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ORIGINAL RESEARCH

The Impact of COVID-19 on the Tuberculosis Features in a Romanian Pneumology Hospital

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Introduction: The COVID-19 pandemic and tuberculosis have epidemiological similarities, being transmitted airborne, favored by direct contact, crowded environments, and vulnerable biological status.

Methods: We performed a retrospective study of 45 cases of pulmonary tuberculosis associated with COVID-19 (TB+COV+) compared to 45 cases with tuberculous monoinfection (TB+COV-), hospitalized during 2021–2022.

Results: The demographic characteristics were similar in the two groups, predominating men, a median age of 51 years, living in rural areas, medium level of education and smoking. Common symptoms of the two groups were cough, weight loss, profuse sweating, loss of appetite and hemoptysis, while fever, headache, myo-arthralgias, and digestive symptoms characterized the TB+COV+ forms. The scores of radiological lesions in the TB+COV+ compared to TB+COV- group were significantly higher and persistent, revealing more frequent bilateral extensive lung lesions. There were no significant differences in the biological parameters between the two groups. Mortality was 2.2%, regardless of the association of COVID-19. The frequency of infections with *Clostridioides difficile* was higher in TB+COV+ cases.

Conclusion: The co-infection of COVID-19 had a mild impact on the clinical and biological expression of tuberculosis diagnosed in a pandemic context.

Keywords: tuberculosis, COVID-19 pandemic, co-infection, Romania

Introduction

Tuberculosis was one of the leading causes of death in human history and remains one of the leading infectious causes of death in the world.[1] Globally, the number of new cases of tuberculosis exceeds 10 million, although the incidence of tuberculosis has fallen slowly over the past decade, and mortality has fallen by almost a third.[1]

Although there has been a downward trend in the incidence of tuberculosis, the achievements are below the indicators established by the World Health Organization [WHO]. The aim of the "END TB" strategy, is to reduce the global TB incidence and mortality rates by 90% and 95%, respectively, in 2035 when compared to 2015. The COVID-19 pandemic has interfered with the diagnosis and care program for tuberculosis, negatively impacting the progress achieved in combating the disease by 2019. The reported number of people diagnosed with TB in 2020 and 2021 has decreased suggesting growing the number of undiagnosed and untreated people, with an estimated 10.6 million reported TB cases in 2021, compared to 10.1 million in 2020. Over more, the number of deaths increased to 1.6 million in 2021 compared to 1.5 million in 2020.[1]

COVID-19 has epidemiological similarities with tuberculosis, both infections being airborne, favored by direct contact, crowded environments, and vulnerable biological status. Both tuberculosis and the COVID-19 infection predominantly affect the lung, although extrapulmonary manifestations are also known. The incubation period differs,

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with variations between 2 and 14 days for COVID-19 and 3–9 weeks for tuberculosis, although they may start with common manifestations, such as cough, chest pain, and asthenia.[2] Tuberculosis is an airborne bacterial infection caused by Mycobacterium tuberculosis that can cause extensive destruction of lung tissue, with the formation of cavities, while COVID-19 is a viral infection primarily transmitted person-to-person, caused by SARS-Cov-2 that alters lung cells, triggering inflammation and acute respiratory dysfunction.[3,4] The infection of COVID-19 can be diagnosed both before, during active tuberculosis, and post-tuberculosis, but the influence of COVID-19 in the reactivation or worsening of active tuberculosis is still unclear.[5,6] Morbidity and mortality risks for COVID-19 and tuberculosis can be influenced by smoking and co-morbidities, such as chronic lung disease, diabetes, or liver failure.[7–11] The convergence of these infections constitutes major challenges for public health globally.[12]

In 2020, of the 33,148 cases of tuberculosis reported by 29 of 30 EU/EEA countries, 23.2% came from Romania. Regarding the number of TB new cases, Romania is at the top ranking of EU countries, though decreasing trend was noted in the last years.[13]

There are some reports regarding the role of COVID-19 to increase the severity and mortality of tuberculosis.[14–16] The purpose of our study is to identify the particularities of the clinical, biological, radiological, and evolutive characteristics on hospitalized patients with tuberculosis-COVID-19 co-infection, from a special hospital of pneumology. To our knowledge, this is the first study on COVID-19 and tuberculosis co-infection from South-East of Romania.

Materials and Methods

We have conducted a descriptive retrospective study on the cases of tuberculosis hospitalized during the COVID-19 pandemic period, from 1.07.2020 to 30.06.2022, from the Clinical Hospital of Pneumophtisiology Galati, located in the South-East of Romania. We specify that the hospital does not have an intensive care unit, and the complicated cases with organ dysfunctions are admitted/transferred to emergency hospitals.

Selection of the Patients

The diagnosis of tuberculosis (TB) was considered according to the case definitions established by the national tuberculosis management guideline, classified into new cases and relapses, according to the TB history and treatment.[13] The etiological diagnosis was based on the classical methods of sputum analysis through culture on Loewenstein-Jenssen medium and/or microscopic examination of Ziehl-Nielson colored smears. The laboratory diagnosis of TB was completed by molecular tests by quantitative polymerization reaction in real-time DNA chain - RT-PCR (GeneXpert MTB-Rif-Cepheid). All hospitalized patients with TB were tested for COVID-19 upon admission and during hospitalization, due to clinical or epidemiological suspicion for this infection. The diagnosis of COVID-19 was confirmed by RT-PCR SARS-CoV-2 test. Considering that the average incubation interval of COVID-19 is 7 days, we have classified the cases as community or health care associated infection, depending on the diagnostic data, in the first 7 days of hospitalization or after 7 days, respective. The study was based on the analysis of data from the hospital's archive of the clinical records, that were selected based on the diagnostic codes ICD-10-CM version 37.1 R1, specified A15 (respiratory tuberculosis), associated or not with U07.1 (COVID-19), for each case of co-infection. The control group included cases of TB mono-infection (A15), selecting a pair with the most proximate hospitalization date of each co-infection case. Two independent researchers, not involved in the patient care or data collection, have selected the patients of the control group.

Data Collection

Demographic, clinical, biological, radiological, and therapeutic data were collected, used according to current hospital procedures for the diagnosis and treatment of TB and COVID-19, according to the recommendations of national protocols.[17–19]

The radiological changes were evaluated by three independent radiologists and were validated by the pneumologist physician. The cavitary, ulcerated, caseous, nodular, infiltrative, fibrous, pleural/extrapulmonary forms of TB have been notified. Chest CT examination was available in isolated cases. The BRIXIA radiological scores for severity were evaluated on the date of COVID-19 diagnosis (baseline) and at discharge (end of study). Extent of lung parenchyma damage evaluation by BRIXIA score, consists of division into six sections of the lung radiologic image, in which each section achieves a damage score of 0, 1, 2 or 3, while total score could sum from 0 to 18.[20–22]

The inclusion criteria were age over 20 years, signing the informed consent for the use of personal data for the purpose of medical statistical studies, according to the standardized form from the clinical observation sheet.

They were excluded the patients vaccinated against COVID-19, patients with HIV infection, with neurocognitive dysfunctions who cannot express their consent, those re-hospitalized for the same episode of the disease of COVID-19 or tuberculosis, as well as cases with incomplete CXR examination of the lung (less than 3 radiological opinions).

Statistical Analysis

The statistical analysis used the XLSTAT.2022.4.5 program. Continuous variables with normal distribution were compared based on t-tests, and categorical variables were compared with chi-squared tests or Fisher exact tests. We calculated the frequency of the variables and the mean ±SD for the data with normal distribution or the median in the case of non-normally distributed data. We used the nonparametric Mann–Whitney *U*-test for data that did not correspond to the standard distribution.

This non-interventional study complies with the Declaration of Helsinki. The institutional approvement of was endorsed by the Medical Council of the Pneumology Hospital from Galati no 1546/15.01.2024.

Results

We analyzed 90 cases hospitalized with tuberculosis during the 2020–2022 pandemic period, of which 45 had the diagnosis of co-infection with COVID-19 and 45 had TB mono-infection.

Demographic Data

The age of the patients varied between 20 and 86 years, with an average of 52.1±14.69 years, without significant statistical differences between the two groups (Mann Whitney test: $p = 0.272$). The demographic characteristics indicated the predominance of male patients (78.8%), from rural areas (62.2%), with medium/higher education level (53.3%), professionally active (43.33%). The frequency of patients with a low level of education was significantly higher in the group with co-infection with COVID-19 compared to mono-infection with TB ($p < 0.001$), without other demographic differences (Table 1).

Table 1 Characteristics of Hospitalized Patients with TB Only Vs COVID-19 Co-Infection

		All	TB+COV+	TB+COV-	OR	CI 0.95	X^2
Gender	Female Male	19 71	6 39	13 32	0.378	0.132;1.084	0.070
Living area	Urban Rural	34 56	15 30	19 26	0.684	0.290;1.609	0.384
Education*	Low Medium/High	42 48	29 16	13 32	4.461	1.874;10.617	<0.001
Employment	Employed Non-employed Retired	39 18 33	22 5 18	17 13 15	3.364 0.320	1.032;10.968 0.095;1.079	0.044 0.066
Smoking	Yes No	64 26	33 12	31 14	1.241	0.498;3.094	0.641
Alcohol use	Yes No	67 23	33 8	30 15	2.312	0.875;6.108	0.090
Underweight (<20 kg/m^2)	Yes No	21 69	7 38	14 31	0.407	0.147;1.117	0.081
Overweight (≥26 kg/m^2)	Yes No	12 78	9 36	3 42	3.5	0.935;13.098	0.0628

Notes: *Low education: less than 8 years; Medium/High education: over 8 years.

Smoking was reported in 71.11% of the patients, with an average lifetime smoking exposure of 29.48 ± 11.74 packs of cigarettes/year. The alcohol use was reported by 74.33% of patients, with average of 4164±1.82 IU/day. The health risk factors, such as smoking, alcohol consumption or altered nutritional status, did not influence the association with COVID-19.

Associated Chronic Co-Morbidities

Chronic co-morbidities have been associated in 57.77% of patients (Figure 1), mainly chronic lung diseases (41.11%), liver chronic disease (18.88%), hypertension (16.66%), heart chronic diseases (11.11%) (Figure 1).

Clinical Presentation and Diagnostic

The inventory of clinical symptoms identified manifestations exclusively associated with COVID-19, such as headache (44.4%), myalgias (35.5%), arthralgias (24.4%), as well as manifestations common to the two groups of patients, but with a higher frequency in the case of co-infection COVID-19/TB: fever (71.1% vs 22.2%), chest pain (82.2% vs 28.8%), shortness of breath (73.3% vs 44.4%), decreased appetite (77.7% vs 60%). Other manifestations had equal frequencies, for example, cough (100%), sweating (88.8%), weight loss (73–74%). Hemoptysis was reported in 22.2%, but the frequency was higher in patients with TB only (Figure 2).

The source of COVID-19 was community acquired in 62.2% of cases and healthcare-associated in 37.7%.

Recurrences constituted 30% of TB cases, more frequent in patients with COVID-19 co-infections compared to TB mono-infections (38% vs 22%). The microscopic examination of acid-alcohol-resistant bacilli (AARB) was positive in 91.1% of the cases.

The majority of cases (86.66%) had complex radiological images, highlighting 46.66% cavitary forms, 40% caseous, 26.66% ulcerated, 21.11% infiltrative, 36.66% fibrous, 43.33% nodular, and 7.7% pleurisy or associated extrapulmonary locations (Table 2).

The biological picture evidenced higher values of inflammation markers and of the Neutrophils/Lymphocytes ratio in patients with co-infection with COVID-19. Overmore, significantly higher differences of values in creatinine, ALT and Brixia scores, both at baseline and during the follow-up examination, were found in COVID-19 group (Table 3).

Non-TB bacterial examination of sputum was performed in 17.77% of patients, with 43.75% showing negative results. Isolates from sputum included Streptococcus spp (3), Moraxella catharalis (1), Klebsiella spp (3), Pseudomonas spp (1), and

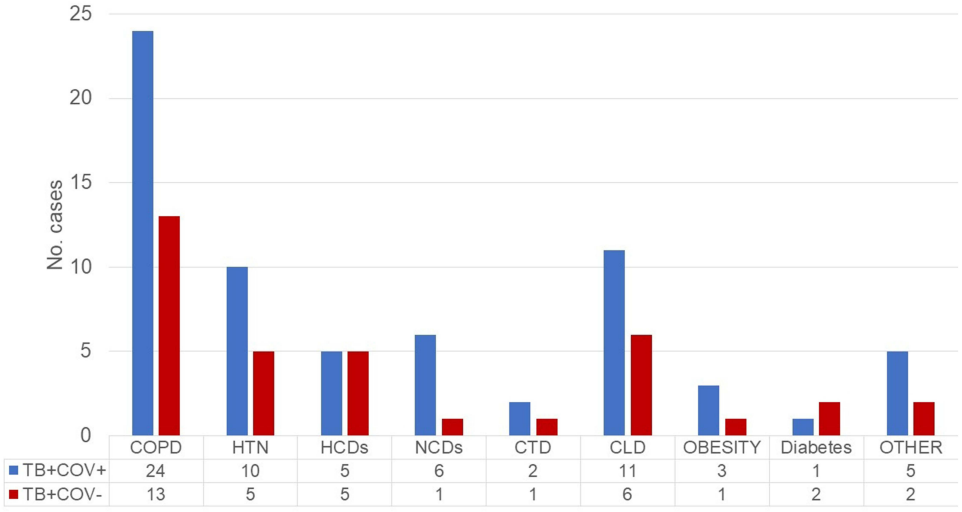

Figure 1 The frequency of TB related chronic co-morbidities.
Abbreviations: COPD, chronic obstructive pulmonary disease; HTN, hypertension; HCDs, heart chronic diseases; NCDs, neurological chronic disease; CTD, connective tissue disease; CLD, chronic liver disease.

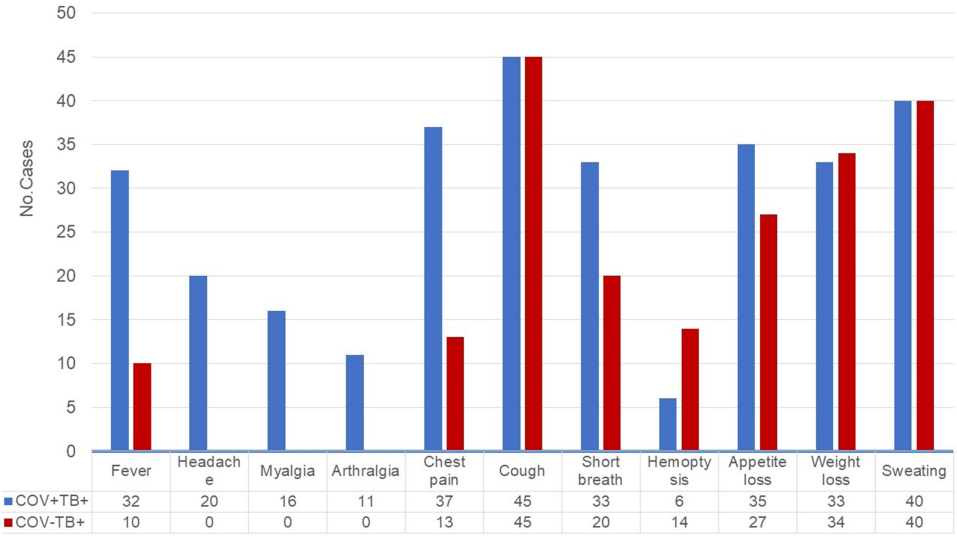

Figure 2 Frequency of Symptoms on patients with TB+ COV- comparative with TB+COV+.

E. coli (1). A higher number of Gram-negative bacteria (BGN) isolates were observed in cases with COVID-19 (3:1), while TB monoinfection had a higher proportion of Gram-positive bacteria (CGP) (3:2).

Drug Therapy and Outcomes

Treatment with the combination of Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol, was administered to 96.6% of TB patients. Individualized antituberculous regimens were provided for 2 patients with TB-MDR and for one case of TB rifampicin resistance detected in the GeneXPERT test.

Table 2 Classification Criteria of in TB Only in Comparison with TB-COVID-19 Co-Infection

		N-All	%	n1 TB+COV+	n2 TB+COV-	p	CI
Evolution	First presentation	63	70%	28	35	0.107	−0.344;0.033
	Recurrence	27	30%	17	10	0.107	−0.033;0.344
Microscopy	Positive AFB	82		40	42	0.458	−0.074;0.163
Radiologic features	Cavitary	43	47.77	21	22	0.996	−0.212;0.211
	Caseous	36	40	15	21	0.223	−0.336;0.079
	Ulcerate	24	26.66	12	12	0.947	−0.184;0.196
	Infiltrative	19	21.11	10	9	0.710	−0.207;0.141
	Fibrous	33		15	18	0.562	−0.146;0.266
	Nodular	39		20	19	0.685	−0.253;0.167
	Pleural/Extrapulmonary	7		6	1	0.049	0.021;0.992
Localization of the lesions	Bilateral	61	67.7	37	24	0.003	0.105;0.475
	Right	15		6	9	0.396	−0.222;0.088
	Left	12		1	11	0.001	−0.358;-0.086
	Miliaria	2		1	1	1	−0.061;0.617

Abbreviations: N-All, number of all patients; n1 TB+COV+, number of patients with co-infection COVID-19 and Tuberculosis; n2 TB+COV-, number of patients with tuberculosis only; CI, 95% confidence interval; AFB, acid fast bacteria.

Table 3 Comparative Features of Biological Data and Radiologic Scores in TB Only and TB-COVID-19 Co-Infection

	NRV	Average ±SD		Median		2t-test	CI 0.95
		COV+	COV-	COV+	COV-		
Leucocytes *10^3/mm^3	4.5–11	13,270±8947	12,300±922	11,400	11,400	0.504	−1.920;3.860
NLR	<3	7.648±8.346	5.468±4.502	4.764	4.229	0.127	−0.641;5.002
CRP [mg/L]	<3	14.448±21.208	8.611±5.63	7	6.7	0.080	−0.732;12.408
ESR [mm/h]	0–22	62.71±31.430	73.2±32.460	55	65	0.123	−23.877;2.898
Creatinine [mg/dL]	0.7–1.3	1.295±1.924	0.678±0.172	0.77	0.66	0.037	0.036;1.197
ALT [U/L]	7–55	72.71±86.69	33.77±27.93	38	22	0.005	11.700;66.166
AST [U/L]	8–48	66.711±73.621	47.667	43	30	0.126	−5.520;43.609
BRIXIA Score-B	0	9.288±3.307	7.688±2.556	9	8	0.012	0.360;2.839
BRIXIA Score C	0	7.266±3.326	3.911±2.172	7	3	<0.001	2.175;4.535

Abbreviations: NRV, Normal Reference Values; N/Ly, Neutrophils/Lymphocytes Ratio; CRP, C-Reactive Protein; ESR, Erythrocytes Sedimentation Rate; ALT, Alanine-amino transferase; AST, Aspartate amino transferase; BRIXIA Score -B, Severity Radiologic Score baseline; BRIXIA Score -C, Severity Radiologic Score Control (on hospital discharge).

Antibiotics for non-tuberculous infections were used in 33.3% of patients, including ceftriaxone (14.4%), amoxicillin (2.2%), tienamicin (3.3%), moxifloxacin (3.3%), levofloxacin (2.2%), linezolid (1.1%), gentamicin (1.1%), sulfamethoxazole (1.1%). Vancomycin (14.4%) and metronidazole (6.6%) were used for the treatment of patients with *Clostridioides difficile*-associated diarrhea.

Oxygen support via nasal cannula or face mask was provided to 31.1% of patients with COVID-19, compared to 6.6% in patients with TB monoinfection. Patients with COVID-19 received antivirals (77.7%) with favipiravir or remdesivir, dexamethasone (51.1%), and anticoagulants (62.2%).

Complications associated with the severe evolution of COVID-19 were observed in 8.8% of cases (coma, sepsis, and pleuropneumothorax), and medication toxicity was reported in 20% of patients (hyperuricemia, renal failure, toxic hepatitis, and anemia). *Clostridioides difficile* associated diarrhea occurred in 27.7% of cases, more frequently in the group with COVID-19 (16/9 vs.), but the difference was not statistically significant (Figure 3).

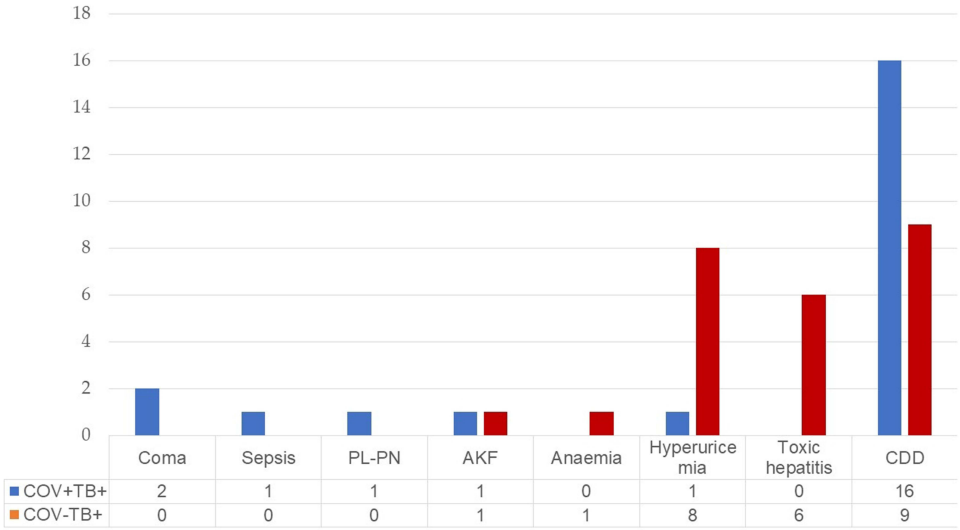

Figure 3 Comparative Complications in Patients Hospitalized with Co-infection TB-COVID-19 and TB only.
Abbreviations: PL-PN, pleuropneumonia; AKF, acute kidney failure; CDD, *Clostridioides difficile* diarrhea.

The outcomes were favorable in 92.2% of patients who were discharged with improved conditions. However, 5.5% of patients with COVID-19 deteriorated, requiring transfer to intensive care units in emergency hospitals, and 2.2% of patients died (1 case of TB-COVID co-infection and 1 case of monoinfection).

Discussion

Impact of COVID-19 on Tuberculosis Outcomes

Mycobacterium tuberculosis, a well-adapted pathogen to humans, has coexisted throughout human history. Approximately 2 billion people worldwide carry latent tuberculosis infections, with an estimated 10% risk of developing active disease during their lifetime, varying geographically and with comorbidities.[23]

COVID-19 induces pulmonary lesions but also affects other compartments of the immune system. In this context, tuberculosis reactivation can be attributed to various mechanisms, such as the immunosuppressive effects of corticosteroid therapy, cytokine storms, and T lymphocyte depletion.[24] An observational case-control study in China highlighted that both active and latent tuberculosis are risk factors for the progression of COVID-19.[25]

Conversely, studies from the early pandemic period provided evidence that COVID-19 increases the frequency and severity of tuberculosis.[18,21,22] The mortality rate in our study for patients with co-infection was 2.2%, comparable to the monoinfection TB group. This hospital mortality rate was lower than reported in some multicenter studies, where rates ranged from 9.2% to 14.2%.[26–28] It should be counting that 5.5% cases with severe evolution were transferred to intensive care units and probably died, increasing the mortality reported per case, and consequent decreasing discrepancy versus other studies. Most radiological lesions observed in our study were cavitary, evenly distributed between the co-infection and monoinfection TB groups, constituting 46.6%. Over 60% of these were new cases of tuberculosis, suggesting that the lesions had been present for at least one month before the onset of the COVID infection, whose incubation period is short.[28]

In view of these observations, our study results in line with the patterns observed in countries with a high prevalence of tuberculosis. In such settings, the diagnosis of COVID-19 might be more of a coincidental revelation of tuberculosis rather than a causative factor for reactivating latent tuberculosis.[23,27,29,30]

Considerations of COVID-19 Impact on Tuberculosis Appearance in Romanian Patients

In comparison with a report from Serbia, patients with tuberculosis-COVID-19 co-infection in our study exhibited more intense symptoms, with a higher frequency of cough (100% vs 69.8%), fever (71.1% vs 30.2%), and shortness of breath (73.3% vs 30.2%). However, the frequency of cases diagnosed with COVID-19 following tuberculosis was lower in our study (37.7% vs 45%).[31] A noteworthy proportion of patients in both the monoinfection TB and co-infection COVID-19 groups received non-tuberculosis antibiotics. Despite the global alert on excessive antibiotic use for COVID-19 without clear evidence of bacterial infections, our study reported lower antibiotic utilization rates compared to other studies.[32]

Demographic characteristics and risk factors such as alcohol and smoking did not influence the occurrence of COVID-19 co-infection. Nevertheless, lower adherence to COVID-19 prevention rules could be related to lower education level that was found more prevalent in co-infected group. Chronic comorbidities, especially chronic obstructive pulmonary disease (COPD), hypertension, chronic liver diseases, or neurological chronic diseases (NCDs), were more frequent in patients with COVID-19 co-infection, consistent with previous findings.[33,34] Most statistics on tuberculosis has reported more frequent the males, according to our findings.[35,36] A slightly higher rate of male/ female was found in co-infection group, probably related to additional risks of comorbidities and smoking that are considered in COVID-19, but are as well in generally observed between males and females.[37–39]

Clinical symptoms highlighted an overlap between manifestations typical of both COVID-19 and tuberculosis, such as cough, sweating, and weight loss. Fever, chest pain, shortness of breath, and loss of appetite were more common in patients with COVID-19 co-infection, whereas hemoptysis was more frequent in TB alone. The pain syndrome was characterized by headache, myalgia, and arthralgia, and has been mentioned exclusively in patients with COVID-19 co-infection. However, the specificity of clinical manifestations for COVID-19 is limited, with none of the symptoms having

the accuracy to confirm or rule out this infection.[40] Moreover, the clinical spectrum of COVID-19 varies from asymptomatic to severe forms, correlated with epidemiological factors and host characteristics.[41] Hemoptysis is an uncommon manifestation of COVID-19, reported with frequencies between 0.9% and 3.3%.[41,42] Hemoptysis in tuberculosis can be caused by bronchiectasis, bronchial artery erosions, and, more rarely, pulmonary artery erosions.[43] The proportion of hemoptysis revealing the onset of tuberculosis and/or the unfavorable evolution of fibrocavitary secondary TB was 20.71%, in line with recent studies in Romania.[44]

Bilateral lung lesions were significantly more frequent in the COVID-19 group compared to monoinfection TB ($p = 0.003$), consistent with a higher BRIXIA radiologic score. Although the BRIXIA score decreased in both groups upon discharge, the difference in values accentuated, likely due to the slow regression of COVID-19 pulmonary lesions. Prospective evaluation of these cases may be useful to clarify whether there is an additional risk for post-COVID fibrosis and respiratory dysfunction in the case of tuberculosis co-infection.

The average NLR was elevated in most patients in our study, but the differences between the COVID-19 co-infection and monoinfection TB groups were not significant, possibly because critical COVID-19 pattern were not evaluated in the study.[45,46]

Clostridioides difficile infection was reported in 27.7% of tuberculosis patients, possibly favored by rifampicin use, listed as one of the antibiotics that can induce diarrhea with this etiology, especially in elderly individuals with chronic comorbidities (underlying conditions).[29] The frequency of *Clostridioides difficile*-associated diarrhea was higher in the COVID-19 co-infection group (35.5% vs 20%), likely explained by the twice as frequent use of non-tuberculosis antibiotics and the occurrence of this type of diarrhea. It could be favored by rifampicin or broad-spectrum antibiotics use, as well as by changes in the intestinal microbiome during COVID-19 infection (fecal microbiota disruption by SARS-CoV-2 infection).[47]

Limitations of the Study

The retrospective design of the study could have limited the accuracy of collecting the data. The number of cases is small, limiting the statistical significance of the results. There were only hospitalized TB cases, with symptomatic COVID-19 during the first 4 to 8 weeks from the admission. Symptomatic or asymptomatic COVID-19 cases preceding tuberculosis were not analyzed. The potential impact of prior asymptomatic COVID-19 infections on tuberculosis, with potential effects on the biological and radiological changes found in the monoinfection TB group, could not be assessed. Intensive care unit was not available and some patients with severe evolution were transferred to other hospitals, with unknown state, that could distort the rate of mortality per case.

Conclusion

Symptomatic non-severe infection COVID-19 had a mild impact on the clinical and biological expression of tuberculosis diagnosed in the pandemic context. The hospital mortality of patients with tuberculosis was not influenced by COVID-19 co-infection in a country with a high tuberculosis prevalence. Persistent structural lung damage is suggested by radiological lesions according to the BRIXIA score and could be an indicator for COVID-19 additional risk on tuberculosis sequelae. Co-infection Covid-19 - tuberculosis should be care by multidisciplinary teams, covering at least specialties as pneumology, infectious diseases, intensive care, microbiology, imagistic, epidemiology. Tuberculosis control strategies should consider intensifying efforts to evaluate tuberculosis in COVID-19 patients, as common clinical manifestations and some pathogenic mechanisms continue to pose challenges for medical research and public health.

Abbreviations

AFB, acid fast bacteria; ALT, Alanine-amino transferase; AKF, acute kidney failure; AST, Aspartate amino transferase; CI, confidence interval; CDD; *Clostridioides difficile* diarrhea; COPD, chronic obstructive pulmonary disease; HCDs, heart chronic diseases; CLD, chronic liver disease; CRP, C-Reactive Protein; CTD, connective tissue disease; ESR, Erythrocytes Sedimentation Rate; GNB, Gram-negative bacilli; GPC, Gram-positive cocci; HTN – hypertension; NCDs, neurological chronic disease; NRV, Normal Reference Values; N/Ly, Neutrophils/Lymphocytes Ratio; OR, Odds Ratio; PL-PN, pleuropneumonia; TB-tuberculosis; WHO, World Health Organization.

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Disclosure

The authors report no conflicts of interest in this work.

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