Prevalence of tuberculosis/COVID 19 co-infection among active tuberculosis patients at a tertiary care hospital in Uttarakhand, India

Abstract

Coronavirus disease 2019 (COVID-19) was spread all over the world and was accepted as a pandemic by the World Health Organization (WHO) on March 11, 2020. Lungs are predominantly affected by tuberculosis and Covid-19. **The objective of the study was to assess the clinical features of COVID-19 in active tuberculosis (pulmonary and extra-pulmonary) and to identify the radiological and laboratory picture of COVID 19 in patients with active tuberculosis**. A cross sectional study was by the Department of Respiratory Medicine, Himalayan Institute of Medical Sciences, among patients of active tuberculosis (pulmonary and extra-pulmonary) presented to the General Outpatient Department(OPD) of the Respiratory Medicine Department. The questionnaire included questions on socio demographic profile, clinical features, comorbidities, clinical history, any substance abuse and laboratory investigations. Data was analyzed by SPSS software version 21.0 while Chi- square test was used for categorical data analysis. The mean age of the study participants was 47.5±5.3 years (Range 18-72). Males constituted the larger group (59.38%) as compared to females (40.63%). The prevalence of COVID19/tuberculosis co-infection in the present study was 21.8%. Positive history of contact, bacterial culture, PCR and CBNAAT, use of drug, presence of cavity and pleural effusion on X Ray, showed all remarkably higher chances ($p < 0.05$) of developing co-infection. The prevalence of COVID19/tuberculosis co-infection in the present study was high. Significantly associated factors can help in identifying Covid 19 infection among tuberculosis patients. Therefore, it is recommended that screening for these factors should be done for all the tuberculosis patients coming for treatment and Covid 19 vaccination.

Keywords: Lung, Xray, Pleural effusion, history, addiction

1. Introduction

A clinical syndrome was reported by doctors from Wuhan city in China in December 2019 and found to be caused by a mutational RNA virus named as Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2). This clinical syndrome was named as the Coronavirus disease 2019 (COVID-19). It was later spread all over the world and was accepted as a pandemic by the World Health Organization (WHO) on March 11, 2020. Over the last two decades, Severe Acute Respiratory Syndrome CoronaVirus (SARS-CoV) and the Middle East Respiratory Syndrome CoronaVirus (MERS-CoV) were the two beta coronaviruses, similar to SARS-CoV-2[1] . As this disease spreads globally, India had also been affected with rapidly escalating numbers of confirmed cases which were currently more than 4 million as reported on 5 September 2020 with total deaths crossing over 70,626, which was increasing on a daily basis as per MOHFW. The spread of COVID-19 human to human is via droplet, direct contact and

also airborne with incubation period of 2-14 days[2]. Lungs are predominantly affected by tuberculosis and Covid-19. During 2018, an estimated 10 million new TB disease cases occurred globally. While 2.8 million cases were only registered in India, the highest in the world[3]. Although,TB-related mortality declined from 56/100000/year in 2000 to 32/100000/ year but still caused an estimated 1.2 million deaths in 2018, globally[3]. Latent mycobacterium tuberculosis infection (LTBI) prevalence is also very high (40%) in India[4]. SARS-CoV-2 infection leads to an 'out-of-control' immune system and 'cytokine storms', ultimately inducing pulmonary and other organ dysfunction[5]. However, there is emerging evidence that patients with LTBI and TB disease have an increased risk of the SARS-CoV-2 infection and predisposition towards developing severe COVID-19 pneumonia[6]. Any relationship of COVID-19 and TB is particularly relevant for the public health system in India since India is one of the major contributors in burden due to TB with the highest number of TB cases in the world. This study was planned to enhance the understanding of the various clinical and radiological findings in the patients with tuberculosis[pulmonary and extrapulmonary(pleural effusion, mediastinal lymphadenopathy)]found to be co-infected with SARS-CoV-2 and the need for early detection and effective management of COVID-19 infection in patients with active TB (less than 2 months of antitubercular treatment).

A substantial focus is recently being given to tuberculosis and covid 19, and studies are underway to establish their association, various socio-demographic risk factors leading to covid 19 infection in tuberculosis patients, as well as its ill effects in developed countries. However, in India, the number of studies regarding this issue is limited. Therefore this study was planned to find out the prevalence of tuberculosis/COVID 19 co-infection among active tuberculosis patients at a tertiary care hospital in Uttarakhand and to assess the clinical features of COVID-19 in active tuberculosis (pulmonary and extra pulmonary) and to identify the radiological and laboratory picture of COVID 19 in patients with active tuberculosis.

2. MATERIALS AND METHODS

2.1 Study area

Himalayan Institute of Medical Sciences, SRHU in Dehradun (Uttarakhand) is a prominent medical institution in India and is well known for its quality of health services to all strata of society. This prospective cross-sectional study was conducted by the Department of Respiratory Medicine, Himalayan Institute of Medical Sciences, among patients of active tuberculosis (pulmonary and extrapulmonary) presented to the General OPD of the Respiratory Medicine Department.

2.2. Study population

All cases presented to the General OPD of the Respiratory Medicine Department who were diagnosed with active tuberculosis (pulmonary and extrapulmonary) were included in the study. Patients who were pregnant, on treatment for multidrug resistance tuberculosis and who did not give consent were excluded from the study. The study was conducted from October 2020 to January 2021.

2.3 Sampling

Complete enumeration by convenient sampling technique of all cases presenting to the General OPD of Respiratory Medicine Department who were diagnosed with active tuberculosis (pulmonary and extrapulmonary) over a period from October 2020 to January 2021, was done. A total of 104 patients during this period were approached to participate in the study out of

which a total of 96 patients satisfying the inclusion and exclusion criteria were included in the final study.

2.4 Data Collection

A predesigned, pretested, semi structured questionnaire was used to collect data. The questionnaire included questions on socio demographic profile e.g. age, gender, education and occupation of the study participants. Subsequent to this, questions on clinical features, comorbidities, clinical history, any substance abuse. Laboratory investigations, Chest X-ray and HRCT thorax (if required) will be performed and data will be recorded. Active tuberculosis was defined as recently diagnosed as tuberculosis by the technique mentioned below or on antitubercular drugs for **less** than 2 months and extrapulmonary cases that were included in study were pleural effusion and mediastinal lymphadenopathy. Tuberculosis was microbiologically confirmed using the Ziehl-Neelsen staining or genotypic (CBNAAT/PCR for TB) or phenotypic (culture) methods of diagnosis depending on the site of involvement. The sputum samples, bronchial lavage, fluid (pleural) samples were used for confirming tuberculosis (pulmonary and extrapulmonary). COVID-19 infection was confirmed by using the RT-PCR for SARS-CoV-2 on the nasopharyngeal swabs in all active tuberculosis patients. All confirmed active tuberculosis patients were recruited in study after they were evaluated for exclusion criteria and further tested for SARS-CoV-2. Also further the clinical and radiological features were recorded for the final study participants. **Voluntary informed consent was taken from all participants after explaining the purpose of the study**.

2.5 Statistical Analysis

The data was exported into Microsoft Office Excel spreadsheet and analysis was done using SPSS version 21. Descriptive analysis was done by calculating proportions, means and standard deviation. Data was presented as tables and appropriate diagrams. Association between qualitative variables was assessed using chi square/fisher's exact test

2.6 Ethics

Permission was obtained from the administrative authorities and approval was sought from the institutional ethics committee. . The data was kept confidential and used for study purposes only.

3. Results

3.1 Socio Demographic characteristics

The mean age of the study participants was 47.5±5.3 years (Range 18-72). About two fifths (39.58%) of study participants belonged to the age group 18-45 years. Among the study participants males (59.38%) were more as compared to (40.63%) females. About half (46.8%) of the study participants were employed while only (8.3%) were retired.

Table 1 shows that about one fourth (28.13%) of study participants had chronic lung diseases while diabetes was present in one fifth (19.79%) of them. None of the study participants was found with chronic kidney disease and immunocompromised status. About three fourth (71.8%) of study participants had no associated comorbidities.

TABLE 1: Distribution of study population according to comorbidities (N=96)

Comorbidities*	Number	Percentage (%)
Chronic lung disease	27	28.13
Chronic liver disease	3	3.13
Heart disease	11	11.46
Chronic Kidney disease	0	0.00
Immunocompromised	0	0.00
Malignancy	1	1.04
Hypertension	6	6.25
Diabetes	19	19.79

***Multiple response

In Table 2, the mean pulse rate of the study participants was 88.8±2.3 while mean SpO2 was 95.7±1.2. About one fifth (20.83%) of them had pallor while only (5.21% and 2.08%) had icterus and clubbing respectively. More than half (59.38%) of the participants were underweight while only (2.08%) were overweight. Among the study participants, the majority (93.75%) of them had no history of contact. Majority (88.54%) of them were using mask cloth while only (1.04%) were using N95 masks. Majority (90.63%) of them were negative on tuberculosis DST

TABLE 2: Distribution of study population according to General physical examination (N=96)

General physical examination	Number	Percentage (%)
Mean pulse rate	88.8±2.3	
Mean SpO2	95.7±1.2	

Mean systolic blood pressure	112.6±4.7	
Mean diastolic blood pressure	83.7±3.8	
Mean respiratory rate	18.2±1.2	
General Physical Examination*		
Pallor	20	20.83
Icterus	5	5.21
Nail/finger clubbing	2	2.08
Lymphadenopathy	0	0.00
Cyanosis	0	0.00
Edema	14	14.58
BMI		0.00
Normal	37	38.54
Underweight	57	59.38
Overweight	2	2.08
Obese	0	0.00

*****Multiple response

In Table 3, on analyzing sociodemographic characteristics with tuberculosis/COVID 19 co-infection, it was found that there was no statistically significant (p> 0.05) association .

TABLE 3: Distribution of sociodemographic characteristics among tuberculosis/COVID 19 co infected study population (N=96)

Age group (years)	Tuberculosis/COVID 19 co infected	Tuberculosis only	Total	P value
< 18	1(33.3%)	2(66.7%)	3(100%)	0.597
18-60	16(23.8%)	51(76.1%)	67(100%)	
> 60	4(15.4%)	22(84.6%)	26(100%)	
Gender				
Male	11(19.3%)	46(80.7%)	57(100%)	0.460

Female	10(25.6%)	29(74.4%)	39(100%)	
Occupation				
Unemployed	12(34.2%)	23(65.7%)	35(100%)	0.757
Employed	19(42.2%)	26(57.7%)	45(100%)	
Student	7(41.1%)	10(58.8%)	17(100%)	

In Table 4, on analyzing the history of tuberculosis with tuberculosis/COVID 19 co-infection, it was found positive history of contact, positive culture, PCR and CBNAAT, consumption of drug has significantly ($p < 0.05$)higher chances of developing co-infection.

TABLE 4: Distribution of history to tuberculosis among tuberculosis/COVID 19 co infected study population (N=96)

	Tuberculosis/COVI D 19 co infected	**Tuberculosis only**	**Total**	**P value**
History of contact				
Present	4(66.67%)	2(33.33%)	6(100%)	**0.001**
Absent	17(18.89%)	73(81.11%)	90(100%)	
AFB staining				
Positive	15(19.48%)	62(80.51%)	77(100%)	0.202
Negative	6(31.57%)	13(68.4%)	19(100%)	
TB culture				
Yes	12(70.58%)	5(29.41%)	17(100%)	**0.001**
No	9(11.39%)	70(88.60%)	79(100%)	
TB PCR				
Yes	16(94.12%)	1(5.88%)	17(100%)	**0.001**
No	5(6.33%)	74(93.67%)	79(100%)	
TB CBNAAT				
Yes	18(51.43%)	17(48.57%)	35(100%)	**0.001**

No	3(4.92%)	58(95.08%)	61(100%)	
Smoking				
Yes	6(15.38%)	33(84.62%)	39(100%)	0.203
No	15(26.32%)	42(73.68%)	57(100%)	
Consumption of alcohol				
Yes	4(40.00%)	6(60.00%)	10(100%)	0.142
No	17(19.77%)	69(80.23%)	86(100%)	
Consumption of drug				
Yes	5(71.43%)	2(28.57%)	7(100%)	**0.008**
No	16(17.98%)	73(82.02%)	89(100%)	

Table 5 shows that on analyzing the clinical sign and symptoms with tuberculosis/COVID 19 co-infection, it was found that headache, vomiting, fever, abdominal pain, nausea, bodyache, sore throat, nasal discharge, Cavity, Consolidation and Pleural effusion on chest X Ray, findings on HRCT thorax are significantly (p<0.05) associated.

TABLE 5: Distribution of clinical sign and symptoms among tuberculosis/COVID 19 co infected study population (N=96)

	Tuberculosis/COVID 19 co infected	**Tuberculosis only**	**Total**	**P value**
Cough	20(25.00%)	60(75.00%)	80(100%)	0.116
Headache	4(50.00%)	4(50.00%)	8(100%)	**0.044**
Diarrhoea	2(66.67%)	1(33.33%)	3(100%)	0.056
Vomiting	5(71.43%)	2(28.57%)	7(100%)	**0.001**
Fever	19(28.79%)	47(71.21%)	66(100%)	**0.015**
Abdominal pain	17(30.91%)	38(69.09%)	55(100%)	**0.013**
Breathlessness	18(26.47%)	50(73.53%)	68(100%)	0.089

Nausea	4(57.14%)	3(42.86%)	7(100%)	**0.019**
Hemoptysis	6(46.15%)	7(53.85%)	13(100%)	0.022
Bodyache	10(47.62%)	11(52.38%)	21(100%)	**0.001**
Chest pain	12(28.57%)	30(71.43%)	42(100%)	0.161
Sore throat	8(61.54%)	5(38.46%)	13(100%)	**0.001**
Nasal discharge	5(71.43%)	2(28.57%)	7(100%)	**0.001**
Weight loss	7(31.82%)	15(68.18%)	22(100%)	0.198
Loss of appetite	15(24.19%)	47(75.81%)	62(100%)	0.458
Cavity on chest X Ray	15(45.45%)	18(54.55%)	33(100%)	**0.001**
Consolidation on chest X Ray	11(15.71%)	59(84.28%)	70(100%)	**0.016**
Pneumothorax on chest X Ray	2 (66.66%)	1(33.33%)	3(100%)	0.056
Pleural effusion on chest X Ray	16(72.72%)	6(27.27%)	22(100%)	**0.001**
HRCT thorax	15(35.71%)	27(64.28%)	42(100%)	**0.003**

4. Discussion

In the present study, a total of 104 patients were approached to participate in the study out of which a total of 96 patients satisfying the inclusion and exclusion criteria were included in the final study. Five patients refused to participate and three patients who were on multidrug resistance tuberculosis treatment were excluded which gave an overall response rate of 92.3%. The mean age of the participants in the present study was 47.5±5.3 years (Range 18-72). About two fifths (39.5%) of study participants belonged to the age group 18-45 years. In a similar study conducted by **Mangamba LME et al[7] in 2022** among tuberculosis patients in Cameroon, the mean age of study participants was reported to be 43.70 ± 17.89 years which is almost similar to present study. Males (59.3%) were more as compared to (40.6%) females in our study and similar results of male predominance (53.3%) were reported by **Mangamba LME et al[7] study** and by **Nuwagira E et al[8] in 2022 from Tanzania**. One or more than one comorbidities were present among one fourth (28.13%) of the participants in the present study. Similar results were reported by **Boushab et al[9] in 2012 in Cameroon**. **Chen et al[10] in 2020 from China** also reported the prevalence of 25% for diabetes mellitus, 22.2% for hypertension. Cough (83.3%), fever (68.7%) and breathlessness (70.8%) were the most common clinical symptoms reported by the participants in the present study which is similar to results reported by **Tekpa et al[11] in 2019** as well as by **Gupta et al[12] 2020 in India**. In another study conducted by **Kunst et al[13] in 2020 in Belgium**, the most common symptoms found were fever (81.2%), dry cough (56.2%) and dyspnea (15.7%). Presence of pleural effusion was significantly associated with higher chance of developing coinfection in our study which is also reported in a study conducted by **Druti H et al[14] in 2023** from Karnataka.

In our study no significant association was found between sociodemographic characteristics and co-infection of COVID19/tuberculosis which is similar to findings reported by **Stochino et al[15] in 2020 in Northern Italy** as well as **Gupta et al[12] 2020 in India**. The prevalence of COVID19/tuberculosis co-infection in the present study was 21.8% among the study participants which is higher than the

prevalence reported by **Tadolini et al[16] in 2020 in Belgium** (18.3%) and Karla et al in 2020 in Philippines. Coinfection of COVID19/tuberculosis was significantly higher among participants with positive TB culture, PCR and CBNAAT. Smoking and alcohol history was not significantly associated with coinfection in our study which is also found by **Nuwagira E et al[8] in 2022 from Tanzania.**

Our study has some strength which makes it more reliable including pilot tested questionnaires and response rate was high. Additionally, the standard operating procedures were followed in collection of samples and their interpretation. First limitation is that the causal relationship between tuberculosis and carriage of Covid 19 infection can't be established as this was a cross sectional study. Second one is that the result of our study cannot be generalized to the entire population of tuberculosis patients across India because of the difference in demographic, lifestyle, environmental condition, and immunity status. The prevalence of COVID19/tuberculosis co-infection in the present study was high (21.8%) among the study participants. Factors like positive history of contact, positive culture, PCR and CBNAAT, consumption of drugs, presence of cavity and pleural effusion have significantly ($p < 0.05$) higher chances of developing co-infection. These significantly associated factors can help in identifying Covid 19 infection among tuberculosis patients. Therefore it is recommended that screening for these factors should be done for all the tuberculosis patients coming for treatment and Covid 19 vaccination.

Conflict of Interest: None

Ethical Statement: Voluntary informed consent and data confidentiality was maintained

Data Availability: Yes

References

1. Q. Li, X. Guan, P. Wu, X. Wang, L. Zhou, Y. Tong, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med. 2020 Mar 26;382(13):1199-1207.

2. World Health Organization. Coronavirus disease (COVID-19) technical guidance: Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases [Internet]. www.who.int. Available from: https://www.who.int/publications/i/item/10665-331501.

3. India Tb Report 2019 :: Central TB Division [Internet]. tbcindia.gov.in. [cited 2024 May 21]. Available from: https://tbcindia.gov.in/index1.php?lang=1&level=1&sublinkid=5365&lid=3450

4. Chadha VK. Tuberculosis epidemiology in India: a review. Int J Tuberc Lung Dis. 2005 Oct;9(10):1072-82.

5. Huang KJ, Su IJ, Theron M, Wu YC, Lai SK, Liu CC, Lei HY. An interferon-gamma-related cytokine storm in SARS patients. J Med Virol. 2005 Feb;75(2):185-94.

6. Chen Y, Wang Y, Fleming J, Yanhong Y, Gu Y, Liu C et al.Active or latent tuberculosis increases susceptibility to COVID-19 and disease severity. medRxiv.2020;03:1-15.

7.Mangamba LME, Medi CI, Tochie JN, Dalle GN, Nkouagmi N, Balkissou AD, et al.Prevalence of tuberculosis/COVID-19 co-infection and factors associated with SARS-CoV-2 infection in pulmonary tuberculosis patients at a respiratory diseases center: a cross-sectional study. Pan African Medical

Journal. 2023;44(204):1-13.

8.Nuwagira E,Mpagama SG,Katusiime A, Natamba B, Baluku JB, Lai PS. Coinfection of COVID-19 and Tuberculosis in Uganda. Am J Trop Med Hyg. 2023 Apr 24;108(6):1240-1243.

9.Boushab BM, Savadogo M, Sow MS. Prevalence of smear-positive pulmonary tuberculosis in Aïoun hospital (Hodh El Garbi)]. Rev Pneumol Clin.2016 Aug;72(4):243-7.

10.Chen Q, Zheng Z, Zhang C, Zhang X, Wu H, Wang J, Wang S, Zheng C. Clinical characteristics of 145 patients with coronavirus disease 2019 (COVID-19) in Taizhou, Zhejiang, China. Infection. 2020 Aug;48(4):543-551.

11.Tékpa G, Fikouma V, Téngothi RMM, Longo JD, Woyengba APA, Koffi B. Epidemiological and clinical features of tuberculosis at the Hôpital de l'Amitié in Bangui]. Pan Afr Med J. 2019 May 15;33:31.

12.Gupta N, Ish P, Gupta A, Malhotra N, Caminero JA, Singla R, Kumar R, Yadav SR, Dev N, Agrawal S, Kohli S, Sen MK, Chakrabarti S, Gupta NK. A profile of a retrospective cohort of 22 patients with COVID-19 and active/treated tuberculosis. Eur Respir J. 2020 Nov 19;56(5):2003408.

13.Kunst H, Burman M, Arnesen TM, Fiebig L, Hergens MP, Kalkouni O et al. Tuberculosis and latent tuberculous infection screening of migrants in Europe: comparative analysis of policies, surveillance systems and results. Int J Tuberc Lung Dis. 2017;21(8): 840-51.

14.Hazra, Druti1; Siddalingaiah, Nayana1; Gupta, Nitin2; Chawla, Kiran1; Prabhu, A Ravindra3; Datta, Divya3; Khader, Nisha3; Swaminathan, Shilna Muttickal3. COVID-19 and tuberculosis coinfection: A case–control study from a tertiary care center in South India. Journal of Family Medicine and Primary Care.2023;12(12):3200-3203.

15.Stochino C, Villa S, Zucchi P, Parravicini P, Gori A, Raviglione MC. Clinical characteristics of COVID-19 and active tuberculosis co-infection in an Italian reference hospital. Eur Respir J. 2020;56(1): 2001708.

16.Tadolini M, Codecasa LR, García-García JM, Blanc FX, Borisov S, Alffenaar JW et al. Active tuberculosis, sequelae, and COVID-19 coinfection: first cohort of 49 cases. Eur Respir J. 2020;56(1): 2001398.