



COVID-19 disease and vaccine status in tuberculosis patients in Sakarya

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Abstract

Tuberculosis was the leading cause of death worldwide before COVID-19. The present study aimed to examine the cases of COVID-19 disease and vaccination against COVID-19 in patients receiving tuberculosis treatment in Sakarya. In this descriptive study, 132 people aged 18 years and over, registered in Sakarya Tuberculosis Dispensary and continuing treatment in 2021, were included. Cases of COVID-19, hospitalization, intensive care unit status and vaccination status against COVID-19 were recorded. Statistical significance level was accepted as $p < 0.05$. The mean age of the patients was 49.8 ± 20.6 years. 65.2% of the patients were male ($n=86$). It has been determined that 21.2% ($n=28$) of the patients have been diagnosed with COVID-19. No statistically significant difference was observed between the patients' gender and history of COVID-19 infection with mortality ($p > 0.05$). There was no statistically significant difference between the ages of groups with and without COVID-19 ($p > 0.05$). Age was statistically significantly different in the surviving and deceased groups ($p < 0.05$). There was a statistically significant difference between the vaccination status of the patients and mortality ($p < 0.05$). People being treated for tuberculosis are at risk as long as the danger of COVID-19 continues. More emphasis should be placed on the importance of vaccination against COVID-19, especially in elderly individuals receiving tuberculosis treatment.

Keywords: COVID-19, tuberculosis, vaccination, mortality

1. Introduction

COVID-19, caused by SARS-COV-2, is a highly contagious acute viral disease. On the other hand, tuberculosis is a chronic bacterial infection, and the most common form is pulmonary tuberculosis. They present with similar symptoms, such as cough, fever, and respiratory distress (1). As of November 16, 2022, the COVID-19 pandemic has been reported to have caused 632 million confirmed cases and 6.5 million deaths worldwide (2). It was revealed that tuberculosis was the leading cause of death worldwide before COVID-19, resulting in the death of approximately 1.5 million people per year (3). Immune status, which makes people susceptible to tuberculosis, may also be a risk factor for COVID-19 infection (4). According to historical evidence, higher mortality is observed in patients with concomitant tuberculosis infection with respiratory viruses (5). Findings indicating a more severe course of COVID-19 in tuberculosis patients have been presented in some studies (6-8) According to a meta-analysis, the prevalence of tuberculosis was between 0.4% and 4.4% among COVID-19 patients. In addition, the prevalence of tuberculosis in severe COVID-19 cases was higher as well (9) People with chronic diseases such as hypertension, diabetes mellitus, lung cancer, and chronic obstructive pulmonary disease are also at higher risk of death and hospitalization associated with COVID-19 and tuberculosis (10,11).

The burden brought by COVID-19 and tuberculosis on the health system is very high and causes many years of life to be

lost (12). Available data are insufficient to understand the potential impact of COVID-19 on treatment outcomes of tuberculosis patients (13,14). With the development of effective vaccines against COVID-19, deaths have decreased, but mortality may still be high in unvaccinated individuals and those with underlying chronic diseases (15,16). Due to the fact that the COVID-19 pandemic has not yet lost its impact worldwide and we are likely to experience a new phase of the epidemic as a result of new variants that may occur at any moment, there is a need to examine the current status of COVID-19 and the vaccination status of current tuberculosis patients. The present study aimed to examine the cases of COVID-19 disease and vaccination against COVID-19 in patients receiving tuberculosis treatment in Sakarya.

2. Materials and Methods

The research was designed as a descriptive study. One hundred thirty-two patients aged 18 and over who were registered in Sakarya Adapazarı Tuberculosis Dispensary, diagnosed with active pulmonary tuberculosis in 2021, and whose treatment was ongoing were included in the study.

According to the Tuberculosis Diagnosis and Treatment guide published by the Ministry of Health of the Republic of Turkey, the diagnosis of pulmonary tuberculosis is made bacteriologically in three methods: (17)

1. Smear-positive pulmonary tuberculosis

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2. Smear-negative pulmonary tuberculosis
3. Molecular test positive pulmonary tuberculosis

SARS-COV-2 positivity is detected by PCR in the combined nose and throat swab obtained as a result of the physician's decision from the people who applied to the hospital with any complaint.

After the approval of the ethics committee, patient records were obtained from the tuberculosis dispensary. The information of the patients about COVID-19 was taken from the digital database. Vaccine data were also questioned from the vaccine tracking system application of the Ministry of Health. In the study, the information of the people who received active pulmonary tuberculosis treatment in 2021 was examined on June 30, 2022. Cases of COVID-19, hospitalization, intensive care unit (ICU) status and vaccination status against COVID-19 were recorded. There are three types of vaccines used against COVID-19 in Turkey at the time of the research. These are Sinovac (CoronaVac), Pfizer/ BioNTech (BNT162b2), and Turkovac (ERUCoV - VAC) vaccines. At the time of our study, it was observed that the Turkovac vaccine was not administered to any patient since it was new. Thus, it will not be mentioned in the rest of the study. The vaccination status of the patients was categorized as follows, considering the guidelines of the Turkish Ministry of Health (18). The first group consisted of patients who had not been vaccinated at all or who had not received two doses of the BNT162b2 vaccine and had less than three doses in total. The patients in the second group were those who did not have two doses of the BNT162b2 vaccine but had at least three doses of the vaccine in total. The third group was those who had at least two doses of the BNT162b2 vaccine.

SPSS 22.0 program was used in the statistical analysis of the data. In descriptive statistics, frequency and percentages were used for qualitative data, and mean, standard deviation, and median (minimum; maximum) values for quantitative data. Pearson Chi-square, Yates corrected Chi-square, Fisher's Exact Test, and Student's t-test performed the statistical analyses. The statistical significance level was accepted as $p < 0.05$.

3. Results

One hundred thirty-two patients were included in the study. The mean age of the patients was 49.8 ± 20.6 years. 65.2% of the patients were male ($n=86$). In addition to pulmonary tuberculosis, 6.1% ($n=8$) of the patients also had extrapulmonary tuberculosis disease. 8.3% ($n=11$) of the patients applied for recurrence.

It was determined that 21.2% of the patients were diagnosed with COVID-19 after the date they started to receive tuberculosis treatment. 28.6% ($n=8$) of those who had the disease were treated in the hospital ward, and 21.4% ($n=6$) were treated in the intensive care unit. The median days of the patients receiving treatment in the ward were 1.5 (min:1 max:10), and the median days that the patients treated in the

intensive care unit received treatment was 10 (min:5 max:21). It was observed that 10.6% ($n=14$) of the patients died during the follow-up. 41.7% ($n=55$) of the patients had at least two doses (BNT162b2) vaccine. 79.2% ($n=84$) of those who had at least one dose of vaccine had at least one dose of vaccine in the last six months. (Table 1)

Table 1. Distribution of Disease and Vaccination Status, Sakarya, 2022

		Frequency (Percent)
COVID-19 Status (n=132)		
	Have-had	28 (21.2)
	Have not had	104 (78.8)
Hospitalization Status (n=28)		
	Those with service admission	8 (28.6)
	Those without service admission	20 (71.4)
Hospitalization in ICU (n=28)		
	Treated in ICU	6 (21.4)
	Not treated in ICU	22 (78.6)
Death Status (n=132)		
	Deceased	14 (10.6)
	Survivors	118 (89.4)
Vaccination Status (n=132)		
*	Group 1	52 (39.4)
	Group 2	25 (18.9)
	Group 3	55 (41.7)
Vaccination Status in the Last Six Months (n=106)		
	Non- vaccinated	22 (20.8)
	Vaccinated	84 (79.2)

*Group descriptions are specified in the methods section.

Table 2. Investigation of the Reasons Affecting the Patients' Status of Passing COVID-19, Sakarya, 2022

		COVID-19 Status		*p
		Not have Had n (%)	Have Had n (%)	
Gender	Male	73 (84.9)	13 (15.1)	0.034^y
	Female	31 (67.4)	15 (32.6)	
Vaccination Status	Group 1	39 (75.0)	13 (25.0)	0.637
	Group 2	21 (84.0)	4 (26.0)	
	Group 3	44 (80.0)	11 (20.0)	

Row percentage is presented * Pearson chi-square test was performed. ^y: Chi-square test with Yates correction was performed. Group descriptions are specified in the methods section.

No statistically significant difference was observed between the vaccination status of the patients and their COVID-19 exposure ($p=0.637$). There was a statistically

significant difference between gender and COVID-19 transmission status ($p=0.034$). (Table 2)

No statistically significant difference was observed between the patients' gender ($p=0.242$) and history of COVID-19 infection ($p=0.076$) with mortality. There was a statistically significant difference between the vaccination status of the patients and mortality ($p=0.013$). It was determined that the effect of vaccination status on survival was caused by the difference between group 3 and both group 2 and group 1. No difference was found between group 1 and group 2. It was revealed that 35.7% ($n=5$) of the deceased died during active COVID-19 disease. When the vaccination status of these five patients was examined, four had no vaccine against COVID-19. (Table 3)

Table 3. Investigation of the Causes Affecting the Survival of the Patients, Sakarya, 2022

		Death Status		
		Survivors n (%)	Deceased n (%)	*p
Gender	Male	79 (91.9)	7 (8.1)	0.242 ^f
	Female	39 (84.8)	7 (15.2)	
Vaccination Status	Group 1	42 (80.8)	10 (19.2)	0.013
	Group 2	22 (88.0)	3 (12.0)	
	Group 3	54 (98.2)	1 (1.8)	
COVID-19 Status	Have had	96 (92.3)	8 (7.7)	0.076 ^f
	Have not had	22 (78.6)	6 (21.4)	

Row percentage is presented * Pearson chi-square test was performed. ^f: Fisher's Exact Test was performed. Group descriptions are specified in the methods section.

There was no statistically significant difference between the ages of groups with and without COVID-19 ($p=0.843$). Age was statistically significantly different in the surviving and deceased groups ($p<0.001$). (Table 4).

Table 4. Examining the Relationship between Patient Age and COVID-19 and Mortality Status, Sakarya, 2022

	Age	*p
	Mean ± Standard Deviation	
COVID-19 Status (n=132)		0.843
Have not had	50.0 ± 20.1	
Have had	49.1 ± 22.6	0.001
Survive Status (n=132)		
Survivors	46.9 ± 19.3	
Deceased	73.8 ± 14.9	

*Student's T-test was performed.

4. Discussion

In the examined period, it was observed that 21.2% of the patients had COVID-19 infection. Considering the factors affecting the status of being COVID-19-positive, a significant

difference was determined only in terms of gender. The incidence of COVID-19 was higher in females. In a qualitative study conducted in Turkey, people with active pulmonary tuberculosis were interviewed, and it was revealed that 28.6% had COVID-19 (19). In a database review performed with a method similar to this study, patients who received tuberculosis treatment in the last five years were examined, and 11.2% had COVID-19 (20).

The present study revealed that 28.6% of the patients were admitted to the hospital ward and 21.4% to the ICU. In one study, the hospitalization rate for COVID-19 was reported as 12% (21). In a study examining 654 patients in Turkey, the rate of ICU admission due to COVID-19 was 7.5% (22). In our example, it has been demonstrated that patients who had recently started tuberculosis treatment had higher rates of hospitalization and ICU admission.

The COVID-19 mortality rate in patients with tuberculosis was 17.8%. In a study conducted in Turkey in the early period when there was no COVID-19 vaccine yet, mortality in the coexistence of tuberculosis and COVID-19 was found to be 6% (23). According to the latest reports of the World Health Organization, as of November 2022, the overall mortality rate of COVID-19 is 1.04% (2). According to the data of the Ministry of Health in Turkey, the overall mortality rate is 0.6% (24). Based on this data, it can be considered that active tuberculosis patients are more likely to die if they have COVID-19 than other COVID-19 patients.

In our study, a significant difference was observed between the deceased and surviving groups regarding age. While the mean age of the deceased group was 73.8±14.9 years, it was 46.9±19.3 years in the survivors. A study performed in California reported that the mean age of those who died in the group with tuberculosis and COVID-19 was significantly different from the group that survived, and the median age of those who died was 81 (25). In a meta-analysis study, it was reported that age affected death in 89 COVID-19 patients with tuberculosis (26).

The present study demonstrated a significant difference between the vaccination statuses against COVID-19 in the deceased and surviving groups. It was observed that those who had at least two doses (BNT162b2) vaccine died less frequently than those in other groups. Only 41.7% of our patients had at least two doses (BNT162b2) vaccine. 39.4% of the patients were either never vaccinated or had at most one dose of any vaccine. As of November 2022 in Turkey, 85.6% of the population received at least two doses of any vaccine (27). This rate was 76.3% for Sakarya province (27). In tuberculosis patients, a very risky group for COVID-19, these rates were even below the general population. A qualitative study performed in Turkey reported that almost all of the 14 tuberculosis patients were vaccinated, and 71% were vaccinated by the (BNT162b2) vaccine (19).

People being treated for tuberculosis are at risk as long as the danger of COVID-19 continues. When combined, the mortality risk of both tuberculosis and COVID-19 causes catastrophic clinical outcomes. More emphasis should be placed on the importance of vaccination against COVID-19, especially in elderly individuals receiving tuberculosis treatment. We believe that more research will be needed on how often booster vaccines should be given to these disadvantaged groups.

Conflict of interest

The authors declared no conflict of interest.

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Authors' contributions

Concept: E.A.G, S.T.Ç, A.Ö Design: E.A.G, S.T.Ç, İ.O Data Collection or Processing: E.A.G, N.A, F.A.K, Z.D.M, Ş.T Analysis or Interpretation: E.A.G, S.T.Ç, N.A, İ.O, F.A.K Z.D.M, Ş.T Literature Search: E.A.G, S.T.Ç, A.Ö Writing: E.A.G, S.T.Ç, Z.D.M

Ethical Statement

Ethics committee approval for the study was obtained from Sakarya University Faculty of Medicine Non-Invasive Research Ethics Committee with the application file number 154 on June 02, 2022.

References

- Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, Ji R, Wang H, Wang Y, Zhou Y. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. *Int J Infect Dis*. 2020 Mar 12;94(1):91-5.
- Weekly epidemiological update on COVID-19 - 16 November 2022 (Internet) Available from: <https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---16-november-2022>
- World Health Organization. Global tuberculosis report 2020, (Internet) 2020. Available from: <https://www.who.int/publications/i/item/9789240013131>
- Sarinoğlu RC, Sili U, Eryüksel E, Yildizeli SO, Cimsit C, Yagci AK. Tuberculosis and COVID-19: An overlapping situation during pandemic. *The Journal of Infection in Developing Countries*. 2020 Jul 31;14(07):721-5.
- Walaza S, Tempia S, Dawood H, Variava E, Moyes J, Cohen AL, et al. Influenza virus infection is associated with increased risk of death amongst patients hospitalized with confirmed pulmonary tuberculosis in South Africa, 2010–2011. *BMC Infectious Diseases*. 2015 Jan 27;15(1)
- Yousaf Z, Khan AA, Chaudhary HA, Mushtaq K, Parengal J, Aboukamar M, et al. Cavitory pulmonary tuberculosis with COVID-19 coinfection. *IDCases*. 2020;22:e00973
- Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, Liu XQ, Chen RC, Tang CL, Wang T, Ou CQ. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *European Respiratory Journal*. 2020 May 1;55(5).
- Chen Y, Wang Y, Fleming J, Yu Y, Gu Y, Liu C, Fan L, Wang X, Cheng M, Bi L, Liu Y. Active or latent tuberculosis increases susceptibility to COVID-19 and disease severity. *MedRxiv*. 2020 Jan 1
- Gao Y, Liu M, Chen Y, Shi S, Geng J, Tian J. Association between tuberculosis and COVID-19 severity and mortality: A rapid systematic review and meta-analysis. *Journal of medical virology*. 2021 Jan 1
- Jeon CY, Murray MB. Correction: diabetes mellitus increases the risk of active tuberculosis: a systematic review of 13 observational studies. *PLoS medicine*. 2008 Aug;5(8):e181.
- Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The lancet*. 2020 Mar 28;395(10229):1054-62.
- Visca D, Ong CW, Tiberi S, Centis R, D'ambrosio L, Chen B, Mueller J, Mueller P, Duarte R, Dalcolmo M, Sotgiu G. Tuberculosis and COVID-19 interaction: a review of biological, clinical and public health effects. *Pulmonology*. 2021 Mar 1;27(2):151-65.
- Tadolini M, Codecasa LR, García-García JM, Blanc FX, Borisov S, Alffenaar JW, Andréjak C, Bachez P, Bart PA, Belilovski E, Cardoso-Landivar J. Active tuberculosis, sequelae and COVID-19 co-infection: first cohort of 49 cases. *European Respiratory Journal*. 2020 Jul 1;56(1).
- Motta I, Centis R, D'Ambrosio L, García-García JM, Goletti D, Gualano G, Lipani F, Palmieri F, Sánchez-Montalvá A, Pontali E, Sotgiu G. Tuberculosis, COVID-19 and migrants: preliminary analysis of deaths occurring in 69 patients from two cohorts. *Pulmonology*. 2020 Jul 1;26(4):233-40.
- Roghani A. The influence of Covid-19 vaccine on daily cases, hospitalization, and death rate in Tennessee: a case study in the United States. *medRxiv*. 2021 Jan 1.
- Xu S, Huang R, Sy LS, Glenn SC, Ryan DS, Morrisette K, Shay DK, Vazquez-Benitez G, Glanz JM, Klein NP, McClure D. COVID-19 vaccination and Non-COVID-19 mortality risk—seven integrated health care organizations, United States, December 14, 2020–July 31, 2021. *Morbidity and Mortality Weekly Report*. 2021 Oct 10;70(43):1520.
- TC Sağlık Bakanlığı, Tüberküloz Tanı ve Tedavi Rehberi (Internet) 2022 [updated 2022 Nov 30; cited 2022 Nov 30]. Available from: https://hsgm.saglik.gov.tr/depo/birimler/tuberkuloz_db/haberler/Tuberkuloz_Tani_Ve_Tedavi_Rehberi_/Tuberkuloz_Tani_ve_Tedavi_Rehberi.pdf
- T.C Sağlık Bakanlığı COVID-19 Bilgilendirme Platformu Temaslı Takibi, Salgın Yönetimi, Evde Hasta İzlemi ve Filyasyon (Internet) 2022 [updated 2022 Nov 30; cited 2022 Nov 30]. Available from: <https://covid19.saglik.gov.tr/Eklenti/42333/0/covid-19gunceldonemdecovid19iliskiliizolasyonvekarantinauygulamalari-2pdf.pdf>
- Öztürk FÖ, Öztomurcuk D, Turan N, Oruç MA. COVID-19 Pandemi Sürecinde Tüberküloz Tanısı Alan Hastaların Deneyimleri: Nitel Araştırma. *Sürekli Tıp Eğitimi Dergisi*.;31(3):193-200.
- Otlu B, Yakupoğulları Y, Tanrıverdi ES, Bentli R. Tüberküloz hastalarında gelişen COVID-19'un klinik özellikleri. *Mikrobiyol Bul* 2022;56(4):722-728.
- Karaca B. Erişkin yaş grubunda Covid-19 klinik bulguları. *Journal of Biotechnology and Strategic Health Research*. 2020;4:85-90.
- Teker AG, Emecen AN, Girgin S, Şimşek-Keskin H, Şiyve N, Sezgin E, Başoğlu E, Yıldırım-Karalar K, Appak Ö, Zeka AN,

- Ömeroğlu G. Türkiye'de Bir Üniversite Hastanesinde COVID-19 Olgularının Epidemiyolojik Özellikleri. *Klimik Journal/Klimik Dergisi*. 2021 Apr 1;34(1).
23. Gül Ş, Akalın Karaca ES, Özgün Niksarlıoğlu EY, Çınarka H, Uysal MA. Coexistence of tuberculosis and COVID-19 pneumonia: A presentation of 16 patients from Turkey with their clinical features. *Tuberk Toraks* 2022;70(1):8-14.
24. T.C Sağlık Bakanlığı Genel Koronavirüs Tablosu 2022 (Internet) Available from: <https://covid19.saglik.gov.tr/TR-66935/genel-koronavirus-tablosu.html>
25. Nabity SA, Han E, Lowenthal P, Henry H, Okoye N, Chakrabarty M, Chitnis AS, Kadakia A, Villarino E, Low J, Higashi J. Sociodemographic characteristics, comorbidities, and mortality among persons diagnosed with tuberculosis and covid-19 in close succession in California, 2020. *JAMA network open*. 2021 Dec 1;4(12):e2136853-.
26. Song WM, Zhao JY, Zhang QY, Liu SQ, Zhu XH, An QQ, Xu TT, Li SJ, Liu JY, Tao NN, Liu Y. COVID-19 and tuberculosis coinfection: an overview of case reports/case series and meta-analysis. *Frontiers in medicine*. 2021 Aug 24;8:657006.
27. T.C Sağlık Bakanlığı COVID-19 Aşısı Bilgilendirme Platformu (Internet) 2022 [updated 2022 Nov 30; cited 2022 Nov 30]. Available from: <https://covid19asi.saglik.gov.tr/>