Original Article

Distinguishing Crohn's Disease from Intestinal Tuberculosis in Nepal: A Prospective Observational Study

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Abstract

Background and Aims: Crohn's disease (CD) and intestinal tuberculosis (ITB) are chronic granulomatous disorders with substantial overlap in clinical, endoscopic and histopathological features, posing significant diagnostic challenges. We aimed to compare demographic characteristics, clinical presentation, endoscopic and histological finding and treatment outcomes of CD and ITB and to identify distinguishing features in a Nepalese cohort.

Methods: This prospective observational study (2017–2024) included adults diagnosed with CD or ITB. CD was diagnosed via standard criteria; ITB was established by histopathology, GeneXpert MTB/PCR, or clinicoradiological response to anti-tubercular therapy (ATT). Patients failing to improve after one month of ATT were re-evaluated. Multivariate logistic regression identified independent predictors of diagnosis.

Results: Six of 75 patients (8.0%) initially treated as presumed ITB failed to respond to ATT at one month and were subsequently reclassified as CD, yielding a final cohort of 263 CD and 69 ITB patients. CD demonstrated male predominance (61.6%), whereas ITB was more common in females (59.4%) (p=0.003). Mean age at diagnosis was similar between CD (31.8 ± 6.7 years) and ITB (32.7 ± 12.9 years). Abdominal pain was reported in 87.5% of CD and 88.4% of ITB patients. Fever was more frequent in ITB (49.3% vs 24.7%), while rectal bleeding (41.8% vs 14.5%) and perianal disease (24.7% vs 0%) favored CD. Ileocecal involvement predominated in both groups. Histopathological confirmation of ITB was achieved in 58.0%. All confirmed ITB and CD patients achieved sustained clinical and endoscopic remission at six months follow-up. Female sex (aOR 2.48) and fever (aOR 2.12) independently predicted ITB, whereas rectal bleeding (aOR 0.18) and perianal disease (aOR 0.12) favored CD.

Conclusion: CD and ITB frequently overlap, limiting the utility of disease location and histopathology alone. Accurate differentiation requires an integrated approach combining demographics, clinical markers, endoscopic findings, and microbiological testing. Prompt reassessment of patients failing to respond to anti-tubercular therapy within one month is critical to prevent misdiagnosis and ensure appropriate management as IBD incidence rises.

Introduction

Crohn's disease (CD) and intestinal tuberculosis (ITB) are chronic inflammatory disorders that frequently present with overlapping clinical, endoscopic, radiological and histopathological features, particularly in tuberculosis-endemic regions.[1–3] While the global incidence of inflammatory bowel disease is rising including across Asia, tuberculosis continues to remain highly prevalent in low and middle-income countries, creating a unique diagnostic challenge for clinicians.[4–8] Both CD and ITB commonly affect young adults and share symptoms such as abdominal pain, diarrhea, weight loss and anemia, often leading to delayed or incorrect diagnosis.[9–11]

Accurate differentiation between these two conditions is critical, as the therapeutic approaches differ fundamentally. Immunosuppressive therapy used for CD may result in catastrophic outcomes if administered to patients with undiagnosed ITB, whereas delayed initiation of anti-tubercular therapy can lead to disease progression and complications in ITB patients.[2,3,10] Histopathological confirmation remains the diagnostic gold standard. However, caseating granulomas and acid-fast bacilli are detected in only a subset of ITB patients due to the paucibacillary nature of intestinal

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disease.[12–14] Consequently, a substantial proportion of patients require empirical treatment based on a composite of clinical, radiological, laboratory and therapeutic response criteria.[15,16]

Several diagnostic models incorporating clinical, endoscopic, histological and radiological parameters have been proposed to improve diagnostic accuracy, yet their applicability varies across populations and healthcare settings.[3,10,17,18] Rapid urbanization and dietary westernization have been implicated in the rising incidence of inflammatory bowel disease across Asia, including Nepal, and may contribute to the evolving clinical spectrum of Crohn's disease in tuberculosis-endemic regions. In Nepal, data comparing CD and ITB remain limited despite the country's high tuberculosis burden and increasing recognition of inflammatory bowel disease. This prospective study aimed to compare the demographic characteristics, clinical presentation, disease distribution, histopathological findings and treatment outcomes of CD and ITB patients in a tertiary setting and to identify key features that may aid in their differentiation.

Methods

Study Design and Setting

This prospective observational study enrolled consecutive adults (≥18 years) diagnosed with CD or ITB between 2017 and 2024 at a tertiary-care centre in Nepal. Patients with indeterminate colitis, isolated extraintestinal tuberculosis without intestinal involvement, prior bowel resection before diagnosis, or incomplete clinical data were excluded. Six patients initially treated as ITB were reassessed at 1 month due to absent clinical response to anti-tubercular therapy (ATT) and were reclassified as CD; therefore, the final analytical cohort comprised 263 CD and 69 ITB patients.

Diagnostic Criteria

CD was diagnosed using a composite of clinical features, ileocolonoscopy, histology, and radiological assessment consistent with established international criteria. ITB was diagnosed by (i) histopathological evidence of caseating granulomas and/or acid-fast bacilli and/or (ii) microbiological confirmation of Mycobacterium tuberculosis using nucleic acid amplification testing (GeneXpert MTB and/or PCR), or (iii) a composite clinicoradiological diagnosis supported by therapeutic response to ATT in a tuberculosis-endemic setting.

Clinical and Endoscopic Assessment

Baseline demographic data, clinical history and presenting symptoms were recorded prospectively. Common symptoms assessed included abdominal pain, diarrhea, weight loss, anorexia, fever and rectal bleeding. The presence of perianal disease (fissure, fistula, or abscess) was specifically documented, given its known diagnostic relevance in differentiating CD from ITB. Disease activity in CD patients was assessed using the Crohn's Disease Activity Index (CDAI), a validated composite scoring system. CDAI parameters included stool frequency, abdominal pain, general well-being, use of antidiarrheal medications, extraintestinal manifestations, abdominal mass, hematocrit, body weight and sex. CDAI scores were calculated using a standardized electronic calculator. Based on CDAI scores, disease activity was categorized as: Mild: 150–219; Moderate: 220–449 and Severe: ≥450. Colonoscopic findings were categorized as ulceration, nodularity, deformed ileocecal valve, mass lesion, stricture, or erythema. Disease location was classified according to standard criteria (L1–L3 for CD; ileal, ileocecal, or colonic for ITB).

Radiological and Ancillary Assessment

Chest radiographs were reviewed and categorized as normal, cavitary disease, pleural effusion or healed tuberculosis changes. Dietary history, including transition from traditional Nepali to Westernized or foreign diets, and self-reported ethnicity were recorded for exploratory analysis.

Treatment and Follow-up

All patients initially diagnosed with ITB commenced standard ATT per national guidelines. Clinical response was assessed at 1 month and 6 months. Patients without meaningful clinical improvement at the 1-month review had ATT discontinued and underwent diagnostic reassessment; six such patients were subsequently reclassified as CD and excluded from the final ITB cohort. Among patients who improved at 1 month and remained classified as ITB, sustained clinical remission was observed at 6 months, with no documented relapses during the observation period.

Statistical Analysis

Categorical variables are presented as n (%) and continuous variables as mean ± SD. Between-group comparisons used Chi-square / Fisher's exact test for categorical variables and Student's t-test or Mann–Whitney U test for continuous variables, as appropriate. Multivariable logistic regression (dependent variable: ITB vs CD) was performed to identify independent predictors of ITB; covariates were prespecified based on clinical plausibility and univariable association, and results are reported as adjusted odds ratios (aOR) with 95% confidence intervals (CI). Two-sided $p<0.05$ was considered statistically significant.

Results

Patient Characteristics and Demographics

A total of 332 patients were included in the study: 263 diagnosed with CD and 69 with ITB.

Table 1. Baseline demographic characteristics of patients with Crohn's disease and intestinal tuberculosis

Variable	Crohn's disease (n = 263)	Intestinal TB (n = 69)	p-value
Mean age, years (SD)	31.8 ± 6.7	32.7 ± 12.9	0.56
Male, n (%)	162 (61.6)	28 (40.6)	0.003
Female, n (%)	101 (38.4)	41 (59.4)	

Among CD patients, there was a clear male predominance (162 males, 61.6% vs 101 females, 38.4%), yielding a male-to-female ratio of 1.6:1. In contrast, ITB patients showed a female predominance (41 females, 59.4% vs 28 males, 40.6%), with a male-to-female ratio of 0.68:1. This difference in sex distribution between CD and ITB was statistically significant ($p = 0.003$). The mean age at diagnosis was comparable between the two groups. CD patients had a mean age of 31.8 ± 6.7 years, while ITB patients had a mean age of 32.7 ± 12.9 years ($p = 0.56$).

Disease Activity Profile in Crohn's Disease

Table 2. Distribution of Crohn's disease activity based on CDAI

Disease activity	CDAI range	n (%)
Mild	150–219	77 (29.3)
Moderate	220–449	164 (62.4)
Severe	≥450	22 (8.4)

Disease activity among CD patients was assessed using the Crohn's

Disease Activity Index (CDAI). Mild disease (CDAI 150–219) was observed in 77 patients (29.3%), moderate disease (CDAI 220–449) in 164 patients (62.4%), and severe disease (CDAI ≥450) in 22 patients (8.4%). The mean CDAI score for mild CD was 183.4 ± 18.0, for moderate CD was 276.5 ± 40.7, and for severe CD was 483.6 ± 15.9.

Clinical Presentation and Symptom Profile

Abdominal pain was the most common presenting symptom in both disease groups, reported in approximately 85–90% of CD patients and 88.4% of ITB patients. Chronic diarrhea and weight loss were also frequently observed in both conditions. However, fever was significantly more common in ITB patients (49.3%), reflecting the systemic inflammatory nature of tuberculosis. Rectal bleeding and perianal disease were notably more frequent in CD patients. Perianal disease (including fissure, fistula, or abscess) was documented in approximately one-quarter of CD patients and was absent in all ITB patients ($p < 0.001$). Mucus or blood in stool was reported in only 14.5% of ITB patients.

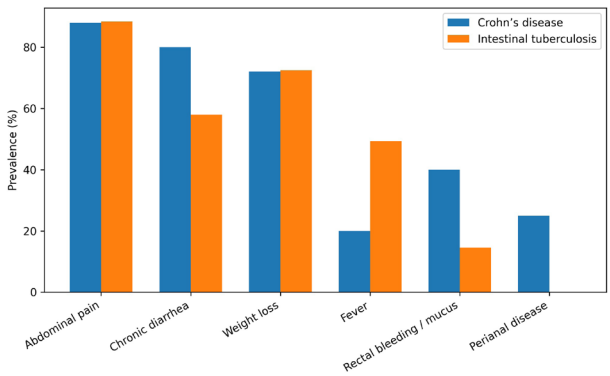

Figure 1. Comparative clinical symptom profile of Crohn's disease and intestinal tuberculosis.

Disease Location and Endoscopic Distribution

Table 3. Disease location in Crohn's disease and intestinal tuberculosis

Location	Crohn's disease n (%)	Intestinal TB n (%)
Ileal	49 (18.6)	16 (23.2)
Colonic	68 (25.9)	16 (23.2)
Ileocolonic / Ileocecal	146 (55.5)	37 (53.6)

In CD patients, ileocolonic involvement (L3) was the most common disease location, affecting 146 patients (55.5%), followed by isolated colonic disease (L2) in 68 patients (25.9%) and isolated ileal disease (L1) in 49 patients (18.6%). In ITB patients, the ileocecal region was the predominant site of involvement, observed in 37 patients (53.6%). Isolated ileal and isolated colonic involvement were each seen in 16 patients (23.2%). Overall, the distribution of disease location showed substantial overlap between CD and ITB, and anatomical site alone was not a reliable discriminator between the two conditions. Intestinal tuberculosis demonstrated nodular lesions (n = 2), deformed ileocecal valve (n = 3), mass-like lesions (n = 4), strictures (n = 5), and erythema (n = 6), while Crohn's disease was predominantly characterized by ulceration and erythema.

Histopathological Diagnosis and Diagnostic Yield

Histopathological confirmation of ITB was achieved in 40 patients (58%) through the identification of caseating granulomas and/or acid-fast bacilli. The remaining 29 patients (42%) were diagnosed empirically based on a combination of clinical presentation, radiological findings, laboratory investigations, and response to anti-tubercular therapy. Among CD patients the majority demonstrated chronic inflammatory changes without granuloma formation.

Table 4. Diagnostic basis for starting ATT in intestinal tuberculosis

Diagnostic basis	n (%)
Histopathology confirmed	40 (58.0)
Empirical (clinical + radiology + labs)	29 (42.0)

Treatment Response and Outcomes in ITB

All patients initially diagnosed with ITB commenced ATT. At the 1-month review, six patients showed no meaningful clinical improvement; ATT was discontinued and these patients were reclassified as CD, yielding a final cohort of 69 ITB patients for analysis. Among the remaining ITB patients who demonstrated clinical improvement at 1 month, sustained clinical remission was observed at 6 months, with no documented relapses during the observation period. Patients diagnosed with Crohn's disease were managed according to disease severity using standard therapeutic protocols. Over six months of follow-up, CD patients demonstrated clinical improvement, with corresponding endoscopic improvement or mucosal healing observed on follow-up colonoscopy. Treatment response patterns in both groups further supported the final diagnostic classification.

Independent Predictors of Diagnosis

On multivariable logistic regression, female sex independently predicted ITB (aOR 2.48, 95% CI 1.32–4.66; p=0.005), and fever was also independently associated with ITB (aOR 2.12, 95% CI 1.10–4.08; p=0.024). In contrast, rectal bleeding (aOR 0.18, 95% CI 0.07–0.42; p<0.001) and perianal disease (aOR 0.12, 95% CI 0.04–0.36; p<0.001) were strongly associated with CD. Age at diagnosis and disease location were not independently discriminatory after adjustment.

Table 5. Multivariate logistic regression analysis for predictors of intestinal tuberculosis

Variable	Adjusted OR	95% CI	p-value
Female sex	2.48	1.32–4.66	0.005
Fever	2.12	1.10–4.08	0.024
Rectal bleeding	0.18	0.07–0.42	<0.001
Perianal disease	0.12	0.04–0.36	<0.001
Disease location	1.09	0.61–1.95	0.77
Age	1.01	0.98–1.04	0.56

Discussion

This prospective study highlights the persistent diagnostic challenge of differentiating Crohn's disease from intestinal tuberculosis in a tuberculosis-endemic setting. Both conditions affected predominantly young adults in their third decade of life, consistent with global epidemiological trends reported for inflammatory bowel disease and extrapulmonary tuberculosis. Notably, we observed a clear divergence

in sex distribution, with CD showing male predominance and ITB affecting more females, a pattern previously reported from South Asian cohorts and other tuberculosis-endemic regions.[1,2,4–6] These differences may reflect variations in exposure risk, healthcare-seeking behavior and underlying immunological susceptibility.[2,3]

Disease activity assessment demonstrated that more than two-thirds of CD patients presented with moderate-to-severe disease at diagnosis. Similar observations have been reported from low- and middle-income countries, where delayed diagnosis and limited access to specialist care remain common.[10,19,20] The use of the Crohn's Disease Activity Index provided an objective measure of disease burden and highlighted the heterogeneity of CD at presentation.[21]

Clinical features alone were insufficient to reliably distinguish CD from ITB. Abdominal pain, diarrhea and weight loss were frequently observed in both conditions, consistent with prior comparative studies.[9,11,19] Fever was significantly more common in ITB, reflecting systemic inflammatory activity related to tuberculosis, whereas rectal bleeding and perianal disease were strongly associated with CD and were absent in ITB patients.[9,10,22] These findings support previous evidence that perianal disease is a useful discriminator favoring CD, although no single clinical feature is diagnostic in isolation.[3,23]

Anatomical distribution of disease showed substantial overlap between CD and ITB. Ileocecal and ileocolonic involvement predominated in both conditions, limiting the discriminatory value of disease location alone. This reinforces prior reports that anatomical site should be interpreted alongside clinical, endoscopic, and histological findings rather than as a standalone diagnostic criterion.[4,18]

Histopathological examination remains a cornerstone of diagnosis but demonstrated limited sensitivity in our cohort. Caseating granulomas or acid-fast bacilli were identified in only 58% of ITB patients, reflecting the known limitations of tissue diagnosis in paucibacillary disease.[12–14] Importantly, all empirically diagnosed ITB patients demonstrated a robust clinical response to anti-tubercular therapy, supporting the pragmatic role of therapeutic trials in selected high-probability cases when histology is inconclusive.[15,16]

Multivariate analysis further strengthened these observations by identifying female sex as an independent predictor of ITB and rectal bleeding as a strong predictor of CD. Age and disease location did not independently discriminate between the two conditions, consistent with previously validated diagnostic models.[17,18] These findings underscore the importance of a composite diagnostic strategy rather than reliance on isolated parameters.

The strengths of this study include its prospective design, real-world patient population, and comprehensive assessment across clinical, endoscopic, histological, and therapeutic domains. Limitations include the single-center design, absence of advanced molecular biomarkers and limited long-term follow-up. Future multicenter studies incorporating immunological, molecular, and imaging-based diagnostics may further refine diagnostic algorithms in tuberculosis-endemic regions.[7,11,16] Crohn's disease and intestinal tuberculosis continue to pose a significant diagnostic dilemma in TB-endemic regions. Our findings emphasize the need for an integrated, multidisciplinary approach that balances diagnostic certainty with timely initiation of appropriate therapy to optimize patient outcomes.[2,3,10]

Conclusion

In this prospective Nepalese cohort CD and ITB showed significant overlap among young adults. CD predominated in men, while ITB was more common in women. Fever independently favored ITB, whereas rectal bleeding and perianal disease strongly predicted CD. Because disease location and histology were often non-discriminatory, accurate diagnosis requires integrating demographics, symptoms, and microbiology with a critical one-month reassessment of treatment response.

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