

TUBERCULOSIS AND COVID-19 CO-INFECTION – CLINICAL CHARACTERISTICS

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Abstract: The threat of contagious infectious diseases is constantly evolving as demographic explosion, travel globalization and changes in human lifestyle increase the risk of speeding pathogens, leading to accelerate changes in disease landscape.(1) Tuberculosis and Covid-19 are both infectious diseases that attack primarily the lungs. Both diseases have similar symptoms such as cough, fever and difficulty breathing. Tuberculosis has a longer incubation period with a slower reset of disease. Experience on Covid-19 infection in TB patient remains limited. 8 studies reported a total of 80 patients with this co-infection. These patients were reported from 9 different countries, with Italy reporting the largest number of cases.(2) The aim of this study is to evaluate the characteristic of TB and Covid-19 co-infection in 10 patients who were admitted in the Pulmonology Hospital of Sibiu between 01.05.2020-30.04.2021. All of these patients were with nosocomial infection Covid-19 and were previously diagnosed with TB.

INTRODUCTION

On 11th March, the World Health Organization declared COVID-19 as a global pandemic and a public health emergency. Pandemic continues to be a significant global health crisis. On 30.04.2021, nearly 170 million people have been affected in more than 188 countries and 3,8 million people died. At the same time Tuberculosis (TB) continues to be a global burden with around 2,5 million new patients and 3 million deaths annually.(2)

There is a paucity in clinical literature reporting interactions and the impact of COVID-19 among patients with TB. The co-infection seems more likely to be a co-incidental occurrence rather than a causal association. It is likely that patients with active TB will have more time to get exposed to COVID-19 infection due to chronic course of TB.(3) The hypothesis is also supported by a higher percentage of multidrug-resistant TB patients with COVID-19, as these patients are on prolonged treatment and harbour TB disease for a long period of time.(3) Covid-19 infection may alter the clinical presentation of TB, and also possibly exacerbate pulmonary TB. Both infections hinder host immune responses. Specifically, Covid-19, infection can impair T-cell immunity and weaken immune responses against secondary bacterial infection. High TB burden countries have a huge number of patients with post TB lung sequelae and the outcome of COVID-19 in such patients is unknown so far.(4) In some cases, Covid-19 infection may promote the progression of latent Mycobacterium tuberculosis (MTB) infection to active TB.(5)

The Covid-19 infection rate is higher in patients with active tuberculosis.

Major clinical complications were seen including, in these patients, oxygen supply, *Clostridium difficile* infection, hyperglycaemia, cardiac failure, deep thrombosis. One of main

concern about this co-infection is the mortality associated with it.

AIM

The aim of the study is to evaluate the impact of Covid-19 among the patients with tuberculosis, patients admitted in Sibiu Pulmonology Hospital between 01.05.2020 and 30.04 2021. We analysed symptoms, laboratory findings, imaging, risk factors, treatment, complications, prognosis, mortality among 10 patients with co-infection.

MATERIALS AND METHODS

From 01.05 2020 to 30.04.2021, 12 patients with active TB and Covid-19 were hospitalized in the Pulmonology Hospital of Sibiu.

We evaluated only the patients who were confirmed as active TB with smear sputum positive, sputum culture positive, GeneXpert test positive to Mycobacterium tuberculosis, which were used as the diagnostic tool for Tuberculosis. COVID-19 diagnosis was based on the result of real-time RT-PCR for SARS CoV-2 and with Rapid Antigen test for SARS-CoV-2 from nasopharyngeal swabs.

The study was observational and based on a relatively small cohort. Ten patients were included in this review. One patient was excluded because he was without bacteriologic confirmation for MTB and one case with active TB and Covid-19 which was referred for treatment in his origin county.

Covid- 19 and TB coinfection: This was defined with the presence of Covid-19 positivity in patient with TB.

Clinical features

The most reported symptom was productive cough in 8 patients (80%) Fever was found in 2 patients (20%) Dyspnea was present in 6 patients (60%). Other

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CLINICAL ASPECTS

symptoms were sputum with blood in 1 patient (10%), diarrhoea in 2 patients (20%), chest pain in 3 patient (30%), muscle aches (10%), loss of appetite (10%), fatigue (10%), sweats (10%) chills (10%).

Laboratory findings

Leukopenia was found in 4 patients (40%) and lymphocytopenia in 6 patients (60%). All 10 patients were with elevated inflammatory markers including PCR, VSH, LDH. (100%) 2 cases were with leucocytosis (20%), 1 case with thrombocytosis (10%) and 2 cases with anaemia (20%).

Other reported laboratory abnormalities were low serum albumin in 3 patients (30%) raised ALT in 3 cases (30%) and high glucose level in 5 patients (50%). 7 Covid-19 patients have been reported to have raised level of D-dimer (70%).

Other laboratory tests such as: fentim, interleukin-2 (IL-2), IL-7, troponin, CK-HB, myoglobin, NTpro BMP could not be provide in our laboratory.

Imaging:

Chest radiograph (CXR) and computed tomography has been used to identify the patterns of pulmonary involvement. Imaging details were available in all of cases. All 10 patients have chest radiograph. Only 2 patients were evaluated using computed tomography (20%). One of this had no abnormalities to indicate COVID-19 and the other one had bilateral ground glass opacity.

Imaging findings in the TB patients with Covid -19 are the development of multiple, bilateral ground glass opacity (1 patient -10%), consolidations with air bronchogram (8 patients-80%), pulmonary infiltrates (1 case-10%), cavitory lesions (8 patients- 80%). 2 of cases have bilateral cavitory lung lesion (20%). None of them have crazy paving imaging.

Risk Factors:

Predisposing factors in TB patients with Covid-19 have been similar to that of TB patients without Covid-19. Medical comorbidities like COPD, diabetes, HIV, renal failure, liver disease, alcohol abuse, and smoking have been reported.(6)

In our study 4 patients were with alcohol abuse (40%), 2 with COPD (20%), 1 with diabetes (10%), 2 with chronic cardio-vascular diseases (20%), one with splenectomy (10%). 3 cases were smokers (30%).

This study also reported demographic factors including male gender and elderly people. 9 of 10 were males (90%), age over 70 - 2 cases (20%), 5 patients were between 55 and 65 and 3 patients were under 50. 3 of them were unemployed which is also a risk factor.(7)

Treatment:

All the patient with active TB were reported to be treated with multidrug regimen antitubercular therapy (100%). Among patients with pan-susceptible organism, treatment regimen consisted of isoniazid, rifampicin, pyrazinamide and ethambutol. In 2 (20%) of them, amikacin was used in addition of first line antitubercular drugs. Various therapeutic agents were used to treat Covid-19 in patients with TB co-infection. We used, as anti-viral agents, favipiravir (7 patients-70%) and remdesivir (3 cases-30%) Glucocorticoids including methylprednisolone and dexamethasone have also been administered in these subsets of patients (10 patients -100%). There have been reports of administration of anticoagulation (enoxaparin, parnaparin) as well in all 10 patients (100%). While the antitubercular regimes used across all patients (100%).

Most treatment details including the reason for the choice of therapy, the doses of medication, the duration of medication, the details of medication interactions, dosage modifications and adverse drug events were not reported for eighter form of therapy consistently.(8)

Complications:

Complications that have been reported in this subset of patient are hypoxemia (3 cases-30%), respiratory failure (5 cases - 50%), glucose abnormalities (5 patients-50%), a prolonged hospital stay (maximum 30 days in hospital in 1 patient) and superimposed bacterial infection (4 cases-40%). 2 cases were with *Clostridium difficile* co-infection (20%).

Mortality

In our study 3 of 10 patients (30%) died, two in first seven days after admitted in COVID Compartment and one after nine days.

DISCUSSIONS

All the patients in this study had acquired Covid 19 via nosocomial transmission. In our COVID Compartment there were not admitted patients primarily diagnosed with SARS-COV-2 and secondary with active TB.

In one study, in a hospital in Sondrio province, Lombardy region, in northern Italy, a number of 20 patients of a total of 24 diagnosticated with active TB were with co-infection. It means there is a high susceptibility in patients with active TB to develop COVID-19.(9)

It is strongly preferred over hospital treatment for TB patients to reduce opportunities for transmission unless serious conditions are requiring hospitalization, unless TB is very severe.(10,11)

Because of a small sample size, this study has not been able to establish the statistical significance of the co-infection. There are few studies with a large number of patients. There are reported 8 studies with a total of 80 patients since 2020 till 09, 2020 when Ajay K M published his study in Acta Biomedica.(12)

This study was limited in defining the severity and patterns of organ involvement in patients with Covid-19, as in a study published by Echverria G, Espinoza. W, DE Vaard J.H in June 2020.(13)

Anti-tuberculosis treatment must be ensured for all TB patients, including those in Covid-19 quarantine and those with Covid-19 disease, as WHO recommended in Tuberculosis and COVID-19 report from 21.09.2020.(14,15)

We could not identify the interactions of various drugs that are used for treating TB and antiviral medication used in Covid-19 protocols of treatment. Interactions amongst multiple medications and adverse drug events were not reported in any study till now.(16)

The standardized multidrug antitubercular regime can be safely continued following physician's recommendations. as WHO mentioned in its report from 08.2020.(17)

We are limited also in terms of laboratory investigations including biochemical profile, inflammatory markers and coagulation profile.(18)

Morbidity was higher in patients with TB and Covid-19 co-infection. In our study, among the TB patients, Covid 19 was contributory to worst outcome and mortality. In the Sandalo Hospital study, fatality rate was 5% (18), in our report being of 30%.

CONCLUSIONS

TB is associated with an increased risk of Covid-19.

TB is associated with high risk of severe Covid-19 disease and increased risk for mortality.

Mortality is likely to occur in elderly patient with co - morbidities.

Hospital treatment for patients with tuberculosis, should be limited to severe cases, to prevent the spread of SARS-CoV-2 in TB cases.

Co-infection rates are higher in males.

TB patients with Covid-19 should continue their TB

CLINICAL ASPECTS

treatment.

The pattern of pulmonary involvement secondary to Covid-19 (clinical, laboratory, imaging, treatment) are the same as that of non-TB patients.

In our experience, there is no evidence that Covid-19 reactivate TB disease.

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