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COVID-19 Disease in Patients with Hematological Disease-Single Center Data

Hematolojik Hastalarda COVID-19 Hastalığı-Tek Merkez Verisi

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Abstract

Objectives: Coronavirus disease-2019 (COVID-19) is a pandemic that has been the main issue of the healthcare since December 2019. There are difficulties in treatment and follow-up for hematology patients. In this study, we aimed to share data about the disease and mortality of patients diagnosed with COVID-19.

Materials and Methods: The patients diagnosed with COVID-19 between March 2020 and February 2021 were included. Patients were retrospectively analyzed.

Results: Forty-nine patients were evaluated. Twenty-one were female, 28 were male, the median age was 64 (19-84) years. Nineteen patients had no comorbidities. Thirty patients had 1-4 comorbid diagnoses. Forty-one (83%) patients had malignant hematological diagnosis, 33 (67%) of them were receiving active chemotherapy. Sixteen (33%) patients were in the cytopenic period. Six patients were asymptomatic at the time of diagnosis. Nineteen (38.8%) of the patients had mild illness, 6 (12.2%) had moderate COVID-19, 24 (49%) had severe disease. Fourteen (29%) patients were followed up at home, while 35 (71%) patients were hospitalized. Twenty-one (60%) of the inpatients were followed up in the intensive care unit. Totally 17 patients (34.6%) died from COVID-19 infection. Being diagnosed with COVID-19 during hospitalization for the hematological causes, hematological disease status, cytopenia on the day of COVID-19 diagnosis, hospitalization for COVID-19 treatment, lung involvement, accompanying extrapulmonary organ involvement, decreased hemoglobin level and thrombocyte count, systemic inflammatory response syndrome development, intensive care admission, intubation and secondary infection during hospitalization were the factors associated with higher mortality.

Conclusion: In this study, we observed that COVID-19 had a higher morbidity and mortality in hematological patients. More attention should be paid to hematological patient groups in the era of COVID-19 to protect them from the disease.

Key Words: Hematological Diseases, COVID-19, SARS-CoV-2

Öz

Amaç: Koronavirüs hastalığı-2019 (COVID-19), Aralık 2019'dan bu yana sağlık hizmetlerinin ana uğraşı haline gelmiş bir hastalıktır. Hematoloji hastalarının COVID-19 tedavi ve takiplerinde zorluklar yaşanmaktadır. Bu çalışmada COVID-19 tanısı alan hematolojik hastaların hastalık seyri ve ölüm oranlarına ilişkin verileri paylaşmayı amaçladık.

Gereç ve Yöntem: Mart 2020 ile Şubat 2021 arasında COVID-19 tanısı konulan hastalar çalışmaya dahil edildi. Hastalar retrospektif olarak incelendi.

Bulgular: Kırk dokuz hasta değerlendirildi. Yirmi biri kadın, 28'i erkek idi, ortanca yaş 64 (19-84) idi. On dokuz hastada komorbidite yoktu. Otuz hastada 1-4 ek tanı vardı. Kırk bir (%83) hastada malign hematolojik tanı saptandı, 33'ü (%67) aktif kemoterapi alıyordu. On altı (%33) hasta sitopenik dönemdeydi. Altı hasta tanı anında asemptomatikti. Hastaların 19'u (%38,8) hafif, 6'sı (%12,2) orta derecede COVID-19, 24'ü (%49) ağır hastalığa sahipti. On dört (%29) hasta evde takip edilirken, 35 (%71) hasta hastaneye yatırıldı. Yatan hastaların 21'i (%60) yoğun bakımda takip edildi. Toplam 17 hasta (%34,6) COVID-19 enfeksiyonundan öldü. Hematolojik nedenlerle hastanede yatışı sırasında COVID-19 tanısı almış olmak, hematolojik hastalık durumu, COVID-19 tedavisi için yatış, akciğer tutulumu, eşlik eden ekstrapulmoner organ tutulumu, anemi, trombositopeni, sistemik enflamatuvar yanıt sendromu gelişimi, yoğun bakıma yatış, entübasyon ve sekonder enfeksiyon gelişimi daha yüksek mortalite ile ilişkili bulundu.

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Sonuç: Bu çalışmada, hematolojik hastalarda COVID-19'un daha yüksek morbidite ve mortaliteye sahip olduğunu gözlemledik. Bu nedenle hematolojik hasta gruplarını COVID-19 döneminde hastalıktan korumak için daha fazla özen gösterilmelidir.

Anahtar Kelimeler: Hematolojik Hastalıklar, COVID-19, SARS-CoV-2

Introduction

Coronaviruses are a group of RNA viruses that can infect animals and humans, causing respiratory infections in humans. Coronavirus disease-2019 (COVID-19) infection is the name given to the infection of the coronavirus subtype, most recently named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) (1). In December 2019, COVID-19 infection was first described as a highly contagious lung infection in China (2). The infection, which affected the whole world in a short time and spread rapidly with the inhalation of viral particles, was defined as a pandemic by the World Health Organization (WHO) in March 2020, and the first cases began to appear in our country at that time.

COVID-19 infection status of hematology patients who have been immunosuppressive due to their diseases and/or treatments often seems to be challenging from the beginning of the pandemic (3). Advanced age, male gender, comorbidities and pregnancy have been defined as risk factors for COVID-19 progression. Among comorbid conditions, hematological malignancies are defined as risk factors because of their immunosuppressive state (4). A multicenter study, which COVID-19 was evaluated in cancer patients, including hematological malignancies, showed that severe COVID-19 development was higher in cancer patients than in patients without cancer (64% vs 32%) (5). The same study identified advanced age, high interleukin 6, procalcitonin, D-dimer levels, low lymphocyte count, advanced tumor stage as risk factors indicating the severity of COVID-19 disease (5). In different series, COVID-19 mortality was found to be higher in patients with malignancies compared to non-cancer patients, and the mortality rate was reported between 23.5-34% (6-9). In this study, we aimed to share descriptive data and to determine the mortality status of hematology patients diagnosed with COVID-19 during their follow-up in our outpatient and inpatient clinic.

Materials and Methods

Patient Characteristics and Selection

Patients following for a hematological disease and diagnosed with COVID-19 between March 2020 and February 2021 were included in the study. The data of patients who were diagnosed during outpatient or clinical follow-up and treated as outpatients or inpatients were recorded.

Patients who were not diagnosed by us and who were not followed up by any of the investigators in the study were excluded.

Patients' Data

Demographic and laboratory data were obtained from the electronic hospital database and medical files of the patients. Patients' age, sex, comorbidities, detailed information about underlying hematological diseases, COVID-19 diagnosis date, symptoms of the disease and symptom onset date, diagnostic procedure of COVID-19, disease severity, COVID-19 treatment modalities, hematological parameters at the diagnosis, development of systemic inflammatory response syndrome (SIRS), maximum level of ferritin and D-dimer, extrapulmonary organ involvement, antiaggregant-anticoagulant therapy status, intensive care unit (ICU) admission and intubation history, secondary infection coexistence, the latest state of COVID-19 infection, COVID-19 related mortality-morbidity status were recorded.

We evaluated the disease severity according to WHO COVID-19 disease severity definitions. Patients with any of the following finding classified as severe COVID-19;

• Severe pneumonia that means clinical signs of pneumonia and having a saturation of peripheral oxygen (SpO_2) <90% on room air or ≥40 breaths in minute.

• Acute respiratory distress syndrome that means patients on mechanical ventilation with partial pressure arterial oxygen /fraction of inspired oxygen ≤300 mmHg with positive end-expiratory pressure or continuous positive airway pressure ≥5 cmH_2O.

• Sepsis.

• Septic shock.

Patients having clinical signs of pneumonia such as fever, cough, dyspnea, tachypnea without a sign of severe pneumonia and SpO_2 ≥ 90% on room air classified as moderate disease. Symptomatic patients without evidence of viral pneumonia or hypoxia classified as mild disease.

Leukopenia, neutropenia, lymphopenia, thrombocytopenia at diagnosis of COVID-19 was defined as values below $4x10^9$/L, $1.5x10^9$/L, $1x10^9$/L and $150x10^9$/L respectively.

Statistical Analysis

Continuous variables were given as median (minimum-maximum). Categorical variables such as gender and comorbidity are represented as percentages (%). Continuous characteristics were compared between groups by Independent samples t-test, Mann-Whitney U test or Kruskal-Wallis test with respect to the distribution of characteristics and the number of the groups. When necessary, Mann-Whitney U test with Bonferroni correction was applied as post-hoc test after Kruskal-Wallis test. Chi-square tests were performed to compared categorical characteristics between groups. Logistic regression analysis was used to determine independent risk factors for ICU mortality. A p-value <0.05 was considered as statistically significant.

All statistical analyses were performed with IBM SPSS Statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.).

Ethical Standards

Ethics committee approval was received from Ministry of Health and Ankara City Hospital Local Ethics Committee with the number E1-21-1715.

Results

Forty-nine patients included in our study. Median age of the patients was 64 (19-84), 21 were female, 28 were male. Fifteen of the patients were being followed up with the diagnosis of acute leukemia, 12 with non-Hodgkin's lymphoma and 10 with multiple myeloma. Other diagnoses were chronic myeloproliferative disease, myelodysplastic syndrome, chronic lymphocytic leukemia, immune thrombocytopenia, aplastic anemia (Figure 1).

Twenty of the patients were diagnosed with hematological disease in the last one year, during COVID-19 period in our country. Characteristics of the patients are given in Table 1. Forty-one (83%) patients had malignant hematological diagnosis, 33 (67%) of them were receiving active chemotherapy. Sixteen (33%) patients were cytopenic at the time of COVID-19 diagnosis and 11 were receiving steroids as a part of their chemotherapy. Thirty (61.2%) of the patients had at least one comorbid disease. Most common comorbid disease in COVID-19 patients with hematological diseases was hypertension. There was no active smoker patient but 28 of them were ex-smokers.

Three patients were diagnosed with COVID-19 until August 2020, while the number of patients diagnosed with COVID-19 after this date was 46 (94%). Twenty-one (43%) patients were diagnosed with COVID-19 during hospitalization due to their hematological disease. The median day from onset of COVID-19 associated symptoms to diagnosis was 2 (0-14). Twenty-three (47%) patients had a history of contact with a COVID-19 positive person. At the time of the diagnosis of COVID-19, 6 (12.2%) patients were asymptomatic. These patients were diagnosed with polymerase chain reaction (PCR) test before hospitalization for their hematological disease or due to test because of a contact history with a COVID-19 positive person. The most common symptom of the patients was fever or fever with

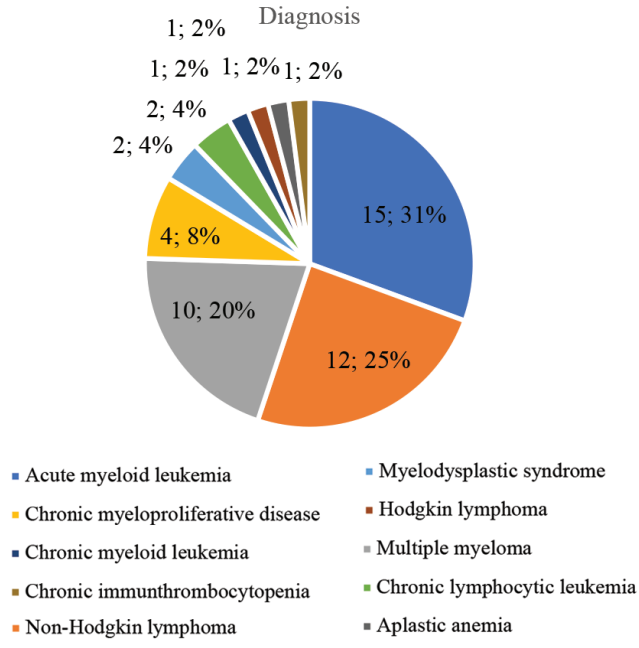

Figure 1: Hematological diseases of the patients

Table 1: Characteristics of the patients

Characteristics	n=49
Median age (years) (Min.-Max.)	64 (19-84)
Gender	
Male (%)	28 (57%)
Female (%)	21 (43%)
Hematological diagnosis	
Acute leukemia	15
Multiple myeloma	10
Non-Hodgkin's lymphoma	9
Other hematological malign diseases	7
Benign hematological diseases	8
Active chemotherapy (%)	
Co-morbidities	33 (67%)
None (%)	19 (38%)
1-4 Co-morbid diseases (%)	30 (62%)
Hypertension	21
Smoking status	
Non-smoker (%)	21 (43%)
Ex-smoker (%)	28 (57%)

Min.: Minimum, Max.: Maximum

other symptoms, respiratory system complaints such as cough, dyspnea and structural symptoms such as weakness, fatigue, muscle and bone pain were the other symptoms following fever. The distribution of symptoms is shown in Table 2. Forty-eight patients were diagnosed with PCR test positivity, only 1 patient was diagnosed with thorax computed tomography (CT). CT was performed simultaneously in 21 (43%) of the patients diagnosed with PCR.

The hematological parameters of the patients at the time of diagnosis of COVID-19 are presented in Table 3. Fourteen (28.5%) of the patients were followed up with outpatient treatment, 2 of them required hospitalization. Thirty-five (71.5%) patients were treated as inpatients from the time of diagnosis. Twenty-one (60%) of the inpatients were followed up in the ICU, and 14 (40%) in the clinic. The number of patients who required intubation was 13. For COVID-19, 3 patients were followed up without treatment, 2 patients received only hydroxychloroquine (HCQ) treatment and 44 (89.7%) patients received favipravir and/or HCQ, colchicine, steroids. Convalescent plasma therapy was given to 3 patients. Disease progression in hospitalized patients was on the median day 4 (1-17). Anti-cytokine treatment was required for 19 patients. Twelve of these patients received steroid and intravenous immunoglobulin (IVIG), 7 of them received steroid therapy alone. All 7 patients who received steroid therapy alone died. Nine of 12 patients who received IVIG and steroids died. Secondary infection development was observed in 22 patients.

The analysis of the data of the patients who were followed up for D-dimer and ferritin showed a median maximum D-dimer level 6,235 mg/L (0.51-60.340) and median maximum ferritin level 1612 µg/L (58-180.498).

Table 2: COVID-19 symptoms of the patients

Symptoms	Number of patients (%)
Asymptomatic	6 (12.2%)
Fever	21 (42.9%)
Respiratory system symptoms	12 (24.5%)
Constitutional symptoms	10 (20.4%)
Total	49 (100%)

COVID-19: Coronavirus disease-2019

Table 3: Hematological parameters on the day of COVID-19 diagnosis

Parameter	Median (Min.-Max.)
Hemoglobin (g/dL)	9.4 (5-15.3)
Leukocyte count (x10^9/L)	3.75 (0.28-50)
Neutrophil count (x10^9/L)	2.32 (0.05-17)
Lymphocyte count (x10^9/L)	0.66 (0.05-39.6)
Platelet count (x10^9/L)	116 (8-693)

COVID-19: Coronavirus disease-2019, Min.: Minimum, Max.: Maximum

During COVID-19 related hospitalization, Guillain Barre syndrome developed in one patient. Acute renal failure development was observed on the basis of chronic renal failure in three patients, acute renal failure in two patients. Pregnancy loss in one patient was observed.

Anticoagulant therapy was used in a total of 35 (71.4%) patients, 24 (49%) of them treated with prophylactic and 11 (22.4%) of them with therapeutic dose. Twelve (24.5%) patients were given antiaggregant therapy. No thromboembolic complications were observed.

The median length of hospitalization of the patients was 12 days (1-39), and the median length of ICU duration was 6 days (1-20). Twenty of the 49 (40.8%) patients died at the end of the follow-up period. While 16 of these 20 patients died from COVID-19 during hospitalization, 4 of them died after discharge or during home monitoring. One patient died at home while he was positive for COVID-19. Three patients recovered from COVID-19 infection and were discharged, one died due to acute myeloid leukemia relapse, one due to sepsis during acute lymphoblastic leukemia treatment, and one patient due to acute myocardial infarction. Totally 17 patients (34.6%) died from COVID-19 infection. Three patients needed long-term oxygen treatment at home after COVID-19 treatment. Treatment follow-up, complications and mortality distribution of the patients are shown in Table 4.

Factors affecting COVID-19-related mortality in logistic regression analysis were detection of the disease during

Table 4: COVID-19 following, complications, mortality of the patients

Parameters	Number of patients (%)
Total patients	49
Outpatients	14 (28.5%)
Inpatients	35 (71.5%)
Inpatients	35
Clinical follow-up	14 (40%)
ICU follow-up	21 (60%)
Intubation	13
COVID-19 treatment	
No treatment	3
HQ	2
Favipravir	13
Favipravir + HQ	5
Favipravir + steroid	21
Favipravir + HQ + steroid	2
Favipravir + HQ + colchicine + steroid	3
Patients developing SIRS	19
Steroid therapy	7
IVIG + Steroid therapy	12
Total mortality at the end of the follow-up	20/49 (40.8%)
COVID-19 related mortality	17/49 (34.6%)
Mortality in ICU patients	18/21 (85.7%)

ICU: Intensive care unit, HQ: Hydroxychloroquine, SIRS: Systemic inflammatory response syndrome, IVIG: Intravenous immunoglobulin

hospitalization of the hematological causes, hematological disease not in complete response, presence of cytopenia on the day of COVID-19 diagnosis, requirement hospitalization for COVID-19 treatment, presence of lung involvement, accompanying extrapulmonary organ involvement, hemoglobin level of 10 g/dL or below on the day of COVID-19 diagnosis, thrombocyte count below $150x10^9$/L, SIRS development, ICU admission, intubation and secondary infection during hospitalization (Table 5).

Age, gender, comorbidity status, type of hematological disease diagnosis, smoking status, duration of hematological disease diagnosis, active immunosuppressive treatment status, receiving steroids and rituximab as part of chemotherapy, modifying/reducing chemotherapy dosage due to COVID-19 pandemic, leukocyte-neutrophil-lymphocyte count on COVID-19 diagnosis day, D-dimer and ferritin levels, SIRS treatment modalities, use of antiaggregant-anticoagulant therapy had no significant effect on mortality (Table 6).

Table 5: Factors not associated with COVID-19 mortality

	p-value
Age	0.97
Gender	0.35
Hematological diagnosis (malign vs benign)	0.10
Comorbidities	0.08
Smoking (Ex-smoker vs non-smoker)*	0.39
Hematological disease duration (in the last year vs earlier)	0.80
Active chemotherapy treatment	0.88
Steroid treatment as a part of chemotherapy	0.32
Rituximab treatment in last year	0.09
Hematological treatment modification	0.36
Leukocyte count ($\geq 4x10^9$/L vs $<4x10^9$/L)	0.33
Lymphocyte count ($\geq 1x10^9$/L vs $<1x10^9$/L)	0.50
Neutrophil count ($\geq 1.5x10^9$/L vs $<1.5x10^9$/L)	0.56
Maximum D-dimer level	0.95
Maximum ferritin level	0.95

*There are no active smokers
COVID-19: Coronavirus disease-2019

Discussion

In this study, we presented COVID-19 infection data of our hematological patients. The mortality rate associated with COVID-19 was 34.5% in our patient group, most of whom had hematological malignancies and were immunosuppressive due to the treatments or their hematological disease. In the literature, COVID-19-related mortality rates in patients with hematological malignancies have been reported between 28% and 40% (10-14). This rate has been reported up to 60% in case series when treatment is not sufficient at the beginning of the pandemic (15). In a retrospective analysis of Turkish Ministry of Health comparing patients with hematologic malignancies and patients without cancer, the mortality rate was 6.8% for the general population and 13.8% for hematological patients (16). The low mortality rates in this study were associated with the high number of chronic myeloproliferative patients who have less immunosuppressive status and the presence of both inpatients and outpatients (16).

According to the current data of WHO on May 28, 2021, the death rate associated with COVID-19 in the world is 2% and in Turkey is 0.8% (17). In our study in which we analyzed both outpatients and inpatients together with a high rate of immunosuppressive patients, mortality rates were found to be compatible with the literature and nearly 20-fold higher from the general population. High mortality rates suggest that more attention should be paid to COVID-19 infection in hematological patients than the general population.

Similar to the general population, it has been shown that advanced age especially >60 years and comorbidities have

Table 6: Factors effecting COVID-19 associated mortality

	p-value	OR, 95% CI
COVID-19 diagnosis while hospitalization	0.04	3.33 (1.01-10.97)
Hematological disease response (CR vs others)	0.04	3.69 (1.05-12.87)
Cytopenia on the day of COVID-19 diagnosis	0.03	3.83 (1.09-13.45)
COVID-19 treatment modality (Inpatient vs outpatient)	0.008	17 (2.08-150.53)
COVID-19 pulmonary involvement	0.001	2.9 (1.75-4.78)
Extrapulmonary involvement	0.002	1.4 (1.0-1.90)
Hemoglobin level on the day of COVID-19 diagnosis (<10 g/dL vs ≥10 g/dL)	0.001	16.87 (3.10-91.84)
Platelet level on the day of COVID-19 diagnosis ($<150x10^9$/L vs $\geq 150x10^9$/L)	0.008	7.36 (1.67-32.31)
SIRS development	0.001	34.66 (6.85-175.40)
ICU admission	0.001	78 (11.81-514.98)
Intubation	0.001	42 (4.71-373.81)
Secondary infection	0.001	27.2 (5.71-129.49)

OR: Odds ratio, CI: Confidence inverval, CR: Complete response, SIRS: Systemic inflammatory response syndrome, ICU: Intensive care unit

been associated with higher mortality in COVID-19 infection in hematological patients (10,12-14,18). No relationship between age, comorbidities and death was found in our study. This may be attributed to the median age of patients in other studies is higher than our population.

Expectedly and in accordance with the literature, unresponsiveness of hematological disease, need for hospitalization for COVID-19 infection, development of SIRS, ICU admission and the need for intubation were found to be associated with higher mortality (10,12-15,18). Although there are different reports in the literature about the level of cytopenias and effect on mortality for hematological patients, in our study, when the leukocyte-lymphocyte-platelet count-hemoglobin level was evaluated individually on the day of COVID-19 diagnosis, the platelet count below $150x10^9$/L and the hemoglobin level below 10 g/dL were found to be associated with mortality. In this respect, we think that our study contributed to this issue, since there is no cut-off in the literature.

Secondary infections in hematologic patients, which are also not mentioned in the literature, are common in the course of treatment of all hematological diseases and are important in the course of COVID-19 and were associated with an increase in mortality in our study.

Confusion has been arising about the treatment of hematological patients in the era of COVID-19. Some studies showed COVID-19 related deaths were higher in patients receiving active chemotherapy or immunotherapy, it was recommended to rearrange immunosuppressive therapies, delay and reduce these treatments as much as possible (10,19). On the other hand, after it has shown in some studies that active cancer treatment has no effect on mortality, guidelines recommend determining the urgency and intensity of hematological treatment needs on the basis of patient and disease (7,12). In our study, we observed that active chemotherapy, steroid, rituximab had no effect on mortality. It can be concluded that immunosuppression attributed to hematological disease is more important than immunosuppression due to chemoimmunotherapy. Hematological patients, with requiring urgent treatment such as aggressive malignancies should be treated without delaying, but with strict attention to COVID-19 infection precautions and screening the patients with PCR regularly as well as before treatments (20-23).

Recently thanks to the increasing number of clinicopathological studies, parallel with three clinicobiological phases of the disease; asymptomatic/pre-symptomatic, respiratory phase and multisystemic syndromic phase are defined (24). Although we could not clearly identify these phases in our patients, according to our patients' symptoms distribution, asymptomatic cases were only 12.2% of our patient group. In our study; the significant scarcity of asymptomatic cases compared to 50-80% reported in the literature confirmed that immunosuppression caused by the hematological disease or treatments causes more symptoms associated with COVID-19 than in a healthy person, as expected (24).

The incubation period for COVID-19 was defined as approximately 5-6 days, and the predicted time for disease progression was defined as 6-12 days (25,26). In our study, the median diagnosis day was 2 days and the median disease progression was on the 4^{th} day. This data showed that the diagnosis of COVID-19 is faster in hematological patients compared to the general population. These findings also showed that the disease progression was faster than expected, and awareness caused acting quickly for the diagnosis of COVID-19 in hematological patients. It is important to show the sensitivity for close monitoring of progression and early treatment interventions to the patients as well as early diagnosis of the disease.

According to studies with a high number of patients in the general population, hospitalization rate due to COVID-19 has been report as 9.5%; ICU admission rates in hospitalized patient have been reported as 7.1%, 22% and 39%; intubation rates in ICU patients have been reported as 60.2% and 86% (27-29). Hospitalization rate in hematological-oncological patients was 78%, 98%; the rate of patients needing ICU follow-up was 27.5%; The rate of patients requiring intubation during ICU follow-up was 65.5% (9,30). In our study, the rate of hospitalization was 71.5%, this rate was slightly lower than the hematological-oncological patient population, on the other hand was very high than the general population. This situation can be explained by the frequent presence of malignant patients in the literature data of hematological oncological patients and the inclusion of benign patients in our study. Rate of patients going to ICU admission in hospitalized patients is 60% and it differs from the literature. We attribute the high rate of ICU admission to the awareness of the rapid progression of hematological patients and admitting patients to ICU as soon as possible in our center. The requirement for intubation in ICU was 13/21 (61.9%), which is similar to both the general population and hematological oncological patients. Hematological oncological patients do not seem to exhibit a difference from the general population in terms of intubation after ICU period.

Study Limitations

There are some limitations in our study. Our study, which includes retrospective single center data, has a limited number of patients. Nevertheless, it is one of the rare studies in Turkey analyzing both benign and malignant hematology patients. It is thought that debates about the COVID-19 in hematological patients can be resolved with multi-center studies with high number of patients.

Conclusion

COVID-19, a multisystemic pandemic disease, appears to be a serious cause of mortality in hematological patients. Hematological diseases have an important effect on COVID-19 related mortality, rapid care of the condition should be done in this patient group as well as prevention of the infection.

Ethics

Ethics Committee Approval: Ethics committee approval was received from Ministry of Health and Ankara City Hospital Local Ethic Committee with the number E1-21-1715.

Informed Consent: Patients were retrospectively analyzed.

Peer-reviewed: Externally peer-reviewed.

Authorship Contributions

Concept: F.C., İ.D., S.A., T.G., Design: F.C., İ.D., S.A., T.G., Data Collection and Processing: F.C., İ.D., S.A., T.G., Statistical Analysis: F.C., İ.D., S.A., T.G., Literature Search: F.C., İ.D., S.A., T.G., Writing: F.C., İ.D., S.A., T.G.

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