sex-female (n %) | 123 (49,8) | - |
| Age (year±SD) | 38,84±14,29 | - |
| Under 30 years of age (n %) | 86 (34,8) | - |
| Over 30 years of age (n %) | 161 (65,2) | - |
| Smoking habit (n %) | 57 (48,3) | 118 |
| Family history | 18 (15,7) | 115 |
| Appendectomy | 45 (18,3) | 243 |

MAIN POINTS

- Irritable bowel syndrome (IBS) is a functional bowel disorder characterized by abdominal pain and changes in defecation habits, with no identifiable organic cause.
- Dysbiosis, or an imbalance in gut microbiota composition, is believed to play a significant role in the etiology of IBS, according to recent research.
- Microbiota awareness involves understanding the relationship between gut microbiota and disease, as well as knowledge about prebiotics and probiotics.
- Higher microbiota awareness has been shown to improve the quality of life in IBS patients by reducing disease symptoms.
- Increasing microbiota awareness through targeted initiatives may be an effective strategy for alleviating symptoms and enhancing the quality of life in individuals with IBS.

32.4%, and proximal gastrointestinal (GI) tract involvement in 7.7% of patients. Patients were divided into two groups: those with isolated ileal involvement and those without. The mean age at diagnosis for 101 patients with isolated ileal involvement was 40.9±13.9 years, with a mean disease duration of 69.8±63.28 months. For 146 patients with non-isolated ileal involvement, the mean age at diagnosis was 37.3±14.42 years, and the mean disease duration was 81.1±63.24 months. The analysis revealed that patients with isolated ileal involvement had a statistically significantly higher age at diagnosis compared to those with non-isolated ileal involvement (21.6±30.5 months vs. 16.2±22.1 months, respectively).

It is noteworthy that the mean time to diagnosis was longer for patients with isolated ileal involvement compared to those without (21.6±30.5 months vs. 16.2±22.1 months).

The Montreal classification system defines disease phenotypes at the time of diagnosis. Among the patients, the majority (80%) presented with an inflammatory phenotype, 13% exhibited a stricturing phenotype, and 7% displayed a fistulizing/penetrating phenotype.

Among the patients evaluated with multiple symptoms, abdominal pain was the most common initial complaint, present in 80.6% of cases. At the time of diagnosis, approximately one-quarter of patients exhibited at least one extraintestinal symptom, with arthritis/arthralgia being the most prevalent.

Regarding the occurrence of extraintestinal findings after diagnosis but before disease progression, 36% of patients exhibited at least one such finding, with arthritis/arthralgia being the most common (26.3%). Evaluation of the data according to gender revealed that the prevalence of this symptom was statistically higher among female patients.

Patients with isolated colonic involvement were more likely to have at least one extraintestinal finding compared to those without (27.7% vs. 26.5%, respectively). However, this difference was not statistically significant.

The distribution of complications was analyzed, including stenosis, restriction, and dilatation in the pathological segment. Intestinal complications were defined as intra-abdominal inflammatory masses, abscesses, perforations, and extra-perianal fistulas. Conversely, perianal

Table 2. Clinical Characteristics of The Study Population

| | | Patients Whose Data Can Be Accessed |
|--|-------------------|-------------------------------------|
| Disease duration | 76,56±63,37 month | - |
| Follow-up | 38,3±31,10 month | - |
| Average time to diagnosis (Average±SD) | 18,4±25,8 month | 117 |
| Gastrointestinal Involvement (N %) | | |
| İleitis | 101 (40,9) | |
| İleocolitis | 80 (32,4) | |
| Colitis | 47 (19) | |
| Upper GI tract | 19 (7,7) | |
| Time to Diagnosis According to Involvement Type | | |
| İleal involvement (Average±SD) | 21,6±30,5 month | 47 |
| Other (Average±SD) | 16,2±22,1 month | 70 |
| Disease Phenotypes (N %) | | |
| İnflammatory type | 198 (80) | |
| Fibrotic type | 32 (13) | |
| Penetrating type | 17 (6,9) | |
| Extraintestinal Manifestation (N %) | | |
| Arthritis/arthralgia | 50 (20,2) | |
| Skin problems | 16 (6) | |
| Ankylosing spondylitis/sacroiliitis | 10 (4) | |
| Eye problems | 8 (3,2) | |
| Osteoporosis | 7 (2,8) | |
| Liver problems | 4 (1,6) | |
| Thromboembolism | 4 (1,6) | |
| Genitourinary disease | 3 (1,2) | |
| Intestinal Complication | | |
| Stricture | 37 (50) | |
| İnflammatory mass | 14 (18,9) | |
| Abscess | 10 (13,5) | |
| Extra-perianal fistula | 9 (12,2) | |
| Perforation | 4 (5,4) | |
| Surgical Treatment | | |
| Number of patients (n %) | 58 (23,5) | |
| Age at diagnosis (Average±SD) | 35,4± 12,5 yıl | |
| Disease duration (Average±SD) | 111,8±82,9 ay | |
| Laboratory Tests (Average±SD) | | |
| Hgb (g/dL) | 12,77±2,05 | |
| Leukocyte(10 ³ /uL) | 9,7±3,7 | |
| Neutrophil(10 ³ /uL) | 6,9±3,6 | |
| Platelet(10 ³ /uL) | 341±135 | |
| CRP (mg/dl) | 18,26±34,70 | |
| ESR (ml/s) | 34,57±23,79 | |
| Albumin (g/dL) | 4,07±0,59 | |
| Medical Treatment (N %) | | |
| 5-aminosalicylates | 234 (98,4) | |
| Immun system suppressors | 147 (59,5) | |
| Anti-TNF | 64 (24,9) | |
| Anti-integrins | 15 (6,1) | |
| Number of relapse sayısı ≥ 2 (n %) | 68 (27,5) | |

disease was classified as perianal fissures and abscesses, which were not included in the category of intestinal complications.

While 70% of patients did not develop complications, 30% did. The mean time from disease onset to complication development was 49.7 ± 50.5 months. Among the 74 patients who developed complications, 74.3% had stenosing complications, while 25.7% experienced fistulizing or penetrating complications.

The most common surgical complications included stenosis or restriction in the pathological segment, as well as prestenotic dilatation (50%). Among patients who developed fistulas, the most common type was perianal (52.6%).

Surgical treatment was performed in 23.5% of patients, with the average age at diagnosis being 35.4 ± 12.5 years. The mean disease duration was 111.8 ± 82.9 months, and the mean time from symptom onset to diagnosis was 20.6 ± 28.8 months among the 26 patients with available data. It was statistically significant that patients undergoing surgical treatment exhibited a younger age at diagnosis and a longer disease duration compared to those who did not undergo surgical treatment.

The range of medical treatment options available to Crohn's disease patients in our study was also analyzed. The majority of patients (98.4%) received 5-aminosalicylate (5-ASA), while approximately 59.5% were treated with immunosuppressive therapy, 25% with anti-TNF therapy, and 6% with anti-integrin therapy.

A total of 226 patients received a diagnosis of Crohn's disease and were treated with steroids. Of these, 29.2% underwent systemic steroid treatment, while the remaining 70.8% did not. Additionally, 11.7% of patients were identified as steroid-dependent, and 17.8% were classified as steroid-resistant.

When the development and distribution of complication subtypes were analyzed in patients who were started on steroids at the time of diagnosis, it was observed that 66.7% of patients had no complications. Among the remaining patients, 13.6% developed surgical stenosis/stricture and prestenotic dilatation in the pathological segment, 10% ($n=7$) had an intra-abdominal inflammatory mass, 4.5% ($n=3$) had an extra-perianal fistula, 3% had an abscess, and 1.5% ($n=41$) experienced perforation.

A systematic evaluation of clinical data, radiologic imaging, endoscopic examinations, and laboratory values was performed, and the frequency of relapse was determined to be 27.5%, with a rate of fewer than two relapses per year.

Among the 55.4% of patients who developed at least one complication, the relapse frequency was two or fewer per year in 100% of cases.

DISCUSSION

Although there is some discrepancy in the literature regarding the prevalence of Crohn's disease (CD) in males versus females, our study found a male-to-female ratio of 1.008. This ratio aligns closely with the findings of other studies reporting similar distributions between genders.

CD typically demonstrates a first peak in incidence between the ages of 20 and 30, with a second peak occurring later in life. One study reported that 25% of patients were under the age of 20.⁶ In our analysis, 34.8% of Crohn's disease patients were aged 30 years or younger.

A study by Tozun et al.³ on patients diagnosed with Crohn's disease in Türkiye reported an average age at diagnosis of 37.4 ± 12.8 years (range: 17-73 years). In comparison, our study found a mean age at diagnosis of 38.84 ± 14.2 years (range: 18-68 years), which is consistent with national data. The observation that the age at diagnosis was below 40 years aligns with the increased prevalence of Crohn's disease among younger individuals observed globally.

The immune response triggered by Crohn's disease in genetically susceptible individuals highlights the importance of a family history of IBD as a significant risk factor. In a study by Farmer et al.,⁴ a family history was identified in 35% of 522 Crohn's disease patients, with 7.5% being close family members. In our study, 15.7% ($n=18$) of the 115 participants with available family history data were found to have a family history of IBD.

A survey of 4,990 individuals diagnosed with inflammatory bowel disease (IBD), conducted in collaboration with the European Crohn's and Colitis Organization (ECCO)⁷, reported that 20% of patients experienced a five-year delay between symptom onset and diagnosis of Crohn's disease (CD). Wagtmans et al.⁸ found no significant differences in the meantime to diagnosis between genders in their study. In contrast, our study revealed a mean time to diagnosis of 18.42 ± 25.8 months, supporting the notion that challenges in diagnosing CD contribute to diagnostic delays.

A study of patients in an American cohort found that 45.1% had ileal involvement, 32% had colonic involvement, 18.6% had ileocolonic involvement, and 4.2% had proximal gastrointestinal involvement.⁹

The proportion of patients with terminal ileal involvement was 40.9% ($n=101$), with 19% presenting with colonic involvement, 32.4% ($n=80$) with ileocolonic involvement, and 7.7% with proximal GI involvement. In our study, isolated terminal ileal involvement was detected with a high frequency, consistent with findings in the existing medical literature.

Data from the IMPACT study in Europe suggest that individuals under the age of 40 with isolated disease are at a heightened risk of delayed diagnosis.¹⁰ The median age at diagnosis for patients with isolated ileal involvement was found to be 13.90 years higher than that for those with isolated colonic involvement, while the median age for patients with isolated ileocolonic involvement was 14.42 years lower. These differences, however, were not statistically significant.

Furthermore, the median time to diagnosis for patients with isolated ileal involvement was 21.6 ± 30.5 months, compared to 16.2 ± 22.1 months for patients with non-isolated involvement. Although this difference suggests a trend toward delayed diagnosis in isolated cases, it did not reach statistical significance. The lack of statistical significance may be attributed to the limited number of patients available for analysis.

The study by Arora et al. reported that the inflammatory phenotype constituted 51% of cases ($n=207$), the stricturing phenotype accounted for 41.4% ($n=168$), and the fistulizing/penetrating phenotype represented 8.1% ($n=31$).¹¹ Similarly, in our analysis, 80% of cases ($n=198$) were classified as the inflammatory phenotype, 13% ($n=32$) as the stricturing phenotype, and 6.9% ($n=17$) as the fistulizing/penetrating phenotype, the least common type.

The shortest interval between the onset of symptoms and diagnosis was observed in patients with the fistulizing/penetrating phenotype, while

the longest was associated with the inflammatory phenotype. Delays in diagnosing the inflammatory phenotype may, in part, be due to the more subtle presentation of intestinal symptoms. In contrast, the fistulizing/penetrating phenotype often significantly impacts a patient's quality of life and may lead to severe or life-threatening complications, prompting earlier diagnosis.

The most common GI symptoms in our study were abdominal pain (80.6%) and diarrhea (55.1%), findings consistent with those reported in the existing literature.

In the community cohort study conducted by Bernstein et al.,¹² 36% of patients experienced at least one extraintestinal manifestation. A study by Tavela Veloso¹³ reported that 26% of patients with inflammatory vertebral involvement exhibited extraintestinal symptoms. In our study, the occurrence of at least one extraintestinal manifestation was identified in 26.7% of patients ($n=66$), which is higher than the rates reported in previous studies. One of the most common symptoms of Crohn's disease (CD) is appendicitis, which occurs in approximately 20% of patients.¹⁴ In our study, the prevalence of rheumatologic conditions, including arthritis and arthralgia, was 20.2% ($n=50$), consistent with findings in the existing literature.

Several studies have demonstrated that colonic involvement is associated with an increased risk of developing extraintestinal symptoms.¹⁵ Although not statistically significant, our study found that patients with isolated colonic involvement had a slightly higher rate of extraintestinal symptoms compared to those without (27.7% vs. 26.5%, respectively).

It is estimated that 21% to 47% of Crohn's disease (CD) patients may experience systemic symptoms and complications.¹⁶ In our study, 30% of patients ($n=74$) developed complications after an average of 49.7±50.5 months. A 2002 study by Cosnes et al.¹⁷ analyzed a retrospective cohort of 646 CD patients with a mean disease duration of more than five years. Of these, 60% ($n=1199$) were found to have either stricturing or penetrating complications.

In our study, 74.3% ($n=55$) of patients with complications developed a stenosing-type complication, while 25.7% ($n=19$) experienced a fistulizing or penetrating complication. The discrepancy in findings between our study and those reported in the literature may stem from differences in follow-up durations. Unlike the common trend in the literature, stenosing complications were more prevalent in our cohort than penetrating complications.

As disease duration increases, the frequency of penetrating complications tends to rise, while the prevalence of inflammatory complications diminishes. This shift may be related to the relatively younger age of the participants in our study, as younger patients may be at an earlier stage in the natural progression of the disease.

In their analysis of data from the Swiss IBH cohort study, Schoepfer et al.¹⁸ reported that patients with delayed diagnoses were at an increased risk of requiring intestinal surgery due to Crohn's disease. Similarly, a prospective cohort study involving several centers in France found that delayed diagnosis heightened the risk of early surgery.¹⁹

In our study, 23.5% of patients ($n=58$) underwent surgery. The median age at which surgical treatment was performed was 35.4±12.5 years, while the median disease duration was 111.8±82.9 months. The relatively younger age at diagnosis among patients who required surgical

treatment compared to those who did not suggests that Crohn's disease may present more severely in younger individuals.

The observation that patients undergoing surgical procedures tend to have a longer history of disease than those who do not may reflect sub-optimal medical management and an associated increased incidence of complications. Crohn's disease is known to exhibit more aggressive behavior in younger patients. A study of 1,188 Crohn's disease patients within the first five years of diagnosis found an association between steroid use at the time of diagnosis, age below 40, and increased clinical severity and morbidity.²⁰

Although not statistically significant, the mean age at diagnosis for patients who developed complications (37.1±14.58 years; range 19-58) was slightly younger than that of those who did not develop complications (39.5±14.15 years; range 18-58).

Systemic steroids are a common treatment for moderate-to-severe Crohn's disease (CD). However, approximately 20% of patients have been reported to show an inadequate response to steroid therapy, while 36% are considered steroid-dependent.²¹ Differentiating between steroid dependence and steroid resistance can be challenging, as the steroid response is often dose-dependent. In contrast to previous studies, our analysis revealed that 11.7% ($n=29$) of patients with available data were steroid-dependent, while 17.8% ($n=44$) exhibited steroid resistance.

This study has some limitations, including a relatively small patient population and missing data, partly attributable to the impact of the COVID-19 pandemic. However, patients diagnosed and followed at our university hospital were thoroughly evaluated.

The majority of CD cases occur in individuals under 40 years of age. Chronic, non-specific symptoms that often mimic irritable bowel syndrome can contribute to delayed diagnosis. CD can affect multiple organs, including the joints, eyes, and skin, in a potentially destructive manner. Early identification of demographic, clinical, and laboratory characteristics is critical for guiding diagnosis, treatment, and follow-up, as well as for reducing complications.

Our study found that isolated terminal ileum involvement was common. Older patients and those with longer disease durations were associated with higher risks of complications, likely due to delays in diagnosis. These findings highlight the importance of further research into the factors contributing to diagnostic delays in CD.

Ethics Committee Approval: Ethics committee approval was obtained from the Eskişehir Osmangazi University Faculty of Medicine Clinical Research Ethics Committee (Approval Number: 20, Date: 3.11.2020).

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