Clinical Characteristics of Crohn’s Disease in a Cohort from Saudi Arabia

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Abstract
Objective: In Saudi Arabia, there are limited studies on the clinical characteristics of patients specifically with Crohn’s disease (CD). This study was conducted to describe the clinical characteristics of CD at a tertiary care center in Jeddah, Saudi Arabia.

Methods: This retrospective study included all patients aged >14 years who had a definitive diagnosis of CD and were managed at King Abdulaziz University Hospital, Jeddah, Saudi Arabia, between 2012 and 2018. Data were collected for the following categories: clinical, laboratory, radiological, histological features at presentation, and disease-related complications.

Results: The study included 245 newly diagnosed CD patients, aged 14–73 years (median: 26.3 years). All subjects presented with abdominal pain. Majority of the patients (59.7%) received a definitive diagnosis of CD >3 months after the onset of symptoms: 15.1% were initially suspected to have intestinal tuberculosis. Diarrhea and bleeding per rectum were reported in 60.8% and 49.7% of the patients, respectively. Sacroiliitis was the most frequent extraintestinal manifestations (11.4%). In terms of disease location, the terminal ileum (L1) was the most affected area (46.9%). Twenty-five patients had perianal disease, of which 40% had complex fistulae and 36% had perianal abscesses. The majority had hemoglobin levels >10 g/dl (74.1%), decreased serum iron (69.6%) and ferritin (50.5%) levels, and elevated erythrocyte sedimentation rate (68.2%) and C-reactive protein (82.2%).

Conclusions: The majority of the patients in our cohort presented with the characteristic quartet of abdominal pain, weight loss, fever, and diarrhea. This study also found a significant number of patients with CD in Saudi Arabia experience diagnostic delay, which may contribute to disease morbidity and complications. These findings highlight the need for future studies to determine factors influencing this diagnostic delay.

Keywords: Crohn’s diagnosis, Crohn’s disease, diagnostic delay, gastrointestinal diseases, inflammatory bowel disease, Saudi Arabia

INTRODUCTION
Crohn’s disease (CD) is a type of inflammatory bowel disease (IBD) that causes chronic granulomatous inflammation of the gastrointestinal tract. It has a high recurrence rate and unpredictable disease course. Recent studies have shown an increased global trend in the prevalence of CD in Western countries,[1‑4] Asia,[5,6] and the Arab world.[7] The incidence of CD is also increasing in Saudi Arabia.[8‑11]

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The disease is characterized by transmural inflammation, which may result in strictures, micro-perforations, and fistulae. Inflammation of the intestinal wall is not necessarily continuous, and thus, CD has a characteristic “skip lesions,” in which the disease is observed intermittently throughout the bowel. Histologically, CD displays transmural lymphoid aggregates, fissuring, non-necrotizing granulomas, and microscopic skip lesions. While granulomas are strongly suggestive of CD, they occur only in 40–60% of the CD patients.

CD may initially manifest as recurrent abdominal pain or diarrhea, symptoms often mistaken for irritable bowel syndrome (IBS) in clinical practice. The symptoms of CD may be present for several months or years prior to diagnosis and the initiation of treatment. A recent study from central Saudi Arabia found that the average duration between the onset of symptoms and diagnosis was 11 months. Many factors were reported to result in delay in CD diagnosis including patient and physician-related factors such as a delay in seeking medical care secondary to patient ignorance, psycho-social or cultural beliefs, inadequate clinical evaluation, and insufficient follow-up. According to several reports from Saudi Arabia, abdominal pain, diarrhea, and weight loss are the most common presenting symptoms in patients with CD. Extraintestinal manifestations such as arthralgia, clubbing of the fingers, and pallor have also been documented. Rare extraintestinal manifestations include ocular manifestations and sclerosing cholangitis, which are observed in <5% of the patients. Data from Saudi Arabia also support an increased risk of CD in relatives of patients with IBD.

There are conflicting results among national and international studies with regards to the median age at diagnosis, symptom duration prior to diagnosis, and gender preponderance in CD. Further, in Saudi Arabia, there are limited studies on the clinical characteristics of patients specifically with CD. An improved understanding of the clinical characteristics and complications of CD would provide a more robust context for evaluating future intervention-based research. This study was conducted with the objective of describing the clinical characteristics of CD in a university hospital from the Western region of Saudi Arabia.

METHODS

Study design, setting, and participants
This retrospective study included all patients aged >14 years who had a definitive diagnosis of CD and were managed at King Abdulaziz University Hospital, Jeddah, Saudi Arabia, between 2012 and 2018. Patients were considered to have “definite” CD when they fulfilled a combination of clinical, endoscopic and histologic criteria, based on the World Health Organization’s diagnostic criteria for Crohn’s disease. The study was conducted after obtaining approval from the Research Ethics Committee of King Abdulaziz University, Jeddah, Saudi Arabia.

King Abdulaziz University Hospital is one of the largest tertiary care government hospitals in the western region of Saudi Arabia and receives patients from across the country. Therefore, the patients from this hospital can be adequately representative of the population.

Data collection
Patient data were collected from the electronic database of the hospital. The study aimed at reporting the most common clinical, laboratory, radiological, and histological features associated with CD. Accordingly, data on demographic variables (age, gender, nationality, and residence location in Saudi Arabia), clinical variables (clinical presentation, symptoms, symptom duration, time interval between the onset of symptoms and diagnosis, extraintestinal manifestations, number of previous hospital admissions, past medical history, past surgical history, and family history), diagnosing physician’s specialty, and treatment offered were collected. In addition, data on laboratory findings (complete blood count, erythrocyte sedimentation rate, C-reactive protein, iron level, total iron binding capacity, ferritin level, and stool analysis) were also extracted, and imaging reports including ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI) of the abdomen and perianal area were reviewed. Endoscopy and histopathological results were also reviewed.

Scoring and categorization
The electronic records did not include unified scores for evaluation of disease activity or severity. However, we categorized the different collected items according to the various reported scores for CD’s activity and severity. Abdominal pain, bowel frequency, presence of abdominal mass and presence of extraintestinal manifestations were categorized into the Harvey–Bradshaw index. Presence of blood in stool was classified into trace, occasionally frank, and usually frank, according to the Clinical Scoring System for the Simple Clinical Colitis Activity Index. Laboratory tests were categorized according to Truelove and Witts’ disease activity grades in inflammatory bowel disease.
L2; ileocolonic, L3; and upper gastrointestinal (GI), L4.[22]
Perianal fistulizing disease was recorded as a modifier of the disease behavior (p), and the fistulas observed on MRI were classified as simple or complex, according to the Perianal Crohn’s Disease Activity Index.[23]

Statistical analysis
Data were analyzed using SPSS version 16 (SPSS Inc., Chicago, IL., US). Descriptive statistics were computed for all variables. Results are expressed as frequency (percentage) for categorical variables and as mean (standard deviation [SD]) and range for continuous variables.

RESULTS
A total of 245 patients newly diagnosed with CD met the inclusion criteria of the study. Patients’ age ranged from 14 to 73 years (median age: 26.3 years). About half of the sample (51%) were males, and 68.5% were Saudi [Table 1].

Diagnosis
Most patients (59.7%) received a definitive diagnosis of CD only >3 months after the onset of symptoms. About 15.1% (n = 37) of the patients were initially suspected to have intestinal tuberculosis, which contributed to delay in the diagnosis; none received antitubercular medication, as definite diagnosis was not reached.[24] The majority of the participants (71.4%) were diagnosed by gastroenterologists, while only 3.5% were diagnosed by general practitioners [Table 2].

Clinical presentation
All participants presented with abdominal pain; central abdominal pain (45.5%) was the most common, followed by the right and left lower quadrants (34.0% and 8.4%, respectively). About 65% reported their abdominal pain intensity as “severe.” Diarrhea was documented in 60.8% of the participants, while the remaining had regular bowel habits. Among those who reported diarrhea, 2.9% experienced alternating bouts of constipation and diarrhea. About half of the patients (49.7%) reported blood in stool; bloody stools were predominant in 23.8%. Weight loss, fever, and vomiting (46.1%, 38.8%, and 38.8%, respectively) were other common presenting symptoms. Of those with weight loss, 19.5% had lost >10% of their body weight at presentation [Table 3].

Extraintestinal manifestations
Sacroiliitis was the most frequent extraintestinal manifestation (11.4%), followed by arthritis or arthralgia (6.5%) and aphthous ulcers of the oral cavity (4.9%). Scleritis, erythema nodosum, and deep venous thrombosis were infrequent extraintestinal manifestations [Table 3].

Medical and surgical history
About 10.2% of the participants had a history of perianal disease, 4.5% of tuberculosis, and 4.1% of contact with an individual diagnosed with tuberculosis. Upper gastrointestinal tract involvement was reported in 4.9% of the patients. Ten patients (4.1%) had a family history of CD and 3 (1.2%) of tuberculosis. Twenty-eight patients underwent bowel surgery (11.4%), either prior to or following CD diagnosis, with right hemicolectomy accounting for three-fourths of all surgeries. The majority were admitted to a hospital at least three times during the illness [Table 4].

Imaging findings
Seventy-nine patients (32.2%) had an ultrasound examination. Findings were suggestive of a thickened bowel (20.3%), intra-abdominal or pelvic collections (16.5%), and an abdominal mass (3.8%). Ultrasound revealed enlarged lymph nodes in 10 patients, of which 60% had >1 cm in diameter [Table 5].

A computed tomography (CT) examination was performed in 123 patients. Findings included abdominal collections (17.9%), abdominal masses (11.4%), and thickened bowel (62.6%). CT revealed enlarged lymph nodes in 61 of 123 abdominal CT examinations (49.6%), the
majority of which were <1 cm in diameter (62.3%) [Table 5]. Based on the Montreal classification for disease location, the terminal ileum (L1) was the most affected area (115 patients; 46.9%) followed by the ileocolonic area (L3) (106 patients; 43.3%) [Table 6]. Twenty-five patients had perianal disease, of which complex fistulae were noted in 10 cases (40%) [Table 5].

**Table 3: Clinical presentations and symptoms of the patients**

| Variables                             | n (%)     |
|---------------------------------------|-----------|
| Abdominal pain at presentation (n=224) |           |
| Mild                                  | 78 (34.8) |
| Severe                                | 146 (65.2) |
| Location of abdominal pain at presentation (n=191) |       |
| Right lower quadrant                  | 65 (34.0) |
| Left lower quadrant                   | 16 (8.4)  |
| Central                               | 87 (45.5) |
| Diffuse                               | 19 (9.9)  |
| Right lower and left lower quadrants  | 4 (2.1)   |
| Abdominal distension at presentation  | 40 (16.3) |
| Nausea at presentation                | 63 (25.7) |
| Vomiting at presentation              | 95 (38.8) |
| Fever at presentation                 | 95 (38.8) |
| Excessive night sweating              | 13 (5.3)  |
| Weight loss                           | 113 (46.1)|
| Degree of weight loss (n=113)         |           |
| <10%                                  | 91 (80.5) |
| >10%                                  | 22 (19.5) |
| Bowel habit (n=245)                   |           |
| None                                  | 78 (31.8) |
| Constipation                          | 11 (4.5)  |
| Diarrhoea                             | 149 (60.8)|
| Diarrhoea and constipation            | 7 (2.9)   |
| Frequency of diarrhoea (times/day) (n=144) |       |
| <4                                    | 94 (65.3) |
| 4-6                                   | 35 (24.3) |
| >6                                    | 15 (10.4) |
| Characteristics of diarrhoea (n=147)  |           |
| Usually frank blood                   | 35 (23.8) |
| Occasionally frank blood              | 39 (26.5) |
| Trace of blood                        | 73 (49.7) |
| Extraintestinal symptoms (n=245)      |           |
| Arthritis                             | 16 (6.5)  |
| Sacroiliitis or back pain             | 28 (11.4) |
| Erythema nodosum                      | 3 (1.2)   |
| Scleritis (painful eyes)              | 5 (2.0)   |
| Aphthous ulceration                   | 12 (4.9)  |
| Deep venous thrombosis                | 2 (0.8)   |

**Table 4: Patients’ medical and surgical histories**

| Variables                                | Frequency (%) |
|------------------------------------------|---------------|
| Family history of Crohn’s disease        | 10 (4.1)      |
| Perianal disease                         | 25 (10.2)     |
| Other percutaneous fistulae              | 6 (2.4)       |
| Upper gastrointestinal involvement       | 12 (4.9)      |
| Personal history of tuberculosis         | 11 (4.5)      |
| Family history of tuberculosis           | 3 (1.2)       |
| Contact with tuberculosis patient        | 10 (4.1)      |
| Previous bowel surgeries                 | 28 (11.4)     |
| Type of surgery                          |               |
| Proctectomy                              | 1 (3.7)       |
| Colostomy                                | 1 (3.7)       |
| Ileostomy                                | 3 (11.1)      |
| Right hemicolectomy                      | 20 (74.1)     |
| Small bowel resection                    | 2 (7.4)       |

**Laboratory and histopathology findings**

Histopathological examination was available in only 126 (51.4%) of the patients’ records, and revealed non-caseating granulomas in 23 (18.2%). Acid-fast bacilli were isolated in only 2 (1.5%) patients. Thirty-five patients underwent polymerase chain reaction to diagnoses tuberculosis, resulting in 3 positive tests (8.5%); that is, three patients had both TB and CD simultaneously [Table 6].

White blood cell counts, platelets, and total iron binding capacity were normal in most patients [Table 7], and the majority (74.1%) had hemoglobin levels >10 g/dl. Serum iron and ferritin were below normal levels in 69.6% and

**Table 5: Radiology investigations**

| Variables                                      | Frequency (%) |
|------------------------------------------------|---------------|
| Ultrasound abdomen and pelvis                  | 79 (32.2)     |
| Lymph node observed on ultrasound (cm) (n=10)  |               |
| <1                                             | 4 (40.0)      |
| >1                                             | 6 (60.0)      |
| Collections observed on ultrasound             | 13 (16.5)     |
| Mass observed on ultrasound                    | 3 (3.8)       |
| CT (n=183)                                     |               |
| No                                             | 58 (31.7)     |
| CT abdomen and pelvis + enterography           | 123 (67.2)    |
| Magnetic resonance enterography               | 2 (1.1)       |
| Lymph node observed on CT (n=68)               |               |
| Few                                            | 30 (44.1)     |
| Many                                           | 38 (55.9)     |
| Lymph node size (cm) (n=61)                    |               |
| <1                                             | 38 (62.3)     |
| >1                                             | 23 (37.7)     |
| Collection observed on CT                      | 22 (17.9)     |
| Mass observed on CT                            | 14 (11.4)     |
| Thick bowel wall observed on CT                | 77 (62.6)     |
| Large bowel involvement observed on CT         | 45 (36.6)     |
| Small bowel involvement observed on CT         | 89 (72.3)     |
| Small and large bowel involvement on CT        | 29 (23.6)     |
| Terminal ileum involved                        | 48 (39.0)     |
| Proximal areas                                 | 8 (6.5)       |
| Areas of involvement in the small bowel (n=59) |               |
| Multiple                                       | 12 (20.3)     |
| Single                                         | 47 (79.7)     |
| MRI of the perianal area                       | 25 (10.2)     |
| Simple fistula                                 | 15 (60)       |
| Complex fistula                                | 10 (40)       |
| Presence of a collection on MRI               | 9 (28.1)      |

**Table 6: Histopathological and endoscopic examinations**

| Variables                                      | n (%)     |
|------------------------------------------------|-----------|
| Histological findings of colonic biopsy        | 126 (51.4)|
| Noncaseating granuloma on histological examination | 23 (18.2) |
| Acid-fast bacilli                              | 2 (1.5)   |
| PCR for tuberculosis                           | 35 (27.8) |
| Positive PCR for tuberculosis                  | 3 (8.5)   |
| Gastrointestinal location on endoscopy (according to Montreal classification) |       |
| Colon (L2)                                     | 24 (9.8)  |
| Illeocolonic (L3)                              | 106 (43.3)|
| Terminal ileum (L1)                            | 115 (46.9)|
| Proximal bowel involvement (L4)                | 8 (3.3)   |

CT: Computed tomography, MRI: Magnetic resonance imaging

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Qari: Characteristics of Crohn’s disease

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| Right hemicolectomy                      | 20 (74.1)     |
| Small bowel resection                    | 2 (7.4)       |
Diagnostic delay was frequent in the cohort. Our findings are consistent with previous hospital-based studies conducted in Western[25–27] and Gulf[28–30] countries. We hypothesize that in our cohort, this delay was secondary to patient characteristics, such as delay in the patients seeking initial medical advice, and practitioner characteristics, such as not considering CD at the initial medical evaluation.

Extraintestinal symptoms were not uncommon in our cohort: approximately one-fifth of the participants reported sacroiliitis or back pain. Joint involvement is the most prevalent extraintestinal manifestations observed in our study, which is different from the data reported in the literature. For example, Card et al.[39] reported skin manifestations such as pyoderma gangrenosum and erythema nodosum were the most common extraintestinal symptoms. As the extraintestinal symptoms in CD often overlap with those of other IBD conditions, diagnosis may be even more challenging in this subset population.[40] The radiologic and endoscopic findings in our patients are similar to that of patients in studies conducted nationally and internationally.

**Limitations**

The current study has limitations such as its small sample size and retrospective design, and thus, the results should be interpreted with caution. Importantly, data regarding follow-up, change in disease behavior, number of flares, types of therapy, and patient outcomes could not be evaluated. Another limitation was that a unified score for evaluation of the disease severity and activity was not used.

**DISCUSSION**

This descriptive study of patients newly diagnosed with CD at a university hospital in the Western region of Saudi Arabia documents three important findings: a significant diagnostic delay, the characteristic presenting symptoms, and radiological findings.

Some authors have also found that diagnostic delay may be affected by patient’s socioeconomic status.[31,32] However, findings from a prospective study conducted at two referral centers in France did not find any significant correlation between socioeconomic status and diagnostic delay.[24] In the current study, other patient demographical factors did not influence diagnostic delay in CD. As our study design precludes determination of causality, future studies are needed to unequivocally determine factors that influence the diagnostic delay in CD patients.

The prevalence of isolated small bowel disease in the current study is relatively higher (46%) compared with other studies in the literature.[53] This high percentage could be due to referral bias, as the data collected are from a large tertiary care referral center for IBD. The majority of the patients in our cohort presented with the characteristic quartet of abdominal pain, weight loss, fever, and diarrhea. These four symptoms have previously been reported in the medical literature as the hallmark symptoms of CD.[34] While the majority of patients in our study presented with diarrhea (60.8%), it was less prevalent than that reported in other studies (70–90%).[35–37] Our findings are consistent with the “red flag” signs and symptoms suggestive of a diagnosis of CD, as reported by Danese et al.[38] The findings from our study indicate the need to educate general practitioners about these red flags to improve the frequency of early diagnosis.

50.5% of the patients, respectively. Most of the cohort had an elevated erythrocyte sedimentation rate (68.2%) and C-reactive protein (82.2%). Stool analysis revealed pustular cells (i.e., white blood cells/neutrophils) in 23 patients (13.9%) and *Entamoeba histolytica* cysts in seven patients (5.3%).

### Table 7: Laboratory investigations

| Variables | Frequency |
|-----------|-----------|
| White blood cell count *(n=231)* |  |
| Low | 14 (6.1) |
| Elevated | 44 (19.0) |
| Normal | 173 (74.9) |
| Platelet count *(n=23)* |  |
| Low | 5 (2.2) |
| Elevated | 41 (17.8) |
| Normal | 184 (80.0) |
| Haemoglobin level *(n=228) (g/dl)* |  |
| >10 | 169 (74.1) |
| <10 | 59 (25.9) |
| Serum iron *(n=115)* |  |
| Normal | 35 (30.4) |
| Low | 80 (69.6) |
| Serum ferritin *(n=111)* |  |
| Normal | 46 (41.4) |
| Low | 56 (50.5) |
| High | 9 (8.1) |
| Total iron binding capacity *(n=83)* |  |
| Low | 12 (14.5) |
| Normal | 48 (57.8) |
| High | 23 (27.7) |
| Erythrocyte sedimentation rate *(n=211)* |  |
| Normal | 67 (31.8) |
| High | 144 (68.2) |
| C-reactive protein *(n=213)* |  |
| Normal | 38 (17.8) |
| High | 175 (82.2) |
| C-reactive protein level *(n=164)* |  |
| <20 | 101 (61.6) |
| 20–40 | 29 (17.7) |
| >40 | 34 (20.7) |
| Pus cells observed on stool examination *(n=165)* |  |
| Yes | 23 (13.9) |
| *Entamoeba histolytica* observed on stool examination *(n=132)* |  |
| Yes | 7 (5.3) |
among the patients, although most cases were diagnosed by gastroenterologists.

CONCLUSIONS

A significant proportion of CD patients in the study cohort experienced diagnostic delay, which may have contributed to disease morbidity. The finding highlights the need for future studies to determine factors that influence diagnostic delay in patients with CD in the region, as well as the need for educating general practitioners for an early diagnosis of CD.

Ethical considerations

The study received ethical approval from the Research Ethics Committee at King Abdulaziz University (Ref. no.: 51-15; date: March 09, 2015). Requirement for consent was waived by the Ethics Committee owing to the study design. The study adhered to the principles of the Declaration of Helsinki, as revised in 2013.

Data availability statement

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

Peer review

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Freeman K, Ryan R, Parsons N, Taylor-Phillips S, Willis BH, Clarke A. The incidence and prevalence of inflammatory bowel disease in UK primary care: A retrospective cohort study of the IQVIA Medical Research Database. BMC Gastroenterol 2021;21:139.
2. Businge D, Pollack A, Chidwick K. Prevalence of inflammatory bowel disease in the Australian general practice population: A cross-sectional study. PLoS One 2021;16:e0252458.
3. Pasvol TJ, Horsfall L, Bloom S, Segal AW, Field N, et al. Incidence and prevalence of inflammatory bowel disease in UK primary care: A population-based cohort study. BMJ Open 2020;10:e036584.
4. Xu F, Carlson SA, Liu Y, Greenlund KJ. Prevalence of inflammatory bowel disease among Medicare fee-for-service beneficiaries – United States, 2001-2018. MMWR Morb Mortal Wkly Rep 2021;70:698-701.
5. Mak WY, Zhao M, Ng SC, Burisch J. The epidemiology of inflammatory bowel disease: East meets west. J Gastroenterol Hepatol 2020;35:380-9.
6. Ng WK, Wong SH, Ng SC. Changing epidemiological trends of inflammatory bowel disease in Asia. Intest Res 2016;14:111-9.
7. Azzam N, Al-Jebreen A, Abdo A, Al-Sawat K, Al-Mofleh I, Al-Rashe R. Emerge in Crohn's disease incidence in Saudi Arabia: Tertiary care centre experience. In: The 9th GI and Liver Disease Conference. Abha: KSA; 2007.
8. Mosli M, Alawadhi S, Hasan F, Abou Rachid A, Sanai F, Danese S. Incidence, prevalence, and clinical epidemiology of inflammatory bowel disease in the Arab world: A systematic review and meta-analysis. Inflamm Intest Dis 2021;6:123-31.
9. Al-Mofarreh MA, Al-Mofleh IA, Al-Temimi IN, Al-Jebreen AM. Crohns disease in a Saudi outpatient population: Is it still rare. Saudi J Gastroenterol 2009;15:111-6.
10. Al-Mofarreh MA, Al-Mofleh IA. Emerging-inflammatory bowel disease in Saudi outpatients: A report of 693 cases. Saudi J Gastroenterol 2013;19:16-22.
11. Al-Mofleh IA, Azzam NA. Crohn's disease: Increasing trend in Saudi Arabia. Saudi Med J 2013;34:1105-13.
12. Vavricka SR, Spigaglia SM, Rogler G, Pittet V, Michetti P, Felley C, et al. Systematic evaluation of risk factors for diagnostic delay in inflammatory bowel disease. Inflamm Bowel Dis 2012;18:496-505.
13. Al Salamah S. Surgery for small bowel Crohn's disease: Experience of a tertiary referral center. Saudi J Gastroenterol 2005;11:85.
14. Contractor Q, Contractor T, UI Haque I, El Mahdi EM. Crohn's disease among Saudis in Al-Gassim region. Saudi J Gastroenterol 2005;11:157-63.
15. Al-Jebreen AM, Alharbi OR, Azzam NA, Almalki AS, Alswat KA, Almadi MA. Clinical epidemiology and phenotypic characteristics of Crohn's disease in the central region of Saudi Arabia. Saudi J Gastroenterol 2014;20:162-9.
16. Mosli M, Atzahrani A, Showlag S, Alshehri A, Hejazi A, Alnefaie M, et al. A cross-sectional survey of multi-generation inflammatory bowel disease consanguinity and its relationship with disease onset. Saudi J Gastroenterol 2017;23:337-40.
17. Hunt R, Armstrong D, Katelaris P, Athene M, Bane A, Bhatia S, et al. World gastroenterology organisation global guidelines. J Clin Gastroenterol 2017;51:467-78.
18. Sturm A, Maaser C, Calabrese E, Annese V, Fioriono G, Kucharzik T, et al. ECCO-ESGAR guideline for diagnostic assessment in IBD part 2: IBD scores and general principles and technical aspects. J Crohns Colitis 2019;13:273-84.
19. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet 1980;315:514.
20. Walmesley RS, Ayres RC, Pounder RE, Allan RN. A simple clinical colitis activity index. Gut 1998;43:29-32.
21. Truelove SC, Witts LJ. Cortisone in ulcerative colitis; final report on a therapeutic trial. Br Med J 1955;2:1041-8.
22. Satsangi J, Silverberg MS, Vermeire S, Colombel JF. The montreal classification of inflammatory bowel disease: Controversies, consensus, and implications. Gut 2006;55:749-53.
23. Jan Irvine E, Castelli M, Collins SM, Goodacre RJ, Hunt RH, Lumb B, et al. Usual therapy improves perianal Crohn's disease as measured by a new disease activity index. J Clin Gastroenterol 1995;20:27-32.
24. Shi XC, Zhang LF, Zhang YQ, Liu XQ, Fei GJ. Clinical and laboratory diagnosis of intestinal tuberculosis. Chin Med J (Engl) 2016;129:1330-3.
25. Nahon S, Lahmek P, Saas C, Durance C, Olympie A, Lesgourgues B, et al. Socioeconomic and psychological factors associated with nonadherence to treatment in inflammatory bowel disease patients: Results of the ISSEO survey. Inflamm Bowel Dis 2011;17:1270-6.
26. Chouraki V, Savoye G, Dauchet L, Vernier-Massouille G, Dupas JL, Merle V, et al. The changing pattern of Crohn's disease incidence in northern France: A continuing increase in the 10- to 19-year-old age bracket (1988-2007). Aliment Pharmacol Ther 2011;33:1133-42.
27. Schoepfer AM, Delhavi MA, Fournier N, Safroneeva E, Straumann A, Pittet V, et al. Diagnostic delay in Crohn's disease is associated with a complicated disease course and increased operation rate. Am J Gastroenterol 2013;108:1744-53.
28. Burisch J, Pedersen N, Čuković-Čavka S, Brinar M, Kaimakliotis I, Duricova D, et al. East-West gradient in the incidence of inflammatory bowel disease among the patients, although most cases were diagnosed by gastroenterologists.

Qari: Characteristics of Crohn's disease
bowel disease in Europe: The ECCO-EpiCom inception cohort. Gut 2014;63:588-97.

29. Nahon S, Lahmek P, Lesgourgues B, Poupardin C, Chaussade S, Peyrin-Biroulet L, et al. Diagnostic delay in a French cohort of Crohn’s disease patients. J Crohns Colitis 2014;8:964-9.

30. Bihan H, Laurent S, Sass C, Nguyen G, Huot C, Moulin JJ, et al. Association among individual deprivation, glycemic control, and diabetes complications: The EPICES score. Diabetes Care 2005;28:2680-5.

31. Sewell JL, Velayos FS. Systematic review: The role of race and socioeconomic factors on IBD healthcare delivery and effectiveness. Inflamm Bowel Dis 2013;19:627-43.

32. Baumgart DC, Sandborn WJ. Crohn’s disease. Lancet. 2012;380:1590-605.

33. Voderholzer WA, Beinhoelzl J, Rogalla P, Murrer S, Schachschal G, Lochs H, et al. Small bowel involvement in Crohn’s disease: A prospective comparison of wireless capsule endoscopy and computed tomography enteroclysis. Gut 2005;54:369-73.

34. Vavricka SR, Schoepfer A, Scharl M, Lakatos PL, Navarini A, Rogler G. Extraintestinal manifestations of inflammatory bowel disease. Inflamm Bowel Dis 2015;21:1982-92.

35. Al-Ghamdi AS, Al-Mofle IA, Al-Rashed RS, Al-Amri SM, Aljebreen AM, Isnani AC, et al. Epidemiology and outcome of Crohn’s disease in a teaching hospital in Riyadh. World J Gastroenterol 2004;10:1341-4.

36. Almadi MA, Aljebreen AM, Sanai FM, Marcus V, Almeghaiseeb ES, Ghosh S. New insights into gastrointestinal and hepatic granulomatous disorders. Nat Rev Gastroenterol Hepatol 2011;8:455-66.

37. Leong RW, Lawrance IC, Chow DK, To KF, Lau JY, Wu J, et al. Association of intestinal granulomas with smoking, phenotype, and serology in Chinese patients with Crohn’s disease. Am J Gastroenterol 2006;101:1024-9.

38. Danese S, Fiorino G, Mary JY, Lakatos PL, D’Haens G, Moja L, et al. Development of red flags index for early referral of adults with symptoms and signs suggestive of Crohn’s disease: An IOIBD initiative. J Crohns Colitis 2015;9:601-6.

39. Card TR, Langan SM, Chu TP. Extra-gastrointestinal manifestations of inflammatory bowel disease may be less common than previously reported. Dig Dis Sci 2016;61:2619-26.

40. Freeman HJ. Granuloma-positve Crohn’s disease. Can J Gastroenterol 2007;21:583-7.