

AN OBSERVATIONAL STUDY, IMPACT OF TUBERCULOSIS ON COVID-19 DISEASE AND ITS EFFECT ON SEVERITY

Virendra Singh¹, Shanu², Sudhanshu Sant³, Rahul Bhargava⁴, S. Kumar⁵

¹Associate Professor, Department of Pulmonary Medicine G.S. Medical College and Hospital, Pilkhuwa, Hapur, U.P, India.

²Phd Nursing Research Scholar, Senior nursing officer CNE Coordinator, DQM (nursing) Quality cell VMMC& Safdarjung Hospital New Delhi, India

³Assistant Professor, Department of Anaesthesia, G.S. Medical College and Hospital, Pilkhuwa, Hapur, U.P, India.

⁴Professor & Head of the Department of Ophthalmology, G.S. Medical College and Hospital, Pilkhuwa, Hapur, U.P, India.

⁵Chief Medical Superintendent & Professor Critical Care Medicine G.S. Medical College and Hospital, Pilkhuwa, Hapur, U.P, India.

Received : 04/08/2022
Received in revised form : 17/09/2022
Accepted : 14/10/2022

Keywords:
Tuberculosis,
COVID-19,
RT-PCR, Spo2

Corresponding Author:
Dr. Virendra Singh,
Email: virendrasingh99aug@gmail.com
ORCID: 0000-0003-4472-5006

DOI: 10.47009/jamp.2022.4.4.82

Source of Support: Nil,
Conflict of Interest: Nondeclared

Int J AcadMedPharm
2022; 4 (4); 416-420



Abstract

Background: covid-19 disease is a new disease of international concern. Till now there is limited studies available on this new disease.it is anticipated that the people suffering from both tuberculosis and covid-19 may have poor outcomes, the present study conducted to find out the impact of tuberculosis on covid-19 disease and its severity. **Materials and Methods:** 486 patients of both genders from general and private ward were enrolled in this study, data of tuberculosis case made as per clinical manifestations, current or old treatment history of ATT and investigations. While covid-19 cases confirmed by RT-PCR and HRCT chest, scoring of covid-19 severity was done by Spo2, HRCT chest and inflammatory markers. **Result:** In enrolled total 486 confirm cases of covid-19,39(8%) patients had history of tuberculosis and 447 (92%) patients without H/o of tuberculosis. It have been seen that severity of covid-19 was significantly low in patients with history of tuberculosis (p value <0.0001). **Conclusion:** Thus in our observational study, it is concluded that the severity of covid-19 was less in patients having tuberculosis as compared to patients without tubercular infection.

INTRODUCTION

Corona virus disease 2019 (COVID-19), the highly contagious infectious disease caused by severe acute respiratory syndrome corona virus 2(SARS-CoV-2). Its first case was reported in Wuhan city of China in early December 2019 and spread quickly over 215 countries worldwide except Antarctica. In India the first case was reported on 31 January 2020. WHO, under International health regulations has declared this outbreak as a "public health emergency of International concern"(PHEIC) on 30th January 2020.WHO subsequently declared COVID-19 as a pandemic on 11th March 2020 till now. In a general estimate 2% of the population are healthy carrier of CoVs and 5% -10% of acute respiratory infections by these viruses.^[1]

SARS-CoV-2 is a novel beta CoV belonging to same subgenus as the severe acute respiratory syndrome corona virus (SARS-CoV) and the middle east respiratory corona virus (MERS-CoV), with mortality up to 10% and 35% respectively.^[2]

Similar to SARS and MERS, it has been hypothesized that SARS-CoV-2 advanced from bats to intermediate hosts such as pangolins and minks, and then to humans.^[3,4]

In US, COVID-19 was the third leading cause of death in 2020 after heart disease and cancer, with approximately 3,75,000 death reported.^[5]

It is estimated that 17.9% to 33.3% of infected patients will remain asymptomatic.^[6,7]

The majority of symptomatic patients present with fever, cough and shortness of breath and less commonly with sore throat, anosmia, dysgeusia, anorexia, myalgias and diarrhea.

Stokes et al. reported that among 373,883 confirmed symptomatic COVID-19 cases in the US, 70% of them presented with fever, cough, shortness of breath,36% reported myalgia and 34% reported headache.^[8]

India has the highest estimated burden of tuberculosis infection(TBI) globally, with nearly 35-40 crores Indian population having TBI, of which 26 lakhs people are estimated to develop tuberculosis(TB) disease annually. India has one

fourth of the global burden of TB i.e. 2.2 million out of 9.6 million new cases annually. Every day >6000 die of tuberculosis, 2 deaths every 5 minutes.

People suffering from COVID-19 and TB have shown similar symptoms such as cough, fever, and difficulty in breathing, both disease attacks primarily the lungs and both biological agents transmit mainly via close contact. The incubation period from exposure to disease in TB is longer. There is insufficient data regarding potential interaction between covid-19 and tuberculosis.

The experience on COVID-19 infection in TB patients remains very limited and till now it is anticipated that the people suffering from both TB and COVID-19 may have poor outcomes, especially if tuberculosis treatment is interrupted, the present study will be conducted to find out the effect of tuberculosis on Covid-19 disease.

Aims and Objectives

1. To estimate the prevalence of covid-19 disease and its severity in pulmonary tuberculosis Patients.
2. To find out the effect of tuberculosis on Covid-19 disease.

MATERIALS AND METHODS

Study Design

It is a retrospective clinical study conducted by department of pulmonary medicine, G.S. Medical

College and Hospital Pilkhuwa, Hapur, after approval by ethical committee. Study conducted w.e.f. April 2020 to March 2022 and 486 covid-19 positive of all severity were enrolled who were admitted in our Institution during covid-19 second wave in general ward, private ward. The patients of both gender and of all age group enrolled in the study. Data of tuberculosis cases made as per clinical manifestations, current or old treatment history of ATT and investigations. The clinical data, spo2 and relevant investigations CBC, ESR, chest x-ray, sputum for AFB (as per need), KFT, LFT, RBS, HIV (as per need), COVID-Ag, RT-PCR for COVID-19, S.CRP, S.LDH, S. ferritin, IL-6 (as per need), D-dimer, ABG (as per need) and HRCT chest get done of all patients admitted.

Exclusion Criteria

Patients Vaccinated to covid-19 vaccine.

Patient with chronic respiratory failure and on Domiciliary O2 therapy (LTOT).

Data Collection

Pulmonary medicine, radiology and pathology department of G. S. Medical College and Hospital, Pilkhuwa, Hapur, U.P, India.

Statistic Analysis

The observed data tabulated and statistical analysis done by using T Test, coefficient statistic and Anova Test by using SPSS28 (IBN INC).

RESULTS

Table 1: Descriptive Statistics

	Mean	Std. Deviation
Age (Yrs)	45.93	15.771
CRP	25.8811	20.23920
LDH	535.066	260.3606
DD	2.56017	33.957738
CTSS	9.08	7.063
Valid N (list wise)	Mean	Std. Deviation

Table 2: Frequencies H/O ATT

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Nil	447	92.0	92.0	92.0
	Yes	39	8.0	8.0	100.0
	Total	486	100.0	100.0	

Table 3: Homogeneous Subset (CTSS)

Tukey HSDa,b			
AGE GROUP	N	Subset for alpha = 0.05	
		1	2
Less than 18	15	1.33	
18.1-40	176		8.11
40.1-60	203		10.05
More than 60	92		10.03
Sig.		1.000	.538

Means for groups in homogeneous subsets are displayed.

- a. Uses Harmonic Mean Sample Size = 45.380.
- b. The group sizes are unequal. The harmonic mean of the group sizes is used. Type I error levels are not guaranteed.

The difference in CTSS score did not differ between different age groups. P value = 0.538 which is non-significant.

Table 4: Correlations Statistic

Variable	Variable2	Correlation	Count	Lower C.I.	Upper C.I.	Notes
CTSS	CRP	.669	486	.616	.715	
	DD	.026	486	-.063	.114	

Missing value handling: PAIRWISE, EXCLUDE. C.I. Level: 95.0

CTSS and CRP have significant correlation with 0.669 correlation coefficient, P value <0.001

CTSS and DD have non-significant correlation with 0.026 correlation coefficient, P value 0.571

Table 5: Group Statistics, T-Test

	H/O ATT	N	Mean	Std. Deviation	Std. Error Mean
CTSS	Nil	447	9.74	6.954	.329
	Yes	39	1.49	2.187	.350

The mean CTSS score in patients with H/o ATT (1.49±2.2) was significantly lower than patients without H/o ATT (9.74±6.9), on independent T Test (P < 0.001).

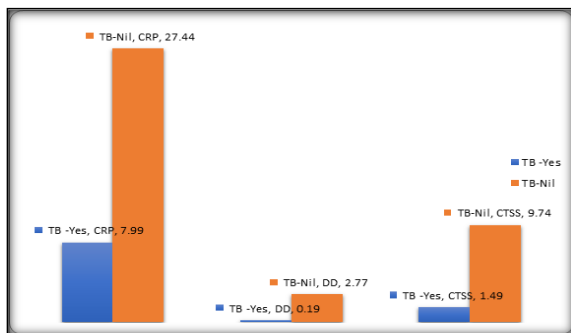
Table 6: Level of CRP, LDH, DD & CTSS (mean±SD) in patients with COVID19 with and without History of ATT.

	H/O ATT		p-value
	Yes (n=39)	No(n=447)	
Age	36±13.37	45.93±15.77	0.002
CRP	7.99±7.56	27.44±20.25	<0.0001
LDH	296.32±95.35	555.69±259.84	<0.0001
DD	0.19±0.47	2.77±35.40	0.650
CTSS	1.49±2.19	9.74±6.95	<0.0001

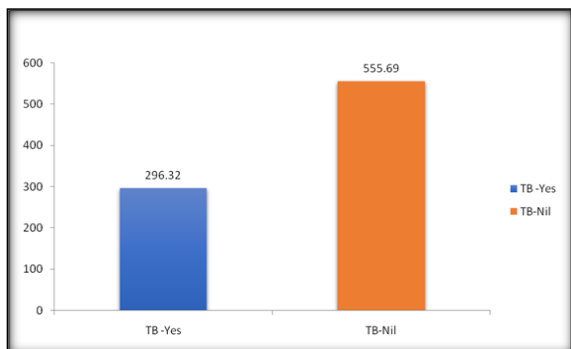
Bar graph: showing age wise distribution of patients as per H/o tuberculosis and without H/o tuberculosis in covid-19 patients.

Table 7: Level of CRP, LDH, DD, CTSS & SPO2 (%) (mean±SD) in covid-19 positive patients admitted in general vs private ward.

	Ward		p-value
	General ward (n=374)	Private ward (n=112)	
CRP	22.66±19.51	35.91±18.62	<0.0001
LDH	501.38±245.77	649.26±277.47	<0.0001
DD	0.34±0.40	0.61±0.66	<0.0001
CTSS	7.18±6.14	15.40±6.22	<0.0001
SPO2%	87.70±14.91	65.32±22.14	<0.0001

**Figure 1: CRP, DD and CTSS**

Bar Graph: Showing level of CRP, DD and CTSS in COVID patients with H/o ATT present and absent

**Figure 2: LDH level in COVID patients with H/O ATT present and absent.**

Bar Graph

showing level of LDH in covid patients with H/o ATT present and absent

DISCUSSION

Results of study were as follow

- Total no of covid-19 positive patients of all severity 486
- Minimum age of patients 1 year.
- Maximum age of patients 87 years.
- Male patients 310(63.8%)
- Female patients 176 (36.2%).
- H/o tuberculosis present in 39 (8%) patients.
- Patients without H/o of tuberculosis 447(92%)
- Patients admitted in general ward 374 and in private ward 112.

As shown in Table 6

Mean age with SD of covid-19 positive with H/O tuberculosis 36±13.37

Mean age with SD of covid-19 positive without H/O tuberculosis 45±15.77

With p value < 0.002, which is significant

Because tuberculosis disease occurs more common in young and reproductive age so mean age of

covid-19 patients with tuberculosis was less (36 ± 13.37)

All inflammatory markers values low in covid-19 positive patients having H/O tuberculosis in comparison to the patients without tuberculosis with p value of < 0.0001 which is significant.

CTSS values less in patients who are with H/O tuberculosis with mean with SD 1.49 ± 2.19 in comparison to the patients with H/O tuberculosis with mean with SD 9.74 ± 6.95 with p value $< .0001$ which is significant.

Patients admitted in general ward have low levels of inflammatory markers in comparison of private ward (p value < 0.0001), so severity of covid-19 less in patients admitted in general ward. Fact behind this may be as tuberculosis is more prevalent in low socio-economic groups so covid-19 cases less severe in tuberculosis patients and need less hospital admission rate.

As covid-19 is a new disease and there is very less data available, meanwhile most of the study related to covid-19 and tuberculosis done from developed world where tuberculosis is very less prevalent and, in these studies, have shown that tuberculosis patients are more prone and more severe to develop covid-19

In developing country and our country India very less research work done on tuberculosis and covid-19.

In our study compare to prior studies shown patients having H/O tuberculosis are less prone and less severe to get covid-19 disease.

In support of our study-

Phase III, two group multicentre randomized controlled in 10078 health workers to determine role of BCG vaccination to reduce the incidence and severity of covid-19 during the 2020 pandemic BCG vaccination to protect health care workers against covid-19 (BRACE).^[9]

Another hypothesis in role of bacilli calmette guerin (BCG) vaccine for protection against COVID-19 generated – BCG protects from tuberculosis by enhancing cellular immunity. IFN γ is a key cytokine produce by CD4 T cells and mediates macrophage activation and resistance to mycobacterium tuberculosis via cellular immune mechanism.^[10] In another interesting study done by Escobar et al, a correlation between BCG index and covid-19 mortality in different socially similar European countries was observed. Every 10% increase in the BCG index was associated with a 10.4% reduction in covid-19 mortality.^[11]

It also has been shown in our study that severity of disease less in low socio-economic group compared to high socio-economic as reported in Urashima M, et al study.

In Urashima M, et al study covid-19 related deaths were higher in countries with higher quality of life compared to developing countries in contrast to general expectation that high income countries would have lower mortality rates due to the better

healthcare systems but effect of BCG vaccination on morbidity was not evident.^[12]

In CADTH report has been proposed that BCG vaccination may be protective against viral pathogens, such as influenza, through non-specific effects and innate immunity.^[13] A rapid review conducted by the centre for evidence-based medicine in April 2020 found evidence that BCG vaccination prevents pneumonia and influenza in children in children and elderly patients.^[14]

It has been suggested that the non-specific immune effects induced by BCG vaccination may have a protective role against COVID-19.^[15]

CONCLUSION

It is concluded in our study that symptomatic cases of covid-19 and severity of disease less in patients having history of tuberculosis and as tuberculosis more prevalent in low socio-economic group population, so symptomatic cases of covid-19 less common in that population. Thus in our study it is concluded that there is some immunogenic correlation between mycobacterium tuberculosis bacteria and covid-19 virus so BCG vaccination may be important key factor to fight against covid-19 to the world although more research work require to reach the final conclusion.

REFERENCES

1. Chan JF, To KK, Tse H, Jin DY, Yuen KY. Interspecies transmission and emergence of novel viruses: lessons from bats and birds. *Trends Microbiol.* 2013;21(10):544-55. doi: 10.1016/j.tim.2013.05.005.
2. Chan JF, Kok KH, Zhu Z, Chu H, To KK, Yuan S, et al. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerg Microbes Infect.* 2020;9(1):221-236. doi: 10.1080/22221751.2020.1719902.
3. Zhang T, Wu Q, Zhang Z. Probable Pangolin Origin of SARS-CoV-2 Associated with the COVID-19 Outbreak. *Curr Biol.* 2020;30(8):1578. doi: 10.1016/j.cub.2020.03.063.
4. Oreshkova N, Molenaar RJ, Vreman S, Harders F, Oude Munnink BB, Hakze-van der Honing RW, et al. SARS-CoV-2 infection in farmed minks, the Netherlands, April and May 2020. *Euro Surveill.* 2020;25(23):2001005. doi: 10.2807/1560-7917.ES.2020.25.23.2001005.
5. Ahmad FB, Cisewski JA, Miniño A, Anderson RN. Provisional Mortality Data - United States, 2020. *MMWR Morb Mortal Wkly Rep.* 2021;70(14):519-522. doi: 10.15585/mmwr.mm7014e1.
6. Mizumoto K, Kagaya K, Zarebski A, Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. *Euro Surveill.* 2020;25(10):2000180. doi: 10.2807/1560-7917.ES.2020.25.10.2000180.
7. Nishiura H, Kobayashi T, Miyama T, Suzuki A, Jung SM, Hayashi K, et al. Estimation of the asymptomatic ratio of novel coronavirus infections (COVID-19). *Int J Infect Dis.* 2020;94:154-155. doi: 10.1016/j.ijid.2020.03.020.
8. Stokes EK, Zambrano LD, Anderson KN, Marder EP, Raz KM, El Burai Felix S, et al. Coronavirus Disease 2019 Case Surveillance - United States, January 22-May 30, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(24):759-765. doi: 10.15585/mmwr.mm6924e2.
9. Ten Doesschate T, van der Vaart TW, Debisarun PA, Taks E, Moorlag SJCFM, Paternotte N, et al. Bacillus Calmette-

- Guérin vaccine to reduce healthcare worker absenteeism in COVID-19 pandemic, a randomized controlled trial. *Clin Microbiol Infect.* 2022;28(9):1278-1285. doi: 10.1016/j.cmi.2022.04.009.
10. Rossouw M, Nel HJ, Cooke GS, van Helden PD, Hoal EG. Association between tuberculosis and a polymorphic NFkappaB binding site in the interferon gamma gene. *Lancet.* 2003;361(9372):1871-2. doi: 10.1016/S0140-6736(03)13491-5.
 11. Escobar LE, Molina-Cruz A, Barillas-Mury C. BCG vaccine protection from severe coronavirus disease 2019 (COVID-19). *Proc Natl Acad Sci U S A.* 2020;117(30):17720-17726. doi: 10.1073/pnas.2008410117.
 12. Urashima M, Otani K, Hasegawa Y, Akutsu T. BCG Vaccination and Mortality of COVID-19 across 173 Countries: An Ecological Study. *Int J Environ Res Public Health.* 2020;17(15):5589. doi: 10.3390/ijerph17155589.
 13. O'Neill LAJ, Netea MG. BCG-induced trained immunity: can it offer protection against COVID-19? *Nat Rev Immunol.* 2020;20(6):335-337. doi: 10.1038/s41577-020-0337-y.
 14. ZhelezovaG, Mateeva V, Mateev G. Is the BCG vaccine a useful tool against COVID-19? *Clin Dermatol.* 2021;39(1):98-103. doi: 10.1016/j.clindermatol.2020.12.018.
 15. GurselM, Gursel I. Is global BCG vaccination-induced trained immunity relevant to the progression of SARS-CoV-2 pandemic? *Allergy.* 2020;75(7):1815-1819. doi: 10.1111/all.14345.