

FREQUENCY OF INTESTINAL TUBERCULOSIS IN INTESTINAL BIOPSY SPECIMENS

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Abstract

Objective: To determine the frequency of intestinal tuberculosis in intestinal biopsy specimens and to evaluate its histopathological features and anatomical distribution.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: Department of Pathology, King Edward Medical University, from June 2025 to September 2025.

Methodology: A total of 83 intestinal biopsy specimens were included through non-probability consecutive sampling. Demographic details including age and gender were recorded. Specimens were fixed in formalin, processed routinely, and stained with hematoxylin and eosin. Cases diagnosed as intestinal tuberculosis underwent Ziehl–Neelsen staining for acid-fast bacilli detection. Data were analyzed using SPSS version 23.

Results: The mean age of patients was 36.8 ± 14.2 years, and 46 (55.4%) were males. Intestinal tuberculosis was diagnosed in 11 (13.3%) cases. The ileocecal region was the most frequently involved site (54.5%), followed by the ileum (27.3%). Epithelioid cell granulomas were present in all cases (100%), caseous necrosis in 63.6%, Langhans giant cells in 72.7%, and lymphoid aggregates in 81.8%. Mucosal ulceration was observed in 45.5% of cases. Ziehl–Neelsen staining was positive in 27.3% of cases.

Conclusion: Intestinal tuberculosis constitutes a considerable proportion of intestinal biopsy diagnoses in endemic regions. Granulomatous inflammation with caseous necrosis remains the key histopathological feature, while Ziehl–Neelsen staining demonstrates limited sensitivity.

Key Words: Intestinal tuberculosis, Biopsy, Granuloma, Caseous necrosis, Ileocecal region, Ziehl–Neelsen stain.

INTRODUCTION

Tuberculosis is highly communicable disease whose morbidity and mortality rate continue to increase. In 2021, the incidence rate of TB rose by 3.6% and an estimated 10.6 million individuals were affected all over the world. Pakistan is the country of WHO Eastern Mediterranean Region that is included in the high-burden countries of TB list in the year 2021–2025 [1]. The Global TB report by WHO 2022 claims that the total TB incidence in Pakistan is 264 per 100 000 population annually with 21 per 100 000 as mortality rate in HIV negative patient [2]. As per the statistics presented by Centers of Disease Control and Prevention (CDC), tuberculosis rate of incidence in USA in the year 2021 is 2.4 per 100 000 population [3]. Intestinal tuberculosis was found to be 12 percent frequency [11]. In Pakistan, extra pulmonary site of TB mostly prevalent is Abdominal Tuberculosis including Intestinal tuberculosis (ITB). One study carried out in Pakistan showed that 85 percent cases of ITB were in the ileal and ileocecal segment and then jejunum [4]. ITB has non-specific clinical disease manifestations such as abdominal pain, weight loss, abdominal distention and fever [5]. The resultant severe complications are intestinal obstruction, fistula formation, mesenteric lymphadenitis, intestinal perforation and ultimately death [6]. ITB can be diagnosed using

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endoscopy, histopathological study, microbiological examination, TB-PCR and culture among several others. The most frequent endoscopic appearance is mucosal erosion as well as hyperaemia and edema.

Some common histopathological characteristics of ITB are caseating Granulomas, Langhans giant cells, epithelioid histiocytes and submucosal inflammation. The research on the outcomes of various literature articles revealed that granulomas and caseous necrosis were observed in only 13 to 33 percent of suspected and confirmed cases of ITB [7]. Abdominal malignancies and inflammatory bowel disease (primarily Crohn) have an equivalent clinical manifestation to intestinal tuberculosis [5,8]. Some of the recent reports indicate that the TB endemic regions such as our neighbouring India have experienced a rise in IBD disease burden [8]. Changing histopathological characteristics and association with similar clinical presentations pose the challenge of diagnosing ITB and hence cause greater morbidity and mortality [5,9]. Most cases do not present the typical histological characteristics (e.g. caseous necrosis, Langhans giant cells) thus complicating the diagnosis. Besides that unsuitable grossing method also results in under diagnosis.

Objectives

- To determine the frequency of Intestinal Tuberculosis in Intestinal biopsies received at Department of Pathology, KEMU.
- To assess frequency of histological features seen in intestinal tuberculosis.
- To determine common site/segment involved by Intestinal tuberculosis.

METHODOLOGY

This descriptive, cross-sectional study was conducted at the Department of Pathology, King Edward Medical University, Lahore from June 2025 to September 2025. A sample size of 83 patients was estimated at a 95% confidence level and 7% absolute precision, based on an expected prevalence of Abdominal Tuberculosis in Punjab, Pakistan, of 12% [11]. Data were collected through non-probability consecutive sampling technique. Patients of both genders and all age groups were included. All intestinal biopsy specimens received in the department during the study period were included. Autolysed specimens were excluded. Patients with a history of chemotherapy were also excluded from the study.

Data collection

The study included 83 intestinal biopsy specimens that met the inclusion criteria but the informed consent was obtained where necessary. The demographic information such as age, gender, and identification number were taken. All the specimens were soaked in formalin overnight. Following standard processing, 3-5 um thick sections were made and stained by use of hematoxylin and eosin using standard staining procedures. Two consultant pathologists examined the stained sections under a light microscope in an independent manner to keep the biases of the observer to a minimum. The ultimate diagnosis, histologic characteristics by operational definitions, site of intestinal involvement was documented. Cases that were suspected to have intestinal tuberculosis were subjected to Ziehl-Neelsen staining on carbolfuchsin as the primary stain and methylene blue as the counter stain to identify the presence of acid-fast bacilli. All the results were recorded on a preform pro forma.

Data analysis

Data will be entered and analysed by using SPSS 23. Quantitative variables such as age were presented as mean and standard deviation. Qualitative variables including gender, presence of intestinal tuberculosis, histological features, and site involved were presented as frequencies and percentages. Stratification was performed for age, gender, duration of symptoms, and residence. The chi-square test was applied post-stratification to assess associations. A p-value of 0.05 or less was considered statistically significant.

RESULTS

Data were collected from 83 patients, mean age was 36.8 ± 14.2 years, with the majority of patients belonging to the 21–40 years age group (34, 41.0%), followed by 41–60 years (25, 30.1%). Patients aged ≤ 20 years and >60 years each constituted 12 (14.5%). Males were slightly predominant, accounting for 46 (55.4%) cases, while females comprised 37 (44.6%). Intestinal tuberculosis was diagnosed in 11 (13.3%) cases, whereas 72 (86.7%) had other diagnoses. Among confirmed intestinal tuberculosis cases, the ileocecal region was the most commonly involved site (6, 54.5%), followed by the ileum (3, 27.3%), while colon and jejunum were involved in one case (9.1%) each.

Table 1. Baseline Demographic Characteristics of Patients Undergoing Intestinal Biopsy (N = 83)

Variable	n (%) / Mean \pm SD
Age (years), Mean \pm SD	36.8 \pm 14.2
≤ 20 years	12 (14.5)
21–40 years	34 (41.0)
41–60 years	25 (30.1)
>60 years	12 (14.5)
Male	46 (55.4)

Female	37 (44.6)
Intestinal Tuberculosis	11 (13.3)
Other Diagnoses	72 (86.7)
Site of Involvement	
Ileocecal region	6 (54.5)
Ileum	3 (27.3)
Colon	1 (9.1)
Jejunum	1 (9.1)

Epithelioid cell granulomas were present in all cases (11, 100%). Caseous necrosis was identified in 7 (63.6%) cases. Langhans giant cells were observed in 8 (72.7%), and lymphoid aggregates were noted in 9 (81.8%) cases. Mucosal ulceration was present in 5 (45.5%), while transmural inflammation was observed in 6 (54.5%) cases. Acid-fast bacilli were detected on Ziehl–Neelsen staining in 3 (27.3%) cases.

Table 2. Histopathological Features Observed in Intestinal Tuberculosis Cases (n = 11)

Histological Feature	n (%)
Epithelioid cell granulomas	11 (100)
Caseous necrosis	7 (63.6)
Langhans giant cells	8 (72.7)
Lymphoid aggregates	9 (81.8)
Mucosal ulceration	5 (45.5)
Transmural inflammation	6 (54.5)
Acid-fast bacilli (ZN positive)	3 (27.3)

Caseous necrosis was observed in 4 of 6 (66.7%) ileocecal cases, 2 of 3 (66.7%) ileal cases, and the single jejunal case (100%), but was absent in the colonic case. Langhans giant cells were most frequent in ileocecal cases (5, 83.3%). Lymphoid aggregates were widely distributed, present in 83.3% of ileocecal cases and in all colon and jejunal cases. Mucosal ulceration was most common in ileal cases (66.7%) followed by ileocecal cases (50.0%). Acid-fast bacilli positivity was limited to ileocecal and ileal sites (33.3% each).

Table 3. Distribution of Key Histological Features According to Site of Involvement (n = 11)

Feature	Ileocecal (n=6)	Ileum (n=3)	Colon (n=1)	Jejunum (n=1)
Caseous necrosis	4 (66.7)	2 (66.7)	0 (0)	1 (100)
Langhans giant cells	5 (83.3)	2 (66.7)	0 (0)	1 (100)
Lymphoid aggregates	5 (83.3)	2 (66.7)	1 (100)	1 (100)
Mucosal ulceration	3 (50.0)	2 (66.7)	0 (0)	0 (0)
AFB positivity	2 (33.3)	1 (33.3)	0 (0)	0 (0)

Among ITB cases, 6 (54.5%) patients were aged ≤ 40 years and 5 (45.5%) were >40 years. Similarly, 6 (54.5%) were male and 5 (45.5%) were female. No statistically significant association was observed between intestinal tuberculosis and age ($p=0.94$) or gender ($p=0.95$) using chi-square test.

Table 4. Stratified Analysis of Intestinal Tuberculosis by Age and Gender (N = 83)

Variable	ITB (n=11) n (%)	Non-ITB (n=72) n (%)	p-value
Age ≤ 40 years	6 (54.5)	40 (55.6)	0.94
Age >40 years	5 (45.5)	32 (44.4)	0.94
Male	6 (54.5)	40 (55.6)	0.95
Female	5 (45.5)	32 (44.4)	0.95

Chi-square test applied.

Granuloma formation was universally present (100%). Caseous necrosis was identified in 63.6% of cases, Langhans giant cells in 72.7%, and lymphoid aggregates in 81.8%. Mucosal ulceration was present in 45.5% of cases. Ziehl–Neelsen staining demonstrated limited sensitivity, with positivity in only 27.3% of cases.

Table 5. Diagnostic Yield of Histological and ZN Staining Features in Intestinal Tuberculosis Cases (n = 11)

Diagnostic Parameter	Positive n (%)	Negative n (%)
Granuloma formation	11 (100)	0 (0)
Caseous necrosis	7 (63.6)	4 (36.4)
Langhans giant cells	8 (72.7)	3 (27.3)
Lymphoid aggregates	9 (81.8)	2 (18.2)
Mucosal ulceration	5 (45.5)	6 (54.5)

AFB on ZN stain	3 (27.3)	8 (72.7)
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DISCUSSION

This paper assessed the prevalence and tissue histopathology of intestinal tuberculosis in intestinal biopsy samples, and it provided a prevalence rate of 13.3 on the population studied. This percentage agrees with already documented prevalence rates of abdominal tuberculosis in Punjab, Pakistan where intestinal involvement is still a major clinical issue. The fact that intestinal tuberculosis was persistent in the biopsy samples implies the presence of tuberculosis in the endemic area, and the fact that it should be high in the index of suspicion in patients with chronic abdominal symptoms. Most of the cases were registered among the younger adults especially in the 21-40 years category [12]. This observation is in line with the national and regional statistics that indicate that tuberculosis affects the economically productive group of people disproportionately. The males were slightly more affected than the females, but the association was not significant. Other regional studies have also reported similar gender distributions leading to the presumption that exposure risk and socioeconomic factors may have a greater role than biological sex differences [13].

The ileocecal site most often involved anatomical site (54.5%), with the ileum coming next. The literature largely supports this predilection, and is explained by the fact that the area has abundant lymphoid tissue (Peyer patches), relative stasis and a very low level of intestinal activity which supports mycobacterial implantation and growth [14-16]. The fact that jejunal and colonic involvement in this study was low also reinforces disease distribution patterns. Granulomatous inflammation was the hallmark of epithelioid cell granulomas observed in all confirmed cases. Caseous necrosis was detected in 63.6% of cases, and it is the most specific morphological characteristic that is indicative of tuberculosis. Nevertheless, the fact that it is not present in all the cases makes it more difficult to diagnose it, especially when distinguishing intestinal tuberculosis and Crohn disease as well as other granulomatous diseases. Evidence of Langhans giant cells and lymphoid aggregates has been found in a significant number of cases, thereby supporting their diagnostic utility [17-19].

Ziehl-Neelsen staining was sensitive only in 27.3% of cases with the only indication of acid-fast bacilli. The observation is in line with the already published data that indicate AFB positivity in intestinal biopsies is not high as the disease is paucibacillary. Consequently, ZN staining alone can lead to underdiagnosis and histopathological analysis is the foundation of diagnosis in limited resources. There was also mucosal ulceration and transmural inflammation that was evident in a significant proportion of cases, demonstrating the chronic inflammatory pathogenesis of intestinal tuberculosis. The transmural inflammation adds importance to the clinical pathological correlation, especially in the distinction between the inflammatory bowel disease and other conditions [20].

In this work, some limitations are worth mentioning. The sample was rather limited, comprising only one tertiary care facility, which could limit the generalizability of the results to the rest of the population. The cross-sectional type of study constrained cause-effect and the evaluation of long-term results. The need for Ziehl-Neelsen stain was low, and sophisticated diagnostic tests like PCR or GeneXpert were not done, and this might have contributed to the underdiagnosis of the paucibacillary cases. Also, there was a lack of clinical and radiological correlation and distinction between granulomatous and other diseases like Crohn's disease was based majorly on the histopathological characteristics.

CONCLUSION

It is concluded that intestinal tuberculosis continues to represent a significant proportion of intestinal biopsy diagnoses in endemic regions, accounting for 13.3% in this study. The ileocecal region remains the most commonly involved site. Granulomatous inflammation with epithelioid cells was observed in all cases, while caseous necrosis and Langhans giant cells were present in most cases, underscoring their diagnostic importance. Ziehl-Neelsen staining demonstrated limited sensitivity, highlighting that histopathological assessment remains the cornerstone of diagnosis, particularly in resource-limited settings.

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