Impact of COVID-19 pandemic on Tuberculosis

Running title: Impact of COVID-19 on TB

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Abstract

Background: Tuberculosis, disease of respiratory system which spreads when patient coughs, sneezes or spits. COVID-19, another respiratory disease created havoc in 2020 and 2021. During this pandemic, the whole healthcare system was diverted into COVID-19 patient care. It is important to determine, what status of Tuberculosis was during COVID-19 period. This study was mainly undertaken, to detect occurrence of *Mycobacterium tuberculosis* (*M.tuberculosis*) and rifampicin resistance before, during, and after COVID-19 restrictions were fully released.

Methods: Pulmonary and extrapulmonary samples from 1st January 2018 till 31st December 2022 were included in present retrospective study. The period was divided as- 2018, 2019 - Before COVID-19 2020, 2021 -COVID-19 period with restrictions (such as use of masks, social distancing, avoiding gatherings) 2022 –COVID-19 period without restrictions. All samples received in TB section were subjected to Cartridge-Based Nucleic Acid Amplification Test (CBNAAT). Samples were processed according to manufacturer's guidelines.

Results: There was no significant difference in samples received per year from 2018 to 2022. The positivity of *M. tuberculosis* decreased from 22.52% in the pre-COVID-19 period to 15.70% in COVID-19 period with restrictions and increased again in 2022 (16.80%). Rifampicin resistance decreased from 10.40% to 6.89% in the COVID-19 period with restrictions. A decrease in positivity was not observed in extrapulmonary tuberculosis cases.

Conclusion: In present study, total samples for tuberculosis received over period of five years were relatively same. Restrictions imposed during COVID-19 period could have decreased Tuberculosis and rifampicin resistance. Thus, imposing restrictions on TB-suspected and positive patients regularly can help prevent the spread of the disease.

Keywords: COVID-19; Mycobacterium *tuberculosis*; Rifampicin

Introduction

India contributes almost a quarter of the global Tuberculosis (TB) burden (1).It is the second most common cause of death among infectious diseases (2).The silent epidemic of TB was been overshadowed by the COVID-19 pandemic which began in March 2020, and majorly continued till January 2022 and few cases are found till now. The focus in the years 2020 to 2021 was completely on COVID-19. The peak of the first wave of the pandemic was in mid-September when there were more than one million active cases in the country, with the highest single-day spike of 97,894 new cases recorded on September 16, 2020 (3). By the end of February 2021, there was a sharp rise in the number of daily reported cases, which culminated in the second wave of the pandemic (4). The third wave began in December 2021 and remained up to January 2022.The pandemic continues and few cases are found till date. But as COVID-19 and TB are the diseases of respiratory system they might have an impact on each other. Having a reliable estimate of the association between tuberculosis and COVID-19 severity and mortality is crucial to ensure specific successful global preventive and treatment strategies for TB patients (5).When a patient suffers from a previous respiratory disease, the patient's lung function is impaired, and their resistance to viruses is low and they tend to develop acute respiratory distress syndrome (6). Both pathogens may lead to an unbalanced inflammatory immune response, and together a shared dysregulation of immune response suggests an increased risk of severity and progression of both diseases (7). This study was mainly conducted to see the impact of COVID-19 on TB whether the cases have raised or have fallen in the pandemic period. This study was conducted mainly to see isolation, lockdown, strict quarantine measures that were taken for COVID-19 were effective for TB also. Our aim of study was to detect the *Mycobacterium tuberculosis* (*M.tuberculosis*) and rifampicin resistance before, during COVID restrictions and after COVID-19 restrictions were fully released.

Methods

Type of study: Retrospective
Duration of study: 1st January 2018 to 31st December 2022. The COVID-19 free period was considered 2018 to February 2020, COVID-19 with restrictions were from March 2020 (8) to June 2021 (9), COVID-19 without restrictions were considered from July 2021-December 2022.
Inclusion criteria: Patients of all age group and gender clinically suspected to have TB.
Exclusion criteria- Samples received for tests other than TB.
Procedure: Early morning deeply expectorated sample were collected from clinically suspected cases of Tuberculosis, was taken in sterile wide mouth container after taking consent from the patient. Extrapulmonary samples were collected depending on the site. The samples were subjected to GeneXpert MTB/RIF manufactured by Cepheid, France for detection of *M.tuberculosis* and rifampicin resistance in them. They were processed according to manufacturer's guidelines.

Results

Our study is a five-year retrospective study conducted from 2018 to 2022. Samples of all age groups and gender irrespective of any co-morbid condition, drug history were included in study. The total number of pulmonary and extra-pulmonary samples received is as given in table no. 1. This study was mainly conducted to see the impact of COVID-19 on TB. To our surprise it was found that, positivity for *M.tuberculosis* was 20.9%, 18.2%, 15.5%, 15.8% and 16.8% from year 2018-2022 respectively (Table 2). The rifampicin resistance detected during same years was

11.0%, 9.8%, 7.3%, 6.4% and 11.9% respectively (Table 2). This result was found to be statistically significant (p value 0.042, significant value < or = 0.05). *M.tuberculosis* detected from extra pulmonary samples was minimum (11.58%) in 2020 which increased in later years (Table no. 3). No significant change in Rifampicin resistance was noted for extrapulmonary samples.

Discussion

This study was conducted in a tertiary care hospital from 1st January 2018 to 31st December 2022.The total samples received for *M.tuberculosis* from 2018-2022 were 3543,3823,3682,3248 and 3381 respectively. Samples positive for *M.tuberculosis* were 20.9%, 18.2%, 15.5%, 15.8% and 16.8% from year 2018-2022 respectively. The rifampicin resistance detected during years 2018-2022 was 11.0%, 9.8%, and 7.3%, 6.4% and 11.9% respectively.

During the period under study, two years i.e. 2020 and 2021 was a COVID-19 pandemic period in India. Moreover, many restrictions were imposed to stop the spread of COVID-19 during these years like wearing masks, avoiding social gatherings, maintaining social distancing etc. which are all the isolation measures. It was observed that, the positivity of Tuberculosis in our tertiary care hospital was decreased in years 2020 and 2021. The rifampicin resistance was also decreased during the same period.

In the present study, 2018 and 2019 can be considered as the pre-COVID-19 period and 2022 as the COVID-19 period without restrictions. *M.tuberculosis* positivity and rifampicin resistance were higher in the pre-COVID-19 (22.5%) and post-COVID-19 period (16.8%) compared to the COVID-19 period with restrictions (15.7%).

Tuberculosis and COVID-19 are diseases of the respiratory system and they spread through droplet nuclei (10). Isolation measures followed during COVID-19 may have contributed in decreasing cases of tuberculosis during 2020 and 2021.

The importance of masks in prevention of airborne diseases has been mentioned by CDC and Asadi et al (11,12). Moreover, the lockdowns would have done a major impact as people were scared of COVID-19 so they had minimal contact with family members also during that period. This must have prevented infection in household contact as well as in community. After that, vaccination was introduced widely in India. In 2021, every hour India reported around 1.6 lakhs vaccination (12). At the same time, COVID-19 cases started decreasing and restrictions were partially released. In 2022, the milder omicron wave was documented but strict restrictions were not imposed again. This could be the major reason for increase in cases in 2022. In the study conducted by G.B.Miligori et al, they found that, TB disease decreased from 32,898 (mean SD 2742±177 per month) in 2019 to 16,396 (1366±308 per month; $p<0.0001$ in 2020 with a sudden decline in March 2020, concomitantly with the commencement of lockdown in majority of the countries (13). This epidemiological change was observed in all countries, except the TB centers in Australia, Singapore and Virginia (13).

In the present study, rifampicin resistance was seen lowest in the year 2021. The possible reason could be, lockdown restricted movement of people and social gatherings. Due to which, people may not have reached diagnostic facility and have resulted in under-reporting of resistance. In the study conducted by Trajman A et al, the COVID-19 pandemic had sufficient impact of TB care cascade resulting in decrease in TB testing and notifications of TB, primarily as a result of disrupted TB services and constrained patient movement (14). But in 2022, restrictions were released, and increase in rifampicin resistance was reported.

Extra pulmonary TB positive cases were not seen to decrease significantly during COVID-19 period. Infact, we saw rise in number of TB positive cases from extrapulmonary samples in year

2021. This clearly indicates, wearing masks has prevented only pulmonary tuberculosis. As very few studies are available on TB in COVID-19 period, we could not compare our results with similar studies.

Conclusion

Restrictions imposed during COVID-19 period could have decreased TB as well as rifampicin resistance. There was not much difference in total sample size received each year from 2018 to 2022. Thus, implication of restrictions for TB suspected and positive patients on regular basis can help in preventing spread of the disease.

Limitations: In case of rifampicin resistant TB, we could not track family members of rifampicin resistant patients to confirm their rifampicin status. These findings cannot be imposed as this is a single center study. More studies of similar kind especially in bigger institutes will let the know the overall status and that can be useful to take further action. There is a need to conduct cohort study on people wearing and not wearing masks.

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Conflict of Interest

None

Declaration

Not applicable.

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Ethical approval

Ethical approval was taken Reference number 1023291-291(Dated 27/10/2023)

Author's contribution

SSP- Idea of manuscript, editing manuscript. PGS- Drafting manuscript,VVG, SND, MVR, RPK- Reviewing the manuscript

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Table 1. Total samples received from 2018 to 2022

Year	Total Pulmonary Samples received (percent)	Total extra-pulmonary samples received (percent)	Total pulmonary+extrapulmonary samples received (percent)
2018	2221 (62.69)	1322 (37.31)	3543 (100)
2019	2609 (68.24)	1214 (31.76)	3823 (100)
2020	2646 (71.86)	1036 (28.14)	3682 (100)
2021	2313 (71.21)	935 (28.79)	3248 (100)
2022	2298 (67.97)	1083 (32.03)	3381 (100)

Table 2. Year-wise distribution of samples received, samples positive for *Mycobacterium tuberculosis* and rifampicin resistance by CBNAAT

Year	Total samples received	*Mycobacterium tuberculosis* detected (percent)	Rifampicin resistant (percent)
2018	3543	744 (20.9)	82 (11.0)
2019	3823	699 (18.2)	69 (9.8)
2020	3682	573 (15.5)	42 (7.3)
2021	3248	515 (15.8)	33 (6.4)
2022	3381	568 (16.8)	68 (11.9)

‘‘p value’’- 0.042 statistically significant

Table 2, indicates decreased positivity and rifampicin resistance in year 2020 and 2021.

Table 3. Total extrapulmonary samples received, positive and negative for *M.tuberculosis* from 2018 to 2022.

Results of EP sample	Year				
	2018	**2019**	**2020**	**2021**	**2022**
Total samples	1322	1214	1036	935	1083
***M.tuberculosis* detected**	269 (20.3%)	167 (13.7%)	120 (11.5%)	136 (14.5%)	136 (12.5%)
Rifampicin Resistant	22 (8.1%)	14 (8.3%)	10 (8.3%)	10 (7.3%)	12 8.8%)

‘‘p value’’- 0.3694 not statistically significant