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Original Article

Microbiology Section

Co-infection of COVID-19 and Tuberculosis in a Tertiary Care Hospital

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ABSTRACT

Introduction: The burden of Tuberculosis (TB) has managed to remain an age old menace to our society, especially India. The potential impact of Coronavirus Disease-2019 (COVID-19) on TB patients continues to be worrisome due to the disruption of the national program and its services.

Aim: To compare the TB infection in COVID-19 vs non COVID-19 patients.

Materials and Methods: This retrospective study was undertaken at Department of Microbiology, ABVIMS, Dr. RML Hospital Delhi, India. The data was collected, retrospectively from 15th September 2020 to 15th January 2021 from admitted 1094 non COVID-19 and 150 COVID-19 patients, >18 years of age, either sex. Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) was done to diagnose COVID-19 and GeneXpert was used to detect *Mycobacterium tuberculosis*. The data entry was done in the Microsoft Excel spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software version 21.0. Two by two contingency table was used for calculating the Odd's ratio.

Results: During the study period, 1094 samples were received from non COVID-19 ward and 150 from COVID-19 ward. Out of 150 COVID-19 positive patients, 30 (20%) were also positive for *Mycobacterium tuberculosis* Complex (MTBC) and 120 (80%) were negative for MTBC. Out of 1094 COVID-19 negative patients, 98 (8.96%) were positive for MTBC and 996 (91.04%) were negative for MTBC. The Odd's ratio/Risk Ratio (RR) of TB infection in COVID-19 infected patients was 3.08 {Confidence Interval (CI) 95%}. The mortality was 10% in the COVID-19 positive group.

Conclusion: It was observed that the chances of contracting TB are thrice in COVID-19 patients and thus TB diagnosis should be equally emphasised and further strengthened in this ongoing pandemic.

Keywords: Coronavirus disease 2019, GeneXpert, *Mycobacterium tuberculosis* complex, Polymerase chain reaction

INTRODUCTION

The COVID-19 pandemic has posed a serious threat to global healthcare and economy. Before COVID-19 pandemic, India was battling with another, much older epidemic-TB, which affected 2.64 million Indians in 2019 and killed nearly 450,000 people in the country [1]. Moreover, it is estimated that two billion people have Latent TB Infection (LTBI) worldwide [2]. The potential impact of COVID-19 on TB patients and services continues to generate significant attention.

The nation-wide lockdown which was announced on 24th March 2020 in India for COVID-19 led to setback in National TB Elimination Program (NTEP) [3]. Modelling studies predict an additional 6.3 million cases of TB and 1.4 million deaths over the next five years, due to the same. This translates to about 5-8 year setback in TB control, receding even further away from the 2030 target of TB elimination in India [4]. From the beginning of COVID-19 positive cases in India, all the focus was put on strengthening the COVID-19 testing. The other pathogens of Lower Respiratory Tract Infections (LRTI), the differential diagnosis was put aside. Co-infections which involve the respiratory tract pose diagnostic predicaments and treatment challenges [5]. Due to the lacunae created, the TB diagnosis was neglected and this lead to the higher mortality [6]. With the COVID-19 pandemic erupting worldwide in the beginning of 2020, a significant rise in the incidence of TB co-infection was noticed [7].

Co-infection with TB and COVID-19 is concerning due to non specific clinical features of both the diseases (TB and COVID-19). COVID-19 may also cause reactivation of latent TB in country like India. Also, pre-existing TB disease and underlying compromised lung can affect the clinical severity score of COVID-19. Co-existing active TB disease may mount to severe illness and higher mortality [5]. Hence, this study was undertaken to compare the positivity of TB in COVID-19 and non COVID-19 patients and also the impact of TB/COVID-19 infection on the outcome of the patient, in a tertiary care hospital.

MATERIALS AND METHODS

The present study was a retrospective study, conducted in Department of Microbiology, Atal Bihari Vajpayee Institute of Medical Sciences, Dr. Ram Manohar Lohia Hospital, New Delhi, Hospital which is a tertiary care centre in North India. The data was collected from 15th September 2020 to 15th January 2021 from the entries included in the department record registers, which incorporates all the samples received for testing by the department along with the appropriate patient credentials. The data was analysed in the month of February 2021.

Inclusion criteria: Patients more than 18 years of age, either sex were included in the study.

Exclusion criteria: Extrapulmonary samples and samples received from patients <18 years of age were excluded from the study.

Study Procedure

Sputum/endotracheal aspirate or bronchoalveolar lavage samples received from non COVID-19 (n=1094) and COVID-19 ward (n=150) for MTBC detection by Cartridge Based Nucleic Acid Amplification Test (CBNAAT) by Cepheid®, a molecular based method, were included in the study. All the samples included, were from admitted patients who presented with complaints of Influenza Like Illness (ILI) and Severe Acute Respiratory Illnesses (SARI) such as cough, fever, chest pain, breathlessness. Considering the ongoing pandemic, nasopharyngeal and oropharyngeal swabs were collected and RT-PCR was done to detect Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-COV-2) infection in all patients prior to the

ward admission by commercially available RT-PCR kits. The patients detected for SARS-COV-2 were admitted in COVID-19 ward and those who were negative for SARS-COV-2 were admitted in non COVID-19 ward.

STATISTICAL ANALYSIS

The data entry was done in the Microsoft Excel spreadsheet and the final analysis was done with the use of SPSS software version 21.0. Two by two contingency table was used for calculating the Odd's ratio.

RESULTS

A total of 1094 samples were received from non COVID-19 ward and 150 from COVID-19 ward during the study period. Out of 1094 (age distribution 18-76 years), 601 were males and 493 were females. The mean age in males was 45.25 years and in females was 38.76 years. Similarly, out of the 150 COVID-19 positive patients (age distribution 19-85 years), 80 were males and 70 were females. Mean age in males was 40.24 years and mean age in females was 35.67 years.

Distribution of MTBC positive status in the COVID-19 vs non COVID-19 patients is shown in [Table/Fig-1]. The Odd's ratio/RR of TB infection in COVID-19 infected patients was 3.08, (CI) 95%.

Non COVID-19 patients (n=1094)		COVID-19 patients (n=150)	
MTB positive	MTB negative	MTB positive	MTB negative
98 (8.96%)	996 (91.04%)	30 (20%)	120 (80%)

[Table/Fig-1]: Distribution of MTB status in the COVID-19 vs non COVID-19 group. MTB: *Mycobacterium tuberculosis*

Of the 98 non COVID-19, MTB infected patients, 58 were males (mean age 35.63 years) 40 were females (mean age 36.22 years) (male:female 1.45:1). Of the 30 TB/COVID-19 co-infected patients, 20 were males (mean age 32.76 years) and 10 females (mean age 28.34 years) (male:female 2:1). All were newly diagnosed cases of active TB. Only two (both females) had Multidrug Resistance (MDR) TB. Three (10%), (two males and one female) succumbed to the diseases and rest 27 (90%) were discharged.

DISCUSSION

In September 2020, the Indian Ministry of Health and Family Welfare (MoHFW) stated that due to the COVID-19 pandemic there was an overall decline by 26% in TB notification during the period of January to June 2020, when compared to previous year [8]. It is noteworthy that apart from impact of COVID-19 on the NTEP, studies have also stated that active as well as latent TB is an important risk factor for SARS-CoV-2 infection, which results in increased susceptibility, development of severe symptoms and rapid disease progression associated with poor outcomes.

In present study, authors have compared the positivity of TB in COVID-19 group vs the non COVID-19 group. It was observed to be more than twice when compared to the non COVID-19 group (20% vs 8.96%). The odds ratio calculated was 3.08. This was similar to reports by other studies [9]. This can be justified by the temporary immunosuppression induced by TB, which may increase the susceptibility of patients to COVID-19, and vice-versa [10]. In other words, immunologically the TB/COVID-19 co-infection has the potential to converge into a "perfect storm". This immunomodulation disturbance induced by each pathogen leads to a conducive unchecked inflammatory response, which worsens the morbidity and mortality [7].

There was no gender preponderance observed in the COVID-19 positive group (80 males and 70 females). This was similar to the data of a brief report published by World Health Organisation (WHO) which shows a relatively even distribution of COVID-19 infections between women and men (47% versus 51%, respectively) [11]. However, in the present study it was found that the co-infection of TB and COVID-19 was more in males as compared to females (2:1). This finding was similar to a recently published review article in January 2021, in which many included studies have has stated co-infection more in males than females [7]. Similarly, the TB in non COVID-19 patients was more in males than females (1.45:1). In our setting this can be explained by the fact that in India, TB infection/LTBI is more common in males than in females.

The mortality was 10% in present study, which was comparable to studies by Tadolini M et al., and Motta I et al., which reported respectively 12.3% and 11.6%, mortality in patients co-infected with TB and COVID-19 [12,13]. None of the demised COVID-19 infected patients had any other co-morbidities than TB. Also, all three were infected by a Rifampicin sensitive TB strain. A recent review article published by Mousquer GT et al., has stated that higher mortality in TB/COVID-19 co-infection is due to an acute, secondary abuse in a previously compromised TB [7]. Amongst COVID-19 patients in India, around 2.3% mortality rate has been witnessed including patients with co-morbidities such as hypertension, diabetes and malignancy [14]. This was observed to be much higher in patients co-infected by TB. An observational study from Wuhan, found *Mycobacterium tuberculosis* infection to be a more common co-morbidity for COVID-19 (36%) and suggested that individuals with latent or active TB were more susceptible to SARS-CoV-2 infection [15].

Tuberculosis and COVID-19 have certain similarities- both present with fever, cough and breathlessness and they mainly invade susceptible population through droplet transmission [16]. Understanding the nature of the interactions between *Mycobacterium tuberculosis* and SARS-CoV-2 will be crucial for the development of therapeutic strategies against co-infection. Therefore, it is important that all LRTI patients are investigated for both SARS-COV-2 and TB as per the bi-directional TB/COVID-19 screening NTEP guidelines. A recent press release from MoHFW, January 2021, stated "The fight against TB needs to be made into a Jan Andolan, a people's movement". The release stated that an effective approach is required which should mainly aim at reaching the maximum population; should supplement the existing strategies of preventive, diagnostic and curative aspects of TB management; should work towards demand generation; ensuring mass-media coverage; and with special spotlight on community participation and mobilisation [17].

Limitation(s)

Due to substantial burden in both COVID-19 RT-PCR and CBNAAT for TB samples, bidirectional testing for all the samples could not be done which is need of the hour. Further prospective studies are required to generate structured algorithms for diagnosis and management of COVID-19- TB co-infection and its outcome.

CONCLUSION(S)

Amidst the rising number of cases and deaths due to COVID-19, it is imperative to not forget TB. Authors have observed that the chance of contracting TB with COVID-19 infection is increased by three times (RR-3.08, CI-95%). Hence, it is important that all LRTI patients should be investigated for both SARS-COV-2 and TB.

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