

**Outcome of COVID-19 in Children With TB: Single-Center Experience**

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**ABSTRACT**

**Objective:** To evaluate the outcome of Coronavirus disease 2019 (COVID-19) infection in children and adolescents with tuberculosis. **Methods:** We analyzed hospital records for the period May, 2020 to September, 2021 for children who were severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reverse transcriptase-polymerase chain reaction (RT-PCR) positive or SARS-CoV-2 antibody positive. They were divided into two group. viz., those with TB (Tuberculosis Group) and those without tuberculosis (non-TB group). Demographic information, symptoms, and outcomes of COVID-19 were compared between the two groups. **Results:** Median (IQR) age of participants was 11 (6) and 4.5 (7) year for the tuberculosis and non-TB groups, respectively. 93.5% and 36.1% of children were asymptomatic in the tuberculosis and non-TB group, respectively. No variable in the study was significantly associated with COVID-19 positivity in children with tuberculosis. No difference was found in the outcomes of COVID-19 infection in children having tuberculosis. **Conclusions:** No differences were noted in the outcomes of COVID-19 infection in children having tuberculosis.

**Keywords:** *Co-infection, Diagosis, Presentation, Severity.*

Coronavirus disease 2019 (COVID-19) is a contagious disease with varied presentations, ranging from asymptomatic or mild features to acute respiratory distress syndrome leading to death. Co-infection of severe acute coronavirus 2 (SARS-CoV-2) with other micro-organisms appears to pose a significant challenge for the management and prognosis of COVID-19 infected patients, one such association being with *Mycobacterium tuberculosis* [1]. In 2020, TB was the commonest cause of death caused by a single infectious pathogen, and India accounted for 26% of the global tuberculosis cases [2]. Of the worldwide tuberculosis, 16% cases were accounted for by children <15 years of age [2].

Only a few studies have highlighted the association between tuberculosis and COVID-19. Having a reliable estimate of the association between tuberculosis and COVID-19 severity and outcomes is crucial to ensure appropriate strategies for these patients. In this study, we have evaluated outcomes of COVID-19 infection in children and adolescents with tuberculosis.

**METHODS**

We extracted hospital records of children with tuberculosis (both new and those on treatment) and those without a tuberculosis diagnosis, attending the outpatient and inpatient department between May, 2020 and September, 2021. All the patients were tested with reverse transcription-polymerase chain reaction (RT-PCR) for SARS-CoV-2 detection at presentation. Those negative on RT-PCR were tested for SARS-CoV-2 nucleocapsid antibody levels in serum, which in the absence of a vaccination mandate for children up to 18 years of age, was considered to indicate a sub-clinical exposure to SARS-CoV-2. As per the directives from the National tuberculosis Elimination Programme (NTEP) [7], all patients with tuberculosis had to be mandatorily screened for COVID-19 and vice versa.

After approval from the institutional ethics committee, the demographics, anthropometry, history, symptomatology, vaccination status, investigations, and outcomes were recorded on a pre-designed proforma,

along with a history of close contact with a confirmed SARS-CoV-2 positive index case. Complete blood counts, liver and renal profile, chest X-ray, and sputum/gastric aspirate for cartridge-based nucleic acid amplification test (CBNAAT) were done for all tuberculosis patients (as per NTEP guidelines). Additionally, MGIT cultures along with line probe assay (LPA) for drug resistance testing and phenotypic drug sensitivity testing (DST) were done, wherever applicable. The antibody test was done by ECLIA (enhanced chemiluminescence immunoassay).

*Statistical analysis:* Data were compiled in a Microsoft office excel sheet and analyzed with IBM SPSS 26.0. Chi-squared test was used to test the association between categorical variables. Kolmogorov-Smirnov was used to test the normality of the data. If the normality was rejected, then non-parametric tests for significance were used. For factors associated with SARS-CoV-2 positive status in children with TB, bivariate logistic regression analysis was applied while adjusting for potential confounders. A *P* value less than 0.05 was considered statistically significant.

## RESULTS

A total of 137 (35% males) and 154 (59.1% males) children were enrolled in the TB and Non-TB groups, respectively. The baseline characteristics of the participants in the two groups are shown in **Table I**.

Out of 137 patients with tuberculosis, 108 had either a positive RT-PCR or COVID-19 antibodies. Of these 108 children, the majority (93.5%) were asymptomatic. Out of 7 symptomatic children, five had a fever, nine had a cough, six had increased respiratory activity, 2 had lethargy, and one had vomiting with abdominal pain. In the non-TB group, 111 children were RT-PCR positive, and 11 were antibody positive, with fever being the most common symptom in 78 children, followed by cough in 65; 36.1% children were asymptomatic. A history of close contact with the SARS-CoV-2 positive index case was found in 10 (9.3%) children in the TB group and 15 (12.3%) children in the non-TB group.

In the TB group, 106 patients with evidence of COVID-19 recovered completely, whereas two patients died. In the Non-TB group, 118 patients recovered completely, and four died. The two deaths in the TB group were patients with disseminated MDR TB. Upon comparing the outcomes of COVID-19 in both groups, there was no difference in mortality risk of COVID-19 infection in children having tuberculosis as compared to those without tuberculosis [95% CI 0.56 (0.09 – 3.10); *P*=0.50]

## DISCUSSION

Majority of children with tuberculosis were asymptomatic for COVID-19, as also reported previously [17]. Amongst those with symptomatic COVID-19 and tuberculosis, cough and fever were the predominant symptoms. Several studies have shown that the most common presentation of COVID-19 infection is fever and cough [17,18].

Similar to a previous Indian study [19], we also found <5% of children with tuberculosis infected with SARS-CoV-2 [19]. A study on mouse models [22], where activation of a stem cell defence mechanism accelerated the activation of dormant tuberculosis, indicates a potential increase in active tuberculosis post-COVID-19 infection.

A meta-analysis reported a 2.1 fold increase in severity of COVID-19 in those with tuberculosis, although it was not statistically significant [10]. Liu, et al. studied the severity of COVID-19 in 36 patients

with tuberculosis in which 78% patients were in the severe/critical category, while mild/moderate cases were just 22% of the total, which was in contrast with our study [25]. However, all these studies have focused only on adult population, in whom the incidence of other co-morbidities is also high.

In both groups, the majority of the mild cases recovered only with symptomatic treatment. The use of immunosuppressive drugs for COVID-19 remains an area of concern, as it can potentially increase the risk of reactivation of latent tuberculosis. In our study, amongst those children who died, only two children were treated with remdesivir and steroids were used in nine children.

No difference was noted in the outcome of SARS-CoV-2 infection in children with or without tuberculosis in this study, as also seen in other studies around the world.

*Ethics clearance:* IEC, Grant Government Medical College; No. IEC/Pharm/RP/570/Sep/2021, dated Sep, 2021.

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*Contributors:* All authors were involved in concept and designed the study, collected and analyzed data, and drafted, revised the manuscript the manuscript. All authors approve the present version for publication, and are accountable for all aspects related to the study.

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#### WHAT THIS STUDY ADDS?

- No difference was noted in the outcome of SARS-CoV-2 infection in children with and without tuberculosis.

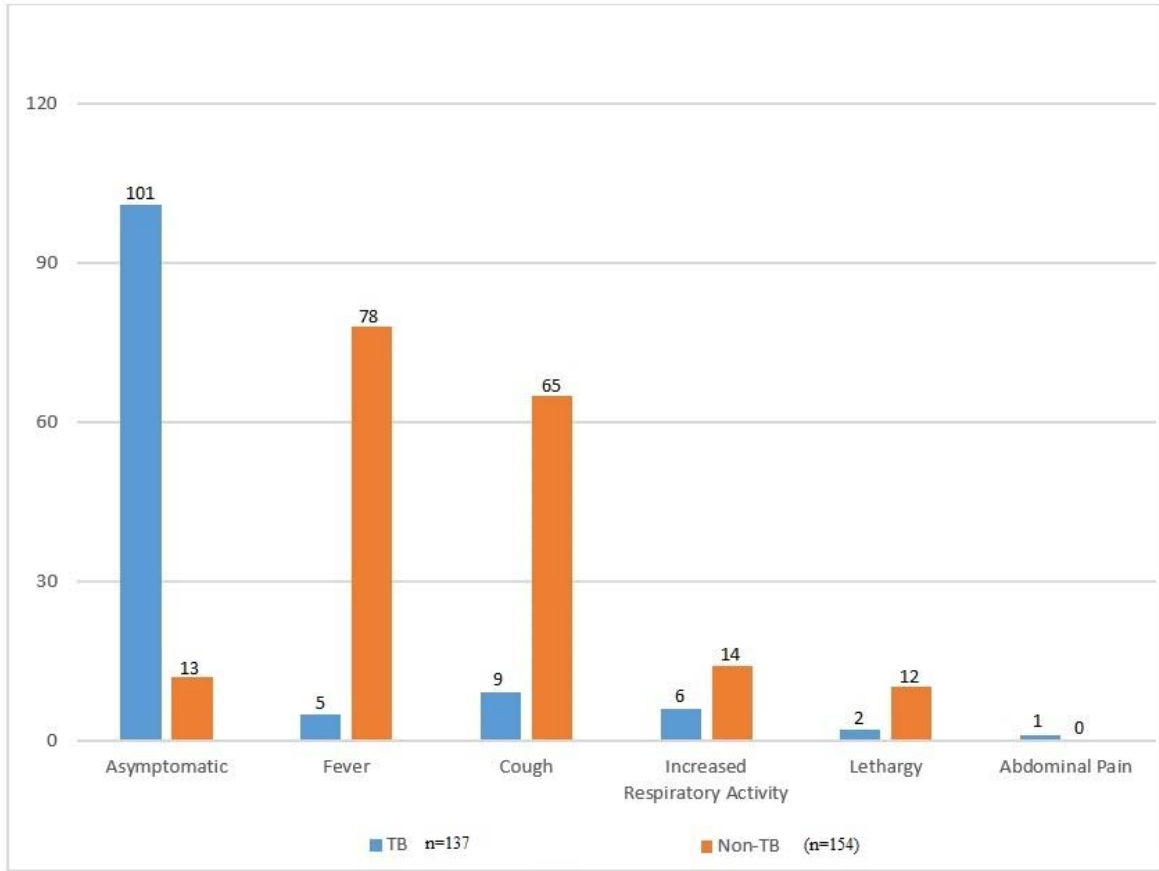
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**Table I Characteristics of Children With COVID-19 With or Without Tuberculosis Enrolled in the Study**

	<i>TB group (n=137)</i>	<i>Non-TB Group (n=154)</i>
Age <sup>a</sup> (y)	11 (6)	4.5 (7)
Females gender	89 (65)	63 (40.9)
RT-PCR Positive	6 (4.3)	111 (79.3)
COVID-19 Antibody positive	102 (74.4)	11 (7.69)
Neither Antibody nor RT-PCR Positive	29 (21.2)	32 (12.9)

*Data in no. (%) or <sup>a</sup>median (IQR). Mortality rate was 1.85% in children with Tuberculosis as compared to 3.27% in non-TB group (P>0.05).*



**Fig. 1** Symptoms of COVID-19 in children with (TB) and without TB (non-TB ).