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# COVID-19 in cancer patients may be presented by atypical symptoms and higher mortality rate, a case-controlled study from Iran

Soodabeh Shahidsales[1]  |  Seyed Amir Aledavood[1]  |  Mona Joudi[1]  |
Fatemeh Molaie[2] [ID]  |  Habibollah Esmaily[3]  |  Seyed Alireza Javadinia[4] [ID]

[1]Cancer Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran

[2]Student Research Committee, Mashhad University of Medical Sciences, Mashhad, Iran

[3]Department of Epidemiology and Biostatistics, School of Health, Mashhad University of Medical Sciences, Mashhad, Iran

[4]Cellular and Molecular Research Center, Sabzevar University of Medical Sciences, Sabzevar, Iran

**Correspondence**
Fatemeh Molaie, Cancer Research Center, Mashhad University of Medical Sciences, Koohsangi Ave., Shariati Sq., Mashhad, 9176613775, Razavi Khorasan, Iran.
Email: molaeif961@mums.ac.ir, fatemeh.mle@gmail.com

**Abstract**

**Background:** Coronavirus disease 2019 (COVID-19) pandemic imposes serious problems to health systems around the world and its rapid expansion makes it difficult to serve patients with certain health conditions such as cancer patients which might be at high risk for mortality if they are infected by the severe acute respiratory syndrome coronavirus 2.

**Aim:** To compare the outcomes of cancer patients admitted due to COVID-19 and compare them with data of COVID-19 infected patients without a history of cancer.

**Methods:** In this case-controlled study, 93 healthy people and 92 patients with malignancy admitted for COVID-19 were enrolled. The clinical features and laboratory indicators were assessed at the presentation and both groups were followed-up for treatment options and outcomes prospectively and compared at the level of $P \leq .05$.

**Results:** COVID-19 related mortality rate in malignant patients was significantly higher than patients without malignancy (41.3% vs 17.2%, $P = .0001$). The risk of death increased significantly in patients with malignancy (OR = 8.4, $P = .007$) and mechanical ventilation (OR = 3.3, $P = .034$) independent of other variables. Fever (64.5% vs 43.5%, $P = .004$), chill (35.5% vs 14.1%, $P = .001$), malaise (49.5% and 30.4%, $P = .008$), dry cough (51.6% vs 26.1%, $P = .0001$), and vomiting (17.2% vs 5.4%, $P = .012$) were reported significantly lower in cancer patients.

**Conclusion:** The results suggest that cancer patients who were infected by COVID-19 may present with atypical symptoms are at higher risk of mortality independent of the demographic data, comorbidities, and treatments.

**KEYWORDS**
COVID-19, malignancy, mortality

## 1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a severely contiguous infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reported for the first time at the beginning of

2020 in Wuhan, China. However, less than 3 months later, the world health organization recognized its spread as a pandemic that influences all countries on different continents.[1] In most clinical scenarios, COVID-19 presented by mild to moderate self-limiting flue like symptoms, however, in some certain populations, COVID-19 infected

**TABLE 1** Characteristics of COVID-19 infected patients with and without malignancy

| | | Malignancy | | |
| --- | --- | --- | --- | --- |
| | | **No** | **Yes** | **P-value** |
| **Demographic data** | | | | |
| Age [median, year] | | 57 | 62 | .078 |
| Gender | Male | 56 (60.2%) | 55 (59.8%) | .952 |
| | Female | 37 (39.8%) | 37 (40.2%) | |
| Comorbidity | | 50 (53.8%) | 33 (35.9%) | .014 |
| Number of comorbidities | 0 | 43 (46.2%) | 59 (64.1%) | .064 |
| | 1 | 25 (26.9%) | 20 (21.7%) | |
| | 2 | 18 (19.4%) | 7 (7.6%) | |
| | 3 | 6 (6.5%) | 6 (6.5%) | |
| | 4 | 1 (1.1%) | 0 | |
| Diabetes mellitus | | 30 (32.3%) | 14 (15.2%) | **.006** |
| Hypertension | | 28 (30.1%) | 17 (18.5%) | .065 |
| IHD/CHF | | 14 (15.1%) | 14 (15.2%) | .975 |
| COPD | | 4 (4.3%) | 1 (1.1%) | .187 |
| Asthma | | 2 (2.2%) | 0 | .251 |
| CKD/ESRD | | 4 (4.3%) | 2 (2.2%) | .346 |
| Hepatitis B | | 0 | 2 (2.2%) | .246 |
| Deep venous thrombosis | | 0 | 1 (1.1%) | .497 |
| **Symptoms** | | | | |
| Fatigue | | 66 (71%) | 66 (71.7%) | .908 |
| Fever | | 60 (64.5%) | 40 (43.5%) | **.004** |
| Chill | | 33 (35.5%) | 13 (14.1) | **.001** |
| Malaise | | 46 (49.5%) | 28 (30.4%) | **.008** |
| Chest pain | | 10 (10.8%) | 10 (10.9%) | .980 |
| Headache | | 9 (9.7%) | 7 (7.6%) | .617 |
| Seizure | | 0 | 5 (5.4%) | .029 |
| Lack of consciousness | | 3 (3.2%) | 15 (16.3%) | **.003** |
| Dry cough | | 48 (51.6%) | 24 (26.1%) | **.0001** |
| Productive cough | | 17 (18.3%) | 18 (19.6%) | .823 |
| Shortening of breath | | 82 (88.2%) | 73 (79.3%) | .104 |
| Hemoptysis | | 0 | 3 (3.3%) | .079 |
| Sore throat | | 5 (5.4%) | 2 (2.2%) | .227 |
| Nausea | | 21 (22.6%) | 13 (14.1%) | .138 |
| Vomiting | | 16 (17.2%) | 5 (5.4%) | **.012** |
| Diarrhea | | 6 (6.5%) | 4 (4.3%) | .747 |
| Constipation | | 1 (1.1%) | 4 (4.3%) | .211 |
| Gastrointestinal bleeding | | 0 | 4 (4.3%) | .059 |
| Bowel obstruction | | 1 (1.1%) | 1 (1.1%) | 1 |
| **Signs** | | | | |
| Systolic blood pressure | [median, mmHg] | 130 | 120 | **.0001** |
| Diastolic blood pressure | [median, mmHg] | 80 | 75 | **.0001** |
| Oxygen saturation | | | | |
| | Normal | 11 (11.8%) | 19 (20.9%) | .383 |
| | O2sat = 90–95% | 41 (41.1%) | 33 (36.3%) | |
| | O2sat = 90–75% | 37 (39.8%) | 35 (38.5%) | |

**TABLE 1**　(Continued)

| | | Malignancy | | |
| --- | --- | --- | --- | --- |
| | | No | Yes | *P*-value |
| | O2sat < 75% | 4 (4.3%) | 4 (4.4%) | |
| Heart rate | | | | |
| | Normal | 58 (62.4%) | 60 (65.2%) | .687 |
| | Bradycardia | 0 | 0 | |
| | Tachycardia | 35 (37.6%) | 32 (34.8%) | |
| Respiratory rate | | | | |
| | Normal | 9 (9.7%) | 5 (54%) | .275 |
| | Bradypnea | 0 | 0 | |
| | Tachypnea | 84 (90.3%) | 87 (94.6%) | |
| Temperature | | | | |
| | Normal | 72 (77.4%) | 81 (88%) | .102 |
| | Hypothermia | 1 (1.1%) | 0 | |
| | Fever | 20 (21.5%) | 11 (12%) | |
| **Laboratory data** | | | | |
| Neutrophil count | | | | |
| | Normal | 64 (69.6%) | 45 (48.9%) | **.002** |
| | Neutropenia | 1 (1.1%) | 11 (12%) | |
| | Neutrophilia | 27 (29.3%) | 36 (39.1%) | |
| Lymphocyte count | | | | |
| | Normal | 25 (26.9%) | 32 (34.8%) | .245 |
| | Lymphopenia | 68 (73.1%) | 60 (65.2%) | |
| Thrombocytopenia | | 7 (7.5%) | 33 (35.9%) | **.0001** |
| Anemia | | 20 (21.5%) | 34 (97%) | **.021** |
| Sodium level | | | | |
| | Normal | 64 (68.8%) | 59 (64.1%) | .239 |
| | Hyponatremia | 28 (30.1%) | 27 (29.3%) | |
| | Hypernatremia | 1 (1.1%) | 6 (6.6%) | |
| Potassium level | | | | |
| | Normal | 73 (78.5%) | 68 (74.7) | .335 |
| | Hypokalemia | 18 (19.4%) | 17 (18.7%) | |
| | Hyperkalemia | 2 (2.2%) | 6 (6.6%) | |
| ESR [mean ± SD, mm/h] | | 54.5 ± 5.3 | 63.14 ± 4.8 | .605 |
| CRP [median, mg/L] | | 58.7 | 89.5 | .109 |
| Cr [median, mg/dL] | | 0.9 | 0.95 | .802 |
| SGOT [median, U/L] | | 30 | 33 | .171 |
| SGPT [median, U/L] | | 24.5 | 29 | .404 |
| LDH [median, U/L] | | 574.5 | 698.5 | .075 |
| Consolidation | | 54 (58.1%) | 51 (57.3%) | .917 |
| Ground glass opacity | | 87 (94.6%) | 79 (88.8%) | .157 |
| Location of lesions | Disseminated | 60 (65.3%) | 48 (53.9%) | .685 |
| | Peripheral | 21 (22.8) | 12 (13.5%) | |
| | Bases | 7 (7.6%) | 19 (21.3%) | |
| | Apical | 1 (1.1%) | 7 (7.9%) | |
| | Peribronchovascular distribution | 3 (3.3%) | 3 (3.%) | |

**TABLE 1** (Continued)

| | Malignancy | | |
| --- | --- | --- | --- |
| | No | Yes | P-value |
| Bilaterality | 88 (94.6%) | 74 (82.2%) | .009 |
| Pleural effusion | 10 (10.8%) | 36 (40.4%) | .0001 |
| Lymphadenopathy | 9 (9.7%) | 20 (22.7%) | .017 |
| Calcification | 3 (3.2%) | 3 (3.4%) | 1 |
| **COVID-19 treatment data** | | | |
| $O_2$ therapy | 91 (97.8%) | 82 (91.1%) | .06 |
| Antibiotic therapy | 92 (98.9%) | 89 (98.9%) | 1 |
| Steroid therapy | 12 (12.9%) | 11 (12.4%) | 1 |
| Antiviral therapy | 56 (60.2%) | 51 (57.3%) | .690 |
| Mechanical ventilation | 10 (10.8%) | 21 (23.6%) | .021 |
| ICU admission | 14 (15.1%) | 22 (24.7%) | .102 |

*Note:* Bold numbers show the *p* values which are significant at the level of *p* < .05.

**TABLE 2** The characteristics of patients with malignancy

| | Frequency | Percent |
| --- | --- | --- |
| **Type of cancer** | | |
| Hematologic cancer | 31 | 33.3 |
| GI cancer | 23 | 24.7 |
| Lung cancer | 9 | 9.7 |
| Breast cancer | 8 | 8.6 |
| Urogenital cancers | 6 | 6.5 |
| Brain tumors | 5 | 5.4 |
| H&N cancer | 5 | 5.4 |
| GYN cancer | 3 | 3.2 |
| Melanoma | 1 | 1.1 |
| Sarcoma | 1 | 1.1 |
| Beast and endometrial cancer | 1 | 1.1 |
| **Stage** | | |
| Metastatic | 41 | 53.9 |
| Nonmetastatic | 33 | 43.9 |
| Relapse | 2 | 2.6 |
| **Current status** | | |
| Follow up | 40 | 44.0 |
| Chemotherapy | 35 | 38.5 |
| Radiotherapy | 2 | 2.2 |
| Targeted therapy | 4 | 4.4 |
| Hormone therapy | 6 | 6.6 |
| New case | 4 | 4.4 |

with a potential fivefold risk of severe events[4,5]; however, the data in this context is conflicting and there is evidence clearly demonstrated no significant effect of recent anticancer therapies on mortality of COVID-19.[6-8] Since COVID-19 is a new medical condition that most health care systems never faced before, data about different aspects of it, that is, high-risk population, criteria for admission of patients, and treatment options are lacking. For example, in Iran, there is no specific report on the features of cancer patients with COVID-19 and only two studies reported them as a part of the general single institutional studies.[9,10] Therefore, along with institutional-based recommendations on the management of patients with cancer suffering from COVID-19,[11,12] there is a need to assess the epidemiologic aspects of this medical situation. In this study, we aimed to assess the clinical features, laboratory values, treatment options, and outcomes of cancer patients admitted due to COVID-19 and compare them with data of COVID-19 infected patients without a history of cancer.

## 2 | METHODS

This case-control study was performed between February 20, 2020 and May 20, 2020 during the first peak of the COVID-19 pandemic in COVID-19 specific treatment centers of Mashhad, Iran. Mashhad is located in northeastern Iran and is the capital of Khorasan Razavi Province neighboring Afghanistan. With more than 6 million inhabitants, it is the second-most-populated city in Iran. Besides, this town is visited by millions of Iranian and international travelers monthly due to the presence of The Holy Shrine of Imam Reza.

The protocol of the study was approved by the Ethics Committee of Mashhad University of Medical Sciences (IR.MUMS.REC.1399.059) and a written informed consent form was obtained from the patients or the legal guardian. Medical documents of patients with malignancy admitted to the Imam Reza Educational Hospital, the Ghaem

patients experience the severe form of disease leading to a higher rate of mechanical ventilation, intensive care unit (ICU) admission, and mortality.[2,3] Patients with malignancy especially if they are on active anti-tumor treatments are among this high-risk population

**TABLE 3** Stepwise binary logistic regression on variables predicting the death in patients with COVID-19

|  | OR | 95% CI | | P-value |
|---|---|---|---|---|
| Age | 1.2 | .977 | 1.079 | .301 |
| Gender (male) | 1.9 | .327 | 3.684 | .881 |
| Comorbidities (yes) | .8 | .083 | 8.725 | .893 |
| Total number of comorbidities | 1.6 | .099 | 27.535 | .727 |
| DM (yes) | 2 | .130 | 31.423 | .614 |
| HTN (yes) | .3 | .025 | 5.227 | .456 |
| IHD/CHF (yes) | .6 | .022 | 17.620 | .777 |
| COPD (yes) | 4 | .062 | 259.718 | .514 |
| Malignancy (yes) | 8.4 | 1.780 | 39.918 | **.007** |
| Systolic blood pressure | 1.1 | .963 | 1.068 | .599 |
| Diastolic blood pressure | 1.4 | .928 | 1.086 | .921 |
| Moderate/severe hypoxemia (yes) | 2.2 | .071 | 12.101 | .068 |
| Tachycardia (yes) | .418 | .112 | 1.552 | .192 |
| Tachypnea (yes) | .157 | .004 | 6.577 | .331 |
| Fever (yes) | 2.9 | .309 | 28.004 | .348 |
| Neutropenia (yes) | .235 | .013 | 4.277 | .328 |
| Neutrophilia (yes) | .685 | .172 | 2.728 | .591 |
| Lymphopenia (yes) | 2.8 | .782 | 10.076 | .113 |
| Anemia (yes) | .201 | .036 | 1.127 | .068 |
| Thrombocytopenia (yes) | .278 | .065 | 1.196 | .086 |
| Bilateral lung involvement (yes) | .160 | .017 | 1.477 | .106 |
| $O_2$ therapy (yes) | .000 | .000 |  | .999 |
| Antibiotic therapy (yes) | 2.2 | .042 | 119.259 | .691 |
| Steroid therapy (yes) | .223 | .043 | 1.150 | .073 |
| Antiviral therapy (yes) | .698 | .191 | 2.550 | .587 |
| Mechanical ventilation (yes) | 3.3 | 1.52 | 10.35 | **.001** |
| ICU admission (yes) | .269 | .053 | 1.368 | .114 |

*Note:* Bold numbers show the *p* values which are significant at the level of *p* < .05.

**TABLE 4** An overview of recent data on COVID-19 and its impact on patients with malignancies

| Authors | Year | Country | Population | ICU admission | Mortality rate |
|---|---|---|---|---|---|
| Guan et al.[14] | 2019 | China | Non-cancer (1089) | 4.8% | 1.4% |
|  |  |  | Cancer (10) | 30% | 0 |
| Huang et al.[15] | 2020 | China | Non-cancer (40) | 31.7% | 15% |
|  |  |  | Cancer (1) | 0 | 0 |
| Yang et al.[16] | 2020 | China | Non-cancer (50) | 100% | 62% |
|  |  |  | Cancer (2) | 100% | 50% |
| Wang et al.[17] | 2020 | China | Non-cancer (128) | 25% | — |
|  |  |  | Cancer (10) | 40% |  |
| Lei et al.[18] | 2020 | China | Non-cancer (25) | 40% | 12% |
|  |  |  | Cancer (9) | 55.5% | 44.4% |
| Lee et al.[19] | 2020 | UK | Cancer (1044) | — | 28.2% |
| Erdal et al.[13] | 2021 | Turkey | Non-cancer (4412) | — | 1.51% |
|  |  |  | Cancer (77) |  | 23.9% |
| Present study | 2020 | Iran | Non-cancer (93) | 15.1% | 17.2% |
|  |  |  | Cancer (92) | 24.7% | 41.3% |

Educational Hospital, and the Shariati Educational Hospital are all affiliated to the Mashhad University of Medical Sciences because COVID-19 were assessed, prospectively. COVID-19 infected patients without previous history of malignancy from the same units were selected randomly and matched based on their gender and age. To perform a randomized selection of the non-malignant patient, they were sorted based on the date of admission and then were enrolled based on the computer-generated random number table.

The COVID-19 was diagnosed based on the presence of signs and symptoms of severe respiratory illness plus the evidence of lung involvement on the high-resolution CT (HRCT) of the chest with or without positive real-time polymerase chain reaction (RT-PCR) test for COVID-19. The decision to include patients only based on their HRCT chest was primarily made because of the limited resources in Iran during the first peak of COVID-19 and not performing the RT-PCR for all patients and the potential false negative of this procedure. The demographic data and signs, symptoms, and laboratory tests result of patients at the presentation were recorded and patients were followed up until the death or discharge. The primary objectives of the study were treatment options, mechanical ventilation, ICU admission, and the final outcome. The time interval between the last oncologic treatment and the beginning of COVID-19 was reported in patients on active oncologic treatments receiving (chemo+/−) radiotherapy or chemotherapy. The level of $O_2$ saturation on pulse oximetry was grouped as normal, mild ($O_2$sat = 90-95%), moderate ($O_2$sat = 90-75%), and severe ($O_2$sat < 75%) hypoxemia.

The sample size was estimated to be at least 33 COVID-19 infected patients in each group based on the results of Erdal et al.[13] who showed that the mortality rates of COVID-19 infected patients with and without malignancy was 23.9% and 1.5%, respectively; using $n = (Z\alpha/2 + Z\beta)2 * (p1(1 − p1) + p2(1 − p2))/(p1 − p2)2$ with a confidence interval of 95% and poser of 90%.

Data were analyzed by SPSS-21 using chi-square and Fisher exact tests for categorical variables and independent $t$-test for quantitative data (or Mann-Whitney $U$ test is a nonparametric test in case of the absence of normal distribution which was tested by Shapiro-Wilk test) at the level of $P \leq .05$. To assess the most parsimonious set of predictors that are most effective in predicting the death [odd ration (OR)], stepwise binary logistic regression was used.

## 3 | RESULTS

Between 20 February 2020 and 20 May 2020, 3373 patients with the diagnosis of COVID-19 were admitted at COVID-19 specific treatment centers of Mashhad, Iran. In this research, 93 non-malignant patients and 92 patients with malignancy admitted for COVID-19 were enrolled. The rate of positive PCR for COVID-19 was significantly higher in non-malignant patients (64% vs 35.1%, P-value = .0001). Comparing COVID-19 infected malignant patients with COVID-19 infected patients without malignancy, non-malignant patients had higher rates of comorbidities (P-value = .014) notably diabetes mellitus (P-value = .006). COVID-19 related mortality rate in malignant patients was significantly higher (41.3% vs 17.2%, P-value = .0001), however, the cause of death was similar between the groups mostly due to acute respiratory distress syndrome (50% vs 60%), multiple organ dysfunction syndromes (41.7% vs 40%), and cardiac arrest (8.3% vs 0%) by P-value = .483. The time interval to admission after the onset of COVID-19 symptoms in malignant and non-malignant patients was 7.16 ± 5.3 and 7.01 ± 7 days (P-value = .089). Also, the duration of admission was the same (medians; 8 vs 6.5 days,

P-value = .155). Table 1 shows characteristics of COVID-19 infected patients with and without malignancy in detail.

As shown in Table 2, most patients with malignancy suffered from hematologic and gastrointestinal cancers (33.3% and 24.7%) that 53.9% of them had metastatic disease. In patients on active treatment (except hormone therapy), the median time interval between the last oncologic treatment and COVID-19 infection was 20 [95%CI 17-29] days.

Regression analysis showed that the risk of death increased significantly in patients with malignancy (OR = 8.4, P = .007) and mechanical ventilation (OR = 3.3, P-value = .034) independent of other variables (Table 3).

Subsequently, the stepwise binary logistic regression was performed in COVID-19 infected patients with cancer to define the predisposing factors of death. However, no factor can predict the outcome including the type of malignancy, stage of the disease, and recent oncologic treatment (chemotherapy or radiotherapy, data not presented).

## 4 | DISCUSSION

This study aimed to assess the clinical features, laboratory values, treatment options, and outcomes of cancer patients admitted due to COVID-19 and compare them with data of COVID-19 infected patients without a history of cancer. Our results showed that mortality was significantly higher in cancer patients infected by COVID-19, although the comorbidities especially diabetes mellitus were more prevalent in non-malignant patients. Moreover, the probability of positive PCR for CODIV-19 was significantly higher in non-malignant patients. Regression analysis showed that the risk of death in COVID-19 infected patients with malignancy was about nine times more than other patients. Also, the patients who needed mechanical ventilation had a significantly higher mortality rate. An overview of recent data on COVID-19 and its impact on patients with malignancies has been provided in Table 4.

As stated earlier, there are limited data on the potential interaction of COVID-19 and malignancy and its treatments, and this specific category of COVID-19 infected patients accounts for a small portion of patients in the recent studies.[14,15,20] However, studies from China, Europe, and the United States proposed the predisposing role of malignancy on the increased mortality rate of COVID-19 with higher rates for patients with active cancer receiving the anti-cancer treatments.[4,7,19,21] Although, there is not a general agreement in this context with lower mortality rates in cancer patients with COVID-19.[6,17]

Our study showed that cancer patients might present less with typical symptoms of COVID-19 and COVID-19 infected patients with malignancy reported a lower frequency of fever and dry cough comparing previous studies.[5,18] However, studies are confirming our results regarding obscuring the main presentation of COVID-19 in cancer patients.[22] Also, the rate of neutropenia, anemia, and thrombocytopenia which mainly had been the side-effects of chemotherapy

was higher in our study as expected. Besides, pleural effusion and lymphadenopathy were reported significantly higher in patients with malignancy that we believed is related to the underlying malignant condition.

Our study has some limitations. Due to limited resources during the first peak of pandemic and special economic conditions of Iran, it was not possible to do PCR tests for all patients and therefore, we had to enroll patients only based on pulmonary symptoms and radiography. Also, our analyses were based on patients with symptomatic cancer admitted to COVID-19 specific treatment centers of Mashhad, and patients who managed in an outpatient setting or were asymptomatic were not included. Therefore, the cohort might not be entirely representative of all patients with cancer. Patients on an end-of-life care pathway would be unlikely to be included in the current study.

## 5 | CONCLUSION

The results suggest that cancer patients who were infected by COVID-19 are at higher risk of mortality independent of the demographic data, comorbidities, and treatments. Also, the false-negative rate of PCR may be higher in COVID-19 infected patients with malignancy and they might present with atypical presentation leading to delay diagnosis, collectively.

## AUTHOR CONTRIBUTIONS
**Soodabeh Shahidsales:** Conceptualization; project administration; supervision; validation. **Seyed Amir Aledavood:** Investigation; methodology; writing-review & editing. **Mona Joudi:** Investigation; methodology; project administration; visualization; writing-review & editing. **Fatemeh Molaie:** Conceptualization; data curation; formal analysis; investigation; methodology. **Habibollah Esmaeili:** Formal analysis; methodology; software; visualization; writing-original draft. **Seyed Alireza Javadinia:** Conceptualization; formal analysis; investigation; methodology; writing-original draft; writing-review & editing.

## CONFLICT OF INTEREST
The authors declare that there is no conflict of interest to be reported.

## ETHICAL STATEMENT
The protocol of the study was approved by the Ethics Committee of Mashhad University of Medical Sciences (IR.MUMS.REC.1399.059) and a written informed consent form was obtained from the patients or the legal guardian.

## DATA AVAILABILITY STATEMENT
All data generated and analyzed during this study can be accessible through direct communication with corresponding author and agreement of all research team members.

## ORCID
*Fatemeh Molaie* https://orcid.org/0000-0002-7267-9943
*Seyed Alireza Javadinia* https://orcid.org/0000-0003-2467-837X

## REFERENCES
1. World Health Organization. *Coronavirus Disease (COVID-19): Weekly Epidemiological Update*. 2020. https://www.who.int/publications/m/item/covid-19-weekly-epidemiological-update.
2. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA*. 2020;323 (18):1775-1776. https://doi.org/10.1001/jama.2020.4683.
3. Zhang J, Wang X, Jia X, et al. Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan, China. *Clin Microbiol Infect*. 2020;26(6):767-772. https://doi.org/10.1016/j.cmi.2020.04.012.
4. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol*. 2020;21(3): 335-337.
5. Zhang L, Zhu F, Xie L, et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. *Ann Oncol*. 2020;31(7):894-901. https://doi.org/10.1016/j.annonc.2020.03.296.
6. Kuderer NM, Choueiri TK, Shah DP, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet*. 2020; 395(10241):1907-1918. https://doi.org/10.1016/s0140-6736(20) 31187-9.
7. Lee LY, Cazier JB, Angelis V, et al. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet*. 2020;395(10241):1919-1926. https://doi.org/10.1016/S0140-6736(20)31173-9. Epub 2020 May 28. Erratum in: Lancet. 2020 Aug 22;396(10250):534. PMID: 32473682; PMCID: PMC7255715.
8. Vuagnat P, Frelaut M, Ramtohul T, et al. COVID-19 in breast cancer patients: a cohort at the Institut Curie Hospitals in the Paris area. *Breast Cancer Res*. 2020;22:1-10.
9. Alamdari NM, Afaghi S, Rahimi FS, et al. Mortality risk factors among hospitalized COVID-19 patients in a major referral center in Iran. *Tohoku J Exp Med*. 2020;252(1):73-84.
10. Nikpouraghdam M, Jalali Farahani A, Alishiri G, et al. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in IRAN: a single center study. *J Clin Virol*. 2020;127:104378. https://doi.org/10.1016/j.jcv.2020.104378.
11. Rakhsha A, Azghandi S, Taghizadeh-Hesary F. Decision on chemotherapy amidst COVID-19 pandemic: a review and a practical approach from Iran. *Infect Chemother*. 2020;52(4):496-502. https://doi.org/10.3947/ic.2020.52.4.496.
12. Siavashpour Z, Taghizadeh-Hesary F, Rakhsha A. Recommendations on management of locally advanced rectal cancer during the COVID-19 pandemic: an Iranian consensus. *J Gastrointest Cancer*. 2020;51(3):800-804. https://doi.org/10.1007/s12029-020-00454-4.
13. Erdal GS, Polat O, Erdem GU, et al. The mortality rate of COVID-19 was high in cancer patients: a retrospective single-center study. *Int J Clin Oncol*. 2021;1-9. https://doi.org/10.1007/s10147-021-01863-6. Epub ahead of print. PMID: 33486624; PMCID: PMC7826293.

14. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382(18):1708-1720. https://doi.org/10.1056/NEJMoa2002032.

15. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395 (10223):497-506. https://doi.org/10.1016/S0140-6736(20)30183-5.

16. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med*. 2020;8 (5):475-481. https://doi.org/10.1016/s2213-2600(20)30079-5.

17. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061-1069. https://doi.org/10.1001/jama.2020.1585.

18. Lei S, Jiang F, Su W, et al. Clinical characteristics and outcomes of patients undergoing surgeries during the incubation period of COVID-19 infection. *EClinicalMedicine*. 2020;21:100331. https://doi.org/10.1016/j.eclinm.2020.100331.

19. Lee LYW, Cazier J-B, Starkey T, et al. COVID-19 prevalence and mortality in patients with cancer and the effect of primary tumour subtype and patient demographics: a prospective cohort study. *Lancet Oncol*. 2020;21(10):1309-1316. https://doi.org/10.1016/S1470-2045(20)30442-3.

20. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507-513. https://doi.org/10.1016/S0140-6736(20)30211-7.

21. Passamonti F, Cattaneo C, Arcaini L, et al. Clinical characteristics and risk factors associated with COVID-19 severity in patients with haematological malignancies in Italy: a retrospective, multicentre, cohort study. *Lancet Haematol*. 2020;7(10):e737-e745. https://doi.org/10.1016/S2352-3026(20)30251-9.

22. Yang F, Shi S, Zhu J, Shi J, Dai K, Chen X. Clinical characteristics and outcomes of cancer patients with COVID-19. *J Med Virol*. 2020;92 (10):2067-2073. https://doi.org/10.1002/jmv.25972.