Original Article

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Clinical Characteristics of COVID-19 in Active or Previously Treated Tuberculosis Patients in Turkey

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Abstract

Aim: There is limited literature on coronavirus disease-2019 (COVID-19) and tuberculosis (TB) coinfection, although high rates of coinfection between COVID-19 and other respiratory pathogens are expected. To the best of our knowledge, this is the first study to examine COVID-19 infection in patients diagnosed with active or previously treated TB in Turkey. In this study, the aim was to examine the frequency of COVID-19 and the factors affecting the frequency of COVID-19 in patients with active or previously treated TB.

Methods: The population of the retrospective cohort type study consisted of patients with TB enrolled in the Elazig Tuberculosis Dispensary between January 2015 and April 2021. The TB-related data of the patients was obtained from the Public Health Management System Tuberculosis System, and the COVID-19 information was obtained from the COVID-19 Case Tracking System. The status of being alive or dead and the date of death if they were dead were obtained from the Central Population Management System.

Results: 23.92% (n=105) of 439 patients with TB were COVID-19 cases. Advanced age, having at least one comorbid disease, and the presence of chronic pulmonary disease, diabetes mellitus, and heart disease increased the risk of developing COVID-19 in active or previously treated patients with TB.

Conclusion: COVID-19 was detected more frequently in active or previously treated TB patients than in the general population. Within the scope of public health services implemented to prevent the spread of COVID-19 infection, priority should be given to the TB patient group and older people, especially those with comorbid chronic pulmonary disease, diabetes mellitus, and heart disease in this group.

Keywords: COVID-19, coinfection, tuberculosis, retrospective studies, diabetes mellitus

Introduction

Tuberculosis (TB) is a public health problem that affects millions of people worldwide. In the World Health Organization (WHO) "2020 Global Tuberculosis Report", it was stated that around 7.1 million people worldwide were diagnosed with TB in 2019, and approximately 1.4 million people died from TB (1). Tuberculosis dispensaries were opened in order to provide assistance, solidarity, and health services in the fight against TB in Turkey. According to the "Tuberculosis War 2019 Report", 11,101 people were newly diagnosed in 2017, and 732 died in 2016 (2).

Coronavirus disease-2019 (COVID-19), which emerged in Wuhan, China, in December 2019 and spread widely in a short time, was declared a pandemic by the WHO on March 11, 2020 (3). On the same day, the first case was seen in Turkey (4). COVID-19 can cause a wide range of clinical symptoms, from asymptomatic infection to severe respiratory failure (5). It has been reported that 396 million people worldwide were diagnosed with COVID-19 on February 8, 2022, and 5.7 million died because of COVID-19 on February 6, 2022 (6). The total number of cases in Turkey has exceeded 12 million, and COVID-19 has caused the death of 89 thousand people (as of February 9, 2022) (7).

Although high coinfection rates are expected between COVID-19 and other respiratory pathogens (8), there is limited literature on COVID-19 and TB coinfection (9). TB infection can cause respiratory dysfunction and specific ventilation defects. This situation is associated with inflammation and proteases that develop to fight infection

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and cause lung damage. Thus, a history of TB constitutes a risk factor for chronic respiratory disorders (10). For these reasons, it is critical to investigate the coexistence of TB and COVID-19.

Although there are few studies examining the TB-COVID-19 coinfection, these studies generally have insignificant sample sizes and short follow-up periods. Another important issue is the lack of information about comorbidities in these studies. In most studies, it is even difficult to determine whether TB was diagnosed before or during treatment for COVID-19 (11). To the best of our knowledge, this is the first study to examine COVID-19 infection in patients diagnosed with active or previously treated TB in Turkey. In this study, the aim was to examine the frequency of COVID-19 and the factors affecting the frequency of COVID-19 in patients with active/previously treated TB.

Materials and Methods

Compliance with Ethical Standards

The ethical permission for the research was obtained from Firat University's Non-Interventional Research Ethics Committee with a letter dated April 27, 2021 and numbered 1908, and the institutional permission was obtained from the Public Health Directorate of the Elazig Provincial Health Directorate with a letter dated June 16, 2021.

Study Design, Setting, and Participants

The universe of the retrospective cohort type study consisted of patients with TB enrolled in the Tuberculosis Dispensary in Elazig province between January 2015 and April 2021. We reached the entire population without using the sample selection method.

Since this study is a retrospective cohort, the starting point of the study was January 2015. From January 2015 to April 2021, patients were followed through their records. A group of people with a certain trait is called a cohort (12). The cohort of this study consists of patients diagnosed with active or previous TB. In cohort studies, exposure status (independent variables, e.g., comorbid diseases) must occur before the outcome (COVID-19) occurs (12). For these reasons, people who have not yet been diagnosed with TB cannot be included in the cohort, so those who were diagnosed with COVID-19 before being diagnosed with TB were excluded from the study. Additionally, those who died before the start of the pandemic in Turkey (the first case of COVID-19 in Turkey) were excluded from the study because they could not be examined in terms of whether they were COVID-19 or not. In conclusion, the criteria for inclusion and exclusion from the study are as follows: The inclusion criterion was the TB diagnosis. Exclusion criteria: i) diagnosed with COVID-19 before being diagnosed with TB; ii) died before March 11, 2020, which is the first COVID-19 case in Turkey (13).

Variables

The dependent variable was whether the patient had COVID-19. Sex, age, comorbidities, the diagnosis year of TB, the case definition of TB, the sites of involvement of the TB disease, culture or smear positivity, drug-resistant TB, the multi-drug regimen used in the treatment and treatment result of patients with TB, and active or previously treated TB were independent variables. Comorbid diseases diagnosed before the COVID-19 diagnosis date were included in the analysis, and comorbid diseases diagnosed later were excluded from the study.

Active TB patients refer to people who are still receiving treatment, and previously treated TB patients refer to people whose treatment has been completed or who have been cured.

According to the 'Tuberculosis Diagnosis and Treatment Guidelines of the Ministry of Health of the Republic of Turkey', the definitions of the variables used in the current study are given below (14):

Case Definitions of TB

New case: patients who have not been treated for TB before or have received treatment for less than a month.

Relapse cases: patients who were previously diagnosed with TB and whose treatment was completed successfully, and who were re-diagnosed with TB with sputum positivity or clinical and radiological findings.

Multi-drug Regimen

First-line drugs: isoniazid, rifampicin, ethambutol, and pyrazinamide. Sensitive ones were used in the treatment.

Second-line drugs: ethionamide, prothionamide, cycloserine, and terizidone (since they were similar drugs, one of ethionamide and prothionamide, one of cycloserine and terizidone were used).

Treatment Results

Cured: it was the demonstration of a negative sputum smear at least twice in a patient with a positive sputum smear at baseline, one during the maintenance period of the treatment and the other at the completion of the treatment, with clinical and radiological improvement.

Completed treatment: it was the termination of the treatment by considering the clinical and radiological findings that was successful in cases where sputum analysis could not be performed during the maintenance period of the treatment or at the end of the treatment for the patient who completed the prescribed treatment within the prescribed time.

Death: death of a patient with TB during treatment.

Abandonment of treatment: tuberculosis patients did not take their medication for two months or longer during treatment.

Transferred: it was the case that the results of the treatment were not known because the patient went to another dispensary area (or abroad).

Ongoing treatment: if the patient's treatment was ongoing, it was considered in this group.

Data Sources

The TB-related data of the patients were obtained from the Public Health Management System Tuberculosis System, and the COVID-19 information was obtained from the Public Health Management System COVID-19 Case Tracking System. The patients' status as being alive or dead and their death dates were obtained from the Central Population Management System.

Statistical Analysis

The data obtained in the study were recorded in the SPSS 21.0 program and analyzed. Descriptive statistics are presented with frequency (n) and percentage (%) for categorical variables; mean ± standard deviation or median; and 1st quarter-3rd quarter or minimum (min.)-maximum (max.) for continuous variables. Normal distribution was tested with the Kolmogorov-Smirnov test. Chi-square and Mann-Whitney U tests were used in bivariate analyses. While presenting the results of the regression analysis, the unadjusted odds ratio (UOR) was used in the univariate logistic regression analysis, and the hazard OR (HOR) was used in the COX regression analysis. Odds ratios are presented with a 95% confidence interval (CI). Statistical significance was evaluated at $p<0.05$.

Results

Between January 2015 and April 2021, there were 496 patients with TB registered in the Elazig Tuberculosis Dispensary. One hundred and twenty-eight of these patients had COVID-19. Twenty-three patients were diagnosed with COVID-19 before being diagnosed with TB; eight patients were diagnosed with TB in 2020 and 15 patients in 2021; they were excluded from the study, and 34 patients died before the first COVID-19 case in Turkey. The remaining 439 patients with TB were included in the study (Figure 1). Of these patients, 23.92% (105/439) were cases of COVID-19 (Table 1).

The demographic, clinical, and laboratory characteristics and frequency of COVID-19 of the patients with TB included in the study are given in Table 1. They were 186 (42.37%) males and 253 (57.63%) females, with a mean age of 42.65±20.29 (median=43, min.=0, max.=95). The average time elapsed between the TB diagnosis date and the COVID-19 process start date for the patients with TB who caught COVID-19 was 35.20±21.74 months (min.=0, max.=71).

A regression analysis was performed using the independent variables (age, having at least one comorbidity, chronic lung disease, diabetes mellitus, and heart disease) that were significant in the bivariate analysis and the dependent variable of the presence or absence of COVID-19. The results of a binary regression analysis with one independent variable are shown in Figure 2. Increasing age by 1 year increased the incidence of COVID-19 by 2% (UOR=1.02, 95% CI=1.01-1.03, $p<0.001$). The incidence of COVID-19 was 81% higher in patients with at least one comorbidity than in those without (UOR=1.81, 95% CI=1.16-2.82, p=0.009). Additionally, the incidence of COVID-19 was significantly higher in patients with chronic pulmonary disease (UOR=2.93, 95% CI=1.42-6.04, p=0.004), diabetes mellitus (UOR=2.27, 95% CI=1.05-4, 87, p=0.036), and chronic cardiac disease (UOR=2.51, 95% CI=1.48-4.28, p=0.001) than in those without. The results of the COX regression analysis with the model created using these five independent variables are presented in Figure 3. The variables of having at least one comorbid disease, diabetes mellitus and chronic cardiac diseases lost their significance in the model. Age (HOR=1.01, 95% CI=1.00-1.03, p=0.009) and chronic pulmonary disease (HOR=2.05, 95% CI=1.10-3.81; p=0.024) variables remained significant.

The clinical characteristics of COVID-19 cases are presented in Table 2. Only one COVID-19 case died; he was a 68-year-old male patient. Here, diabetes mellitus and epilepsy were comorbidities, and TB involvement was extrapulmonary. It had a computed tomography result that was compatible with COVID-19. The COVID-19 fatality rate was determined at 0.95%.

Discussion

In this study, the frequency of COVID-19 in patients with active/previously treated TB and the factors affecting the frequency of COVID-19 were investigated. To the best of our knowledge, the current study is the first to examine COVID-19 infection in patients diagnosed with active or previously treated TB in Turkey. According to the results of the study; the incidence of COVID-19 in the current cohort was found to be 23.92%. Advanced age, having at least one comorbid disease, and the presence of chronic pulmonary disease, diabetes mellitus, and heart disease increase the risk of developing COVID-19 in active or previously treated patients with TB.

The prevalence of COVID-19 in active or previous patients with TB in the current study (23.92%, Table 1) was higher than the prevalence in the population in Turkey (5.78%, when the data from the onset of the pandemic to

Table 1. Demographic, clinical, laboratory characteristics and frequency of COVID-19 of tuberculosis patients					
Variables	**Total, n (%)**	**COVID-19 case, n (%)**		**p-value**	**COVID-19 frequency %**
		Yes	**No**		
Total	439 (100)	105 (100)	334 (100)		23.92
Sex				0.430*	
Male	186 (42.37)	41 (39.05)	145 (43.41)		22.04
Female	253 (57.63)	64 (60.95)	189 (56.59)		25.30
Age [median (Q1-Q3)]	43 (25-61)	49 (29-67)	41 (24-57)	**<0.001****	-
At least one comorbid disease	158 (35.99)	49 (46.67)	109 (32.63)	**0.009***	31.01
Comorbidities					
Chronic pulmonary diseases	33 (7.52)	15 (14.29)	18 (5.39)	0.003*	45.45
Chronic renal disease	14 (3.19)	6 (5.71)	8 (2.40)	0.110*	42.86
Cerebrovascular diseases	7 (1.59)	3 (2.86)	4 (1.20)	0.365*	42.86
Diabetes mellitus	30 (6.83)	12 (11.43)	18 (5.39)	**0.032***	40.00
Chronic cardiac diseases	73 (16.63)	29 (27.62)	44 (13.17)	**0.001***	39.73
Cancer	21 (4.78)	7 (6.67)	14 (4.19)	0.300*	33.33
Neurological diseases	11 (2.51)	3 (2.86)	8 (2.40)	0.729*	22.27
Gastrointestinal system diseases	8 (1.82)	1 (0.95)	7 (2.10)	0.686*	12.50
Rheumatological diseases	17 (3.87)	2 (1.90)	15 (4.49)	0.383*	11.76
Diagnosis year of TB				0.119*	
2015	86 (19.59)	18 (17.14)	68 (20.36)		20.93
2016	77 (17.54)	22 (20.95)	55 (16.47)		28.57
2017	65 (14.81)	16 (15.24)	49 (14.67)		24.62
2018	69 (15.72)	13 (12.38)	56 (16.77)		18.84
2019	71 (16.17)	15 (14.29)	56 (16.77)		21.13
2020	60 (13.67)	21 (20.00)	39 (11.68)		35.00
2021	11 (2.51)	0	11 (3.29)		0
Case definition of TB (n=416)				0.694*	
New	388 (93.27)	96 (94.12)	292 (92.99)		24.74
Relapse	28 (6.73)	6 (5.88)	22 (7.01)		21.43
The involvement sites of the TB disease				0.334*	
Pulmonary	197 (44.87)	41 (39.05)	156 (46.71)		20.81
Pulmonary + extrapulmonary	19 (4.33)	6 (5.71)	13 (3.89)		31.58
Extrapulmonary	223 (50.80)	58 (55.24)	165 (49.40)		26.01
Extrapulmonary involvement (n=235)					
Bone involvement	17 (7.23)	7 (11.29)	10 (5.78)	0.160*	41.18
Breast involvement	15 (6.38)	5 (8.06)	10 (5.78)	0.549*	33.33
Pleural membrane involvement	40 (17.02)	13 (20.97)	27 (15.61)	0.335*	32.50
Lymphatic system involvement	123 (52.34)	35 (56.45)	88 (50.87)	0.450*	28.46
Abdominal involvement	27 (11.49)	6 (9.68)	21 (12.14)	0.602*	22.22
Central nervous system involvement	10 (4.26)	2 (3.23)	8 (4.62)	1.000*	20.00
Cutaneous involvement	27 (11.49)	5 (8.06)	22 (12.72)	0.324*	18.52
Culture positivity	95 (50.80)	26 (59.09)	69 (48.25)	0.209*	27.37
Smear positivity	115 (61.50)	23 (52.27)	92 (64.34)	0.150*	20.00
Resistance to at least one drug	20 (4.56)	4 (3.81)	16 (4.79)	0.794*	20.00
Multi-drug regimen (n=424)				0.397*	
First-line drugs	402 (94.81)	97 (97.00)	305 (94.14)		24.13

Table 1. Continued					
Variables	**Total, n (%)**	**COVID-19 case, n (%)**		**p-value**	**COVID-19 frequency %**
		Yes	**No**		
First-line drugs and second-line drugs	17 (4.01)	3 (3.00)	14 (4.32)		17.65
Second-line drugs	5 (1.18)	0	5 (1.54)		0
Treatment result (n=438)				0.716*	
Cure	99 (22.60)	27 (25.71)	72 (21.62)		27.27
Completed treatment	282 (64.38)	66 (62.86)	216 (64.86)		23.40
Death	2 (0.46)	0	2 (0.60)		0
Abandonment of treatment	3 (0.68)	0	3 (0.90)		0
Transferred	18 (4.11)	3 (2.86)	15 (4.50)		16.67
Ongoing treatment	34 (7.76)	9 (8.57)	25 (7.51)		26.47
Active/previously treated TB (n=415)				0.789*	
Active tuberculosis	34 (8.19)	9 (8.82)	25 (7.99)		26.47
Previously treated tuberculosis	381 (91.81)	93 (91.18)	288 (92.01)		24.41
*Chi-square were used, **Mann-Whitney U were used COVID-19: Coronavirus disease-2019, TB: Tuberculosis					

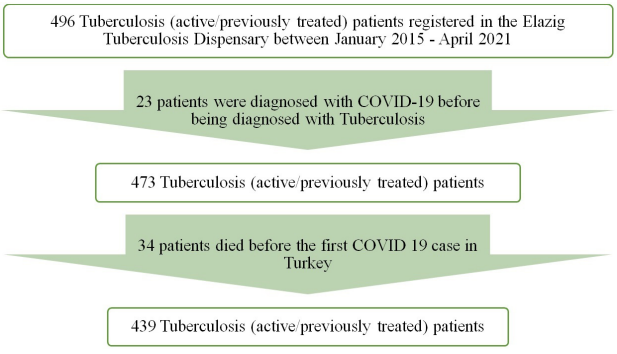

Figure 1. Flow chart of study sample identification

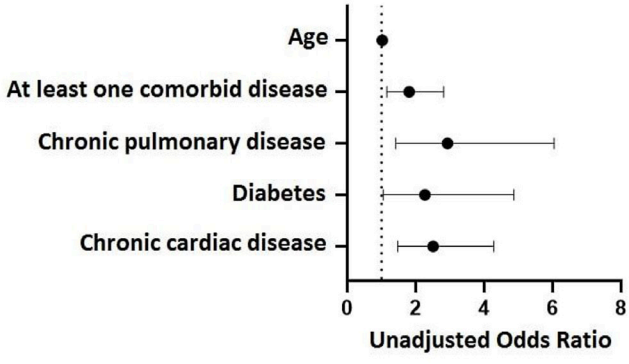

Figure 2. Univariate logistic regression analysis predicting COVID-19 with factors associated with the frequency of COVID-19 in tuberculosis patients
COVID-19: Coronavirus disease-2019

April 30, 2021 were analyzed) (7,15). Patients who have previously been affected by a respiratory disease have impaired lung function and decreased resistance to the virus, and they tend to develop Acute Respiratory Distress Syndrome (16). Therefore, the incidence of COVID-19 in

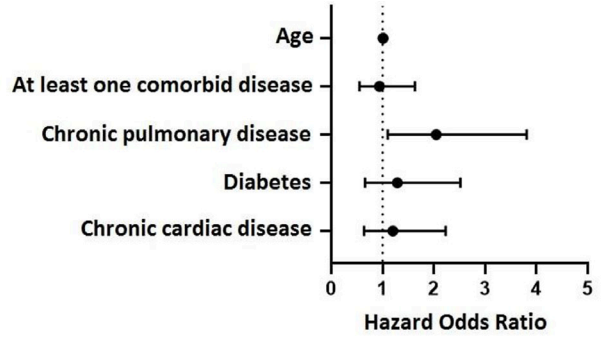

Figure 3. Multivariate logistic regression analysis predicting COVID-19 with factors associated with the frequency of COVID-19 in tuberculosis patients
COVID-19: Coronavirus disease-2019

Table 2. Clinical characteristics of COVID-19 cases	
Variables	**n (%)**
Total	105 (100)
Tuberculosis and COVID-19 status	
COVID-19 after the previously treated tuberculosis	89 (84.76)
COVID-19 while active tuberculosis (now tuberculosis is not active)	4 (3.81)
COVID-19 during active tuberculosis (also active now)	9 (8.57)
Unknown due to transferred	3 (2.86)
Symptomatic case	67 (63.81)
Contacted	26 (24.76)
COVID-19 case status	
Recovered from COVID-19	100 (95.24)
Currently in treatment	4 (3.81)
Death	1 (0.95)
Hospitalization in intensive care	1 (0.95)
Intubation	0
COVID-19: Coronavirus disease-2019	

patients with TB may be higher than that in the general population. Another possible cause of TB-COVID-19 infection may be that both diseases reinforce each other, with a temporary reduction in cellular immunity leading to new infection or exaggerated reactivation of latent infection (17).

Due to biological factors, social roles, and behavioral differences, the distribution of some diseases by sex differs. It has been reported that TB is more common in males in Turkey (2). However, with the increase in extrapulmonary TB, which is more common in females recently, female dominance can be observed in TB cases (18,19). Therefore, the fact that more than half (50.80%) of the TB cases in the current study were extrapulmonary TB can be explained by the fact that the frequency of female patients (57.63%) is higher than that of males (Table 1). It was reported that the frequency of COVID-19 did not change according to sex (Table 1), in accordance with the current study (20).

In the study of Tadolini et al. (21) examining the TB - COVID-19 coinfection, the median age of the patients was 48 (32-69), and in the study of Sy et al. (9), 48.92±19.63. In this study, the median age of TB-COVID-19 co-infected patients was 49 (29-67), and this finding was consistent with the literature (Table 1). TB and COVID-19 have overlapping risk factors such as advanced age, diabetes, smoking, and other chronic respiratory diseases (17). According to the results of the current study, age was significantly associated with the frequency of COVID-19 both when examined alone and in the presence of comorbid diseases (Table 1, Figure 2, Figure 3).

In studies examining both COVID-19 patients (22-24) and TB-COVID-19 co-infected patients (21,25), the most frequently reported comorbidities were cardiovascular diseases, diabetes, and chronic lung diseases (Table 1), which was consistent with the findings of the present study. The coexistence of these diseases with COVID-19 may be related to the pathogenesis of COVID-19 (23). Although the underlying mechanism of COVID-19 remains unclear, it has been determined that the virus uses angiotensin converting enzyme-2 (ACE-2) receptors on the surface of host cells to enter the cell (26). The association between cardiovascular diseases and COVID-19 may be due to the weakening of the immune system in people with cardiovascular disease (23,27) and/or the presence of ACE-2 receptors in cardiac muscle cells (28). People with diabetes tend to get infections due to impaired phagocytic cell abilities. Elevated ACE-2 receptor levels have been associated with diabetes and may sensitize people with diabetes to COVID-19 infection (29). Additionally, impaired function of T cells and elevated interleukin-6 levels may also play a decisive role in the development of COVID-19 in diabetics (27,30).

In this cohort of patients with TB, although there was no correlation between pulmonary and extrapulmonary TB disease and the frequency of COVID-19 infection, COVID-19 infection was observed most frequently in those with chronic pulmonary disease compared with other comorbidities (Table 1). Additionally, in the presence of other comorbid diseases, chronic pulmonary diseases were found to be the only risk factor for comorbid COVID-19 infection (Figure 3). Further studies are needed to examine the effect of chronic respiratory system diseases as a mediator variable in the TB-COVID-19 relationship. Additionally, experimental data on the immunopathological mechanism underlying the TB-COVID-19 coinfection may further explain this relationship (11).

In this study, the most common extrapulmonary involvement in COVID-19 patients with TB was found to be lymphatic system, pleura, and bone involvement (Table 1), consistent with the literature (21).

In this study, the incidence of COVID-19 was found to be higher in patients with active TB than in patients with previously treated TB, in patients diagnosed with TB in 2020 compared with patients with TB diagnosed in previous years (Table 1). However, no significant relationship was found between being a patient with active or previously treated TB or the year of diagnosis of TB and the incidence of COVID-19 (Table 1). The relationship between TB and COVID-19 coinfection can be explained by the presence of damage to the lungs due to fibrosis or cavitation in patients with previously treated TB and impaired lung function in patients with active TB (31). Although there is limited information on the TB-COVID-19 relationship in the literature, there is also limited information on the distinction between active and previously treated TB as a risk factor for COVID-19 (32).

In a study conducted in India, a country with a high TB burden, examining TB and COVID-19 coinfected patients, the mortality rate among TB and COVID-19 coinfected patients was found to be 27.3% (31). In another study conducted in eight countries examining TB and COVID-19 coinfected patients, this frequency was found to be 12.3% (21), and in a study conducted in Italy, it was 11.6% (33). In the study, which included the data of 37 countries, the mortality rates were 14.2% in Europe, 9.2% outside Europe, and 11.08% (34). However, in the current study, only one of the 105 TB-COVID-19 coinfected patients died (Table 2). This can be explained by the fact that both the TB estimated incidence rate and the TB estimated mortality rate in Turkey are lower than the rates of both the world and all WHO regions, including the European and American regions (35). Additionally, according to the results of the study evaluating TB-COVID-19 infection in South Africa, another country with a high TB burden,

it was determined that underlying conditions such as advanced age, male sex, and diabetes mellitus increase COVID-19-related hospital mortality (25). Therefore, it should be emphasized that the TB-COVID-19 coinfected patient who died in this study was an advanced-age male patient who was diagnosed with diabetes mellitus. When the data from the beginning of the epidemic to the date of April 30, 2021, in Turkey showed a COVID-19 fatality rate of 0.83% (7), it was calculated as 0.95% in the current study. In this study, in which we examined COVID-19 patients in the patient population with TB, it was seen that the COVID-19 fatality of the population with TB is similar to that of the general population.

Study Limitations

This study has some limitations. First, COVID-19 is rapidly evolving globally. Therefore, information regarding COVID-19 may change as new literature continues to be reported. Second, the results may not be representative of COVID-19 cases nationwide or globally, as the current research only includes data for one city. Third, some data are missing because the study's data was derived from health information systems.

This study has some strengths. Compared to similar studies, a larger sample size was used in the study, and a longer follow-up period was determined. The comorbid diseases of patients with TB were also examined. Additionally, it was clearly stated that the patients with TB included in the study were people who had not been diagnosed with COVID-19 yet since the study was a retrospective cohort. For all these reasons, this study offers stronger and more precise results than similar studies.

Conclusion

COVID-19 was detected more frequently in active or previously treated patients with TB than in the general population. Advanced age, chronic pulmonary diseases, diabetes mellitus, and chronic cardiac diseases have also been identified as risk factors for COVID-19 infection in patients with TB. For these reasons, within the scope of public health services implemented to prevent the spread of COVID-19 infection, priority should be given to the TB patient group and those with advanced age and comorbid diseases in this group. Furthermore, there was no correlation between the frequency of COVID-19 and the year of TB diagnosis, TB case definition (new or relapse), TB involvement sites (pulmonary or extrapulmonary TB), culture or smear positivity, anti-tuberculosis drug resistance status, the multi-drug regimen used in treatment, or active or previously treated TB. The fatality of COVID-19 in patients with TB has been found to be similar to that in the general population. The relationship between TB and COVID-19 severity was not evaluated in this study. Evaluation of this issue in future studies may contribute to further elucidating the TB-COVID-19 relationship.

Ethics

Ethics Committee Approval: The ethical permission for the research was obtained from Firat University's Non-Interventional Research Ethics Committee with a letter dated April 27, 2021 and numbered 1908, and the institutional permission was obtained from the Public Health Directorate of the Elazig Provincial Health Directorate with a letter dated June 16, 2021.

Informed Consent: Retrospective cohort type study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: S.K., F.N.K., M.Y., Z.A.T., E.P., Design: S.K., F.N.K., M.Y., Z.A.T., E.P., Data Collection and/or Processing: S.K., F.N.K., Analysis and/or Interpretation: S.K., F.N.K., Literature Research: S.K., F.N.K., Writing: S.K., F.N.K., M.Y., Z.A.T., E.P.

Conflict of Interest: No conflict of interest was declared by the authors.

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