

## Clinical profile of Tuberculosis in COVID-19 patients at tertiary care center- An observational study

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**Type of Publication:** Original Research Article

**Conflicts of Interest:** Nil

### Abstract

**Background:** This study is aimed to determine the prevalence of tuberculosis in COVID-19 patients in a tertiary care hospital.

**Methods:** The is a hospital - based prospective observational study carried out at a tertiary care center in vidharbha region of Maharashtra, to analyze the clinical profile of tuberculosis in COVID-19 patients.

**Results:** 230 Covid-19 patients were included in this study. Total 33 (14.34%) were detected as Tuberculosis of which PTB in 27(81%) & EPTB in 6(18.18%). From this study, mean age of patients with COVID-19/TB patients was found to be  $51.87 \pm 11.78$

years, males outnumbered females, more than fifty percentage (52.6%) participants were from rural area, most common comorbidity recorded was acute respiratory diseases (ARDS) (42.4%), cough (90.9%) was predominant symptom, 50% of patients needed oxygenation, mortality in COVID-19 with TB group was in 3 (9.1%) found to be significantly less than COVID-19 group in 31 (15.7%).

**Conclusion:** Patients with pulmonary TB suspect are considered a vulnerable group for COVID-19 and require special attention and appropriate preventive measures to prevent development of COVID-19. Early detection, isolation and prompt management of both

covid and PTB is crucial to prevent the progression, complications and mortality, ther by reducing the need for critical care in patients co-infected with COVID-19 & Tuberculosis

**Keywords:** COVID-19, Tuberculosis, PTB & EPTB, COVID-19/TB group, ARDS.

## Introduction

The World Health Organization declared the novel coronavirus outbreak a public health emergency, and the Coronavirus disease 2019 (COVID-19) pandemic remains a major global health crisis. As of September 30th, more than 33 million people in 188 countries had been affected. More than a million people have been reported dead. Respiratory manifestations continue to predominate among symptomatic patients.<sup>1</sup>

Patients with advanced chronic obstructive pulmonary disease, multiple comorbidities, and associated cardio vascular illnesses are reported to have the worst outcome.<sup>2</sup> At the same time, tuber culosis (TB) remains a global burden, with approximately 2.5 million new patients and 0.3 million deaths each year.<sup>3</sup> COVID-19 pandemic caused by the novel coronavirus SARS-CoV-2 is primarily a respiratory illness with symptoms ranging from a common cold to more severe disease, including pneum onia.<sup>4,5</sup>

Human to human transmission occurs through droplet infections, which are inhaled or enter the body by touching infected surfaces. Currently, supportive therapy is the primary treatment modality, though serious illnesses may necessitate ventilator assistance.<sup>6,7</sup>

The ongoing COVID-19 pandemic has wreaked havoc on TB patients. According to the Government of India's Central TB Nikshay portal, the number of new TB cases diagnosed has dropped dramatically since the lockdown. The estimated number of new cases of tuberculosis

detected in government healthcare facilities as of April 27, 2020 was 34,342 compared to 1,56,000 cases in April month of 2019, a 78% decrease.<sup>8</sup> The COVID-19 pandemic has created a global health crisis. However, national TB programmes must be actively engaged to ensure an effective, timely response to COVID-19 while maintaining TB services.<sup>9</sup>

## Materials and Methods

### Study design

The is a hospital-based observational, prospective cross-sectional study carried out at tertiary care Centre to analyze clinical profile of tuberculosis in COVID-19 patients, carried out from 1 May 2021 to 30 November 2022.

**Sample size:** According to study done by Tadolini et al (2020) an active TB & COVID-19/SARI infection 18.3% patients developed TB in COVID-19 patients.<sup>38</sup>

Taking prevalence of 18.3% by formula –

$$n = Z^2 p (1 - p) / d^2$$

where,

Z = statistic corresponding to level of confidence (95%) = 1.96

p = prevalence of TB in COVID-19 patients (18.3%)

d = Margin of error – 5%

The sample size is- 230.

### Patient selection

All the potential candidates with positive rt PCR for Covid -19 admitted in SARI ward and DCH were included in the study, applying exclusion criteria. Written informed consent of the study participants were taken in a local language before collection of information. The information regarding the study variables were recorded on predesigned, predefined questionnaire. Detailed clinical history, personal history,

past history was taken. Physical examination and systematic examination of patients were undertaken after the interview was over. Appropriate sample of patient send for diagnosis of tuberculosis and report were noted.

**Diagnosis of tuberculosis**

was made as per recent guideline by NTEP, based on following criteria-

**Pulmonary tuberculosis**

- Sputum positive for AFB/ CB - NAAT (myco bacterium tuber culosis)- Two sputum samples was collected in screw cap container and one sample in falcon tube. Micro bio logical examination was conducted by ZN/ Floro scent staining at Designated Micro scopy Centre at our college. All samples collected in Falcon tube were processed for CBNAAT/ Truenat. Patients with MTB detected and Rif resistance was subjected for 1<sup>st</sup> line and 2<sup>nd</sup> line Probe Assay at Intermediate Reference Laboratory.
- Mantoux test- It is carried out by injecting intradermaly on the volar surface of forearm 1 TU of PPD in 0.1ml. The result of the test is read after 48 -72 hours. Usually, the induration is measured in the transverse diameter. Reactions of 10 mm or more are considered positive reactions, 6 – 9 mm are considered

doubtful and less than 6 mm are considered negative. More than 20 mm reactions are considered as strongly positive.

- Chest X-Ray positive cases / Sputum negative -Upper zone infiltrates Cavity, Bilateral apical infiltrates, Pulmonary fibrosis

**Extrapulmonary tuberculosis**

Lymph node

- Histopathological study by FNAC/Excision biopsy of Lymph node showing tuberculous granuloma.

**Pleural effusion**

- Pleural fluid analysis showing exudative pattern (increased protein and decreased sugar, ADA) with lymphocytosis

**Pleural fluid**

- AFB/CBNAAT positive
  - Radiological diagnosis (chest X ray, USG, HRCT) and other specific investigations like Lumbar Puncture (for CSF study) for various types of tuberculosis

**Results and Discussion**

Tuberculosis found in 33 patients of COVID-19 with the period prevalence rate of 14.3%.

Table 1: Demographic characteristics And Symptoms

Characteristics	COVID-19 with TB (n= 33)	COVID-19 (n= 197)	Total (n= 230)	P-value
Age (Years)	51.36 ± 10.13	51.41 ± 13.26	51.40 ± 12.84	0.791
Male	23 (69.7)	123 (62.4)	146 (63.5)	0.423
Female	10 (30.3)	74 (37.6)	84 (36.5)	
Urban	22 (66.7)	87 (44.2)	109 (47.4)	0.023
Rural	11 (33.3)	110 (55.8)	121 (52.6)	
Total	33 (100.0)	197 (100.0)	230 (100.0)	
Characteristics	COVID-19/TB (n= 33)	COVID-19 (n= 197)	Total	P value
Fever	29 (87.9)	137 (69.5)	166 (72.2)	0.03
Cough	30 (90.9)	149 (75.9)	179 (77.8)	0.051
Nasal congestion	26 (78.8)	87 (44.2)	113 (49.1)	<0.001
Dyspnea	19 (57.6)	85 (43.1)	104 (45.2)	0.123

Sore throat	20 (60.6)	66 (33.5)	86 (37.4)	0.003
Headache	1 (3.0)	22 (11.2)	23 (10.0)	0.149
Loss of taste	6 (18.2)	36 (18.3)	42 (18.3)	0.990
Loss of smell	13 (39.4)	35 (17.8)	48 (20.9)	0.005
Chest pain	10 (30.3)	18 (9.1)	28 (12.2)	0.001

Mean age of patients with COVID-19/TB patients was found to be 51.87 ± 11.78 years, males outnumbered females, more than fifty percentage (52.6%) participants

were from rural area, most common comorbidity recorded was acute respiratory diseases (ARDS) (42.4%), cough (90.9%) was predominant symptom,

Table 2: Site of TB

Site of TB	Frequency	Percentages
Pulmonary	27	81.82
Extrapulmonary	6	18.18
Tubercular pleural effusion	3	9.09
Tubercular lymphadenitis	2	6.06
Miliary tuberculosis	1	3.03
Total	33	100.0

Among thirty-three patients, twenty-seven (81.82%) patients had pulmonary tuberculosis whereas six patients had extrapulmonary tuberculosis in the form of pleural

effusion (9.09%), tubercular lymphadenitis (6.06%), miliary tuberculosis (3.03%).

Table 3: Diagnosis and diagnostic tests

Diagnosis and diagnostic tests	Frequency	Percentage
Pulmonary TB (n= 27)		
Sputum smear positive	23	85.19
CBNAAT confirmed	27	100.0
Mantoux test	19	70.37
Radiologically positive finding	21	77.78
X- ray	20	
HRCT	1	
ZN staining	23	69.70
Plural effusion (n=3)		
ZN stain	0	0.0
Culture	0	0.0
CBNAAT	1	33.33
Plural fluid ADA (>40 IU)	3	100.0
Tubercular lymphadenitis (n= 2)		
FNAC suggestive of TB	2	100.0
USG (mesenteric lymphadenopathy)	2	100.0
Miliary TB (n= 1)		
X ray (miliary pattern)	1	100.0
HRCT (consolidation)	1	100.0

CBNAAT conformed diagnosis of pulmonary tuberculosis in 100% patients. Plural fluid ADA level of >40 IU were found in 100% patients with tuberculosis plural effusion. For tuberculosis lymphadenitis, FNAC shows

pathological abnormalities were noted in all patients. Miliary tuberculosis were diagnosed with miliary pattern on X ray and consolidation on HRCT.

Table 4: Comparative analysis of complications

Complications	COVID-19/TB (n= 33)	COVID-19 (n= 197)	P value
ARDS	11 (33.3)	68 (34.5)	0.052
DVT	0 (0.0)	3 (1.5)	0.475
PE	0 (0.0)	4 (2.0)	0.439
Sepsis	4 (12.1)	6 (3.0)	0.043
Respiratory failure	1 (3.0)	21 (10.6)	0.031
Myocardial infarction	1 (3.0)	13 (6.6)	0.077
CVA	1 (3.0)	14 (7.1)	0.061

The complication rate comparisons are ARDS – 33.3% in the COVID-19/TB group versus 34.5% in the COVID-19 group (P =0.052); respiratory failure – 3.0% versus 10.6% (P =0.031); DVT – 0.0% versus 1.5% (P =

0.764). Sepsis was recorded in the COVID-19/TB group (12.1%), compared with 3.0% in the COVID- 19 group (P= 0.043).

Table 5: Need for Oxygenation

Ventilation and oxygen therapy	COVID-19/TB (n= 33)	COVID-19 (n= 197)	Total (n= 230)	P value
No ventilation	23 (69.7)	79 (40.1)	102 (44.3)	0.002
Nasal cannula	3 (9.1)	17 (8.6)	20 (8.7)	0.845
Oxygen mask	4 (12.1)	63 (32.0)	67 (29.2)	0.029
Mechanical ventilation	1 (3.0)	29 (14.7)	30 (13.0)	0.708
CPAP	2 (6.1)	9 (4.6)	11 (4.8)	0.710

We analyzed the need for oxygen (Table 5). A total of nearly 50.0% of all patients required oxygenation. At the same time, the need for oxygen therapy in patients with

COVID-19/TB was significantly less than in the group of patients without TB (4 [12.1] vs 63 [32.0], P = 0.029).

Table 6: Outcome of COVID-19 patients and COVID-19 with TB patients

Outcome	COVID-19 with TB	COVID-19	Total	P-value
Death	3 (9.1)	31 (15.7)	34 (14.8)	<0.001
Discharge	30 (90.9)	166 (84.3)	196 (85.2)	
Total	33 (100.0)	197 (100.0)	230 (100.0)	

Mortality in COVID-19 with TB group was in 3 (9.1%) found to be significantly less than COVID-19 group in 31 (15.7%).

**Discussion**

- In present study, mean age of patients with COVID-19/TB patients was about 51.87 ± 11.78 years. Similarly,

Parolina L et al<sup>10</sup> reported mean age of COVID-19/TB patients were 48 years.

- Male outnumbered the female. Number of males in COVID-19/TB group and COVID-19 group were 23 (69.7%) and 123 (62.4%) respectively. It is similar to the study conducted by Mane SS et al<sup>11</sup> number of male in COVID-19/TB and COVID-19 group were 65.0% and 40.9% respectively.

- Of all the patients 52.6% participants were from rural area and 44.2% from urban area. In COVID-19/TB group 66.7% of patients belong to urban area and in COVID-19 group 55.8% of patients belong to rural patients. The association between place of residence and status of tuberculosis in COVID -19 patients were statistically significant ( $P= 0.023$ ). Also, in a study conducted by Sereda Y et al<sup>12</sup>, most of the participants were from urban area (81.8%). Among urban residents 4.9% of residents belong to tuberculosis group.

- Most common comorbidity recorded among COVID 19/ TB cases were chronic respiratory diseases (21.3%) followed by DM (18.2%), chronic kidney disease (15.2%). Comorbidities noted in another study by Tadolini Met al<sup>13</sup> were COPD (17.0%), DM (16.3%), HIV infection (12.5%), renal disease (10.2%), liver diseases (14.3%).

- Cough (90.9%) was found most prominent symptom in patients with COVID-19/TB patients. Fever was reported among 87.9% patients followed by nasal congestion (78.8%), sore throat (60.6%), dyspnea (57.6%). Other noted symptoms include headache, loss of taste, loss of smell and chest pain. Similar to current study Radulescu et al<sup>14</sup>, most common reported symptom were cough (80.0%) followed by fever (20.0%), dyspnea (60.0%), hemoptysis (10.0%).

- In this study, mechanical ventilation was needed to 3.0% patients with COVID-19/TB patients, while 6.1% needed CPAP. Oxygen was supplied with O<sub>2</sub> mask in 12.1 patients, by nasal canula in 9.1% patients. In a study undertaken by Karthik Adegga B et al<sup>15</sup> 19% patients needed mechanical ventilation.

- Mortality rate in COVID-19 with TB group (9.1%) was found to be less than COVID-19 group (15.7%). This difference was found to be significant statistically ( $P < 0.001$ ). Outcome of present study also contrast to the study by Serede Y et al<sup>12</sup> where mortality rate were 2.3%

#### **Limitations and future prospectives:**

1. Although the group of patients without TB was recruited randomly, its size implies that the results should be interpreted with caution. As more data becomes available, it will be important to identify factors that influence mortality and complications in patients with TB diagnosed with COVID-19.

2. The limitations of the study were that the role of pathological and biochemical factors, such as D-dimer, C reactive protein, IL-6 and ferritin, etc., and use of investigational drugs, such as tocilizumab, remdesivir, favipiravir and steroids

3. for patient management were not studied, as neither of these were a component of national treatment guidelines during the study period. Also, because of the small sample size, analysis of various risk factors was not carried out.

#### **Conclusion**

Patients with Tuberculosis are considered another vulnerable group for COVID-19 and require special attention and appropriate preventive measures in this ongoing COVID-19 pandemic. Further early diagnosis and isolation of Tuberculosis and COVID-19 is the key to prevent future spread in the community and thereby

minimizing the need of critical care and to prevent the morbidity and mortality of COVID-19/TB coinfecting patients.

#### Ethics approval and consent to participate

The Study was approved by Institutional Ethics Committee. Complete confidentiality of the data is maintained by the principal investigator.

#### List of Abbreviations

AFB- Acid Fast Bacilli, ALT- Alanine Transaminase, AOR- Adjusted Odds Ratio, ARDS- Acute Respiratory Distress Syndrome, AST- Aspartate Trans amine, CBNAAT- Cartridge Based Nucleic Acid Amplification Test, CI- Confidence Interval, COVID-19- Coronavirus Disease, CPAP- Continuous Positive Airway Pressure, CVD- Cardiovascular diseases, DM- Diabetes Mellitus, DVT- Deep Venous Thrombosis, DOTS- Directly observed treatment, short-course, DLC- Differential Leukocyte Count, FNAC- Fine Needle Aspiration Cytology, GFR- Glomerular Filtration Rate, HRCT- High resolution computer tomography, SARS- Severe Acute Respiratory Syndrome, TB- Tuberculosis, TLC- Total Leukocyte Cell, WBC- White Blood Cell, WHO- World Health Organization, ZN stain- Ziehl-Neelson stain

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