Int J Biochem Mol Biol 2022;13(6):77-86
www.ijbmb.org /ISSN:2152-4114/IJBMB0145875

Original Article

Evaluation of clinical outcomes, laboratory and imaging data of patients with solid tumor infected with COVID-19 infection

Somayeh Sadeghi[1,2], Mohammadsaleh Peikar[3], Erfan Sadeghi[4], Ali Darakhshandeh[3], Safie Ghafel[5], Marzieh Aalinezhad[6], Alireza Sadeghi[3], Mehran Sharifi[3,7], Elahe Nasri[1]

[1]Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Isfahan, Iran; [2]Acquired Immunodeficiency Research Center, Al-Zahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran; [3]Department of Internal Medicine, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran; [4]Research Consultation Center (RCC), Shiraz University of Medical Sciences, Shiraz, Iran; [5]Mycology Reference Laboratory, Research Core Facilities Laboratory, Isfahan University of Medical Sciences, Isfahan, Iran; [6]Department of Radiology, Medical School, Isfahan University of Medical Sciences, Isfahan, Iran; [7]Cancer Prevention Research Center, Seyed Al-Shohada Hospital, Isfahan University of Medical Sciences, Isfahan, Iran

Received August 11, 2022; Accepted November 13, 2022; Epub December 15, 2022; Published December 30, 2022

Abstract: Background: COVID-19 is associated with higher mortality rates in patients with cancer. In this study, we aimed to evaluate the clinical outcomes, and laboratory and imaging data of patients with solid tumor infected with COVID-19 infection. Methods: This is a cross-sectional retrospective study performed in 2020-2022 on 85 patients with a previous diagnosis of solid tumors infected with COVID-19. We included all patients with tumors of solid organs that were diagnosed with COVID-19 infection and required hospitalization those patients previously hospitalized for treatments and were infected with COVID-19 during hospitalization. Demographic data of patients were collected using a checklist. We collected data regarding clinical outcome (discharge, hospitalization or death), duration of hospitalization, requiring ICU admission, duration of hospitalization divided by received drugs and type of tumor and mean survival time. Furthermore, we collected laboratory data from all patients. The radiologic characteristics of patients were also extracted from their data. Results: Breast cancer was the most common solid tumor (34.9%), followed by lung cancer (19.3%). The mortality rate was 24.1% (20 patients). The highest mortality rate in this study was for metastatic intestinal cancer to the lung (100%, one patient), followed by metastatic prostatic cancer to lung (50%, three patients). The highest hospitalization duration was for patients with glioblastoma multiform (GBM) (30 days). The mean survival time among patients with mortality was 19.15±1.80 days. The mean CT severity score of all patients was 27.53±22.90. Patient's most common radiologic sign was air space consolidation (89.1%). The highest CT severity score was found in patients with stomach cancer (46.67±5.77). Conclusion: The mortality rate in this study was 24.1%. Based on the results of our study and previous research, special care should be provided to patients with solid tumors during the COVID-19 pandemic and in infected cases.

Keywords: COVID-19, cancer, solid tumor, survival

Introduction

Coronaviruses are enveloped viruses with single-stranded RNA in the family Coronaviridae. 2019-nCoV acute respiratory disease (COVID-19) is an infectious disease caused by coronavirus acute respiratory syndrome 2 (SARS-CoV-2) [1]. This disease is the reason for the coronavirus pandemic in 2019-2020. Common symptoms are fever, cough, shortness of breath, and lethargy [2]. Muscle pain, sputum production, sore throat, nausea and red eyes are some of the less common symptoms. Although the majority of cases of the disease cause mild symptoms, some patients progress to pneumonia and multiple organ failure [3]. Mortality rates are estimated at between 1% and 5% but vary with age and other health conditions [4]. The disease is spread mainly to other people through cough droplets when they

cough or sneeze. The interval between exposure to the disease and the onset of symptoms is between 2 and 14 days [5].

Risk factors for the disease depend on viral load and the host's immune system status. Conditions with reduced immune responses including steroid use and chemotherapy regimens, could increase the risks of infections [6]. Patients with cancer and undergoing chemotherapy and patients with bone marrow transplants are at the highest risk of coronavirus mortality [7]. Because patients with cancer undergoing chemotherapy are often neutropenic and tests such as ESR, CRP are often distorted, clinical symptoms such as fever are less seen in these patients due to immunosuppressive drugs [8]. On the graph and CT scan in these patients, there could be evidence of diseases indistinguishable from other non-infectious causes such as (pulmonary edema and pulmonary hemorrhage and pulmonary alveolar proteinosis) and infectious causes of viruses (influenza and para-influenza and RSV, CMV and bacteria (tuberculosis)) and fungi (Pneumocystis carinii). Therefore, it is necessary to use clinical and paraclinical tests for the early diagnosis of patients [9, 10].

On the other hand, it is essential to note that these patients are more prone to drug interactions with the regimens recommended for treating coronavirus. For example, due to problems such as anemia, the use of ribavirin in these patients is limited [11]. Therefore, the existence of fast and reliable diagnostic methods is critical to implementing a timely and sufficient standard treatment program in reducing the length of hospital stay and improving the outcome of these patients [12].

Previous studies have evaluated the prognosis and treatment trend of patients with malignancies infected with COVID-19. These studies have reported different mortality and morbidity rates that were generally more than the general population. The present study aims to evaluate the mortality, hospitalization duration and intensive care unit (ICU) admission rate of patients with solid tumors infected with COVID-19 in Isfahan, Iran. Only a few studies have been conducted in our region, so that similar evaluation could have high clinical importance.

Methods and material

Study design

This is a retrospective cross-sectional study performed in 2020-2022 in Omid hospital affiliated to Isfahan University of Medical Sciences. The current study was conducted on patients with previous diagnosis of solid tumors that were infected with COVID-19. The study protocol was approved by the Research Committee of Isfahan University of Medical Sciences and the Ethics committee has confirmed it (Ethics code: IR.MUI.MED.REC.1400.195).

Inclusion and exclusion criteria

The inclusion criteria were age of more than 18 years, previously diagnosed tumors in solid organs (any organ other than hematologic organs), infection with COVID-19 based on polymerase chain reaction (PCR), admission to our medical center and signing the written informed consent to participate in this study. The exclusion criteria were lack of consent and incomplete data.

The sampling method of this study was a census, and we included all eligible patients.

COVID-19 confirmation tests

COVID-19 testing was performed by oropharyngeal and nasopharyngeal real-time polymerase chain reaction (RT-PCR) tests. Samples were collected by hospital staff using swabs of Dacron material with a plastic handle inside the sterile screw tube. The prepared samples were then placed in viral transfer media, collected and sent for RT-PCR molecular analysis.

To extract RNA by the kit, according to the protocol of the consumable kit, RNA purification steps were performed on the samples collected from patients. The cDNA synthesis as a PCR reaction pattern was performed by the cDNA synthesis kit. Some cDNA is then transferred to another microtube for amplification by PCR. In the first stage, the E gene is used as an amplification target in PCR, and if necessary, the target gene (other genes) was used for the genetic similarity of Iranian samples. The sequence of primers and probes used was as follows: E-F: ACAGGTACGTTAATAGTTAATAGCGT; E-R1: ATATTGCAGCAGTACGCACACA; E-P1: hex-ACACTAGCCATCCTTACTGCGCTTCG-Bh.

The RT-PCR method was performed according to the manufacturer's instructions for the detection of COVID-19 nucleic acid. Determining the results were as follows: Positive test result = Ct-value <37; Negative test result = Ct-value ≥40.

Data collection

Demographic data of patients were collected using a checklist. The data included age, gender, and type of tumor. The type of tumor was determined based on patient's clinical and imaging data (CT scan), medical records and after consultation with 2 oncologists.

We ordered the following data from all cases:
- Clinical outcome (discharge, hospitalization, or death).
- Duration of hospitalization.
- Requiring ICU admission.
- Duration of hospitalization is divided by type of received drugs and type of tumor, and mean survival time.

The types of medications were also extracted from patient's files. These data were classified into these categories:
- Antiviral
- Antibiotic
- Corticosteroid
- Anticoagulant
- Antifungal
- Anti-PCP
- Non-invasive oxygen therapy
- Invasive oxygen therapy

The duration of hospitalization was calculated for patients based on their medications.

Furthermore, we collected laboratory data from all patients and evaluated them based on their tumor types. The laboratory tests were as follows: D-dimer, arterial blood gas analysis (PH, PCo2 and HCO3), number of white blood cells (WBC), polymorphonuclear (PMN), lymphocytes, hemoglobin (Hb), platelets (PLT), blood urea nitrogen (BUN), creatinine (Cr), Sodium (Na), potassium (K), calcium (Ca), albumin (Alb), magnesium (Mg), erythrocyte sedimentation rate (ESR), lactate dehydrogenase (LDH), ferritin, fibrinogen, Fibrin Degradation Product (FDP), aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), creatine kinase (CPK), direct bilirubin (Bill-D), partial thromboplastin time (PTT), prothrombin time (PT) and INR.

The chest CT scan of all cases were reviewed. Frequencies of different CT scan findings were evaluated based on tumor types. These CT scan findings were CT severity score, presence of a halo sign, ground glass opacity (GGO), air space consolidation, crazy paving sign, and pleural effusion (PE). To calculate the CT severity score according to the anatomical structure of the lung, 18 segments of both lungs were divided into 20 separate areas so that the apicoposterior segment of the left upper lung was divided into the apical and posterior regions and the antromediobasal segment of the left lung was also divided into the anterior and basal regions. The radiologists examined the presence and spread of opacity in all 20 areas and scored each area as 0, 1, and 2 for 0%, below 50%, and above 50%, respectively. The final score was obtained from the sum of points in each of the 20 areas and was considered as CT severity score, which had a range of 0-40.

Statistical analysis

The obtained data were entered into the Statistical Package for Social Sciences (SPSS) (version 24, SPSS Inc., Chicago, IL). Quantitative data were reported as mean ± standard deviation and qualitative data as frequency distribution (percentage).

Results

Study population

A total number of 85 patients were assessed for eligibility. During the study, two patients were excluded due to incomplete data. In the end, data from 83 patients were analyzed. The study population consisted of 43 males (51.8%) and 40 females (48.2%) with a mean age of 57.92±14.69 years. By evaluating the age distribution, it was shown that three patients (3.6%) had 18-30 years of age, seven patients (8.4%) had 30-40 years, 18 patients (21.7%) had 40-50 years, 42 patients (50.7%) had 50-60 years, eight patients (9.6%) had 60-70 years and five patients (6%) had >70 years.

Cancer data

Preliminary analysis of patients' data indicated that breast cancer was the most common solid tumor (34.9%), followed by lung cancer (19.3%) and metastatic colorectal cancer to lung and metastatic prostatic cancer to lung (7.2% each).

Table 1. Clinical outcomes of patients based on the tumor types

	Death N (%)	Discharge N (%)	Hospitalization duration Median (CI)	ICU N (%)
Brain N = 1 (1.2%)	0 (0)	1 (100)	10 (10-10)	0 (0)
GBM N = 1 (1.2%)	0 (0)	1 (100)	30 (30-30)	1 (100)
Breast N = 29 (34.9%)	7 (24.1)	22 (75.9)	7 (4-8)	8 (27.6)
Pancreas N = 5 (6%)	1 (20)	4 (80)	5 (4-7)	1 (20)
Prostate N = 6 (7.2%)	3 (50)	3 (50)	6.5 (6-11)	3 (50)
Skin N = 1 (1.2%)	0 (0)	1 (100)	18 (18-18)	0 (0)
Pelvic mass N = 1 (1.2%)	0 (0)	1 (100)	7 (7-7)	0 (0)
Larynx N = 3 (3.6%)	1 (33.3)	2 (66.7)	7 (2-9)	2 (66.7)
Intestine N = 1 (1.2%)	1 (100)	0 (0)	6 (6-6)	1 (100)
Lung N = 16 (19.3%)	5 (31.3)	11 (68.8)	6.5 (5-16.5)	5 (31.3)
Sarcoma N = 2 (2.4%)	0 (0)	2 (100)	11.5 (8-15)	0 (0)
Osteosarcoma N = 1 (1.2%)	0 (0)	1 (100)	6 (6-6)	0 (0)
Liver N = 3 (3.6%)	0 (0)	3 (100)	6 (5-11)	0 (0)
Colon N = 6 (7.2%)	2 (33.3)	4 (66.7)	6 (4-13)	2 (33.3)
Esophagus N = 1 (1.2%)	0 (0)	1 (100)	3 (3-3)	0 (0)
Stomach N = 4 (4.8%)	0 (0)	4 (100)	5 (4-5.50)	0 (0)
Melanoma N = 2 (2.4%)	0 (0)	2 (100)	7 (6-8)	0 (0)
Total N = 83 (100%)	20 (24.1)	63 (75.9)	7 (5-10)	23 (27.7)

ICU: intensive care unit, GBM: Glioblastoma.

Analysis of patient outcomes showed that the mortality rate was 24.1% (20 patients), and 63 patients (75.9%) were discharged. The highest mortality rate in this study was for metastatic intestinal cancer to the lung (100%, one patient), followed by metastatic prostatic cancer to the lung (50%, three patients), metastatic colorectal cancer to the lung (33.3%, two patients), larynx cancer (33.3%, 1 patient) and breast cancer (24.1%, seven patients). The highest hospitalization duration was for patients with glioblastoma multiform (GBM) (30 days) and metastatic malignant melanoma to lung (18 days). The highest rate of ICU admission was for patients with metastatic intestinal cancer to the lung (100%), GBM (100%), larynx cancer (66.7%), and metastatic prostatic cancer to the lung (50%). These data are summarized in **Table 1**.

We also assessed patients' hospitalization duration based on the type of received medications. As the data in **Table 2** shows, the patient with GBM had the highest period of hospitalization (30 days) and received antiviral, antibiotic, corticosteroid, anticoagulant, and invasive oxygen therapy. Similar data were observed for the patient with metastatic malignant melanoma to the lung, except that this case received non-invasive oxygen therapy.

Cumulative survival time

As shown in **Figure 1**, the cumulative survival time decreased significantly as hospitalization duration increased. The mean survival time among patients with mortality was 19.15±1.80 days.

Laboratory data

We also assessed the different laboratory data of patients based on the tumor type. These data showed that the highest D-dimer was observed in patients with metastatic colorectal cancer to the lung (713.80±1025.64), the lowest hemoglobin was observed in patients with colon cancer (7.68±2.3), and the highest creatinine was observed in patients with brain tumors (3.5). These data are shown in **Table 3**.

Imaging evaluations of patients

The imaging evaluations of patients are shown in **Table 4**. Based on these data, the mean CT severity score of all patients was 27.53±22.90. Patients' most common radiologic sign was air space consolidation (89.1%), followed by GGO (80.7%). The highest CT severity score was found in patients with stomach cancer (46.67±5.77).

Table 2. Hospitalization duration among patients received specific medications

	Antiviral	Antibiotic	Corticosteroid	Anticoagulant	Antifungal	Anti-PCP	Noninvasive oxygen therapy	Invasive oxygen therapy
Brain	10 (10-10)	10 (10-10)	10 (10-10)	10 (10-10)	-	-	10 (10-10)	-
GBM	30 (30-30)	30 (30-30)	30 (30-30)	30 (30-30)	-	-	-	30 (30-30)
breast	7 (5-8)	7 (5.5-9)	7 (5-9)	7 (5-9)	4 (4-4)	-	7 (5-9)	7 (5-13.5)
pancreas	6 (4.5-13.5)	5 (4-7)	5 (4-7)	5 (4-7)	-	-	6 (5-7)	2 (2-2)
prostate	7 (6-11)	6.5 (6-11)	6.5 (6-11)	6 (6-7)	-	-	6 (6-7)	11 (4-15)
skin	18 (18-18)	18 (18-18)	18 (18-18)	18 (18-18)	-	-	18 (18-18)	-
pelvic mass	7 (7-7)	7 (7-7)	7 (7-7)	7 (7-7)	-	-	7 (7-7)	-
larynx	7 (2-9)	7 (2-9)	7 (2-9)	7 (2-9)	-	-	8 (7-9)	2 (2-2)
intestine	6 (6-6)	6 (6-6)	6 (6-6)	-	-	-	-	6 (6-6)
lung	7 (5-19)	6.5 (5-16.5)	6.5 (5-16.5)	6.5 (5-16.5)	9 (4-14)	17 (14-20)	7 (5-19)	5 (4-14)
sarcoma	11.5 (8-15)	11.5 (8-15)	11.5 (8-15)	11.5 (8-15)	-	-	11.5 (8-15)	-
osteosarcoma	6 (6-6)	6 (6-6)	6 (6-6)	6 (6-6)	-	-	-	-
liver	6 (5-11)	6 (5-11)	6 (5-11)	6 (5-11)	-	-	-	-
colon	6 (4-13)	6 (4-13)	6 (4-13)	6 (4-13)	-	-	4.5 (4-6)	19 (13-25)
esophagus	3 (3-3)	3 (3-3)	3 (3-3)	3 (3-3)	-	-	3 (3-3)	-
stomach	5 (4-5.5)	5 (4-5.5)	5 (4-5.5)	5 (4-5.5)	-	-	5 (4-5.5)	-
melanoma	8 (8-8)	7 (6-8)	7 (6-8)	7 (6-8)	-	-	8 (8-8)	-
Total	7 (5-10)	7 (5-10)	7 (5-10)	7 (5-10)	4 (4-14)	17 (14-20)	7 (5-8.5)	7 (4-15)

Values are presented as Median (Q1-Q3).

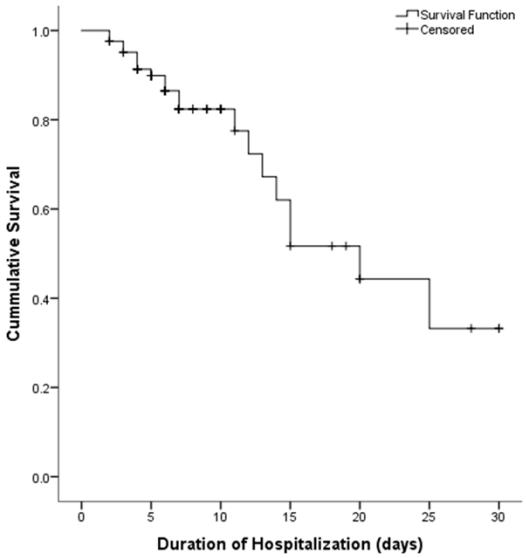

Figure 1. Relationship between survival time and hospitalization duration.

Discussion

In this study, data from 85 patients with solid tumors that were infected with COVID-19 were analyzed. Our data showed that breast cancer was the most common solid tumor, followed by lung cancer and metastatic colorectal cancer to lung and metastatic prostatic cancer to the lung. The mortality rate in this study was 24.1%. We also showed that patients with GBM had highest the hospitalization duration and ICU admission rates.

Evaluation of radiologic findings showed that the mean CT severity score of all patients was 27.53±22.90. Patients' most common radiologic sign was air space consolidation, followed by GGO. The highest CT severity score was found in patients with stomach cancer. Previous reports have shown the association of COVID-19 in patients with solid tumors. In 2021, Fuentes-Antrás and others assessed the outcomes of 73 patients with solid tumors with COVID-19. They demonstrated that the most frequent malignancy was lung cancer (19%). The mortality rate of this study was 24.7%, with higher rates in patients with longer hospitalization duration. It was explained that 73% of patients presented an abnormal pattern, the most frequent being infiltrates 64% [13]. In another study by Özdemir and colleagues in 2021, clinical features and outcomes of COVID-19 in 1523 patients with solid tumors were analyzed. They showed that the most common types of cancers were breast (19.8%), metastatic prostatic cancer to the lung (10.9%), and metastatic colorectal cancer to lung (10.8%). The mortality rate of this study was 11.4% and highest among patients with metastatic intestinal cancer to lung and metastatic

Table 3. Laboratory data of patients based on tumor types

	brain	GBM	breast	pancreas	prostate	skin	pelvic mass	larynx	intes-tine	lung	sarcoma	osteosa-rcoma	liver	colon	esoph-agus	stomach	mela-noma	Total
D-dimer (ng/mL)	2600	145.91	1840.80± 2819.03	3786.80± 3789.34	2327.80± 3345.38	150	140	150	-	1698.80± 2449.8	5060.80± 6308.52	150	233.80± 76.73	713.80± 1025.64	-	1840.80± 3380.15	5471.1	1861.4± 2734.13
PH	7.33	7.35	7.41±0.06	7.43±0.11	7.35±0.19	7.48	-	7.45±0.21	7.13	7.4±0.1	7.41	-	7.45	7.44±0.08	-	7.43±0.01	7.38±0.04	7.4±0.1
PCo2 (mmHg)	50.3	23.8	35.59± 9.92	29.15± 2.73	25.48± 5.66	33.3	-	47.9± 18.39	29.5	38.82± 11.66	39.4	-	20.1	19.66± 10.03	-	35.47± 11.21	41.6± 3.11	34.4± 11.62
HCO3 (mmHg)	25.5	12.8	20.89± 6.58	19.85± 4.17	14.82± 6.22	25.4	-	25.17± 5.87	11	22.78± 3.96	24.3	-	14.2	18.23± 6.64	-	24.1± 6.86	24.05± 4.31	20.82± 6.02
WBC (cells per microliter)	13.8	5.9	7.05± 4.95	13.23± 8.69	12.58± 7.81	4.11	-	10.67± 12.12	16.9	11.68± 9.14	2.82± 2.55	3.1	13.2± 6.98	7.73±5.61	3.6	4.32± 2.05	11.1±7.21	9.07±7.01
PMN (cells per microliter)	85.3	85.5	75.42± 20.14	66.28± 22.51	71.45± 34.23	88.5	-	78.47± 17.74	88.6	65.36± 27.84	65.8± 11.46	84.6	85.53± 6.17	52.6± 36.27	73	78.25± 16.2	78.8± 13.15	72.1± 23.3
Lymphocytes (cells per microliter)	7.9	12.1	15.57± 16.01	27.62± 21.68	5.06±5.24	7.7	-	17.1±16.2	4.7	13.81± 17.67	21.55± 3.04	8.7	11.5±3.7	32.63± 30.62	12.5	12.53± 10.9	14.25± 10.25	15.96± 16.99
Hb (g/dl)	11.6	9.7	15.33± 23.82	9.2±1.55	9.12±1.86	8.1	-	10.07± 3.18	12.2	10.69± 2.64	7.9±0.14	9.6	9.63± 2.93	7.68±2.3	11.2	8.98±1.5	10.95± 1.63	11.68± 14.39
PLT (per mcL)	155	205	171.74± 93.54	116.23± 104.61	195± 194.1	47	-	242± 149.19	412	227.56± 156.48	140.5± 169	38	162.33± 53.78	148.4± 109.51	230	136.25± 108.37	291.5± 40.31	182.86± 123.82
BUN (mg/dL)	75	16	15.17± 9.96	24.68± 13.54	46.55± 44.08	50	13	18±9.85	28	25.52± 12.06	17±5.66	6	34.67± 38.18	29.17± 14.95	12	19.75± 7.09	13±1.41	23.17± 19.15
Cr (mg/dL)	3.5	0.8	1.05±0.37	1.36±1.06	2.57±2.85	1.7	1.3	0.87±0.15	0.8	1.25±0.66	1.3±0.14	0.8	2.47±2.44	1.53±0.76	1.3	0.9±0.22	1.2	1.33±1.07
Na (mEq/L)	149	135	136.38± 6.12	138.8±1.3	134±4.1	144	139	130.33± 8.08	127	135.56± 6.99	135	129	132±8.54	134.33± 3.61	138	138.75± 5.06	135.5± 6.36	135.81± 6.02
K (mEq/L)	4.5	3.1	3.8±0.37	3.86±1.47	4.42±0.87	4.1	4	3.73±0.15	3.7	4.06±0.55	3.9±0.57	4.9	3.5±0.62	3.9±1.1	4.3	3.7±0.57	4±0.14	3.92±0.65
Ca (mEq/L)	14.7	7.9	8.37±0.89	7.36±0.61	7.52±1.2	9.2	8.9	8.2±1.25	-	8.79±1.83	9.9	9.3	6.37±2.51	7.78±0.73	8.8	8.4±0.54	8.7±0.42	8.32±1.49
Alb (g/dL)	3.2	3	3.74±0.7	2.73±0.64	2.97±0.87	3	3.8	3.77±0.23	-	3.27±0.83	4.1	3.8	2.95±0.49	2.82	3.7	3.25±0.52	3.7	3.36±0.73
Mg (mEq/L)	1.7	1.6	1.92±0.19	1.54±0.22	37.42± 86.51	-	2	1.57±0.23	-	2.05±0.6	2.2±0.57	-	1.63±0.45	1.76±0.11	1.9	1.83±0.29	1.85± 0.35	5.05± 25.92
ESR (mm)	40	119	57.74± 32.68	47±16.97	53±23.38	-	140	66.33± 41.79	55	76.4± 34.29	-	-	51.67± 49.4	81±24.64	61	51.5± 31.82	65.5± 0.71	64.1±32.8
CRP (mg/L)	57	54	41.64± 20.63	61±14.2	60.67± 19.44	64	62	44.33± 24.21	61	51.91± 21.01	37.8± 18.67	34	54.67± 6.43	67.23± 23.54	19	63±6.98	65.6± 6.93	50.81± 20.44
LDH (units/L)	365	709	1215.79± 911.73	751.33± 227.55	791.9± 587	-	1271	300.33± 68.38	3570	1482.25± 1870.38	1314± 758.02	1360	584± 112.34	1101.5± 628.78	-	583± 148.85	1822± 1241.68	1155.58± 1143.74
Ferritin (μg/L)	1295	1766	2371.68± 3250.87	769± 887.1	8848.5± 15655.46	3675	755	1162.5± 208.6	-	13838.07± 43532.31	2540± 2552.66	7080	6655± 7647.52	1459.5± 88.81	-	4181.75± 6593.58	1430.5± 833.68	5436.43± 20530.32
Fibrinogen (mg/dL)	390	550	334.06± 61.34	319± 128.69	327± 153.13	396	562	392.5± 44.55	-	368.25± 139.87	-	493	351± 137.18	440±8	-	330.5± 83.58	417	363.38± 100.92
FDP (mg/dL)	25	45	21.93± 10.02	31.67± 11.55	20.2± 8.41	31	22	14.5± 14.85	-	16.83± 6.43	-	45	32.5± 17.68	20.33± 11.55	-	29.25± 14.45	-	23.69± 11.3
AST (IU/L)	23	69	66.44± 60.91	251.75± 441.75	38.8± 12.76	25	35	20.33	470	50.38± 48.85	30	80	-	69.6± 55.86	23	23.5	23	70.31± 118.65

ALT (IU/L)	44	132	48.78± 42.41	128.75± 164.76	33.2± 29.98	24	92	12±4.24	190	39.81± 42.87	28±18.38	27	60±35.51	89.2± 139.28	17	15±6.63	11	51.82± 64.94
ALP (U/L)	379	153	243.74± 138.65	1878± 3264.17	412± 186.67	310	398	176.33± 41.36	2380	217.21± 78.03	296	-	1213.33± 1435.74	763.5± 1189.89	119	177.33± 55.52	167	450.39± 933.63
CPK (IU/L)	64	50	134.6± 223.93	89.5±7.78	8050	-	39	46	-	72±27.87	-	-	173.5± 180.31	70.33± 43.19	-	62±45.25	-	395.26± 1536.49
Bill-D (mg/dL)	-	0.2	0.27±0.14	1.87±2.71	0.5±0.2	0.2	-	0.33±0.12	16.2	0.38±0.21	0.3	-	4.8±6.09	1.5±0.57	0.2	0.3±0.28	-	1.08±2.86
PTT (sec)	37	28	28.6±6.81	27.75± 2.75	32.17± 10.44	21	29	33.33± 10.5	55	28.93± 6.59	27.5±2.12	-	38.67± 12.42	30.58± 12.72	-	28.75± 2.22	31.5±0.71	30.09± 8.07
PT (sec)	13.2	13.9	10.89± 2.02	15.68± 4.04	12.75± 2.81	12.5	-	13.2±2.33	24	15.78± 12.23	10.3±0.42	32	17.3±5.58	13.67± 3.57	-	13.1± 0.96	11.4±0.57	13.51± 6.51
INR	1.06	1.11	0.96±0.12	-	1.08±0.06	-	-	1.13±0.13	2.05	1.57±1.4	1.03±0.04	17.8	1.74±0.99	1.32±0.34	-	-	1.1±0.13	1.55±2.42

Values are presented as mean ± standard deviation. GBM: Glioblastoma, WBC: white blood cells, PMN: polymorphonuclear, HB: hemoglobin, PLT: platelets, BUN: blood urea nitrogen, Cr: creatinine, Na: sodium, K: potassium, Ca: calcium, Alb: albumin, Mg: magnesium, ESR: erythrocyte sedimentation rate, LDH: lactate dehydrogenase, FDP: Fibrin Degradation Product, AST: aspartate transaminase, ALT: alanine transaminase, ALP: alkaline phosphatase, CPK: creatine kinase, Bill-D: direct bilirubin, PTT: partial thromboplastin time, PT: prothrombin time.

Table 4. Imaging findings of the study by case

		CT severity score	Halo sign	GGO	air space consolidation	crazy paving	PE
Total		27.53±22.90	3 (3.6)	67 (80.7)	74 (89.1)	5 (6.1)	19 (22.9)
By case	Brain	6.25	0	1 (100)	0	0	0
	GBM	12.25	0	1 (100)	1 (100)	0	1 (100)
	breast	25.41±21.19	1 (8.3)	25 (89.3)	22 (84)	1 (8.3)	5 (38.5)
	pancreas	36.04±21.83	0	5 (100)	4 (80)	1 (100)	1 (50)
	prostate	26.8±22.86	1 (20)	4 (66.7)	5 (100)	0	1 (25)
	skin	40	0	1 (100)	1 (100)	0	1 (100)
	pelvic mass	30	0	1 (100)	1 (100)	0	1 (100)
	larynx	33.65±49.03	0	3 (100)	3 (100)	0	0
	intestine	0.96	0	1 (100)	1 (100)	1 (100)	1 (100)
	lung	40.08±20.25	1 (7.7)	14 (87.5)	14 (100)	1 (20)	3 (60)
	sarcoma	15.3±20.79	0	2 (100.)	2 (100)	1 (100)	0
	osteosarcoma	40	0	1 (100)	1 (100)	0	1 (100)
	liver	30.01±26.43	0	3 (100)	2 (66.7)	0	0
	colon	10.21±22.24	0	4 (66.7)	5 (100)	0	2 (50)
	esophagus	0.2	0	1 (100)	0	0	0
	stomach	46.67±5.77	0	3 (75)	1 (100)	0	1 (50)
	melanoma	0.1±0.08	0	1 (50)	2 (100)	0	1 (50)

Values are presented as number (percent) or mean ± standard deviation. GGO: ground glass opacity, PE: pleural effusion.

prostatic cancer to the lung. They also showed that the presence of leukocytosis (OR 6.7, 95% CI 3.3-13.7, P<.001), lymphocytopenia (OR 3.1, 95% CI 1.6-6.1, P = .001) and thrombocytopenia (OR 3.4, 95% CI 1.5-8.1, P = .005) were found to be associated with increased 30-day mortality [14]. These data were in line with the findings of our study. We also showed that patients with metastatic intestinal cancer and metastatic prostatic cancer to the lung had the highest mortality rates. Still, we also reported higher rates than these two studies.

Another study found the lowest Hb levels in colon and skin cancer patients. The lowest platelet levels were also observed in patients with osteosarcoma and skin cancer. It could be determined that patients with colon and skin cancers and osteosarcoma could be at higher risk of hematologic disorders. Patients with metastatic cancer to the intestine, GBM, and pancreas had the lowest sodium, potassium, and calcium levels. Patients with prostate cancer had the highest levels of magnesium compared to others.

A study was performed by Marté and colleagues in 2020. They assessed the changes in immune cell subsets in response to COVID-19 in patients with solid tumors. By evaluating data of 48 patients, they showed that the early drop in absolute lymphocyte counts with persistent lymphopenia and the prolonged total neutrophil counts elevation seen in response to corticosteroid administration is similar to trends associated with increased mortality in several coronavirus studies to include the current SARS-CoV-2 pandemic. Furthermore, the mortality rate in this study was 20.8% among hospitalized patients, with higher rates of brain tumors [15]. These data are consistent with our findings. The critical point was that we evaluated the imaging characteristics of the patients. It was shown that the mean CT severity score of all patients was 27.53±22.90. Patients' most common radiologic sign was air space consolidation, followed by GGO. The highest CT severity score was found in patients with stomach cancer.

In 2020, Chiaravalli and others our study suggested a possible collateral effect of the COVID pandemic to bear in mind were the reduced likelihood of pediatric cancer patients accessing referral centers and their consequently worse chances of a timely diagnosis [16]. Wysocki and colleagues also mentioned that the mortality rates of patients with solid tumors

infected with COVID-19 could range from 15-35% and is highest among patients with longer hospitalization duration [17].

In another study by Madan and others, implications of COVID-19 on clinical outcomes of cancer patients and management of solid tumors during the pandemic were evaluated. Based on this study, they suggested an increased mortality risk and serious clinical events from COVID-19 infection in cancer patients. However, the risk of adverse events does not seem to be increased by cancer therapies [18]. The critical issue is that our study and previous reports have shown 24.1% mortality rates in patients. This rate is not considered significantly higher compared to patients with solid tumors without COVID-19 infection. However, it is believed that special care should be given to patients with solid tumors.

As shown by Liu and colleagues in 2020, they investigated data of 216 patients with COVID-19 with solid tumors. It was indicated that increasing age, receipt of antitumor treatment within three months before COVID-19 diagnosis, elevated WBC count and dNLR, and having dyspnea on admission were independent risk factors for mortality among patients with COVID-19 and solid tumors. The mortality rate in this study was 17% which was lower than our reported rate [19]. It is recommended that patients with malignant tumors are more prone to be infected and develop severe infections. Prevention and control of the pandemic and ensuring the progress of cancer diagnosis and treatment is a significant problem in the current scenario [20]. These data were also in line with our reports.

Another critical point was that we assessed the radiologic data of patients. Based on our findings, the mean CT severity score of all patients was 27.53±22.90. Patients' most common radiologic sign was air space consolidation, followed by GGO. Ghetti and colleagues reported that infiltrations in CT scans could significantly diagnose COVID-19, but different patterns could be observed in patients with reduced immune responses [21].

The shortcomings of our study were restricted study population and duration and not considering the relative risk factors of mortality among patients. It is noteworthy that based on our study's results and previous research, special care should be provided to patients with solid tumors during the COVID-19 pandemic and in infected cases. We recommend that further studies be conducted on larger populations to evaluate and compare different COVID-19-related complications in patients with cancer.

Conclusion

The mortality rate in this study was 24.1%. We also showed that patients with GBM had the highest hospitalization duration and ICU admission rates. The mean CT severity score of all patients was 27.53±22.90. Patients' most common radiologic sign was air space consolidation, followed by GGO.

Disclosure of conflict of interest

None.

Address correspondence to: Elahe Nasri, Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Hezar Jarib St., Isfahan City, Isfahan Province, Iran. Tel: +989131278762; Fax: +983137265007; E-mail: elahe.nasri@yahoo.com

References

[1] Ogimi C, Kim YJ, Martin ET, Huh HJ, Chiu CH and Englund JA. What's new with the old coronaviruses? J Pediatric Infect Dis Soc 2020; 9: 210-217.

[2] Struyf T, Deeks JJ, Dinnes J, Takwoingi Y, Davenport C, Leeflang MM, Spijker R, Hooft L, Emperador D, Domen J, Tans A, Janssens S, Wickramasinghe D, Lannoy V, Horn SRA and Van den Bruel A; Cochrane COVID-19 Diagnostic Test Accuracy Group. Signs and symptoms to determine if a patient presenting in primary care or hospital outpatient settings has COVID-19. Cochrane Database Syst Rev 2022; 5: CD013665.

[3] Fernández-de-Las-Peñas C, Palacios-Ceña D, Gómez-Mayordomo V, Florencio LL, Cuadrado ML, Plaza-Manzano G and Navarro-Santana M. Prevalence of post-COVID-19 symptoms in hospitalized and non-hospitalized COVID-19 survivors: a systematic review and meta-analysis. Eur J Intern Med 2021; 92: 55-70.

[4] Yanez ND, Weiss NS, Romand JA and Treggiari MM. COVID-19 mortality risk for older men and women. BMC Public Health 2020; 20: 1742.

[5] Menni C, Sudre CH, Steves CJ, Ourselin S and Spector TD. Quantifying additional COVID-19

symptoms will save lives. Lancet 2020; 395: e107-e108.
[6] Gao YD, Ding M, Dong X, Zhang JJ, Kursat Azkur A, Azkur D, Gan H, Sun YL, Fu W, Li W, Liang HL, Cao YY, Yan Q, Cao C, Gao HY, Brüggen MC, van de Veen W, Sokolowska M, Akdis M and Akdis CA. Risk factors for severe and critically ill COVID-19 patients: a review. Allergy 2021; 76: 428-455.
[7] Jee J, Foote MB, Lumish M, Stonestrom AJ, Wills B, Narendra V, Avutu V, Murciano-Goroff YR, Chan JE, Derkach A, Philip J, Belenkaya R, Kerpelev M, Maloy M, Watson A, Fong C, Janjigian Y, Diaz LA Jr, Bolton KL and Pessin MS. Chemotherapy and COVID-19 outcomes in patients with cancer. J Clin Oncol 2020; 38: 3538-3546.
[8] Lee LY, Cazier JB, Angelis V, Arnold R, Bisht V, Campton NA, Chackathayil J, Cheng VW, Curley HM, Fittall MW, Freeman-Mills L, Gennatas S, Goel A, Hartley S, Hughes DJ, Kerr D, Lee AJ, Lee RJ, McGrath SE, Middleton CP, Murugaesu N, Newsom-Davis T, Okines AF, Olsson-Brown AC, Palles C, Pan Y, Pettengell R, Powles T, Protheroe EA, Purshouse K, Sharma-Oates A, Sivakumar S, Smith AJ, Starkey T, Turnbull CD, Várnai C, Yousaf N; UK Coronavirus Monitoring Project Team, Kerr R and Middleton G. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. Lancet 2020; 395: 1919-1926.
[9] Luciani M, Bentivegna E, Spuntarelli V, Lamberti PA, Cacioli G, Del Porto F, Sesti G, Martelletti P and De Biase L. Recurrent COVID-19 pneumonia in the course of chemotherapy: consequence of a weakened immune system? J Med Virol 2021; 93: 1882-1884.
[10] Lin DD, Meghal T, Murthy P, Mo L, D'Silva A, Huang Y and Xu Y. Chemotherapy treatment modifications during the COVID-19 outbreak at a community cancer center in New York City. JCO Glob Oncol 2020; 6: 1298-1305.
[11] Jafari A, Dadkhahfar S and Perseh S. Considerations for interactions of drugs used for the treatment of COVID-19 with anti-cancer treatments. Crit Rev Oncol Hematol 2020; 151: 102982.
[12] Sahu KK, Jindal V and Siddiqui AD. Managing COVID-19 in patients with cancer: a double blow for oncologists. JCO Oncol Pract 2020; 16: 223-225.
[13] Fuentes-Antrás J, Manzano A, Marquina G, Paz M, Aguado C, Granja M, Benítez J, Ortega J, Priego A, González C, Tejerina-Peces J, Flores P, de Sa AL, Toledano C, Olalla J, de Luna A, Bartolomé J and Pérez-Segura P. A snapshot of COVID-19 infection in patients with solid tumors. Int J Cancer 2021; 148: 2389-2397.
[14] Özdemir N, Dizdar Ö, Yazıcı O, Aksoy S, Dede DS, Budakoğlu B, Metan G, Alp A, Budakoğlu II, Öksüzoğlu ÖBÇ, Özet A, Kılıçkap S, Turhal NS, Çelik İ, Erman M, Ata N, Çelik O and Hayran M. Clinical features and outcomes of COVID-19 in patients with solid tumors: Turkish National Registry Data. Int J Cancer 2020; [Epub ahead of print].
[15] Marté JL, Toney NJ, Cordes L, Schlom J, Donahue RN and Gulley JL. Early changes in immune cell subsets with corticosteroids in patients with solid tumors: implications for COVID-19 management. J Immunother Cancer 2020; 8: e001019.
[16] Chiaravalli S, Ferrari A, Sironi G, Gattuso G, Bergamaschi L, Puma N, Schiavello E, Biassoni V, Podda M and Meazza C. A collateral effect of the COVID-19 pandemic: delayed diagnosis in pediatric solid tumors. Pediatr Blood Cancer 2020; 67: e28640.
[17] Wysocki PJ, Kwinta Ł, Potocki P, Konopka K, Streb J, Wojtukiewicz MZ, Radecka B, Tomczak P, Jarząb M and Kawecki A. Systemic treatment of patients with solid tumors during the COVID-19 (SARS-CoV-2) pandemic-comprehensive recommendations of the Polish Society of clinical oncology. Oncol Clin Pract 2020; 16: 41-51.
[18] Madan A, Siglin J and Khan A. Comprehensive review of implications of COVID-19 on clinical outcomes of cancer patients and management of solid tumors during the pandemic. Cancer Med 2020; 9: 9205-9218.
[19] Liu C, Li L, Song K, Zhan ZY, Yao Y, Gong H, Chen Y, Wang Q, Dong X, Xie Z, Ou CQ, Hu Q and Song Q. A nomogram for predicting mortality in patients with COVID-19 and solid tumors: a multicenter retrospective cohort study. J Immunother Cancer 2020; 8: e001314.
[20] Cai J, Zheng L, Lv D, He M, Xiong J, Mao J and Wang J. Prevention and control strategies in the diagnosis and treatment of solid tumors in children during the COVID-19 pandemic. Pediatr Hematol Oncol 2020; 37: 620-629.
[21] Ghetti C, Ortenzia O, Maddalo M, Altabella L and Sverzellati N. Dosimetric and radiation cancer risk evaluation of high resolution thorax CT during COVID-19 outbreak. Phys Med 2020; 80: 119-124.