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Original article

TB positive cases go up in ongoing COVID-19 pandemic despite lower testing of TB: An observational study from a hospital from Northern India

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Abstract

The whole world is wrestling against SARS-CoV-2 infection (COVID-19). COVID-19-TB co-infection is also reported but there are limited number of studies which analyze the impact of COVID-19 pandemic in TB diagnosis and management. In this retrospective study, we observed that the TB diagnosis was reduced in pandemic time. Before COVID-19 pandemic (March–December 2019), there were 644 TB tests out of which 127 were TB positive. In ongoing COVID-19 pandemic (January–October 2020), 484 TB tests were performed and 146 patients were TB positive. Male accounted for 64%/57% of TB cases in 2019/2020 whereas female patients were 35%/42% in 2019/2020. Increase in female TB positive cases was a noticeable feature. The newly diagnosed with TB cases in 2019/2020 were 112/130 respectively. Though, we have seen only 7 COVID-TB co-infection cases, we could not establish the causal relationship in COVID-TB co-infection. The increase in the number of TB positive cases during COVID-19 pandemic clearly showed how adversely COVID-19 has affected TB diagnosis and management. Anticipating the increase in TB cases in future, we emphasize the need to ensure continuous TB testing and treatment despite the pandemic burden. Further study on the COVID-TB co-infection in high TB-burden countries like India, is required to enable analyses of interactions, risk factors in COVID-19-TB co-infection.

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Abbreviations: TB, Tuberculosis; AIDS, MERS, SARS, Chronic obstructive pulmonary disease, COPD; Human immunodeficiency virus, HIV; Diabetes mellitus, DM; Hypertension, HTN.
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1. Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease (COVID-19) pandemic has attracted the interest due to its worldwide reach, clinical severity and higher mortality rate. SARS-CoV-2 transmission is mainly through droplets, although aerosol transmission and surface contamination is still a subject of continuous debate. The initial symptoms of COVID-19 infection are similar to Middle East respiratory syndrome (MERS). Influenza, severe acute respiratory syndrome (SARS), tuberculosis (TB), though the immune response and disease manifestation are different. Most of the COVID-19 infected patients show mild or no symptoms. Elderly patients or, persons with underlying medical conditions are at higher risk of developing severe outcome. Thus it is important to study the associated factor along with COVID-19 infection to know more about this novel disease. The TB-COVID-19 co-infections are not rare and both are associated with weaken protective immune responses. TB care and management program has already suffered in the past during HIV/AIDS emergencies, outbreak of EBOLA, H1N1, MERS. Currently, the unprecedented demand required by COVID-19 has hindered TB management in many countries as lab personnel and laboratory facilities are re-assigned for COVID-19 testing, a major chunk of budget goes for the procurement of consumables. The supply for scientific as well as general goods has suffered during worldwide lock-down.

Thus, the aim of the study was to analyze the effect of COVID-19 pandemic on TB diagnosis. The present study describes the first-ever comparative study of TB diagnosis in pre-COVID-19 period. It is a purely observation study and no analysis for outcome assessment is performed.

2. Study setting and design

The study was performed in a 300-bed tertiary care private hospital in Gurgaon, Haryana (India). A retrospective observational analysis was undertaken of all patients with confirmed TB cases from GENEXpert test-a CBNAAAT (cartridge based nucleic acid amplification test). For COVID-19 patients, patients with confirmed RT-PCR test were included in the study. The duration of time-period studied were, pre-COVID-19 time (From March–December 2019) and ongoing COVID-19 time (from January–October 2020).

Patient demographics gender, age, microbiology data, co-morbidities and death-record extracted from hospital information system (HIS) were de-identified as part of an ongoing outbreak investigation. Thus, institutional review board approval was deemed unnecessary. Also, due to the retrospective and purely observational nature of the study, the written informed consent from patients is not required.

The information available on patients details were as far as could be, is accurate, however, some details of patients were missing because either the patients did not continue the treatment at the hospital or left against medical advice.

3. Statistical analysis

Continuous variables are presented as medians (interquartile ranges, IQR), and categorical variables as counts (percentages). Fisher’s exact test (two-tailed) was performed was performed with GraphPad to compare data from pre-COVID-19 and ongoing COVID-19 period.

4. Results

4.1. Ongoing COVID pandemic (from January–October 2020) sees lesser number of TB diagnostic tests

From March 2019 to December 2019, 644 TB tests were performed and TB was detected in 127/644 (19.72%). In COVID time, total 484 TB tests were performed out of which 146/484 were TB positive (30.16%) (Table 1). TB positivity has gone up to 30% in 2020 from ~20% in 2019 despite decline in lesser tests in 2020 (484) as compared to 2019 (644).

In 2020, out of 146 confirmed TB cases, 134 were sensitive and 12 were resistant. Whereas in 2019, out of 127 confirmed TB cases, 101 were sensitive and 23 were resistant (Table 1).

Male (M) accounted for 64% of TB cases in 2019 and 57% in 2020 patients. Female (F) accounted 35% of TB cases in 2019 and 42% in 2020 patients (Table 1). One interesting feature is that female % in TB positive cases have increased from 2019.

The no. of patients newly diagnosed with TB in 2019/2020 was 112/130 respectively.

The median age was 46.5 years (IQR 2020): 36, M: 32, F: 37.5), and 53 years IQR (2019) = 38 M: 37 F: 39.

5. COVID-TB Co-infection

In 2020, approximately 71 COVID-19 tests (RT-PCR based) were conducted for confirmed TB cases and we observed 7 cases of COVID-TB co-infection (Table 2). All COVID-TB co-infection patients survived except one (Table 1). In COVID-TB co-infection (Table 2), 4/7 (57.14285714%) had TB (ongoing anti-TB treatment) before COVID-19, 2/7 (28.5%) had COVID-19 first and 1/7 (14.2%) had both diseases diagnosed within the same week. Signs and symptoms of COVID-19 infection were fever, cough and breathlessness (in different combinations). All the COVID-TB co-infection patients had at least one co-morbidity (Table 2) and were sensitive. The median age was 60 years, (IQR: 27, Coefficient of Variation (CV) = 0.23) in COVID-TB co-infection. Unfortunately, BCG vaccination status was not available; hence no significant correlation can be ascertained to BCG vaccination mediated protection from COVID-19 infection.

In patients, where COVID-19 was detected first, probably, an overlap of signs/symptoms of COVID-19 and TB have occurred and COVID-19 was diagnosed earlier because of a higher degree of suspicion. On a different note, suspicion of COVID-19 infection and overlapping symptoms with TB might have led to TB diagnosis before the onset of TB-related
This could be the reason behind higher percentage of confirmed TB cases in 2020 despite lower testing (Table 1). In India where majority of the population is asymptomatic for COVID-19 infection (or who are missed in testing and contact tracing), it is pertinent to monitor the development of TB. We cannot either report or rule-out the potential contribution of COVID-19 towards development of TB based on this study. Although the diagnosis of TB preceded that of COVID-19 in 4/7 patients, any contribution of COVID-19 to TB pathogenesis or vice-versa can neither be excluded nor confirmed. We believe larger numbers of patient data are required to fully understand the impact of COVID-19 pandemic on TB diagnosis and treatment.

| Table 1 — Demographic and clinical characteristics of TB patients. |
|---------------------------------------------------------------------|
| **Pre-COVID-19 period** | **Ongoing COVID-19 period** | **p value** |
| No. of patients (n) | 644 | 484 |
| Confirmed TB patients | 127/644 (19.72%) | 146/484 (30.16%) | p = 0.0001 |
| Age (years) | 53 (IQR: 38) | 46.5 (IQR: 36) | - |
| Median (min–max) | 53 (0–82) | 46.5 (0–94) | - |
| Age (years) | | |
| Sex | | |
| Male | 82/127 (64.5%) | 84/146 (57.5%) | p = 0.26 |
| Female | 45/127 (35.4%) | 62/146 (42.4%) | p = 0.26 |
| Co-morbidities in TB patients | | |
| Sepsis (all died) | 3/127 (2.36%) | 9/146 (6.16%) | p = 0.1489 |
| Carcinoma | 17/127 (13.38%) | 21/146 (14.8%) | p = 0.8621 |
| HIV | 0 | 1/146 (0.68%) | p = 1 |
| DM/HTN | 21/127 (16.53%) | 20/146 (13.69%) | p = 0.61 |
| COPD | 6/127 (4.72) | 4/146 (2.73) | p = 0.52 |
| Alcohol | 2/127 (1.57%) | 1/146 (0.68%) | p = 0.59 |
| Smoker | 3/127 (2.36%) | 3/146 (2.05%) | p = 1 |
| Candida/yeast infection | 3/127 (2.36%) | 3/146 (2.05%) | p = 1 |
| Pneumonia | 0 | 8 | - |
| History of Tuberculosis | | |
| Previous history of TB | 15/127 (11.81%) | 16/146 (10.95%) | p = 0.85 |
| Newly Diagnosed TB | 112/127 (88.18%) | 130/146 (89.04%) | p = 0.85 |
| Resistant | 23/127 (18.11%) | 12/146 (8.21%) | p = 0.01 |
| Sensitive | 101/127 (79.52%) | 134/146 (91.78%) | p = 0.0047 |
| Death | 8/127 (6.29%) | 13/146 (8.90%) | p = 0.49 |
| COVID-19 infection in TB patients | | |
| No. of COVID-19 test | - | 71 | - |
| Male | - | 32 | - |
| Female | - | 39 | - |
| Confirmed COVID-19 infection | - | 7 | - |
| Median age in years | - | 60 (IQR: 27) | - |
| Asymptomatic | - | 3/7 (42.85%) | - |
| Symptomatic | - | 4/7 (57.14%) | - |
| Female | - | 3/7 (42.85%) | - |
| Male | - | 4/7 (57.14%) | - |
| Death | - | 1/7 (14.28%) | - |

| Table 2 — Characteristics of patients with COVID-TB co-infection. |
|------------------------------------------------------------------|
| **Patient** | **Age/Sex** | **Co-morbidities** | **TB Type** | **Sensitive/Resistant TB** | **COVID Severity** | **Recovered/Death** |
| Patient 1 | 60/F | CKD | EPTB | Sensitive | Severe, COVID pneumonia | Left hospital |
| Patient 2 | 65/M | Hypothyroidism, Cholelithis | PTB | Sensitive | Mild | Delayed viral clearance |
| Patient 3 | 67/M | Metastatic NSCLC | PTB | Sensitive | Severe, COVID pneumonia | Death |
| Patient 4 | 39/F | Relapsed AML | PTB | Sensitive | Mild | Recovered |
| Patient 5 | 40/F | DM | EPTB | Sensitive | Severe | Recovered |
| Patient 6 | 68/M | DM | PTB | Sensitive | Mild | Delayed viral clearance |
| Patient 7 | 47/M | DM, CAP-PTCA | PTB | Sensitive | Moderate | No info |

*Pre-COVID-19 period (March–Dec 2019), ongoing COVID-19 period (Jan–Oct 2020), Chronic obstructive pulmonary disease (COPD), Human immunodeficiency virus (HIV), Diabetes mellitus (DM), Hypertension (HTN). Death is the number of patients who died during anti-TB treatment.

*Abbreviations: Chronic kidney disease(CKD), coronary artery perforation (CAP), Percutaneous transluminal coronary angioplasty (PTCA), Acute myeloid leukemia (AML), Nonsmall-cell lung carcinoma (NSCLC), Diabetes mellitus (DM), Multiple Organ Dysfunction Syndrome (MODS), Pulmonary tuberculosis (PTB), Extrapulmonary tuberculosis (EPTB).
6. Discussion and conclusion

Due to the disruption in healthcare system caused by COVID-19 pandemic, TB reporting and diagnosis in 2020 sees a significant fall (Table 1). In 2020, we observed increase in confirmed TB cases as compared to 2019. It is possible that undiagnosed and untreated TB cases are contributing to TB transmission among household contacts. Longer indoor stay, failure to follow-up due to lock-down, discouraged-hospital visit, all these factors not only poses health hazard to the existing TB patient but also increases the chances of transmission within house-hold contacts or care-givers. Crowded live-in conditions, poor hygiene, are contributing factor for both COVID and TB infection, thus it is pertinent to identify and isolate TB patients at an earliest to reduce the severe outcome due to suppressed immunity.

In high risk group or in TB-endemic areas like India, COVID-TB co-infection should be assessed critically. Present study is an attempt to study COVID-TB co infection in a high burden country, India to fill the knowledge-gap in the concern area. The identification of COVID-TB co infection is important for proper disease management. This is, to our knowledge, the first comparison study of TB diagnosis/reporting in the pre and ongoing COVID-19. Our study represents a “snapshot” of TB diagnosis at different times. No attempt was made to represent the casual relationship on co-occurrence of both diseases. Given the small size of data and single-institutional study, we cannot directly correlate/or establish the relationship in COVID-TB co infection or its outcome, but such studies are important for prevention, treatment and management of TB, COVID-19 like infectious diseases in future. We believe that this observational research can motivate for larger studies to enable analyses of interactions, risk factors and determinants of outcomes in patients with COVID-TB co infection.

Author contribution statement

Shruti Srivastava: Conceptualization, Methodology, Investigation, Writing- Original draft preparation, reviewing, editing and manuscript submission.

Namita Jaggi: revised and approve the manuscript.

Both authors read and approved the final manuscript.

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Conflicts of interest

The authors have none to declare.

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