Metabolomics (2026) 22:1
https://doi.org/10.1007/s11306-025-02377-2

ORIGINAL ARTICLE

NMR based human gut metabolomic profiling reveals altered metabolites associated with pulmonary and extra-pulmonary tuberculosis

Vishal Sharma[1] · Anoop Singh[1] · Sonam Sharma[2] · Mohita Gaur[1] · Arun Kumar Malaisamy[2] · Deepti Rawat[1] · Anjali Yadav[1] · Bolaji Fatai Oyeyemi[2,3] · Aarushi Vasudeva[1] · Anil Chaudhry[4] · Ashwani Khanna[5] · Vishal Khanna[6] · Sheelu Lohiya[6] · Reema Arora[6] · Anannya Bandyopadhyay[1] · Neel Sarovar Bhavesh[2] · Yogendra Singh[1,7] · Richa Misra[1,8]

Received: 4 June 2025 / Accepted: 30 October 2025 / Published online: 29 November 2025

Abstract

Introduction Tuberculosis remains one of the world's deadliest infectious diseases. The pathophysiology of the two manifestations of *Mycobacterium tuberculosis* infection, pulmonary TB (PTB) and extrapulmonary TB (EPTB) is still not fully understood. Understanding the metabolic profile of both disease manifestations in patients is important for developing therapeutic approaches and molecular diagnosis.

Objective The current study aimed to elucidate differences in the gut metabolic profile of PTB and EPTB patients compared to healthy controls (HCs).

Method We used an untargeted approach through ^{1}H Nuclear Magnetic Resonance (NMR) spectroscopy to perform metabolomic profiling of stool samples from 77 TB patients [pulmonary TB (PTB, $n=33$), cervical lymph node TB (CrLNTB, $n=30$), abdominal TB (ATB, $n=14$)], and 30 HCs. Multivariate and univariate analyses were performed to identify the differential gut metabolites associated with TB patients.

Results PTB patients showed greater metabolic perturbation than either EPTB group, with 24 metabolites significantly altered compared to 13 in ATB and 12 in CrLNTB, relative to HCs (adjusted $p<0.05$). Each TB subtype displayed distinct metabolic profiles, yet several metabolites were commonly altered across all TB groups, including valine, N-formyl-L-methionine, choline, dimethylsulfone, tryptophan, valerate, N-acetylglutamate, creatine, and malonate. In the combined TB cohort versus controls, the most discriminatory metabolites were valine and N-formyl-L-methionine (AUC$\geq$0.80). Overall, these findings offer insights into the gut metabolome of TB patients in India and characterize for the first time metabolic perturbations in EPTB patients.

Conclusion The study highlights the metabolic disruptions associated with PTB and EPTB patients.

Keywords Tuberculosis · Diagnosis · Pulmonary TB · Extra-pulmonary TB · ^{1}H NMR spectroscopy · Gut metabolites

1 Introduction

Tuberculosis (TB), despite being an ancient disease, has re-emerged as the leading cause of death from a single infectious agent worldwide following the COVID-19 pandemic (Global tuberculosis report, 2024). The causative agent of the disease *Mycobacterium tuberculosis* (Mtb) typically infects the lungs causing pulmonary tuberculosis (PTB). The other clinical manifestation of TB where bacilli infect other body organs except the lungs is extra-pulmonary tuberculosis (EPTB), known to contribute 15–20% of all TB cases (Global tuberculosis report, 2020). The most

Vishal Sharma, Anoop Singh and Sonam Sharma contributed equally to this work.

Extended author information available on the last page of the article

Richa Misra