

Are the frequency and severity of COVID-19 infection higher in cancer patients than in the general population?

Önder Bağcı¹, Levent Korkmaz², Mehmet Zahid Kocak^{1*}

¹Department of Medical Oncology, Konya City Hospital, Konya, Türkiye

²Department of Computer Engineering, İstinye University Engineering Faculty, İstanbul, Türkiye

ABSTRACT

Aim: To investigate whether cancer increases the frequency and severity of coronavirus disease (COVID-19).

Methods: A total of 641 cases were included in this study, comprising 425 cancer cases and 216 non-cancer cases. The non-cancer subjects were spouses and first-degree relatives of cancer patients, all residing in the same household as the cancer subjects included in the study.

Results: In both the patient and the control groups, the history of COVID-19 infection and disease severity were evaluated. There was no statistically significant difference in the frequency of COVID-19 infection between cancer and control groups (30.3% vs. 24.6%, $p = 0.133$). Additionally, there was no statistically significant difference between metastatic and non-metastatic cancer cases regarding the frequency of COVID-19 infection (36% vs. 29%, $p = 0.236$). The frequency of COVID-19 infection was also comparable between vaccinated cancer patients and vaccinated control subjects ($p = 0.108$). No statistically significant difference was observed between the cancer patients and control groups in terms of disease severity among patients with COVID-19 ($p = 0.406$). Regression analysis showed that age ≥ 65 years and vaccination were significantly associated with a lower risk of COVID-19 infection. Cancer group and gender were not found to have an independent association with COVID-19 infection.

Conclusion: This study found no difference in the frequency or severity of COVID-19 infection between the cancer and control group. Additionally, older age and vaccination were protective factors against COVID-19, while cancer status did not appear to affect the risk of infection.

Keywords: Cancer, COVID-19, frequency, severity, real-life data.

✉ Dr. Mehmet Zahid Kocak*

Department of Medical Oncology, Konya City Hospital,
Konya, Türkiye

E-mail: mehmetzahidkocak@hotmail.com

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1. Introduction

The novel coronavirus (COVID-19) was first identified in December 2019 in Wuhan, China, as an infectious disease that resulted in severe acute respiratory syndrome. In a

relatively short period, the virus caused a global pandemic that threatened lives worldwide [1]. As of June 7, 2023, the total number of confirmed cases reached 767,750,083, with 6,941,095 reported deaths and 13,396,086,098 vaccinations [2].

The COVID-19 pandemic created an exceptional burden on healthcare systems and greatly impacted the delivery of medical services. During the acute phase of the pandemic, many nonurgent oncologic services were delayed, and the number of patients

accessing hospitals for emergency reasons decreased [3].

The total number of deaths attributed to cancer as the underlying cause showed a slight decrease, which may reflect COVID-19 as a competing disease for the underlying cause [4, 5]. Some studies reported a higher frequency and mortality rate of COVID-19 among cancer patients [6,7]. Malignancies and chemotherapeutics may be associated with suppression of the immune response, increasing the severity of COVID-19 and decreasing the response to SARS-CoV-2 vaccines [8, 9].

As the disease continued to spread, clinical deterioration and deaths resulting from the infection were attributed to an excessive immune system response [10]. Some studies conducted during this period reported a lower prevalence of COVID-19 infection in individuals with cancer [11, 12]. One study indicated that the frequency and mortality rates related to COVID-19 in cancer patients were comparable to those observed in control groups [13].

The aim of this study was to compare the frequency and severity of COVID-19 infection between cancer patients and healthy control groups, as well as to evaluate the frequency of COVID-19 infection in vaccinated and unvaccinated cancer patients.

2. Materials and methods

A retrospective study was conducted between September 2021 and January 2022 in the Medical Oncology Department, involving 641 participants—425 cancer patients and 216 healthy controls. The patient group included individuals receiving active treatment (adjuvant hormonal therapy, adjuvant chemotherapy, or palliative chemotherapy due to metastatic disease, etc.) and surveillance patients. The control group consisted of healthy volunteers

with no history of malignant disease, all of whom shared a household with the cancer patients. This study received ethical approval from the local ethics committee (approval number: 2023/386) and was conducted in accordance with the Declaration of Helsinki and all applicable regulations.

In both the patient and control groups, the history of COVID-19 infection and the severity of the disease were assessed. The severity of the disease was classified into three groups: mild, moderate, and severe disease. Mild disease included patients who were not hospitalized and recovered at home (COV19-Mild); moderate disease included patients who were hospitalized due to the need for oxygen inhalation but did not require intensive care unit follow-up (COV19-Moderate); severe disease included patients who required intensive care unit follow-up (COV19-Severe).

The frequency of COVID-19 was evaluated in both groups. Additionally, age, gender, vaccination status (yes, no), vaccine type (Sinovac [Chinese], BioNTech [Germany] + Turkovac [Turkey]), COVID-19 disease (yes, no), and COVID-19 severity (mild, moderate, severe) were compared between the patient and control groups.

COVID-19 vaccine products administered to the cases were also grouped for cancer and control groups. The vaccine products were categorized into five groups: Sinovac only, BioNTech only, Sinovac + BioNTech, BioNTech + Turkovac, and Sinovac + Turkovac. The frequency of COVID-19 infection was evaluated in vaccinated and unvaccinated cases.

2.1. Statistical Methods

Statistical analysis was performed using W-analyzer version 1.4.53, a data analytics platform that incorporates tools such as the SciPy v1.2.3 Python library for statistical

testing. Comparisons of continuous variables between groups were conducted using the independent samples t-test. Categorical variables were analyzed using the Chi-square test. P values < 0.05 were considered statistically significant.

3. Results

A total of 425 cancer patients were included in the study, with 216 participants assigned to the control group. The distribution of cancer types in the cancer group was as follows: breast cancer (55.9%, $n = 236$), colorectal cancer (11.1%, $n = 47$), lung cancer (10.7%, $n = 45$), gastric cancer (5.7%, $n = 24$), ovarian cancer (3.0%, $n = 13$), prostate cancer (1.9%, $n = 8$), pancreatic cancer (1.7%, $n = 7$), and other cancers (10.0%, $n = 42$).

Among the cancer patients, 128 (30.3%) had COVID-19 infection, compared to 53 (24.6%) in the control group. The frequency of COVID-19 infection was not significantly different between the cancer and control groups ($p = 0.133$, Figure 1). In the control group, 198 (92.5%) were vaccinated, while 16 (7.5%) were not. In the cancer group, 354 (84%) patients were vaccinated, and 68 (16%) were not. The vaccination rate was significantly higher in the control group compared to the cancer group ($p = 0.002$). Among patients vaccinated at least once, 45 (22.7%) in the control group had COVID-19, while 153 (77.3%) did not. In the cancer group, 102 vaccinated patients (29%) had COVID-19, while 249 cancer patients (71%) did not have COVID-19. The frequency of COVID-19 infection was not significantly different between the vaccinated cancer and control groups ($p = 0.108$). In the cancer group, 346 patients (81.4%) had non-metastatic cancer, and 79 (18.6%) had metastatic cancer. Among metastatic cancer patients, 28 (36%) had COVID-19, and 51 (64%) did not. Among

non-metastatic cancer patients, 100 (29%) had COVID-19, and 246 (71%) did not. There was no statistically significant difference in the frequency of COVID-19 infection between metastatic and non-metastatic cancer patients ($p = 0.236$).

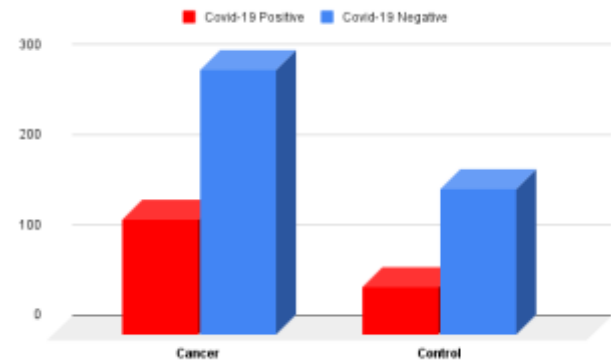


Figure 1. Frequency of Covid-19 in cancer patients and healthy volunteers.

Most patients in this study cohort were vaccinated with the Sinovac vaccine. The distribution of vaccine types was as follows: only Sinovac ($n = 235$, 42.6%), only BioNTech ($n = 184$, 33.3%), Sinovac + BioNTech ($n = 131$, 23.7%), BioNTech + Turkovac ($n = 1$, 0.2%), and Sinovac + Turkovac ($n = 1$, 0.2%). Multiple subgroup analyses by vaccine type revealed no statistically significant difference in the frequency of COVID-19 infection between the cancer and control groups (Table 1).

Data on COVID-19 severity were available for 171 cases. Most cases were classified as COV19-mild. The distribution of COVID-19 severity was as follows: COV19-mild ($n = 137$, 80.1%), COV19-moderate ($n = 28$, 16.4%), and COV19-severe ($n = 6$, 3.5%). Subgroup analyses of severity groups showed no statistically significant differences in COVID-19 severity between the cancer and control groups (Table 1).

A binary logistic regression analysis was performed to identify factors associated with

Table 1. Study characteristics and comparative results between groups.

Parameters	Cancer (N:425) n (%)	Control (N:216) n (%)	All Cases (N:641) n (%)	P
Age (mean)	57.2	57.6	57.3	
Gender				
Male	102 (24)	161 (74.5)	263 (41.0)	<0.001
Female	323 (76)	55 (25.5)	378 (59.0)	
Vaccination *				
Yes	354 (84.0)	198 (92.5)	552 (86.8)	0.002
No	68 (16.0)	16 (7.5)	84 (13.2)	
Vaccination Type *				
Sin	173 (48.9)	62 (31.3)	235 (42.6)	<0.001
Bio	98 (27.7)	86 (43.4)	184 (33.3)	
Bio-Sin	82 (23.2)	49 (24.8)	131 (23.7)	
Bio-Tur	0 (0.0)	1 (0.5)	1 (0.2)	
Sin-Tur	1 (0.2)	0 (0.0)	1 (0.2)	
Covid-19 All *				
Yes	128 (30.3)	53 (24.6)	181 (28.4)	0.133
No	294 (69.7)	162 (75.4)	557 (86.7)	
Covid-19 Vacc *				
Yes	102 (29.0)	45 (22.7)	147 (26.8)	0.108
No	249 (71.0)	153 (77.3)	402 (73.2)	
Covid-19 Vacc-S *				
Yes	66 (26.0)	21 (19.0)	87 (23.8)	0.145
No	188 (74.0)	90 (81.0)	278 (76.2)	
Covid-19 Vacc-B *				
Yes	55 (30.7)	34 (25.0)	89 (28.2)	0.264
No	124 (69.3)	102 (75.0)	226 (71.8)	
Covid-19 Un-Vacc *				
Yes	23 (33.8)	7 (43.8)	30 (35.7)	0.456
No	45 (66.2)	9 (56.2)	54 (64.3)	
Covid-19 Severity				
COV19-Mild	102 (81.0)	35 (77.8)	137 (80.1)	0.406
COV19-Moderate	21 (16.7)	7 (15.6)	28 (16.4)	
COV19-Severe	3 (2.3)	3 (6.7)	6 (3.5)	

* Covid-19 ALL, Covid-19 infection in all cases. Covid-19 Vacc, Covid-19 infection in vaccinated cases. Covid-19 Vacc-S, Covid-19 infection in at least one Sinovac vaccinated cases. Covid-19 Vacc-B, Covid-19 infection in at least one BioNTech vaccinated cases. Covid-19 Un-Vacc, Covid-19 infection in unvaccinated cases.

Table 2. Binary logistic regression analysis of factors associated with COVID-19 infection.

Variable	Odds Ratio	95% Confidence interval	p
Age ≥ 65 years	0.50	0.31-0.80	0.004
Gender (male)	1.55	0.94-2.54	0.08
Cancer patient group	0.94	0.82-1.57	0.07
Vaccination (yes)	0.31	0.17-0.55	<0.001

COVID-19 infection. Age (≥ 65 years), sex, group (cancer patients vs. controls), and vaccination status were included as independent variables, while COVID-19 infection status was the dependent variable. The analysis demonstrated that being aged ≥ 65 years was associated with significantly lower odds of COVID-19 infection (OR = 0.50, 95% CI: 0.31–0.81, $p = 0.004$). In addition, vaccination was found to significantly decrease the odds of infection (OR = 0.32, 95% CI: 0.18–0.56, $p < 0.001$). Being in the cancer patient group and gender were not significantly associated with infection risk ($p = 0.07$, $p = 0.083$, respectively) (Table 2).

4. Discussion

This study demonstrated that there was no significant difference in the frequency or severity of COVID-19 infection between cancer patients and controls, nor was there a significant difference in the severity of infection between cancer patients and the control group. Furthermore, there was no significant difference in the frequency of infection between subjects with metastatic and non-metastatic cancer.

Studies conducted in the early stages of the epidemic reported that COVID-19 infection was more common and more fatal in cancer patients than in non-cancer cases [6, 12]. In this study, there was a large numerical difference between cancer ($n = 18$) and non-cancer ($n = 1572$) patient groups [6]. His study included 425 cancer patients, of whom 128 had COVID-19, with no difference in frequency or severity of COVID-19 infection between cancer patients and controls. Rasheed et al. reported a study of 7,877 cancer patients, 170 (2%) of whom had COVID-19 [14]. This study lacked a control group. In analyzing their study, they compared the rate of COVID-positive cancer patients with

national COVID-positive case rate data (0.1%), which diminishes the study's value in terms of fair evaluation. Several meta-analyses on the severity and frequency of COVID-19, which included cancer patients, reported that COVID-19-infected cancer patients had a higher mortality rate than infected non-cancer patients [7, 15]. COVID-19 patients with hematologic cancers have a more aggressive process and have higher mortality compared to COVID-19 patients with solid cancers [16]. Hematologic cancer, lung cancer, or with metastatic cancer (stage IV) patients had the highest frequency of severe COVID-19 [17]. In one study, the most common cancer types infected with COVID-19 are as follows: lung: 37.8%, breast: 13.3%, colorectal: 13.3% and prostate: 11.1% [18]. Patients hospitalized with a diagnosis of COVID-19 had a history of breast, colorectal, prostate, bladder, melanoma, uterine, and kidney cancer, respectively, according to their frequency [19].

The limitations of these meta-analyses are similar, with large numerical differences between infected cancer and non-cancer patient groups. Ethnic, socioeconomic differences, and variations in treatment conditions between countries may reduce the value of these meta-analyses for accurate assessment.

However, one study found that the prevalence of COVID-19 infection was lower in cancer patients than in the non-cancer population [11]. Another study indicated that the incidence and mortality rates of COVID-19 were no different in cancer and non-cancer patients [13]. These results support the findings of the present study. Different results have been reported about the frequency of COVID-19 in patients with cancer [6, 12]. Other studies conducted in the early stages of the pandemic had a very small number of cancer patients infected with COVID-19. The infection rates in

the present study are higher. Compared to other studies, two features of our study make it unique. First, this study was conducted at the end of the pandemic process, when vaccination was nearly complete. Second, the control group consisted of spouses and first-degree relatives of cancer patients who shared the same home, which is a significant factor. Cancer and non-cancer cases had the same socioeconomic status and living conditions in our study. They were exposed to COVID-19 strains with similar virulence and had the same treatment conditions.

Our findings suggest that older age (≥ 65 years) and vaccination are protective factors against COVID-19 infection. This may indicate that older adults may be more likely to adhere to preventive measures and vaccination campaigns. Vaccination has been confirmed to significantly reduce the likelihood of infection. Although cancer patients are generally assumed to be more susceptible to COVID-19 due to their immunosuppressed status, our regression analysis did not demonstrate an increased risk of infection in this group. After adjusting for gender and vaccination status, being in the cancer group was not identified as an independent predictor of COVID-19 infection. This finding suggests that the observed infection rates among cancer patients may be largely explained by other factors, such as age distribution, vaccination coverage, or preventive behaviors, rather than cancer status itself.

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