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Original Research Article

Clinical profile of patients with COVID-19 and tuberculosis co-infection in a tertiary care hospital

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ABSTRACT

Background: Historical evidences suggest that Tuberculosis (TB) with concurrent respiratory viral infections, such as, Influenza has been associated with higher mortality. TB and COVID-19 co-infection has implications beyond mortality at the individual level. Hence there is a need to study the clinical characteristics and outcomes in COVID-19 and TB co-infection.
Methods: In this retrospective observational study, COVID-19 cases admitted to Victoria Hospital, a tertiary care hospital in Bengaluru, twenty-six patients with COVID 19 and TB co-infection were observed and their clinical characteristics, radiological and laboratory parameters were recorded and analyzed for the impact of COVID-19 on TB.
Results: Raised inflammatory markers, high neutrophil to lymphocyte ratio (NLR), lymphocytopenia were observed in majority of the cases. There was worsening of Tubercular lesions on Chest radiography in eighteen patients (69%). Out of the twenty six, sixteen patients (61%) needed supplemental oxygen therapy at admission, Five (19%) of them needed Assisted ventilation and intensive care. Out of the five patients who needed intensive care, two (7.6%) patients succumbed to death owing to Severe COVID-19 pneumonia, respiratory failure and other co-morbid conditions.
Conclusions: Co-infection with COVID-19 and TB alters the severity, the course and management of the disease and can be associated with adverse outcomes and is associated with high mortality; a high index of suspicion is required for the detection of this co-infection and bi-directional screening of COVID-19 and TB must be carried out for the early detection and management of this co-infection.

Keywords: SARS-CoV-2, COVID-19, Tuberculosis, Co-infection

INTRODUCTION

Co-infections involving the respiratory tract pose clinical dilemmas and diagnostic and therapeutic challenges. The World health organization declared the outbreak of novel corona virus disease COVID-19, caused by the Severe acute respiratory syndrome Coronavirus 2, as a Pandemic on 11, March 2020. India also has the majority of global burden of tuberculosis, having an estimated incidence of 26.9 lakh cases in 2019.[1] Tuberculosis, the leading cause of death worldwide from a single infectious agent, like COVID-19, is mainly transmitted through respiratory route and which primarily affect the lungs; present with similar complaints of cough, fever and difficulty in breathing, although the incubation period and onset of Tuberculosis is slower. There has been an overall decline of TB notification by 26% during January to June 2020 as compared to previous year, due to COVID-19 pandemic.[2]

Risk factors such as advanced age, diabetes mellitus, chronic respiratory diseases are associated with Poor outcomes in both TB and COVID-1910, however there is

sparse data available about TB and COVID-19 co-infection. Historical evidences suggest that TB with concurrent respiratory viral infections, such as, Influenza has been associated with higher mortality.[3] Co-infection with Severe Acute respiratory syndrome Corona virus or Middle east respiratory syndrome corona virus has been associated with increased Intensive care unit admissions.[4]

Hence TB and COVID-19 co-infection has implications beyond mortality and is of rising concern. This study describes the clinical, radiological and laboratory characteristics of patients with COVID-19 and Active TB co-infection, admitted at Victoria Hospital, a tertiary respiratory care hospital in Bangalore, India.

Aims and objectives

The aim of the study was to describe the clinical, radiological and laboratory characteristics of a series of COVID-19 patients with concurrent active tuberculosis admitted at a tertiary care hospital.

METHODS

A retrospective observational study was conducted at Victoria Hospital, Bangalore Medical College and Research Institute, Bangalore, a tertiary care hospital in for a period of 15 months. Out of the COVID -19 patients admitted to Victoria Hospital, Bangalore between April 2020 to July 2021, twenty-six patients were found to have concurrent active Tuberculosis. This study was cleared from Institutional Ethical Committee, BMCRI to which the hospital is attached.

Inclusion criteria

Patients who were admitted with already diagnosed with Active Tuberculosis and later developed COVID-19 infection, patients admitted as SARI and diagnosed with Active tuberculosis with concurrent COVID-19 infection; patients willing to give written informed consent.

Exclusion criteria

Patients not willing to give written informed consent; Patients with history of old treated pulmonary Tuberculosis without Active Tuberculosis; Patients who were COVID positive by RTPCR but opted for home isolation.

The diagnosis of Tuberculosis was done on the basis of either CBNAAT, chest radiography, histopathological examination or body fluid analysis. COVID-19 diagnosis was based on the result of RTPCR for SARS-CoV-2 from Orophrayngeal and nasopharyngeal swabs. Chest radiograph taken at the time of diagnosis of COVID-19 was compared with the most recent radiograph which was available after diagnosis of tuberculosis, to assess any change in Tubercular lesions. Patient clinical and laboratory data were recorded from the date of diagnosis of COVID-19 up to discharge/death of the patient.

RESULTS

Among twenty-six patients, seventeen patients were males (65%) and Nine patients were female (35%) (Figure 1). The mean age of the patients was 45 years (16-87 years). Nineteen patients were from urban area (73%), while seven patients were from rural areas (27%) (Figure 2).

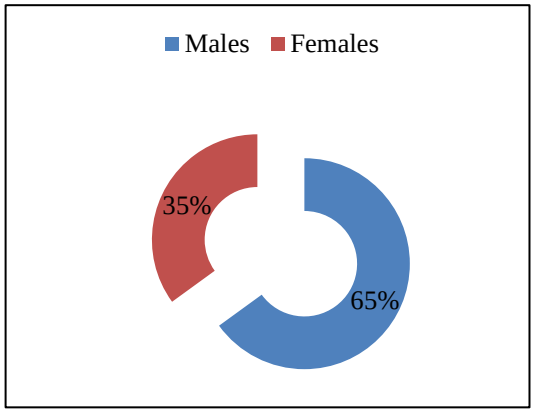

Figure 1: Gender distribution of patients.

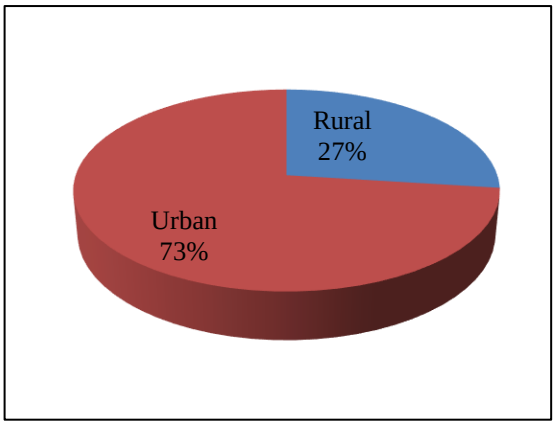

Figure 2: Demography of patients with TB and COVID co-infection.

Twenty four patients (92%) presented with a history of cough for more than two weeks duration. Sixteen patients (61%) had history of fever. Eleven patients (42%) had dyspnea. Only one patient had hemoptysis (Figure 3).

History of weight loss and loss of appetite was present in all the patients. Two patients had complaints of vomiting out of which one patient had drug induced liver injury with deranged liver functions.

At admission, eight patients had pre-existing type-2 diabetes mellitus (30.7%) and three had history of hypertension (11.5%), four patients had HIV co-infection (15%), one had chronic kidney disease (3%), one had

ischemic heart disease (3%), one had seizure disorder (3%) and one patient had hypothyroidism (3%). Among twenty six patients, twenty two had pulmonary tuberculosis (84.6%), four had extrapulmonary tuberculosis (15%) in the form of: one had tubercular pyopneumothorax (3%), one had tubercular pleural effusion (3%) and one had gastrointestinal tuberculosis (3%) and one had neurological tuberculosis (3%) (Figure 4).

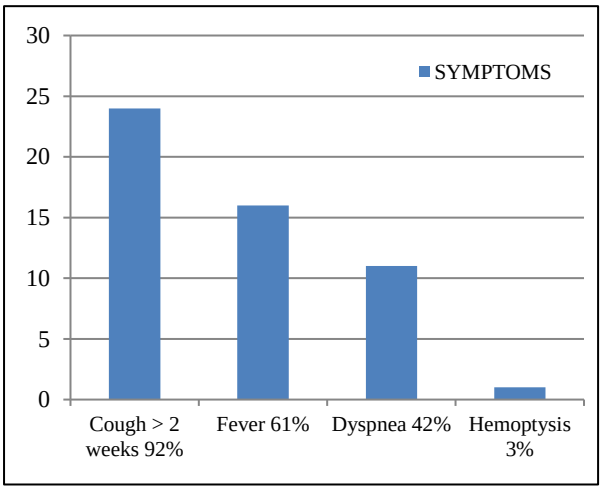

Figure 3: Symptomatology of patients with TB and COVID co-infection.

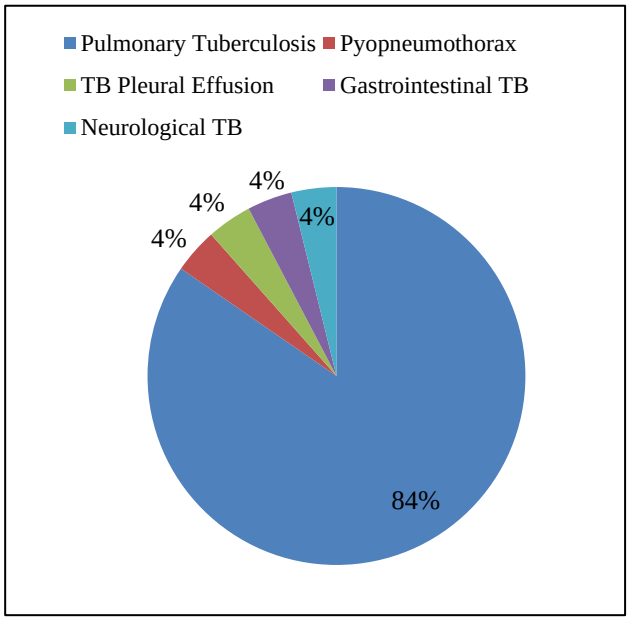

Figure 4: Site of involvement of TB.

Lymphocytopenia was observed in all the cases and mean NLR was 9.32. Six patients had Neutrophilic Leucocytosis (TLC >11,000 cell/cumm) (23%). Eight patients had a hemoglobin of less than 10 g/dl (30.7%) and three of them had severe anemia (11.5%), who received blood transfusion.

Table 1: Radiological features of TB and COVID co-infection.

Findings	N	%
Nodular Opacities	10	38
Cavities	7	27
Consolidation	5	19
Pleural Effusion	2	7.6
Hydropneumothorax (pyopneumothorax)	1	3

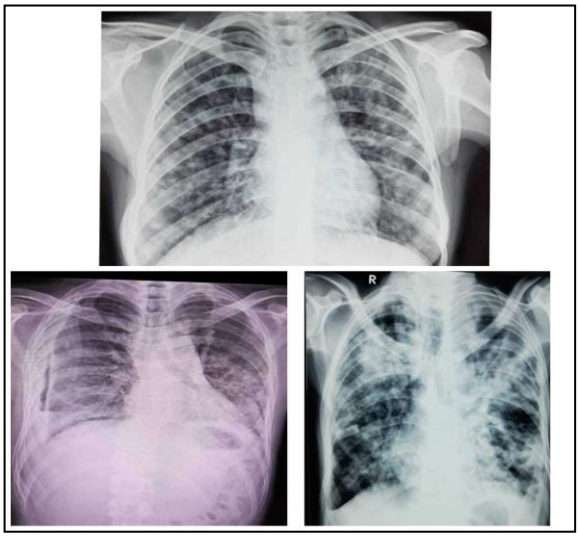

Figure 5: Chest radiography images showing patterns of involvement in TB and COVID patients.

Twenty four patients (92%) had high D-dimer levels (>500 ng/ml) (Mean D-dimer was 3264 ng/ml), eighteen patients (69%) had elevated ferritin levels (>1000 ng/ml) (mean S. ferritin was 862 ng/ml), twenty patients (77%) had raised CRP levels (>90 mg/l) (Mean CRP was 91 mg/l), LDH was elevated in fifteen patients with mean being 368 U/l. Four patients had elevated liver enzymes (AST and ALT >100 IU/l).

In all twenty six patients, COVID-19 diagnosis was based on the result of RTPCR for SARS-CoV-2 from Orophrayngeal and Nasopharyngeal swabs. Sputum CBNAAT was positive in twenty two patients, pus (from Pyopneumothorax) CBNAAT was positive in one patient, one patient was diagnosed on the basis of pleural fluid analysis. Two patients with pulmonary tuberculosis, one patient with gastrointestinal tuberculosis and one with ependymal tuberculosis were diagnosed on the basis of radiological investigations.

Chest radiography showed bilateral or unilateral nodular opacities in ten patients (38%), cavitation was observed in seven patients (27%), pleural effusion was observed in two patients (7.6%), consolidation was observed in five patients (19%), while pyopneumothorax (3%) was seen in one patient who subsequently underwent tube thoracostomy (Table 1, Figure 5). Worsening of

tubercular lesions as compared to previous available chest radiography was seen in eighteen patients (69%).

Predominant zone involved was right upper zone (11/22, 50%), followed by multiple zone (>2 zone) involvement (7/22, 31%) and 4 patients had other zone involvement (18%).

Twenty five patients received standard anti TB treatment with isoniazid, rifampicin, ethambutol and pyrizinamide as per NTEP guidelines. One patient was on Non-DOTS treatment in view of underlying ATT induced Hepatitis. Twenty five (96%) patients received Remdesivir, appropriate antibiotics and other symptomatic treatment were given to all patients. Twenty five patients received Steroids and all twenty six received Low molecular heparin (Enoxaparin) as per the existing COVID-19 treatment protocols in the state 11.

At admission, oxygen supplementation was required in sixteen (61%) patients with SpO_2<92%, and ten patients were gradually weaned from oxygen therapy as their Saturation improved during the course of hospital stay and none required home oxygen therapy. Ventilatory support and intensive care support was needed for five patients (19%). Three patients recovered and was gradually weaned from NIV support. Two patients required invasive mechanical ventilation. Both patients who were on IMV, succumbed to death due to severe COVID 19 pneumonia and tuberculosis (7.6%).

One patient underwent tube thoracostomy in view of tubercular pyopneumothorax. Patient eventually recovered from COVID-19 infection and was shifted to general wards.

The mean time between from TB diagnosis and SARS-CoV2 detection was 25 days (0-95 days). Mean duration of hospital stay was 20 days. Inflammatory markers and neutrophil to lymphocyte ratio were elevated in majority of the patients, along with a generalized lymphocytopenia. Chest radiographic worsening of Tubercular lesions were seen in eighteen patients (69%). Twenty four out of the twenty six patients were discharged without requirement of home oxygen therapy.

Sixteen patients needed supplemental oxygen therapy in view of hypoxia (SpO_2<92%) at admission, five of them deteriorated and needed assisted ventilation late and were shifted to Intensive care unit. Three of the five patients who were in ICU, on NIV support recovered and was shifted to HDU and later discharged without any sequelae in the due course. The other two admitted to ICU succumbed to death (7.6%).

One patient died on the third day of admission to ICU in view of severe COVID-19 pneumonia, respiratory failure, severe anemia and multiorgan dysfunction. Other patient succumbed to death due to progressive respiratory failure, due to severe COVID pneumonia.

DISCUSSION

Studies have suggested that history of TB, both active and treated is an important risk factor for SARS-CoV-2 infection.[5] This not only results in increased susceptibility, but also rapid and severe symptom development and disease progression with poorer outcomes. TB patients also tend to have co-morbid conditions like malnutrition, HIV, Diabetes that increase the vulnerability.[2]

Only limited data is reported on Tuberculosis and COVID-19 co-infection, which is probably due to lack of screening for TB in COVID-19 patients and for COVID-19 in patients with TB. The current guidelines have emphasized the importance of bidirectional screening in COVID-19 and TB patients.[2] Paucity of data on co-infection can also be attributed for under-reporting of cases, early mortality in such patients and due to late presentations.

The exact mechanism of interaction between TB and COVID-19 is largely unknown, however several mechanisms are under study. Interleukins which are triggered by the inflammatory response to viral infections affect the T-cell response, which may result in rapid disease progression in cases of COVID-19 with active tuberculosis. Type-1 Interferon has antiviral properties, however mistimed IFN-1 response in Viral infection may promote susceptibility for the development of Tuberculosis.[6] Factors like Impaired glucose metabolism in Diabetics predispose to an excessive uncontrolled inflammatory response, lead to a higher risk of developing COVID-19 pneumonia and rapid disease progression.

In our current series of twenty six patients, the overall mortality is lower compared to other studies (7.6%). Though preliminary, this is lower compared to other studies by Gupta et al (27.3%), Tadolini et al (12.3%), Motta et al (11.6%) in TB and COVID 19 co infection.[7-9] In India, mortality rate of around 2.3% has been observed among COVID-19 patients including patients with comorbid conditions such as diabetes, hypertension, malignancy, tuberculosis etc., This higher mortality in TB and COVID-19 co-infection could be explained by the damage to lungs by active Tuberculosis superimposed with COVID-19 infection, leading to further deterioration of already compromised lung functions.

Kumar et al in their study have observed that, co-infection of TB and COVID-19 is of particular importance due to various reasons such as, missed diagnosis due to non-specific clinical features, use of steroids in the disease may itself lead to reactivation of latent TB, pre-existing TB disease and the underlying lung condition will affect the clinical categorization of COVID-19 severity, also the possibility of drug interactions and hepatotoxicity due to simultaneous use of ATT and available COVID-19 drugs.[10,12]

Limitations of this study included the small sample size of study population, limited analysis of various other risk factors, patients with old treated tuberculosis without current active TB was not considered for the study and lastly, follow-up of ATT adherence and smear negativity status and post COVID sequealae and related complications were not considered in this study.

CONCLUSION

Patients with active TB require special attention and appropriate preventive measures for the development of COVID-19, and strategies like bi-directional screening of COVID-19 and TB must be emphasized in patients presenting with common complaints of cough and fever. A higher mortality and greater need of Intensive care including assisted ventilation was found in TB patients co-infected with COVID-19. Thus, co-infection with COVID-19 and TB alters the severity, the course and management of the disease and can be associated with adverse outcomes, and a high index of suspicion is required for the detection of this co-infection.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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