Journal of Medicinal and Chemical Sciences 7 (2024) 352-362

Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/

Original Article

Mortality and Prevalence of COVID-19 in Variable Cancer Subtypes with Radiological Correlation at the King Hussein Cancer Center

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ARTICLE INFO

Article history

Receive: 2023-07-09
Received in revised: 2023-08-18
Accepted: 2023-08-18
Manuscript ID: JMCS-2308-2224
Checked for Plagiarism: **Yes**
Language Editor:
Dr. Fatima Ramezani
Editor who approved publication:
Dr. Ali Delpisheh

DOI:10.26655/JMCHEMSCI.2024.2.7

KEYWORDS

COVID-19
Cancer
Mortality rate
Radiological findings

ABSTRACT

Purpose: Radiographic abnormalities on first CT scans may correspond with increased risk of severe COVID-19 infections in cancer patients. Therefore, the purpose of this study is to use CT scans to identify the radiological characteristics of COVID-19 in deceased cancer patients from Jordan's King Hussein Cancer Centre (KHCC), and to quantify the mortality rate in a subgroup analysis of individual cancers, all while comparing our findings to the existing literature.

Methods: The inpatient and outpatient records of 785 patients diagnosed with cancer who tested positive for COVID-19 by RT-PCR between September 2020 and December 2020 were reviewed, along with the chest CT scans of 24 patients who died of the disease. Microsoft Excel 2013 was used for all data analysis. We just make use of descriptive statistics.

Results: In total, 82 (10.5%) of COVID-19-positive cancer patients passed away. Patients' median ages at death were 58.8 15.5. There were 38 male deaths (47.3%) and 44 female deaths (53.7%). In our research, COVID-19 was most frequently associated with diagnoses of breast cancer. Patients with gastrointestinal (GI) cancer and hematological cancer had the highest rates of death due to COVID-19. Multiple myeloma patients had the greatest mortality rate compared to the total number of cases. Ground glass opacities with or without consolidations were the most often observed CT finding in the deceased. CT scans showing pleural effusion were more common in patients with severe COVID-19 infection.

Conclusion: COVID-19 clinical features of KHCC cancer patients are assessed in this study. Patients with COVID-19-related malignancy had a low overall death rate, and the radiological findings of COVID-19 in the deceased were determined to be typical for the population as a whole.

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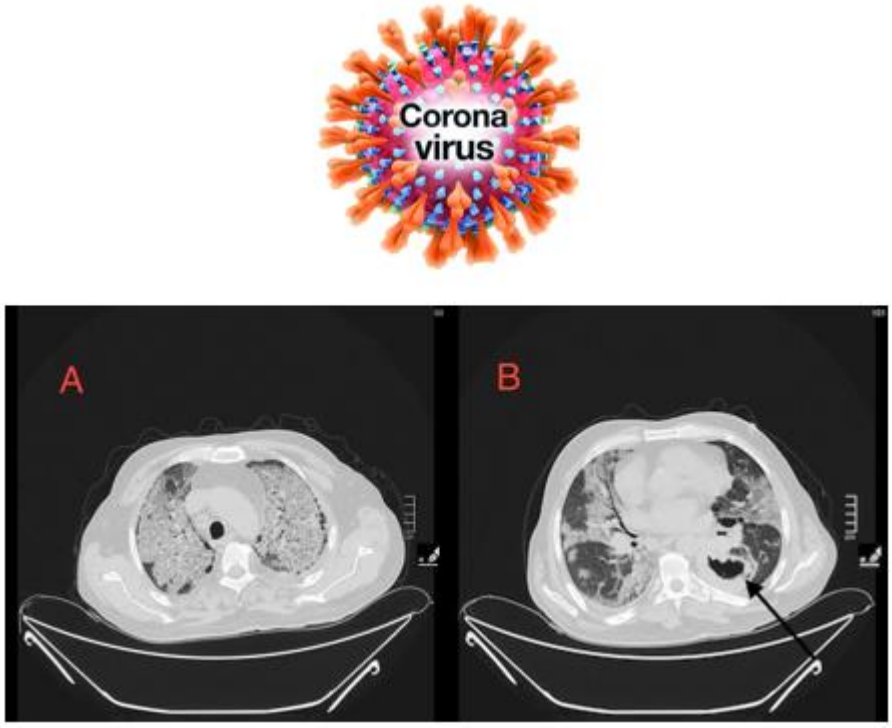
GRAPHICALABSTRACT



Introduction

More than 4.6 million people would die from the SARS-CoV-2 virus-caused COVID-19 pandemic between 2019 and July 2021 [1-5]. The first case of COVID-19 in Jordan was recorded in early March 2020. Since then, Jordan has recorded over 700,000 cases and over 10,000 deaths of COVID-19 as of July 2021 [6]. The typical incubation period of COVID-19 lasts 4-5 days, but may present within 14 days following exposure to the virus. Common symptoms of the viral infection are cough, shortness of breath, and sore throat. In more severe cases, infection of the lower airways and acute respiratory distress syndrome (ARDS) may ensue, leading to death [7, 8]. Deep vein thrombosis (DVT) and pulmonary embolism (PE) are two types of venous thromboembolism (VTE) and another consequences are cardiac complications such as myocardial infarction (MI) as well as neurological and immunological complications [9]. Furthermore, several studies have shown that COVID-19 mortality is higher among men, older age populations, and people suffering from multiple diseases at once; examples include diabetes, cardiovascular disease, and chronic renal disease [10-12].

One of the most reliable ways to diagnose COVID-19 is with a positive Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) [13]. Radiographs of the chest and computed tomography (CT) scans are two more diagnostic tools. Despite the superior sensitivity of CT scans, the ACR advises against routinely using them outside of a hospital setting [14]. Ground glass opacities (GGO) and consolidations are two CT findings that are indicative of a COVID-19 infection. These characteristics typically manifest themselves bilaterally in the lower lobes, and at the periphery. Air bronchograms, interlobular septal thickening, and adjacent pleural thickening are all less frequent findings [15, 16]. In addition, radiographic grading criteria can be used to measure the severity of a COVID-19 infection, which can help in predicting long-term prognoses of the patients [17].

Multiple reports have linked COVID-19 infection with an increased risk of developing cancer. Hematological and lung malignancies, especially those accompanied by other comorbidities, appear to have the highest COVID-19 incidence among cancer patients. Cancer patients, although having similar COVID-19 clinical features to those without current malignancies, are more likely to get life-threatening infections and have higher mortality rates. Patients with hematological cancers are particularly susceptible to the side effects of weakened immunity as a result of chemotherapy used to treat their disease. [18-21]. These factors make cancer patients more at risk for contracting COVID-19 and highlight the need for more monitoring and attention to these patients.

Ultimately, there remains a scarcity in the literature regarding the association between initial CT scan findings of COVID-19 and the resulting mortality rate among cancer patients. This data is especially limited in the Middle East. Our study's overarching objective is to use CT scans to identify radiological characteristics of COVID-19 among recently deceased cancer patients from Jordan's King Hussein Cancer Centre. In addition, a subgroup analysis of individual cancers will be conducted to quantify the mortality rate in COVID-19 cancer patients and compare the results to existing literature.

Materials and Methods

We conducted a retrospective analysis of 785 cancer patients with positive COVID-19 RT-PCR who presented to the King Hussein Cancer Center (KHCC) inpatient and outpatient departments between September 2020 and December 2020. Types of patients were extracted from the hospital database, including age, gender, and primary cancer. Furthermore, general demographic data from KHCC from 2015 until 2020 was also extracted from the hospital database.

SARS-CoV-2 nasal swab positive at the KHCC confirmed the COVID-19 diagnosis in patients. Patients who had previously been diagnosed with COVID-19 outside of the KHCC were re-examined to ensure correctness of their diagnosis. In addition, patient information at the time of diagnosis was obtained, such as presenting symptoms and the reason for obtaining a radiographic study. For this study, patients who died from an active COVID-19 infection were considered dead due to COVID-19. Patients excluded from the study were those with incomplete medical records or who were lost to follow-up.

CT Scan

Twenty-four of the eighty-two COVID-19-related cancer deaths occurred in individuals who had a chest CT scan within ten days of learning their SARS-CoV-2 swab results. A supine patient was given an IV injection of contrast medium before undergoing the CT scans. The chest CT scans were done in multi-detector CT (MDCT) with variable slice thickness. Three CT machines were used: Philips Brilliance 64, Philips Ingenuity 128, and Philips ICT 256. Optiray Injection 300 (Ioversol Injection) and Omnipaque (Iohexol Injection) were available contrast medium agents. Independently, four board-certified radiologists analyzed each CT image, and then they reached an agreement to settle any discrepancies that arose. The CT scans were evaluated based on unilateral or bilateral changes.

Furthermore, the number of lobes was assessed, and the spared lobes were recorded. The CT changes were stratified based on their appearances according to the Fleischner Society Glossary of terms, which included: GGOs, consolidations, nodular changes, and tree-in-bud patterns [22]. The results were stratified in a semi-quantitative scoring system based on the number of lobes involved in both lungs, with the results ranging between 0 (no lobes involved) to 5 (all lobes involved) [23]. Other pathologies such as pleural effusions, primary lung masses, tumor metastases, and pulmonary embolisms were further recorded if present.

Statistical analysis

Microsoft Excel 2013 was used for all data analysis. We just use the descriptive statistics. Means and standard deviations were provided

for continuous data. The percentage and frequency distributions of the categorized data were presented.

Ethical considerations

The IRB at King Hussein Cancer Centre gave their stamp of approval to the study after looking through the proposal and procedure. The procedures included in the study's protocol are also in conformity with the Declaration of Helsinki's principles.

Results and Discussion

Clinical characteristics of the study population

There was a total of 785 people who had cancer and were infected with COVID-19. Table 1 indicates that of the total patients, 437 were female (55.6%) and 348 were male (44.3%). Patients' ages ranged from 2 to 87, with a mean age of 51 years 31.1. The most frequent cancers were breast and hematological, occurring in 179 (22.8%) and 155 (19.7%) patients. The most common presenting symptoms of COVID-19 were cough (n = 60) and shortness of breath (n = 57). Table 2 presents the distribution of cases according to primary cancer. Furthermore, data from KHCC demonstrated that in 2020, 2275 (55%) female and 1894 (45%) male patients received cancer treatment.

COVID-19 mortality

Among those diagnosed with cancer and COVID-19, 82 people sadly passed away (10.5%). Patients' median ages at death were 58.8 15.5. Two of the patients were minors. Totally, 44 deaths were recorded with 53.7% being female and 46.3% being male (Table 1). Of the total number of people who lost their lives due to COVID-19, 16 (14.7%) were patients with gastrointestinal (GI) cancer and 14 (19.7%) were patients with hematological cancer. The highest percentage of deaths occurred in multiple myeloma patients, which were 11 deaths out of 37 patients (29.7%).

Table 1: The study population

	Cases with COVID-19	Cases died of COVID-19
Total number of cases	785	82 (10.5%).
Male (n, %)	348 (44.3%)	38 (46.3%)
Female (n, %)	437 (55.6%)	44 (53.7%)
Mean age (years)	51	58.8

Table 2: The distribution of cases according to the primary cancer

N (%)	Total Number of Cases	Total Number of Deaths
All hematological malignancies	192 (24.5%)	25 (13%)
Lymphoma and leukemia	155 (19.7%)	14 (9%)
Multiple myeloma	37 (4.7%)	11 (29.7%)
Brain tumors	38 (4.8%)	3 (7.9%)
Thyroid cancer	9 (1.2%)	1 (11.5%)
Bladder cancer	30 (3.82%)	4 (13.3%)
Breast cancer	179 (22.8%)	14 (7.8%)
Gastrointestinal cancers	115 (14.7%)	16 (13.9%)
Female genital tract malignancies	8 (1%)	2 (25%)
Hepatobiliary tumors	9 (1.2%)	1 (11%)
Head and neck cancer	25 (3.2%)	4 (16%)
Intrathoracic cancer	46 (5.6%)	8 (17.4%)
Sarcoma	24 (3.1%)	1 (4.2%)
Prostate cancer	14 (1.8%)	2 (14.3%)
Renal cancer	16 (2%)	1 (6.2%)
Others	80 (10.2%)	0

Figure 1: A chest CT scan of a 70-year-old woman with lymphoma and COVID-19 infection. There are diffuse bilateral ground glass opacities and bilateral pleural effusions (arrows)

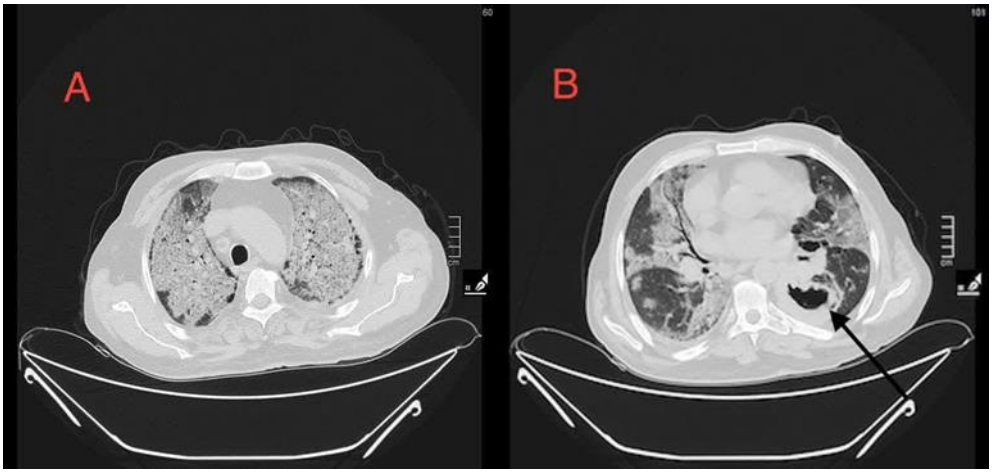


Figure 2: A chest CT scan of a 56-year-old man with lung cancer and a COVID-19 infection. There are extensive bilateral consolidations on top of smoking-related pulmonary interstitial disease (A and B). In addition, a cavitating mass is noted at the superior segment of the left lower lobe (arrow), in keeping with the primary lung cancer

COVID-19 radiographic findings

Out of the 82 patients who had died due to COVID-19, 24 were stable enough to receive CT scans (29.3%), whereas the rest received portable chest X-Rays. The CT findings revealed that 20 (83.3%) patients had bilateral lung involvement (Figures 1, 2, and 3), while 4 had no lung involvement (16.7%). Of those who had lung involvement, 17 (70.8%) patients had five lobes affected, 2 (8.3%) patients had four lobes involved, and 1 (4.2%) patient had two lobes involved (Table 3). The most common spared lobes were the right middle lobe (RML) and the left upper lobe (LUL), which were involved in 2 patients each. Most patients had both central and peripheral lung involvement (54.2%), whereas 29.2% had peripheral involvement only. The most common CT findings were ground glass opacities (83.3%), consolidations (50%), and nodular patterns (4.2%). In addition, 7 (29.2%) patients had both GGOs and consolidations. Only four patients received follow-up CT scans, revealing no changes in the score. Other CT findings included 14 (58.3%) patients with pleural effusion, 10 (41.7%) of which were bilateral (Figure 1) and 2 (8.3%) were right-sided and 2 (8.3%) were left-sided. Moreover, 4 (16.7%) patients had a lung mass (Figure 2) and 6 (25%) had metastases (Figure 3), and 2 (8.3%) had a pulmonary embolism (Table 4).

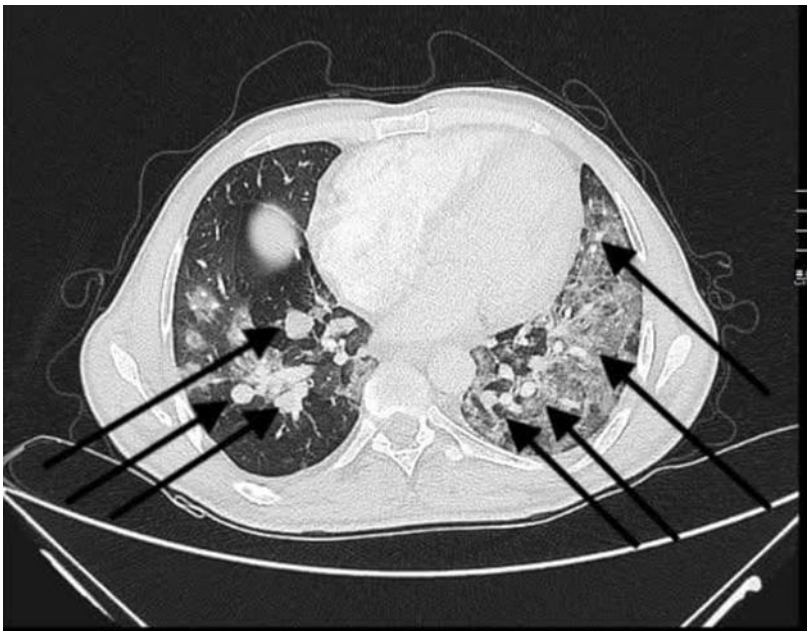


Figure 3: A chest CT scan of a 43-year-old man with renal cell carcinoma and COVID-19 infection. There are extensive bilateral consolidations with bilateral pulmonary metastases (arrows)

Regarding the four patients who did not have COVID-19-related findings on CT scan, there was a limited assessment of the underlying aerated parenchyma due to the following reasons: Two patients had progression of diffuse extensive bilateral pulmonary metastases, one patient had bilateral extensive lymphangitis carcinomatosis, in addition, one individual had a central left lung tumor that was completely collapsing the left lung as a result of obstructing the left major bronchus.

We report a retrospective review of 785 patients with laboratory-confirmed SARS-CoV-2 virus infection who have active malignancies and are being treated at the designated cancer hospital in Jordan. Our analysis demonstrates mortality and associated radiographic characteristics of cancer patients with a positive SARS-CoV-2 test.

The study found that among patients with COVID-19, breast (22.8%) and hematological (24.5%) cancers were the most prevalent subtypes of malignancies. There was a little rise in the number of female patients at KHCC with a positive nasopharyngeal COVID-19 swab, which we reported as 55.6%. This may be due to the high frequency of breast cancer. This is because, regardless of sex, breast cancer accounts for roughly 20.6% of all cases of cancer in Jordan [24]. Furthermore, data at our center notes that there has been a consistently higher percentage of female cancer patients at KHCC over the past five years. Moreover, these results are in alignment with other studies. F. Yang *et al.* performed a retrospective analysis of the clinical characteristics of 52 Chinese cancer patients with COVID-19 and found that lung cancer and breast cancer are the most typically encountered cancers with a positive nasopharyngeal swab with a record of 19.2% and 17.3%, respectively [18].

Table 3: The number of affected lobes

No. of affected lobes/score	No. of cases
0	4 (16.7%)
I	0
II	1 (4.2%)
III	0
IV	2 (8.3%)
V	17 (70.8%)

Table 4: Other CT findings

Findings	No. of CT scans
Pleural effusion	14 (58.3%)
Pulmonary embolism	2 (8.3%)
Metastases	6 (25%)
Lung mass	4 (16.7%)

K. Yang *et al.* analyzed 205 cancer patients with a positive COVID-19 infection in Hubei; China reported the most common malignancies to be affected breast, colorectal, and lung carcinomas [19].

Our study yielded similarities between the clinical features of COVID-19 within cancer patients in our cohort and those within the general population, as the most frequently documented symptoms were dry cough and dyspnea, which were similar to those documented worldwide [25]. The mortality rate of our study was found to be 10.5%. When compared to the fatality rates found in other trials, this one was remarkably low. For example, f. Yang *et al.* found that COVID-19 was responsible for the deaths of 21.2% of cancer patients. In addition, a retrospective case-control examination of cancer patients in Turkey by Acar *et al.* revealed a death rate of 46.5% [26]. This difference could be because our study population was larger and included more women than theirs did, and because male patients tend to have a greater mortality rate.

The highest deaths recorded in our study were in hematological, gastrointestinal, and breast malignancies, which all comprise a significant number of the cancer patients in our center. Moreover, hematological cancer patients are at a higher risk of acquiring a severe COVID-19 infection and dying from it, as they are usually immunodeficient due to several reasons, including the effects of the malignancy and the immunosuppressive treatment, which may include stem cell transplantation [27]. This is reinforced by the fact that multiple myeloma patients had the highest mortality rate (29.7%). Chari *et al.* have suggested that due to the nature of the highly immunosuppressive treatment of multiple myeloma and other associated factors, including older age and the presence of renal disease, hospitalized patients with multiple myeloma and COVID-19 have a high mortality rate ranging between 29% to 57% [28]. The mortality rate among breast cancer patients in our study was reasonably low (7.8%). A prospective research by Vuagnat *et al.* found no increased incidence of severe COVID-19 or death among breast cancer patients compared to the general population [29].

The most prominent CT findings of our study's deceased COVID-19 patients were GGOs, either alone or in combination with consolidations. We noted the presence of GGOs in 83.3% of CT scans, consolidations in 50%, and bilateral involvement in 83.3%. This is comparable to findings documented in the literature. CT results of GGOs with or without consolidations were the most common in a retrospective investigation of deceased COVID-19 patients conducted by Hu *et al.* [30]. Furthermore, in a case series of CT findings in COVID-19 patients in Italy, Polistina *et al.* noted similar findings of GGOs in 88.0% of cases and bilateral involvement in 87.5%, which indicates that our findings are comparable to those of the general population [31].

In our study, 17 (70.8%) patients had all five lobes affected. In addition, most patients had central and peripheral lung involvement (54.2%). Patients who died with COVID-19 had greater severity CT ratings, as found by Hu *et al.* In a comprehensive analysis of 919 cases with COVID-19, Salehi *et al.* concluded that findings in a severe COVID-19 infection were characterized by bilateral and multifocal involvement with peripheral or posterior distribution [32]. The most commonly spared lobes in our study were the RML and the LUL. This is in concordance with other studies; a retrospective study by Ng *et al.* on CT findings of patients with COVID-19 found that the RML is the least involved, which is supported by similar findings by Chung *et al.* [33, 34].

Furthermore, our study found that 58.3% of our deceased patients had pleural effusion, the majority of which were bilateral (41.7%), which could be related to severe COVID-19 pulmonary disease, as several studies concluded that pleural effusions on the initial CT scans were uncommon and associated with more severe COVID-19 infections and poor clinical outcomes [35-37].

Limitations

The retrospective nature of the design limits our study. Moreover, it is evident from the high number of breast cancer patients in the study

that the overall prognosis of SARS-CoV-2 infection may ultimately be skewed to more positive results.

Conclusion

This is the first report of COVID-19 in Jordanian hospitalized cancer patients. Our research has outlined the demographic and clinical features of COVID-19 in cancer patients and shown that postmortem radiological findings of COVID-19 are similar to those reported in the general population. The low overall mortality rate associated with COVID-19 suggests that the virus itself is the primary cause of death, rather than the cancer presence. Therefore, with further follow-up, the findings of this study could improve the quality and safety of cancer treatment during the current COVID-19 epidemic.

Abbreviations

CT: Computerized tomography; GI: Gastrointestinal; ARDS: Acute respiratory distress syndrome; VTE: Venous thromboembolism; DVT: Deep vein thrombosis; PE: Pulmonary embolism; MI: myocardial infarction; RT-PCR: Reverse-transcriptase polymerase chain reaction; ACR: American College of Radiology; KHCC: King Hussein Cancer Center; IRB: Institutional review board; GGO; ground glass opacities; RML: Right middle lobe; LUL: Left lower lobe.

Disclosure Statement

No potential conflict of interest was reported by the authors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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HOW TO CITE THIS ARTICLE
Mousa El Khaldi, Mira Al Jabi, Dana Alkhulaifat, Mais Zmaily, Maysa Al-Hussaini, Mariam Kharroubi, Tala Ghatasheh, Samar Taqatqeh, Abdallah Nofal. Mortality and Prevalence of COVID-19 in Variable Cancer Subtypes with Radiological Correlation at the King Hussein Cancer Center. *J. Med. Chem. Sci*., 2024, 7(2) 352-362.
DOI: https://doi.org/10.26655/JMCHEMSCI.2024.2.7
URL: https://www.jmchemsci.com/article_182906.html