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Original Article

Surviving the Double Threat: A Holistic Study on Clinical Manifestations of SARS-CoV-2 and Mortality among Patients with Cancer

Mehdi Norouzi[1], Omid Salahi Ardekani[1], Mohammad Reza Mohammadi[2], Erfan Kordi[1], Roxana Tajdini[1], Zahra Aboughadareh Nasab[1], Parsa Ghafari[3], Mahya Arabi[1], Mohammad Sina Khanbabazade[1], Mina Naderisemiromi[4*]

1. Research Center for Clinical Virology, Tehran University of Medical Science, Tehran, Iran.
2. Department of Bacteriology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran.
3. Iranian Network for Research in Viral Diseases (INRVD).
4. Department of Infectious Immunology, Manchester University, Manchester, UK.

Abstract

Background and Aims: The appearance of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) gave rise to the global coronavirus disease 2019 (COVID-19) pandemic. SARS-CoV-2 primarily affects the respiratory system, ranging from mild to severe symptoms. Cancer patients are at higher risk of severe outcomes and mortality rates due to compromised immune systems.This study aims to evaluate the clinical findings of cancer patients following infection with SARS-CoV-2, emphasizing the need for tailored approaches to address challenges during the COVID-19 pandemic.

Methods: The study enrolled a total of 158 individuals, all of whom had previously been diagnosed with various cancers and tested positive for SARS-CoV-2 with Real-time PCR. Demographic information of patients, characteristics of underlying diseases, type of cancer and clinical symptoms with geographical distribution of Iranian provinces by the Iran Viral Research Network were investigated.

Results: Among 158 patients, 62.65% were male and 37.34% were female. The majority were over 60 years old (55.69%). Leukemia was the predominant cancer (37.34%), followed by genital cancers and breast cancer (each at 13.51%). Respiratory symptoms were prominent, with shortness of breath (59.49%) and dry cough (41.77%) being the most common. Other symptoms such as runny nose (6.32%), sore throat (6.96%), and lethargy (41.77%) were common. Digestive symptoms like anorexia (25.31%) and nausea (10.75%) were also observed in a significant percentage of patients. In total, nine (5.6%) patients passed away during the study.

Conclusion: In conclusion, this study provides insights into the clinical manifestations of SARS-CoV-2 infection in cancer patients, revealing a higher susceptibility to severe outcomes due to compromised immune systems. The majority of patients exhibited respiratory symptoms, with leukemia being the most prevalent cancer type. These findings underscore the importance of tailored approaches in managing COVID-19 in cancer patients. As the pandemic continues, it is imperative to implement strategies that mitigate the risk and optimize care for this vulnerable population.

Keywords: Cancer, SARS-CoV-2, COVID-19, pandemic, Clinical symptoms.

Introduction

The emergence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS- CoV-2) in late 2019 led to the ongoing coronavirus disease 2019 (COVID-19) pandemic, posing significant challenges to global health and economies (1). SARS-CoV-2 is a highly transmissible virus that primarily affects the respiratory system and can lead to a wide range of clinical symptoms, ranging from mild flu-like symptoms to severe respiratory distress and multi-organ failure (2). The importance of understanding SARS-CoV-2 and cannot be

[*] **Corresponding author;**
Mina Naderisemiromi, Ph.D
Email: minanaderi767@yahoo.com

overstated, as it continues to affect millions worldwide and has strained healthcare systems worldwide (2, 3). Investigations in the context of cancer is of ut-most importance as it affects millions worldwide. Among the vulnerable populations at higher risk of severe COVID-19 are cancer patients. The intersection between cancer and SARS-CoV-2 infection has garnered substantial attention from the scientific and medical communities (4, 5). Cancer patients often have compromised immune systems due to their underlying disease or treatments such as chemotherapy, which makes them more susceptible to many infection agents, including SARS-CoV-2. Additionally, the direct and indirect effects of viruses on cancer patients, such as delayed treatments and healthcare disruptions, further compound the challenges faced by this already vulnerable population (6, 7).

In this study, we have investigated clinical manifestations of SARS-CoV-2 in cancer patients and shedding light on its impact on this specific population. Our primary objectives included assessing the common clinical symptoms experienced by COVID-19 positive cancer patients, evaluating the death rate among this group, and exploring other potential factors that may influence disease severity and outcomes.

Methods and Materials

Study Population

This retrospective study aimed to gather information regarding patients suffering from various cancers (Table 1) who also tested positive for SARS-CoV-2. The data collection was conducted at hospitals supervised by the country's viral diseases research network, encompassing Ali Asghar, Amin, Amiralmomenin, Imam Khomeini, Hajar, Khansari, Razi, Rouhani, Shariati, Sina, Vali Asr, and Yas Medical Center. All data were collected from March 2020 to May 2021.

The eligibility criteria for participation in the study involved individuals who had previously received a diagnosis of cancer and rolled out for other respiratory infections. Additionally, participants needed to provide demographic information and have their clinical symptoms and characteristics documented. The study enrolled a total of 158 individuals, comprising 59 women and 99 men, all of whom had previously been diagnosed with cancer. It was imperative to include individuals of all age groups, and hence, there was no age limit set for participation. The comprehensive demographic information of the patients can be found in Table 2, which provides a detailed overview of the studied population's characteristics. During this research study, all patients underwent routine examinations to ensure they were free from any other viral diseases or co-infections with viruses in associated hospitals by ELISA. Additionally, their clinical history was reviewed to check for inclusion in the study.

Sample Collection and Molecular Assay

Nasal swabs were collected from patients with respiratory symptoms in the mentioned hospitals (By physicians in the associated hospital). To maintain the accuracy of the study, all samples that showed simultaneous infection with other viruses detected by ELISA or PCR were excluded. By implementing these stringent criteria, we aimed to ensure the reliability and validity of the data, thereby enhancing the overall quality and significance of the research findings (Table 2). With Real-time PCR we verified the infection in cases (both RdRP and E genes were examined) (8).

Statistical Analysis

To analyze data, we used the statistical package IBM SPSS v.27. To describe data, frequency and percentage were applied. Pearson's chi-square test was used to investigate the independence of symptoms of COVID-19 from sex and age categories. Fisher's exact test was performed where assumptions of the chi-square test were not met.

Results

Demographic Data

In this research, a retrospective study of 158 patients underwent examination, with a break-

down of 99 (62.65%) male and 59 (37. 34%) female participants.

Table 1. Percentage of each cancer in patients involved in the study.

Variable	N	Percentage
Blood Cancer	59	37.34
Gastrointestinal Cancer	20	12.78
Genitourinary Cancer	25	13.51
Head and neck cancer	6	3.79
Breast Cancer	25	13.51
Lung cancer	4	2.53
head cancer	8	5.06
Multiple	5	3.16
other	6	3.79

Table 2. Demographic data of individuals participated in the study.

Variable	N	Percentage
	Gender	
Male	99	62.65
Female	59	37.34
	Age	
0-20	3	1.89
20-60	67	42.40
60<	88	55.69
	City	
Tehran	106	67.08
Mazandaran	17	10.75
Fars	7	4.43
Markazi	6	3.79
Esfahan	5	3.16
Alborz	5	3.16
Hamedan	4	2.53
Khuzestan	4	2.53
Khorasan, south	2	1.26
Gilan	1	0.63
Ghom	1	0.63

The study categorized individuals into three age groups: up to 20 years, 20-60 years, and over 60 years. Within these groups, there were 3 individuals (1.89%) in the up to 20-year-old category, 67 individuals (42.4%) in the 20-60-year-old category, and 88 individuals (55.69%) in the over 60-year-old category. Most of the studied people (106 patients), were from Theran province. Out of the total participants, 58 individuals passed away during the examination.

Cancer and Underlying Disorders

The predominant cancer observed in the study was leukemia, affecting 59 (37.34%) individuals. genital cancer (Bladder 6, Uterus 4, Prostate 15) and breast cancer were among the most prevalent cancers after leukaemia, each accounting for 25 participants (13.51%).

Table 1 provides an overview of the cancer prevalence among the patients under examination. In addition to cancer, the most prevalent underlying condition among the studied subjects was related to blood pressure, affecting 46 indivi-duals (29.11%). A history of surgery was re-ported in 38 people (24.05%), while diabetes followed closely with a prevalence of 36 individuals (22.78%). Table 3 provides details of other underlying diseases, including heart problems, kidney problems, COPD, asthma, allergies, obesity, and immunodeficiency due to transplantation and the use of immunosuppressive drugs. In total, nine patients (all had leukaemia cancer) had passed away during the period of the study (P-Value<0.05).

Table 3. Underlying disorders of patients included in the study.

Variable	N	Percentage
Cigarettes	8	5.06
Blood pressure	46	29.11
Diabetes	36	22.78
Heart problem	30	0.18
Fatty liver	1	0.63
History of stroke	6	3.79
Chronic renal	15	9.49
COPD	7	4.43
tuberculosis	2	1.26
hyperthyroidism	6	3.79
Asthma	2	1.26
Allergy	1	0.63
History of surgery	38	24.05
Obesity	1	0.63
Bone marrow transplant	2	1.26
Immunosuppress	2	1.26
Total	203	100

Table 4. Clinical manifestations of SARS-CoV-2 positive individuals.

Variable	N	Percentage	*P*-value
Nausea			
Positive	17	10.75	0.593
Negative	141	89.24	
Diarrhea			
Positive	24	15.18	0.556
Negative	134	84.81	
Vomiting			
Positive	16	10.12	0.050
Negative	142	89.87	
Lethargy			
Positive	66	41.77	0.751
Negative	92	58.22	
Breath_ shortness			
Positive	94	59.49	0.958
Negative	64	40.50	
Headache			
Positive	15	9.49	0.963
Negative	143	90.50	
Dizziness			
Positive	8	5.06	0.304
Negative	150	94.93	
Myalgia			
Positive	52	32.91	0.900
Negative	106	67.08	
Cough			
Positive	66	41.77	0.01
Negative	92	58.22	
Rhinorrhea			
Positive	10	6.32	1.000+
Negative	148	93.67	
Sore_throat			
Positive	11	6.96	0.315
Negative	147	93.03	
Anorexia			
Positive	40	25.31	0.332
Negative	118	74.68	
Chills			
Positive	32	20.25	0.450
Negative	126	79.74	

Clinical Manifestations

Among the prevalent respiratory symptoms observed in patients, shortness of breath stood out as the most common (59.49%), followed by dry cough (41.77%), runny nose (25.31%), and sore throat (6.96%) as notable presentations. Additionally, other clinical symptoms such as lethargy, muscle pain, confusion, fever, chills, and headache were also reported (Table 4). Regarding digestive symptoms, the study highlighted the presence of nausea (10.75%), diarrhoea (15.18%), heartache (13.44%), and anorexia (25.31%) among the subjects. The most prevalent digestive symptom in cancer patients exposed to COVID-19 is anorexia and reversely the lowest prevalence is for nausea and vomiting. For respiratory symptoms, the most prevalent symptom is shortness of breath and the lowest is sore throat and rhinorrhea.

Discussion

Emerging and re-emerging viral diseases continue to threaten human health. The emergence of viruses such as SARS-CoV-2 and Monkeypox poses great danger with increased mortality rates among nations (9, 10). The COVID-19 pandemic had a significant impact on clinical research and is expected to affect critical study outcomes. Iran has experienced hardships due to the COVID-19 pandemic (11, 12). Emerging research has indicated that individuals who have recuperated from severe COVID-19 might face an increased vulnerability to accelerated cancer progression (13).

Nowadays, several studies are reporting an association between different viruses and cancers that exhibit their connection and physiologic functions. The connection between viruses

and cancer triggers is among the most controversial research and new findings are helpful toward future treatment of this disease such as HHV-6 for primary brain cancer (14, 15). There are several reports which indicate SARS-CoV-2 clinical manifestations in different groups of individuals. In a study, it was found that fever and cough were the most common symptoms observed in paediatrics, which is consistent with the symptoms experienced by the general population with COVID-19 (16).

In a study across China, Liang et al. found that cancer patients had a higher risk of contracting SARS-CoV-2 and experiencing severe clinical outcomes like ICU admission, invasive ventilation, or death compared to non-cancer patients. According to the findings of this research, 39% of individuals diagnosed with cancer who contracted COVID-19 experienced severe symptoms, a stark contrast to the 8% rate observed among COVID-19 patients without a history of cancer (17). Another multi-centre retrospective study involving 105 cancer patients diagnosed with COVID-19 revealed that individuals with haematological malignancies faced a notably elevated risk of severe symptoms, with a rate of 66.67%. Similarly, those with metastatic solid tumours exhibited a relatively high risk, with 34.29% experiencing severe symptoms (18). These studies align with our study which we found that patients with blood cancer had a higher mortality rate which has a correlation with their more severe symptoms following COVID-19.

According to another retrospective study, the mortality rate among 218 COVID-19 patients with cancer from a single medical centre in New York City surpassed 25%. This rate was notably 2-3 times higher than that of individuals without cancer of the same age group, after adjustment for age (19). Information gathered from the COVID-19 and Cancer Consortium (CCC19) cohort study, encompassing 1,018 patients, indicated markedly elevated rates of mortality and severe illness among COVID-19 patients with cancer compared to the broader population (20). Moreover, findings from another multicenter study revealed that COVID-19 patients with cancer who underwent immunotherapy exhibited elevated rates of severe symptoms (66.67%) and mortality (33.33%). Conversely, patients who underwent radiotherapy did not demonstrate a noteworthy rise in the occurrence of severe events (18).

In our study, 5.6% of our cases with both cancer and COVID-19 passed away. This percentage is much more than what we have predicted and shows that cancer patients are at higher risk of severe symptoms and increased mortality rate following COVID-19.

In the context of presenting clinical manifestations, various studies have reported different symptoms regarding COVID-19 infection. In a study, Twenty-eight COVID-19-infected cancer patients were analyzed, with 60.7% being male and a median age of 65.0 years. Lung cancer was predominant (25.0%). Hospital-associated transmission was suspected in 28. 6% of cases. Common clinical features included fever (82.1%), dry cough (81%), and dyspnea (50.0%) (21). In our study, breath shortness, lethargy and cough were among the most prevalent clinical symptoms linked to COVID-19-positive patients with cancer.

Another study found that individuals who received the vaccine experienced coughing at the highest rate of 100%, followed by sore throat at 72%, and runny nose at 65%. However, our research has identified distinct symptoms, particularly shortness of breath with a 59% incidence rate, followed by dry cough at 41%, runny nose at 25%, and sore throat at 6% (16). Analysis of clinical symptoms in another study revealed a similar pattern to our study. In this study, Cough emerged as the predominant symptom, affecting over 79% of participants. Following closely, fever was the second most common complaint, reported by approximately 62% of individuals. Fatigue ranked third, impacting 57% of the subjects. Conversely, vomiting was the least commonly mentioned symptom, with an incidence of only 14.3% (2). In another study, sore throat at 65.3% (32/49), headache at 59.2% (29/49), and cough at 57. 1% (28/49) were reported in patients following COVID-19 infection which aligns with our study (22).

The HIV-positive group are another immunocompromised group besides cancer patients, and SARS-CoV-2 in this group is very important due to the probable higher mortality rate. A study conducted a comparative analysis of various clinical parameters between COVID-19 patients with and without HIV infection at Zhongnan Hospital of Wuhan University from January 20th to February 14th, 2020. Parameters included maximum body temperatures, duration of fever, chest CT findings, viral shedding, lymphocyte counts, and levels of SARS-CoV-2 antibody (23).

In contrast, a study examined PLHIV hospitalized for COVID-19 in Chile, comparing their outcomes with the general population. Among 36 PLHIV, severe COVID-19 occurred in 44. 4%, with 13.9% mortality. Hypertension and cardiovascular disease were significant mortality risk factors. PLHIV were more likely male and younger. While PLHIV had higher ICU admissions, no differences were found in mechanical ventilation or mortality compared to the general population (24).

Recent research suggests a potential link between the N (nucleocapsid) gene of SARS-CoV-2, the virus responsible for COVID-19, and its ability to inhibit apoptosis, a process of programmed cell death. The N gene plays a crucial role in viral replication and assembly within host cells. Studies have shown that this gene may interfere with cellular pathways involved in apoptosis, potentially leading to prolonged cell survival. In cancer, cells often evade apoptosis, leading to uncontrolled proliferation and tumour growth. If the N gene of SARS-CoV-2 indeed inhibits apoptosis in infected cells, it could have significant implications for cancer patients. Cancer cells already possess mechanisms to resist apoptosis, and the additional inhibition by the virus could potentially exacerbate tumour progression. This could result in more aggressive cancer behaviour, metastasis, and poorer outcomes for cancer patients who contract COVID-19 (25). However, it's essential to note that this area of research is still in its early stages, and further studies are needed to fully understand the interaction between SARS-CoV-2 and apoptosis, as well as its potential impact on cancer progression. The prevalent types of cancer observed in this research were in the order of blood, genitourinary, breast and gastrointestinal. Adding that we haven't studied all sorts of cancers and cancer stages which might present different clinical conditions. Patients exhibited a range of clinical symptoms, such as diarrhoea, shortness of breath, lethargy, muscle pain, headache, anorexia, nausea, vomiting, and confusion. Being a prospective study, it doesn't need a control group. The forthcoming research directions should concentrate on documenting the gaps that have been identified in this paper and making sure that data is collected consistently.

The outcomes observed in these findings could potentially be affected by the administration of drug medications and cancer interventions such as chemotherapy treatments. To enhance our understanding, future studies should take into account these medications and the stage of cancer as well. Our study had proper population numbers by statistical analysis. However, larger populations may be needed for more accurate results in future studies.

Conclusions

In this research, we investigated to determine the prevalence of SARS-CoV-2 in individuals with cancer, aiming to better understand its effects on this vulnerable population. The results of this study add to the existing knowledge about the relationship between SARS-CoV-2 and cancer, offering vital insights to aid in the management and mitigation of COVID-19's impact on cancer patients.

The most prevalent respiratory symptoms in patients included shortness of breath (59.49%) and dry cough (41.77%). Other respiratory symptoms such as runny nose, phlegm cough, and sore throat were also noted. The high mortality rate among the participants underscores the severity of COVID-19 in this vulnerable population. The study highlights the importance of close monitoring and tailored care for cancer patients during the ongoing pandemic. Understanding the impact of COVID-19 on cancer patients is crucial for optimizing treat-

ment strategies and enhancing the outcomes of this susceptible population.

Acknowledgment

None

Conflict of Interest

No conflict of interest is declared.

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Ethics Approval and Consent to Participate

This study is approved by the Ethics Committees of Tehran University of Medical Sciences (IR.TUMS.VCR.REC. 1399.599).

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