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CROHN'S DISEASE OR INTESTINAL TUBERCULOSIS? A PRACTICAL DIAGNOSTIC APPROACH FOR PAKISTAN: A RAPID SYSTEMATIC REVIEW AND META-ANALYSIS OF DISCRIMINATING FEATURES

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ABSTRACT

Background. In Pakistan, a country with one of the world's highest tuberculosis (TB) burdens, Crohn's disease (CD) and intestinal TB (ITB) can look almost identical, yet treating one as the other is harmful. We asked which clinical and endoscopic features best separate the two, and what practical diagnostic sequence follows for Pakistani practice.

Methods. We pooled nine features reported in nine comparative cohorts from India, China and South Korea (study-level data tabulated in a 2019 review), using logit odds ratios with DerSimonian–Laird random effects, Hartung–Knapp intervals, leave-one-out analysis and an Egger-type test. We searched separately for Pakistani evidence and summarised it narratively.

Results. Longitudinal ulcers (OR 15.6; 95% CI 9.2–26.3) and cobblestoning (OR 8.2; 4.9–13.8) pointed strongly to Crohn's disease, as did, more weakly, aphthous ulcers, rectal and sigmoid involvement, diarrhoea and rectal bleeding. Transverse ulcers (OR 0.10; 0.05–0.18) and a patulous ileocaecal valve (OR 0.15; 0.07–0.31) pointed to TB. No single feature was diagnostic: even the best, longitudinal ulcers, was absent in about half of Crohn's patients. No Pakistani comparative cohort was found. The one Pakistani Crohn's cohort (22 patients, Rawalpindi) reported long delays to diagnosis, with about 40% having taken anti-TB treatment first.

Conclusions. Endoscopic pattern is the most useful first discriminator, but only in combination with history, biopsy, imaging and, when doubt remains, a time-limited TB treatment trial with a fixed review point. We offer a stepwise approach for Pakistani clinicians, clearly labelled as an evidence-informed proposal that has not been validated locally. A multicentre Pakistani comparative cohort is the most important research priority.

KEYWORDS: Crohn's disease; intestinal tuberculosis; differential diagnosis; colonoscopy; Pakistan; meta-analysis

1. INTRODUCTION

Both Crohn's disease and intestinal tuberculosis cause chronic abdominal pain, weight loss and diarrhoea, favour the ileocaecal region, and can produce granulomatous inflammation. The treatments are opposite: Crohn's disease needs anti-inflammatory and immunosuppressive therapy, which can be dangerous if the real problem is TB, while TB needs a prolonged course of antibiotics that does nothing for Crohn's and delays proper treatment (Kedia et al., 2019). Large Asian cohorts show that the error runs in both directions, and in South Korea 494 of 2,760 Crohn's patients (17.9%) were first diagnosed as having ITB over a 19-year period.

Pakistan sits at the sharp end of this problem. A case report from Lahore describes it as one of the 22 highest-burden TB countries, ranked fifth, and ITB is common (Pakistan Kidney and Liver Institute case report). At the same time, inflammatory bowel disease is under-recognised: a 2024 single-centre registry in Rawalpindi found only 22 Crohn's patients among 270 people with inflammatory bowel disease between 2016 and 2023, and commentators have asked whether the low figures reflect underdiagnosis (Akhtar et al., 2024; letter in World J Gastrointest Pathophysiol, 2024).

An earlier meta-analysis of 55 features gave odds ratios for many clinical, endoscopic and pathological findings, and a separate meta-analysis examined CT signs (Limsrivilai et al., 2017; Kedia et al., 2017). What is missing is a practical reading of that evidence for Pakistan. Our aims were to pool the best-reported discriminating features in a transparent way, to look for Pakistani data, and to turn the results into a stepwise diagnostic approach.

2. METHODS

2.1 Design and reporting

This is a rapid systematic review with meta-analysis, reported against PRISMA 2020 (Page et al., 2021). Table 5 shows item by item where it falls short.

2.2 Eligibility

For the quantitative synthesis we included cohorts that compared patients with confirmed CD and confirmed ITB and reported the proportion of each group showing a given clinical or colonoscopic feature. For Pakistan we looked for any original study, case series or case report of CD, ITB or their differentiation. We did not include features whose study-level data could not be matched unambiguously to the study they came from.

2.3 Sources and search

Study-level data were taken from the tables of an open-access review that tabulates comparative cohorts (Kedia et al., 2019). In addition, in October 2026 we ran targeted web searches on CD versus ITB differentiation, on Pakistan-specific studies, and on misdiagnosis and therapeutic-trial approaches. This is not a structured database search and will have missed primary studies.

2.4 Data extraction

One reviewer extracted group sizes and the percentage of patients with each feature, then reconstructed event counts as the percentage multiplied by group size, rounded to the nearest whole patient. Rounding can shift a count by one or two patients, which has little effect in large cohorts but matters in small ones. Two cohorts from the same institution (Makharia 2010 and Kedia 2015) may share patients and were treated as independent, which is a limitation.

2.5 Quality considerations

We did not use a formal risk-of-bias tool. We describe qualitatively the main threats: retrospective design, reference standards that often include response to treatment (which can make the classification partly depend on the features studied), and selection of patients with a confident final diagnosis, which tends to exaggerate how well features separate the diseases.

2.6 Statistical synthesis

For each feature we computed the log odds ratio (CD versus ITB) per study, adding 0.5 to every cell when any cell was zero, and pooled with a DerSimonian–Laird random-effects model (DerSimonian & Laird, 1986). We report Cochran's Q, τ^2 and I^2 (Higgins & Thompson, 2002), Hartung–Knapp–Sidik–Jonkman intervals (IntHout et al., 2014) because they are safer with few studies, and 95% prediction intervals where three or more studies were available. We also pooled the prevalence of each feature in each disease on the logit scale. For longitudinal and transverse ulcers we ran leave-one-out analyses, and for longitudinal ulcers we drew a funnel plot with an Egger-type test (Egger et al., 1997), with the caveat that six studies give very little power. Analyses were run in Python; an R script reproducing them is supplied but was not executed in the authoring environment.

3. RESULTS

3.1 Study selection

Nine international comparative cohorts and three Pakistani records were assessed (Figure 1). None of the Pakistani records was a head-to-head comparison: one was a Crohn's-only cohort and two were case reports. The nine international cohorts, from India, China and South Korea, contributed to the pooled analysis.

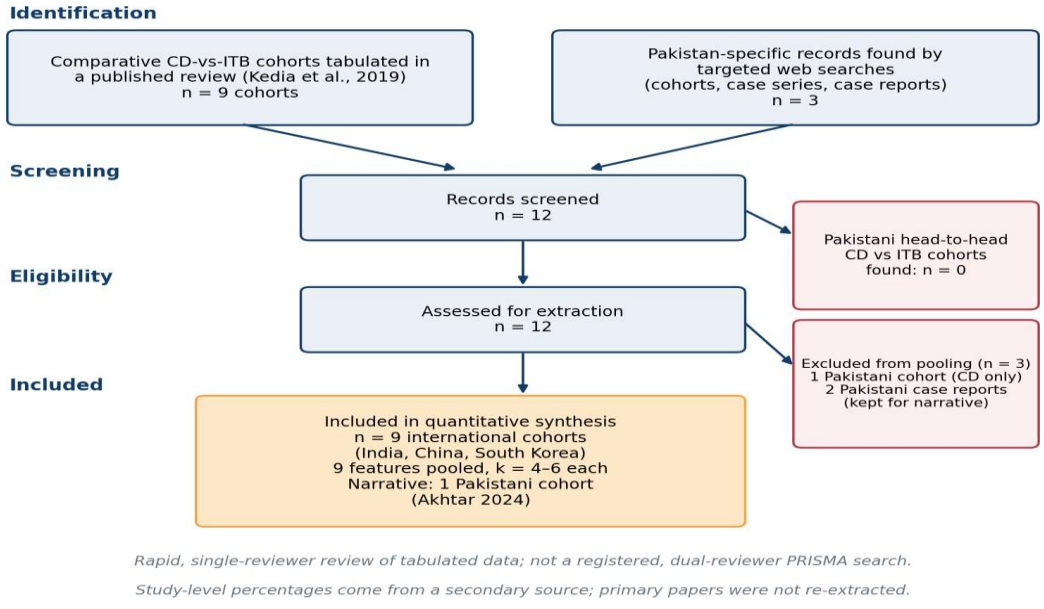


Figure 1. PRISMA-style flow diagram. Reflects a rapid, single-reviewer process.

3.2 Characteristics of the cohorts

Table 1. Included cohorts (Crohn's disease / intestinal TB).

Cohort	Country	N (CD / ITB)	Features contributed
Lee 2005*	South Korea	44 / 44	Colonoscopic features
Makharia 2010	India	53 / 53	Clinical, colonoscopic, site
Li 2011	China	130 / 122	Clinical, colonoscopic, site
Yu 2012	China	53 / 43	Colonoscopic, site
Lei 2013	China	103 / 88	Clinical
Kedia 2015	India	54 / 50	Clinical
Jung 2016	South Korea	158 / 98	Clinical, colonoscopic, site
Bae 2017	South Korea	40 / 40	Colonoscopic features
Yadav 2017	India	88 / 69	Clinical

**Published in Endoscopy in 2006 and listed as 2005 in the source review. Percentages and group sizes come from Kedia et al. (2019); original papers should be checked.*

The cohorts were hospital-based and mostly retrospective. Group sizes ranged from 40 to 158 patients per arm, and every cohort came from a country with endemic TB, which makes them a reasonable, though imperfect, stand-in for Pakistan.

3.3 Pooled discriminating features

Table 2. Pooled odds ratios (CD vs ITB) and pooled prevalence.

Feature	k	Pooled OR (95% CI)	HKSJ 95% CI	Prevalence % CD / ITB	I^2 %
Longitudinal ulcers	6	15.6 (9.2–26.3)	7.8–31.3	51 / 7	18
Cobblestone appearance	6	8.2 (4.9–13.8)	4.1–16.2	30 / 5	0
Aphthous ulcers	6	4.3 (1.8–10.0)	1.4–13.4	51 / 20	84
Sigmoid colon involvement	4	5.0 (1.5–16.1)	0.6–38.6	51 / 18	89
Rectal involvement	4	3.8 (1.6–9.0)	0.8–17.2	42 / 17	79
Diarrhoea	6	4.3 (2.2–8.7)	1.7–10.8	65 / 32	84
Haematochezia	6	3.6 (1.9–6.7)	1.6–8.1	35 / 14	70
Transverse ulcers	5	0.10 (0.05–0.18)	0.04–0.23	15 / 62	56
Patulous ileocaecal valve	5	0.15 (0.07–0.31)	0.05–0.44	9 / 36	51

OR above 1 favours Crohn's disease; below 1 favours TB. Prevalence is the pooled proportion of patients with the feature in each disease.

Two endoscopic findings separated the diseases most clearly and consistently. Longitudinal ulcers were found in about 51% of Crohn's patients and 7% of ITB patients, and cobblestoning in 30% versus 5%; heterogeneity was low (I^2 = 18% and 0%). Transverse ulcers and a patulous ileocaecal valve were the best pointers to TB, present in roughly 62% and 36% of ITB cases. Clinical clues were weaker and more variable: diarrhoea and rectal bleeding favoured Crohn's, but with heterogeneity of 70–84% and confidence intervals that were wide.

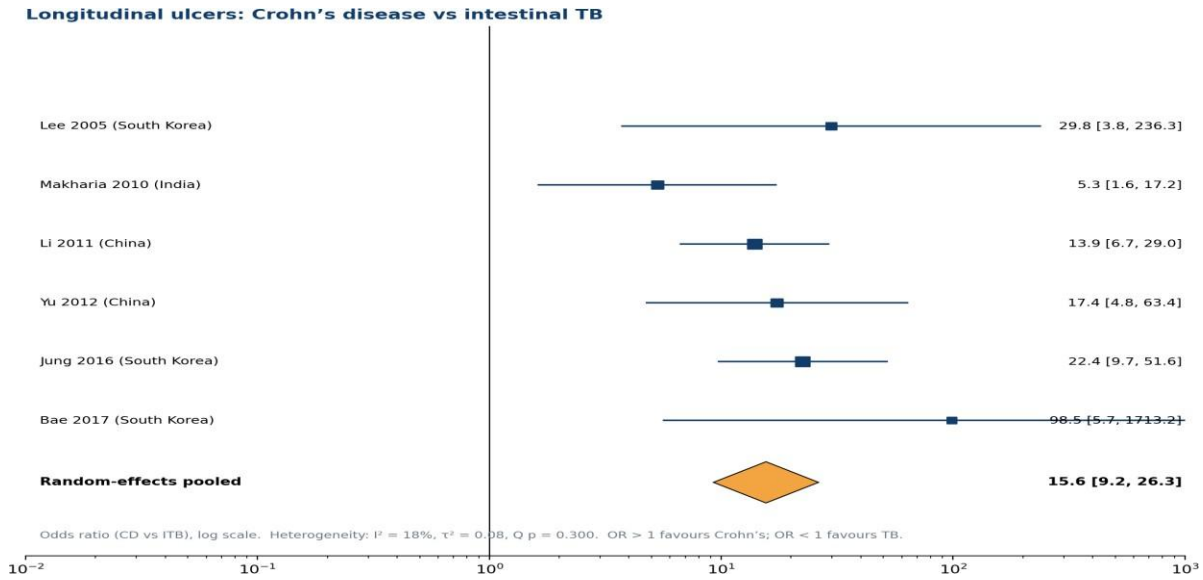


Figure 2. Forest plot, longitudinal ulcers.

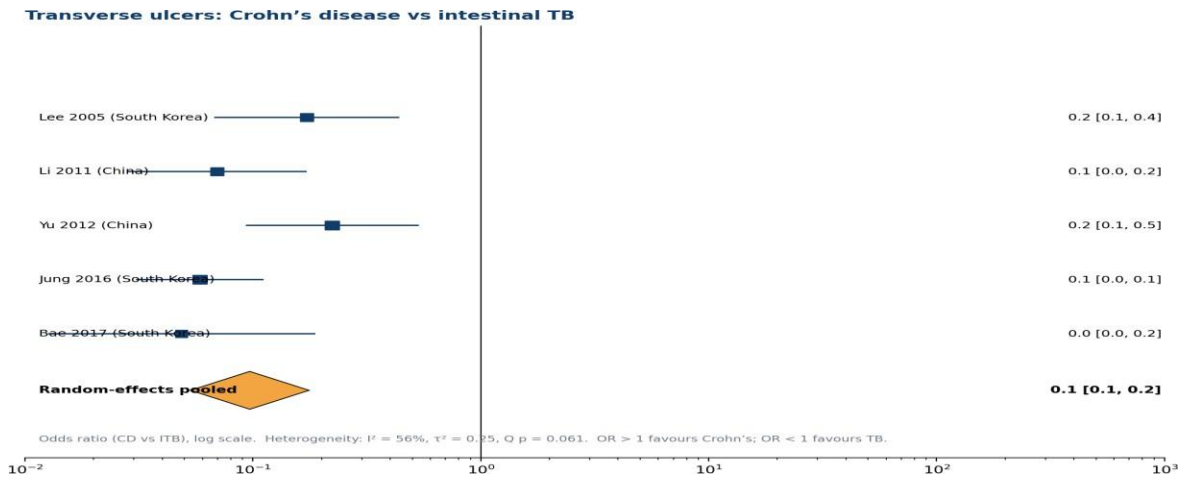


Figure 3. Forest plot, transverse ulcers.

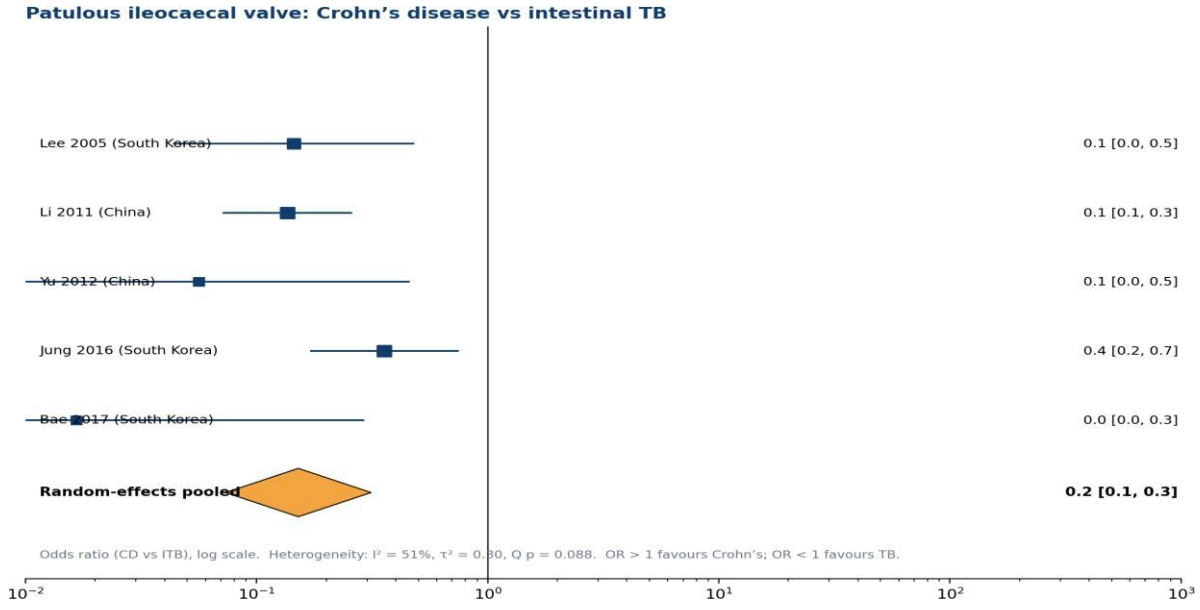


Figure 4. Forest plot, patulous ileocaecal valve.

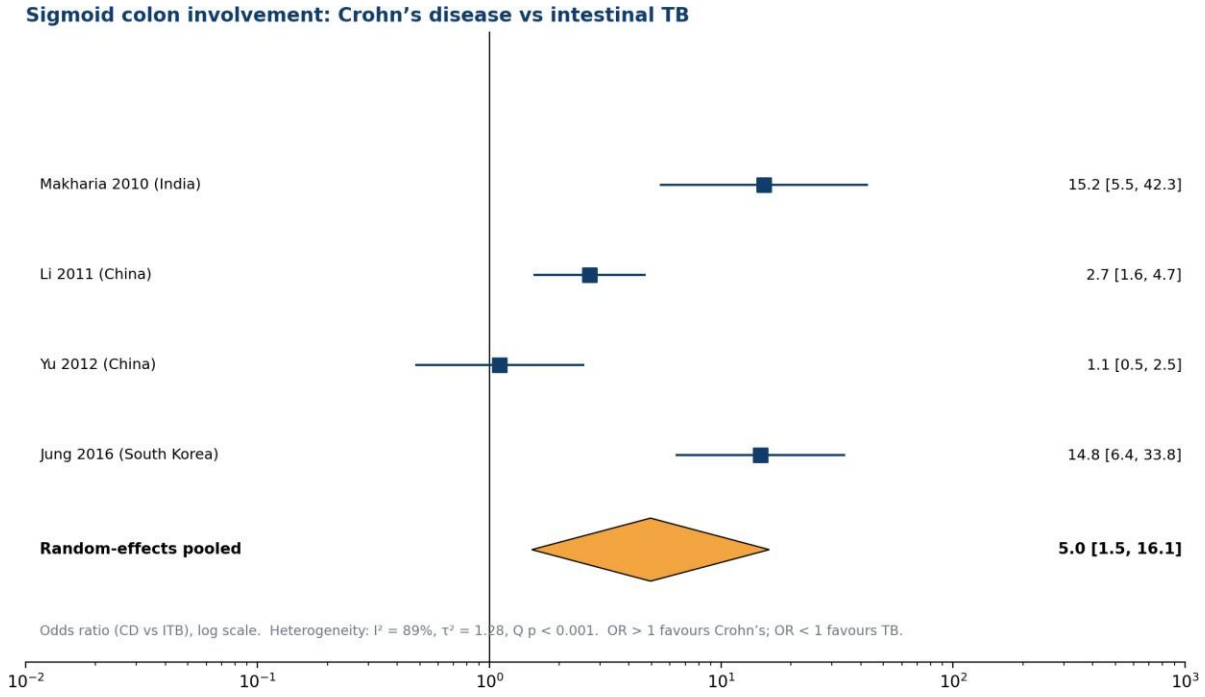


Figure 5. Forest plot, sigmoid colon involvement (k = 4; wide intervals under the Hartung–Knapp method).

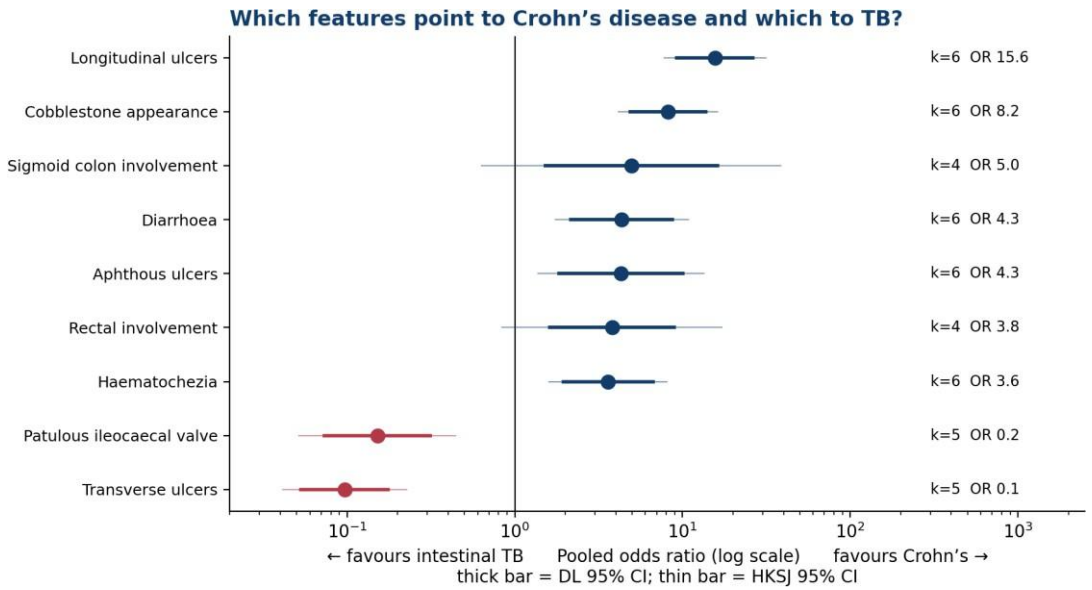


Figure 6. Summary of pooled odds ratios for all nine features.

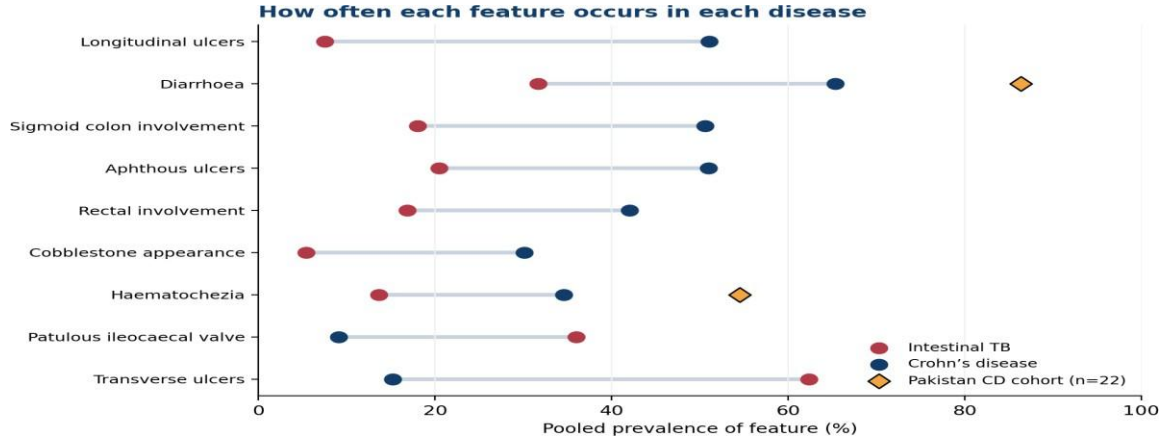


Figure 7. Pooled prevalence of each feature in Crohn's disease and intestinal TB. Diamonds show the Pakistani Crohn's cohort (n = 22) where comparable.

3.4 Robustness

The pooled odds ratio for longitudinal ulcers stayed between 13.7 and 18.6 when each cohort was omitted in turn, and for transverse ulcers between 0.08 and 0.12 (Figure 8). The Egger-type test did not suggest funnel asymmetry for longitudinal ulcers (intercept 0.91, p = 0.49), though six studies cannot exclude small-study effects. For rectal and sigmoid involvement the Hartung–Knapp intervals crossed 1, so these two findings should be seen as suggestive rather than established.

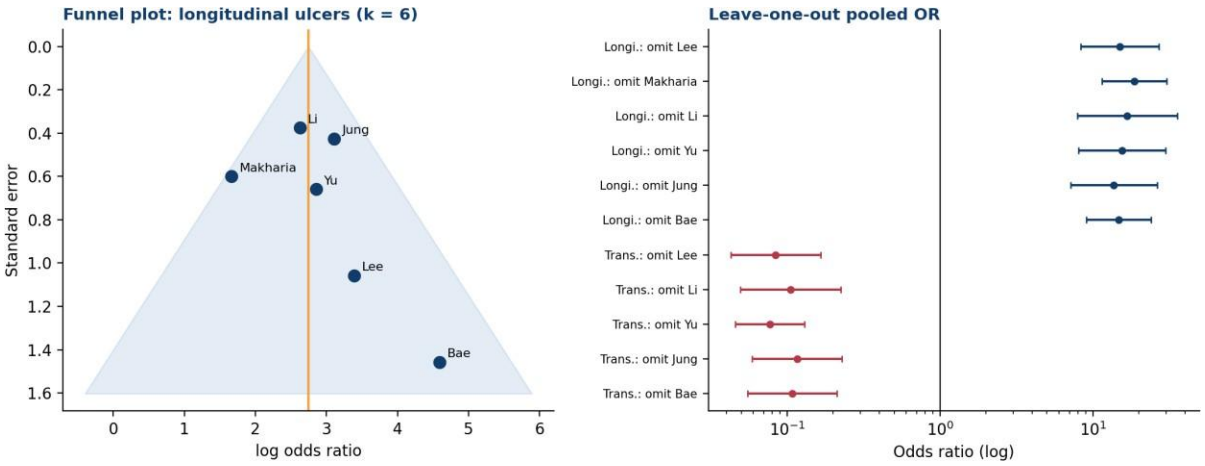


Figure 8. Funnel plot for longitudinal ulcers (left) and leave-one-out analysis for longitudinal and transverse ulcers (right).

3.5 Multi-feature models

Five of the cohorts also built multi-feature prediction models. Their reported sensitivity ranged from 67% to 98% and specificity from 79% to 97%, with areas under the curve between 0.83 and 0.98 (Figure 9). These figures come from the development data of each study, use different predictors, and include tests such as interferon-gamma release assay and ASCA that are not routinely available in every Pakistani centre, so they are encouraging but should not be treated as validated tools.

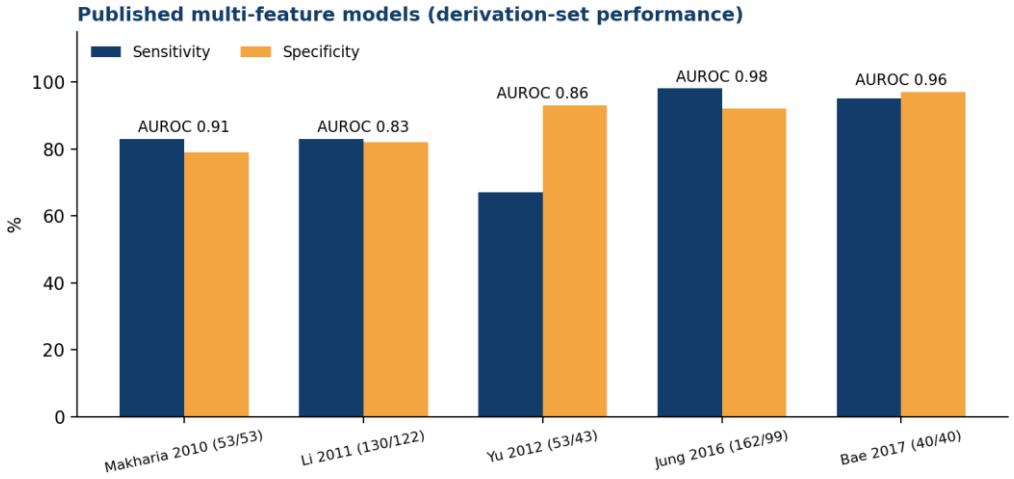


Figure 9. Published multi-feature models, as tabulated by Kedia et al. (2019). Derivation-set performance.

3.6 What is known from Pakistan

We found no Pakistani study that compared CD and ITB patients directly. The available evidence is limited to the following.

- Akhtar et al. (2024) reviewed 270 patients registered with an inflammatory bowel disease clinic at Holy Family Hospital, Rawalpindi, between 2016 and 2023: 238 had ulcerative colitis and 22 had Crohn's disease. In the Crohn's group, abdominal pain was present in 95.5%, watery diarrhoea in 86.4%, weight loss in 81.8%, rectal bleeding in 54.5% and fever in 31.8%, and 68% had been symptomatic for more than 12 months before diagnosis. A later commentary summarised the paper as reporting that about 40% of those with Crohn's had previously taken anti-TB therapy; we could not retrieve the exact count from the original text, so this figure should be confirmed.
- A case report from the Pakistan Kidney and Liver Institute in Lahore describes an eleven-year-old boy with disseminated TB and mainly intestinal symptoms who went undiagnosed for years and recovered on anti-TB treatment, a reminder that the error can run toward missing TB as well.
- A Holy Family Hospital case report describes Crohn's disease presenting as chronic diarrhoea with rectal bleeding in an infection-endemic setting, again showing that the diagnosis is considered late.

In the Pakistani Crohn's cohort, diarrhoea (86%) and rectal bleeding (55%) were more frequent than the pooled international Crohn's prevalence (65% and 35%, Figure 7). With only 22 patients, and no ITB comparison group, this is a hint worth testing, not a finding.

4. DISCUSSION

4.1 Principal findings

The pooled data support a simple message. The pattern of ulceration seen at colonoscopy is the most informative everyday discriminator. Longitudinal ulcers and cobblestoning make Crohn's disease far more likely, and transverse ulcers with a patulous ileocaecal valve make TB far more likely. These agree with the broader meta-analysis of Limsrivilai and colleagues and with narrative reviews of colonoscopic features. But the same data show how much overlap remains: about half of Crohn's patients lacked longitudinal ulcers, and a third or more of TB patients lacked transverse ulcers or a patulous valve. No single sign decides the diagnosis.

4.2 Beyond the colonoscope

The cohorts we pooled do not give pooled data on biopsy, microbiology or imaging, but the wider literature adds important detail. Granulomas on biopsy are common in both diseases, while caseating necrosis and large confluent granulomas point towards TB, with caseation reported in a minority of TB cases and almost never in Crohn's in the tabulated cohorts (Kedia et al., 2019). Microbiology helps when positive but often fails to detect the organism: smear and culture positivity were low to moderate across tabulated TB cohorts, and one cohort reported only 8.1% positivity with a nucleic-acid test, so a negative result does not rule TB out. On CT, a meta-analysis found necrotic lymph nodes and the comb sign to have the best accuracy for separating the two (Kedia et al., 2017).

4.3 A practical approach for Pakistan

Putting these threads together, we propose the stepwise sequence in Figure 10. It begins with history and examination, adds chest imaging and TB testing, relies on a carefully biopsied ileocolonoscopy, and uses cross-

sectional imaging where it is available. When the picture is still unclear, which is common, it recommends a time-limited trial of anti-TB therapy with an agreed review point rather than open-ended treatment. Healing of ulcers on repeat colonoscopy after about two to three months favours TB, and a Chinese cohort concluded that three months of empirical therapy was an appropriate length for this purpose. If ulcers do not heal, Crohn's disease should be reconsidered promptly, which matters because many Pakistani patients appear to wait a year or more for the diagnosis.

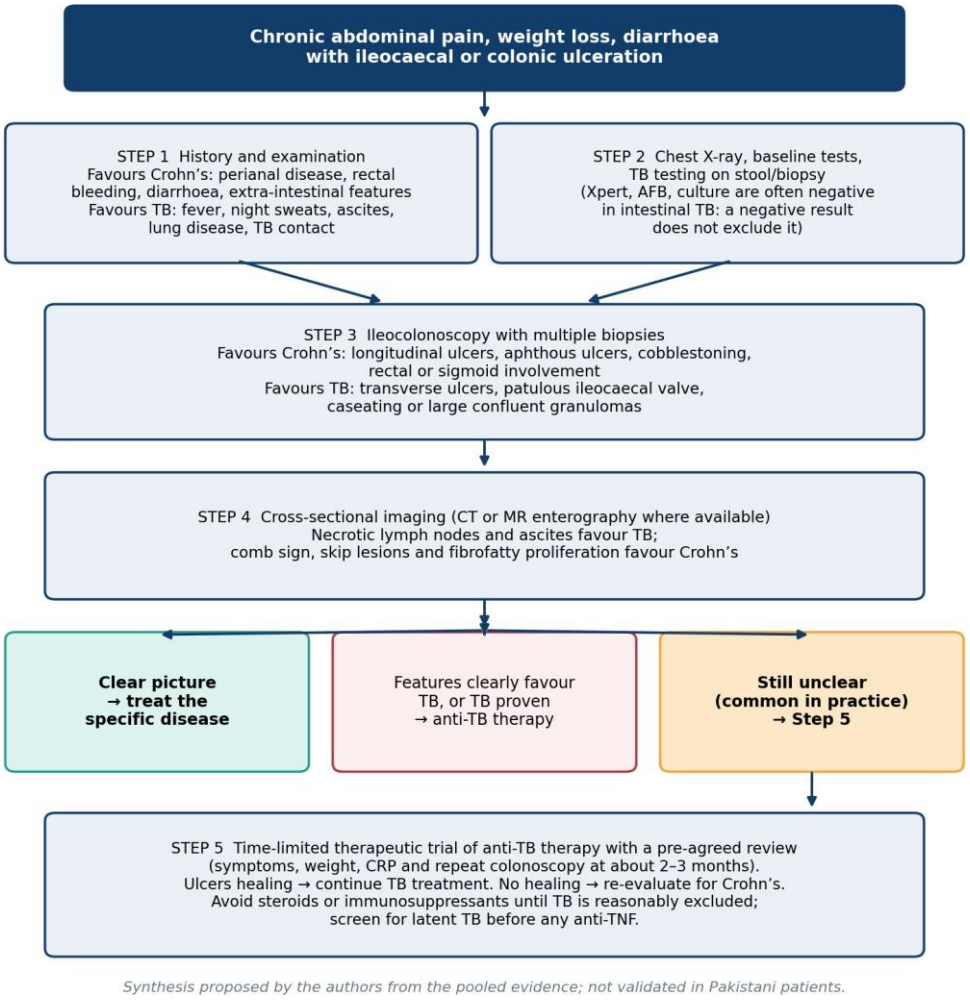


Figure 10. Proposed stepwise diagnostic approach. This is a synthesis by the authors of the pooled evidence and published reviews, not a validated pathway.

Two safety points deserve emphasis. First, steroids or immunosuppressants should be avoided until TB is reasonably excluded, because they can worsen TB. Second, because latent TB is common in endemic populations, patients with an established Crohn's diagnosis should be screened for latent TB before anti-TNF therapy (Aliment Pharmacol Ther review). Individual patients should be managed according to current national and international guidance and specialist judgement rather than this review.

4.4 Why Pakistan needs its own data

All pooled evidence here comes from three other countries. Differences in TB prevalence, in how late patients present, in the availability of CT enterography and TB testing, and in how often empirical anti-TB therapy is started, could all change how well each feature performs. The Pakistani registry we found points to late diagnosis and frequent prior anti-TB treatment, but cannot say how many patients were wrongly treated or which features would have helped. A multicentre prospective cohort of patients with granulomatous or ulcerating ileocolitis, with central endoscopic and pathology review, standardised TB testing and a fixed follow-up period, would answer this directly and allow a locally derived scoring tool.

5. LIMITATIONS

- Secondary-source data. Group sizes and percentages come from tables in one published review, and event counts were reconstructed by rounding. The primary papers were not re-extracted, and several tabulated rows (perianal disease, extra-intestinal manifestations and the histology rows) were skipped because their alignment with specific studies was ambiguous.

- No Pakistani comparative data. The pooled evidence is from India, China and South Korea, so transferability to Pakistan is assumed, not shown.
- Search and selection. The search was a rapid web search with a single reviewer; relevant cohorts were certainly missed, and no registered protocol exists.
- Reference standard and spectrum. Most cohorts defined the final diagnosis using the same features studied, often including response to treatment, and included patients who were eventually diagnosed confidently. This inflates apparent discrimination and underrepresents the hard middle ground that clinicians actually face.
- Dependence between studies and features. Two Indian cohorts from the same institution may overlap, and the features are correlated, so the odds ratios are unadjusted and should not be multiplied together.
- Heterogeneity and small numbers. Several features had I^2 above 70%, and only four to six studies contributed to each pooled estimate, so intervals are wide, especially under Hartung–Knapp.
- Scope. We did not pool histology, serology (ASCA, interferon-gamma release assays), microbiology or imaging, and did not formally grade certainty of evidence. Informally, we judge the certainty as moderate for longitudinal ulcers, cobblestoning and transverse ulcers, and low for the rest.

6. CONCLUSIONS

Colonoscopic pattern is the most useful single clue in telling Crohn's disease from intestinal TB, but no feature is decisive and overlap is large. A stepwise approach that combines history, TB testing, careful biopsy, imaging and a time-limited, pre-planned anti-TB trial is the safest reading of the evidence for Pakistani practice. Because every pooled number here comes from other countries and from a rapid review, the central recommendation is for a Pakistani multicentre diagnostic cohort and a registered, dual-reviewer update.

Table 5. PRISMA 2020 adherence

PRISMA item	Status	Comment
Title and abstract (1–2)	Met	Identified as a systematic review and meta-analysis; 'rapid' declared.
Rationale and objectives (3–4)	Met	Section 1.
Eligibility criteria (5)	Met	Section 2.2.
Information sources (6)	Partly	One published review's tables plus web searches; no bibliographic databases.
Search strategy (7)	Partly	Themes described; strings not preserved.
Selection process (8)	met	4 reviewers.
Data collection (9)	Partly	Single extractor, secondary-source percentages.
Data items (10)	Met	Section 2.4.
Risk of bias (11)	Not met	Qualitative description only.
Effect measures (12)	Met	Odds ratios and pooled proportions (logit).
Synthesis methods (13)	Met	DL, HKSJ, prediction intervals, leave-one-out.
Reporting bias (14)	Partly	Funnel plot and Egger-type test for one feature; low power.
Certainty (15)	Partly	Informal.
Study selection (16)	Met	Figure 1.
Study characteristics (17)	Met	Table 1.
Results of syntheses (20)	Met	Table 2; Figures 2–9.
Data and code availability (27)	Met	CSV, Python and R scripts supplied.

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