Variables associated with progression of moderate-to-severe Crohn's disease

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ABSTRACT

Objective Determine the variables associated with hospitalisations in patients with Crohn's disease and those associated with surgery, intestinal resection, hospital readmission, need for multiple operations and immunobiological agent use.

Design A cross-sectional study was conducted from 2019 to 2021, using two centres for inflammatory bowel diseases in the Brazilian Public Health System.

Results This study included 220 patients. Only perianal disease was associated with hospitalisation (31.6% vs 13.0%, p=0.012). Stricturing or penetrating behaviour (35.8% vs 12.6%, p<0.001) and perianal disease (45.9% vs 9.9%, p<0.001) were associated with surgery. Ileal or ileocolonic location (80.0% vs 46.5%, p=0.044) and stricturing or penetrating behaviour (68.0% vs 11.2%, p<0.001) were associated with intestinal resection. Steroids use at first Crohn's disease occurrence and postoperative complications were associated with hospital readmission and need for multiple operations, respectively. Age below 40 years at diagnosis (81.3% vs 62.0%, p=0.004), upper gastrointestinal tract involvement (21.8% vs 10.3%, p=0.040) and perianal disease (35.9% vs 16.3%, p<0.001) were associated with immunobiological agent use.

Conclusion Perianal disease and stricturing or penetrating behaviour were associated with more than one significant outcome. Other variables related to Crohn's disease progression were age below 40 years at diagnosis, an ileal or ileocolonic disease localisation, an upper gastrointestinal tract involvement, the use of steroids at the first Crohn's disease occurrence and history of postoperative complications. These findings are similar to those in the countries with a high prevalence of Crohn's disease.

INTRODUCTION

Crohn's disease (CD) is characterised by chronic and transmural inflammation of the digestive tract and is often associated with complications such as strictures and fistulas.[1 2] More than 50% of patients with CD will develop serious medical complications over time, and the estimated global surgical

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Knowing the variables associated with moderate-to-severe disease progression is crucial for optimal treatment protocols for patients with Crohn's disease (CD). In newly industrialised countries, including Brazil, variables associated with CD progression lack sufficient research.

WHAT THIS STUDY ADDS

⇒ Our results show that Brazil, which has distinct sociodemographic characteristics and intermediate incidence and prevalence of CD, has CD disease progression similar to those of developed countries, including Europe and North America.

HOW THIS STUDY MIGHT AFFECT THE RESEARCH, PRACTICE OR POLICY

⇒ These findings reveal important information on the progression of moderate-to-severe CD in a Latin American country, which could be applicable in other newly industrialised countries. Knowing these variables is useful in identifying the severity profile of CD and selecting the most appropriate management and treatment.

risk is 60%–80%.[3 4] CD has a high morbidity, predominantly affecting the economically active population and women of childbearing age. This condition can significantly compromise education, professional development and family planning.[5] One of the primary goals of rational drug therapy for CD is to delay or even prevent the phenotype progression of this disease. This goal would allow the early individualised and conscious use of more intensive therapies to control patients with a higher risk of serious complications.[6]

Identifying variables associated with progression to moderate-to-severe CD in outpatient clinics may aid in deciding the best management option. Intensive treatment is recommended for high-risk patients, but its risk and benefits must be evaluated.

Furthermore, up-to-date prescription protocols may lead to increased costs in the short term, mostly due to more expensive treatment options.[7 8] Some studies have attempted to identify different factors involved in the development and progression of moderate-to-severe CD.[9] However, factors and clinical prediction tools for disease progression remain poorly understood and are not routinely implemented. Prediction of specific outcomes based on multiomic approaches has also lacked clinical translation. In newly industrialised countries such as Brazil, these CD-associated variables are still insufficiently investigated.

In this study, we aimed to identify distinct variables associated with CD hospitalisation and those associated with hospital readmission, surgeries, intestinal resection, need for multiple operations and immunobiological agents used for CD.

METHODS
Study design
This study is an observational cross-sectional research and data were retrieved retrospectively. Patients with CD were interviewed and had their medical records reviewed. It involved two medical referral centres for inflammatory bowel diseases (IBDs) in the public health system from the capital of notheatern Brazil, the only ones in the state. Participants had been diagnosed with CD at least 1 year before the date of inclusion in the survey. The 1-year follow-up time was defined arbitrarily, being considered the minimum time to have an outcome that represents CD'progression.

Data were collected during patient appointments at the IBD clinic. Patients were approached and evaluated in terms of the inclusion and exclusion criteria. Informed consent was then requested to eligible participants. They filled up a questionnaire specifically designed for this research. We then evaluated their data from the physical and/or electronic medical records. Data collection occurred from July 2019 to February 2020 at the one medical referral centre and from August 2020 to July 2021 at another. However, it was interrupted or delayed in commencement in both centres because of the suspension of outpatient activities due to the coronavirus disease 2019 pandemic.

Population
By consecutive sampling, the sample population consisted of outpatients with CD. Diagnosis of CD was based on European Crohn's and Colitis Organisation recommendations.[10] The inclusion criteria applied during the survey were as follows: 18 years of age or more, diagnosis of CD for at least 1 year and regular follow-up at the two medical referral centres. We excluded those who were not cognitively able to answer the questionnaire. In total, we included 220 patients. The sample size was calculated using the Open Source Epidemiologic Statistics for the Public Health System and p<0.05 (n=205, minimum).[11] Epidemiological data were found in Lima *et al.*[12]

Variables
Moderate-to-severe CD was defined as hospitalisation for clinical disease decompensation and/or a surgical procedure, the primary outcome. Secondary outcomes were abdominal or perianal surgery, intestinal resection (large and/or small intestine), clinical or surgical hospital readmission, need for multiple operations and immunobiological agent use. The hospitalisations, surgeries and immunobiological agent use were CD-related only as the main outcome and according to the indication of the assistant physician. The need for multiple operations was defined as another bowel resection. Immunobiologicals included adalimumab, certolizumab pegol, infliximab, ustekinumab and vedolizumab.

The analysed variables were sex, origin, self-reported skin colour, education, income level and smoking at diagnosis. Age, location and behaviour of CD at diagnosis were categorised according to the Montreal classification.[13] The following data were also collected and evaluated: perianal disease at diagnosis, upper gastrointestinal (GI) tract involvement, any ulceration seen in some colonoscopy during follow-up, granulomas observed in the anatomopathological examination of any colonoscopy, first-degree relatives diagnosed with IBD and any steroid use at first CD occurrence.

In patients requiring readmission, the following variables were analysed at diagnosis: hospitalisation, admission to the intensive care unit, infectious conditions and parenteral nutrition requirement. Regarding the need for multiple operations, the following were evaluated: diagnosis of CD after surgical procedures and postoperative complications.

Physical and/or electronic medical records were reviewed to confirm the data and avoid information bias. Given the lack of uniformity in diagnosis, extraintestinal manifestations were excluded from the analysis.

Statistical analysis
Variables are expressed as absolute frequencies, percentages, means and medians. Initially, the association between variables was evaluated using a χ^2 test with a 95% CI. Variables whose associations obtained a p value of less than 0.05, which was considered statistically significant, were later evaluated in a multivariate binary logistic regression model. When only one variable was associated with the outcome in the univariate analysis, multivariate logistic regression analysis was not required. As far as the patient's age at the time of diagnosis is concerned, patients were classified into two categories: those of age ≤40 years and those of age >40 years. This categorisation was done because the category younger than 16 years obtained a small n value and did not reach the minimum count expected for the cell in the χ^2 analysis for all outcomes, indicating the possibility of committing a statistical error. Missing data were excluded from

Table 1 Demographic and clinical characteristics of patients with Crohn's disease treated at two reference centres in Salvador, Bahia, Brazil (2019–2021)

	Hospitalised n=174 (79.1%)	Non-hospitalised n=46 (20.9%)	Total n=220
Females	87 (50.0)	25 (54.3)	112 (50.9)
Urban area	136 (78.2)	38 (82.6)	174 (79.1)
Black and brown ethnic	152 (87.4)	38 (82.6)	190 (86.4)
Education			
Illiterate	10 (5.7)	1 (2.2)	11 (5.0)
Incomplete middle school	21 (12.0)	8 (17.4)	29 (13.2)
Complete middle school	13 (7.5)	3 (6.5)	16 (7.3)
Incomplete high school	12 (6.9)	4 (8.7)	16 (7.3)
Complete high school	85 (48.9)	21 (45.6)	106 (48.1)
Higher education	33 (19.0)	9 (19.6)	42 (19.1)
Family income of <US$220	133 (76.4)	34 (73.9)	167 (75.9)
Smoker at diagnosis	20 (11.5)	4 (8.7)	24 (10.9)
Familial IBD	15 (8.6)	5 (10.9)	20 (9.1)
Ulceration at colonoscopy	132 (75.9)	28 (60.9)	160 (72.7)
Granuloma at anatomopathological examination	12 (6.9)	1 (5.9)	2,2 (5.9)
Steroid use at the first disease occurrence	119 (68.4)	24 (52.2)	143 (65.0)

IBD, inflammatory bowel disease.

the analysis. All statistical data were analysed using SPSS V.21.0 (SPSS).

RESULTS

Demographic data and clinical characteristics

Overall, we included 220 patients, with 112 (50.9%) females, 174 (79.1%) living in urban areas and 24 (10.9%) smokers. The mean age at diagnosis was 32.9 years. During the first CD occurrence, 143 (65.0%) patients were treated with steroid therapy. Table 1 presents the demographics and clinical characteristics of the participants.

Table 2 shows the Montreal classification of the sample. The most common age group at diagnosis was 17–40 years, with 149 (67.7%) patients. At diagnosis, colon disease was the most prevalent (45.0%). In addition, the most frequent behaviour at diagnosis was non-stricturing, non-penetrating, with 167 patients (75.9%) and perianal disease was found in 61 (27.7%) patients at diagnosis. The median time of diagnosis was 6 years (range 1–43), and the mean was 8.4 years.

Variables associated with hospitalisation

Hospitalisation occurred at some point in 174 (79.1%) patients, with 65 (37.4%) clinical hospitalisations and 109 (62.6%) surgical hospitalisations. Hospitalisation was performed within 1 year in 144 (81.6%) patients, 3 years in 150 (86.2%) and 5 years in 157 (90.2%) patients. Through univariate analysis, three independent variables, namely, perianal disease at diagnosis, ulceration at colonoscopy and steroid use during the first CD occurrence, were significantly associated with hospitalisation. In the logistic regression, only perianal disease at diagnosis showed a significant association (31.6% vs 13.0%, p=0.012) (table 3). In an additional analysis, we separated clinical and surgical hospitalizations. Considering only clinical hospitalizations, the perianal disease remained an independent variable associated with hospitalization (p < 0.001, data not shown).

Variables associated with surgery

A total of 109 patients (49.5%) underwent surgery during CD. The most common surgical procedure was seton placement in 38 (34.9%) patients, followed by perianal fistulectomy in 34 (31.2%) and right hemicolectomy in 28 (25.7%). Surgery was performed within 1 year in 76 (71.0%) patients, 3 years in 82 (76.6%) and 5 years in 86 (82.2%) patients. Two variables associated with surgery were identified with statistical significance both after univariate analysis and logistic regression. These variables were stricturing or penetrating behaviour (35.8% vs 12.6%, p<0.001) and perianal disease (45.9% vs 9.9%, p<0.001) (table 3).

Variables associated with bowel resection

Fifty (22.7%) patients underwent bowel resection, and the most common was right hemicolectomy in 28 (56.0%) patients, followed by enterectomy, total colectomy and left hemicolectomy in 27 (54.0%), 6 (12.0%) and 3 (6.0%), respectively, patients. In the univariate analysis, three variables, namely, involvement of the upper GI tract, location and stricturing or penetrating

Table 2 Montreal classification at the time of diagnosis of patients with Crohn's disease treated at two reference centres in Salvador, Bahia, Brazil (2019–2021)

	n=220
Age	
A1 (<16 years or younger)	12 (5.5%)
A2 (17–40 years)	149 (67.7%)
A3 (>40 years)	59 (26.8%)
Location	
L1 (terminal ileum)	35 (15.9%)
L2 (colon)	96 (43,6%)
L3 (ileocolon)	55 (25.0%)
L4 (isolated upper GI)	2 (0.9%)
L1L4	17 (7.7%)
L2+L4	3 (1.4%)
L3+L4	12 (5.5%)
Behaviour	
B1 (non-stricturing, non-penetrating)	119 (54.1%)
B2 (stricturing)	20 (9.1%)
B3 (penetrating)	20 (9.1%)
B1p	48 (21.8%)
B2p	7 (3.2%)
B3p	6 (2.7%)
Upper GI involvement	34 (15.4%)
Perianal disease	61 (27.7%)

GI, gastrointestinal; p, perianal disease; y, years.

behaviour, were significantly associated with bowel resection. After logistic regression, ileal or ileocolonic location (80.0% vs 46.5%, p=0.044) and stricturing or penetrating behaviour (68.0% vs 11.2%, p<0.001) showed a significant association with bowel resection (see table 3).

Variables associated with hospital readmission
Of the 174 patients who had already been hospitalised, 106 (60.9%) were hospitalised more than once. Sixty-six patients were hospitalised one time (40.2%), 37 (22.6%) two times and 61 (37.2%) more than three times. The only variable associated with hospital readmission was steroid use in the first CD occurrence (77.7% vs 54.4%, p=0.001) (table 3).

Variables associated with need for multiple operations
Of the 50 patients who underwent bowel resection during disease follow-up, 13 (26.0%) were reoperated. The average time to perform a new surgery was 3.2 years. The operations were enterectomy in 10 (76.9%) patients, right hemicolectomy in 2 (15.4%) and total colectomy in 1 (7.7%). The presence of postoperative complications was the only variable associated with the need for multiple operations (53.8% vs 21.6%, p=0.029) (see table 3).

Variables associated with immunobiological agent use
A total of 128 (58.2%) patients used immunobiological agents previously for CD. In both univariate analysis and logistic regression, three independent variables, namely, age below 40 years at diagnosis (81.3% vs 62.0%, p=0.004), upper GI tract involvement (21.8% vs 10.3%, p=0.040) and perianal disease (35.9% vs 16.3%, p<0.001) were significantly associated with immunobiological agent use (see table 3).

DISCUSSION
Knowing the variables associated with moderate-to-severe disease progression is crucial for optimal treatment protocols in patients with CD. This knowledge will aid in optimising therapeutic interventions and altering natural disease progression.[8 14] Reliable variables of unfavourable progression would enable medically customising individual therapy within a properly planned clinical follow-up.[15] This study is pioneering research conducted in Latin America aimed at determining the variables associated with moderate-to-severe CD progression. In this study, perianal disease was a substantial variable related to moderate-to-severe progression. It was significantly associated with hospitalisation, surgery and immunobiological agent prescription. Stricturing or penetrating behaviour was another variable that was consistently associated with moderate-to-severe CD progression, being related to surgery and intestinal resection. Other detected variables were the age of younger than 40 years at diagnosis, ileal or ileocolonic location, upper GI tract involvement, steroid use during the first CD occurrence and postoperative complications.

The incidence and prevalence of CD in Brazil and other newly industrialised countries are still intermediate compared with those in industrialised countries, but they have increased in recent years.[16–18] In 2020, the incidence of CD in Brazil was 2.7/100 000, and the prevalence was 33.7/100 000. In Bahia state, where the study was performed, the incidence of CD was 1/100 000 and the prevalence was 22/100 000 in 2020.[16] This increment has led to a greater interest in the study of clinical characteristics and course of CD in newly industrialised countries.[19–21] Our study showed equivalent results between sexes, similar to those of the previous studies.[7 20 21] The most common age group at diagnosis was 17–40 years (67.7%), consistent with other national and international studies.[1 12 19] Colonic location (45.0%) was the most frequent, similar to the results of Parente et al's study in the Northeast region of Brazil as well as other studies in newly industrialised countries.[19 22 23] However, the prevalent location of CD at diagnosis varies in several international studies. This is common with ileocolonic predominance or equivalence between locations.[4 12 24] Moreover, non-stricturing and non-penetrating was the most frequent CD behaviour at diagnosis (75.9%), similar to previous studies in Brazil and worldwide.[12 19 24] Perianal disease at diagnosis was found in 27.7% of patients,

Table 3 Variables associated with hospitalisation, surgery, intestinal resection, hospital readmission, need for multiple operations and the therapeutic use of immunobiologicals in patients with Crohn's disease treated at two reference centres in Salvador, Bahia, Brazil (2019–2021)

	Univariate analysis			Logistic regression		
	Yes* (%)	No* (%)	P value	OR	95% CI	P value
Hospitalisation (n=174)						
Perianal disease†	31.6	13.0	0.012	3,32	1.31 to 8.43	0.0012‡
Ulceration at colonoscopy	75.9	60.9	0.042	1.91	0.94 to 3.89	0.076
Steroid use at first disease occurrence	68.4	52.2	0.040	1.94	0.98 to 3.85	0.058
Surgery (n=109)						
Stricturing or penetrating behaviour†	35.8	12.6	<0.001	5.34	2.55 to 11.18	<0.001‡
Perianal disease†	45.9	9.9	<0.001	9.72	4.54 to 20.84	<0.001‡
Intestinal resection (n=50)						
Ileal or ileocolonic location†	80.0	46.5	<0.001	2.82	1.10 to 7.22	0.044‡
Stricturing or penetrating behaviour†	68.0	11.2	<0.001	12.3	5.26 to 28.95	<0.001‡
Upper GI involvement§	34.0	12.0	<0.001	1.81	0.434 to 3.22	0.613
Hospital readmission (n=106)						
Steroid use at first disease occurrence	77.7	54.4	0.001‡	NA		
Surgical recurrence (n=13)						
Postoperative complications	53.8	21.6	0.029‡	NA		
Use of immunobiologicals (n=128)						
Age of <40 years†	81.3	62.0	0.001	2.67	1.36 to 5.23	0.004‡
Perianal disease†	35.9	16.3	0.001	3.50	1.62 to 7.54	<0.001‡
Upper GI involvement§	21.8	10.3	0.035	2.53	1.04 to 6.13	0.040‡

*Frequencies related to endpoints.
†At diagnosis.
‡Significant.
§23 patients did not undergo investigation of the small intestine.
GI, gastrointestinal; NA, not applicable.

consistent with past studies.[12 15 25] Generally, most of the patient's clinical characteristics in this study are similar to those yet described.

In this study, perianal disease at diagnosis was the only independent variable associated with hospitalisation. It is a poor prognostic factor associated with a disabling clinical progression, as represented in several studies.[26–28] Golovics *et al* also deemed perianal disease as a predictor of hospitalisation, in addition to stricturing or penetrating behaviour at diagnosis and the use of azathioprine and antitumour necrosis factor.[29] In an Australian study, perianal disease, ileocolonic location and stricturing or penetrating behaviour at diagnosis were all associated with hospitalisation.[30] Unlike these two studies, the current study did not show stricturing or penetrating behaviour at diagnosis as a hospitalisation-associated variable.

Torres *et al*'s review revealed that only a few studies have evaluated variables associated with hospitalisation in CD, despite being widely regarded as predictors of high activity or disease severity.[5] Most of the studies investigating the predictors of CD severity included hospitalisation along with other factors and did not perform the analysis separately. Hence, only a few international medical studies reported variables specifically associated with hospitalisation. Nonetheless, this study confirmed the previously recognised association between perianal disease at diagnosis and hospitalisation. Thus, it becomes evident that perianal disease at diagnosis is an independent variable associated with CD severity in Brazil, and probably in newly industrialised countries.

In this study, stricturing or penetrating behaviour and perianal disease were independent variables associated with surgery. Oostenbrug *et al* also showed that these two variables are predictors of surgery, in addition to ileocolonic location.[31] A similar study was conducted in a referral centre in India; it found that variables, as well as the male sex and the disease location in the small intestine, are associated with surgery.[32] In this study, sex and location were not identified as independent variables associated with surgery.

Furthermore, ileal or ileocolonic location and stricturing or penetrating behaviour were independent variables associated with surgical resection in this study. Several previous surveys evaluated these variables. In Torres *et al*'s review, stricturing or penetrating disease at the time of diagnosis was the most important independent

factor associated with surgery requirements. Ileal or ileo-colonic location is among the most important prognostic factors for surgery in CD and should be actively incorporated into clinical decision-making.[5] A large population cohort study recently conducted in European countries and Israel also showed stricturing or penetrating behaviour as a surgery-associated factor.[33]

The Epidem-IBD study, which was conducted in Spain and presented at the Congress of the European Organization of Crohn's and Colitis in 2021, also revealed stricturing or penetrating behaviour as a factor associated with intestinal resection.[34] This study confirms this important association. This relationship is already well documented in industrialises countries and now was observed in the newly industrialised countries as well.

This study also found that age below 40 years, perianal disease and upper GI tract involvement were independent variables associated with immunobiological agent use. In other studies, patients diagnosed at an age younger than 40 years are a clinical predictor of unfavourable development in CD.[23 26 35] Most studies refer only to factors associated with the use of infliximab or unspecified immunosuppressants. Moon *et al* showed that age below 40 years at diagnosis and presence of perianal disease are predictors of infliximab treatment, in addition to ileal involvement and penetrating behaviour. Upper GI tract involvement also exhibited association in Korean research, although it was not selected in the multivariate model.[25] Oostenbrug *et al* reported that apart from penetrating behaviour, perianal disease and ileocolonic location were associated with infliximab use.[31] Wenger *et al* found that male sex, young age at diagnosis and loss of response to steroids were associated with immunosuppressant use.[36] This study established that the relevant association between age below 40 years with perianal disease and the involvement of the upper GI tract, correlates with immunobiological agent use. This finding can significantly contribute to the treatment protocol for patients with CD.

Moreover, steroid use during the first CD occurrence was the only independent variable associated with hospital readmission. Golovics *et al* observed that steroid use was related to hospital readmission risk in patients with CD, in addition to arthritis, inflammatory behaviour change and immunobiological agent and azathioprine use.[29] In this study, the three preceding variables were not evaluated, and the use of immunobiological agents was considered as an outcome. Typically, steroid use during the first CD occurrence indicates a severity factor, as shown in several original and review studies.[5 26 27] Currently, variables associated with long-term hospital readmission in patients with CD remain unreported. However, this study presents important additional information substantiating that steroid use during the first CD occurrence is associated with hospital readmission.

In addition, operative complications were the only variables associated with the need for multiple operations. CD is often associated with the potential risk factors

of postoperative complications. However, reports on the relationship between these complications and the recurrence rate are still few.[36] Yamamoto reviewed some studies that identified this relationship and suggest that postoperative complications are a variable associated with the need for multiple operations.[37] Smoking is also commonly associated with CD recurrence,[37–39] but this association was not confirmed in this study.

This study has some limitations. First, it was performed in only two centres specialising in IBD in the Brazilian Public Health System. Thus, patients cared for in the private health system and those cared for by physicians in primary public healthcare were not examined. Therefore, other variables may play a role in non-specialised centres. Similar to the studies of Beaugerie *et al* and Stallmach *et al*, more than 70% of the patients in our study achieved the defined primary outcome (CD-related hospitalisation),[26 35] demonstrating that severe cases in medical specialty centres are over-represented. Moreover, the survey was performed through a questionnaire with self-reported responses, which could lead to memory bias. To avoid this effect, physical and/or electronic medical records were reviewed to confirm the data. Although this was a cross-sectional study, causality could have been established by implementing well-defined demographic and clinical data at the time of diagnosis to establish a consistent temporal relationship. In fact, the Montreal classification, which is a widely accepted classification with established criteria,[11] was applied at diagnosis. In addition, the participants had different follow-up times. However, we defined a follow-up time greater than 1 year as the minimum period necessary to assess CD progression in these patients.

Phenotypic and clinical differences in CD have been observed among different regions in the world.[25] This raised the question of whether the factors associated with the moderate-to-severe occurrence of CD would be similar among industrialised countries, such as Europe and North America, and newly industrialised countries, such as Brazil. Reliable and early predictors of the disease course are essential for the development of personalised medicine in patients with IBD.[40] In this study, factors associated with the moderate-severe evolution of CD in Brazil were found to be mostly similar to those in industrialised patients, despite all their differences. This can directly influence the therapeutic decision in clinical practice, even public policies, modifying the natural course and preventing the progression and complications of CD in Brazil.

The use of prognostic factors to guide therapy in CD is constantly evolving. Genetic markers and the use of multiple omics technologies are still poorly investigated, but they seem to be promising. This study should become a reference for the development of other studies in our research group, and even other groups, aiming at greater knowledge on the subject.

Newly industrialised countries such as Brazil, which has distinct sociodemographic characteristics and

intermediate incidence and prevalence of CD, have CD disease progression similar to developed countries, including Europe and North America. This study recognised perianal disease, stricturing or penetrating behaviour, age below 40 years at diagnosis, ileal or ileocolonic location, upper GI tract involvement, steroid use at first CD occurrence and postoperative complications as possible independent variables significantly associated with moderate-to-severe disease progression of CD. This finding is similar to the reports obtained from countries with high CD prevalence, and it could be applicable in other developing countries as well. Knowing these variables is useful in identifying the severity profile of CD and selecting the most appropriate management and treatment.

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