

The characteristics of cancerous patients infected with COVID-19 in hospital setting

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Summary. *Purpose:* recently, Covid 19 as a fatal virus has been known as the cause of the pandemic. Different number of the mortality rate in various societies have been reported. However, it seems the underlying comorbidities increase the risk of mortality and the severity of presentation. In this study we evaluated the pattern of presentation of COVID-19 among cancerous patients in terms of severity. *Method:* Between 20th February to 22nd April of 2020, in Taleghani Hospital as a COVID-19 referral hospital, among 214 hospitalized patients because of COVID-19. 41 patients revealed the cancer as a synchronous comorbidity. These patients based on the severity of COVID-19 infection presentation were divided to mild and severe groups. Then, the demographic characteristics, manifestation and laboratory data between these groups were compared. *Result:* about 19 (46.34%) of 41 cases were categorized as severe forms of COVID-19 with malignancy. The mean age of severe groups was significantly higher (P=0.00). Dyspnea (48.78%), cough (46.34%) and myalgia (24.39%) were the most common clinical features among cancerous patients with COVID-19. Diarrhea caused significant effects on severe form of presentation of COVID-19 infection (P=0.05). Hematological cancers were the most frequent types of cancer among these patients (46.34%). *Conclusion:* The elderly age, the positive chemotherapy history, diarrhea, cough, PLT and elevated CRP correlated with a severe form of this infection in malignant cases. (www.actabiomedica.it)

Keywords: Malignancy, COVID-19, Clinical Characteristic

Introduction

On March 11 of 2020, according to the world health organization (WHO) report, the world was afflicted with a new pandemic condition that was previously initiated from Wuhan city, China (1). An unknown contagious fatal pneumonia associated with Wuhan wild animal and seafood markets reported as a cause of this pandemic by the Chinese government(2). Genetic studies showed that this pneumonia agent is the 7th member of the coronavirus family. Hence, the virus was identified as a severe acute respiratory

syndrome coronavirus 2 (SARS-CoV-2) and COVID-19 was commonly used for identifying this virus (3, 4). As of July 31 of 2020, approximately 17 106 007cases were polluted with this new type of coronavirus family all around the world. Also, about 668 910deaths have recorded according to the 193rd situation report published by the WHO (5)

Meta-analysis findings showed that cancer and other comorbidities play as an important risk factor in the mortality rate and also the severity of COVID-19 (6). The primary Chinese data reported that mortality rates among cancerous patients and all COVID-19

patients are 28.6% and 2.3%, respectively, suggesting that fatality rates are 12.5 times more in patients with cancer (7, 8). Moreover, other Chinese study showed that ICU admission or mechanical ventilation support is 3.5 times more required in a cancerous patient (9). According to high mortality and severity rates of COVID-19 in cancerous patients, to provide better care to patients, it is crucial to describe demographics, clinical characteristics, diagnose these patients, and classify severe patients from first admission day. However, few studies have focused on those patients and additionally the majority of those COVID-19 infected cancerous patient studies face various limitations including sample size and cancer types. Several questions about this patient are still unresolved. Thus, we attempted to design the present study to identify COVID-19 characteristics and prognosis among cancerous patients in Taleghani hospital in Tehran, capital of Iran.

Methods

This observational, retrospective, single study was conducted in Taleghani hospital from 20th February to 22nd April of 2020. During this period, about 3000 patients were referred to our center due to a similar manifestation of COVID-19. In our study, COVID-19 positive patients were recognized based on SARS-cov-2 nucleic acid RT-PCR using the oropharyngeal sputum and swabs samples. 214 patients were admitted to our hospital as COVID-19 positive patients. A total of 43 patients among them (approximately 20% of all patients) had a history of malignancy among our patients. According to the main goal of our study, which is evaluating admission laboratory data among adult cancerous patients, eventually, 41 patients who were over 18 years old or did not have the previous admission to other hospitals due to COVID-19 participated in this investigation. Medical records for all of those patients were gathered from patients' electronic medical records by trained researchers.

Written informed consent was obtained in this study from all included patients. This investigation was approved by the ethics committee Shahid Beheshti University of Medical Sciences, in accord with the

World Medical Association's Declaration of Helsinki about the human involved studies.

Data collection and definitions: The first manifestation of the disease, demographics, and laboratory data including complete blood cell counts, blood coagulation function, blood biochemistry, liver, and renal function tests, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were recorded at the first day of admission for all patients. The entire laboratory specimens were tested through the same sets of standards. All specimens were collected when the patient was admitted in the Emergency ward and was checked in the same laboratory with the same laboratory kits. Type of cancer and previous history of chemotherapy were also collected. In this study, we categorized all of patients in severe and mild groups. Patients who have had confusion or respiratory rate ≥ 30 beats/minute or admission O₂ saturation $\leq 90\%$ were categorized as a severe group according to the Iranian ministry of health COVID-19 critical managing guideline. Moreover, the requirement of ventilation support was recorded for all of our patients during hospitalization.

Statistical Analysis: Continuous and categorical variables were reported as mean (\pm SD) and percentages, respectively. The Mann-Whitney U test and t-test were applied to compare continuous variables due to the normality assumption. Fisher's exact test was used to compare categorical variables. A p-value < 0.05 was assumed statistically significant. All statistical analyses were performed using R software version 3.6.3.

Results

Between 20th February to 22nd April of 2020, approximately 214 patients with confirmed diagnosis of Covid-19 were admitted in Taleghani hospital center. As a referral hospital, more critically and ill patients were admitted in our center. During this time, approximately, 41 (19.1%) of 214 patients with malignancy were admitted in this hospital.

Based on critical criteria, about 19 (46.34%) of 41 cases were categorized as severe forms of COVID-19 with malignancy, and need the critical care. In current study the demographic characteristics, the cancer types, the admission clinical features, and laboratory

admission data between mild and severe groups were compared (Table.1, 2)

The mean age of all cancerous patients with COVID-19 infection was about 61.78 ± 16.44 . However, the mean age of severe groups was significantly higher ($P=0.00$). The gender had no effect on the severity of COVID-19 infection among malignant patients.

Dyspnea (48.78%), cough (46.34%) and myalgia (24.39%) were the most common clinical features among cancerous patients with COVID-19. Other features with less frequency included fever, myalgia vomiting and diarrhea.

Among the onset features of COVID-19 infection, it seems diarrhea and nearly cough caused significant effects on severe form of presentation of COVID-19 infection ($P=0.05$, $P=0.06$, respectively).

Approximately no-one of the patients with severe presentation had the diarrhea at onset of their disease. Furthermore, the malignant patients were divided to different types of cancers. Hematological cancers were the most frequent types of cancer among these patients (46.34%). Breast cancer is another common cancer (12.19%). Nevertheless, based on our results, the type of cancer had no significant effect on the severe or mild presentation of COVID-19 infection. In addition, 53.65% of these patients from both mild and severe arms needed invasive ventilation during their hospitalization. However, there was no difference based on the need for invasive ventilation between mild and severe groups in our population ($P=0.35$). The positive history of chemotherapy was represented in 41.46% of malignant patients, surprisingly the patients with

Table 1. The comparison of demographic, manifestation characteristics and medical history between severe and mild groups of cancer patients infected with COVID-19

	No. (%)		Sig.
	Mild (N = 22)	Severe(N = 19)	
Age, mean (SD)	54.4 (15.9)	70.3 (12.8)	0.001
Sex			
Male	14 (63.6)	12 (63.2)	1.000
Female	8 (36.4)	7 (36.8)	1.000
Symptoms			
Fever	5 (22.7)	4 (21.1)	1.000
Myalgia	4 (18.2)	6 (31.6)	0.469
Cough	7 (31.8)	12 (63.2)	0.063
Dyspnea	8 (36.4)	12 (63.2)	0.121
Sore throat	0 (0.0)	2 (10.5)	0.209
Pleuritic pain	3 (13.6)	1 (5.3)	0.610
Vomit	6 (27.3)	3 (15.8)	0.466
Headache	2 (9.1)	2 (10.5)	1.000
Abdominal pain	5 (22.7)	1 (5.3)	0.191
Diarrhea	5 (22.7)	0 (0.0)	0.051
Cancer type			
Breast cancer	4 (18.2)	1 (5.3)	0.350
Colorectal cancer	1 (4.5)	3 (15.8)	0.321
Haematological cancer	12 (54.5)	7 (36.8)	0.350
Other cancer	5 (22.7)	8 (42.1)	0.313
Invasive Ventilation	10 (45.5)	12 (63.2)	0.350
Chemo therapy	14 (63.6)	3 (15.8)	0.004

Table 2. the comparison of laboratory data between severe and mild groups of cancer patients infected with COVID-19

	Total	Mean (SD)		Sig.
		Mild	Severe	
RBC ¹ (million/mm ³)	40	3.7 (0.9)	3.3 (1.2)	0.211
HCT ²	40	30.6 (6.3)	29.8 (9.8)	0.587
WBC ³ (× 10 ⁹ cells/L)	40	5.3 (3.5)	4.7 (3.2)	0.578
PLT ⁴ (* 10 ⁹ cells/L)	39	236.9 (139.1)	152.1 (93.4)	0.035
Hb ⁵ (g/dl)	40	10.1 (2.1)	9.7 (3.1)	0.590
AST ⁶ (IU/Liter)	35	36.2 (16.4)	50.6 (26.4)	0.063
ALT ⁷ (IU/Liter)	35	28.9 (15.2)	30.4 (18.5)	0.804
CRP ⁸ (mg/L)	36	46.2 (34.7)	67.5 (31.1)	0.064
Neutrophil (× 10 ⁹ cells/L)	30	4.2 (2.8)	3.5 (1.9)	0.514
Lymphocyte (× 10 ⁹ cells/L)	30	0.7 (0.5)	1.4 (2.5)	0.279
LDH ⁹ (units/L)	24	758.6 (609.7)	731 (296.8)	0.883

¹Red Blood Cells, ²Hematocrit, ³White Blood Cells, ⁴Platelet, ⁵Hemoglobin, ⁶Aspartate amino Transferase, ⁷ Alanine Transaminase, ⁸C-Reactive Protein, ⁹ Lactate Dehydrogenase.

severe presentation of COVID-19 infection revealed the less positive history of chemotherapy (P=0.00). 14 (63.6%) cases in mild group and 3 (15.8%) in severe group revealed the history of chemotherapy.

Contrarily to previous studies, among our study population, no lung cancer case was detected. Among these 41 cancerous cases, 63.41 % of them finally dead during the hospitalization due to COVID-19 infection.

The comparison of important prognostic items between severe and mild groups showed that platelet levels were significantly lower in severe groups (P=0.03). C-reactive protein is another item that nearly significantly was higher in severe groups of cancerous patients (P=0.06).

Discussion

The persistent risk factors of COVID-19 infection include the elderly age, male gender, and co-morbidities such as hypertension or cardiovascular diseases (10). Cancer-related immunosuppressive therapies expose cancerous patients to the high risk of infection with COVID-19(11). To the best of our knowledge, the underlying immunosuppression disorders have not been considered as the definitive risk factor for COVID-19 infection yet (12) , although, in many

clinical centers, malignant patients are considered as the high-risk group (13). According to previous studies, the malignant patients encounter a more serious and severe presentation of COVID-19 compared with normal patients (14, 15). The present study aims to determine the items that differed between severe and mild presentation among cancerous patients in COVID-19 infection. For this purpose, we separated the cancerous patients into mild and severe groups according to their admission vital signs and compared the manifestations, and demographic characteristics, positive previous history of chemotherapy, and laboratory data. Nevertheless, a large share of malignant patients has simultaneous co-morbidities that could worsen the outcome of COVID-19 infection.

Thus, determining the effect of malignancy as an independent factor had a bias. The support of the cancer patients in the early onset of manifestations could help to decrease the need for later advanced intensive care and invasive ventilation (12).

Principally, patients with hematologic cancers, including leukemia, lymphoma, or the cases who received recent chemotherapy confront a higher risk of COVID-19 infection (11, 16). The mortality rate of cancer patients infected with COVID-19 in China has been reported about 28%, which was remarkably higher than that of normal infected patients (17).

However, the response to COVID-19 infection is different among malignant patients. For example, in more immunocompromised patients including the hematologic cancers, the immune system response is too weak (11). In comparison, in patients with non lymphopenic malignancies, lower severity of infection has been detected (11). Among the population of the current study, the major proportion of malignancy belonged to hematologic cancers that seem to cause a high risk of poor prognosis among the patients (11).

Besides, more than half of our malignant patients infected with COVID-19 died during the hospitalization. This number was higher than the previously reported mortality rates (18). Such a difference could be because our center is a referral hospital for malignant cases. Previous studies reported lung cancer as the most common cancer among COVID-19 infected patients (19). However, in the current study, no patient had lung cancer to evaluate. Recent studies showed that cancer patients were significantly older than the normal population infected with COVID-19. Further, the elderly age could significantly worsen the outcome of the COVID-19 infection (12). Same as the previous studies, the mean age of cancerous patients was significantly higher than the normal group. Moreover, this number was remarkably higher in the severe group.

Although the outcome of the cancer patients is worse than the normal population, the onset manifestations are similar to non-malignant patients (17). Fever, dyspnea, cough, and myalgia were the common manifestations among our patients, which were similar to other groups of infected patients in our hospital. Although the pattern of admission manifestations between the mild and severe malignant patients had no remarkable difference, diarrhea and cough were significantly differencing among these two groups. Furthermore, it appears that COVID-19 infection could lead to more severe complications among malignant patients. Previous studies revealed that malignant patients infected with COVID-19 required invasive ventilation and intensive care three times more than normal infected patients (17).

Although, overall the number of cancer patients who needed intensive care and invasive ventilation was remarkably higher, these needs in severe group was not significantly higher than mild group.

Chemotherapy and radiotherapy suppressed the immune system of patients. Therefore, recent chemotherapy could worsen the prognosis of cancer patients infected with COVID-19 (20). Contrarily, chemotherapy and radiotherapy, especially in the early stages of malignancy, could improve the surveillance (21). Hence, it is essential to determine the cut-point time of recent chemotherapy to avoid bias (20). Unfortunately, we could not separate the cancer patients who had chemotherapy in terms of the exact time of previous chemotherapy. So, it seems the role of recent chemotherapy on the prognosis of COVID-19 infection in malignancy should be evaluated more accurately in separated groups. However, in our study, the recent history of chemotherapy did not represent the severe presentation of COVID-19. This result could be because of different variations of our regional/local population or the small number of the study population (17).

These evaluations showed the decreased counts of PLT at admission time could significantly correlate the chance of severe presentation of COVID-19 infection and the need for critical care among malignant patients (22). Besides, the significant increase in CRP indicated an inflammatory reaction in severe forms of infection among cancerous cases.

Conclusion

In this study, we report the demographic, clinical, and laboratory characteristics factors at the admission time of Covid-19 infected patients with malignancy. Also, we attempted to determine the factors associated with the severe presentation of this infection among these high-risk populations. According to the obtained results, the elderly age, the positive chemotherapy history, diarrhea, and cough correlated with a severe form of this infection in malignant cases. Among laboratory data, PLT counts significantly declined in the severe group of these patients. Moreover, elevated CRP represented inflammatory reactions among patients with the severe presentation of COVID-19 infection. The close monitoring of these features during the first days of presentation could help us to achieve better outcomes among the patients with underlying malignant diseases. Also, it could help us to allocate the facilities,

including ICU beds and intensive care to the severe group of patients with these interfered items during the first days of admission.

Acknowledgements: We would like to thank the participants in the study for their cooperation.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 8 July 2020

Accepted: 3 August 2020

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