Mortality of TB-COVID-19 coinfection in India

M. S. Kumar,[1] D. Surendran,[1] M. S. Manu,[2] P. S. Rakesh,[3] S. Balakrishnan[4]

[1]State TB Cell, and [2]State TB Training and Demonstration Centre, Directorate of Health Services – Kerala, Thiruvananthapuram, [3]State TB Cell, WHO NTEP Technical Support Network, Thiruvananthapuram, [4]Regional Team Lead (South), WHO NTEP Technical Support Network, Cochin, India

Correspondence to: P. S. Rakesh, State TB Cell, WHO NTEP Technical Support Network, Thiruvanathapuram, India. email: rakeshrenjini@gmail.com

Running head: Mortality of TB-COVID coinfection.

Dear Editor,

Kerala, a state in southern Indian, notified 25,617 (750 per million population) TB cases in 2019. The mean age of TB patients in Kerala was 50.27 years (standard deviation [SD] ±17.3); and 21.1% of microbiologically confirmed TB cases were over 65 years of age. Among the cases notified in 2019, death as an outcome was reported in 1,951 cases (7.6%). The mean age of TB patients with death as an outcome was 64.75 (SD ±14.52); 68% of deaths occurred in people over the age of 65. A detailed audit in 2018 revealed that 70% of those deaths were attributed to non-communicable diseases.[1] Preliminary audits for all deaths among TB patients used to be done by a Medical Officer based on all available medical records.

Kerala reported the first COVID-19 case in India, and has had over 20,000 cumulative confirmed cases per million population. The peak of COVID-19 cases in the state was in October 2020 (260 cases per million per day), and overall case fatality due to COVID-19 was 0.4%.[2] The state experienced a reduction of up to 50% in TB notification from April to July

2020 because of COVID-19, but managed to identify 90% of expected TB cases in 2020 through active case finding activities in subsequent months of the year. Because of the difficulty of gaining access to TB services posed by the COVID-19 pandemic, extra effort was made to deliver services for TB patients at their homes, including the provision of medicines for comorbidity management and proactive fortnightly clinical reviews through phone consultations.[3]

The state initiated bidirectional screening of COVID-19 and TB from September 2020,[4] and all TB patients were screened for COVID-19 symptoms. All confirmed COVID-19 patients were screened for TB using the four symptoms complex (cough, fever, weight loss, haemoptysis). COVID-19 patients requiring hospital admissions were also screened for TB using chest X rays. Individuals with influenza-like illness and severe acute respiratory illnesses were also tested for COVID-19 and screened for TB. All identified presumptive TB cases from the above categories were offered testing for TB using an upfront molecular test. Population-based data were captured systematically regarding individuals with TB-COVID-19 coinfection and were recorded real time on NIKSHAY, a case-based, web-based programme management information system of the National TB Elimination Programme.

Among the 177 cases diagnosed with active TB-COVID-19 coinfection, 27 (15.2%) deaths were reported. Among the people who died with TB-COVID-19, COVID-19 was diagnosed only after their death in two cases. Primary death audit reports of all 27 cases were available. The profile of people with TB-COVID-19 is shown in the Table. Death as an outcome was 50% in persons aged >50 years, which increased to 90% among those aged >65 years. Of the 27 who died, 23 had at least one other major comorbidity along with COVID-19 and TB: diabetes ($n = 9$, 30%), systemic hypertension ($n = 6$, 22.2%), chronic kidney diseases ($n = 5$, 18.5%), chronic obstructive pulmonary disease ($n = 3$, 11.1%), hepatic problems ($n = 2$, 7.4%), cerebrovascular accident ($n = 2$, 7.4%), HIV and cancer ($n = 1$ each, 3.7%). Thirteen (48.1%) had more than one major comorbidity other than TB and COVID-19. One died due to myocardial infarction.

Of the 27 who died, the gap between the diagnosis dates for TB and COVID-19 was <7 days in 12 cases, between 8 and 30 days in 12 cases and >30 days in 3 cases. COVID-19 was diagnosed before TB in one patient and both conditions were diagnosed on the same day in two patients. Among the 27 people who died, 7 died within 1 week of diagnosis of TB, 9 between 8 and 30 days, 6 between 31 and 60 days, 2 between 61 and 90 days and 4 after 90 days. Among those who died, the mean delay in initiating treatment for TB after diagnosis was 4.2 days (standard error: 0.93, range 0–18). Five people died before initiating treatment for TB. One

person was diagnosed to have rifampicin resistance and one had extrapulmonary TB. It is anticipated that people who are ill with both TB and COVID-19 may have poorer treatment outcomes. Tadolini et al. and Motta et al. reported respectively 12.3% and 11.6% mortality among individuals with TB-COVID-19 co-infections.[5,6]A recent report from a tertiary care hospital in India among 22 patients with TB and COVID-19 coinfection reported an overall mortality rate of 27.3%.[7]

This is one of the first reports on TB-COVID-19 deaths using state-wide programme data. Because the state has a robust TB surveillance system, including real-time information from the private sector, we believe that there are no missing cases. However, data on any deaths that might have occurred before the attempt to diagnose TB or COVID-19 may not have been captured. This report has limitations as it has not looked into in-depth clinical details. We suggest that mortality among people with TB-COVID-19 co-infection could be attributed to 1) presence of severe comorbidity other than TB and COVID-19; 2) a delayed diagnosis of TB; and 3) further damage to the lungs of already compromised lung function among TB patients from the added insult of COVID-19 co-infection. A comparison of clinical details of deaths due to TB without COVID-19 and TB-COVID-19 coinfection will provide further insight into the risk factors for death.

An early diagnosis of both TB and COVID-19 is important in the care of the elderly and those with non-communicable diseases, who are particularly vulnerable to unfavourable outcomes.

References

1   Karthika M, et al. Why are people dying due to tuberculosis? A study from Alappuzha District, Kerala, India. Indian J Tuberc 2019; 66(4): 443–447.

2   Government of India. COVID-19-19 state-wide status. New Delhi, India: GOI, 2020. https://www.mohfw.gov.in/ Accessed December 2020

3   Government of Kerala. Advisory for ensuring continuity of TB services in Kerala in the context of COVID-19. No 31/F2/2020 20th April 2020. Thiruvananthapuram, India: Government of Kerala, 2020. https://dhs.kerala.gov.in/wp-content/uploads/2020/04/Advisory-on-TB.pdf

4   Government of Kerala. Integrated diagnostic algorithm for diagnosis of TB in Kerala in the context of COVID-19. No 31/F2/2020 11th September 2020. Thiruvananthapuram, India: Government of Kerala, 2020. https://dhs.kerala.gov.in/wp-content/uploads/2020/09/Guidelines-Integrated-TB-Diagnosis-algorithm-in-context-COVID-19.pdf

5   Tadolini M., et al. Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases. Eur Respir J https://doi.org/10.1183/13993003.01398-2020

6   Motta I, et al. Tuberculosis, COVID-19-19 and migrants: Preliminary analysis of deaths occurring in 69 patients from two cohorts. Pulmonology 2020; 26(4): 233–240.

7   Gupta N, et al. A profile of a retrospective cohort of 22 patients of COVID-19-19 with active/treated tuberculosis. Eur Respir J 2020; https://doi.org/10.1183/13993003.03408-2020

Table. Profile of individuals with TB-COVID-19 coinfection in Kerala, October–November 2020

Characteristics	A. Deaths among individuals with both TB and COVID-19 ($n = 27$) n (%)	B. Total individuals with TB-COVID-19 coinfection ($n = 177$) n (%)	Fatality rate (%) (A/B*100)
Age group, years			
<15	0 (0)	1 (0.5)	0
15–24	1 (3.7)	34 (19.2)	2.9
25–34	0 (0)	32 (18.0)	0
35–44	4 (14.8)	38 (21.4)	10.5
45–54	4 (14.8)	35 (19.7)	11.4
55–64	9 (33.3)	26 (14.6)	34.6
65–74	6 (22.2)	7 (3.9)	85.7
≥75	3 (11.1)	3 (1.6)	100
Sex			
Male	22 (81.5)	138 (77.9)	15.9
Female	5 (18.5)	39 (22.1)	12.8
Comorbidity			
Diabetes mellitus	9 (33.3)	53 (29.9)	16.9
Hypertension	6 (22.2)	71 (40.1)	8.4
Chronic kidney disease	5 (18.5)	11 (6.2)	45.4
Chronic respiratory diseases	3 (11.1)	12 (6.7)	25.0
Liver diseases	2 (7.4)	4 (2.2)	50.0
Cerebro vascular accident	2 (7.4)	5 (2.8)	40.0
Cancer	1 (3.7)	2 (1.1)	50.0
HIV	1 (3.7)	2 (1.1)	50.0
More than one comorbidity other than TB and COVID-19	13 (48.1)	32 (19.1)	40.6