Section: Respiratory Medicine

Original Research Article

COMPARISON OF CLINICAL PRESENTATION OF TUBERCULOSIS AMONG ADULTS DURING PRECOVID COVID AND POSTCOVID PERIOD IN A TERTIARY CARE CENTRE

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ABSTRACT

Background: Tuberculosis (TB) remains a major public health problem, and the COVID-19 pandemic disrupted TB diagnostic and treatment services worldwide. Reduced access to healthcare, lockdown-related restrictions, fear of infection, diversion of healthcare resources, and overlap of respiratory symptoms between TB and COVID-19 may have altered the clinical profile of patients reaching tertiary care hospitals. The present study evaluated changes in the clinical presentation, site distribution, diagnostic characteristics, drug sensitivity, comorbidities and treatment outcomes of adult TB patients across pre-COVID, COVID and post-COVID periods.

Materials and Methods: This retrospective observational study was conducted at Sree Gokulam Medical College and Research Foundation, Trivandrum. All eligible adult TB records available for the defined study periods were included using universal sampling. Data included age, sex, residence, pulmonary versus extrapulmonary/disseminated TB, anatomical site, diagnostic modality, microbiological confirmation, drug sensitivity, comorbidities and treatment outcome. Categorical variables were compared using Pearson chi-square or Fisher's exact test; ordered trends in age were assessed using the Jonckheere–Terpstra test with permutation-based significance. Logistic regression was used to identify factors independently associated with extrapulmonary/disseminated TB.

Results: A total of 469 TB records were analysed: 153 (32.6%) in the pre-COVID period, 148 (31.6%) during COVID and 168 (35.8%) in the post-COVID period. Median age increased progressively from 53 years (IQR 35–65) to 56 years (IQR 37.5–65) and 60.5 years (IQR 48.5–70), respectively (P=0.002; Jonckheere–Terpstra permutation P=0.0008). Pulmonary TB decreased from 52% pre-COVID to 35% during COVID and 41% post-COVID, whereas extrapulmonary TB increased from 48% to 59% and 58%, respectively (P<0.001). Disseminated TB was documented in 0%, 6.1% and 0.6% of patients. Site distribution differed significantly (P=0.008), with pleural disease increasing from 7.2% to 16% post-COVID. Histopathology-based diagnosis varied significantly across periods (P=0.004). Treatment outcomes also differed (P=0.006), with mortality of 8.5%, 1.4% and 6.0% across the three periods. In multivariable analysis, COVID and post-COVID periods were independently associated with higher odds of extrapulmonary/disseminated TB compared with pre-COVID (adjusted OR 2.27 and 2.03, respectively). Female sex and non-

diabetes/other comorbidity category were also independently associated with extrapulmonary/disseminated presentation.
Conclusion: The study demonstrates a sustained shift in the clinical spectrum of TB toward extrapulmonary disease during and after the COVID-19 period in a tertiary care setting. The findings highlight the need for continued vigilance for extrapulmonary TB, preservation of diagnostic capacity during health emergencies, and strengthened post-pandemic case finding and referral pathways.
Keywords: Tuberculosis; COVID-19; extrapulmonary tuberculosis; pulmonary tuberculosis; tertiary care; India; diagnosis; treatment outcome; pandemic.

INTRODUCTION

Tuberculosis remains one of the most important infectious diseases worldwide and continues to cause substantial morbidity, mortality and socioeconomic consequences. Although modern molecular diagnostics, standardized treatment regimens and national TB programmes have improved detection and outcomes, TB control remains highly dependent on timely access to healthcare, uninterrupted diagnostic services, reliable laboratory networks, treatment availability and sustained patient engagement. The WHO End TB Strategy emphasizes early diagnosis, universal access to appropriate drug-susceptibility testing, patient-centred care and strong health systems as central components of TB control.[1-3]

The COVID-19 pandemic created an unprecedented interruption in these systems. During the early pandemic, hospitals redirected staff, laboratory capacity, oxygen supplies, beds and administrative resources toward COVID-19. At the same time, lockdowns and restrictions on movement reduced access to outpatient clinics, diagnostic laboratories and public-health services. Patients with cough, fever, fatigue and breathlessness faced another layer of uncertainty because these symptoms overlapped with COVID-19. Fear of acquiring COVID-19 in healthcare facilities, stigma and economic disruption further affected healthcare-seeking behaviour. WHO documented a major decline in TB notifications globally in 2020, including a particularly large reduction in India.[4-7]

The reduction in notification should not automatically be interpreted as a reduction in TB incidence. A substantial proportion of the decline may have represented missed or delayed diagnoses. Modelling studies predicted that interruptions in TB diagnosis and treatment could increase transmission, disease burden and mortality over subsequent years. As healthcare services recovered, increased notifications could reflect both recovery of diagnostic activity and identification of patients whose diagnosis had been delayed during the pandemic. Thus, examining only the number of TB cases is insufficient; changes in the phenotype of disease presenting to hospitals may provide additional insight into the indirect consequences of healthcare disruption.[8-11]

Extrapulmonary tuberculosis (EPTB) is particularly relevant in this context. Compared with pulmonary TB, EPTB can be diagnostically challenging because symptoms may be nonspecific, microbiological confirmation may be less frequently obtained, and tissue sampling or imaging may be required. EPTB encompasses lymph-node, pleural, central nervous system, abdominal, osteoarticular, genitourinary, skin and other forms of disease. Female sex has been associated with greater odds of extrapulmonary dissemination in published studies, and South Asian data indicate an important burden of EPTB among women.[12,13]

A tertiary care centre is especially suitable for studying these changes because it receives patients with complicated, atypical, advanced or diagnostically difficult disease, including patients referred after evaluation at peripheral centres. The present study therefore compares adult TB presentations across pre-COVID, COVID and post-COVID periods, with particular emphasis on pulmonary versus extrapulmonary/disseminated disease, anatomical distribution, diagnostic methods, microbiological confirmation, drug resistance, comorbidity and treatment outcome.

Aim and Objectives

Aim: To evaluate the impact of the COVID-19 pandemic on the clinical presentation of tuberculosis cases in a tertiary care centre.

Primary objective: To compare the clinical presentation of tuberculosis among adults during the pre-COVID, COVID and post-COVID periods.

Secondary objectives: (1) to assess differences in treatment outcomes including cure/completion, mortality and loss to follow-up; and (2) to evaluate the occurrence of drug-resistant TB across study periods.

MATERIALS AND METHODS

Study design and setting

This was a retrospective observational study conducted at Sree Gokulam Medical College and Research Foundation, Trivandrum. The protocol describes the pre-COVID, COVID and post-COVID periods as January 2017–December 2019, January 2020–December 2022 and January 2023–December 2025, respectively. All eligible adult TB records available for the defined study periods were considered using universal sampling. The protocol

states that patients with incomplete or missing records were excluded.

Study population and data collection

Records of confirmed pulmonary or extrapulmonary TB patients attending the TB unit were reviewed. Data extracted from TB registers and electronic medical records included age, sex, residence, clinical presentation, pulmonary versus extrapulmonary disease, anatomical site, diagnostic modality, microbiological confirmation, drug sensitivity status, comorbidities and treatment outcome.

Statistical Analysis

For the primary analysis, TB presentation was categorized into pulmonary TB and extrapulmonary/disseminated TB. Pulmonary TB was used as the reference category in regression analysis. Anatomical site was separately categorized as pulmonary, lymph-node, pleural effusion, meningitis/brain, abdomen, spine/bone, genitourinary, skin, eye and vocal cord disease. Disseminated TB was retained as a separate category in descriptive analysis and grouped with extrapulmonary disease for the regression outcome.

The analysis was performed using the R statistical package. Categorical variables were summarized using frequency and percentage, while continuous variables were summarized using median and interquartile range. Pearson chi-square or Fisher's exact test was used for associations between categorical variables and study periods. For sparse expected frequencies, Fisher's exact test with 10,000 Monte Carlo simulations was used. The ordered trend in age across the three periods was assessed using the Jonckheere–Terpstra test with a permutation-based P value using 10,000 permutations. Univariate logistic regression generated crude odds ratios with 95% confidence intervals. Variables of clinical importance were included in multivariable binary logistic regression, with study period as the principal predictor and adjustment for age, sex, residence and comorbidity. Male sex, urban residence and pre-COVID period were the reference categories. Model calibration was assessed using the Hosmer–Lemeshow test and discrimination using the area under the receiver operating characteristic curve. A two-tailed $P<0.05$ was considered statistically significant.

The statistical methods and regression model were retained from the supplied analysis. The analysis reports Hosmer–Lemeshow $\chi^2=12.28$, $P=0.139$ and AUC=0.707 (95% CI 0.660–0.754), indicating no evidence of poor calibration and moderate discriminative performance.

RESULTS

A total of 469 adult TB records were included. Of these, 153 (32.6%) were from the pre-COVID period, 148 (31.6%) from the COVID period and 168 (35.8%) from the post-COVID period. The distribution demonstrates that the study included broadly comparable numbers of patients across the three periods, supporting period-wise comparison of the clinical characteristics.

The median age increased progressively across the study periods. Patients in the pre-COVID period had a median age of 53 years (IQR 35–65), compared with 56 years (IQR 37.5–65) during COVID and 60.5 years (IQR 48.5–70) in the post-COVID period. The overall difference was statistically significant (P=0.002). Bonferroni-adjusted post-hoc comparisons showed significant differences between pre-COVID and post-COVID patients (P=0.002) and between COVID and post-COVID patients (P=0.026). The Jonckheere–Terpstra test confirmed a significant increasing age trend across the three periods (JT=42,144; permutation P=0.0008).

Sex distribution did not differ significantly across the periods. Men accounted for 61% of pre-COVID cases, 59% of COVID cases and 64% of post-COVID cases (P=0.666). In contrast, residence changed significantly (P=0.006), with the proportion of rural patients increasing from 82% before COVID to 93% during COVID and 90% after COVID.

The most important change was in the type of TB. Pulmonary TB accounted for 52% of pre-COVID cases but decreased to 35% during COVID and 41% after COVID. Conversely, extrapulmonary TB increased from 48% before COVID to 59% during COVID and 58% after COVID. Disseminated TB, which was not recorded in the pre-COVID period, accounted for 6.1% of cases during COVID and 0.6% after COVID. The overall variation in pulmonary, extrapulmonary and disseminated disease was highly significant (P<0.001).

Anatomical site distribution also differed significantly (P=0.008). Lymph-node disease remained relatively stable at 24%, 24% and 25%. Pleural effusion increased from 7.2% pre-COVID to 9.5% during COVID and 16% post-COVID. Abdominal TB was 6.5%, 11% and 6.5%, respectively. Spine/bone disease was 5.2%, 7.4% and 5.4%. Genitourinary TB increased from 0.7% to 2.7% and 3.6%. CNS disease decreased from 4.6% to 4.1% and 1.2%.

Diagnostic patterns also changed significantly (P=0.004). AFB smear/NAAT/culture accounted for 52% of diagnoses before COVID, 41% during COVID and 44% after COVID. Imaging-based diagnosis was used in 12%, 20% and 8.9%, respectively. Histopathology accounted for 21%, 21% and 26%, while specimen-based testing accounted for 15%, 14% and 20%. Skin testing was recorded in 0%, 4.7% and 0.6%.

Microbiological confirmation was positive in 52% of pre-COVID cases, 41% of COVID cases and 44% of post-COVID cases, with no statistically significant difference (P=0.132). Drug sensitivity was also broadly similar (P=0.166): all pre-COVID cases were reported as sensitive, compared with 98% during COVID and 99% post-COVID. Resistance was documented in 3 cases (2.0%) during COVID and one case (0.6%) post-COVID.

Diabetes was the principal specifically reported comorbidity, present in 42% of pre-COVID, 40% of COVID and 46% of post-COVID cases. HIV was recorded in one patient during COVID and one after COVID. The overall comorbidity distribution did not differ significantly (P=0.636).

Treatment outcomes varied significantly by study period (P=0.006). Cure/completion occurred in 92% of pre-COVID patients, 95% during COVID and 93% post-COVID. Mortality decreased from 8.5% pre-COVID to 1.4% during COVID and increased again to 6.0% post-COVID. Loss to follow-up was absent before COVID, 2.7% during COVID and 0.6% post-COVID. No treatment failures were reported in any period.

Table 1: Sociodemographic and clinical characteristics of tuberculosis patients across study periods

Variable	Pre-COVID (n=153)	COVID (n=148)	Post-COVID (n=168)	P value
Age, median (IQR), years	53.0 (35.0–65.0)	56.0 (37.5–65.0)	60.5 (48.5–70.0)	0.002
Age range, years	18–95	20–88	18–97	
Male	93 (61%)	87 (59%)	107 (64%)	0.666
Female	60 (39%)	61 (41%)	61 (36%)	
Urban	28 (18%)	10 (6.8%)	17 (10%)	0.006
Rural	125 (82%)	138 (93%)	151 (90%)	
Pulmonary TB	80 (52%)	52 (35%)	69 (41%)	<0.001
Extrapulmonary TB	73 (48%)	87 (59%)	98 (58%)	
Disseminated TB	0 (0%)	9 (6.1%)	1 (0.6%)	
Lymph node	36 (24%)	35 (24%)	42 (25%)	
Pleural effusion	11 (7.2%)	14 (9.5%)	27 (16%)	
Meningitis/Brain	7 (4.6%)	6 (4.1%)	2 (1.2%)	
Abdomen	10 (6.5%)	16 (11%)	11 (6.5%)	0.008
Spine/Bone	8 (5.2%)	11 (7.4%)	9 (5.4%)	
Genitourinary	1 (0.7%)	4 (2.7%)	6 (3.6%)	
Skin	0 (0%)	2 (1.4%)	1 (0.6%)	
Eye	0 (0%)	6 (4.1%)	1 (0.6%)	
Vocal cord	0 (0%)	1 (0.7%)	0 (0%)	

Figure 1. Distribution of pulmonary, extrapulmonary and disseminated tuberculosis across pre-COVID, COVID and post-COVID periods

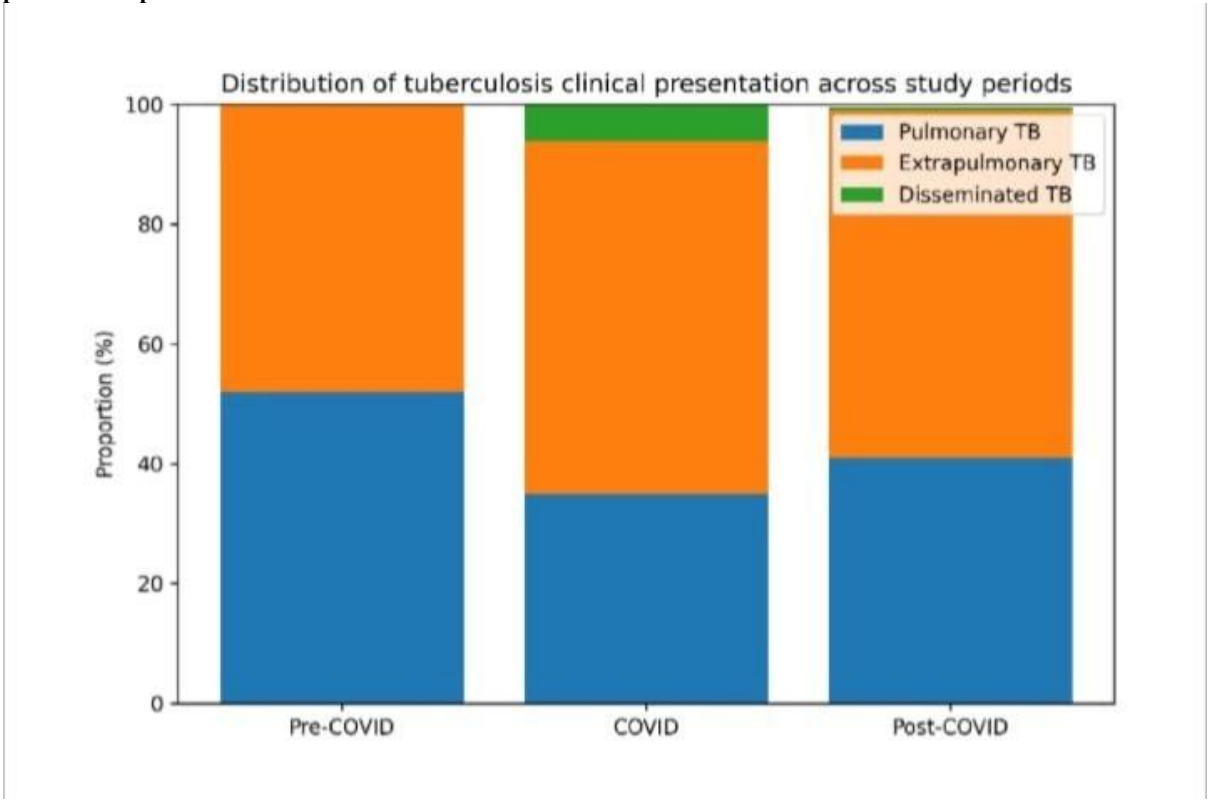

Figure 2. Median age of Tuberculosis patients across the three study period

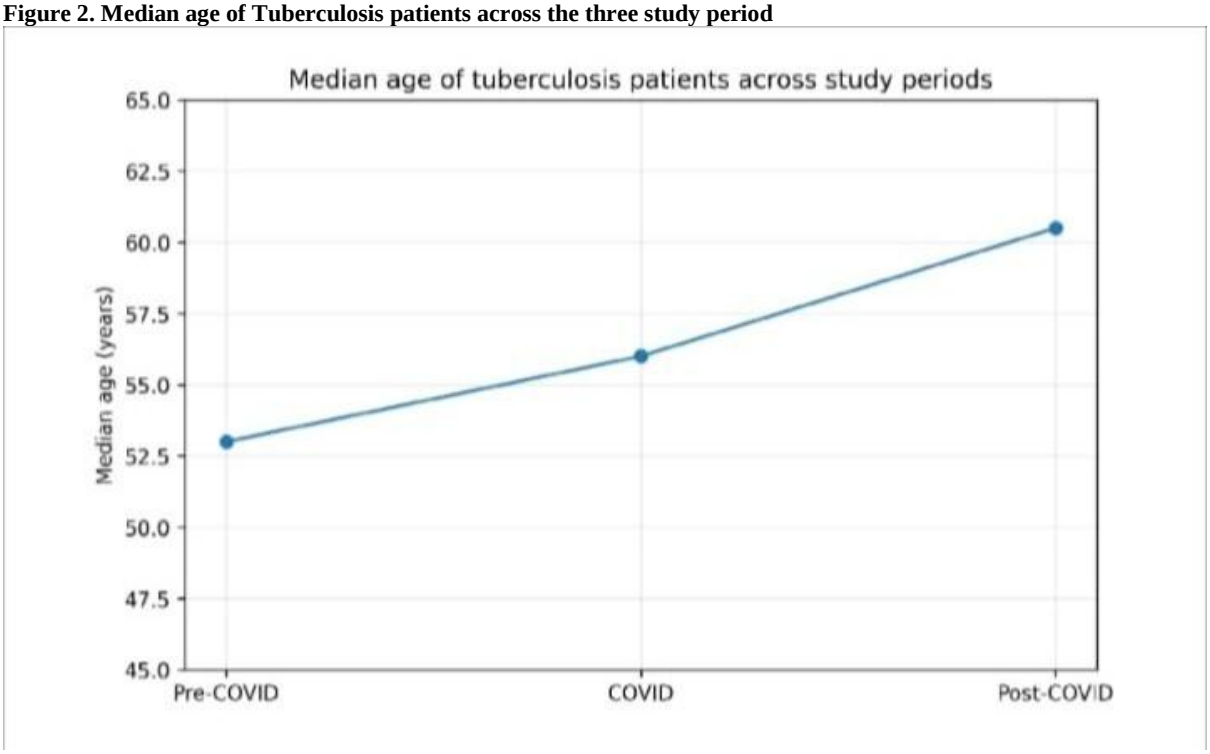

Table 2: Diagnostic characteristics, drug sensitivity, comorbidities and treatment outcomes

Variable	Pre-COVID (n=153)	COVID (n=148)	Post-COVID (n=168)	P value
AFB smear/NAAT/culture	79 (52%)	60 (41%)	74 (44%)	0.004
Imaging	19 (12%)	29 (20%)	15 (8.9%)	
Histopathology	32 (21%)	31 (21%)	44 (26%)	
Specimen test	23 (15%)	21 (14%)	34 (20%)	
Skin test	0 (0%)	7 (4.7%)	1 (0.6%)	
Microbiologically positive	80 (52%)	61 (41%)	74 (44%)	0.132
Microbiologically negative	73 (48%)	87 (59%)	94 (56%)	
Drug sensitive	153 (100%)	145 (98%)	167 (99%)	0.166
Drug resistant	0 (0%)	3 (2.0%)	1 (0.6%)	
Diabetes	64 (42%)	59 (40%)	78 (46%)	
HIV	0 (0%)	1 (0.7%)	1 (0.6%)	
Other comorbidities	89 (58%)	88 (59%)	89 (53%)	0.636
History of COVID-19	0 (0%)	5 (3.4%)	4 (2.4%)	
Cure/Completed	140 (92%)	141 (95%)	157 (93%)	
Death	13 (8.5%)	2 (1.4%)	10 (6.0%)	0.006
Lost to follow-up	0 (0%)	4 (2.7%)	1 (0.6%)	
Failure	0 (0%)	0 (0%)	0 (0%)	
Other diagnosis	0 (0%)	1 (0.7%)	0 (0%)	

Table 3: Logistic regression analysis of factors associated with extrapulmonary/disseminated tuberculosis

Variable	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Study period: Pre-COVID (reference)	1.00	—	1.00	—
COVID	2.02 (1.28–3.23)	0.003	2.27 (1.38–3.77)	0.001
Post-COVID	1.57 (1.01–2.45)	0.045	2.03 (1.25–3.31)	0.004
Age, per year	0.977 (0.966–0.988)	<0.001	0.984 (0.972–0.996)	0.009
Male (reference)	1.00	—	1.00	—
Female	2.39 (1.62–3.56)	<0.001	2.02 (1.34–3.06)	<0.001
Urban (reference)	1.00	—	1.00	—
Rural	0.95 (0.53–1.68)	0.868	0.83 (0.45–1.52)	0.550
Diabetes (reference)	1.00	—	1.00	—
Other comorbidities	2.94 (2.01–4.31)	<0.001	2.31 (1.53–3.49)	<0.001

Reference categories: pre-COVID period, male sex, urban residence and diabetes. The multivariable model was adjusted for study period, age, gender, residence and comorbidity. HIV (n=2) and HBsAg (n=0) were not retained as separate categories because of sparse observations and were included in

the "Others" category. Model diagnostics: Hosmer–Lemeshow χ^2=12.28, P=0.139; AUC=0.707 (95% CI 0.660–0.754).

DISCUSSION

The present study provides a detailed comparison of adult TB presentations before, during and after the COVID-19 pandemic in a tertiary care centre in Trivandrum. The most important observation is the substantial shift from pulmonary toward extrapulmonary/disseminated disease during the COVID period, with this pattern persisting into the post-COVID period. In parallel, the median age of patients increased progressively, anatomical site distribution changed, diagnostic pathways showed significant variation, and treatment outcomes differed across periods.

Increase in extrapulmonary and disseminated tuberculosis

The most clinically important finding was the increase in extrapulmonary TB from 48% before COVID-19 to 59% during COVID-19 and 58% after COVID-19. Pulmonary TB declined from 52% to 35% during the pandemic and remained below the pre-pandemic proportion at 41% after recovery. Disseminated TB was newly prominent during COVID-19, occurring in 6.1% of patients compared with no recorded cases in the pre-COVID period. This pattern is not simply a change in one anatomical site; it represents a broad alteration in the phenotype of TB reaching the tertiary hospital.

Several mechanisms may explain this observation. First, patients with pulmonary symptoms may have had easier access to COVID-oriented screening and respiratory pathways, while patients with less typical TB symptoms may have experienced delayed recognition. Second, lockdowns and reduced access to outpatient services could have preferentially delayed patients with slowly progressive extrapulmonary disease. Third, prolonged diagnostic delay may have allowed localized disease to progress or disseminate before definitive diagnosis. Fourth, the referral pattern of a tertiary hospital may have changed during the pandemic, with peripheral facilities managing straightforward pulmonary cases while complicated or diagnostically uncertain patients were referred later.

The finding is also biologically plausible. EPTB often presents with constitutional symptoms or organ-specific manifestations rather than classical respiratory symptoms. Lymphadenopathy, pleural effusion, abdominal disease, bone involvement or CNS disease can therefore be missed when health systems are overwhelmed by a respiratory pandemic. The requirement for imaging, aspiration, biopsy or histopathological confirmation can add further delay. The present data support the hypothesis that disruption of routine diagnostic pathways may have changed not only the number of TB cases diagnosed but also the type of disease detected.

The persistence of a high EPTB proportion in the post-COVID period is particularly important. If the increase had represented only a transient diagnostic artefact during lockdown, one might expect a return toward the pre-COVID distribution once services normalized. Instead, EPTB remained at 58% after COVID. This may reflect a backlog of delayed cases being diagnosed after recovery of healthcare services, as well as consequences of prolonged periods of underdiagnosis. WHO has similarly suggested that increased TB notifications in the recovery period partly reflect diagnosis of patients whose TB diagnosis had been delayed during the pandemic.[6,7]

Female sex and extrapulmonary disease

Female sex emerged as an independent predictor of extrapulmonary/disseminated presentation. Women had approximately twice the adjusted odds of extrapulmonary/disseminated TB compared with men (aOR 2.02, 95% CI 1.34–3.06; P<0.001). This is consistent with published evidence. A meta-analysis reported higher odds of extrapulmonary dissemination among females, and South Asian literature has specifically highlighted the relatively greater representation of EPTB among women. [12]

The reasons for this association are multifactorial and may include biological differences in host immune responses, differences in exposure, healthcare-seeking patterns, nutritional and socioeconomic factors, and the anatomical distribution of disease. The present study cannot determine the mechanism because individual-level behavioural, socioeconomic, immunological and hormonal variables were not available. Nevertheless, the finding is clinically useful because female patients with constitutional or organ-specific symptoms may warrant a lower threshold for considering EPTB.

Ageing of the TB population

Another striking observation was the progressive increase in patient age. Median age increased from 53 years before COVID to 56 years during COVID and 60.5 years after COVID. The trend was statistically significant by both overall comparison and Jonckheere–Terpstra testing. This suggests that the post-pandemic TB population attending the tertiary centre may have become older.

Several explanations are possible. Older adults were among the groups most affected by healthcare access restrictions and may have postponed medical evaluation during the pandemic. Older individuals also have greater risk of comorbid disease and reactivation TB, and their presentation may be atypical. In addition, changes in referral patterns may have resulted in a greater proportion of older and medically complex patients reaching tertiary care. The dataset does not establish causality, but the progressive trend is clinically relevant because age may influence symptom recognition, diagnostic yield, treatment tolerance and mortality.

Changes in anatomical distribution

The overall site distribution changed significantly. Pleural TB showed the clearest sustained increase, from 7.2% before COVID to 9.5% during COVID

and 16% after COVID. Abdominal TB increased during COVID to 11% before returning to 6.5%. Genitourinary TB increased progressively from 0.7% to 3.6%. Conversely, CNS/brain disease decreased from 4.6% before COVID to 1.2% after COVID. These changes should be interpreted cautiously because individual site categories were relatively small and the study was not designed to establish causal mechanisms for each anatomical site.

The increase in pleural disease may nevertheless be clinically meaningful. Pleural TB often requires imaging, pleural fluid analysis and sometimes pleural biopsy, and microbiological confirmation can be difficult. A higher proportion of pleural disease in the post-COVID period could therefore indicate a greater burden of diagnostically challenging TB. The rise in genitourinary disease may similarly reflect delayed presentation or increased detection through organ-specific investigations, although the small numbers preclude firm conclusions.

Diagnostic pattern and microbiological confirmation

Diagnostic modality differed significantly across study periods. AFB smear/NAAT/culture represented 52% of diagnostic approaches before COVID but 41% during COVID and 44% after COVID. Imaging-based diagnosis increased during COVID to 20%, compared with 12% before COVID, before falling to 8.9% after COVID. Histopathology remained at 21% during the pre-COVID and COVID periods but increased to 26% after COVID. Specimen testing also increased post-COVID.

The diagnostic shift is consistent with the observed increase in EPTB. Extrapulmonary disease frequently requires tissue or fluid sampling rather than routine sputum testing. Thus, the higher proportion of histopathology and specimen-based diagnoses in the post-COVID period may partly reflect the changing disease phenotype. At the same time, the overall microbiological confirmation rate did not differ significantly, suggesting that the increase in EPTB was not simply the result of a change in laboratory positivity.

The WHO diagnostic framework emphasizes rapid molecular testing and appropriate testing of relevant specimens. Modern NAATs have expanded the ability to diagnose TB rapidly and identify drug resistance, while molecular testing of non-respiratory specimens can be important in EPTB. The present findings reinforce the need for diagnostic pathways that remain functional during health emergencies and are capable of handling both pulmonary and extrapulmonary disease.[14,15]

Drug resistance

Drug resistance was uncommon in this cohort. No resistance was recorded before COVID, while three cases were reported during COVID and one after COVID. The difference was not statistically significant. Therefore, this study does not demonstrate an increase in drug-resistant TB associated with the pandemic.

This finding should not be interpreted as evidence that the pandemic had no effect on drug resistance at the population level. The study is hospital-based, the number of resistant cases is very small, and the analysis is underpowered for this outcome. Globally, WHO documented reductions in detection and treatment of drug-resistant TB during the pandemic, raising concern about missed resistance and treatment interruptions. Continued universal access to rapid drug-susceptibility testing remains essential.[4-7]

Comorbidities and the association with extrapulmonary presentation

Diabetes was common across all periods, ranging from 40% to 46%, but the overall distribution of comorbidities did not differ significantly. In regression analysis, the “other comorbidities” category was independently associated with extrapulmonary/disseminated TB compared with diabetes (aOR 2.31, 95% CI 1.53–3.49; P<0.001). This category included sparse HIV and other comorbidity observations and therefore should be interpreted with caution.

Diabetes is an established risk factor for TB and may influence disease severity and treatment outcomes. However, the current analysis was not designed to compare individual comorbid conditions, and the grouping of several conditions into “others” limits mechanistic interpretation. Future studies should collect sufficiently large numbers of individual comorbidity categories, including HIV, chronic kidney disease, malignancy, immunosuppressive therapy and other immunocompromising conditions.[3,20-22]

Treatment outcomes and mortality

Treatment outcomes differed significantly across periods. The mortality rate was 8.5% before COVID, decreased to 1.4% during COVID and subsequently increased to 6.0% after COVID. Cure/completion remained high at 92–95%. The mortality pattern is therefore not parallel to the increase in extrapulmonary disease, and the low mortality during COVID should not be interpreted as evidence of improved disease severity or care.

Several factors may explain the mortality pattern. Differences in case mix, referral patterns, admission thresholds, availability of inpatient care and completeness of outcome documentation may all contribute. During COVID, tertiary hospitals may have experienced selective referral of patients who could be managed successfully through established TB pathways, while patients with severe COVID or other illnesses may have been managed through separate pathways. The subsequent increase in post-COVID mortality may reflect a return of complex cases and delayed presentations. Because this was a retrospective study, causal attribution cannot be established.

Interpretation of the regression model

The multivariable model provides important evidence that the increase in extrapulmonary/disseminated TB was not explained

entirely by demographic differences. After adjustment for age, sex, residence and comorbidity, the odds of extrapulmonary/disseminated presentation were 2.27-fold higher during COVID and 2.03-fold higher post-COVID compared with pre-COVID. Female sex remained independently associated with extrapulmonary/disseminated disease.

The age association requires careful interpretation. The adjusted OR per year was 0.984, indicating a small decrease in the odds of the defined extrapulmonary/disseminated outcome with each additional year after adjustment, despite the overall increase in median age over time. This apparent difference between descriptive age trends and adjusted regression results illustrates why age should not be interpreted as the principal driver of the period effect. The period association remained strong after adjustment.

Model calibration was acceptable by the Hosmer–Lemeshow test (P=0.139), while the AUC of 0.707 indicates moderate discrimination. The model therefore provides useful evidence of association but is not intended as a clinical prediction tool.

Implications for TB control

The findings have several implications. First, pandemic preparedness plans should explicitly protect TB diagnostic and treatment services. TB cannot be treated as a programme that can be temporarily paused during respiratory epidemics. Second, case-finding should continue after the acute phase of a health emergency because delayed cases may present later and may have different clinical phenotypes. Third, clinicians should maintain a high index of suspicion for EPTB, particularly among women and patients with unexplained systemic or organ-specific symptoms. Fourth, diagnostic networks should retain access to molecular tests, imaging, cytology and histopathology even when laboratory resources are redirected toward emerging infections.

The results also support stronger integration between TB services and general hospital services. EPTB may present to neurology, gastroenterology, surgery, orthopaedics, gynaecology, nephrology or dermatology rather than directly to a TB clinic. Education of non-respiratory specialties and streamlined referral pathways can therefore improve case detection. The post-COVID period offers an opportunity to identify residual gaps and redesign TB services to remain resilient during future public-health emergencies.

Strengths and Limitations

The principal strengths are the inclusion of all eligible records using universal sampling, comparison across three clinically meaningful periods, detailed anatomical categorization of TB, assessment of diagnostic and treatment variables, and multivariable adjustment for important demographic and clinical factors. The study also provides a real-world tertiary-care perspective that complements national notification data.

Several limitations should be considered. First, the study is retrospective and depends on the accuracy and completeness of medical records. Second, it was performed at a single tertiary care centre, so the findings may not be generalizable to the wider community or to primary and secondary care. Third, referral patterns may have changed substantially during the pandemic, creating selection bias. Fourth, the study measures cases presenting to the hospital rather than population-level incidence, so the observed increase in EPTB cannot be interpreted as an increase in population incidence of EPTB. Fifth, some subgroups, particularly HIV and drug-resistant TB, were very small, limiting statistical power. Sixth, the regression model could not account for potentially important factors such as socioeconomic status, duration of symptoms before presentation, vaccination status, prior TB history, immunosuppressive medications, nutritional status and exact duration of diagnostic delay. Finally, the reasons for the increase in EPTB cannot be established from the available retrospective data and require prospective multicentre investigation.

CONCLUSION

This tertiary-care study demonstrates a significant and clinically important change in the presentation of tuberculosis across the pre-COVID, COVID and post-COVID periods. The most prominent finding was a shift from pulmonary toward extrapulmonary and disseminated TB during the COVID period, with the increased proportion of extrapulmonary disease persisting into the post-COVID period. The odds of extrapulmonary/disseminated presentation remained significantly higher during both COVID and post-COVID periods even after adjustment for age, sex, residence and comorbidity.

The study also demonstrates a progressive increase in the age of patients presenting with TB, significant changes in anatomical site distribution and diagnostic pathways, and significant variation in treatment outcomes. Female sex was independently associated with extrapulmonary/disseminated disease. Although drug resistance remained uncommon in this cohort, the small number of resistant cases prevents definitive conclusions regarding pandemic-related changes in resistance.

Overall, the findings suggest that the indirect effects of COVID-19 on TB extended beyond reduced case detection. Healthcare disruption may have altered the phenotype of TB reaching tertiary care, resulting in a greater relative burden of extrapulmonary and diagnostically challenging disease. Strengthening diagnostic capacity, maintaining continuity of TB services during future emergencies, improving post-pandemic active case finding, and maintaining a high index of suspicion for EPTB are essential to prevent similar disruptions. Multicentre prospective studies are warranted to determine whether the observed increase in EPTB represents a wider epidemiological

phenomenon or a change in tertiary-care referral patterns.

Ethical Considerations

The Institutional Ethics Committee approval was obtained (SGMC IEC72/996/06/2026F) and that patient confidentiality will be maintained. Because this is a retrospective study, informed consent may be waived subject to Institutional Ethics Committee approval.

Data availability

The study used retrospective hospital records. Data availability should follow the institutional policy and applicable ethics approval.

Conflict of interest

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