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A Retrospective Study of Covid-19 Disease in Confirmed Tuberculosis Patients from a Tertiary Care Centre in Ahmedabad

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ABSTRACT

Background: Tuberculosis (TB) is long standing disease and SARS-COV-2 being global pandemic in current era. Interactions between SARS-COV-2 and TB needs analysis, as both has major infection-related morbidity and mortality worldwide. This study was conducted to evaluate impact of super imposing viral pandemic over chronic diseases like tuberculosis.

Methodology: A Retrospective study done in 75 patients registered under RNTCP program at our centre. Epidemiological data, diagnostic timing of TB, duration of AKT, history of SARS-COV-2 symptoms and SARS-COV-2 diagnostic result were evaluated. Analysis conducted based on incidence of COVID-19 infection in active cases of TB.

Results: Male: Female ratio was 1.88:1 with majority belongs to age group of 35 to 55years. Only 3 patients developed influenza like symptoms who tested negative for SARS-COV-2. None COVID-19 suspected or positive patient were reported amongst laboratory confirmed TB patients taking AKT, indicating TB drugs definitely have some impact on SARS-COV-2 virus.

Conclusion: TB and COVID-19 co-infection has limited cases. Very few individuals who were exposed to SARS-COV-2 during AKT treatment developed influenza like symptoms, however tested negative for SARS-COV-2. A larger study is needed to understand any role played by TB infection or AKT drugs on covid-19 disease.

Keywords: Covid -19, Tuberculosis, Co-Infection

INTRODUCTION

The WHO suggests a "pandemic" is defined as the worldwide spread of a new disease. At present whole world is facing one of such pandemics called corona virus disease-19. (Declared on 11march 2020 by WHO)[1].

The novel coronavirus-19 (nCoV-19) or severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a new corona virus that is recently discovered[2] in 2019. The virus causes corona virus disease 2019 (COVID-19). It has rapid global spread with extreme clinical severity and pneumonia with high transmissibility and significant mortality rate [3]. India has reported **6,650,456** total cases with **102685** deaths so far as per ICMR and MoHFW (India) [4] till 05 October 2020.

Tuberculosis remains a global health emergency invariably [5]. It is caused by *Mycobacterium tuberculosis*, a bacterium discovered by Dr Robert Koch in 1882. It is ranked as the ninth leading cause of death worldwide and the leading cause from a single infectious agent [6] (especially in most middle-income and emerging-economy countries.) India alone accounts for 6.25 lakh new cases and nearly one lakh deaths annually (mortality rate 20%) [1].

Hence it becomes important to study the interactions between COVID-19 and tuberculosis (TB) since both causes major infection-related morbidity and mortality around the world. Both COVID-19 and tuberculosis can present with respiratory

symptoms like viral influenza. With similar clinical picture the diagnosis and treatment of patients with tuberculosis OR tuberculosis and COVID-19 co-infection, are likely to be compromised during the COVID-19 pandemic. Also, both diseases have considerable economic impact and social impact including stigma, discrimination, and isolation[7].

The purpose of this paper is to predict the impact of superimposing COVID-19 pandemic on individuals with Mycobacterium TB with ongoing treatment and its sequelae. Experience with concomitant TB and COVID-19 is extremely limited, we need more longitudinal studies to determine the factors and outcomes in patients with both disease[3].

MATERIAL AND METHODS

The study was a retrospective review of 75 randomly selected patients out of 82 patients, who were registered under RNTCP from March 2020 to July 2020 at the TB and Chest Unit of S.C.L. General Hospital, Ahmedabad, Gujarat, India. Patients who were lost in follow-up, non-cooperative and not responded for survey were excluded. All the information was retrieved from patient medical records as per standard guidelines and ethical standards. This data was evaluated for the epidemiological data, timing of diagnosis of Mycobacterium TB, duration of AKT taken, history of covid-19 symptoms, and status of COVID-19 diagnosis testing. The patients selected are laboratory confirmed cases of tuberculosis (including pulmonary and extra pulmonary). The patients were assessed on basis of the incidence of COVID-19 disease, history of exposure to lab-confirmed COVID-19 positive patient, history of travelling, resident of containment/non-containment zone, mortality or any other complications as parameters. Furthermore, an analytical study report was made on incidence of COVID-19/SARS-COV-2 in active cases of tuberculosis and influence of AKT was studied. The association between variables was assessed using chi-square test. P value <0.05/0.001 was considered as statistically significant/highly significant.

RESULTS

The study was attempted on cohort of 75 patients (registered under RNTCP) who have ongoing AKT or were previous TB patients (post TB treatment sequelae). Out of 75 cases, 49 (65%) were male and 26 (35%) were female. The study has Male: Female ratio of 1.88:1.

The patients included were of age ranging from 17 years to 70 years. Out of 75 cases 36% were below 35 years, 45% aged between 35 to 55 years and 19% were above 55 years. The median age was 45years. All the patients were scanned if they had COVID-19 symptoms or not and for result of COVID-19 diagnosis test. We found only 6 patients suffering from influenza symptoms; however, they were tested negative for COVID-19 done after 4 days of symptom **(Table 1)**. All patients had undergone Covid-19 RT-PCR testing, all of which came out to be negative.

67 patients (89.3%) patients had active T.B and 8 (10.6%) had post-TB treatment (direct sequelae).

Out of these, 10 patients (13.33%) belonged to Containment Zone and 06 patients (8.0%) were in direct contact with COVID-19 positive patient, however none of them were tested positive for COVID-19 **(Table 2 and Table 3)**.

The overall mortality in our study was 12% (9/75); 6 out of 9 were >60years old and all of them had ≥ 1 co-morbidities, 2 had HIV co-infection, 1 had chronic kidney disease. Given the smaller number of deaths, larger studies are necessary.

The results were further analyzed to draw a comparison using the above same parameters to understand the effect of tuberculosis and its treatment on SARS-COV-2.

Table 1: Duration of TB and Symptoms of COVID-19

Duration of TB	Symptoms of COVID-19		Total
	Yes (%)	No (%)	
< 3 months	4(66.67)	30(50)	34(51.51)
> 3 months	2(33.33)	30(50)	32(48.49)
Total	6	60	66

P value is 0.430. (Limitation-due to less sample size);
There is insignificant association between duration of TB and symptoms of COVID-19; Excluded 9 patients who got expired.

Table 2: Containment Zone and Symptoms

Containment Zone	Symptoms of COVID-19		Total
	Yes (%)	No (%)	
Yes	5(83.33)	5(7.25)	10(13.33)
No	1(16.67)	64(92.75)	65(86.67)
Total	6	69	75

P value < 0.001. Association between TB patients in containment zone and no. of patients having symptoms is significant.

Table 3: Direct Contact Exposure and Symptoms

Direct Contact Exposure	Symptoms of COVID-19		Total
	Yes (%)	No (%)	
Yes	5(83.33)	1(1.45)	6(8)
No	1(16.67)	68(98.55)	69(92)
Total	6	69	75

P value < 0.001. Association between who had Direct Contact Exposure history and No. of patients having symptoms is significant.

DISCUSSION

Tuberculosis is an airborne infection i. e. can cause an infection in humans by being inhaled, or breathed in. It is transmitted by respiratory droplets which can remain suspended in air up to 6 hours. The infection transmitted by inhalation of TB bacilli from close contact with someone with TB disease, especially with symptoms such as cough. The tuberculosis infection can be prevented by decrease in concentration by movement of air (open windows, well ventilated spaces), exposure to direct sunlight which kills bacilli and Face mask

SARS-CoV-2 spreads by droplets, not by aerosols. It is transmitted by droplet if inhaled while it is still airborne or Direct contact with virus-containing droplets that fall onto surface (Stays up to hours). Sneeze or cough generate droplets containing SARS-CoV-2 become airborne immediately. Spread of infection can be prevented by hand-washing to eliminate virus after touching an infected surface, and by using ace mask

For limiting the spread of SARS-COV-2 in TB cases, self-isolation or quarantine is necessary and hospital-based treatment should be given to only severe cases.

The present study observed a male preponderance, most of the patients being adults belonging to the age group of 35-55 years. This agrees with the reports from previously published studies done by Tadolini M et al and Wingfield et al. Male young adults, being the breadwinners of the family are thus more vulnerable while young females likely to have iron deficiency anemia increases the risk for catching MTB.

In our present study, we found that along with comorbid conditions, poor hygiene, and overcrowding, lesser awareness to safety and isolation measures are leading factors for developing these diseases which agrees with report from [6]. According to Chopra et al in their study stated, One SARS-cov-2 infected person could have infected 2.5 people in 5 days which in turn could infect 406 people over 30 days but with proper isolation & containment measures the transmission rate could be decreased to as low as 1.05. On the other hand, a person infected with TB has a lifetime risk of 5–15% of developing an active disease and an active TB patient could infect 10–15 people per year.

One latest report stated that SARS-CoV-2 is in emerging phase, the basic reproduction number (R_0) is 2.2, i.e. each person with SARS-COV-2 can pass the infection on to an additional 2.2 individuals[7].

The R_0 value for TB in low-incidence countries can be below 1 so has little transmission rates. However, in low-income settings with a high TB burden like India, the R_0 value has been 3.55 [7].

We found that older age group and co-morbidities, such as hypertension, diabetes and coronary heart disease, chronic kidney disease makes individual more prone for poor outcome and mortality. Our study results are comparable to Tadolini M. et al.

Few reports published agreed that increasing evidences shown that having chronic respiratory disease increases the chance of poor outcomes with COVID-19 disease[2].

TB and COVID-19 both present with respiratory symptoms like cough and shortness of breath associated with fever and weakness. Both have different time of onset.

TB symptoms start appearing with gradual onset, over period of weeks or longer and not immediately after infection unlike COVID-19, where symptoms appear within 2-14 days after exposure with incubation period of 5 days[2].

In present study we found that those who were on anti TB treatment did not had any symptoms or did not get covid-19 infection. We concluded that there is role of tuberculous drugs on SARS-COV-2.

Literature also suggested that SARS-CoV-2 infection initiates an aggressive inflammation by increasing cytokines secretion such as interleukin-1β (IL-1β), interferon-γ (IFN-γ), tumour necrosis factor-α (TNF-α), interleukin-2(IL-2), interleukin-4 (IL-4), interleukin-10 (IL-10), their plasma levels being associated with disease severity, leading to a so-called "*cytokine storm*" [6].

Comparison of TB and COVID-19 disease [2]

Comparison	Tuberculosis	Covid-19 disease
Pathogen	Mycobacterium tuberculosis complex	Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
Spread	Airborne	Droplet spread
Specimen for Diagnosis	Sputum tests	Nasopharyngeal swab
Infectivity	Range from less than 1 to up to 4 people infected per one person with TB	Average of 2.2 people infected per one person with COVID-19
Treatment	Antibiotics. (Drug-sensitive TB: 4 antibiotics for 6 months. Drug resistant TB: antibiotics for 9-24months)	Supportive treatments Antibiotics with antivirals
Vaccine	BCG vaccine	No vaccine

Few other studies reported that influenza aggravated pulmonary status of individuals with TB, so that latent TB could become active, a closed cavity might open, and various lesions might progress leading to further deterioration of pulmonary function

Previous reports also show that TB status plays a major role in a rapid development of severe acute respiratory syndrome in SARS-CoV-2 co-infection[6].

With limited data on TB and COVID-19 infection in the present study, it's difficult to compare the co-existence of both diseases. Others reports also concluded that its inadequate data currently on those with or who have a previous history of TB are more at risk of worse outcomes[7]. However, COVID-19 affects the lungs, and as we know that there is usually some left-over damage in the lungs following TB disease, which may increase the risk of developing more severe COVID-19 symptoms.

However, we need such longitudinal prospective studies to prove impact and burden of both diseases on each other. Further to determine the role of AKT drugs and its interactions with SARS-COV-2 virus.

CONCLUSION

TB and COVID-19 co-infection has limited cases. Patients with anti-TB treatment were found negative in COVID-19 testing. Very few individuals who were exposed to SARS-COV-2(containment zone resident/direct positive patient contact) during anti-TB treatment developed influenza like symptoms, however they tested negative for COVID-19 disease. Mortality was seen in older age group with co-morbidities and has been confirmed negative for COVID-19. We understand that pre-existing TB, its pathogenesis or its treatment has some influence in SARS-COV-2 Though we need larger studies to understand role played by TB infection or AKT drugs on COVID-19 disease. We believe that this descriptive research can motivate larger studies to enable analyses of interactions and determinants of outcomes in patients with both diseases.

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