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Research Article

COVID-19 Pandemic is More Dangerous Than We Think

Elvina Almuradova,[1] Denis Cetin,[2] Mustafa Murat Midik,[2] Erdem Goker,[1] Ulus Ali Sanli,[1] Burcak Karaca[1]

[1]Department of Medical Oncology, Ege University Faculty of Medicine, Izmir, Turkey
[2]Department of Internal Medicine, Ege University Faculty of Medicine, Izmir, Turkey

Abstract

Objectives: The Coronavirus disease-19 (COVID-19) pandemic continues to pose a threat to humanity without pausing. The difficulties in the diagnosis and treatment of cancer patients arising from the outbreak are worrisome.

Methods: The data of 1060 adult patients who applied to the Department of Medical Oncology with the new diagnosis of solid cancer between February 2019 and March 2021 were analyzed retrospectively. Applications between February 2019 - 2020 were defined as pre-pandemic, and those between March 2020 - 2021 were defined as post-pandemic group. Groups were compared according to demographic characteristics, cancer types, stages, time to treatment initiation, and reasons for the delay in medical treatment.

Results: There were 711 (54% female, 46% male) applications in the pre-pandemic period and 349 (48.4% female, 51.6% male) in the post-pandemic period ($p<0.001$) with no difference according to age and gender distribution. In the post-pandemic period, decreases to hospital admission were observed in all cancer types except lung and central nervous system cancers. The frequency of stage 4 disease at diagnosis increased significantly compared to the pre-pandemic period ($p=0.039$). Postpones in surgical procedures due to the pandemic conditions was the most common cause of medical treatment delay, while pandemi-phobia was the second leading cause.

Conclusion: This study revealed that the COVID-19 pandemic has severely limited the newly diagnosed cancer applications. At the same time, the increase in the frequency of stage 4 disease at the time of diagnosis with the pandemic may be a harbinger of increased mortality.

Keywords: Cancer, COVID-19, pandemic

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On December 31, 2019, the World Health Organization (WHO) China office reported cases of pneumonia of unknown etiology in the city of Wuhan, and on January 7, 2020, the cause was revealed to be a new coronavirus that has not been detected in humans before.[1,2] Later, the disease was identified as Coronavirus disease-19 (COVID-19) and the virus was named severe acute respiratory syndrome coronavirus 2.[3] The WHO classified the COVID-19 outbreak as an "international public health emergency" on 30 January and was finally declared a pandemic on 11 March 2020. The first COVID-19 case in Turkey was seen on March 11, 2020, and until July 2021, a total of 5,440,368 people were infected, and the daily number of cases is still over 5000.[4] Due to the lack of a specific treatment against the virus, governments saw the solution in quarantine. In addition to the closure of all social places, the outpatient services of hospitals were restricted in service to reduce both the risk of transmission and the risk of overloading the health system.[5] Many units of hospitals were organized to care for patients with COVID-19. In Turkey, the

Address for correspondence: Elvina Almuradova, MD. Ege Universitesi Tip Fakultesi, Tıbbi Onkoloji Anabilim Dali, Izmir, Turkey
Phone: +90 553 431 98 03 **E-mail:** elvinaalmuradova@yahoo.com.tr

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Ministry of Health started to take precautions from March 2020. Some of these measures were the postponement of non-emergency hospital admissions and elective surgeries, increasing intensive care capacities, the restriction of social life, and intercity travel with a national quarantine. [4] In addition, studies reported from various countries showed that the incidence of cancer during quarantine decreased compared to previous years.[6,7] It is known that cancer incidence is increasing gradually, and the decline in the pandemic period can only be explained by challenges in the detection of new cases. Studies conducted in European clinics revealed that the incidence of prostate, bladder, and colorectal cancers decreased significantly.[7-9] Early diagnosis and curative treatment of these cancers are usually possible with screening programs. COVID-19 may divest the chance of early diagnosis and cure of these patients. All these may be an indication that cancer-related deaths will increase in the coming years.[10] This might be an another fortcoming result of Covid-19 pandemic.

As one of the most important oncology centers in Turkey, we have never stopped our outpatient and inpatient services during the pandemic. In this study, we investigated the effect of the COVID-19 outbreak on newly diagnosed cancer applications.

Methods

The data of 1060 newly diagnosed cancer patients who applied to the Department of Medical Oncology between February 2019 and March 2021 were analyzed retrospectively. Ethics committee approval was obtained from the Medical Research Ethics Committee and the Ministry of Health for the study. Inclusion criteria were to be over 18 years of age and to have a newly diagnosed solid tumor. Children and hematological cancers were excluded. Applications between February 2019 - 2020 were defined as pre-pandemic, and those between March 2020-2021 were defined as post-pandemic group. Demographic data (age and gender), cancer type, disease stage, time to treatment initiation (TTI, days), and the reasons for delay in medical treatment (over 1 month) were obtained from the hospital electronic database. Ovarian, cervical, vulvar, vaginal, endometrial cancers, malignant sex cord tumors and trophoblastic diseases were grouped as gynecological; gallbladder, bile duct cancers and hepatocellular carcinoma as hepatobiliary; esophageal, gastric and pancreatic cancers as upper gastrointestinal system (GIS) cancer; small intestinal, colorectal and anal cancers were grouped as lower GIS cancer. Other cancers were named after themselves. Each cancer type was staged according to its own TNM classification and stratified into 4 stages to facilitate comparison.

The primary outcome of this study was to reveal the impact of the COVID-19 pandemic on the number of newly diagnosed cancer admissions. Secondary outcomes were to investigate the effects of the pandemic on the cancer subtypes, stages and TTI in newly diagnosed cancers and to determine the reasons for delay in medical treatment.

Statistical Analysis

All data were analyzed with IBM SPSS (Statistical Package for the Social Sciences) v.25.0 software. Descriptive statistics were specified with frequency and percentage for qualitative, and median, minimum and maximum values for quantitative data. Crosstabs and Chi-square tests were used to compare categorical variables. Conformity of continuous variables to normal distribution was examined by Kolmogorov-Smirnov and Shapiro-Wilk tests. Mann-Whitney U test was performed to compare non-parametric data. A level of $p<0.05$ was considered statistically significant.

Results

Of the 1060 patients included in the study, 711 (54% female, 46% male) were pre-pandemic and 349 (48.4% female, 51.6% male) were post-pandemic group ($p<0.001$). Gender distributions were not significantly different between the groups ($p=0.087$). The median age of the patients who applied before the pandemic was 60 years (range, 18 to 92) and those who applied during the pandemic were 61 years (range, 18 to 88) ($p=0.638$), almost the same.

The three most common cancer types were lower GIS, breast, and upper GIS cancers in both groups, respectively. When the cancer types of the groups were compared, decreases were observed in all types except lung and central nervous system (CNS) cancers (Table 1). A 10.3% ($p=0.001$) increase in lung cancer and a 50% ($p=0.09$) increase in CNS cancer was noted in the pandemic. The cancers with the highest decline in admissions during the pandemic were neuroendocrine tumors (NET) (80%), melanoma (66.7%), breast (63.5%), and prostate cancers (62.5%). Among the decreased cancers, only a 63.5% decrease in breast cancer was found to be statistically significant ($p=0.025$).

The fourth stage was the most detected stage at the time of admission, both before and during the outbreak (Table 2). When the stages of the groups were compared, significant increases in stages 1 and 4 and a decrease in stage 3 were found in the pandemic ($p<0.05$).

Although the median TTI was similiar (28 vs 29 days pre/post-pandemic), the most common reasons for the delay in medical treatment were surgical complications (52.9%) and examinations (15.8%) in the pre-epidemic period and surgical complications (43%) and pandemi-phobia (25%) during the post-pandemic period (Table 3).

Table 1. Comparison of pre-pandemic and pandemic cancer types

Cancer type	Pre-pandemic, n (%)	Pandemic, n (%)	Change, %	p
Sarcoma	26 (3.7)	15 (4.3)	-42.3	0.734
Upper GIS	106 (14.9)	52 (14.9)	-50.9	0.997
Lower GIS	171 (24.1)	83 (23.8)	-51.5	0.923
Hepatobiliary	25 (3.5)	15 (4.3)	-40	0.648
Gynecological	49 (6.9)	30 (8.6)	-38.8	0.321
Lung	29 (4.1)	32 (9.2)	10.3	**0.001**
CNS	4 (0.6)	6 (1.7)	50	0.09
Urothelial	36 (5.1)	17 (4.9)	-52.8	1
Head and neck	14 (2)	7 (2)	-50	1
NET	10 (1.4)	2 (0.6)	-80	0.356
Breast	167 (23.5)	61 (17.5)	-63.5	**0.025**
Melanoma	27 (3.8)	9 (2.6)	-66.7	0.396
Prostate	8 (1.1)	3 (0.9)	-62.5	1
Testicular	19 (2.7)	8 (2.3)	-57.9	0.872
Other	20 (2.8)	9 (2.6)	-55	0.985
Total	711 (100)	349 (100)	-50.9	**<0.001**

GIS: Gastrointestinal system; CNS: Central nervous system; NET: Neuroendocrine tumor

Discussion

In this study, we investigated the relationship between the COVID-19 pandemic and the diagnostic or treatment delays in cancer patients. We revealed a 50.9% reduction in newly diagnosed cancer applications with no significant difference in age and gender, during the first year of the COVID-19 outbreak. Although it is known that oncological diseases are scaling up all over the world, data from many countries during the pandemic shows a decline in the number of newly diagnosed cancer patients.[6,9,11,12] In the pandemic, it has been reported that the number of newly diagnosed cancers decreased by 46.4% per week in the United States and by 26-60% per month in Nederland.[12,13] Data from Germany shows that there are significantly fewer new cancer diagnoses, especially in the first three months of the pandemic, compared to the previous period.[8] This cannot represent a true reduction in cancer incidence, and its relevance to the pandemic is obvious. During the pandemic period, non-urgent radiological imaging, endoscopic procedures and even elective operations were postponed in Turkey as it was the situationfor all countries.[14,15] Within the context of the precautions, outpatient clinics were completely closed in the first months of the pandemic and attenuated in the following months. Many physicians were sent to Covid -19 wards or ICU to back up their collegaues. This has changed the routine medical prodecures to be applied in cancer diagnoisi and teratment clinics. For instamce, NET incidence has dropped dramatically during post- pendemic period,it should be emphasized that NET is usually detected incidentally during endoscopic procedures.[16] Another example for this is; dermatological examinations for screening melanoma and routine mammography screenings for breast cancer are required for early

Table 2. Comparison of pre-pandemic and pandemic cancer stages

Stages	Pre-pandemic, n (%)	Pandemic, n (%)	p
1	100 (14.1)	66 (18.9)	**0.041**
2	181 (25.5)	77 (22.1)	0.226
3	181 (25.5)	61(17.5)	**0.004**
4	249 (35)	145 (41.5)	**0.039**
Total	711 (100)	349 (100)	

Table 3. Pre-pandemic and pandemic reasons for delay in medical oncological treatment

Delay reasons	Pre-pandemic, n (%)	Pandemic, n (%)
Pandemy	-	77 (22.1)
Surgical complications	324 (45.6)	130 (37.2)
Nonappointment	97 (13.6)	6 (1.7)
Infection	7 (1)	3 (0.9)
Re-biopsy	21 (3)	3 (0.9)
Examination	137 (19.3)	68 (19.5)
RT related complications	26 (3.7)	11 (3.2)
Unspecified	99 (13.9)	51 (14.6)
Total	711 (100)	349 (100)

RT: Radiation therapy

diagnosis,[17,18] but these procedures were almost stopped for months. Due to the asymptomatic course of prostate cancer in the early period, patients may not be diagnosed until the metastatic stage if screening is not performed.[19] In our study, especially more reduction in numberof these tumors may be related to the inability to perform routine screenings. These findings are also consistent with studies reported from different countries.[20] Studies conducted in the United Kingdom revealed that endoscopic procedures decreased by 88% per week in the first months of the pandemic compared to previous months.[14] In a study conducted with dermatologists in the United States, it was reported that both the number of patients examined and the rate of biopsy from suspicious lesions declined in the pandemic.[21] During the outbreak, there was a 34%-43.9% reduction in surgical procedures, especially for elective cases.[22-24] It was also clarified that mammography and breast ultrasound decreased by 100% in the first months and 60% in the following months of the pandemic in Fortaleza, and up to 37.2% in Taiwan.[25,26] In studies conducted from different centers in our country, it was observed that surgical interventions are performed up to two times less.[27]

The augmentation of lung cancers in our study may be related to the referral of these patients to Medical Oncology Department after the pandemic, while they were treated mainly by the Chest Diseases Unit before the pandemic in our hospital. On the other hand, the increased frequency of thoracic computed tomography due to COVID-19 may raise the incidence of lung cancer detection. Long-term epidemiological studies will show whether COVID-19 causes lung cancer on the fibrosis that the disease is causing. Despite the small number of patients, CNS cancers may not be affected by the pandemic, as they often present with immediate neurological symptoms.[28]

In our study, it was determined that 41.5% of the patients presented in the metastatic stage in pandemic, which was significantly higher than the pre-pandemic period. The relationship between delayed diagnosis and poor prognosis is well known in cancer.[29,30] In a study from the United Kingdom, models were constructed based on three new scenarios reflecting the best, worst and real situation, and analyzed how delays due to COVID-19 would affect survival. Although it varies according to tumor types, it was determined that there would be a significant increase in mortality.[10] On the other side, Austrian clinics notified more aggressive histologies in bladder cancers after the pandemic.[31] It can be estimated how this will upstage the patients who could not apply to our center due to the pandemic.

In our study, TTI in the pandemic was found to be almost the same as in the pre-pandemic period. This may be due to the fact that oncology/hematology clinics continue to provide services in our country both during the strict quarantine period and in the following months.

In our study, when the reasons for delay in admission were examined, it was seen that the second most common reason was the pandemic (25%). This tardiness may also be caused by COVID-19 phobia.[32] In a study conducted in our country, a high level of coronophobia was observed in cancer patients, which is also valid for healthy people.[33] Studies show that people see hospitals as a source of infection, and even emergency room visits are reduced by 50%.[34,35]

The limitations of our study was that it was single-centered and therefore did not reflect the whole country, besides it reflects a short term analysis.

The COVID-19 pandemic, along with mutant strains, still continues to pose a significant threat. Problems in reaching the vaccine continue in many countries and many countries cannot even reach the first dose. It is clear that the decrease in the incidence of cancer with COVID-19 is not real, but it is veiled by Covid-19 and thus most of the patients wait till they have seriosu symptoms of cancer. For years, many studies and organizations were carried out to increase the cure rates of cancer by early diagnosis all over the world. We can say that the pandemic overthrow all of them. We need to encourage our patients to continue standard cancer screening during these difficult times, so that progress in cancer diagnosis, treatment and survival continues to improve in the coming decades.

Disclosures

Ethics Committee Approval: The study was approved by The Ege University Medical Research Ethics Committee (Date: 06/05/2021, No: 21-5T/72).

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Conflict of Interest: None declared.

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