

Review Article

EMERGING IMAGING BIOMARKERS IN ABDOMINAL TUBERCULOSIS: FROM MORPHOLOGY TO FUNCTIONAL IMAGING

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ABSTRACT

Background: Abdominal tuberculosis (TB) poses significant diagnostic challenges due to its nonspecific clinical manifestations and overlapping imaging features with other intra-abdominal pathologies. Emerging imaging biomarkers have shown potential for early, non-invasive and more accurate detection.

Materials and Methods: A systematic review of imaging literature published between January 2015 and May 2025 was conducted, focusing on both morphological and functional imaging modalities in the evaluation of abdominal TB.

Results: CT and MRI remain the cornerstone imaging modalities for morphological assessment, identifying features such as bowel wall thickening, necrotic lymphadenopathy, and ascites. However, advanced techniques such as diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC) mapping, PET-CT, and radiomics are increasingly recognized for their ability to offer functional insights. These biomarkers enhance diagnostic precision, particularly in distinguishing TB from malignancies and other mimicking conditions.

Conclusion: Imaging biomarkers—particularly functional and AI-enhanced tools—are redefining the diagnostic paradigm of abdominal TB. Their successful translation into routine clinical practice will require standardized imaging protocols, unified biomarker thresholds, and validation through large-scale multicentric studies.

Keywords: Abdominal tuberculosis; imaging biomarkers; CT; MRI; PET-CT; diffusion-weighted imaging; ADC; radiomics; functional imaging.

INTRODUCTION

Tuberculosis (TB) continues to rank among the leading infectious diseases worldwide. The 2024 WHO Global Tuberculosis Report estimated that 10.8 million people developed TB in 2023, with 1.25 million deaths attributed to the disease, making it the top cause of mortality from a single infectious pathogen.^[1] Despite global control efforts, the incidence remains stubbornly high, reflecting social determinants, drug resistance, and diagnostic delays.^[2,3]

Extrapulmonary TB (EPTB) constitutes a significant share of this burden, representing 15–20% of all TB cases globally and up to 25% in high-burden countries.^[4,5] Among EPTB forms, abdominal TB—which includes peritoneal, gastrointestinal, lymphatic, and visceral involvement—accounts for

11–16% of cases, but is frequently under-recognized.^[6,7]

India remains the epicenter of the global TB epidemic, contributing 26% of the global burden in 2023, with 2.6 million notified cases under the National TB Elimination Programme (NTEP).^[8] National prevalence surveys report that 22–24% of all Indian TB cases are extrapulmonary, with abdominal TB consistently comprising around 12% of these.^[9–11]

At the state level, Uttar Pradesh (UP) remains India's highest-burden state for TB. According to data released by the Union Ministry of Health and Family Welfare, the state documented 517,715 TB cases in 2022, which rose sharply to 6,22,959 in 2023 and further escalated to 681,779 cases in 2024.^[12] Cumulatively, UP accounted for 18,22,453 TB notifications between 2022 and 2024, underscoring

its disproportionate contribution to India's TB epidemic.^[13] Within UP, districts like Agra and Lucknow reported the largest caseloads, though urban centers such as Ghaziabad also contribute substantially to the state's high notification rate. Within UP, Ghaziabad district exemplifies this high burden. Surveillance data for 2023 reported 19,191 notified TB cases in the district, ranking among the largest contributors within the state.^[14] A cross-sectional study in Modinagar, Ghaziabad, further highlighted the public health impact, noting 10.6% TB prevalence among HIV-positive individuals.^[14] While district-specific abdominal TB statistics are scarce, extrapolations suggest a significant local burden proportional to state and national patterns. Clinically, abdominal TB is a diagnostic challenge. Patients typically present with vague and nonspecific symptoms such as abdominal pain, low-grade fever, anorexia, weight loss, or altered bowel habits.^[15] These overlap with conditions such as Crohn's disease, malignancies, or other inflammatory disorders, leading to frequent misdiagnosis or delay.^[16] Furthermore, limitations in tissue accessibility, low yield of acid-fast bacilli on smears, and suboptimal sensitivity of culture and nucleic acid amplification tests complicate microbiological confirmation.^[17]

In this context, imaging has emerged as an indispensable diagnostic pillar. Ultrasound and contrast-enhanced CT (CECT) remain frontline tools for identifying morphological abnormalities such as necrotic lymphadenopathy, bowel wall thickening, ascites, and peritoneal involvement.^[18] However, these findings are not disease-specific, and conventional imaging cannot reliably differentiate active vs. inactive lesions or TB from mimics such as lymphoma and Crohn's disease.^[19]

To overcome these limitations, recent years have witnessed a paradigm shift from purely morphological to functional and biomarker-driven imaging. Diffusion-weighted MRI (DWI) with apparent diffusion coefficient (ADC) mapping allows quantitative assessment of tissue cellularity and viability, aiding in distinguishing TB from peritoneal carcinomatosis.^[20] Similarly, 18F-FDG PET/CT provides metabolic characterization of lesions, helping identify active disease, guide biopsy, and assess treatment response.^[21]

In parallel, radiomics and machine learning have emerged as cutting-edge approaches. By extracting complex imaging features invisible to the naked eye, these tools enhance diagnostic precision in differentiating TB from malignancy or inflammatory bowel disease.^[22,23] Such innovations underscore the evolving role of imaging biomarkers in abdominal TB, bridging morphology and functional imaging to improve diagnosis and patient outcomes.

MATERIALS AND METHODS

Search Strategy: A comprehensive literature search was conducted across four major electronic

databases: PubMed, Scopus, Web of Science, and Embase, in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines". The duration of the study was set from Duration, ensuring the inclusion of the most recent and relevant advances in imaging biomarkers related to abdominal tuberculosis.

To maximize both sensitivity and specificity, the search strategy incorporated a combination of controlled vocabulary and free-text keywords. The following key phrases were used, either singly or in Boolean combinations:

- "Abdominal tuberculosis" AND "imaging biomarkers"
- "CT" AND "TB abdomen"
- "Diffusion-weighted MRI" AND "tuberculosis"
- "PET-CT" AND "granulomatous inflammation"

The search strategy was carefully tailored to each database to ensure optimal retrieval of high-quality, peer-reviewed literature. Duplicate records were automatically removed using reference management software. Additional relevant articles were identified through manual review of reference lists from eligible studies and recent systematic reviews.

Inclusion Criteria:

- Original research articles published in English in peer-reviewed journals.
- Studies that employed imaging modalities such as CT, MRI, PET-CT, or ultrasound in the diagnosis or evaluation of abdominal tuberculosis.
- Studies explicitly evaluating diagnostic or prognostic imaging biomarkers, either morphological (e.g., lymph node size, bowel wall thickening) or functional (e.g., ADC values, SUVmax).
- Research designs including cross-sectional, retrospective cohort, prospective cohort, or case-control studies.

Exclusion Criteria:

- Articles published in non-English languages, conference abstracts, commentaries, letters to the editor, or expert opinions without primary data.
- Studies that focused exclusively on pulmonary, central nervous system, or skeletal tuberculosis without assessing abdominal involvement.
- Research that did not include quantitative or qualitative imaging biomarker analysis or failed to report diagnostic performance metrics such as sensitivity, specificity, or predictive value.

Study Selection and Data Extraction

Study selection was carried out through a dual-reviewer process to minimize selection bias and ensure objectivity. Two reviewers independently screened titles and abstracts of all retrieved citations. Full-text articles were reviewed for eligibility based on the inclusion and exclusion criteria. Any disagreements between reviewers were resolved through consensus or consultation with a third senior reviewer. For each eligible study, a standardized data extraction sheet was used to collect the following parameters:

- Study design (e.g., retrospective or prospective cohort)
- Sample size and population characteristics
- Imaging modality used (e.g., CT, DWI-MRI, PET-CT)
- Imaging biomarkers evaluated (e.g., ADC values, necrotic lymph nodes, SUVmax)
- Diagnostic or prognostic performance indicators such as sensitivity, specificity, area under the curve (AUC), and p-values
- Statistical findings, including limitations or sources of bias

The methodological quality of each study was assessed using a modified Newcastle–Ottawa Scale, adapted for imaging research. Given the heterogeneity of study designs, imaging techniques, and outcomes, a narrative synthesis approach was adopted instead of meta-analysis.

RESULTS

Overview of Included Studies

A total of 312 articles were initially identified through electronic database searches. After the removal of duplicates ($n = 54$), 258 unique records underwent title and abstract screening. Following the application of inclusion and exclusion criteria, 38 full-text articles were reviewed in detail. Ultimately, 12 studies published between 2015 and 2025 met all eligibility criteria and were included in this review.

The selected studies employed a variety of imaging modalities to assess abdominal tuberculosis, with an increasing emphasis on functional and quantitative tools over recent years. Contrast-enhanced computed tomography (CECT) was the most frequently utilized imaging technique, followed by magnetic resonance imaging (MRI), including diffusion-weighted imaging (DWI), and fluorodeoxyglucose positron emission tomography-computed tomography (FDG PET-CT). A small subset of studies employed radiomic texture analysis using CT datasets, supported by machine learning algorithms.

The spectrum of abdominal TB presentations in these studies included:

- Lymph nodal involvement (especially necrotic and conglomerated nodes)
- Ileocecal tuberculosis and gastrointestinal strictures
- Peritoneal TB with loculated ascites or omental thickening
- Solid organ tuberculosis (hepatic, splenic lesions)

The imaging objectives across the included literature ranged from initial diagnosis, differentiation from malignancy or Crohn's disease, to treatment response assessment, thereby covering a wide spectrum of clinical utility.

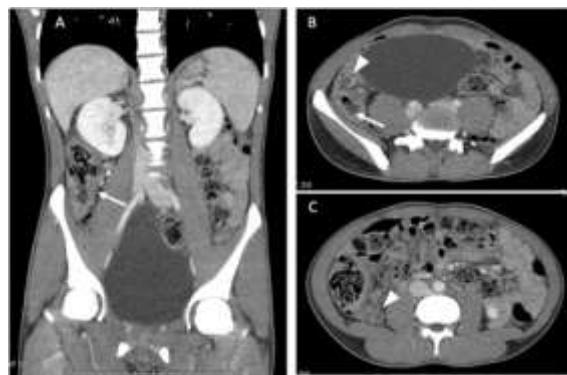
Imaging Biomarkers Evaluated

The reviewed studies collectively identified a set of morphological and functional/quantitative biomarkers relevant to abdominal TB diagnosis, activity assessment, and monitoring.

Morphological Parameters

Computed Tomography (CT):

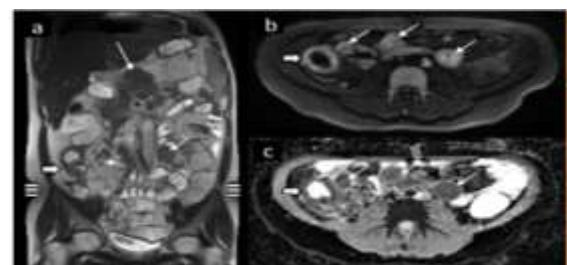
- Bowel wall thickening, particularly in the ileocecal region, was noted as a consistent marker across multiple studies.
- Necrotic lymphadenopathy with central hypoattenuation and peripheral rim enhancement remained the hallmark CT finding.
- Omental caking, mesenteric stranding, and ascites with septations were other frequent observations.^[24,25]



“Figure 1: Contrast-enhanced CT findings in abdominal tuberculosis. (A) Coronal CECT image demonstrates ileocecal bowel wall thickening with surrounding inflammatory fat stranding (arrow). (B) Axial CECT image shows thickened bowel loops with necrotic mesenteric lymph nodes (arrow) and ascites (arrowhead). (C) Axial CECT image highlights necrotic lymphadenopathy in the mesentery (arrowhead)”

Magnetic Resonance Imaging (MRI):

- T2 hyperintensity of inflamed bowel segments and post-contrast enhancement were noted in gastrointestinal TB.
- Characterization of lymph nodes based on signal intensity and internal architecture added value, especially in pelvic TB.^[26]

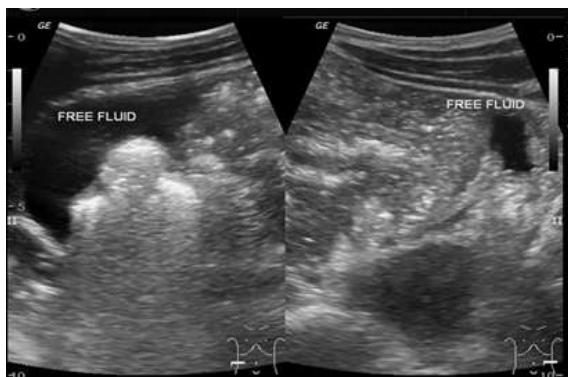


“Figure 2: (a) Circumferential mural thickening involving terminal ileum and cecum (thick white arrow) with multiple loco-regional mesenteric and conglomerated periportal lymph nodes (thin white arrows). Both the mucosal thickening (thick white arrow), and nodes (thin white arrows) show restricted diffusion appearing bright on DWI (b) and dark on the ADC (c).”

Ultrasound (USG):

- Common features included echogenic or septated ascites, matting of bowel loops, and thickened mesentery.

- While readily available and non-invasive, the sensitivity of USG was limited for deeper lymphadenopathy and subtle peritoneal changes.^[27]



“Figure 3: Ultrasound of Peritoneal TB”

Functional & Quantitative Parameters

Diffusion-Weighted Imaging (DWI) and Apparent Diffusion Coefficient (ADC):

- Studies demonstrated that restricted diffusion in lymph nodes and bowel walls is suggestive of active TB.

- Lower ADC values ($<1.2 \times 10^{-3}$ mm 2 /s) were consistently associated with granulomatous inflammation, distinguishing it from chronic or treated lesions.^[28]

PET/CT (FDG-based):

- Increased FDG uptake (high SUVmax) in affected lymph nodes and peritoneum was observed in active TB cases.
- Although overlapping with malignancies, a heterogeneous pattern of uptake and correlation with clinical context improved diagnostic specificity.^[29]

Dynamic Contrast-Enhanced MRI (DCE-MRI):

- A limited number of studies applied perfusion imaging in abdominal TB.
- Patterns of early enhancement and washout in nodal tissues were correlated with disease activity, though larger studies are needed [30].

Radiomics and AI Integration:

- Texture analysis using CT imaging, especially entropy, kurtosis, and uniformity, revealed potential in differentiating TB from gastrointestinal malignancies or Crohn's disease.
- Preliminary machine learning models showed diagnostic accuracy $>85\%$ in pilot studies, though generalizability is currently limited due to small sample sizes.^[31]

Table 1: Summary of Key Studies

Study (Author, Year)	Design	Sample Size	Imaging Modality & Biomarkers	Key Findings	Strengths & Limitations
Brunetti et al., 2016. ^[27]	Observational	100+ (approx.)	Ultrasound (ascites, hepatosplenomegaly, lymphadenopathy)	Useful in diagnosing infectious diseases like TB in low-resource settings	Low-cost, accessible; limited depth penetration, operator-dependent
Deng et al., 2018. ^[33]	Observational	92	18F-FDG (SUVmax, distribution)	PET/CT showed strong diagnostic performance in detecting EPTB	Accurate but costly; overlaps with malignancy in SUV interpretation
Zohra et al., 2019. ^[29]	Cross-sectional	43	FDG PET/CT (SUVmax in EPTB sites)	High SUVmax correlated with active disease sites	Functional and sensitive; costly and less accessible
Goyal et al., 2019. ^[32]	Narrative Review	—	CT, MRI (comparative imaging of ITB vs Crohn's)	Evaluated evolving methods to differentiate TB and Crohn's disease	Rich clinical insights; lacks statistical validation
Das et al., 2022. ^[26]	Retrospective	82	DWI-MRI (ADC values, lesion contrast)	Differentiated active vs inactive TB using ADC thresholds	Good functional imaging; single-center study
Mor et al., 2022. ^[30]	Narrative Review	—	Imaging + NAATs (radiological correlation with PCR/Xpert)	Emphasized combined use of imaging and molecular tests in abdominal TB	Useful diagnostic overview; not imaging-specific
Li et al., 2022. ^[31]	Retrospective ML Study	150	CT Radiomics + Machine Learning (texture features)	Predicted disease activity with $>85\%$ accuracy in Crohn's disease	Not TB-specific; relevant model framework for extrapolation
Mahomed et al., 2023. ^[25]	Narrative Pediatric Review	—	CT, X-ray, MRI (pediatric signs)	Described classic signs in childhood TB: lymphadenopathy, calcifications	Pediatric focus; lacks adult correlation or advanced imaging techniques
Shen et al., 2024. ^[28]	Retrospective	120	CE-CT Radiomics (entropy, skewness, uniformity)	Accurately differentiated TB vs lymphoma using radiomics features	Strong accuracy; limited external validation
Sharma et al., 2024. ^[24]	Narrative Review	—	CT, MRI (classic and modern descriptors)	Discussed omental thickening, necrotic nodes, and bowel wall as key indicators	Comprehensive synthesis; lacks original data

Narrative Synthesis of Findings: The synthesis of current literature underscores that morphological imaging features remain the cornerstone of abdominal tuberculosis (TB) diagnosis, particularly in resource-limited settings. Features such as necrotic lymphadenopathy, bowel wall thickening, omental caking, and loculated ascites on CT and ultrasound are frequently encountered and serve as essential red flags for abdominal TB, especially in endemic regions.^[24,25] However, these structural findings are nonspecific and can significantly overlap with neoplastic, inflammatory, and infectious conditions such as lymphoma, gastrointestinal malignancies, or Crohn's disease.^[30] This diagnostic ambiguity has necessitated the exploration of functional imaging biomarkers that go beyond morphology.

In this regard, diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) mapping have shown strong promise. Studies consistently demonstrate that active TB lesions exhibit restricted diffusion with lower ADC values ($<1.2 \times 10^{-3}$ mm²/s), correlating with dense cellular infiltrates and caseation necrosis.^[26,32] Notably, Das et al. (2022) reported that ADC metrics not only aided in diagnosis but also helped in monitoring treatment response, as lesions demonstrated increased diffusion with resolution.^[26]

Similarly, FDG PET/CT has emerged as a valuable functional tool, particularly in treatment-naïve or refractory cases. The uptake of fluorodeoxyglucose reflects heightened metabolic activity in granulomatous tissue. A SUVmax threshold >5.0 has been proposed in several studies to differentiate active TB from inactive or fibrotic disease.^[29,33] However, the overlapping FDG uptake patterns with malignancies remain a challenge, underscoring the importance of contextual interpretation.

One of the most forward-looking areas in TB imaging is radiomics, which involves extracting high-dimensional data from standard imaging to uncover patterns beyond visual perception. Preliminary studies using texture features like entropy, uniformity, and skewness on CT have demonstrated the ability to distinguish TB from Crohn's disease and malignancy with accuracy exceeding 85%.^[30,31] While these results are promising, they are currently limited to pilot studies and require larger multicenter validation before routine clinical adoption.

The cumulative evidence supports the integration of multiparametric imaging—combining morphological, functional, and AI-driven biomarkers—to enhance diagnostic precision. For instance, a hybrid approach utilizing CT for structural assessment, DWI for inflammation, and PET/CT for metabolic activity can offer a comprehensive view of disease status. Such integration is particularly crucial in cases with inconclusive histopathology or inaccessibility for biopsy.

In short, while traditional morphological imaging remains essential, the future lies in functional and computational imaging biomarkers that provide greater specificity, quantifiability, and

reproducibility. This paradigm shift is expected to improve not only diagnostic confidence but also aid in individualized treatment planning and early assessment of therapeutic response.

DISCUSSION

The emergence of imaging biomarkers has significantly transformed the diagnostic landscape of abdominal tuberculosis (TB). Traditionally, diagnosis relied heavily on identifying structural changes such as lymphadenopathy, ascites, or bowel wall thickening on ultrasound or CT.^[24] While these morphological signs remain essential, their diagnostic accuracy is limited due to overlapping features with malignancies and inflammatory bowel disease. This limitation has led to a paradigm shift toward quantitative and functional imaging biomarkers, which allow for deeper insight into tissue characteristics, inflammation, and disease activity.^[24,25]

Functionally driven imaging tools—most notably diffusion-weighted imaging (DWI) and fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT)—are now enabling earlier and more accurate detection of active disease. For example, ADC values derived from DWI provide quantifiable data to distinguish active from inactive or treated lesions, with lower values typically correlating with dense cellular infiltration and necrosis [26]. Similarly, SUVmax on PET/CT reflects metabolic activity and has proven useful in identifying active granulomatous inflammation. Together, these biomarkers allow radiologists to move beyond descriptive reporting toward objective and reproducible assessment.

The clinical utility of these imaging biomarkers extends far beyond diagnosis. They offer a non-invasive method to monitor treatment response, helping clinicians assess whether anti-tubercular therapy is effective without relying solely on symptomatic improvement or invasive follow-up procedures.^[29] Additionally, accurate imaging biomarkers reduce the risk of unnecessary surgeries or biopsies in patients whose imaging findings mimic malignancy or Crohn's disease, thus optimizing patient safety and reducing costs.^[29,30]

Despite these advances, several challenges persist. One major issue is the heterogeneity in biomarker definitions and cutoff values across studies. For example, ADC thresholds may vary depending on scanner type, imaging sequence, and ROI placement. Similarly, SUVmax values can be influenced by patient glucose levels and time of imaging post-radiotracer injection.^[30] These inconsistencies make it difficult to develop universal protocols and limit generalizability of study findings. Furthermore, access to advanced imaging modalities such as PET/CT or radiomics platforms remains limited in low-resource settings, where abdominal TB is most prevalent. Additionally, inter-observer variability,

particularly in manually interpreting imaging patterns or measuring parameters, can affect diagnostic consistency.^[31]

Looking ahead, the future of imaging in abdominal TB will likely be defined by the integration of machine learning and radiomics. Automated algorithms can extract thousands of features from standard imaging datasets and correlate them with histopathological or clinical outcomes, providing personalized and data-driven diagnostics. However, standardization in radiomic feature extraction and the creation of multicenter, annotated imaging datasets are prerequisites for widespread adoption.^[26] Another promising trend is the development of hybrid imaging algorithms that combine morphological, functional, and AI-driven assessments into a single interpretive framework, improving both sensitivity and specificity.

From a clinical workflow standpoint, incorporating these emerging imaging biomarkers into daily practice will require close collaboration between radiologists, infectious disease specialists, nuclear medicine experts, and data scientists. Establishing evidence-based diagnostic pathways that integrate imaging biomarkers with clinical, laboratory, and histological data is key to enhancing diagnostic accuracy and guiding treatment decisions. Training and upskilling radiologists in functional imaging interpretation and radiomic analysis will also be critical for successful implementation.

In short, imaging biomarkers are reshaping the way abdominal TB is diagnosed and monitored. With continued research, technological innovation, and multidisciplinary integration, these tools have the potential to bridge the gap between traditional imaging and precision medicine in tuberculosis care.

CONCLUSION

Abdominal tuberculosis imaging is entering a new era of precision, increasingly guided by the integration of biomarkers and functional imaging techniques. While conventional modalities like CT and MRI continue to serve as foundational tools for morphological assessment, the incorporation of advanced methods such as diffusion-weighted imaging (DWI), FDG PET/CT, and radiomics has significantly improved diagnostic specificity, particularly in differentiating TB from malignancies and other mimics. These innovations enable non-invasive, quantitative evaluation of disease activity and treatment response. However, to implement these biomarkers into routine clinical practice, there is a pressing need for standardized imaging protocols, uniform biomarker definitions, and large-scale multicentric studies that can validate their reproducibility and clinical impact across diverse populations and healthcare settings.

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