A profile of a retrospective cohort of 22 patients with COVID-19 and active/treated tuberculosis

To the Editor:

We read with interest the two articles by Tadolini *et al.* [1] and Stochino *et al.* [2], which described recent cohorts of either current or former tuberculosis (TB) patients with coronavirus disease 2019 (COVID-19) and studied their clinical course. India has the majority of global burden of TB, along with highest rising number of daily COVID-19 cases in the world [3, 4]. The information about COVID-19 and active/former TB co-infection reported so far is sparse, but it can be assumed that person with TB, when co-infected with COVID-19, may be at more risk of poor outcomes [1, 5]. The present study describes the first-ever cohort of current or treated TB patients co-infected with COVID-19 from a high TB burden country, recruited by a tertiary care hospital in India.

This was a retrospective observational study from 1 February 2020 to 14 June 2020, during which a total of 1073 consecutive COVID-19 patients were admitted. Out of these, 22 cases with a diagnosis of active/treated TB and COVID-19 co-infection were included in the study.

Among 22 patients with COVID-19 and TB co-infection, 13 (59.1%) patients had active TB (median age (interquartile range (IQR)) 36 (27–59.5) years) and nine (40.9%) patients had been treated for TB (median age (IQR) 44 (28–51) years) in the past. Among the active TB group, 11 (84.6%) were females and among the treated TB group, all patients were females. Out of the 13 active TB patients, 12 patients were already receiving anti-TB treatment (ATT) (median duration (IQR) 2 (1–3) months) at the time of admission, while one patient was newly diagnosed with pulmonary TB within a week of admission. The demographic, clinical, radiological and laboratory investigation details, and outcomes of each of the 22 patients, are described in table 1.

All patients, except one, were symptomatic at the time of presentation. All 12 patients with active TB, who were already receiving ATT at the time of admission, had become almost asymptomatic for TB symptoms. Among them, signs and symptoms attributed to COVID-19 included fever (100%), dry cough (53.8%) and dyspnoea (30.8%) (median (range) duration 2 (2–30) days). Nine treated TB patients were also almost asymptomatic for TB prior to the development of current COVID-19 infection. Among them fever (88.9%), dry cough (44.4%) and dyspnoea (33.3%), respectively were present (median (range) duration of 5 (2–30) days), which could be attributed to COVID-19 disease. Radiological examination, conducted at admission, revealed pulmonary parenchymal fibrosis in all patients in the treated TB group with three (33.3%) patients having accompanying residual cavitation as well. Among the 13 active TB patients, nine (69.2%) had pulmonary TB and four (30.8%) had extra-pulmonary TB. Among the nine active pulmonary TB patients, cavitation was present in three (33.3%), and six (66.7%) had parenchymal infiltrates/consolidation on chest radiography but no cavitation. Among four active extra-pulmonary TB patients, one had cerebral tuberculoma, two had pleural effusion, and one patient had only cervical lymphadenopathy. One active pulmonary TB patient had multidrug-resistant (MDR) TB (isoniazid and rifampicin resistant), receiving conventional MDR treatment regimen as per national guidelines. All treated TB cases had had pulmonary TB.

Lymphopenia was found in only one patient. In all, seven patients (31.8%) required critical care, 4/13 (30.7%) in the active TB group and 3/9 (33.3%) in the treated TB group. All but one patient who required

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TABLE 1 Characteristics of 22 patients co-infected with active/treated tuberculosis (TB) and coronavirus disease 2019 (COVID-19)

Patient	Age years/ gender	TB status	Site of TB	ATT history	Clinical presentation on admission	Comorbidities	S_{pO_2} %, respiratory rate per min, GCS, qSOFA	Laboratory findings	Findings in chest radiograph prior to COVID-19	Bilateral new infiltrates, consistent with COVID-19, on CXR	Required critical care, required IMV	Duration of hospital stay days	Endpoint attained (discharged/ died)
1	54/Male	Treated	PTB	Completed DS-TB regimen 2 years earlier	Fever for 2 days	Hypertension, hypothyroidism	S_{pO_2} 98, RR 19, GCS 15, qSOFA 0	TLC 4800 (48% lymphocytes)	Right lung fibrosis	Yes	No	15	Discharged
2	58/Male	Treated	PTB	Completed DS-TB regimen 1 year earlier	Fever for 5 days		S_{pO_2} 95, RR 24, GCS 15, qSOFA 1	TLC 8500 (40% lymphocytes)	Right lung fibrosis	Yes	No	7	Discharged
3	44/Male	Treated	PTB	Completed DS-TB regimen 2 years earlier	Fever for 6 days		S_{pO_2} 98, RR 20, GCS 15, qSOFA 0	TLC 4100 (31% lymphocytes)	Left lung fibrosis	No	No	15	Discharged
4	19/Male	Treated	PTB	Completed DS-TB regimen 1 year earlier	Asymptomatic		S_{pO_2} 95, RR 18, GCS 15, qSOFA 0	TLC 4400 (45% lymphocytes)	Left lung fibrosis	No	No	15	Discharged
5	26/Male	Treated	PTB	Completed DS-TB regimen 2 years earlier	Fever and cough 3 days		S_{pO_2} 95, RR 18, GCS 15, qSOFA 0	TLC 5300 (30% lymphocytes)	Right lung fibrosis	No	No	5	Discharged
6	48/Male	Treated	PTB	Completed DS-TB regimen 1 year earlier	Breathlessness for 2 days, fever and cough for 2 weeks	Diabetes mellitus	S_{pO_2} 80, RR 38, GCS 4, qSOFA 3	TLC 8200 (42% lymphocytes)	Left lung fibrosis and left upper zone cavity	Yes	Required critical care and IMV	<1	Died
7	30/Male	Treated	PTB	Completed DS-TB regimen 2 months earlier	Fever for 3 days		S_{pO_2} 99, RR 20, GCS 15, qSOFA 0	TLC 7700 (42% lymphocytes)	Right lung fibrosis and right upper zone cavitation	No	No	16	Discharged
8	38/Male	Treated	PTB	Completed DS-TB regimen 6 years earlier	Fever, cough and breathlessness for 5 days		S_{pO_2} 81, RR 38, GCS 3, qSOFA 3		Left lung fibrosis	Yes	Required critical care and IMV	<1	Died
9	45/Male	Treated	PTB	Completed DS-TB regimen 6 months earlier	Breathlessness for 2 days, fever for 5 days, cough for 1 month		S_{pO_2} 78, RR 32, GCS 3, qSOFA 3	ABGA, respiratory acidosis	Left lung fibrosis and upper and mid zone cavitation	Yes	Required critical care and IMV	<1	Died
10	45/Male	Active	PTB	On DS-TB regimen for 1 month	Fever, headache, cough, breathlessness for 3 days		S_{pO_2} 86, RR 32, GCS 3, qSOFA 2	Hb 10.4, TLC 15000 (10% lymphocytes), Plt 180000, blood urea 125, creatinine 6.5, total bilirubin 0.5, AST 456, ALT 178	Left upper zone cavitation	Yes	Required critical care and IMV	2	Died
11	26/Male	Active	PTB	On DS-TB regimen for 3 months	Fever for 2 days		S_{pO_2} 94, RR 20, GCS 15, qSOFA 0	TLC 8000 (20% lymphocytes)	Right upper zone infiltrates	No	No	20	Discharged
12	63/Male	Active	PTB	On DS-TB regimen for 2 months	Breathlessness for 5 days, fever for 12 days		S_{pO_2} 92, RR 24, GCS 15, qSOFA 1	TLC 9000 (40% lymphocytes)	Right upper zone cavitation	Yes	No	24	Discharged

Continued

TABLE 1 Continued

Patient	Age years/ gender	TB status	Site of TB	ATT history	Clinical presentation on admission	Comorbidities	S_{pO2} %, respiratory rate per min, GCS, qSOFA	Laboratory findings	Findings in chest radiograph prior to COVID-19	Bilateral new infiltrates, consistent with COVID-19, on CXR	Required critical care, required IMV	Duration of hospital stay days	Endpoint attained (discharged/ died)
13	29/Male	Active	PTB	On DS-TB regimen for 1 month	Fever for 2 days		S_{pO_2} 98, RR 16, GCS 15, qSOFA 0	TLC 8500 (30% lymphocytes)	Left mid zone consolidation	No	No	15	Discharged
14	65/Female	Active	PTB	On MDR-TB regimen for 1 year	Fever, cough and breathlessness for 5 days	Diabetes mellitus, hypertension	S_{pO_2} 76, RR 34, GCS 4, qSOFA 3	ABGA, high anion gap metabolic acidosis, diabetic ketoacidosis with blood sugar value of 470 mg·dL^{-1}), blood urea 70, creatinine 3.8, TLC 17300 (22% lymphocytes)	Right upper, mid and lower zone consolidation	Yes	Required critical care and IMV	1	Died
15	29/Male	Active	EPTB (CNS-TB)	On ATT for CNS-TB for 12 months	Fever and cough for 1 month with weight loss	Seizure disorder	S_{pO_2} 90, RR 24, GCS 15, qSOFA 1	TLC 800 (26% lymphocytes)		Yes	Required critical care but not IMV#	20	Discharged
16	26/Male	Active	PTB	On DS-TB regimen for 4 months	Fever and cough for 2 days		S_{pO_2} 95, RR 20, GCS 15, qSOFA 0	TLC 8100 (40% lymphocytes)	Right upper zone infiltrates	Yes	No	8	Discharged
17	56/Male	Active	PTB	On DS-TB regimen for 3 months	Fever and cough for 3 days	Hypertension	S_{pO_2} 93, RR 18, GCS 15, qSOFA 0	TLC- 9700 (36% Lymphocytes)	Left upper zone infiltrates	Yes	No	7	Discharged
18	36/Male	Active	Disseminated TB (pulmonary and abdominal)	On DS-TB regimen for 2 months	Fever for 2 days		S_{pO_2} 98, RR 18, GCS 15, qSOFA 0	TLC 7900 (47% lymphocytes)	Left upper zone cavitation	Yes	No	10	Discharged
19	40/Male	Active and newly diagnosed concommitantly with COVID-19	EPTB (pleural effusion)	Initiated on DS-TB regimen	Fever and cough for 2 days		S_{pO_2} 99, RR 16, GCS 15, qSOFA 0	TLC 8300 (39% lymphocytes)	Left pleural effusion	No	No	10	Discharged
20	21/Male	Active	EPTB (cervical LN-TB)	On DS-TB regimen for 1 month	Fever for 2 days		S_{pO_2} 75, RR 36, GCS 4, qSOFA 1	ABGA, high anion gap metabolic acidosis, blood urea 72, creatinine 3.8, TLC 19600 (27% lymphocytes)		Yes	Required critical care and IMV	5	Died
21	28/Female	Active	PTB	On DS-TB regimen for 1 month	Fever for 2 days		S_{pO_2} 95, RR 18, GCS 15, qSOFA 0	TLC 6300 (32% lymphocytes)	Left upper zone infiltrates	No	No	12	Discharged
22	67/Male	Active	EPTB (pleural effusion)	On DS-TB regimen for 2 months	Fever, cough and breathlessness for 3 days	Diabetes mellitus, hypertension, seizure disorder	S_{pO_2} 95, RR 20, GCS 15, qSOFA 0	TLC 3700 (34% lymphocytes)	Right pleural effusion	Yes	No	14	Discharged

PTB: pulmonary tuberculosis; EPTB: extra-pulmonary tuberculosis; CNS-TB: central nervous system tuberculosis; LN-TB: lymph node tuberculosis; ATT: anti-tubercular treatment; DS-TB: drug sensitive tuberculosis; MDR-TB: multi-drug resistant tuberculosis; S_{pO_2}: oxygen saturation by pulse oximetry; GCS: Glasgow coma scale score; qSOFA: quick sepsis related organ failure score; TLC: total leukocyte count (unit: per mm^3); ABGA: arterial blood gas analysis; Hb: haemoglobin (unit: g·dL^{-1}); Plt: platelet count (unit: per mm^3), AST: aspartate transaminase (unit: IU·L^{-1}); ALT: alanine transaminase (unit: IU·L^{-1}); CXR: chest radiograph; IMV: invasive mechanical ventilation. Laboratory parameters for blood urea, creatinine and bilirubin are provided in units of mg·dL^{-1}. #: patient's duration of stay in intensive care unit was 5 days, and on ward was 15 days.

critical care also required invasive mechanical ventilation. Among these, 3/13 (23.1%) patients were from the active TB group and 3/9 (33.3) patients were from the treated TB group. All these six patients died; this group also included one MDR-TB patient.

All six patients who died had hypoxaemia and a Glasgow Coma Scale (GCS) score of 3–4 on admission. Quick sepsis-related organ failure scores were 3 in four patients, and 2 and 1 in one patient each. Death in all deceased patients was attributed to COVID-19 co-infection, as all were otherwise responding clinically and radiologically to ATT in the active TB group or were clinically stable in the treated TB group. Comorbid diabetes mellitus was observed in 3/22 (13.6%) patients and two (66.7%) among them died. None of the patients had HIV. Of the 22 patients, 16 patients (72.7%) were discharged. During the study period, 14 days of admission was mandatory for COVID-19 patients as per national guidelines [6]. Among those discharged, the mean±SD duration of stay was 13.3±5.3 days.

In the present series, among 22 patients with TB and COVID-19 co-infection, the overall mortality rate was 27.3%. This mortality rate, though preliminary, is higher as compared to other studies by Tadolini *et al.* [1] (12.3%) and Motta *et al.* [7] (11.6%) in TB and COVID-19 co-infected patients. A review by Ong *et al.* [8] also found a higher mortality in TB with COVID-19. In India, a mortality rate of around 2.3% has been observed among COVID-19 patients, including patients with comorbid conditions such as diabetes, hypertension, malignancy and tuberculosis, *etc.* [4]. This higher mortality in TB and COVID-19 co-infection could be explained by damage to the lungs by fibrosis or cavitation in treated TB cases, or by active TB disease with superimposed insult of COVID-19 co-infection leading to further deterioration of already compromised lung function.

In the initial cohort of 40 COVID-19 patients who had been admitted to the authors' centre up to 31 March 2020, no patient had active or previously treated TB; however, over the subsequent 6 weeks, the incidence of active and treated TB went up to 1.21 and 0.83 per 100 hospital admissions for COVID-19, respectively [9].

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, for patient management were not studied, as neither of these were a component of national treatment guidelines during the study period [6]. Also, because of the small sample size, analysis of various risk factors was not carried out.

In conclusion, patients with treated or active TB may be considered another vulnerable group for COVID-19 and may require special attention and appropriate preventive measures for development of COVID-19. Further, a high mortality, along with a greater need for critical care, was found in active as well as treated TB patients co-infected with COVID-19.

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Declaration of patient consent: the authors certify that they have obtained written informed consent from the patients to publish their personal details and follow up. The patients understand that their name and initials will not be published but, anonymity cannot be guaranteed. Ethics committee approval was not required as it was a retrospective observational study.

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