Internal and Emergency Medicine (2022) 17:135–139
https://doi.org/10.1007/s11739-021-02784-y

IM - ORIGINAL

Patients with hematologic cancers are more vulnerable to COVID-19 compared to patients with solid cancers

Semih Başcı[1] · Naim Ata[2] · Fevzi Altuntaş[1,3] · Tuğçe Nur Yiğenoğlu[1] · Mehmet Sinan Dal[1] · Serdal Korkmaz[4] · Sinem Namdaroğlu[5] · Abdülkadir Baştürk[6] · Tuba Hacıbekiroğlu[7] · Mehmet Hilmi Doğu[8] · İlhami Berber[9] · Kürşat Dal[10] · Mehmet Ali Erkurt[9] · Burhan Turgut[11] · Osman Çelik[12] · Mustafa Mahir Ülgü[13] · Şuayip Birinci[14] on behalf of Turkish Ministry of Health, Hematology Scientific Working Group

Received: 7 February 2021 / Accepted: 31 May 2021 / Published online: 10 June 2021

Abstract
Previous studies reported that COVID-19 patients with cancer had higher rates of severe events such as intensive care unit (ICU) admission, mechanical ventilation (MV) assistance, and death during the COVID-19 course compared to the general population. However, no randomized study compared the clinical course of COVID-19 in patients with hematologic cancers to patients with solid cancers. Thus, in this study, we intend to reveal the outcome of COVID-19 in hematologic cancer patients and compare their outcomes with COVID-19 patients with solid cancers. The data of 926 laboratory-confirmed COVID-19 patients, including 463 hematologic cancer patients and an age-gender paired cohort of 463 solid cancer patients, were investigated retrospectively. The frequencies of severe and critical disease, hospital and ICU admission, MV assistance were significantly higher in hematologic cancer patients compared with the solid cancer patients ($p=0.001$, $p=0.045$, $p=0.001$, and $p=0.001$, respectively). The hospital stay was longer in patients with hematologic cancers ($p=0.001$); however, the median ICU stay was 6 days in both groups. The case fatality rate (CFR) was 14.9% in patients with hematologic cancers, and it was 4.8% in patients with solid cancers, and there was a statistically significant difference regarding CFR between groups ($p=0.001$). Our study revealed that COVID-19 patients with hematologic cancers have a more aggressive course of COVID-19 and have higher CFR compared to COVID-19 patients with solid cancers and support the increased susceptibility of patients with hematologic cancers during the outbreak.

Keywords COVID-19 · SARS-CoV-2 · Hematologic cancer · Solid tumor

Introduction

In China, SARS-CoV-2 was first discovered and subsequently disseminated across the globe. The World Health Organization (WHO) has precisely defined the disease caused by SARS-CoV-2 as Coronavirus Disease 2019 (COVID-19). Symptomatic patients with COVID-19 usually present with dyspnea and fever, and in patients with pneumonia, multilobed lesions can be observed in thorax computed tomography. It was acknowledged a pandemic by WHO on 11 March 2020 [1–4].

In adults with COVID-19, advanced age and chronic conditions, for instance, hypertension, diabetes, or heart disorders, are vulnerabilities for the severe disease [5]. Moreover, in a previous study, 39% of cancer patients with COVID-19 experienced serious events, such as admission to the intensive care unit (ICU), mechanical ventilation (MV) support, and death; on the other hand, only 8% of cancer-free patients with COVID-19 had such serious conditions [6]. In another study, researchers reported a case fatality rate (CFR) of 5.6% in cancer patients with COVID-19, whereas, in the same study, they reported a CFR of 2.3% in cancer-free patients with COVID-19 [7]. The high risk of cancer patients for more severe course of COVID-19 can be related to immunosuppression due to chemotherapy, radiotherapy, or worsened co-existing medical problems or metastases. Because of the underlying immune system deficiency, patients with hematologic cancers (HC) may be more vulnerable to COVID-19 [6]. Some concerns desperately require answers, such as whether COVID-19 in patients with solid

✉ Semih Başcı
dr.semihbasci@gmail.com

Extended author information available on the last page of the article

cancers (SC) and HC has a worse outcome than cancer-free patients and whether cancer patients can undergo anticancer therapies as regular in outbreak regions. Nevertheless, only a small number of COVID-19 reports in SC and HC patients have been proposed in the literature. Thus, we aim to reveal the outcome of COVID-19 in HC patients and compare it with COVID-19 patients with SC. The primary outcome of the study was case fatality rate; secondary outcomes were COVID-19 clinical severity, the rates of hospital admission, intensive care unit admission, and mechanical ventilation.

Materials and methods

Patients

Laboratory-confirmed SARS-CoV-2-infected patients identified in the Republic of Turkey, Ministry of Health records, between 11 March 2020 and 22 June 2020 were examined retrospectively. This is a retrospective observational study, including patients aged 18 and over with HC. A cohort of age, gender, and co-existing diseases (diabetes mellitus, hypertension, cardiovascular diseases) matched COVID-19 patients with invasive SC (excluding basal cell carcinoma of the skin) at 1:1 proportion was allocated for assessment.

Laboratory analysis

Nasopharyngeal swabs were utilized to operate a real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test for SARS-CoV-2 RNA. Utilizing coyote and biospeedy extraction processes (Coyote Bioscience Ltd and Bioeksen Ltd.), complete nucleic acid extraction of nasopharyngeal swab samples of virus isolates was undertaken.

Clinical parameters

Demographic information, concomitant diseases, medications used to treat COVID-19, hospital admission, hospital stay, ICU admission, length of ICU stay, the assistance of MV, and the patients' survival status were recorded.

The presence of dyspnea, blood oxygen saturation below 93%, $PaO_2/FiO_2 < 300$, and deterioration of lung infiltrations more than 50% in 24–48 h were defined as severe COVID-19. Deterioration of clinical condition to respiratory distress, septic shock, and/or multiple organ failure were defined as critical COVID-19 [8]. COVID-19 severity regarding the criteria stated above was recorded.

Statistical analysis and power analysis

The data processing was carried out by the IBM SPSS v26 program. Age, gender, and co-existing disease paired cohorts were allocated for assessment. Categorical variables were reported as number-percentages, and quantitative variables were reported as median (minimum–maximum). The variables were examined with the Kolmogorov–Smirnov test for normal distribution. Distinctions among the categorical variables were explored with the χ^2 test, and the quantitative variables were assessed with the Mann–Whitney U test. A two-sided p value of ≤ 0.05 was assumed significantly important.

The power analysis for sample size estimation was conducted using G*Power version 3.1.9.7 to test the difference between two independent groups using a two-tailed test based on the pilot study conducted by Mehta et al. ($N = 218$) [9, 10]. The result indicated that a total sample of 464 participants with two equal-sized groups of $n = 232$ was necessary to achieve a power of 0.80 with an alpha of 0.05.

Results

Patients

Laboratory-confirmed 926 patients with COVID-19 were included; 463 had HC and the remaining 463 consisted of age, gender, and co-existing diseases matched cohort of patients with SC. Hypertension was observed in 40.6% of the patients with HC and 39.5% of the patients with SC and was the most prevalent co-existing disease in both groups. The frequency of diabetes mellitus, hypertension, and cardiovascular diseases was similar across the groups. The rates of favipiravir and high-dose vitamin C use were higher in HC patients ($p = 0.001$, $p = 0.02$, respectively). The clinical and demographic features of all cases are shown in Table 1. The frequencies of the diseases are shown in Table 2.

Outcome

The frequency of severe and critical disease, hospital and ICU referral, MV support were significantly higher in HC patients compared with the SC patients ($p = 0.001$, $p = 0.045$, $p = 0.001$, and $p = 0.001$, respectively). Duration in the hospital was longer in patients with HC ($p = 0.001$); however, median duration of ICU stay was 6 days in both groups. The CFR was 14.9% in patients with HC, and it was 4.8% in patients with SC, and there was a significant difference regarding CFR among groups ($p = 0.001$) (Table 3).

Discussion

This is one of the most extensive studies examining HC patients with COVID-19 and comparing their outcomes with SC patients with COVID-19. In our study, we revealed that

Table 1 Clinical and demographic features of the cases

Clinical and demographic features	Patients with hematologic cancers ($n=463$)	Patients with solid cancers ($n=463$)	P value
Gender			
Male, *n* (%)	256 (55.3%)	252 (54.4%)	0.8
Female, *n* (%)	207 (44.7%)	211 (45.6%)	
Median age (years)	57 (18–93)	59 (19–86)	0.1
Comorbidity, *n* (%)			
Diabetes mellitus	101 (21.8%)	78 (16.8%)	0.06
Hypertension	188 (40.6%)	183 (39.5%)	0.7
Cardiovascular diseases	59 (12.7%)	46 (9.9%)	0.2
Additional treatment, *n* (%)			
Favipiravir	133 (28.7%)	61 (13.2%)	0.001*
Lopinavir/ritonavir	23 (5%)	15 (3.2%)	0.2
Hydroxychloroquine	332 (71.7%)	349 (75.4%)	0.2
High dose vitamin C	82 (17.7%)	56 (12.1%)	0.02*
Azithromycin	208 (44.9%)	208 (44.9%)	1

Table 2 Diagnosis of the patients

Patients with hematologic cancers	$N=463$, %	Patients with solid cancers	$N=463$, %
Non-Hodgkin lymphoma	214 (46.2%)	Breast cancer	128 (27.6%)
Multiple myeloma	74 (16%)	Lung cancer	91 (19.7%)
Chronic lymphocytic leukemia	54 (11.7%)	Colon cancer	59 (12.7%)
Acute myeloid leukemia	39 (8.4%)	Prostate cancer	89 (19.2%)
Chronic myeloid leukemia	30 (6.4%)	Skin cancer	29 (6.3%)
Hodgkin lymphoma	25 (5.4%)	Stomach cancer	33 (7.1%)
Acute lymphoblastic leukemia	18 (3.9%)	Brain cancer	19 (4.1%)
Hairy cell leukemia	9 (2%)	Endometrial cancer	15 (3.2%)

Table 3 The outcome of COVID-19 in each group

Factors	Patients with hematologic cancers ($n=463$)	Patients with solid cancers ($n=463$)	P value
Hospital admission	290 (62.6%)	260 (56.2%)	0.045*
Hospital stay (day)	15 (2–42)	12 (2–44)	0.001*
ICU admission, *n* (%)	96 (20.7%)	44 (9.5%)	0.001*
ICU stay (day)	6 (1–37)	6 (1–39)	0.97
MV, *n* (%)	69 (14.9%)	31 (6.7%)	0.001*
COVID-19 severity, *n* (%)			
Severe	74 (16%)	57 (12.3%)	0.001*
Critical	86 (18.6%)	38 (8.2%)	
CFR, *n* (%)	69 (14.9%)	22 (4.8%)	0.001*

CFR case fatality rate, *MV* mechanical ventilation, *ICU* intensive care unit

frequency of severe and critical disease, hospital and ICU referral, and MV assistance were significantly higher in HC patients compared with SC patients; hospital stay was longer in patients with HC; ICU stay was similar in both groups, and CFR was higher in HC patients compared with the SC patients.

In a previous report, 53.6% of the patients with cancer had dramatic outcomes, 21.4% were referred to ICU, 35.7% had serious conditions, and 28.6% of the patients died [11]. In the community with COVID-19, 4.7% of cases were reported as critical, and almost half of the critical patients (2.3%) died [7]. In our study, the frequencies of severe and critical disease in SC patients were 12.3% and 8.2%, respectively. The frequency of ICU admission was 9.5%, and the frequency of MV assistance was 6.7% among patients with SC. The CFR was 4.8% in COVID-19 patients with SC.

There are still limited data regarding COVID-19 patients with HC in the literature so far. In a prior report, investigators presented data from 105 hospitalized COVID-19 patients with cancer and compared their findings with those without cancer. Of the 105 COVID-19 patients with cancer, 9 had HC. They reported that patients with cancer had higher mortality rate, higher rate of ICU admission, and MV assistance, and higher rate of severe COVID-19 when compared with cancer-free patients. Moreover, they identified the highest frequency of worse incidents in patients with HC, lung

cancer, and metastatic cancer [12]. In the study conducted by Mehta et al., ICU referral and MV assistance was observed to be higher in HC patients (26%) compared with SC patients (19%) though statistical significance was not reached. In the same report, CFR was 37% in COVID-19 patients with HC [9].

In another research, He et al. reported the result of 128 hospitalized HC patients with COVID-19 and 16 medical professionals with COVID-19, 11 of whom were admitted to the hospital. They observed that patients with HC had a more severe condition and higher CFR than admitted medical professionals [13]. Another study from Spain examined 34 hospitalized COVID-19 patients with HC and stated that the CFR was 32%. They indicated that the HC remission status during COVID-19 was associated with death; patients without active cancer had better outcome [14]. A previous report including 35 hemato-oncology patients has documented a CFR of 40% [15]. In our analysis, the frequencies of severe and critical COVID-19 in HC patients were 16% and 18.6%, respectively. The rate of ICU admission was 20.7%, and the rate of MV assistance was 14.9% among patients with HC. The CFR was 14.9% in COVID-19 patients with HC.

This study has some limitations. The data about the disease status (active cancer/remission) and anticancer treatments are not available. On the other hand, the report's positive aspect is that groups were matched on various factors.

Cancer patients need prompt diagnosis, assessment, and care, including during an outbreak. Nevertheless, it is essential to address that cancer patients are immunodeficient and at an elevated risk of adverse events (ICU admission, MV need, or mortality) linked to COVID-19 relative to the general population [6, 16]. Studies suggest that cancer patients are highly susceptible to a more severe course of COVID-19 than cancer-free patients. Our research revealed that HC patients with COVID-19 have a more aggressive course of COVID-19 and higher CFR relative to SC patients with COVID-19 and endorsed the high risk of HC patients in the outbreak. The high susceptibility of patients with HC may be attributed to immune function dysfunction and hypogammaglobulinemia that are found in most patients. Due to the high infectivity of SARS-CoV-2, HC patients without COVID-19 should receive health care outside of the COVID-19 pandemic hospitals. Hematology departments should be isolated, and patient follow-up should be maintained as much as feasible by alternative methods, such as teleconference services.

Author contributions SB, NA, FA, SK, and TNY performed research; MSD, MHD, TH, and SN designed the research study; SB and AB analyzed and interpreted the data; TNY and SK wrote the paper. OÇ and MMÜ collected and processed data; İB, KD, MAR, BT and FA reviewed the manuscript.

Funding No funding received.

Declarations

Conflict of interest The authors declare no conflict of interest.

Ethics approval The research was in accordance with the 1964 Helsinki Declaration and ethical approval received from the Ministry of Health, Turkey.

Human and animal rights The study was conducted on human subjects, ethical standards were followed.

Informed consent Informed consent was not applicable since this is a retrospective study, and the research data were obtained from the Health Ministry's digital database.

References

1. Yigenoglu TN, Ata N, Altuntas F, Bascı S, Dal MS, Korkmaz S et al (2021) The outcome of COVID-19 in patients with hematological malignancy. J Med Virol 93(2):1099–1104. https://doi.org/10.1002/jmv.26404
2. Başcı S, Ata N, Altuntaş F, Yiğenoğlu TN, Dal MS, Korkmaz S et al (2020) Outcome of COVID-19 in patients with chronic myeloid leukemia receiving tyrosine kinase inhibitors. J Oncol Pharm Pract 26(7):1676–1682. https://doi.org/10.1177/1078155220953198
3. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J et al (2020) A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 395(10223):514–523. https://doi.org/10.1016/S0140-6736(20)30154-9
4. World Health Organization Press Conference (2020) The World Health Organization (WHO) Has Officially Named the Disease Caused by the Novel Coronavirus as COVID-19. https://www.who.int/emergencies/diseases/novel-coronavirus-2019. Accessed 30 Aug 2020
5. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, China Medical Treatment Expert Group for Covid-19 et al (2020) Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 382(18):1708–1720. https://doi.org/10.1056/NEJMoa2002032
6. Liang W, Guan W, Chen R, Wang W, Li J, Xu K et al (2020) Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol 21(3):335–337. https://doi.org/10.1016/S1470-2045(20)30096-6
7. Wu Z, McGoogan JM (2020) Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese center for disease control and prevention. JAMA 323(13):1239–1242. https://doi.org/10.1001/jama.2020.2648
8. Food and Drug Administration (2020) Investigational covid-19 convalescent plasma-emergency INDs. https://www.fda.gov/vaccines-blood-biologics/investigational-new-drug-ind-or-device-exemption-ide-process-cber/investigational-covid-19-convalescent-plasma-emergency-inds. Accessed 13 Aug 2020
9. Mehta V, Goel S, Kabarriti R, Cole D, Goldfinger M, Acuna-Villaorduna A et al (2020) Case fatality rate of cancer patients with COVID-19 in a New York hospital system. Cancer Discov 10(7):935–941. https://doi.org/10.1158/2159-8290.CD-20-0516
10. Faul F, Erdfelder E, Buchner A, Lang AG (2009) Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. Behav Res Methods 41(4):1149–1160. https://doi.org/10.3758/BRM.41.4.1149

11. Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R et al (2020) Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan. China Ann Oncol 31(7):894–901. https://doi.org/10.1016/j.annonc.2020.03.296
12. Dai M, Liu D, Liu M, Zhou F, Li G, Chen Z et al (2020) Patients with cancer appear more vulnerable to SARS-CoV-2: a multicenter study during the COVID-19 outbreak. Cancer Discov 10(6):783–791. https://doi.org/10.1158/2159-8290.CD-20-0422
13. He W, Chen L, Chen L, Yuan G, Fang Y, Chen W et al (2020) COVID-19 in persons with haematological cancers. Leukemia 34(6):1637–1645. https://doi.org/10.1038/s41375-020-0836-7
14. Martín-Moro F, Marquet J, Piris M, Michael BM, Sáez AJ, Corona M et al (2020) Survival study of hospitalised patients with concurrent COVID-19 and haematological malignancies. Br J Haematol 190(1):e16–e20. https://doi.org/10.1111/bjh.16801
15. Aries JA, Davies JK, Auer RL, Hallam SL, Montoto S, Smith M et al (2020) Clinical outcome of coronavirus disease 2019 in haemato-oncology patients. Br J Haematol 190(2):e64–e67. https://doi.org/10.1111/bjh.16852
16. Ueda M, Martins R, Hendrie PC, McDonnell T, Crews JR, Wong TL et al (2020) Managing cancer care during the COVID-19 pandemic: agility and collaboration toward a common goal. J Natl Compr Canc Netw 20:1–4. https://doi.org/10.6004/jnccn.2020.7560

Authors and Affiliations

Semih Başcı[1] · Naim Ata[2] · Fevzi Altuntaş[1,3] · Tuğçe Nur Yiğenoğlu[1] · Mehmet Sinan Dal[1] · Serdal Korkmaz[4] · Sinem Namdaroğlu[5] · Abdülkadir Baştürk[6] · Tuba Hacıbekiroğlu[7] · Mehmet Hilmi Doğu[8] · İlhami Berber[9] · Kürşat Dal[10] · Mehmet Ali Erkurt[9] · Burhan Turgut[11] · Osman Çelik[12] · Mustafa Mahir Ülgü[13] · Şuayip Birinci[14] on behalf of Turkish Ministry of Health, Hematology Scientific Working Group

Naim Ata
naim.ata@saglik.gov.tr

Fevzi Altuntaş
faltuntas@hotmail.com

Tuğçe Nur Yiğenoğlu
dr.nuryigenoglu@gmail.com

Mehmet Sinan Dal
dr.sinandal@gmail.com

Serdal Korkmaz
baranserdalkorkmaz@gmail.com

Sinem Namdaroğlu
dr.sinemnamdaroglu@gmail.com

Abdülkadir Baştürk
drbasturk@yandex.com

Tuba Hacıbekiroğlu
tubahacibekiroglu@sakarya.edu.tr

Mehmet Hilmi Doğu
mhdogu@yahoo.com

İlhami Berber
drilhamiberber@hotmail.com

Kürşat Dal
kursat.dal1@saglik.gov.tr

Mehmet Ali Erkurt
erkurtali@hotmail.com

Burhan Turgut
burhanturgut@hotmail.com

Osman Çelik
osman.celik10@saglik.gov.tr

Mustafa Mahir Ülgü
mahir.ulgu@saglik.gov.tr

Şuayip Birinci
suayip.birinci@saglik.gov.tr

[1] Department of Hematology and Bone Marrow Transplantation Center, Ankara Oncology Training and Research Hospital, University of Health Sciences, Ankara, Turkey

[2] Department of Strategy Development, Republic of Turkey, Ministry of Health, Ankara, Turkey

[3] Department of Hematology, School of Medicine, Ankara Yıldırım Beyazıt University, Ankara, Turkey

[4] Department of Hematology, Kayseri City Hospital, Kayseri, Turkey

[5] Department of Hematology, Bozyaka Training and Research Hospital, İzmir, Turkey

[6] Department of Hematology, School of Medicine, Selçuk University, Konya, Turkey

[7] Department of Hematology, School of Medicine, Sakarya University, Sakarya, Turkey

[8] Department of Hematology, İstanbul Training and Research Hospital, İstanbul, Turkey

[9] Department Hematology, School of Medicine, İnönü University, Malatya, Turkey

[10] Department of Internal Medicine, Keçiören Training and Research Hospital, Ankara, Turkey

[11] Department of Hematology, School of Medicine, Namık Kemal University, Tekirdağ, Turkey

[12] Public Hospitals General Directorate, Ministry of Health, Republic of Turkey, Ankara, Turkey

[13] General Directorate of Health Information Systems, Ministry of Health, Republic of Turkey, Ankara, Turkey

[14] Deputy Minister of Health, Republic of Turkey, Ankara, Turkey