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Severe acute respiratory syndrome coronavirus 2 seroprevalence among patients with pulmonary tuberculosis

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SUMMARY

OBJECTIVE: The objective of this study was to estimate the seroprevalence of severe acute respiratory syndrome coronavirus 2 antibodies in patients with tuberculosis.

METHODS: This cross-sectional study was conducted at an outpatient tuberculosis clinic in Alvorada, RS, Brazil, with data collection between October and December 2020. Outpatients aged>18 years with active pulmonary tuberculosis, no prior history of coronavirus disease 2019, and no suspected coronavirus disease 2019 were included in the study. Whole blood samples were collected to perform the severe acute respiratory syndrome coronavirus 2 antibodies test.

RESULTS: During the study period, 52 patients met the inclusion and were included in the analysis. Severe acute respiratory syndrome coronavirus 2 antibodies were positive in 16 (30.8%) patients. Male sex was more frequent among patients with negative severe acute respiratory syndrome coronavirus 2 antibodies than in patients with positive severe acute respiratory syndrome coronavirus 2 antibodies (86.1 vs. 56.3%, p=0.031). Contact with coronavirus disease 2019 case was more common in patients with positive severe acute respiratory syndrome coronavirus 2 antibodies compared with patients with negative severe acute respiratory syndrome coronavirus 2 antibodies (87.5 vs. 8.3%, p<0.0001). In a multivariate analysis, in a model including the variables such as male sex and contact with coronavirus disease 2019 case, only contact with coronavirus disease 2019 was independently associated with positive severe acute respiratory syndrome coronavirus 2 antibodies (OR 77.0, 95%CI 11.5–512.4, p<0.0001).

CONCLUSION: This study revealed a seroprevalence of 30.8% severe acute respiratory syndrome coronavirus 2 among patients with tuberculosis.

KEYWORDS: Tuberculosis. SARS-CoV-2. Seroepidemiologic studies. COVID-19. Antibodies.

INTRODUCTION

Tuberculosis (TB) is a worldwide public health concern, with a global incidence of 6.4 million people in 2021[1]. Brazil is among the 30 high TB burden countries, with an incidence of 32 cases/100,000 population in 2021; in the State of Rio Grande do Sul, the incidence is 36.5 cases/100,000 population in 2021[2]. The association between TB and coronavirus disease 2019 (COVID-19) has been described since the beginning of the COVID-19 pandemic[3,4]. Both diseases can present simultaneously and have similar symptoms[3], so diagnosing TB during the COVID-19 pandemic requires a high degree of clinical suspicion. In addition, TB and COVID-19 co-infected individuals may be at a greater risk of morbidity and mortality. The risk of mortality was demonstrated to be 2.17 times higher in patients with concomitant COVID-19 and pulmonary TB[5]. In a large cohort of 767 patients co-infected with TB and COVID-19, from 172 centers in 34 countries, the authors showed that age, male gender, and invasive ventilation were independent contributors to mortality. Among the patients who died, 42 (49.4%) died from COVID-19; 31 (36.5%) from COVID-19 and TB; and 1 (1.2%) died from TB only[6].

Although studies have described the association between TB and COVID-19, emphasizing that the overlap of these diseases can cause more severe clinical conditions, no study has evaluated the prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies in TB patients. Seroprevalence studies are important because they enable the detection of asymptomatic and subclinical infections, not usually included in the reported cases[7,8]. Identification and isolation

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of asymptomatic carriers and patients with mild COVID-19 are very important in preventing the disease spread, especially in these high-risk populations, helping to prevent COVID-19 morbidity and mortality[9,10]. Therefore, the objective of this study is to estimate the seroprevalence of SARS-CoV-2 antibodies in patients with TB without symptoms suggestive of COVID-19, in an outpatient TB clinic, before the widespread introduction of COVID-19 vaccines.

METHODS

Study design and location

We conducted a cross-sectional study, from October to December 2020, with prospective data collection in an outpatient TB clinic in Alvorada, RS, Brazil. This clinic is the only reference center for TB in the city and treated 252 confirmed cases of TB in 2022. Alvorada is a city with 211,352 inhabitants, located in the metropolitan area of Porto Alegre, which has a TB incidence of 89.9 cases/100,000 inhabitants[2]. Despite the sanitary restrictions in force during the study period, the care service for patients with TB has not changed in Alvorada. The study was approved by the Ethics Committee of Hospital de Clínicas de Porto Alegre (number 20-0490 – CAAE: 38370330.8.0000.5327). All patients signed informed consent before the start of the study.

Patients and data collection

Outpatients aged>18 years with active pulmonary TB, no history of COVID-19, and no suspected COVID-19 were included in the study. Patients with extrapulmonary TB were excluded from this study. Pulmonary TB was diagnosed according to the Brazilian Guidelines for Tuberculosis[11].

After signing informed written consent, enrolled subjects were interviewed using a standardized questionnaire. The following data were collected: demographic data (i.e., sex and age), medical history (i.e., presence of comorbidities, smoking habits, alcohol abuse, and use of drugs), and history of contact with a suspected or confirmed case of COVID-19.

Whole blood samples were collected to perform the test. The VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Test (Ortho Clinical Diagnostics, USA) was performed using the VITROS Anti-SARS-CoV-2 Total Reagent Pack and the VITROS Anti-SARS-CoV-2 Total Calibrator in the VITROS ECi/ECiQ/3600 Immunodiagnostic Systems and in the VITROS 5600/XT 7600 Integrated Systems. The test assesses the immune response by qualitatively measuring total antibodies (including IgG, IgM, IgA, and other isotypes) against SARS-CoV-2. The result takes 48 min and is described as <1 (anti-SARS-CoV-2 non-reactive sample) or ≥1 (anti-SARS-CoV-2 reactive sample). According to the manufacturer, the sensitivity of the test ranged from 79.4 to 100% and the specificity from 99.1 to 100%[12].

Statistical analysis

Data analysis was performed using SPSS 18.0 (Statistical Package for the Social Sciences, Chicago, IL). Data were presented as number of cases, mean±standard deviation (SD), or median with interquartile range. Categorical comparisons were performed by chi-square test using Yates's correction if indicated or by Fisher's exact test. Continuous variables were compared using *t*-test or Wilcoxon test. Multivariate logistic regression analysis was performed to assess factors associated with the presence of antibodies against SARS-CoV-2. Hierarchical logistic regression models with predictors added one at a time were examined to assess possible collinearity between the predictors. The predictors selected in the final model were based on numerical and clinical significance. The quality of fit of the multiple logistic regression models was evaluated with the Hosmer-Lemeshow test. Odds ratios (ORs) and 95% confidence intervals (CI) were presented. A two-sided p-value<0.05 was considered significant for all analyses.

To calculate the sample size, we considered a SARS-CoV-2 seroprevalence of approximately 30% based on previous studies[13-16]. Thus, with an alpha error of 0.5 and a power of 80%, it would be necessary to include at least 42 patients in the study.

RESULTS

During the study period, 52 patients met the inclusion criteria and were included in the analysis. Only two patients did not accept to participate in the study. SARS-CoV-2 antibodies were positive in 16 (30.8%) patients. The characteristics of the study population are shown in Table 1, according to the results of SARS-CoV-2 antibodies.

Male sex was more frequent among patients with negative SARS-CoV-2 antibodies than in patients with positive SARS-CoV-2 antibodies (86.1 vs. 56.3%, p=0.031). Contact with COVID-19 case was more common in patients with positive SARS-CoV-2 antibodies compared with patients with negative SARS-CoV-2 antibodies (87.5 vs. 8.3%, p<0.0001). All other characteristics were not statistically different comparing patients with negative SARS-CoV-2 antibodies with patients with positive SARS-CoV-2 antibodies.

In a multivariate analysis, in a model including the variables male sex and contact with COVID-19 case, only the last one was independently associated with positive SARS-CoV-2 antibodies (OR 77.0, 95%CI 11.5–512.4, p<0.0001) (Table 2).

DISCUSSION

We aimed to estimate the prevalence of SARS-CoV-2 antibodies among TB patients with no prior history of COVID-19 and no suspected COVID-19. SARS-CoV-2 seroprevalence was 30.8%. In addition, in a multivariate analysis, a history of contact with COVID-19 case was independently associated with positive SARS-CoV-2 antibodies.

Our result of 30.8% of SARS-CoV-2 seroprevalence is similar to the range of percentage reported in other studies[13-16]. In a serological survey conducted on 1,141 healthcare workers in Brazil, the serum prevalence for the virus was 30%[13]. In another study in Brazil[14], the SARS-CoV-2 seroprevalence among 3,046 asymptomatic and symptomatic individuals, selected from a convenience sample, was estimated at 29.1%. In a national survey in Mexico, the authors found a seroprevalence of 24.9% after the first epidemic wave, from August to November 2020[16]. In a meta-analysis[15] of nine studies from South America (i.e., Argentina, Brazil, Colombia, and Peru), the pooled seroprevalence was estimated at 33.6%.

As the clinical manifestation of SARS-CoV-2 infection is largely variable, ranging from asymptomatic to fatal, the number of reported cases does not reflect the actual number of infections because asymptomatic cases are not regularly tested. In the present study, all included patients were COVID-19 asymptomatic. In a seroprevalence study[16] in Mexico, among seropositive individuals, 67.3% were asymptomatic. Recently published studies confirm that a surveillance strategy that relies only on detected cases by RT-PCR will underestimate the true number of SARS-CoV-2 infections[8,17,18].

History of contact with a COVID-19 case was the most important factor associated with positive SARS-CoV-2 antibodies in our study. According to these results, Halili et al.[19] found that having an infected family member is related to seropositivity to SARS-CoV-2 antibodies. In addition, in univariate analysis, males had more positive SARS-CoV-2 antibodies than females. This is in accordance with other studies that found that males have higher odds of seropositivity[19-21]. In contrast, Airoldi et al.[22] reported higher seropositivity among females.

This study has some limitations. First, it was carried out in a single center; thus, considering the locoregional differences and the different waves of the pandemic, it is possible that these results cannot be generalized. Second, although this was not the focus of the study, we did not collect data on mask use and social distancing, measures that may influence the seroprevalence of SARS-CoV-2. However, this is the first study that evaluated the prevalence of SARS-CoV-2 antibodies in TB patients.

CONCLUSIONS

This study revealed a seroprevalence of SARS-CoV-2 of 30.8% among patients with TB. These data help understand the

Table 1. Characteristics of study patients according to severe acute respiratory syndrome coronavirus 2 antibodies.

Characteristics	SARS-CoV-2 antibodies positive (n=16)	SARS-CoV-2 antibodies negative (n=36)	p-value
Age, years	47.3±23.3	41.3±15.9	0.364
Male sex	9 (56.3)	31 (86.1)	0.031
Active smoking	5 (31.3)	10 (27.8)	0.999
Alcohol abuse	1 (6.3)	3 (8.3)	0.999
Use of drugs	1 (6.3)	4 (11.1)	0.999
Previous TB	3 (18.8)	7 (19.4)	0.999
HIV	2 (12.5)	3 (8.3)	0.637
DM	3 (18.8)	2 (5.6)	0.163
Presence of any comorbidity	8 (50.0)	12 (33.3)	0.406
Contact with COVID-19 case	14 (87.5)	3 (8.3)	<0.0001

SARS-CoV-2: seroprevalence of severe acute respiratory syndrome coronavirus 2; TB: tuberculosis; HIV: human immunodeficiency virus; DM: diabetes mellitus; COVID-19: coronavirus disease 2019.

Table 2. Multivariate analysis of factors associated with positive severe acute respiratory syndrome coronavirus 2 antibodies.

Characteristics	β	SE	Wald	OR (95%CI)	p-value
Male sex	-2.21	1.28	3.01	0.11 (0.01–1.33)	0.083
Contact with COVID-19 case	4.34	0.97	20.18	77.0 (11.5–512.4)	<0.0001

SARS-CoV-2: seroprevalence of severe acute respiratory syndrome coronavirus 2; COVID-19: coronavirus disease 2019; SE: standard error; OR: odds ratio; CI: confidence interval.

epidemiology of COVID-19 in this population and to raise awareness that many patients have asymptomatic disease, with the potential for transmission to other patients in TB clinics and to family members. In addition, due to the high seroprevalence and the possibility of severe COVID-19, vaccination efforts must be intensified in TB patients. Also, other measures to mitigate the transmission of the disease from asymptomatic patients and potentially reduce morbidity and mortality would be the maintenance of the use of masks in TB clinics and low-threshold testing (testing patients with mild symptoms)[23,24].

AUTHORS' CONTRIBUTIONS

NJDD: Conceptualization, Methodology, Investigation, Data curation, Project administration, Writing – review & editing. **MSS:** Conceptualization, Methodology, Investigation, Writing – review & editing. **MSB:** Conceptualization, Methodology, Investigation, Writing – review & editing. **GRP:** Conceptualization, Methodology, Investigation, Writing – review & editing. **DRS:** Conceptualization, Methodology, Investigation, Data curation, Project administration, Supervision, Writing – original draft.

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