



# Crohn's Disease Among the Poorest Billion: Burden of Crohn's Disease in Low- and Lower-Middle-Income Countries

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## Abstract

**Background** To establish the epidemiology and patterns of care of Crohn's Disease in low- and lower-middle-income countries.

**Methods** A cross-sectional survey of gastroenterology providers in countries where the world's poorest billion live was conducted to learn more about the state of diagnostic and treatment capacity for Crohn's. Quantitative data were analyzed in R and Excel.

**Results** A total of 46 survey responses from 15 countries were received, giving a response rate of 54.8%. All responses collected were from providers practicing in Africa and South Asia. The mean number of patients with Crohn's cared for in the last year was 89.5 overall but ranged from 0 reported at one facility in Rwanda to 1000 reported at two different facilities in India. Overall, Crohn's disease made up 20.6% of the inflammatory bowel disease diagnoses reported by survey respondents, with Africa exhibiting a larger proportion of Crohn's compared to ulcerative colitis than Asia. Most providers reported that patients with Crohn's have symptoms for 6–24 months prior to diagnosis and that 26–50% of their patients live in rural areas. The most reported diagnostic challenges are differentiating between Crohn's and intestinal tuberculosis, poor disease awareness, and lack of trained pathologists. The most widely reported challenge in managing Crohn's disease is patients' inability to afford biologics, reported by 65% of providers.

**Conclusion** Our study suggests there may be a greater burden of Crohn's disease in low- and lower-middle-income countries than is indicated in prior literature. Respondents reported many challenges in diagnosing and treating Crohn's disease.

**Keywords** Crohn's disease · Crohn's and Colitis · Epidemiology · Inflammatory bowel disease · Health systems

## Introduction

Crohn's disease (CD) is a type of inflammatory bowel disease (IBD) where any part of the gastrointestinal tract may be affected in a non-contiguous pattern and inflammation may extend through multiple layers of the intestinal walls. When left untreated, severe complications such as fistulas and strictures can result, often requiring surgery [1].

Previous systematic reviews of the published literature on CD epidemiology have identified few studies on either the prevalence or incidence of CD in low- and lower-middle-income countries (LLMICs) [2, 3]. A review of population-based studies published between 1990 and 2016 found data from only four LLMICs (Sri Lanka, India, the Philippines, and Indonesia), all of which were in Asia and focused on urban areas [4]. As a result of the poor availability of CD data in LLMICs, the 2017 Global Burden of Disease study largely based its CD estimates for these countries on global trends [5]. As the vast majority of the world's poorest billion people live in the rural areas of LLMICs, particularly in sub-Saharan Africa and South Asia [6], the absence of primary population data regarding CD in these countries has contributed to a perception that the burden of CD remains low among the global poor.

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However, the diagnosis of CD requires a combination of specialized imaging studies, colonoscopy, and gastrointestinal pathology services. Many LLMICs do not have such diagnostic capabilities, except in very specialized tertiary centers in large cities. Diagnosis of CD in LLMICs is further complicated by its overlap with endemic infectious diseases, such as intestinal tuberculosis [7]. Individuals diagnosed with CD in LLMICs may face additional barriers including the availability and high cost of diagnostics and treatments, like biologic therapies [7, 8].

As disease burden data from LLMICs are limited, there is a pressing need to study the unpublished data on the current state of CD in the poorest parts of the world. Understanding the state of CD in LLMICs is crucial because of the high costs to patients and to the health system to diagnose and treat even a small number of patients. As part of an effort to gain a more complete view of how IBD and CD impacts the world's poorest, we conducted a cross-sectional survey of gastroenterology providers in LLMICs. Most LLMICs do not have population-based or even hospital-based disease registries, so we determined that a provider survey would be the most effective barometer with which to measure CD burden in these countries. This survey seeks to answer the following questions: (1) What is the unpublished burden of CD in communities and health facilities in LLMICs? (2) What services, equipment, and medications are available to providers to diagnose and manage CD in LLMICs? (3) What are the typical pathways by which individuals diagnosed with CD in LLMICs receive care? (4) What challenges and barriers are there to individuals with CD and their providers in LLMICs? (5) What are the social and demographic characteristics of individuals with CD in LLMICs?

## Materials and Methods

### Study Design and Data Collection

Our team conducted a cross-sectional survey of gastroenterology providers in countries where the poorest billion live to determine the state of diagnostic and treatment capacity for CD in 79 LLMICs. The 79 countries identified are designated as either low-income countries (LICs) or lower-middle-income countries (LMICs) by the World Bank [9]. These countries of interest have gross national incomes per capita of US \$3895 or less.

The provider survey consisted of eight sections and included 75 questions regarding CD frequency, patient characteristics, diagnosis, treatment, monitoring & maintenance, provider demographic characteristics, and health facility characteristics. Most survey questions were multiple choice, but some allowed respondents to type their answer (e.g., “What was the number of patients diagnosed with

Crohn's that you cared for in the last year?”). Data collection occurred from March 2019 to January 2020. Surveys were administered online via Partners REDCap secure web platform (<https://redcap.partners.org/redcap/surveys/?s=7JF9EKJK73>) both in-person and virtually. In-person interviews occurred during a series of limited endoscopy site visits in South Asia and Sub-Saharan Africa; however, most surveys were delivered virtually via secure web platform. Survey questions focused on the availability of necessary IBD diagnostic and treatment technology and resources. These included laboratory testing of stool and blood, endoscopy, radiography, colonoscopy, and pathology services. Availability of treatments and drugs was also included on the survey, such as anti-inflammatory agents, corticosteroids, immunomodulators, anti-TNF agents, antibiotics, and probiotics, as well as surgical capacity. The survey also inquired about availability of clinical registries and the nature and quality of such registries. A full list of survey domains can be found in the supplementary material file. Our goal in carrying out this survey was to reach at least one gastroenterology provider in each of the 79 LLMICs.

### Participant Selection and Recruitment

We recruited medical professionals who provide gastroenterology care to patients in an LLMIC to complete the study survey. Gastroenterology providers of all levels and working at any type of health facility were eligible for the study. Providers were eligible to participate regardless of their credentials and affiliations. Participation was not restricted by age, race, sex, or any other demographic characteristics. Both convenience sampling and snowball sampling were used to recruit providers for the survey. We started by recruiting gastroenterology providers from LLMICs at World Gastroenterology Organization's Gastro 2018 conference in Bangkok, Thailand in December 2018. Then, we sent a follow-up email to the providers we met at Gastro 2018 to confirm their willingness to participate. We also asked these providers to refer other gastroenterologists in their countries who may be willing to participate. The remainder of the participants were recruited through this referral strategy, internet searches, or LinkedIn. We also conducted a limited number of in-person interviews during a series of site visits to endoscopy facilities in Sub-Saharan Africa and South Asia.

### Statistical Analysis

Descriptive summary statistics were generated regarding provider and facility characteristics, and samples were described using counts and percentages. Categorical data regarding the burden of CD, care pathways, and the availability of diagnostics and treatments collected from provider

surveys were analyzed using Chi-Square or Fisher's exact tests. Quantitative data were analyzed in both R and Excel.

## Ethical Considerations

This study was approved by the Partners Human Research Committee, the Institutional Review Board of Partners Healthcare (now Mass General Brigham). Interviewed providers were given a detailed fact sheet in lieu of formal written consent.

## Results

### Provider Demographic Characteristics

Of the 84 providers who expressed interest and were sent the survey link, a total of 46 completed the survey, yielding a response rate of 54.8%. All the responses received were from providers practicing in either Africa or South Asia. The most highly represented LLMIC is India (21.7%), followed by Ethiopia (17.4%), Nepal (13.0%), Egypt (8.7%), and Nigeria (6.5%) (Table 1). Indonesia, Malawi, Pakistan, Rwanda, and Sudan, each have two responses (4.3%) and Bangladesh, the Philippines, Kenya, Tunisia, and Zimbabwe each have one response (2.2%) (Fig. 1). The majority of providers who have completed the survey are men (80.4%), between the ages of 35 and 54 years (34.8%), with an MD or DO degree (82.6%) and some formal gastroenterology (87.0%) and training, but vary in their years of experience as a gastroenterologist and years of experience managing CD (Table 1).

Of the 15 countries included in the survey, providers from India, Egypt, Pakistan, and Bangladesh report the greatest availability of gastroenterologists and endoscopy centers nationally (Fig. 1). In contrast, those from Malawi and Rwanda reported only one medically trained gastroenterologist in each country and fewer than 11 endoscopy centers (Fig. 1). The ratio of private to public endoscopy centers also varied from country to country, with the majority reporting more centers in the private sector and only one country (Indonesia) with providers reporting more in the public sector. Malawi, Rwanda, and Tunisia both reported equivalent numbers of endoscopy centers in the private and public sectors.

### Health Facility Characteristics

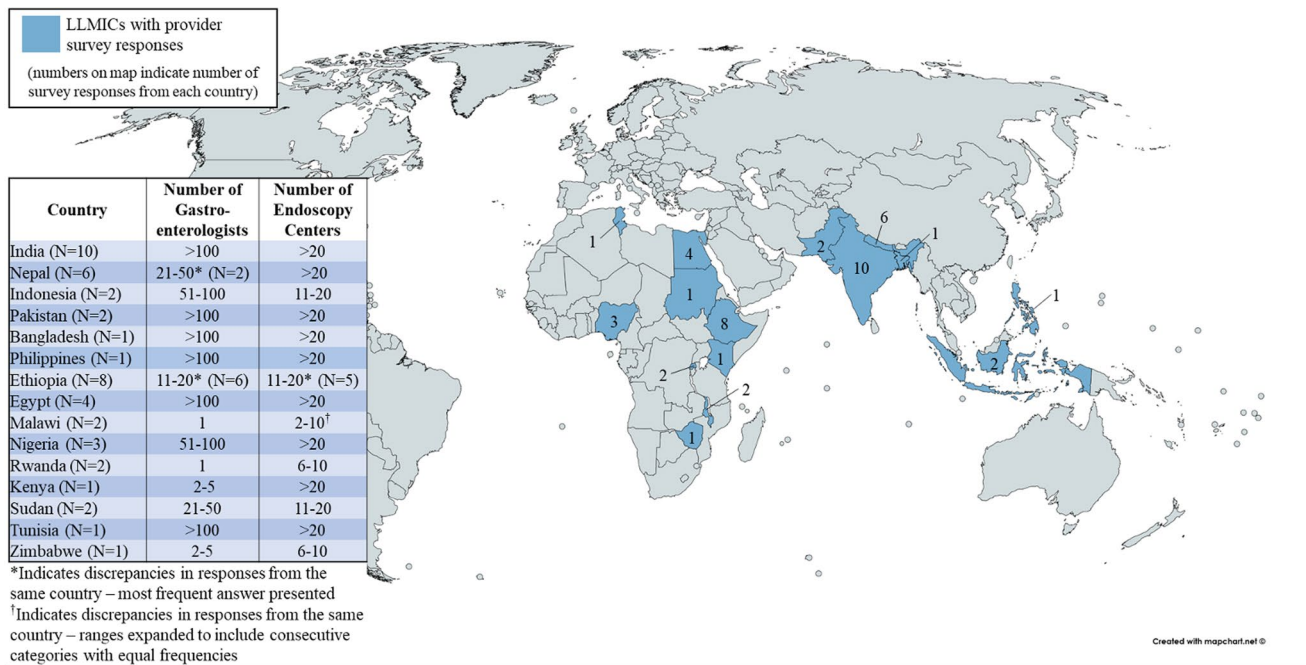
The 46 survey respondents who have taken the survey so far represent 33 health facilities across 15 LLMICs

**Table 1** Survey respondent demographic characteristics overall and by region

	Overall	Asia	Africa
<i>Total N</i>	46 (100)	22 (47.8)	24 (52.2)
<i>Age group in years</i>			
<25	–	–	–
25–34	3 (6.5)	–	3 (12.5)
35–44	16 (34.8)	6 (27.3)	10 (41.7)
45–54	12 (26.1)	5 (22.7)	7 (29.2)
55–64	7 (15.2)	4 (18.1)	3 (12.5)
≥65	3 (6.5)	3 (13.6)	–
Missing	5 (10.9)	4 (18.1)	1 (4.2)
<i>Gender</i>			
Male	37 (80.4)	19 (86.4)	18 (75.0)
Female	7 (15.2)	2 (9.1)	5 (20.8)
Missing	2 (4.3)	1 (4.5)	1 (4.2)
<i>Level of training</i>			
MD/DO	38 (82.6)	18 (81.8)	20 (83.3)
MBBS	3 (6.5)	1 (4.5)	2 (8.3)
Other	2 (4.3)	1 (4.5)	1 (4.2)
Missing	3 (6.5)	2 (9.1)	1 (4.2)
<i>Formal gastroenterology training</i>			
Yes	40 (87.0)	21 (95.5)	19 (79.2)
No	3 (6.5)	–	3 (12.5)
Missing	3 (6.5)	1 (4.5)	2 (8.3)
<i>Years as gastroenterologist</i>			
<5	9 (19.6)	1 (4.5)	8 (33.3)
5–10	7 (15.2)	4 (18.1)	3 (12.5)
11–20	8 (17.4)	3 (13.6)	5 (20.8)
≥20	9 (19.6)	6 (27.3)	3 (12.5)
Missing	13 (28.3)	8 (36.4)	5 (20.8)
<i>Years managing Crohn's</i>			
<5	10 (21.7)	1 (4.5)	9 (37.5)
5–10	13 (28.3)	6 (27.3)	7 (29.2)
11–20	6 (13.0)	3 (13.6)	3 (12.5)
≥20	6 (13.0)	5 (22.7)	1 (4.2)
Missing	11 (23.9)	7 (31.8)	4 (16.7)

All values presented as mean (percent)

in two world regions (Table 2). Most of these facilities were public and located in urban centers, with only three of the 33 facilities located in rural areas (Table 2). All the facilities included at least one provider that performs endoscopy and colonoscopy, with the majority having between two and five. Overall, more upper endoscopies are performed compared to colonoscopies, with 84.8% of facilities performing more than 200 upper endoscopies in the last 6 months, compared to 60.6% for colonoscopies (Table 2). Most facilities have access to biopsy and pathology services (97.0%) and most had some form of patient registration system (81.8%).



**Fig. 1** Number of survey responses from each LLMIC included in the analysis and Number of gastroenterologists and endoscopy centers in each country as reported by survey respondents

### Frequency of IBD and Crohn’s Diagnosis

Overall, 44 of 46 respondents reported numbers of patients with IBD and CD. The mean number of patients diagnosed with CD cared for in the last year reported was 89.5 overall and varied widely from 0 reported at one facility in Rwanda to 1000 reported at two different facilities in India (Table 3). Overall, CD comprised approximately 20.6% of the IBD diagnoses reported by survey respondents. This percentage also varied between countries and regions, with Africa having a larger proportion of CD diagnoses compared to ulcerative colitis (UC) than Asia. These differences were most pronounced in Ethiopia, where almost 69.4% of the mean number of IBD cases are diagnosed as CD, in contrast to Indonesia and Pakistan where less than 10% of the mean number of IBD cases are diagnosed as CD (Table 3).

### Crohn’s Patient Characteristics

Most of the providers who took the survey reported that their patients with CD typically have symptoms for between 6 and 24 months prior to diagnosis (Fig. 2). Only two providers from Nigeria and the Philippines, respectively, reported that their patients with CD typically have symptoms for fewer than 6 months, whereas five providers from India, Ethiopia, Nepal, Nigeria, and Zimbabwe reported that their patients typically have symptoms for more than 24 months (Fig. 2). It should be noted that bias

may influence these estimates, as objectively measuring the duration of symptoms pre-diagnosis can be challenging in these settings.

Most of the providers who participated in the survey estimated that approximately 26–50% of their patients diagnosed with CD live in rural areas (Fig. 2). When stratified by region, Asian providers reported higher proportions of rural patients. Three participants from Asia reported that more than 50% of their patients with CD are from rural regions, whereas none of the providers from Africa did (Fig. 2). Responses from African providers were variable. While eight of the 19 participants from Africa reported that less than 10% of individuals diagnosed with CD are from rural areas, an equal number estimated that 26–50% are from rural areas. The remaining three African providers estimated that 10–25% of patients reside in rural areas (Fig. 2). The differences observed in these responses could be indicative of varying degrees of provider knowledge regarding the demographic characteristics of their patients. More plausible, however, is the issue of location bias. Most health facilities observed were in large, urban areas and naturally reported more urban patients than rural. Conversely, smaller facilities located in peri-urban settings may have reported a greater distribution of rural patients based on their geographic positioning alone. As with the duration of CD symptoms prior to diagnosis, the question of urban versus rural patient distribution was subject to bias and may prove challenging to measure objectively in LLMICs.

**Table 2** Health facility characteristics overall and by region

	Overall	Asia	Africa
# of providers	44*	21 (47.7)	23 (52.3)
# of facilities	33	18 (54.5)	15 (45.5)
<i>Facility geographic setting</i>			
Urban	30 (90.9)	16 (88.9)	14 (93.3)
Rural	3 (9.1)	2 (11.1)	1 (6.7)
<i>Facility type</i>			
Public	20 (60.6)	9 (50.0)	11 (73.3)
Private	9 (27.3)	8 (44.4)	1 (6.7)
Other	4 (12.1)	1 (5.6)	3 (20.0)
<i>Number of upper endoscopies performed in the last 6 months per facility</i>			
1–10	–	–	–
11–50	1 (3.0)	–	1 (6.7)
50–100	–	–	–
101–200	3 (9.1)	2 (11.1)	1 (6.7)
≥201	28 (84.8)	14 (77.8)	14 (93.3)
Missing	2 (6.1)	2 (11.1)	–
<i>Number of colonoscopies performed in the last 6 months per facility</i>			
1–10	1 (3.0)	–	1 (6.7)
11–50	3 (9.1)	–	3 (20.0)
50–100	7 (21.2)	3 (16.7)	4 (26.7)
101–200	3 (9.1)	2 (11.1)	1 (6.7)
≥201	20 (60.6)	11 (61.1)	9 (60.0)
Missing	2 (6.1)	2 (11.1)	–
<i>Availability of biopsy and pathology services</i>			
Available	32 (97.0)	18 (100.0)	13 (86.7)
Not available	2 (6.1)	–	2 (13.3)

All values presented as mean (percent)

\*Two responses missing facility information excluded: one from India and one from Sudan

### Crohn's Disease Diagnosis

All or most of the providers surveyed reported having access to basic CD diagnostic testing, such as tissue pathology, C-reactive protein (CRP), TB testing modalities, upper endoscopy, colonoscopy, barium enema, small bowel follow-through, and abdominal CT scans (Fig. 3A). Of note, stool calprotectin was widely available to respondents from Asian LLMICs (100%) but only 52.2% of providers from Africa. Video capsule endoscopy is the least available advanced endoscopic procedure, especially in Africa, with only 40.9% of respondents having access (66.7% in Asia, 17.4% in Africa). Advanced imaging technology such as CT enterography is available to most (95.2%) respondents from Asia and 52.2% from Africa, and MR enterography is available to 76.2% of respondents from Asia and 34.8% from Africa (Fig. 3A). Differentiation between CD and intestinal tuberculosis (ITB) is a major challenge in LLMICs due to

the high prevalence of TB in Africa and South Asia. For both Asian and African providers, the most frequently used methods for distinguishing between CD and ITB are imaging (59.1% of providers overall) and AFB stain of biopsy samples (54.5% of providers overall) (Fig. 4). Asian providers reported using considerably more PCR of biopsy samples and empirical treatment of TB before considering CD (57.1% and 61.9% of providers, respectively), compared to African providers (30.4% and 39.1% of providers, respectively) (Fig. 3A).

The most reported challenge in diagnosing CD overall is differentiating between CD and ITB, particularly in Asian countries where it was reported by 79.5% of providers (Fig. 5). Distinguishing between CD and other infectious diseases was also a frequently reported challenge in both Asia (57.1%) and Africa (52.2%), as was patients' inability to afford diagnostic testing (52.4% in Asia and 60.9% in Africa) (Fig. 5). Gastroenterologists in Africa particularly struggle with poor CD awareness among providers (47.7%) and lack of trained pathologists (36.4%) in accurately diagnosing CD (Fig. 5).

### Crohn's Disease Management

First-line CD medications, such as Prednisolone, Mesalamine, Sulfasalazine, and Azathioprine, are widely reported to be available by providers across all the included LLMICs (Fig. 3B). The two most critical IBD surgeries, colectomy and small bowel resection, are also commonly available. The availability of more advanced surgeries and alternative medications are much more variable across world regions and between countries. Infliximab and Adalimumab are available to most providers in Asia, but not to any of the surveyed providers in Africa, except for Egypt (Fig. 3B).

The most widely reported challenge in managing CD overall is patients' inability to afford biologics, particularly in African countries where it was reported by 72.7% of providers (Fig. 3B). This challenge is similarly the most common challenge reported by providers in Asian countries, identified by 57.1% of these providers. Lack of access to biologics is also a major challenge for African gastroenterologists (68.2%), as is patients' inability to afford other treatments (50.0%). Among Asian providers, TB reactivation on immunosuppressant therapy (33.3%) and patients' inability to afford other treatments (33.3%) are common challenges in CD management.

### Costs of Crohn's Care

Colonoscopy with biopsy and upper endoscopy with biopsy in both Asia and Africa were reported by the most providers for a cost range less than US \$50 (see supplementary data). Abdominal CT scans are more costly to patients, with most

**Table 3** Mean and range number of patients diagnosed with IBD, Crohn’s cared for in the last year, and percentage of IBD that is diagnosed as Crohn’s, reported overall, by region, and by country

	N	Total IBD*	Crohn’s*	% IBD diagnosed as CD
<i>Overall</i>	44 <sup>a</sup>	434.5 (0–5840)	89.5 (0–1000)	20.6
<i>Asia</i>	21	858.1 (6–5840)	165.0 (0–130)	19.2
India	9 <sup>a</sup>	1860.0 (20–5840)	362.3 (2–1000)	19.5
Nepal	6	129.2 (6–500)	14.5 (1–40)	11.2
Indonesia	2	120.0 (120)	10.0 (10)	8.3
Pakistan	2	32.5 (15–50)	2.8 (1–5)	8.7
Bangladesh	1	150.0 (150)	60.0 (60)	40.0
The Philippines	1	50.0 (50)	30.0 (30)	60.0
<i>Africa</i>	23	47.7 (0–150)	20.7 (0–130)	43.4
Ethiopia	8	61.3 (15–150)	42.5 (5–130)	69.4
Egypt	4	86.3 (25–110)	5.8 (5–8)	6.7
Nigeria	3	5.0 (4–6)	1.3 (1–2)	26.6
Malawi	2	2.0 (0–4)	1.0 (0–2)	50.0
Rwanda	2	2.0 (2)	0 (0)	0.0
Kenya	1	100.0 (100)	5.0 (5)	5.0
Sudan	1	25.0 (25)	10.0 (10)	40.0
Tunisia	1	100.0 (100)	90.0 (90)	90.0
Zimbabwe	1	15.0 (15)	2 (2)	13.3

<sup>a</sup>Excludes missing data from one participant from India, one participant from Kenya, and one participant from Sudan

\*Mean (range)

falling in the US \$50–100 range, and one provider in Malawi reporting it costing more than US \$500 (see supplementary data). Basic stool testing is considerably less expensive, with most providers reporting costs to patients under US \$25.

Overall, the most frequently reported cost of a hospitalization for a CD flare was between US \$101 and \$500 (39.5%) (Table 4). One provider in Pakistan reported that being hospitalized for a CD flare could cost a patient over US \$5000 (Table 4). The most frequently reported cost of biologics overall is over US \$500 (32.6%), followed closely by the US \$100–500 category (27.9%) (Table 4). It should be noted there is a substantial amount of missing data for the cost-related survey questions. In addition, these costs should be seen in light of total health expenditure per capita of \$44 in low-income countries and \$80 in lower-middle-income countries [10].

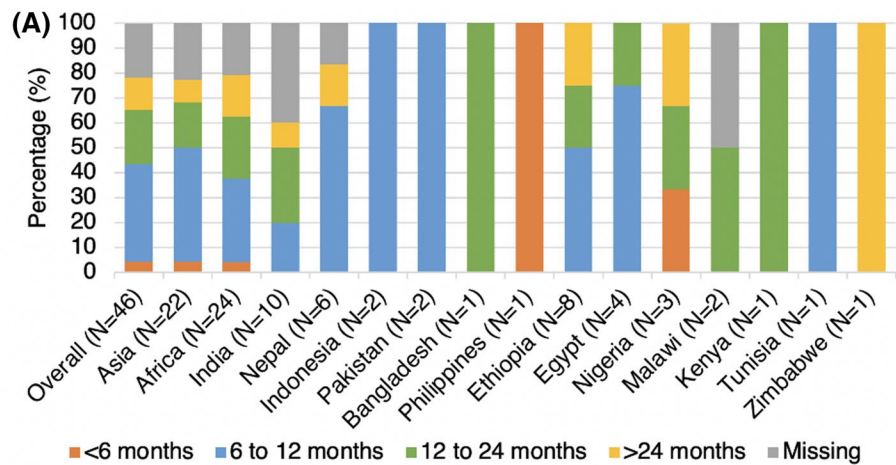
## Discussion

Our survey results suggest a greater burden of CD in LLMICs than is indicated in existing literature. This is particularly true in Ethiopia, which has virtually no published IBD data but has several gastroenterology providers reporting rising IBD cases and a high proportion of CD compared to UC. Similar discrepancies are evident in Nepal and Sudan. While existing literature indicates that most patients with

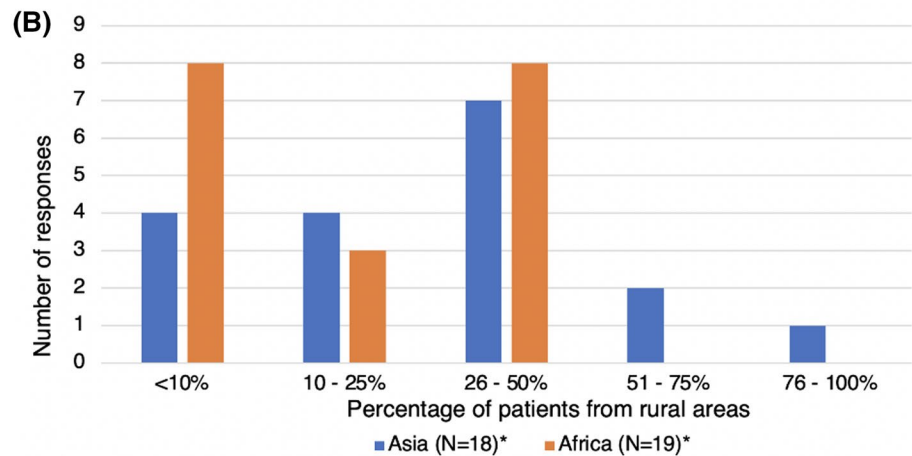
CD reside in urban areas compared to rural areas, our survey respondents indicated that between 10 and 50% of their patients with CD come from rural areas. These numbers may be even higher given the lack of access to diagnostics in most rural areas, although such estimates are challenging to verify and may be subject to both location and provider bias. Survey respondents reported facing many challenges in diagnosing CD, including differentiation from ITB, poor awareness among providers, and patients’ inability to afford diagnostic testing and treatment.

This study suggests the possibility that current literature underestimates the amount of CD present in LLMICs. For example, there are no published cases of CD in Zimbabwe, yet this survey sample includes one respondent from Zimbabwe who reported having two patients with CD in the last year (see supplementary data). For some countries included in existing literature on CD, this survey suggests that the burden of CD is likely higher than has been reported previously. In Ethiopia, for example, two previously published studies [11, 12] reported a total of 8 cases in the country, but the survey respondents of this study from Ethiopia reported caring for a mean of 42.5 for patients with CD in the past year (see supplementary data). Similar disparities were observed for other countries, such as Nepal [13, 14] and Sudan [15, 16], where the relatively few published studies reported a low number of cases, but participants of this study reported a much higher burden

**Fig. 2** Typical duration of symptoms prior to diagnosis for individuals with Crohn's in LLMICs (A) and Estimated percentage of patients with Crohn's who live in rural regions by region (B)



Participants from Rwanda and Sudan did not report typical symptom duration



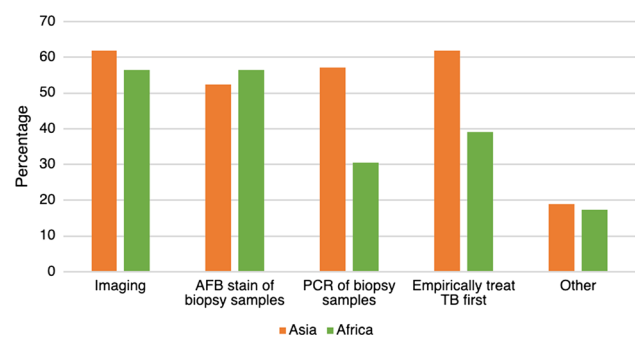
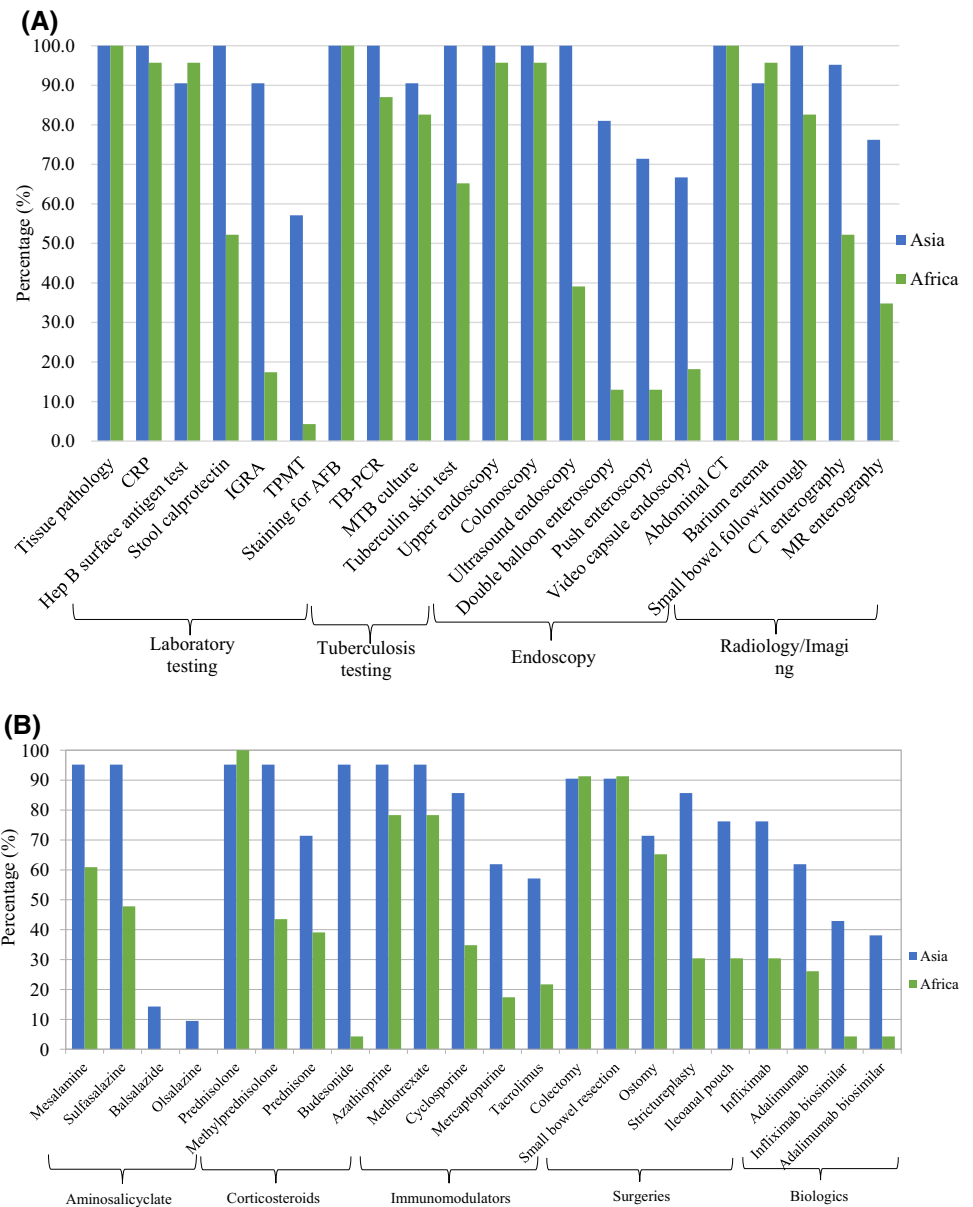
of CD. A scoping review conducted earlier this year by Rajbhandari et al. found that very little literature exists overall with respect to CD and IBD in LLMICs [17]. The absence of recent peer-reviewed literature on this topic makes it challenging to verify estimates or evaluate the change in CD prevalence over time. This dearth of evidence also warrants further investigation into the topic of CD in LLMICs [17].

This survey suggests that overall, CD cases accounted for 20.6% of reported IBD cases. The percentage of CD among IBD diagnoses appeared higher in Africa (43.4%) than in Asia (19.2%). This difference was largely attributable to the high percentage of CD reported among providers in Ethiopia (69.4%) and Tunisia (90.0%), respectively (Table 3). To our knowledge, there is no published literature reporting that CD represents a higher proportion of IBD in Africa than in Asia. The only studies we could locate on this topic were from upper-middle- income and high-income countries, which report that CD represents between 27 and 45% of all IBD diagnoses [18–20].

Based on existing literature, CD is thought to be linked with the environmental conditions of urbanization, and the majority of existing studies exploring CD epidemiology report a higher likelihood of urban residence [4, 21–26]. However, our results show that a significant number of CD cases were reported in rural areas of LLMICs, with 15 providers in the survey reporting that 26–50% of patients are from rural areas (Fig. 2). It is possible that this question was subject to bias and that providers may have varying degrees of knowledge regarding their patients' residence. Even so, of the 33 facilities represented in our survey sample, only 3 (9.1%) were located in rural areas (Table 2). At the very least, this indicates that representation of rural facilities in the survey is unlikely to artificially inflate the number of reported rural patients overall.

The most frequently reported challenge respondents face in diagnosing CD in LLMICs is differentiating it from ITB due to the high prevalence of TB in many of these countries (Fig. 5). While many providers use traditional methods of differentiation, such as imaging and AFB

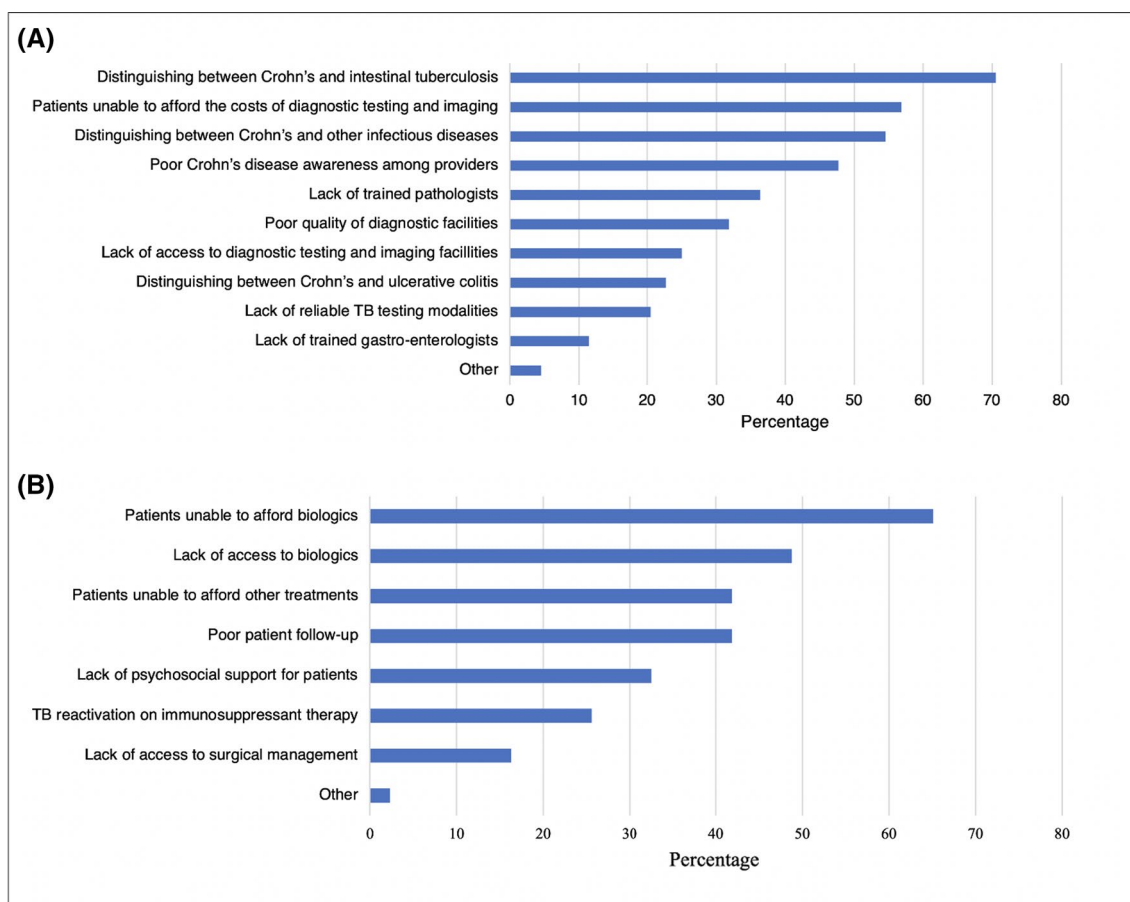
**Fig. 3** **A** Availability of Crohn’s diagnostic technology in LLMICs, by world region. **B** Availability of Crohn’s treatments in LLMICs, overall and by region



**Fig. 4** How providers in LLMICs differentiate between Crohn’s disease and intestinal Tuberculosis, overall and by region

staining of biopsy samples, a large proportion will also empirically treat suspected cases with a course of anti-TB therapy and only consider CD if patients do not respond [27–29]. This can lead to significant delays in diagnosis and the initiation of appropriate treatment (Fig. 5). Other identified challenges included poor awareness of CD among providers in LLMICs and patients’ inability to afford diagnostic testing (Fig. 5). Upper endoscopies tend to cost patients under \$50, but colonoscopies with biopsies and abdominal CT scans can be much more costly, especially for patients of lower socio-economic status (see supplementary data). Although providers reported diagnostics to be widely available, this result is subject





**Fig. 5** Challenges faced by providers in diagnosing (A) and managing (B) Crohn's disease, across all LLMICs

**Table 4** Ranges of costs to patients of common Crohn's disease treatments

	Hospitalization for Crohn's flare						Missing
	< \$100	\$101–500	\$501–1000	\$1001–2000	\$2001–5000	> \$5000	
Overall (N=43)*	5 (11.6)	17 (39.5)	4 (9.3)	5 (11.6)	1 (2.3)	1 (2.3)	10 (23.3)
Asia total (N=21)	1 (4.8)	8 (38.1)	2 (9.5)	1 (4.8)	–	1 (4.8)	8 (38.1)
Africa total (N=22)	4 (18.2)	9 (40.1)	2 (9.1)	4 (18.2)	1 (4.5)	–	2 (9.1)
	Biologic agents					Missing	
	< \$50	\$50–100	\$100–500	> \$500			
Overall (N=43)*	2 (4.7)	4 (9.3)	12 (27.9)	14 (32.6)	11 (25.6)		
Asia total (N=21)	1 (4.8)	2 (9.5)	4 (19.0)	8 (38.1)	6 (28.6)		
Africa total (N=22)	1 (4.5)	2 (9.1)	8 (36.4)	6 (27.3)	5 (22.7)		

All values presented as mean (percent)

\*Excludes missing data from one participant from India, one participant from Kenya, and one participant from Sudan

to bias given the high representation of providers working in urban, tertiary care centers. Reported diagnostic availability in these urban centers may not be reflective of diagnostic availability throughout entire countries. In rural areas, access to diagnostics may remain a challenge to CD

diagnosis, and further research is needed to quantify the availability of diagnostic technology. Access to medications, including biologics, is also a challenge to treating confirmed cases of CD—28 (65.1%) respondents identified this challenge, noting that a single dose of a biologic

therapy can exceed US \$500. It is important to note that in many countries, these costs exceed 10 percent of an individual's annual income, making treatment exceptionally cost-prohibitive. The challenges identified in our survey echo those identified by existing literature. Prior studies have similarly noted differentiating between CD and ITB [27–29] and lack of clinician awareness [30–32] as diagnostic challenges faced by providers in LLMICs. While the high cost of biologic therapy and inability of patients to afford medications were identified as barriers to care in other studies [32–35], most existing literature focused on diagnosis rather than management-related challenges.

This study has several potential limitations. It is challenging to know how generalizable our survey results are, as they are merely suggestive and not conclusive. Population-based data are needed to verify the testimony of the limited number of providers we were able to interview. Similarly, another potential limitation of this study is sample size, with a total of 46 providers representing 15 countries and only a handful of facilities (see supplementary data). Many LLMICs have very few if any gastroenterologists available to participate. The lack of trained providers was identified not only as a barrier to our data collection but also by our respondents as a barrier to CD diagnosis and care (Fig. 5).

## Conclusion

Although CD has traditionally been thought of as a disease of affluence, our survey data demonstrate that it exists in both rural and urban areas of LLMICs. Furthermore, our results indicate that existing literature alone does not represent its true burden. The resource-intensive nature of diagnosing and managing CD potentially contributes to the underreporting of CD in LLMICs. There is an urgent need to study the true epidemiology of CD in LLMICs through population-based IBD registries and rigorous epidemiologic studies. Improving access to CD diagnostics and improving awareness of CD among gastroenterology providers in LLMICs will hopefully catalyze CD diagnosis and treatment worldwide. There is also an urgent need to decentralize diagnosis to lower-level facilities like district hospitals so that patients residing outside of urban areas have access to care. Further research is additionally needed regarding the differentiation of CD from ITB, a disease with high prevalence in LLMICs. Finally, the high cost and unavailability of biologics should be addressed via inclusion in essential medicine formularies, increased global advocacy, collective demand creation, and generic production.

**Supplementary Information** The online version contains supplementary material available at <https://doi.org/10.1007/s10620-022-07675-6>.

**Author's contributions** RR, NG, and GB planned and designed the study; RR and SB implemented surveys and managed data collection; SB, SM, KN, AY, and LD performed data cleaning and analysis; RR, SB, NG, SM, KN, AY, and LD contributed to the writing and editing of the final manuscript.

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## Declarations

**Conflict of interest** The authors have no competing interests to declare.

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