Clinical characteristics and risk factors for mortality of hospitalized cancer patients with COVID-2019 in Mecca, Saudi Arabia

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Abstract:
BACKGROUND: Cancer patients are particularly vulnerable during the coronavirus disease 2019 (COVID-19) pandemic. This study aimed to evaluate clinical characteristics and mortality among cancer patients with COVID-19.

METHODS: This retrospective, observational cohort study included 53 patients with a malignancy and reverse-transcription polymerase chain reaction-confirmed severe acute respiratory syndrome coronavirus-2 infection in a tertiary care center in Mecca, Saudi Arabia, from March 14, 2020, to October 29, 2020. Clinical, laboratory, and radiological data were collected from institutional electronic records and analyzed.

RESULTS: Overall, 53 patients (62% male) were enrolled. The mean age of the patients was 54.9 ± 19.0 years, with 76% aged <65 years. The most common symptoms were fever (66%), dry cough (40%), and dyspnea (36%). Most infections (89%) were community acquired. Hematological malignancies (36%) were the most common cancer type. The most common solid tumors were breast cancer (23%) and colon cancer (9%). Just over half (51%) had a stage 4 tumor, and 30% of the patients had received chemotherapy within 2 weeks before the onset of COVID-19 symptoms. Initial chest radiographs showed pneumonia in 43% of patients; 38%, 9%, and 6% required oxygen support, intensive care unit admission, and invasive mechanical ventilation, respectively. The most common complication was secondary bacterial infection (13.2%). The all-cause mortality rate was 17%. In the multivariable logistic regression, dyspnea, leukocytosis, use of systemic steroids, and secondary bacterial infection were found to be risk factors for death.

CONCLUSION: Hospitalized cancer patients with COVID-19 have a high mortality rate. Our study finds a correlation between multiple independent risk factors and mortality. Patients with dyspnea, leukocytosis, systemic steroid use, or secondary bacterial infection require more care, attention, and possibly more aggressive treatment.

Keywords: Cancer, COVID-19, mortality, Saudi Arabia

The COVID-19 outbreak has heavily impacted a wide range of vulnerable patient groups since it was declared a pandemic by the World Health Organization in March 2020.[1] Cancer patients are particularly vulnerable to COVID-19, as they have a greater risk of serious clinical events and mortality than those without cancer.[2] This is attributed to immunosuppression as a result of cancer itself and its associated treatment. Providing care for cancer patients...
during the COVID-19 pandemic is difficult because they require frequent hospital visits and are more susceptible to infection than healthy people owing to their immunocompromised status.\textsuperscript{1,4}

Few studies have focused on this distinct group of patients, such as those by Liang \textit{et al.} and Mehta \textit{et al.} in China and the USA, respectively.\textsuperscript{2,3}

In our study, we aimed to assess the clinical characteristics of the studied patients, track their clinical course and outcome, and identify specific risk factors associated with mortality rate.

\section*{Methods}

\subsection*{Study design and participant selection}

This retrospective study included all hospitalized cancer patients with COVID-19 at King Abdullah Medical City (KAMC), Mecca, Saudi Arabia, from March 14, 2020, when the COVID-19 hospital committee started releasing the daily COVID-19 patient list, till the end of the study on October 29, 2020. We included male and female patients who were older than 12 years and had a confirmed hematological or solid malignancy. Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection was confirmed with reverse transcription–polymerase chain reaction (RT-PCR) testing of nasopharyngeal samples.

\subsection*{Study procedures and outcomes}

A checklist was prepared to collect patient data from institutional electronic medical records using the electronic filing system. The collected data included clinical features such as demographics, comorbidities, symptomatology, and physical examination findings. We collected the result of laboratory tests that included complete blood count, electrolytes, inflammatory markers, liver, and renal profiles. The administered therapy, clinical course, and outcome were collected as well. The primary outcome was the identification of risk factors for mortality.

\subsection*{Ethical approval}

The Institutional Review Board of KAMC approved this study (approval number: 20–665). The requirement for informed consent was waived because the study was a retrospective record review.

\subsection*{Statistical analysis}

Data were analyzed using STATA/IC version 16.1 software (StataCorp LLC, College Station, TX, USA). Qualitative data were expressed as numbers and percentages, and the Fisher’s exact test was used to assess the relationship between variables. Quantitative data were expressed as mean and standard deviation, and the Mann–Whitney U- and Kruskal–Wallis tests were applied for continuous variables with a skewed distribution. Binary logistic regression was used to assess the independent predictors (risk factors) for COVID-19 severity and mortality. Multivariate models were adjusted for age, sex, body mass index (BMI) >30 kg/m\textsuperscript{2}, nature of malignancy (hematological versus solid), and intensive care unit (ICU) admission. The variables were selected based on previous studies and clinical relevance. Two-tailed \( P < 0.05 \) indicated statistical significance.

\section*{Results}

A total of 53 patients (62.3\% male) were enrolled in this study. The mean age of the patients was 54.9 ± 19.0 years, with 75.5\% aged <65 years. The mean BMI was 27.24 ± 5.79 kg/m\textsuperscript{2}. Most (66.0\%) had a fever, with a mean fever duration of 3.4 ± 3.5 days. Other common symptoms were dry cough (39.6\%), sore throat (17.0\%), and dyspnea (35.8\%). Only 18.9\% had fatigue, myalgia, or gastrointestinal symptoms; 1.9\% had anosmia/dysgeusia. Five cancer patients (11.4\%) had a hospital-acquired COVID-19 infection. The most common type of cancer was hematological malignancy (35.8\%), while the most common solid tumors were breast cancer (22.6\%) and colon cancer (9.4\%). Just over half (50.9\%) of the patients had a stage 4 tumor [Table 1]. Approximately 30.2\%, 11.3\%, and 7.5\% of patients had received chemotherapy, immunotherapy, and hormonal therapy, respectively, within 2 weeks before the onset of infection. Almost all patients (96.2\%) received venous thromboembolism prophylaxis; 64.2\% received antibiotics and 43.4\% had pneumonia on initial chest radiography. A total of 24.5\% received lopinavir/ritonavir, ribavirin, and interferons as an antiviral treatment. About one-third of patients (37.7\%) needed oxygen support, and 5.7\% needed mechanical ventilation (MV). The most common complications were secondary bacterial infection (13.2\%) and the need for ICU admission (9.4\%). The mean period from symptom onset to viral clearance and the mean duration of ICU stay, MV, and total hospital stay were 20.6 ± 19.25, 0.19 ± 0.39, 1.51 ± 5.4, and 1.06 ± 4.95 days, respectively. One-quarter of the patients (24.5\%) had a C-reactive protein (CRP) level >10 mg/dL, 39.6\% had a D-dimer level >1 µg/mL, and 30.2\% had a ferritin level >600 ng/mL [Table 2]. Nine patients (16.9\%) died.

Male patients and patients aged <65 years had significantly higher survival rates. Conversely, mortality was significantly more likely in patients with the following characteristics: dyspnea on initial presentation; receipt of favipiravir and tocilizumab as antiviral treatments, systemic steroids, or vasopressor support; requirement for dialysis; leukocytosis; D-dimer levels >1 µg/mL; older age; longer duration of MV...
and total hospital stay; and complications during hospitalization (secondary bacterial infection and cerebrovascular events, acute coronary syndrome, acute respiratory distress syndrome [ARDS], septic shock, ICU admission, and requirement for MV) [Tables 3 and 4].

The multivariable logistic regression analysis found that dyspnea odds ratio (OR) 33.26, leukocytosis OR 81.37, use of systemic steroids OR 22.99, and secondary bacterial infection OR 23.39 were risk factors for death [Table 5].

### Discussion

Cancer patients are at an increased risk of mortality following SARS-CoV-2 infection, owing to their underlying malignancy and treatment-associated immunosuppression. We described the clinical characteristics and risk of mortality of 53 patients with confirmed solid and hematological malignancies and RT-PCR-confirmed SARS-CoV-2 infection in a tertiary care center in Mecca, Saudi Arabia. We found that 11% of the SARS-CoV-2 cases were due to nosocomial transmission. This finding indicates the need for strict infection control measures, especially in cancer patients.

The case fatality rate in our cohort was 17%. This mortality rate is much higher than that in the general population (2.3%).[6] Previous studies have reported that the mortality rate of patients infected with SARS-CoV-2 is higher among cancer patients than among noncancer patients. Mehta et al.[5] reported a 28% mortality rate in a series of 218 cancer patients with SARS-CoV-2 infection evaluated at Montefiore Network Medical Centers in New York. Lee et al.[7] and Yang et al.[8] reported mortality rates of 30.6% and 20%, respectively, in cancer patients with SARS-CoV-2 infection.

Our results were consistent with those of Mehta et al.,[5] who reported that hematological malignancies were associated with a higher mortality rate than solid malignancies in patients with COVID-19. However, in...
Table 2: Clinical and laboratory findings and treatment of cancer patients with coronavirus disease-2019 (n=53)

| Variable                                      | n (%)               |
|-----------------------------------------------|---------------------|
| On chemotherapy (within 2 weeks)              | 16 (30.2)           |
| On immunotherapy (within 2 weeks)             | 6 (11.3)            |
| On hormonal therapy (within 2 weeks)          | 4 (7.5)             |
| Antiviral treatment                           |                     |
| No                                            | 16 (30.2)           |
| Lopinavir/ritonavir/ribavirin/IF              | 13 (24.5)           |
| Favipiravir                                    | 11 (20.8)           |
| Lopinavir/ritonavir/ribavirin/IF and favipiravir| 10 (18.9)          |
| Favipiravir and tocilizumab                   | 3 (5.7)             |
| Other treatment                               |                     |
| Hydroxychloroquine                            | 9 (17)              |
| Systemic steroids                             | 16 (30.2)           |
| Vasopressor support                           | 3 (5.7)             |
| Antibiotics                                    | 34 (64.2)           |
| Dialysis                                       | 2 (3.8)             |
| Venous thromboembolism prophylaxis            | 51 (96.2)           |
| Initial chest radiography (pneumonia)         | 23 (43.4)           |
| O₂ support                                     |                     |
| No                                            | 3 (56.6)            |
| Regular O₂                                     | 18 (34)             |
| NRM                                           | 1 (1.9)             |
| High-flow nasal cannula                        | 1 (1.9)             |
| Mechanical ventilation                         | 3 (5.7)             |
| Complications                                  |                     |
| Superadded bacterial infection                 | 7 (13.2)            |
| CVA                                           | 2 (3.8)             |
| ACS                                           | 1 (1.9)             |
| Acute respiratory distress syndrome            | 3 (5.7)             |
| Septic shock                                   | 3 (5.7)             |
| ICU admission                                  | 5 (9.4)             |
| Mechanical ventilation                         | 3 (5.7)             |
| Days in ICU                                    | 0.19±0.39           |
| Days on mechanical ventilation                 | 1.51±5.40           |
| Total hospital stays                           | 1.06±4.95           |
| Days from the beginning of symptoms to viral clearance | 20.60±19.25 |
| Laboratory findings                           |                     |
| Leukopenia                                     | 12 (22.6)           |
| Leukocytosis                                   | 12 (22.6)           |
| Neutrophilia                                   | 17 (32.1)           |
| White blood cell (mean±SD)                    | 8.96±10.27          |
| Lymphocytes (mean±SD)                         | 2.33±7.96           |
| Hemoglobin (mean±SD)                          | 10.65±2.30          |
| Platelets (mean±SD)                           | 244.51±114.68       |
| Albumin (mean±SD)                             | 2.54±0.62           |
| Creatinine (mean±SD)                          | 0.90±0.81           |
| Lactate dehydrogenase (mean±SD)               | 517.77±385.48       |
| D-dimer (mean±SD)                             | 2.78±4.06           |
| Troponin (mean±SD)                            | 1.27±2.25           |
| Fibrinogen (mean±SD)                          | 5.29±1.80           |
| Ferritin (mean±SD)                            | 822.33±1004.6       |
| C-reactive protein (mean±SD)                  | 8.27±7.95           |
| Erythrocyte sedimentation rate (mean±SD)      | 73.47±45.44         |

Table 2: Contd.

| Variable                                    | n (%)               |
|---------------------------------------------|---------------------|
| Procalcitonin (mean±SD)                     | 4.49±18.04          |
| AST (mean±SD)                               | 49.91±38.19         |
| ALT (mean±SD)                               | 40.92±54.57         |
| High neutrophil: lymphocyte ratio           | 32 (60.4)           |
| C-reactive protein (mg/dL)                  |                     |
| Normal (<0.29)                              | 2 (3.8)             |
| 0.29-10                                     | 33 (62.3)           |
| >10                                         | 13 (24.5)           |
| Unspecified                                 | 5 (9.4)             |
| D-dimer (µg/mL)                             |                     |
| Normal (<252)                               | 6 (11.3)            |
| 0.55-1                                      | 20 (37.7)           |
| >1                                          | 21 (39.6)           |
| Unspecified                                 | 6 (11.3)            |
| Ferritin (ng/mL)                            |                     |
| Normal (<252)                               | 10 (18.9)           |
| 252-600                                     | 12 (22.6)           |
| >600                                        | 16 (30.2)           |
| Unspecified                                 | 15 (28.3)           |
| Low hemoglobin                              | 18 (34)             |
| Low platelets                               | 12 (22.6)           |
| Low albumin                                 | 51 (96.2)           |
| High creatinine                             | 11 (20.8)           |
| High low-density lipoprotein                | 39 (73.6)           |
| High fibrinogen                             | 25 (47.2)           |
| High erythrocyte sedimentation rate         | 40 (75.5)           |
| High procalcitonin                          | 9 (17)              |
| High AST                                    | 18 (34)             |
| High ALT                                    | 6 (11.3)            |

ACS=Acute coronary syndrome, ALT=Alanine aminotransferase, AST=Aspartate aminotransferase, CVA=Cerebrovascular accident, ICU=Intensive care unit, IF=Interferon, NRM=Nonrebreather mask, SD=Standard deviation

In our study, the difference was not found to be statistically significant, the value of P was 0.555.

Patients with hematological malignancies may potentially be more susceptible to cytokine storms, owing to hyperinflammation that is related to disturbances in myeloid and lymphocyte cell compartments.\[9\]

We found that dyspnea on initial presentation was an independent risk factor for mortality and was correlated with the presence of pneumonia on initial chest radiography. Pneumonia on initial chest radiography was present in 43.4% of the total cohort, and two-thirds of these patients died. Univariate regression analysis suggested that age >65 years was associated with an increased risk of mortality; however, correction for other confounders in the multivariate regression analysis indicated that age >65 years was not a significant factor for mortality. Yang et al.,[8] and Asghar et al.,[10] reported similar results. In contrast, a study conducted by Lee et al.[11] found that the risk of mortality increased with age.
Table 3: Comparison of outcomes in cancer patients with coronavirus virus-2019 across patient and cancer characteristics (n=53)

| Variable                                      | Outcome                  | P      |
|-----------------------------------------------|--------------------------|--------|
| Age (mean±SD)                                 |                          |        |
| <65                                           | 51.43±18.61              | 0.001* |
| ≥65                                           | 71.67±10.63              |        |
| Sex                                           |                          |        |
| Female                                        | 14 (70)                  | 0.049  |
| Male                                          | 30 (90.9)                |        |
| BMI (mean±SD)                                 |                          |        |
| <30                                           | 27.60±5.97               | 0.387**|
| ≥30                                           | 25.44±4.72               |        |
| Symptoms                                      |                          |        |
| Fever                                         | 29 (65.9)                | 0.9651 |
| Dry cough                                     | 8 (40.9)                 | 0.672  |
| Sore throat                                   | 7 (15.9)                 | 0.646  |
| Dyspnea                                       | 11 (25)                  | <0.001 |
| Fatigue                                       | 9 (20.5)                 | 0.514  |
| Myalgia                                       | 9 (20.5)                 | 0.514  |
| Diarrhea/nausea/vomiting                      | 10 (22.7)                | 0.1121 |
| Anosmia/dysgeusia                             | 1 (2.3)                  | 0.648  |
| Community acquired versus hospital acquired   |                          |        |
| Community acquired                            | 39 (88.6)                | 0.983  |
| Hospital acquired                             | 5 (11.4)                 |        |
| System involved                               |                          |        |
| Breast                                        | 12 (27.3)                | 0.384  |
| Gastrointestinal tract                        | 9 (20.5)                 |        |
| Gynecological                                 | 4 (9.1)                  |        |
| Hematological                                 | 15 (34.1)                |        |
| Respiratory                                   | 2 (4.5)                  |        |
| Skin                                          | 1 (2.3)                  |        |
| Urology                                       | 1 (2.3)                  |        |
| Type of malignancy                            |                          |        |
| Breast cancer                                 | 12 (27.3)                | 0.482  |
| Cancer colon                                  | 4 (9.1)                  |        |
| Colorectal cancer                             | 0                       |        |
| Folliculotropic mycosis fungoides             | 1 (2.3)                  |        |
| Ileocecal metastasis                          | 1 (2.3)                  |        |
| Leukemia                                      | 7 (15.9)                 |        |
| Lung cancer                                   | 2 (4.5)                  |        |
| Lymphoma                                      | 7 (15.9)                 |        |
| Metastatic gallbladder cancer                  | 1 (2.3)                  |        |
| Myeloma                                       | 1 (2.3)                  |        |
| Esophageal cancer                             | 1 (2.3)                  |        |
| Ovarian cancer                                | 1 (2.3)                  |        |
| Pancreatic cancer                             | 0                       |        |
| Prostate cancer/HCC                           | 1 (0.0)                  |        |
| Prostate cancer                               | 1 (2.3)                  |        |
| Stomach cancer                                | 1 (2.3)                  |        |
| Uterine cancer                                | 3 (6.8)                  |        |
| Hematological versus solid malignancy         |                          |        |
| Solid                                         | 29 (65.9)                | 0.555  |
| Hematological                                 | 15 (34.1)                | 0.556  |
| Stage 4 versus non-stage 4 solid malignancy   |                          |        |
| Non-stage 4                                   | 14 (38.9)                | 0.293  |
| Stage 4                                       | 22 (61.1)                |        |

*Independent sample t-test, **Mann-Whitney (U-test). BMI=Body mass index, HCC=Hepatocellular carcinoma, SD=Standard deviation
### Table 4: Relationship between patient treatment, laboratory results, treatment, hospital stay, and days from the beginning of symptoms to viral clearance in cancer patients with coronavirus virus-2019 (n=53)

| Variable                                      | Survived | Died | P        |
|-----------------------------------------------|----------|------|----------|
| **Patient age (mean±SD)**                     | 51.43±18.61 | 71.67±10.63 | 0.001*  |
| **BMI (mean±SD)**                             | 27.60±5.97 | 25.44±4.72 | 0.387** |
| **Days of fever (mean±SD)**                   | 3.11±3.46 | 4.78±3.80 | 0.145*  |
| On chemotherapy (within 2 weeks)              | 14 (31.8) | 2 (22.2) | 0.568   |
| On immunotherapy (within 2 weeks)             | 5 (11.4)  | 1 (11.1)  | 0.983   |
| On hormonal therapy (within 2 weeks)          | 2 (4.5)   | 2 (22.2) | 0.069   |
| **Antiviral treatment**                       |          |      |         |
| No                                            | 16 (36.4) | 0    | 0.047   |
| Lopinavir/ritonavir/ribavirin/interferon       |11 (25)    | 2 (22.2) |          |
| Favipiravir                                    | 7 (15.9)  | 3 (33.3) |          |
| Lopinavir/ritonavir/ribavirin/interferon and favipiravir | 9 (20.5) | 2 (22.2) |          |
| Favipiravir and tocilizumab                    | 1 (2.3)   | 2 (22.2) |          |
| **Other treatment**                           |          |      |         |
| Hydroxychloroquine                            | 7 (15.9)  | 2 (22.2) | 0.646   |
| Systemic steroids                             | 8 (18.2)  | 8 (88.9) | <0.001  |
| Vasopressor support                           | 0         | 3 (33.3) | <0.001  |
| Antibiotics                                   | 27 (61.4) | 7 (77.8) | 0.349   |
| Need for dialysis                             | 0         | 2 (22.2) | 0.001   |
| Venous thromboembolism prophylaxis            | 42 (95.5) | 9 (100) | 0.514   |
| Initial chest radiography (pneumonia)         | 17 (38.6) | 6 (66.7) | 0.122   |
| **Laboratory findings**                       |          |      |         |
| Leukopenia                                    | 12 (27.3) | 0    | 0.075   |
| Leukocytosis                                   | 5 (11.4)  | 7 (77.8) | <0.001  |
| Neutrophilia                                   | 17 (38.6) | 0    | 0.024   |
| High neutrophil/lymphocyte ratio              | 25 (61.4) | 7 (55.6) | 0.241   |
| C-reactive protein                            |          |      |         |
| Normal                                        | 2 (4.5)   | 0    | 0.253   |
| 0.29-10                                       | 29 (65.9) | 4 (44.4) |          |
| >10                                           | 9 (20.5)  | 4 (44.4) |          |
| High D-dimer                                  |          |      |         |
| Normal                                        | 6 (13.6)  | 0    | 0.003   |
| 0.55-1                                        | 20 (45.5) | 0    |          |
| >1                                            | 13 (29.5) | 8 (88.9) |          |
| Ferritin                                      |          |      |         |
| Normal                                        | 9 (20.5)  | 1 (11.1) | 0.219   |
| Yes                                           | 11 (25)   | 1 (1.1)  |          |
| >600                                          | 11 (25)   | 5 (55.6) |          |
| Low platelets                                 | 9 (20)    | 3 (33.3) | 0.4     |
| Low albumin                                   | 42 (95.5) | 9 (100) | 0.514   |
| High creatinine                               | 7 (16.3)  | 4 (36.4) | 0.054   |
| High low-density lipoprotein                  | 31 (15.9) | 8 (44.4) | 0.452   |
| High fibrinogen                               | 18 (40.9) | 7 (77.8) | 0.117   |
| High erythrocyte sedimentation rate           | 32 (72.7) | 8 (88.9) | 0.498   |
| High procalceitonin                           | 6 (13.6)  | 3 (33.3) | 0.349   |
| High AST                                      | 15 (34.1) | 3 (33.3) | 0.965   |
| High ALT                                      | 6 (13.6)  | 0    | 0.239   |
| **Complications**                             |          |      |         |
| O₂ support                                     |          |      |         |
| No                                            | 29 (65.9) | 1 (11.1) | <0.001  |
| Regular O₂                                     | 14 (31.8) | 4 (44.4) |          |
| NRM                                           | 0         | 1 (11.1) |          |
| High-flow nasal cannula                       | 1 (2.3)   | 0    |          |
| Mechanical ventilation                        | 0         | 3 (33.3) |          |

Contd...
Sixteen patients (30%) underwent chemotherapy within 2 weeks before COVID-19 onset, but this was not associated with an increased risk of mortality. This result is consistent with that of a study conducted by Jee et al. who found that recent cytotoxic chemotherapy was not associated with adverse COVID-19 outcomes. Asghar et al. also found no significant difference in mortality in a retrospective cohort of cancer patients with COVID-19 who received chemotherapy within 4 weeks before the onset of symptoms. Lee et al. conducted a prospective observational study on 800 cancer patients with symptomatic COVID-19 and also reported that chemotherapy in the past 4 weeks had no significant effect on mortality due to COVID-19. In contrast, Zhang et al. found that cancer treatment within 14 days of COVID-19 diagnosis was a risk factor for the composite endpoint of ICU admission, the requirement for MV, or death.
et al.\cite{10} also reported that patients who had undergone chemotherapy or surgery in the preceding month had a higher risk of clinically severe events (ICU admission, requirement for invasive ventilation, or death) than those not receiving chemotherapy or surgery. Lee et al.\cite{7} found that patients with hematological malignancies who had recently undergone chemotherapy had an increased risk of death during COVID-19-associated hospital admissions. Yang et al.\cite{8} found that receiving chemotherapy within 4 weeks before the onset of COVID-19 symptoms was a risk factor for in-hospital death. They speculated that receiving systemic anticancer treatments increases the risk of mortality in patients with COVID-19 due to the increased risk of immunosuppression. However, withholding effective cancer treatments during the pandemic poses the risk of increased cancer morbidity and mortality; furthermore, the risk posed by untreated cancers may be greater than that posed by COVID-19. Different studies have yielded conflicting results in this regard. Considering the prolonged period of the COVID-19 pandemic, patients with cancer should not be prevented from receiving critical antitumor treatment on the grounds that it increases the risk of death if they acquire SARS-CoV-2 infection. The decision to proceed with antitumor therapy should be based on the risk–benefit ratio, and the clinician should decide the best option for the patient on a case-by-case basis.

On multivariate regression analysis, we found that administering systemic steroids to our patients was an independent risk factor for mortality. However, due to the retrospective design of this study, we were unable to exclude the effects of confounding by indication. Using systemic steroids prolongs the viral shedding time and has an immunosuppressive effect that is often associated with an increased risk of superimposed infections, especially in patients on MV.\cite{14-16} Conversely, steroids have a systemic anti-inflammatory effect that could minimize the development of severe pneumonia and ARDS.\cite{17} However, previous studies found that steroid therapy did not improve clinical outcomes among patients with SARS or Middle East respiratory syndrome.\cite{15,16} The majority of studies that have evaluated the effect of steroids in COVID-19 patients have been conducted on noncancer patients. Liu et al.\cite{17} found that the administration of corticosteroids in patients with severe COVID-19-related ARDS was associated with an increased 28-day mortality rate and delayed SARS-CoV-2 ribonucleic acid clearance. Zhang et al.\cite{13} reported that steroid treatment did not reduce the incidence of severe events. Similarly, Zha et al.\cite{18} found no association between steroid therapy and outcomes in patients without ARDS. In systematic analysis, Wang et al.\cite{19} found that steroid use in patients with severe COVID-19 delayed viral clearance and did not markedly improve survival. No prior randomized controlled trials have assessed the safety and effectiveness of steroids in cancer patients with COVID-19. Although the RECOVERY Trial found that the use of dexamethasone in hospitalized noncancer patients with COVID-19 resulted in lower 28-day mortality among those who were receiving either invasive MV or oxygen alone,\cite{20} it is not known whether administering dexamethasone to immunocompromised cancer patients with COVID-19 would have similar results. Further randomized controlled trials are needed to determine the effect of systemic steroids in cancer patients with COVID-19.

Serious complications including ARDS, stroke, acute coronary syndrome, septic shock, and secondary bacterial infection were observed in some patients in our cohort and were associated with an increased risk of mortality. On multivariate regression analysis, we found that leukocytosis was an independent risk factor for increased mortality. Two-thirds (66%) of the patients had increased neutrophil: lymphocyte ratios, but we did not find an association between a high neutrophil: lymphocyte ratio and an increased risk of mortality. Zhang et al.\cite{13} reported that in cancer patients with COVID-19, the significant increase in pro-inflammatory neutrophils and CRP reflected a more critical illness and was associated with adverse clinical outcomes. Asghar et al.\cite{10} also observed higher neutrophil counts in nonsurvivors than in survivors among cancer patients with COVID-19.

Inflammatory markers, including CRP, D-dimer, and ferritin, are elevated in many cases of severe COVID-19 pneumonia. These markers are key for the diagnosis of cytokine storms and hyperinflammation (induced by the uncontrolled immunologic response to human coronaviruses), which are associated with an increased risk of mortality.\cite{22,23} Coagulopathy with an increase in D-dimer levels could be explained by direct viral involvement of endothelial structures leading to endotheliitis, a finding observed by Varga et al.\cite{24} on postmortem analysis of COVID-19 microscopic lesions. We observed that D-dimer levels >1 μg/mL were associated with an increased risk of mortality in our cohort. Asghar et al.\cite{10} also reported increased D-dimer levels in cancer patients with COVID-19 who
did not survive. In our cohort, we did not observe an association between mortality risk and high CRP or ferritin levels.

Our study has some limitations. The sample size was small; thus, the results are inconclusive. Furthermore, it was an observational study and lacked a control group of noncancer patients. We did not consider that some patients who died were terminally ill and had signed “do not resuscitate” forms; thus, their deaths were primarily related to advanced malignancy.

**Conclusion**

Cancer patients are particularly vulnerable to COVID-19 and have a high risk of mortality following infection. As such, they require a higher level of care and attention. Dyspnea on initial presentation, leukocytosis, use of systemic steroids, and secondary bacterial infection are indicators of a high risk of mortality in cancer patients with COVID-19. This knowledge will help clinicians identify patients who have a high risk of poor outcomes.

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**Conflicts of interest**

There are no conflicts of interest.

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