Original Article

The Impact of non-COVID-19 Infections to COVID-19 Disease in Hematological and Solid Organ Malignancies

Hematolojik ve Solid Organ Malignitelerinde COVID-19 Dışındaki Enfeksiyonların COVID-19 Hastalığına Etkisi

Atakan Tekinalp[1], Hilal Akay Çizmecioğlu[2], Mevlüt Hakan Göktepe[2], Sinan Demircioğlu[1], Ali Kürşat Tuna[2], Melek Karakurt Eryılmaz[3]

[1]Necmettin Erbakan University Meram Faculty of Medicine, Division of Internal Medicine, Department of Hematology
[2]Necmettin Erbakan University Meram Faculty of Medicine, Division of Internal Medicine
3Necmettin Erbakan University Meram Faculty of Medicine, Division of Internal Medicine, Department of Oncology

ABSTRACT

Introduction: The aim of this study is to evaluate the clinical differences of COVID-19 infection in hematological and solid organ malignancy patients.
Methods: In the study, patients who have followed up in the Necmettin Erbakan University Meram Medical Faculty Clinic of COVID-19 with a diagnosis of malignancy between 01 September 2020 and 01 January 2021 were compared in terms of epidemiological and clinical characteristics.
Results: The study included 134 patients. Hospitalization day, intensive care need, convalescent plasma need, sedimentation and ferritin levels of patients diagnosed with hematological malignancies were significantly higher (p: 0.001, 0.008, 0.001, 0.001, <0.001 respectively), and the neutrophil, lymphocyte, platelet, and neutrophil-lymphocyte ratio was found to be low, according to the findings of the study. The cure rate of COVID infection was significantly lower with additionally infection in hematological malignancies (OR: 3.1, 95%; CI: 1.4-6.9; p: 0.004). In multivariate analysis, it was determined that an presence of non-COVID-19 infection increased the risk of death 2.8 times (95% CI; 1.3-6.5, p: 0.010).
Discussion and Conclusion: Patients with hematological malignancy have experienced a more severe clinical course of COVID-19 and higher mortality than those with solid tumors. The use of a model in the COVID-19 pandemic that summarizes these non-COVID-19 infections, hematological parameters, age, and comorbidities can help in the method of malignant patients with high mortality risk.

Keywords: SARS COV-2, COVID-19 Virus, pandemics, Hematologic Malignancies, cancer.

ÖZET

Giriş ve Amaç: Çalışmanın amacı, hematolojik ve solid organ maligniteli hastalarda COVID-19 enfeksiyonundaki klinik farkların değerlendirilmesidir.
Yöntem ve Gereçler: Çalışmada 01.09.2020-01.01.2021 tarihleri arasında Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi COVID-19 kliniğinde yatarak takip edilen malignite tanılı hastalar epidemiyolojik ve klinik özellikleri açısından karşılaştırıldı
Bulgular: Çalışmaya 134 dahil edildi. Hematolojik maligniteli hastalarda hastanede yatış günü, yoğun bakım ihtiyacı, konvelesan plazma ihtiyacı, sedimentasyon ve ferritin düzeyleri daha yüksek (sırasıyla; p: 0.001, 0.008, 0.001, 0.001, <0.001); nötrofil, lenfosit, trombosit ve nötrofil/lenfosit oranı daha düşük bulundu. COVID-19 enfeksiyonundan iyileşme oranı, ilave enfeksiyonun olduğu hematolojik maligniteli hastalarda, daha düşüktü (OR: 3.1, 95%; CI: 1.4-6.9; p: 0.004). Çok değişkenli analizde, COVID-19 dışında bir enfeksiyon varlığının ölüm riskini 2,8 kat arttırdığı tespit edildi (%95 GA; 1.3-6.5, p: 0.010).

First Received: 21.04.2022, Accepted: 06.07.2022 doi: 10.5505/aot.2022.03206

Tartışma ve Sonuç: COVID-19 enfeksiyonu hematolojik maligniteli hastalarda solid organ maligniteli hastalara göre daha şiddetli seyretmektedir. COVID-19 pandemisinde COVID-19 dışı enfeksiyonlar, hematolojik parametreler, yaş ve ko-morbiditeden oluşan bir modelin kullanılması, yüksek mortalite riski olan malign hastaların yönetiminde yardımcı olabilir.

Anahtar Kelimeler: SARS COV-2, COVİD-19 Virus, Hematoloji Maligniteler, kanser

Introduction

In 2003, the first global health emergency with the sickness termed Severe Acute Respiratory Syndrome was enrolled as the world entered the 21st century (SARS). In addition, pneumonia in the city of Wuhan, Hubei province of China was reported as of 31 December 2019 [1]. The disease was designated coronavirus-2 (COVID-19) because of its similar to SARS CoV, and it was called the cause agent SARS-CoV-2 [2]. On 11 March 2020, the WHO identified COVID-19 as a pandemic. The sickness has infected over 100 countries. At least 186 million people were afflicted as of July 13, 2021, with nearly four million deaths [3].

Due to the presence of COVID-19, an infection with the potential for nosocomial transmission could not be treated in the emergency due to individuals with high fatality [4]. Many respiratory therapies for critical ill patients are considered high risk factors for nosocomial transmission (intubation, manual ventilation, etc) [5]. Cancer patients are particularly susceptible to infections during viral outbreaks because of immunosuppression, one of the most sensitive patient groups. The tumor itself and anticancer therapy lead to immunosuppressive conditions [6]. According to 2015 cancer epidemiology statistics, a China report identified cancer history in 18 (1,13 percent) of the 1,590 COVID-19 cases, which was higher than the overall Chinese population for cancer. Research in China indicated that in all patients, the death rate of COVID 19 patients was 2,3%, however in cancer patients the rate was 5,6% [7].

Patients with solid organ and hematological malignancies may present to emergency services with oncological emergencies, primary disease progression or metastasis, metabolic effects of the malignancy, unfavorable treatment effects, or other diseases. These patients must reduce malignancy-related symptoms, manage treatment-related side effects, and treat oncological emergencies and associated diseases in the emergency department [8-11].

Treatment management of patients diagnosed with malignancy with COVID-19 during the epidemic is difficult. Treatment of COVID-19-positive patients diagnosed with cancer during the outbreak is tough. COVID-19 complications can occur as a result of immunosuppression caused by malignancy and anti-tumor treatment [12,13]. Delaying anti-tumor therapy, on the other hand, may result in tumor progression. Patients who become infected within the first 30 days after completing chemotherapy had a higher mortality rate [14] Furthermore, the fact that the malignancy is not under control contributes to COVID-19's more severe course. Infected patients who are in remission may lose their remission due to SARS-CoV-2 infection [15]. Data on the management of malignant patients with COVID-19 infection were obtained from retrospective studies. The general implementation is to interrupt specific treatment and modify the treatment in the presence of suspected or diagnosed COVID-19 [16]. Based on this context, the aim of the study is to examine the management of COVID-19 infection in hematological and solid organ malignancies patients with tertiary hospital experience.

Materials and Methods

The work plan. This study was designed as a single-center study where epidemological features, malignancy types and laboratory parameters of patients with malignancy who were hospitalized in Necmettin Erbakan University Meram Faculty of Medicine Clinic of COVID-19 between 01.09.2020-01.01.2021 were analyzed. All those patients were included the study.

Ethics committee approval of the study was received from Necmettin Erbakan University Meram Faculty of Medicine Clinical Research Ethics Committee with the number 2021/3034 and by signed form related to Helsinki Declaration.

The epidemiological characteristics (age, gender) and malignancy types of the patients constituting the sample of the study were determined. The patients were analyzed in two groups as hematological malignancy (HM) and solid organ malignancy (SM). The two groups were compared in terms of laboratory values, computed tomography (CT) results, convalescent plasma (CP), intensive care unit (ICU) and mechanical ventilation (MV) needs, hospitalization days and healing status, treatment for malignancy, and presence of additional infection.

Clinical Evaluation. Severe COVID infection was defined as dyspnea, >50% increase in lung infiltration on CT within 24-48 hours, oxygen saturation <93%, PaO2/FiO2 <300, and septic shock [17]. In our center where the study was conducted, CP was applied to these cases.

Statistical Analysis. IBM SPSS Statistics for Windows, Version 22.0 program was used for statistical analysis. Distribution analysis of continuous numerical variables was evaluated with the Kolmogorov-Smirnov Test and, variables were presented by median (minimum-maximum). Mann-Whitney U test was applied for comparison of two groups. Categorical variables were expressed as percent (%) and compared with the Chi-Square test. In Spearman correlation analysis, 0.00-0.24 weak, 0.25-0.49 moderate, 0.50-0.74 strong and 0.75-1.00 very strong correlations were accepted for the coefficient (rho). Multivariate analysis was performed with Logistic regression modeling using the Backward method. Parameters considered to be of clinical importance and resulting in $p<0.25$ in univariate analysis were included in the modeling. One of the correlated parameters was included in the model. $p<0.05$ results were considered statistically significant.

Results

The study included a group 134 patients. Of the patients, 70 (52.2%) were male, 64 (47.8%) were female, and the median age was 66 (24±87). All patients included in the study were diagnosed with COVID-19 according to their clinical and radiological characteristics, and the nasal PCR test was positive in only 17 (12.7%) patients. According to malignancy types, 68 (50.7%) of the patients were diagnosed as solid organ malignancies and 66 (49.3%) of them were diagnosed as hematological malignancies. Diagnostic distribution of patients included in the study by malignancy types is given in Table 1.

The comparison of malignancies in terms of laboratory of the patients is given in Table 2. Sedimentation and ferritin were significantly higher in patients diagnosed with HM; neutrophil, lymphocyte, platelet and neutrophil lymphocyte ratio (NLR) was found to be lower. Additionally, the need for CP was found to be significantly higher in patients diagnosed with HM than in patients diagnosed with SM (HM: 71.2%; SM: 42.6%, p: 0.001). Additionally, patients diagnosed with HM had a significantly longer hospitalization and a higher need for intensive care (HM: 11.5; SM:

Table-1: The Frequency of Malignancies, n(%)

Hematological Malignancies	
Multiple Myeloma	22 (16,4)
Non-Hodgkin Lymphomas	14 (10,4)
Myelodysplastic Syndrome	12 (9,0)
Acute Myeloid Leukemia	10 (7,5)
Chronic Lynphocytic Leukemia	4 (3,0)
Acute Lynphoblastic Leukemia	2 (1,5)
Hodgkin Lymphoma	2 (1,5)
Solid Organ Malignancies	
Colorectal Cancer	14 (10,4)
Breast Cancer	11 (8,2)
Lung Cancer	9 (6,7)
Pancreatic Cancer	8 (6,0)
Gastric Cancer	7 (5,2)
Over Cancer	4 (3,0)
Prostate Cancer	3 (2,2)
Nasopharyngeal Cancer	2 (1,5)
Others*	10 (7,0)

8, p: 0.008). Mortality rate was found to be higher in HM patients, although not significant (HM: 66%; SM: 27.9%, p; 0.458). When all the patients included in the study were analyzed, it was found that 41 (30.6%) patients died.

The number of patients diagnosed with COVID-19 during active chemotherapy (CT) was 111 (82.8%). The need for CP was 60.8% (n:67) in patients in the CT period and 39% (n:9) in the others. The cure rate was 61.2% (n:41) in patients undergoing CT, and 88.9% (n:8) in those who did not. When all patients included in the study were evaluated, the cure rate was 64.5% (n:49) in those who underwent CP.

The distribution of clinical features of all patients included in the study is given in Table 3. According to Table 3, growth in blood, urine or sputum cultures other than COVID-19 was detected in 39 (29.1%) of the patients included in the research. In the presence of additional infection, the cure rate was found to be significantly lower in HM ([HM: 51.3%; SM: 76.9%]; [OR: 3.1-95%; CI: 1.4-6.9], p:0.004). While the need for CP was 71.8% (n:28) in patients with additional infection, the need for CP was 50.5% (n:48) in patients who did not, and it was statistically significant (OR:2.4 9%; CI 1.1-5.5, p: 0.024). When 76 patients who underwent CP were evaluated, the cure rate was 75% (n:36) in patients without growth, while the cure rate was significantly lower at 46.4% (n:13) in patients with growth (OR:3.4-95%; CI:1.3-9.3 p:0.012). Additionally, the frequency of active infection was found to be higher in patients receiving CT, even though it was not statistically significant (32.4% vs. 13%, p:0.062). Multivariate logistic regression analysis in Table 4 showed that the presence of non-COVID-19 infection increased the risk of death 2.8-fold (95% CI; 1.3-6.5, p:0.01).

When the correlation analyzes were analyzed, a moderate correlation (rho: 0.427, p:0.007) was found between female gender and culture positivity, and a strong correlation between the application of CP and the day of hospitalization (rho: 0.62, p<0.001).

Discussion

In the COVID-19 pandemic, patients with malignancy are considered a particularly vulnerable group. To date, nothing is known about the clinical characteristics of COVID-19-infected malignancy patients. COVID-19 infection, on the other hand, is known to worsen in malignant patients [18]. On February 26, 2020, the clinical characteristics of 28 cancer patients from three designated hospitals in Wuhan, China, who had a laboratory-confirmed diagnosis of COVID-19 were described. In 53.6% of the patients, serious events occurred, 21.4% were hospitalized to the intensive care unit, 35.7% suffered life-threatening complications, and 28.6% died [19]. ICU admission, mechanical ventilation, or death were all considered significant events in this study. The percentage of patients with severe infection was 56.7% in our study, with a 30.6% mortality rate. In the general COVID-19 infected population, 4.7% of cases have evolved to a clinical critical state, with almost

Table-2. Comparison of malignancies in terms of laboratory

	Hematological Malignancies (n: 66)	Solid Organ Malignancies (n:68)	p
Age	66 (24-87)	66 (38-85)	0,74
CRP (mg/L)	98,8 (0,9-411)	87,7 (1,7-438)	0,50
Sedimentation (mm/h)	98,5 (5-140)	76 (6-140)	0,001*
Fibrinogen (mg/dL)	481 (182-1032)	445 (147-988)	0,69
D-Dimer (mg/mL)	771,5 (72-46692)	777,5 (61-62560)	0,14
Ferritin (ng/mL)	1539 (77-36472)	865 (13-11691)	<0,001*
Procalcitonin (ng/mL)	0,4 (0,02-67,5)	0,3 (0,03-68)	0,75
Neutrophil (/µL)	1,2 (0,01-21,8)	4,8 (0,05-18,7)	<0,001*
Lymphocyte (/µL)	0,42 (0,01-2,55)	0,65 (0,02-18,7)	0,001*
PLT (/µL)	51,5 (2-494)	190 (12-470)	<0,001
NLR	3,1 (0,01-1227)	5,6 (0,18-54,5)	0,001*

Note: Variables were presented as median (minimum-maximum)
PLT; Platelet, NLR; Neutrophil/Lymphocyte Ratio
*Mann-Whitney U Test

Table-3. Clinical Comparison of Malignancies

	Hematological Malignancies (n: 66)	Solid Organ Malignancies (n:68)	p
Hospitalization day*	11,5 (2-64)	8 (3-23)	0,001[a]
CP Need, n (%)	47 (71,2)	29 (42,6)	0,001[b]
İntensive Care Need, n (%)	31 (47)	17 (25)	0,008[b]
MV Need, n (%)	17 (25,8)	10 (14,7)	0,11
After Treatment, n (%)			0,50
Recovery	44 (33,3)	49 (72,1)	
Dead	22 (66,7)	19 (27,9)	
Degree of CT imaging, n (%)			0,17
Low	16 (24,2)	24 (35,3)	
Mild	21 (31,8)	13 (19,1)	
High	29 (43,9)	31 (45,6)	
Culture, n (%)			0,15
Positive	23 (34,8)	16 (23,5)	
Negative	43 (65,2)	52 (76,5)	
During Chemotherapy, n (%)	53 (80,3)	58 (85,3)	0,44

CP; Convalescent Plasma, MV; Mechanical Ventilator, CT; Computerized Tomography
*Median (minimum-maximum)
[a]Mann-Whitney U test
[b]Pearson's chi-square test

Table 4: Multivariate Analysis of Risk Factors for Death*

Risk Factor	Hazard Ratio (95% CI)	P
Age	1,1 (0,993-1,060)	0,12
Sex (female vs male)	0,7 (0,318-1,551)	0,38
During Chemotherapy (yes vs no)	3,2 (0,857-12,176)	0,84
Non-COVID-19 infection (yes vs no)	**2,8 (1,264-6,422)**	**0,01**

*The possible factors identified by univariate analyses were included into the model. In order to determine independent predictors on death, Logistic regression analysis with backward selection was used and, statistical significantly step was added on the table.

half of critical cases (2.3%) being fatal [20]. In our study, the percentage of patients with severe infection was 56.7%, with a 30.6% mortality rate. The frequency of severe infection in HM patients was 15.5%, the need for intensive care was 18.9%, and the need for MV was found to be significantly higher in a study comparing HM patients with the non-HM population [21]. In similar studies, the duration of mechanical ventilation and ICU stay were found to be lower in patients with mortality [22].

Males were prominent in fatal cases of COVID-19 infection, according to a Wuhan study, and the median age was 65.8 years [23]. Furthermore, patients with lung cancer (>60 years old) from solid organ malignancies are at risk of COVID-19 infection, according to the findings. However, we know that lung cancer is more common in the sixth decade and in males [24]. These two deadly diseases can be seen together in the risk population, given their similar demographic characteristics. In our research, it was found that multiple myeloma (16.4%) was the most common among patients diagnosed with hematological malignancies according to malignancy types, and colorectal carcinoma (10.4%) was the most common among patients diagnosed with solid organ malignancies. This is thought to be due to the patient groups included in the study. Patients with malignancy are especially vulnerable to respiratory infections and severe pneumonia because they are immunosuppressed as a result of their disease and anti-tumor treatment. The presence of non-COVID 19 infections raised the risk of death by 2.8 times in our study, which is linked to the prevalence of serious clinical events in COVID-19 infection. According to Liang and et al., a lower percentage of cancer patients (7 out of 18) have serious events [25]. In a study by Chen et al (2020) with eleven patients (10 with nasal oxygen demand, 8 with severe comorbidity), nasopharyngeal PCRs were still positive in 8 of 10 patients 5-6 days after treatment. It was claimed that 6 of these patients had solid/hematological malignancies as a comorbidity [26]. The main reasons for the difference can be attributed to variation in the definition of serious events and study populations. Liang and et al. defined clinical severe events as an admission of patients to the intensive care unit requiring invasive ventilation or death [25].

Given the rise of COVID-19 disease despite recent advancements, rapid and reliable biomarkers are required for the early diagnosis of patients with high mortality risk, such as those diagnosed with COVID-19 malignancy. To evaluate the severity of a disease, some biomarkers have been proposed [27]. While there was a significant difference in laboratory parameters such as sedimentation and ferritin values in patients

with HM, the neutrophil, lymphocyte, platelet, and neutrophil-lymphocyte ratio (NLR) was found to be low in this study. In severely ill patients with COVID-19 infection, lymphocytopenia is a prominent feature among hematological parameters. The cytoplasmic component of the lymphocyte is damaged and destroyed by the targeted invasion of COVID-19 viral particles [28]. Findings that lymphocytes express ACE-2 receptors on their cell membranes support this hypothesis [29]. Furthermore, pro-inflammatory cytokines including tumor necrosis factor-alpha and (IL-6) can cause a reduction in lymphocyte count [30]. The lymphocyte counts of patients who died with COVID-19 were found to be significantly lower than those of survivors [27]. Lymphocytopenia was found in more than 80% of severely ill patients in one research [31]. In a meta-analysis of 21 studies involving COVID-19 patients, it was determined that patients with critical illness and developing mortality had a decreased lymphocyte count compared to survivors [32]. Lymphocytopenia can be used in the clinical diagnosis of new coronavirus infections or to predict the clinical course.

Sedimentation levels are more stable among inflammatory biomarkers, but CRP levels increase significantly in the early stages of the disease, with a positive correlation between increased CRP levels and disease severity [33,34]. In COVID-19 patients, more severe cases revealed a more dramatic PCT increase than non-severe cases, similar to our findings in studies [35,36]. In a retrospective clinical serial, non-survivors had higher CRP and ferritin levels than survivors [37]. In another study, researchers found increased ferritin levels in patients who died [32]. Additionally, when the Charlson comorbidity index (CCI) is examined, the frequency of solid organ malignancies among the patients who developed mortality is higher than the patients who survived. Accordingly, as the COVID-19 epidemic intensifies, it is considered that it will be beneficial for clinicians to consider low lymphocyte count, ferritin, CRP, and PCT serum levels, considering that the need for early identification biomarkers will increase, especially in patients with high mortality risk such as patients diagnosed with malignancy.

Within 14 days of being diagnosed with COVID-19, patients with a history of malignant tumors were found to undergo anti-tumor treatment and patchy consolidation on computed tomography (CT), independently increasing the risk of serious complications [38]. The frequency of active infection was shown to be greater in patients undergoing active chemotherapy in our study, despite the fact that it was not statistically significant. The cure rate for patients who underwent CP was 64.5% among those who received active chemotherapy in the research. In the study conducted by Shen et al., the detection of an increase in the lymphocyte count and a significant decrease in CRP values in patients who underwent CP, and a regression in the radiological findings of the lung at the end of one week, supports the results of the study [19]. Additionally, the strong correlation between the length of hospital stay and the beneficial effects on the patients who underwent CP is an indicator of this result.

The limitations of our study are that it was retrospective, the stage and risk groups of malignancies were not included, and other infection types were not specified. We believe that our study will contribute to the literature in terms of showing that COVID-19 infection is more severe in patients with hematological malignancies than in patients with solid organ malignancies.

Low lymphocyte count, high CRP, ferritin, and PCT levels, according to the findings, can help clinicians identify patients with malignant diagnosis with a high mortality risk. The use of a model in the COVID-19 pandemic that summarizes the sum of these

non-COVID infections, hematological parameters, age and comorbidities can help in the method of patients with a history of malignant tumors with a high mortality risk.

REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020; 382: 727–733.
2. Statement on the second meeting of the International Health Regulations (2005). Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). World Health Organization.
3. WHO Coronavirus Disease (COVID-19) Dashboard | WHO Coronavirus Disease (COVID-19) Dashboard, 2021. Available from: https://covid19. who.int/
4. Zhonghua Liu Xing Bing Xue Za Zhi. Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID19) in China. Chin J Epidemiol. 2020; 41: 145-151.
5. Zhonghua Jie He He Hu Xi Za Zhi. Respiratory care committee of Chinese Thoracic S. Expert consensus on preventing nosocomial transmission during respiratory care for critically ill patients infected by 2019 novel coronavirus pneumonia. Chin J Tuberc Respir Dis. 2020; 17: E020.
6. Wang D, Hu B, Hu C, Zhu F, Liu X et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020; 323: 1061-1069.
7. Wu Z, McGoogan JM. 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. JAMA. 2020; 323(13): 1239-1242.
8. Swenson KK, Rose MA, Ritz L, Murray CL, Adlis SA. Recognition and evaluation of oncology-related symptoms in the emergency department. Ann Emerg Med. 1995; 26(1): 12-17.
9. Mayer DK, Travers D, Wyss A, Leak A, Waller A. Why do patients with cancer visit emergency departments? Results of a 2008 population study in North Carolina. J Clin Oncol. 2011; 29(19): 2683-2688.
10. Barbera L, Taylor C, Dudgeon D. Why do patients with cancer visit the emergency department near the end of life? Can Med Assoc J.2010; 182(6): 563-568.
11. Guddati AK, Kumar N, Segon A, Joy PS, Marak CP et al. Identifying oncological emergencies. Med Oncol. 2013; 30: 669-675.
12. Shereen NG, Salman D. Delivering chemotherapy at home: How much do we know? Br J Community Nurs. 2019; 24: 482-484.
13. You B, Ravaud A, Canivet A, Ganem G, Giraud P et al. The official French guidelines to protect patients with cancer against SARS-CoV-2 infection. Lancet Oncol. 2020; 21(5): 619-621.
14. Yekedüz E, Utkan G, Ürün Y. A systematic review and meta-analysis: the effect of active cancer treatment on severity of COVID-19. Eur J Cancer. 2020; 141: 92–104.
15. Li W, Wang D, Guo J, Yuan G, Yang Z et al. COVID-19 in persons with chronic myeloid leukaemia. Leukemia. 2020;34(7):1799–1804.
16. Weinkove R, McQuilten ZK, Adler J, Agar MR et al. Managing haematology and oncology patients during the COVID-19 pandemic: interim consensus guidance. Med J Aust. 2020; 212(10): 481–489.
17. U.S. Food and Drug Administration (FDA). Recommendations for Investigational COVID-19 Convalescent Plasma. Food Drug Adm. 2020; 1–7.
18. He W, Chen L, Chen L, Yuan G, Fang Y et al. COVID-19 in persons with haematological cancers. Leukemia. 2020; 34(6): 1637–1645.
19. Zhang L, Zhu F, Xie L, Wang C, Wang J et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. Ann Oncol. 2020; 31(7): 894–901.
20. Wu Z, McGoogan JM. 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. 2020; 323(13): 1239-1242.
21. Yigenoglu TN, Ata N, Altuntas F, Bascı S, Dal MS et al. The outcome of COVID-19 in patients with hematological malignancy. J Med Virol. 2021; 93(2): 1099–1104.
22. Guan WJ, Ni ZY, Hu Y, Liang WH, Qu CQ et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020; 382: 1708-1720.
23. Du Y, Tu L, Zhu P3 Mu M, Wang R, Yang P et al. Clinical Features of 85 Fatal Cases of COVID-19 from Wuhan: A Retrospective Observational Study. Am J Respir Crit Care Med. 2020; 201(11): 1372-1379.
24. Barta JA, Powell CA, Wisnivesky JP. Global Epidemiology of Lung Cancer. Ann Glob Health. 2019; 85: 8.
25. Liang W, Guan W, Chen R, Wang W, Li J et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol. 2020; 21(3): 335-337.
26. Chen Z, Hu J, Zhang Z, Jian S, Han S et al. Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial. medRxiv preprint doi: 10.1101/ 2020.03.22. 20040758.

27. Velavan TP, Meyer CG. Mild versus severe COVID-19: Laboratory markers. Int J Infect Dis. 2020; 95: 304-307.
28. Gu J, Gong E, Zhang B, Zheng J, Gao Z et al. Multiple organ infection and the pathogenesis of SARS. J Exp Med. 2005; 202: 415-424.
29. Xu H, Zhong L, Deng J, Peng J, Dan H et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci. 2020; 12: 8.
30. Liao YC, Liang WG, Chen FW, Hsu JW, Yang JJ et al. IL-19 induces production of IL-6 and TNF-alpha and results in cell apoptosis through TNF alpha. J Immunol. 2002; 169: 4288-4297.
31. Yang X, Yu Y, Xu J, Shu H, Xia J et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single centered, retrospective, observational study. Lancet Respir Med. 2020; 8: 475-481.
32. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a metaanalysis. Clin Chem Lab Med. 2020; 58: 1021-1028.
33. Wang L. C-reactive protein levels in the early stage of COVID-19. Med Mal Infect. 2020; 50: 332-334.
34. Yang W, Cao Q, Qin L, Wang X, Cheng Z et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): A multicenter study in Wenzhou city, Zhejiang, China. J Infect. 2020; 80: 388-393.
35. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS et al. China Medical Treatment Expert Group for COVID19. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Eur Respir J. 2020; 14 ;55(5): 2000547.
36. Zhang G, Hu C, Luo L, Fang F, Chen Y et al. Clinical features and shortterm outcomes of 221 patients with COVID-19 in Wuhan, China. J Clin Virol. 2020; 127: 104364.
37. Zhou F, Yu T, Du R, Fan G, Liu Y et al. Clinical course and risk factors for mortality of adult inpatients with COVID19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395: 1054-1062.
38. Shen C, Wang Z, Zhao F, Yang Y, Li J et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. Jama. 2020; 323 (16): 1582-1589.

Corresponding author e-mail: atakantekinalp@hotmail.com

Orcid ID:
Atakan Tekinalp 0000-0001-7937-4045
Hilal Akay Çizmecioğlu 0000-0002-3312-4638
Mevlüt Hakan Göktepe 0000-0003-1711-5157
Sinan Demircioğlu 0000-0003-1277-5105
Ali Kürşat Tuna 0000-0002-7453-326X
Melek Karakurt Eryılmaz 0000-0003-2597-5931

Doi: 10.5505/aot.2022.03206

