

Constitutional Symptoms, Radiological Findings, and Ascitic Fluid Adenosine Deaminase versus CBNAAT in Peritoneal Tuberculosis - A Prospective Study from Northern India.

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Abstract

Gastrointestinal tuberculosis remains a demanding diagnostic problem in regions where the disease is endemic, and peritoneal involvement is often the anatomical subtype that is hardest to confirm without invasive sampling. This prospective cross-sectional study examined the pattern of constitutional symptoms, the findings on contrast-enhanced computed tomography, and the comparative diagnostic performance of two Ascitic fluid tests, adenosine Deaminase estimation and cartridge-based nucleic acid amplification testing, in confirmed peritoneal tuberculosis patients drawn from a larger cohort of 155 gastrointestinal tuberculosis patients evaluated at a tertiary teaching hospital in Kanpur, Uttar Pradesh, between August 2024 and March 2026. Thirty-nine patients (25.2% of the parent cohort) fulfilled diagnostic criteria for peritoneal tuberculosis. Fever was the most common constitutional symptom, present in

74.4% of these patients, followed by anorexia (64.1%), weight loss (48.7%), and night sweats (38.5%). Computed tomography most often showed free as cites (62%), followed by mesenteric fat stranding (54%), loculated or septated as cites (38%), and Omental thickening (24%). Adenosine Deaminase, at the standard threshold of 40 international units per litre, correctly identified 34 of the 39 patients, a sensitivity of 87.18%, with a positive predictive value of 100%. Cartridge-based testing identified 24 of the 39 patients, a lower sensitivity of 61.54%, but an equally strong positive predictive value of 100%. These findings support adenosine Deaminase as the primary rapid screening test for suspected peritoneal tuberculosis in resource-limited settings, with cartridge-based testing applied alongside it for confirmatory evidence and resistance profiling, since neither symptoms nor either single test in isolation can be relied upon for a confident diagnosis.

Keywords: Peritoneal tuberculosis; Tuberculous ascites; Adenosine Deaminase; CBNAAT; Constitutional symptoms; Contrast-enhanced computed tomography; Gastrointestinal tuberculosis; Diagnostic accuracy.

Introduction

Tuberculosis remains one of the major causes of morbidity and mortality due to infectious disease globally and India continues to share the largest burden worldwide¹. Extra pulmonary disease is increasingly being recognized, and among its numerous presentations, gastrointestinal tuberculosis is widely considered one of the most difficult to diagnose because its course is often prolonged and nonspecific and may closely mimic inflammatory bowel disease or abdominal malignancy².

Peritoneal involvement is frequently reported as the most difficult to diagnose anatomical subtype of gastrointestinal tuberculosis. Ascitic fluid in tuberculous peritonitis is paucibacillary, so smear microscopy and even mycobacterial culture reveal organisms in only a minority of patients. The clinical picture of ascites with low grade fever and weight loss can be difficult to differentiate from cirrhotic or malignant ascites on presentation alone³. Peritoneal disease is thus a common and persistent diagnostic challenge in endemic settings such as Northern India and should not be considered a rare curiosity, accounting for approximately one quarter of cases of gastrointestinal tuberculosis on regional reviews⁴.

Two minimally invasive tests for ascitic fluid have emerged as the mainstay in the evaluation of suspected peritoneal tuberculosis without resorting to laparoscopic biopsy in all patients: estimation of adenosine Deaminase, an enzyme released by activated T-lymphocytes during the granulomatous response to mycobacterial antigens, and cartridge-based nucleic acid amplification testing that directly detects *Mycobacterium*

tuberculosis DNA and rifampicin resistance from the ascitic fluid within hours. Both tests are incorporated into national diagnostic algorithms for extra pulmonary tuberculosis in India⁵. Contrast-enhanced computed tomography (CECT) complements these biochemical and molecular tests by characterizing the distribution of ascites and any accompanying mesenteric or omental change, and continues to play an established role in raising and supporting clinical suspicion of peritoneal disease³.

Although several Indian and multinational series have documented the clinical profile of gastrointestinal tuberculosis as a whole^{6,7}, comparative data confined specifically to a well-characterised peritoneal tuberculosis subgroup, combining constitutional symptom pattern, radiological findings, and head-to-head ascitic fluid test performance within the same cohort, remain relatively limited from the Kanpur/western Uttar Pradesh region. This study was therefore undertaken to describe the constitutional symptom pattern, characterise the contrast-enhanced computed tomography findings, and compare the diagnostic sensitivity of ascitic fluid adenosine Deaminase against cartridge-based nucleic acid amplification testing in a cohort of confirmed peritoneal tuberculosis patients identified from a larger prospective study of gastrointestinal tuberculosis conducted at a tertiary teaching hospital in Northern India.

Materials and Methods

Study Design and Setting

This analysis is drawn from a prospective, hospital-based cross-sectional study of gastrointestinal tuberculosis conducted jointly in the Departments of General Medicine and Gastroenterology at G.S.V.M. Medical College and L.L.R. Hospital, Kanpur, Uttar Pradesh, between August 2024 and March 2026. The parent study

enrolled 155 patients with confirmed gastrointestinal tuberculosis across three anatomical subtypes: luminal tuberculosis, tubercular lymphadenopathy, and peritoneal tuberculosis. The present analysis focuses specifically on the 39 patients within that cohort (25.2% of the total) who fulfilled diagnostic criteria for peritoneal tuberculosis, and reports their constitutional symptom pattern, contrast-enhanced computed tomography findings, and Ascitic fluid test performance in detail.

Participants and Diagnostic Criteria

Adults over 18 years of either sex with a confirmed diagnosis of gastrointestinal tuberculosis were eligible for the parent study. Patients already receiving anti-tubercular therapy at presentation, those with an alternative confirmed diagnosis accounting for their symptoms (malignancy, Crohn's disease, ulcerative colitis, cirrhosis with portal hypertension, or another confirmed infection), and those whose diagnostic evaluation remained incomplete or who could not be traced through to a confirmed diagnosis were excluded.

Peritoneal tuberculosis was defined using a composite reference standard incorporating four domains ^[8]: (i) clinical features (fever, abdominal pain, anorexia, weight loss, night sweats); (ii) Ascitic fluid analysis showing an Exudate (protein above 2.5 g/dL), a serum-as cites albumin gradient below 1.1 g/dL, and lymphocytic predominance (over 50%), with an adenosine Deaminase value above 40 IU/L taken as biochemically supportive; (iii) imaging evidence of free, loculated or septated ascites, mesenteric fat stranding or thickening, and/or omental thickening or caking on ultra sonography or contrast-enhanced computed tomography of the whole abdomen; and (iv) bacteriological confirmation, where obtained, by a positive acid-fast bacilli smear, culture, or cartridge-based nucleic acid amplification test on Ascitic fluid.

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee (for Biomedical Health and Research), G.S.V.M. Medical College, Kanpur (reference EC/ BM HR/2024/159, dated 7 August 2024). Written informed consent was obtained from every participant in Hindi or English prior to enrolment, and patient identity was anonymised using a unique study number for all data analysis.

Sample Collection and Diagnostic Procedures

Ascitic fluid was obtained by diagnostic paracentesis under local anaesthesia from each of the 39 peritoneal tuberculosis patients. A single fluid sample from each patient was used for parallel testing: adenosine Deaminase was estimated with a threshold of 40 IU/L taken as positive, and cartridge-based nucleic acid amplification testing (CBNAAT/ Gene X pert) was performed on the same aliquot. All patients additionally underwent ultra sonography of the whole abdomen and/or contrast-enhanced computed tomography of the abdomen as part of the routine diagnostic work-up; radiological features recorded for the peritoneal subgroup included the pattern of as cites (free, loculated or septated), mesenteric fat stranding or thickening, and Omental thickening.

Statistical Analysis

Data were entered in Microsoft Excel and analysed using SPSS version 27.0 (IBM Corp., Armonk, New York, USA). Continuous variables were expressed as mean $\pm$ standard deviation or median and inter quartile range according to their distribution, which was assessed graphically by quantile - quantile plots. Categorical variables such as frequency of individual constitutional symptoms and radiological features in the subgroup of peritoneal tuberculosis were expressed as frequency and percentage. Sensitivity and positive predictive value of

Ascitic fluid adenosine Deaminase and CBNAAT were calculated against the composite reference standard as described above and reported with 95% confidence intervals.

Results and Discussion

Baseline Profile of the Peritoneal Tuberculosis Subgroup

Of the 155 patients in the parent cohort, 39 (25.2%) met the diagnostic criteria for peritoneal TB, the third most common anatomical subtype after luminal TB (45.8%) and tubercular lymphadenopathy (29.0%). This number is in accordance with previous reports that Ascitic presentations account for approximately one quarter of gastrointestinal tuberculosis cases in endemic settings [4] and that peritoneal disease remains a significant proportion of the spectrum of abdominal tuberculosis and is not an uncommon presentation.

Constitutional Symptom Pattern

Table 1: Constitutional and local symptoms in the peritoneal tuberculosis subgroup (n=39)

Symptom	Peritoneal TB (n=39)
Fever	29 (74.4%)
Abdominal pain	30 (76.9%)
Anorexia	25 (64.1%)
Weight loss	19 (48.7%)
Night sweats	15 (38.5%)

TB: tuberculosis.

In the peritoneal tuberculosis subgroup, fever was the most common constitutional symptom (29 out of 39 patients, 74.4%). Other constitutional symptoms included anorexia (25 out of 39 patients, 64.1%), weight loss (19 out of 39 patients, 48.7%), and night sweats (15 out of 39 patients, 38.5%). Abdominal pain was also common (30 out of 39 patients, 76.9%), however this is a local symptom, not a constitutional symptom.

The pronounced constitutional symptom burden observed in this cohort is consistent with the recognised systemic

inflammatory character of peritoneal disease; a systematic review of tuberculous peritonitis has similarly reported that peritoneal involvement produces more marked systemic manifestations, including high rates of anaemia and hypoalbuminemia, than other abdominal presentations of tuberculosis³. The fever prevalence recorded here is broadly in keeping with regional series: a North Indian cohort reported fever in a slightly higher proportion of abdominal tuberculosis patients overall ⁶, while a multinational study spanning 8 countries recorded a comparable fever prevalence of 66.3% of patients, alongside a high burden of anorexia (90.2%) and weakness (87.5%) ⁹. A South Asian series similarly documented a high frequency of constitutional complaints, including anorexia and night sweats, in abdominal tuberculosis, though frequently to a somewhat greater degree than observed in the present cohort, a difference that may reflect variation in disease duration at presentation or in nutritional baseline between populations¹⁰. Even so, constitutional symptoms were not universal in this cohort, and their presence or absence with variability, adds evidence to a point made elsewhere in the literature on differentiating tuberculosis from its principal mimics; clinical features overlap considerably between tuberculosis and other causes of as cites, including malignancy and Crohn's disease, and cannot by themselves reliably confirm the diagnosis¹¹. This underlines why laboratory and radiological corroboration, rather than symptom pattern in isolation, is required before a diagnosis of peritoneal tuberculosis is accepted.

Radiological Findings on Contrast - Enhanced Computed Tomography

Table 2: Contrast-enhanced computed tomography findings in the peritoneal tuberculosis subgroup (n=39)

Radiological feature on CECT abdomen	Peritoneal TB (n=39)
Free ascites	62%
Mesenteric fat stranding / thickening	54%
Loculated / septated ascites	38%
Omental thickening / caking	24%

Percentages are of the 39 confirmed peritoneal tuberculosis patients; features were not mutually exclusive and could co-exist in the same patient.

Contrast-enhanced computed tomography of the abdomen in the peritoneal tuberculosis subgroup most frequently demonstrated free ascites, present in 62% of patients, followed by mesenteric fat stranding or thickening in 54%, loculated or septated ascites in 38%, and Omental thickening in 24%.

These proportions correspond closely to the exudative, fibrino-purulent peritoneal reaction that is considered characteristic of tuberculous peritonitis in the radiological literature, where smooth peritoneal thickening, Omental caking, and loculated or septated ascites have long been described as hallmark computed tomography features of the disease¹². More recent series applying multi detector computed tomography have similarly emphasised nodular as well as smooth peritoneal thickening as a discriminating feature in abdominal tuberculosis¹³, and broader reviews of the abdominal tuberculosis imaging spectrum have reported comparable patterns of ascites, mesenteric involvement, and Omental change across luminal, nodal, and peritoneal disease^{14,15}. A recognised limitation of computed tomography in this context is that these same features, Omental caking, ascites, and peritoneal thickening, can be difficult to distinguish from peritoneal carcinomatosis on imaging alone; a dedicated meta-analysis comparing the two conditions found that no single computed tomography sign reliably separates

tuberculous from malignant peritoneal disease, and that tissue or biochemical confirmation therefore remains necessary even when the radiological appearance is highly suggestive¹⁶. In the present cohort, none of the four radiological features was interpreted in isolation from clinical and biochemical evidence of disease, consistent with the view that computed tomography is best used to raise and support suspicion of peritoneal tuberculosis rather than to confirm it independently.

Diagnostic Performance of Ascitic Fluid Adenosine Deaminase

Table 3: Diagnostic performance of Ascitic fluid adenosine Deaminase and CBNAAT in peritoneal tuberculosis (n=39)

Diagnostic parameter	Ascitic fluid ADA (cut-off >40 IU/L)	CBNAAT (GeneXpert)
True positive / total confirmed cases	34 / 39	24 / 39
False negative	5	15
Sensitivity (95% CI)	87.18% (72.57–95.70%)	61.54% (44.62–76.64%)
Positive predictive value (95% CI)	100% (89.72–100%)	100% (85.75–100%)

ADA: adenosine Deaminase; CBNAAT: cartridge-based nucleic acid amplification test; CI: confidence interval. Mean Ascitic fluid ADA in this subgroup was 92.7 ± 32.2 IU/L; median 95 IU/L (inter quartile range 76–111). Adenosine Deaminase of Ascitic fluid with standard cut-off of 40 IU/L was positive in 34 out of 39 cases with confirmed peritoneal tuberculosis with sensitivity of 87.18% (95% CI 72.57-95.70%) and positive predictive value of 100% (95% CI 89.72-100%). In this subgroup mean adenosine Deaminase value was 92.7 ± 32.2 IU/L with a median of 95 IU/L (inter quartile range 76–111) which was well above the diagnostic cut-off in most of the patients.

This sensitivity is within the range quoted in the published literature on Ascitic adenosine Deaminase. Despite variation in the populations and the cut-offs studied, this test has consistently been found to be a reliable marker of tuberculous peritonitis. An early

Indian series reported a sensitivity of 93% at a cut-off of 33 U/L¹⁷, a meta-analysis of 14 studies comprising 1,083 patients reported a pooled sensitivity of 92% at cut-offs of 30–40 IU/L¹⁸, and a more recent meta-analysis including 28 studies and 3,842 patients reported a pooled sensitivity of 90% with the highest accuracy at cut-offs of 39–40 IU/L¹⁹. Another prospective series with a slightly lower cut-off of 36 IU/L reported a sensitivity of 91.7%²⁰.

A multidisciplinary consensus statement on tuberculous peritonitis supported a similar cut-off of 39 IU/L in 2025²¹, supporting the use of the 40 IU/L cut-off in the current cohort. The 5 false-negative results in this study are most plausibly attributable to early-stage or lower-burden disease rather than any deficiency of the assay itself, though the absence of a parallel non-tuberculous as cites comparison group in the present cohort meant that an independently optimised local cut-off could not be derived.

Diagnostic Performance of CBNAAT

Cartridge-based nucleic acid amplification testing was positive in 24 of the 39 patients, giving a sensitivity of 61.54% (95% CI 44.62–76.64%) and a positive predictive value of 100% (95% CI 85.75–100%), identical to that achieved by adenosine Deaminase despite the marked difference in sensitivity between the two tests.

This figure lies between the 59% pooled sensitivity reported for peritoneal fluid specimens in a Cochrane systematic review²² and the 71.4% sensitivity reported in a separate Ascitic fluid series compared against culture²³, and it is considerably higher than the 23.8% sensitivity reported for Ascitic fluid specimens in another Indian cohort using the same platform, where sensitivity on tissue specimens from the same patients was substantially higher²⁴. This spread of reported sensitivities most likely

reflects genuine variation in bacillary burden, sample volume, and processing across settings rather than any single “correct” figure for the test. What is clinically more informative than the sensitivity comparison alone is that CBNAAT achieved a positive predictive value identical to that of adenosine Deaminase in this cohort: a positive result on either test can be acted upon with confidence, whereas a negative result on one test, particularly CBNAAT, does not exclude peritoneal tuberculosis if clinical, radiological, or biochemical suspicion remains high, or if the companion test is positive.

Adenosine Deaminase versus CBNAAT - A Comparative Appraisal

Together these results support a combined approach, rather than either/or, to the testing of Ascitic fluid in suspected peritoneal tuberculosis. Adenosine Deaminase is inexpensive, rapid and easy to perform. It is well suited to be the initial screening test in resource-poor government hospital settings such as the present one, where its much higher sensitivity directly translates to fewer missed diagnoses. CBNAAT is less sensitive from Ascitic fluid but has an additional advantage over adenosine Deaminase, in that rifampicin resistance can be determined almost simultaneously from the same paracentesis sample within 2 hours. This role for Gene Xpert-based testing has been demonstrated on tissue specimens in gastrointestinal tuberculosis²⁵. Combined Ascitic fluid evaluation with biochemical and molecular testing, instead of a single modality, is already recommended in national diagnostic guidelines for extra pulmonary tuberculosis⁵, and the current results, showing an identical positive predictive value and a broad sensitivity gap, offer direct empirical support for applying this recommendation specifically to the peritoneal subgroup. Performing both tests on the same

specimen of paracentesis fluid, rather than sequentially, maximizes diagnostic yield without adding to patient discomfort or requiring a repeat procedure.

The present analysis has several limitations, which should be acknowledged. The peritoneal tuberculosis subgroup was derived from a reasonably large parent cohort but still a relatively small sample size of only 39 patients and the confidence intervals around the CBNAAT sensitivity estimate, in particular, remain wide. No parallel group of patients with non-tuberculous ascites was studied so specificity could not be calculated and the adenosine Deaminase cut-off could not be independently re-derived in this population; the single-centre tertiary-care setting may also limit generalisability to primary or secondary care settings where disease severity at presentation may differ.

Conclusions

In this prospective analysis of 39 patients with confirmed peritoneal tuberculosis from a larger cohort of gastrointestinal tuberculosis, fever was the most common constitutional symptom (74.4% of patients), followed by anorexia, weight loss and night sweats. Contrast-enhanced computed tomography was the most common modality demonstrating free ascites, followed by mesenteric fat stranding, loculated ascites, and omental thickening, a pattern consistent with the well-recognized imaging spectrum of tuberculous peritonitis but one that can overlap with peritoneal carcinomatosis and therefore requires biochemical or bacteriological corroboration. Ascitic fluid adenosine Deaminase was significantly more sensitive than CBNAAT for diagnosis of peritoneal tuberculosis while both tests had very high positive predictive value. These findings therefore support adenosine Deaminase as the primary rapid screening test for suspected peritoneal tuberculosis in resource-limited settings, used in combination with CBNAAT to provide

confirmatory evidence and same-day rifampicin resistance profiling on the same ascitic fluid sample, and not either test in isolation.

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