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Original Article

Prevalence of Tuberculosis/COVID 19 Co-Infection among Active Tuberculosis Patients at a Tertiary Care Hospital in Uttarakhand, India

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ABSTRACT

The Coronavirus disease 2019 (COVID-19) 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 conducted by the Department of Respiratory Medicine, Himalayan Institute of Medical Sciences, among patients of active tuberculosis (pulmonary and extra-pulmonary) who 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 COVID-19/tuberculosis co-infection in the present study was 21.8%. Positive history of contact, bacterial culture, PCR, and CBNAAT, use of the 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 COVID-19/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 tuberculosis patients coming for treatment and Covid 19 vaccination.

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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 Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). This clinical syndrome was named Coronavirus disease 2019 (COVID-19). It was later spread worldwide and was declared 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 Middle East Respiratory Syndrome Coronavirus (MERS-CoV) were the two beta coronaviruses, similar to SARS-CoV-2 (1). As this disease spreads globally, India has 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 daily as per the MOHFW. The spread of COVID-19 from human to human is via droplet, direct contact, and also airborne, with an incubation period of 2-14 days (2). Lungs are predominantly affected by tuberculosis and COVID -19. During 2018, an estimated 10 million newTB disease cases occurred globally. While 2.8 million cases were only registered in India, making it the highest in the world (3). Although TB-related mortality declined from 56/100000/year in 2000 to 32/100000/ year,it 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 causing pulmonary and other organ dysfunction (5). However, there is emerging evidence that patients with LTBI and TB disease have an increased risk of SARS-CoV-2 infection and a predisposition towards developing severe COVID-19 pneumonia (6).

Any relationship between COVID-19 and TB is particularly relevant for the public health system in India, since India is one of the major contributors to burden due to TB, with the highest number of TB cases in the world. This study was planned to enhance understanding of the various clinical and radiological findings in patients with tuberculosis [pulmonaryand extrapulmonary (pleuraleffusion,mediastinal lymphadenopathy)] who are found to be coinfected with SARS-CoV-2 and to emphasize 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 has recently been given to tuberculosis and COVID -19, and studies are underway to establish their association, including various socio-demographic risk factors leading to COVID- 19 infection in tuberculosis patients, as well as its adverse effects in developed countries. However, in India, the number of studies addressing this issue is limited. Therefore, this study was planned to determine 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 patterns 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 with active tuberculosis (pulmonary and extrapulmonary) presenting to the General OPD of the Respiratory Medicine Department.

2.2. Study Population

All cases presenting 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, or 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 using a 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 performed. A total of 104 patients during this period were approached to participate in the study, out of which 96 patients satisfying the inclusion and exclusion criteria were included in the final study.

2.4 Data Collection

A predesigned, pretested, and 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. Subsequently , questions on clinical features, comorbidities, clinical history, any substance abuse were included. Laboratory investigations, Chest X-ray ,and HRCT thorax (if required) will be performed and data will be recorded. Active tuberculosis was defined as recent diagnosis of tuberculosis by the technique mentioned below or as patients on antitubercular drugs for less than 2 months. The extrapulmonary cases included in study were pleural effusion and mediastinal lymphadenopathy.

Tuberculosis was microbiologically confirmed using the Ziehl-Neelsen staining, genotypic methods (CBNAAT/PCR for TB), or phenotypic methods (culture) ,depending on the site of involvement. 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 evaluation for exclusion criteria and further testing for SARS-CoV-2. Additionally, the clinical and radiological features were recorded for the final study participants. Voluntary informed consent was obtained from all participants after explaining the purpose of the study.

2.5 Statistical Analysis

The data were exported into Microsoft Office Excel spreadsheet, and analysis was performed using SPSS version 21. Descriptive analysis was conducted by calculating proportions, means and standard deviation. Data were presented as tables and appropriate diagrams. The 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 were kept confidential and used solely for study purposes.

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 age group. Among the study participants, males (59.38%) were more than females (40.63%). 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 had chronic kidney disease or immunocompromised status. About three -fourth (71.8%) of study participants had no associated comorbidities.

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. The majority (88.54%) were using mask cloth, while only 1.04% were using N95 masks. The majority (90.63%) were negative on tuberculosis DST.

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.

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 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, body ache, sore throat, nasal discharge, Cavity, Consolidation and Pleural effusion on chest X Ray, findings on HRCT thorax are significantly ($p<0.05$) associated.

4. Discussion

In the present study, a total of 104 patients were approached to participate, 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-resistant 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).

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

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
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

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

Age group (years)	Tuberculosis/C OVID 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
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%)	

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

	Tuberculosis/CO VID 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**
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**

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 the present study. Males (59.3%) were more predominant than females (40.6%) in our study, and similar results of male predominance (53.3%) were reported by Mangamba LME et al (7). 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, and 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), 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%). The presence of pleural effusion was significantly associated with higher chance of developing coinfection in our study, which was 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 socio-demographic characteristics and coinfection 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 by Karla et al. in 2020, in the Philippines. Coinfection of COVID19/tuberculosis was significantly higher among participants with positive TB culture, PCR, and CBNAAT. Smoking and alcohol history were 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 strengths, which make it more reliable, including pilot -tested questionnaires, and the response rate was high. Additionally, the standard operating procedures were followed in the collection of samples and their interpretation. The first limitation is that the causal relationship between tuberculosis and the carriage of Covid 19 infection can't be established, as this was a cross sectional study. The second limitation 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 conditions, 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, as well as consumption of drugs, presence of cavity and pleural effusion had a 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.

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Authors' Contribution

Conceived the idea and conducted the literature search: V. J, R. K, S. J.
Prepared the data extraction sheet and compiled the data: S. KS, V. J.
Quality assessment of the studies: A. S, A. K, M. G.
Performed the analysis: S. KS, S. J.
Drafted the manuscript: S. KS, V. J, R. K.

Ethics

None

Conflict of Interest

None

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None

Data Availability

This study

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