Clinical Characteristics and Risk Factors of COVID-19 in 60 Adult Cancer Patients

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ABSTRACT

BACKGROUND: During the pandemic of COVID-19, cancer patients have been considered as one high-risk group in the morbidity and mortality of COVID-19. This study aimed to describe the clinical symptoms and risk factors of COVID-19 in cancer patients.

METHOD: In a prospective cross-sectional study, during a year, all cancer patients who underwent chemotherapy and/or targeted therapy in our clinic (Kermanshah, Iran) were followed up in terms of getting COVID-19. We analyzed the effect of tumor features and demographic information on clinical manifestations, survival status, therapeutic outcomes, and severity of the disease COVID-19 in 2 categories of cancer (hematologic and solid cancers).

RESULTS: Most of the patients (68%) were in the solid tumor category, including breast cancer (24.4%), colon cancer (22%), and gastric cancer (9.8%). There was a statistically significant difference between 2 categories of cancer in the clinical manifestations: the stage of cancer and survival status ($P < .05$). Logistic regression analysis showed that the risk of death in cancer patients with COVID-19 along with symptoms of diarrhea (odds ratio [OR] = 12.8, $P = .004$), the difficulty of breath (OR = 10.73, $P = .034$), drop of SO2 (OR = 1.334, $P = .003$), thrombocytopenia (OR = 1.022, $P = .02$), anemia (OR = 2.72, $P = .011$), requiring mechanical ventilation (OR = 9.24, $P = .004$), pleural infusion (OR = 10.28, $P = .02$), and intensive care unit (ICU) admission (OR = 7.389, $P = .009$) increases independent of other variables. The COVID-19 mortality rate in our cancer patients was 23%.

CONCLUSIONS: Thrombocytopenia, anemia, and diarrhea are symptoms that, along with common symptoms such as lung involvement, difficulty breathing, and the need for a ventilator, increase the risk of death in cancer patients with COVID-19.

KEYWORDS: Risk factor, hematologic neoplasms, COVID-19, malignant neoplasms, mortality

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Introduction

One of the strategies in the control of morbidity of disease is to characterize the high-risk groups. In this way, supportive proceedings apply to prevent the prevalence of the disease. Among all literature published during the pandemic, this fact was clarified that there are high-risk groups in the morbidity and mortality of COVID-19. The male gender (vs female), old people, some with comorbidities (such as hypertension, diabetes, obesity, chronic liver disease, and cardiovascular and respiratory disorders), and cancer patients were regarded as high-risk groups.[1]

The cancer patient is a general epithet while this group of patients encompasses a diversity of tumor subtypes, stages, treatment options, and dissimilar prognosis and sequels. Despite some suggestions for managing cancer patients, including instructions in the ESMO site,[2] COVID-19 is controversial among oncologist specialists. Some studies have been performed comparing the clinical symptoms of COVID-19 between cancer patients and those without malignancy; age > 60, raised C-reactive protein (CRP), male gender, Asian race, hematologic malignancies, and cancer diagnosis > 2 years had been considered as some risk factor for the severity of COVID-19 in cancer patients.[3,4] Based on an analysis of a nationwide EHR database in the United States, patients with recently diagnosed cancer, particularly leukemia, lung cancer, and non-Hodgkin lymphoma (NHL), are at a higher risk of COVID-19. Also, the race of the patients is notable, as the same analysis suggested that compared with white patients with cancer, blacks were more at risk of COVID-19.[5] Awareness of the clinical symptoms and prevalence of COVID-19 in subgroups of cancer patients can help their clinical management during the outbreak. This is especially challenging in developing countries where health care systems lack comprehensive prioritization and management and appropriate guidelines for specific patients.[6] The dwindling of available services, lack of hospital beds for cancer patients, and the use of nursing and hospital staff of cancer centers in COVID-19 wards are some of the troubles that these patients faced during the pandemic

outbreak. All the mentioned factors have led to a kind of phobia for the presence in medical centers. As a result, missing outpatient visits, ignoring to continue the treatment process, cancelation of radiotherapy, and surgery have been reported in these patients.[7]

In this study, we aimed to describe the clinical symptoms, survival status, and risk factors of COVID-19 in cancer patients who were visited in our clinic during the COVID-19 pandemic in Kermanshah, Iran (January 2020-December 2020). Besides, we compared our results in the different cancer subtypes and stages among various ages/sexes and treatment methods.

Subjects and Method

Approval was obtained from the ethics committee of Kermanshah University of Medical Sciences (IR.KUMS.REC.1400.285). The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

In a prospective cross-sectional study, during a year (from January 2020 to the end of December 2020), all cancer patients who underwent chemotherapy and/or targeted therapy in our clinic (Mahdieh Clinic, Kermanshah, Iran) were followed up in terms of COVID-19 symptoms. This group was continuously present in the study and followed the prevention health instructions provided to them. As this study was performed in the first and second waves of coronavirus and access to the vaccine was very limited, patients were required to follow disease prevention protocols. Promoting self-care behaviors, staying in quarantine, preventing unnecessary travel, avoiding crowded places with a high risk of transmission, washing hands, wearing masks, avoiding stress or anxiety, training companions and caregivers and medical staff in dealing with cancer patients, providing the access to laboratory diagnostic equipment, and continuous monitoring of hematologic tests to prevent neutropenia and thrombocytopenia were included the prevention health instructions.

During the study period, a total of 60 patients experienced COVID-19, and based on the detection of SARS-CoV-2 DNA at the polymerase chain reaction of nasopharyngeal cells and/or computed tomography (CT) lung screening, their disease was confirmed. All clinical information about these patients was extracted and the primary outcomes were recorded in a specific form. Different information, including clinical manifestations, hematologic reports, treatment options, the diagnosis method of disease, survival status, and severity of the disease, were recorded under different cancer subtypes and stages. Besides the risk factors, we analyzed the effect of tumor features (subgroups and stages) and demographic information (age and sex) on clinical manifestations, survival status, therapeutic outcomes, and severity of the disease COVID-19 in 2 categories of cancer (hematologic and solid cancers).

Descriptive indicators, including frequency, percentage, mean, and standard deviation (SD), were applied to analyze the data. Also, an independent *t* test, Mann-Whitney *U*, chi-square, Fisher tests, and binary logistic regression were used. The SPSS 22 statistical software was used for data analysis and the significance level was considered $<.05$.

Results

During 1 year, among cancer patients who had been included in our study, 60 experienced COVID-19 disease and we evaluated their symptoms. Most of the patients (60%) were infected with COVID-19 in the last 3 months of the study. While in the first trimester of the pandemic, the number of patients with COVID-19 was only 7, due to the observance of hygienic principles and adherence to self-care education.[8]

Patients included 27 men (45%) and 33 women (55%) with a mean age of 51.1 ± 13.8 (range = 24-77) years. There was no statistically significant difference in the prevalence of the disease between the 2 sexes. The mean age of the men was 52 ± 13 years and of the women was 47 ± 13 years. There was a statistically significant difference in the age of infection between men and women ($P < .05$).

In terms of cancer type, patients were divided into 2 categories: patients with hematologic malignancy (including lymphoma, leukemia, myeloma, and Hodgkin) and patients with solid tumor (including the brain, breast, gastrointestinal tract, larynx, lung, ovary, pancreas, prostate, and skin cancers). Among all patients, 68% were in the solid tumor categories and 32% in the hematologic categories. In order of number, most cases of COVID-19 in the solid tumors were observed in breast cancer (24.4%), colon cancer (22%), gastric cancer (9.8%), lung cancer (7.3%), and ovarian cancer (7.3%), whereas in hematologic malignancy, most cases were observed in lymphoma (31.6%), chronic lymphocytic leukemia (CLL) (31.6%), and acute leukemia (21.1%) (Table 1). There was no statistically significant difference between the 2 categories in terms of age and sex.

The most clinical manifestations (70%-60%) of COVID-19 were fever, tiredness, exhaustion, and dry cough. Other symptoms such as aches and pains, sore throat, headache, difficulty breathing or shortness of breath, and frailty (severe weakness) were observed in 40% to 55% of cases.

Less common symptoms (<30%) were diarrhea, conjunctivitis, ageusia (loss of taste) and anosmia (loss of smell), dysarthria (difficulty speaking), confusion, and bewilderment (Table 2). The clinical manifestations of solid and hematologic cancers are listed in Table 2. There was a statistically significant difference between the 2 groups in the incidence of frailty ($P = .029$) and dysarthria ($P = .009$) symptoms. Patients with solid tumors experienced dysarthria (26%) and frailty more than patients with hematologic cancer.

Regarding blood findings and pulse oximetry results of patients, the percentage of saturated oxygen (SO2%) before oxygen therapy was in the range of 76% to 96%, and after oxygen therapy was 80% to 96%. According to the paired *t* test, there was a significant difference between the mean of SO2 before and after treatment: 83.81 vs 89.31 ($P < .001$) but there was no statistically significant difference between the 2 cancer groups (Table 3). Other blood factors are listed in Table 3.

Table 1. Frequency of all cancer subtypes according to their categories and the basis of chemotherapy for cancer patients during the COVID-19 pandemic.

CANCER CATEGORIES	CANCER SUBTYPES	CHEMOTHERAPY	FREQUENCY	VALID PERCENT	TOTAL
Solid cancer	Brain	Temo/PCV	1	1.7	41
	Breast	Gem/Nav, FAC, Herceptin, TEC	10	16.7	
	Cholangiocarcinoma	Gem/Cis/5FU	2	3.3	
	Colon	Folfox/Ave, Folfiri/ERB, Pembrolizumab, Oxall/capa	9	15.0	
	Esophageal	Tax/Cis/5FU	1	1.7	
	Gastric	Folfiri/Herceptin, Tax/Cis/5FU	4	6.7	
	Germ T cell	TAX/Cis	1	1.7	
	Larynx	Tax/Cis/5FU	1	1.7	
	Lung	Gem/Cis, Etopos/Cis, Taol/Car	3	5.0	
	MUO	Gem/Cis/5FU	1	1.7	
	Ovary	Carbo/cam/Av, Tax/Carb/Av, BEP	3	5.0	
	Pancreas	Gem/Cis/5FU	2	3.3	
	Pancreatobiliary	Gem/Cis/5FU	1	1.7	
	Prostate	Taxoter/BIC	1	1.7	
	SCC	Tax/Cis/5FU	1	1.7	
Hematologic cancer	Lymphoma	Rituximab, R-CVP, Flu/Cyc/R, Hyper-CVAD	6	10.0	19
	Acute leukemia[a]	FLANG, ATRA/Chem, Arsenic	4	6.7	
	CLL	Chlora/PRD	6	10.0	
	Myeloma	Velcade	1	1.7	
	Hodgkin	ABVD	2	3.3	
Total			60	100.0	60

ABVD, adriamycin, bleomycin, vinblastine, dacarbazine; BEP, bleomycin, etoposide, and cisplatin; Cap, capecitabine (Xeloda); Carbo, carboplatin; Cis, cisplatin; CLL, chronic lymphocytic leukemia; Etop, etoposide; FAC, fluorouracil, adriamycin, and cytoxan; 5FU, 5-fluorouracil; Folfox, leucovorin, 5FU, oxaliplatin; folinic acid (leucovorin, calcium folinate or FA); FLANG, fludarabine, cytosine arabinoside, mitoxantrone, and G-CSF; Gem, gemcitabine; Hyper-CVAD, hyperfractionated cyclophosphamide, vincristine, doxorubicin, and prednisolone; MIC, mitomycin, ifosfamide, cisplatin; MUO, metastatic of unknown origin; Nav, vinorelbine; P, cisplatin; PCV, procarbazine, lomustine (CCNU), and vincristine; RCVP, rituximab, cyclophosphamide, vincristine sulfate, and prednisone; PRD, prednisolone; SCC, squamous cell carcinoma; Tax, paclitaxel; TEC, docetaxel/epirubicin/cyclophosphamide; Temo, temozolomide; VP, etoposide.
[a]Acute lymphocytic leukemia, acute myeloid leukemia, and acute promyelocytic leukemia.

Among hematologic factors, there was a statistically significant difference between the 2 groups only in the mean platelet count ($P = .044$).

Reverse transcription–polymerase chain reaction (RT-PCR) was the main laboratory technique in the diagnosis of COVID-19; in 33.3% of patients despite the symptoms, RT-PCR was negative. The relationship between cancer type and the RT-PCR test result was not significant.

In terms of pulmonary involvement in the computerized tomography (CT) scan report, 50.3% had pulmonary involvement, of which 16.7% had unilateral involvement, 22% bilateral, and 8.3% had pleural effusion combined with unilateral or bilateral pulmonary involvement. There was no statistically significant difference between the 2 groups in terms of pulmonary involvement parameters.

Patients were treated with chemotherapy based on the type of cancer (Table 1), and in COVID-19 cases, based on national treatment guidelines[9] patients were treated to control the disease. Overall, 40% of patients used single-dose or combination medications of ReciGen (interferon β1a) (36.7%), antiviral drugs (remdesivir, Sovodak, favipiravir, Kaletra) (21.7%), corticosteroids (2%), and hydroxychloroquine (8.3%). Intravenous (IV) antibiotics, including ceftriaxone and vancomycin, were prescribed to patients with fever and persistent fever, respectively. There was no significant relationship between the treatment options and the type of cancer.

Other treatment regimens used in different courses based on national treatment guidelines,[9] patient response, and access to available medications. Among patients with breast cancer (10 cases), only supportive treatments were prescribed (supportive

Table 2. Frequency of symptoms of COVID-19 according to cancer category.

SYMPTOMS		CANCER CATEGORY		TOTAL FREQUENCY, N (%)	*P* VALUE
		SOLID FREQUENCY, N (%)	HEMATOLOGIC FREQUENCY, N (%)		
Fever	No	14 (34.1)	4 (21.1)	18 (30.0)	.307
	Yes	27 (65.9)	15 (78.9)	42 (70.0)	
Dry cough	No	14 (34.1)	2 (10.5)	16 (26.7)	.056
	Yes	27 (65.9)	17 (89.5)	44 (73.3)	
Tiredness	No	12 (29.3)	5 (26.3)	17 (28.3)	.815
	Yes	29 (70.7)	14 (73.7)	43 (71.7)	
Pain and ache	No	18 (43.9)	9 (47.4)	27 (45.0)	.803
	Yes	23 (56.1)	10 (52.6)	33 (55.0)	
Sore throat	No	20 (48.8)	13 (68.4)	33 (55.0)	.158
	Yes	21 (51.2)	6 (31.6)	27 (45.0)	
Diarrhea	No	36 (87.8)	15 (78.9)	51 (85.0)	.175
	Yes	5 (12.2)	4 (21.1)	9 (15.0)	
Conjunctivitis	No	40 (97.6)	19 (100.0)	59 (98.3)	.496
	Yes	1 (2.4)	0 (0.0)	1 (1.7)	
Headache	No	16 (39.0)	11 (57.9)	27 (45.0)	.175
	Yes	25 (61.0)	8 (42.1)	33 (55.0)	
Ageusia (loss of taste)	No	36 (87.8)	16 (84.2)	52 (86.7)	.706
	Yes	5 (12.2)	3 (15.8)	8 (13.3)	
Anosmia (loss of smell)	No	33 (80.5)	17 (89.5)	50 (83.3)	.389
	Yes	8 (19.5)	2 (10.5)	10 (16.7)	
Difficulty breathing	No	23 (56.1)	12 (63.2)	35 (58.3)	.609
	Yes	18 (43.9)	7 (36.8)	25 (41.7)	
Shortness of breath	No	23 (56.1)	11 (57.9)	34 (56.7)	.897
	Yes	18 (43.9)	8 (42.1)	26 (43.3)	
Chest pain	No	24 (58.5)	13 (68.4)	37 (61.7)	.468
	Yes	17 (41.5)	6 (31.6)	23 (38.3)	
Dysarthria (difficulty speaking)	No	30 (73.2)	19 (100.0)	49 (81.7)	.009*
	Yes	11(26.8)	0(0.0)	11(18.3)	
Frailty	No	18 (43.9)	14 (73.7)	32 (53.3)	.029*
	Yes	23 (56.1)	5 (26.3)	28 (46.7)	
Exhaustion	No	10 (24.4)	4 (21.1)	14 (23.3)	.778
	Yes	31 (75.6)	15 (78.9)	46 (76.7)	
Confusion and bewilderment	No	40 (97.6)	19 (100.0)	59 (98.3)	.380
	Yes	1 (2.4)	0 (0.0)	1 (1.7)	

Table 3. Hematologic results in COVID-19 cancer patients.

VARIABLE	CANCER CATEGORY	N	MEAN	SD	*P* VALUE
SO2 (%) before oxygen therapy	Solid	41	88	6.611	.610
	Hematologic	19	88	5.981	
SO2 (%) after oxygen therapy	Solid	21	89	4.745	.858
	Hematologic	11	89	4.905	
WBC × 1000/mm^3	Solid	39	14702	24718	.233
	Hematologic	19	31367	33432	
Hb (g/dL)	Solid	41	10.76	1.150	.167
	Hematologic	19	10.13	1.558	
Plt	Solid	41	140227	57046	.044
	Hematologic	19	109315	68220	

Hb, hemoglobin; Plt, Platelet; SD, standard deviation; SO2, saturated oxygen; WBC, white blood cells.

treatments include relieving the symptoms of fever, cough, and pain); one of these patients was treated with remdesivir + corticosteroids. Two patients with acute promyelocytic leukemia (one of whom had Down syndrome) received only supportive treatment. Two patients with acute myeloid leukemia received the antiviral drug Kaletra + hydroxychloroquine but died due to chronic neutropenia and refractory status. Two patients with cholangiocarcinoma were treated with remdesivir + corticosteroids; however, one of them died. Most patients with chronic lymphocytic leukemia (6 cases) received supportive treatment, and one of them received remdesivir + corticosteroids + ReciGen.

A total of 68.3% of patients with severe symptoms were admitted to the intensive care unit (ICU), of which 13.3% needed a ventilator. The rest of the patients (31.7%) developed a moderate form of COVID-19 (the moderate condition was defined as being feverish and showing respiratory symptoms, and the radiology evidence indicating pneumonia) who were treated on an outpatient clinic; in all cases, prompt treatment was performed. There was no statistically significant relationship between the type of cancer and hospitalization in the intensive care unit (ICU) and the need for a ventilator.

In the solid tumors, 9.8% of patients and in hematologic malignancy 15.8% of patients died. There was no statistically significant relationship between cancer type and patients' survival status.

Among various types of cancer, only patients who were stage IV died of COVID-19 and in the other stages, there was no death report. There was a statistically significant difference between the stage of cancer and survival status ($P = .043$).

A total of 7 deaths were reported, of which 4 were related to solid tumors (2 cases of lung cancer, 1 case of the brain, and 1 case of cholangiocarcinoma) and 3 cases were related to hematologic malignancy (myeloma and refractory acute leukemia). The COVID-19 mortality rate in our cancer patients was 23%.

There were no statistically significant differences between hematologic and solid cancers in terms of survival, but there was a statistically significant difference between hematologic malignancy and survival status (Table 4). The deceased patients had no comorbidity except cancer. All patients had a dry cough, but none had conjunctivitis, confusion, and bewilderment. The PCR test was positive in all patients and all required a ventilator. The deceased solid tumor patients had symptoms of fever, shortness of breath, chest pain, and frailty. Diarrhea was common in the deceased hematologic cancer patients, but none had pain, sore throat, ageusia and anosmia, dysarthria, or frailty.

Logistic regression analysis showed that the risk of death in cancer patients with COVID-19 along with symptoms of diarrhea (odds ratio [OR] = 12.8, $P = .004$), the difficulty of breath (OR = 10.73, $P = .034$), drop in SO_2 (OR = 1.334, $P = .003$), thrombocytopenia (OR = 1.022, $P = .02$), anemia (OR = 2.72, $P = .011$), requiring mechanical ventilation (OR = 9.24, $P = .004$), pleural effusion (OR = 10.28, $P = .02$), and ICU admission (OR = 7.389, $P = .009$) increases independent of other variables.

Discussion

Studies have displayed that cancer patients are more likely to develop COVID-19 and its severe form than people who do not have cancer.[10,11] From the beginning of the coronavirus pandemic in Iran (January 2020), all cancer patients who underwent chemotherapy and/or targeted therapy in our clinic (Mahdieh Clinic, Kermanshah, Iran) were followed up in terms of COVID-19 symptoms. During our study, 60 cancer patients experienced COVID-19 disease. As patients with different types of cancer have different phenotypes and vulnerabilities in COVID-19, patients were divided into 2 categories, namely, solid tumor and hematologic malignancy, and various aspects of COVID-19 symptoms in these 2 patients groups were

Table 4. Frequency of COVID-19 symptoms according to cancer category in deceased patients.

TUMOR CATEGORY	SOLID CANCER				HEMATOLOGIC CANCER		
	BRAIN	LUNG	CHOLANGIOCARCINOMA	LUNG	ALL	MM	AML
Sex[a]	1	1	2	2	1	1	2
Age range	51-60	61-70	51-60	31-40	51-60	61-70	31-40
Stage	—	IV	IV	IV	Refractory	—	Refractory
Fever	Yes	Yes	Yes	Yes	Yes	No	Yes
Tiredness	Yes	Yes	Yes	No	No	No	Yes
Pain	Yes	No	Yes	No	No	No	No
Sore throat	Yes	No	Yes	No	No	No	No
Diarrhea	No	Yes	No	No	Yes	Yes	Yes
Headache	Yes	Yes	Yes	No	Yes	Yes	No
Ageusia (loss of taste)	Yes	No	Yes	No	No	No	No
Anosmia (loss of smell)	Yes	No	No	No	No	No	No
Difficulty breathing	Yes	Yes	Yes	Yes	Yes	Yes	No
Shortness of breath	Yes	Yes	Yes	Yes	Yes	Yes	No
Chest pain	Yes	Yes	Yes	Yes	No	Yes	No
Dysarthria (difficulty speaking)	Yes	No	Yes	Yes	No	No	No
Frailty	Yes	Yes	Yes	Yes	No	No	No
Exhaustion	Yes	No	Yes	Yes	Yes	Yes	No
SO2% before O_2 therapy	79	76	78	76	76	76	92
SO2% after O_2 therapy	82	82	85	81	80	83	—
WBC × 1000/mm^3	3500	3500	3200	21 000	1200	2200	800
Hb (g/dL)	10.4	11	8.9	11	7	8	8
Plt	90 000	120 000	58 000	80 000	20 000	65 000	12 000
Treatment option	ReciGen	Hydroxychloroquine & ReciGen	ReciGen, remdesivir, corticosteroid	ReciGen	Hydroxychloroquine	Hydroxychloroquine & ReciGen	ReciGen
Pulmonary involvement	Bilateral	Bilateral	Bilateral	Bilateral	Bilateral	Bilateral	No
Plural involvement	No	Yes	Yes	Yes	No	No	No

ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia; Hb, hemoglobin; MM, multiple myeloma; Plt, platelet; SO2, saturated oxygen; WBC, white blood cells.
[a]1: Male; 2: Female.

Table 5. Binary logistic regression on variables predicting the death in cancer patients with COVID-19.

VARIABLE	OR	95% CI FOR OR	*P* VALUE
Age	0.979	0.922-1.039	.482
Sex (male)	0.575	0.117-2.827	.496
Type of cancer	1.734	0.347-8.657	.502
Fever (yes)	2.833	0.316-25.422	.352
Dry cough (yes)	1.556	0.293-8.246	.604
Tiredness (yes)	0.479	0.095-2.411	.372
Aches and pains (yes)	0.284	0.05-1.599	.153
Sore throat (yes)	0.448	0.08-2.518	.362
Diarrhea (yes)	12.80	2.207-74.221	.004
Headache(yes)	2.232	0.397-12.543	.362
Loss of taste (yes)	3.133	0.494-19.866	.226
Loss of smell (yes)	0.815	0.087-7.617	.857
Difficult breathing (yes)	10.737	1.201-95.953	.034
Shortness of breath (yes)	9.90	1.109-88.339	.040
Chest pain (yes)	4.861	0.857-27.573	.074
Fatigue	0.732	0.126-4.259	.728
SO2	1.334	1.101-1.616	.003
WBC	1.000	1.000-1.000	.282
Anemia	2.723	1.263-5.872	.011
Plt	1.022	1.003-1.040	.020
Mechanical ventilation (yes)	9.214	2.064-41.140	.004
Pleural effusion	10.286	1.453-72.806	.020
ICU admission (yes)	7.389	1.648-33.120	.009
Multilobar involvement of the lung	6.231	0.701-55.364	.101
Unilobar involvement of the lung	10.125	1.116-91.879	.040

CI, confidence interval; ICU, intensive care unit; OR, odd ratio; Plt, Platelet; SO2, saturated oxygen; WBC, white blood cells.

assessed separately. Most patients were women and their age was lower than men.

The mean age of COVID-19 in our cancer patients was 51.1 ± 13.8, which was lower than the mean age in previous studies. A systematic review of risk factors for mortality among 1169 patients with hematologic malignancy affected with COVID-19 revealed that age >60 years is a risk factor for mortality in these patients.[12] Similar results have been reported in other studies that contradict the results of our study.[13]

Similar to Ma Ja et al's findings,[14] in our study most patients with COVID-19 were from the solid tumor group, and most cases were observed in patients with breast and colon cancers. In contrast to our findings, in a nationwide cohort study conducted in the Netherlands, the results of COVID-19 in 442 registered patients revealed that patients with hematologic malignancy or lung cancer were at higher risk of a worse COVID-19 outcome.[15] In some other previous studies, lung cancer has been reported as the most common cancer associated with COVID-19 disease.[16-18]

In addition to the usual symptoms of COVID-19 disease, which include a dry cough, fever, and fatigue, there were also symptoms associated with the involvement of certain organs of the body, such as respiratory symptoms (cough, shortness of breath, sore throat, rhinorrhea, hemoptysis, and chest pain) due to pulmonary involvement, gastrointestinal symptoms (diarrhea, nausea, and vomiting) due to gastrointestinal involvement, physical pain due to skeletal muscle involvement, and neurological symptoms (headache, confusion, ageusia,

Table 6. A summary of some published results of COVID-19 mortality rate.

AUTHOR(S)	YEAR	COUNTRY	POPULATION	ICU ADMISSION	MORTALITY RATE	REFERENCE
Meng et al	2020	Wuhan, China	Non-cancer: 2556	Non-cancer: NM	Non-cancer: 10.2%	30
			Cancer: 109	Cancer: NM	Cancer: 29.4%	
Bertuzzi et al	2020	Lombardy, Italy.	Non-cancer: —	Non-cancer: —	Non-cancer: 20%	31
			Cancer: 1267	Cancer: —	Cancer: 29%	
Erdal et al	2020	Istanbul, Turkey	Non-cancer: 68	Non-cancer: NM	Non-cancer: 1.5%	32
			Cancer: 17	Cancer: NM	Cancer: 23.9%	
Sanchez-Pina et al	2020	Madrid, Spain	Non-cancer:53	Non-cancer:0	Non-cancer: 13.2%	4
			Cancer: 39	Cancer: 100%	Cancer: 35.9%	
Guan et al	2019	China	Non-cancer:1089	Non-cancer:4.8%	Non-cancer: 1.4%	33
			Cancer: 10	Cancer: 30%	Cancer: 0%	
Huang et al	2020	China	Non-cancer: 40	Non-cancer: 31.7%	Non-cancer: 15%	20
			Cancer: 1	Cancer: 0	Cancer: 0	
Aznab et al	2020	Kermanshah, Iran	Non-cancer: not studied	Non-cancer: not studied	Non-cancer: not studied	Present study
			Cancer: 60	Cancer: 3.1%	Cancer: 23%	

ICU, intensive care units; NM, not mentioned.

anosmia, dysarthria, confusion, and bewilderment) due to involvement of the nervous system.[19,20] The most clinical manifestations of our patients, as in previous reports of cancer patients with COVID-19,[21] were fever, dry cough, and fatigue. Only in terms of dysarthria and frailty, differences were observed between the 2 groups of hematologic and solid tumors. Besides common symptoms, the patients presented neurological symptoms such as headache, inactivity, dysarthria, confusion, bewilderment, anosmia, and ageusia. Many reports point to these neurological conditions in patients with COVID-19.[22-24] There are several reasons for these neurological manifestations; a case report of dysarthria in a 72-year-old woman showed a deficiency of 25-OH vitamin D, parathyroid hormone, and blood calcium.[25] Other causes of neurological manifestations due to viral infections include increased levels of interleukin-6 and its subsequent infiltration of the blood-brain barrier, which has been associated with cognitive and neurodegenerative disorders.[26]

The COVID-19 mortality rate in our cancer patients was 23%; there was no statistically significant difference in the mortality rate between hematologic and solid tumor groups. In a prospective cohort study, of 1044 patients with cancer, 30% died. In this study, the risk factor for mortality was mentioned in elderly patients and hematologic malignancies undergoing chemotherapy.[27] Studies have suggested that the prognosis of COVID-19 patients with 2 or more comorbidities is not pleasant,[28] while patients who died of COVID-19 in our study had no underlying disease other than cancer. Some published results of the COVID-19 mortality rate are provided in Table 6. In a similar study conducted in Iran, a mortality rate was 40%,[29] which was higher compared with our study. One of the reasons for the difference in mortality rate results is the adherence of our patients to the instructions given to them in the control and prevention of COVID-19.

In deceased hematologic cancer patients, there was a decrease in the total platelet count. Platelet depletion was a blood factor that was significantly reduced in the hematologic group versus the solid tumor group. Platelet depletion was also a risk factor for COVID-19 death in cancer patients. Previous research has revealed that platelets besides other arms of the immunity, including neutrophils, monocytes, dendritic cells, B cells, and T cells, play an important role in the immune system and even have antiviral effects, so in hematologic malignancy, thrombocytopenia is usual and immunodeficiency exacerbates their disease.[34]

Since the outbreak of the COVID-19 epidemic until the time of this study, no reliable treatment had been definitively provided to reduce the course and improve the complications of the disease. The proposed treatments were based on clinical trials and valid guidelines[2,9] but did not produce the

desired results. As these guidelines have been updated, treatment methods have changed as well. However, the use of several common COVID-19 treatment options, namely, ReciGen, antiviral drugs (remdesivir, Sovodak, favipiravir, Kaletra), hydroxychloroquine, and corticosteroids, failed to control the devastating effects of the disease in patients who died. The previous study demonstrated that the important factors in the severity and the mortality rate in cancer patients are neutropenia and being in the end stages of the disease. The type of treatment regimen in cancer patients is completely dependent on the stage of the disease; one of the most common treatments in patients with early stages of the disease is hormone therapy which is not along with neutropenia and mortality. In our study, none of the deceased patients were among those receiving hormone therapy and developing Covid-19. there is little chance for systemic problems, especially bone marrow suppression or neutropenia, in radiotherapy.[8] Bertuzzi et al[31] described the prognosis of SARS-CoV-2-positive cancer patients on active oncologic treatment and suggested that active oncologic treatments do not represent a risk factor for SARS-CoV-2 infection in cancer patients.

In our study, among the 7 patients who died, 3 were in the advanced stage of the disease (stage IV) and 2 patients (AML and ALL) were in the refractory group. The disease status of these patients puts them at risk of death due to their extreme vulnerability to disease progression, common and unusual infections. Therefore, the cause of death alone cannot be attributed to COVID-19. In our study, none of the patients with stage I, II, or III have died. None of the patients with chronic leukemia and lymphoma have died, as well. The risk factors that determine the progression of the disease in COVID-19 disease, severe pulmonary involvement, and more severe and fatal complications among patients with malignancy need further evaluation.

However, to reduce the risk of solid tumor patients in epidemic conditions, it is better for these patients not to develop neutropenia and to use granulocyte colony-stimulating factors (G-CSFs) at the appropriate time.[35,36]

In the category of patients with hematologic malignancy, patients with acute leukemia need more attention.[8,37,38] Therefore, in this group, the priority should be on prevention. Vaccination of COVID-19 in patients with acute leukemia requires further studies regarding the initiation of vaccination. Recent studies suggested that vaccines, whether inactivated[39] or mRNA,[40,41] in cancer patients have immunogenicity and safety. In addition, cancer patients who receive active systemic therapy had adequate antibody responses to mRNA vaccines.[40] In these studies, 2 doses of vaccine to create adequate immunization have been emphasized.[41] Generally, the data support the vaccination of cancer patients as a priority even during treatment.

Conclusions

According to the results of our study, thrombocytopenia, anemia, and diarrhea are symptoms that, along with common symptoms such as lung involvement, difficulty breathing, and the need for a ventilator, increase the risk of death in cancer patients with COVID-19. What is more important than the proposed treatments in controlling COVID-19 disease in cancer patients is informing patients to observe hygienic principles, promoting self-care behavior, preventing unnecessary commute, avoiding being in places with a high risk of transmission, hand washing, wearing a mask, avoiding stress and anxiety, training of patients' companions and caregivers and treatment staff in dealing with cancer patients, providing access to laboratory diagnostic equipment, and continuous monitoring of hematologic tests to prevent neutropenia and thrombocytopenia.

Availability of data and material

No additional data are available.

Author contributions

MA contributed to concepts, design, the definition of intellectual content, clinical studies, manuscript preparation, manuscript editing, manuscript review, and data acquisition and is the guarantor; NER contributed to concepts, design, literature search, data acquisition, data analysis, manuscript preparation, manuscript editing, and manuscript review; HM contributed to literature search, data acquisition, statistical analysis, manuscript preparation, and manuscript review.

Ethics approval

Approval was obtained from the ethics committee of Kermanshah University of Medical Sciences. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

Consent to participate

Verbal informed consent was obtained before the interview.

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