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CORRESPONDENCE

COVID-19 in hematopoietic cell transplant recipients

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Abstract

In this study, we aim to report the outcome of COVID-19 in hematopoietic cell transplant (HCT) recipients. HCT recipients ($n = 32$) with hematological disease and hospitalized for COVID-19 were included in the study. A cohort of age and comorbid disease-matched hospitalized COVID-19 patients with hematological malignancy but not underwent HCT ($n = 465$), and another cohort of age and comorbid disease-matched hospitalized COVID-19 patients without cancer ($n = 497$) were also included in the study for comparison. Case fatality rate (CFR) was 5.6% in patients without cancer, 11.8 in patients with hematological malignancy and 15.6% in HCT recipients. The CFR in HCT recipients who were not receiving immunosuppressive agents at the time of COVID-19 diagnosis was 11.5%, whereas it was 33% in HCT recipients who were receiving an immunosuppressive agent at the time of COVID-19 diagnosis. In conclusion, our study reveals that for the current pandemic, HCT recipients, especially those receiving immunosuppressive drugs, constitute a special population of cancer patients.

SARS-CoV-2 spread all over the world rapidly and on March 11, 2020, it was declared a pandemic by the World Health Organization (WHO) [1–3]. Older age and comorbidities such as diabetes, hypertension, or cardiac disease are risk factors for a more aggressive clinical course in patients with COVID-19 [4]. In addition, in a previous report, it was reported that 39% of COVID-19 patients with cancer had severe events such as intensive care unit (ICU) admission, mechanical ventilation (MV) support and death during the COVID-19 course whereas only 8% of COVID-19 patients without cancer had those severe events [5].

Hematopoietic cell transplantation (HCT) recipients are vulnerable to a variety of infections because of the high dose immunosuppressive agents they received to prevent graft failure. In addition, patients with hematological malignancy (HM) have varying degrees of immune dysfunction. Therefore, these patients are immunocompromised and may be susceptible to a more aggressive course of COVID-19. In this study, we aim to report the outcome of COVID-19 in HCT recipients.

The data of laboratory-confirmed COVID-19 patients diagnosed between March 11, 2020 and May 29, 2020 included in the Republic of Turkey, Ministry of Health database, were analyzed retrospectively. As of May 29, 2020, there were 162.120 laboratory-confirmed COVID-19 cases in Turkey. All of the HCT recipients ($n = 32$) with hematological disease and hospitalized for COVID-19 were included in the study. A cohort of age and comorbid disease matched hospitalized COVID-19 patients with HM but not underwent HCT ($n = 465$), and another cohort of age and comorbid disease matched hospitalized COVID-19 patients without cancer ($n = 497$) were also included in the study for comparison.

Demographic and clinical characteristics of patients are given in Table 1. 20 HCT recipients had autologous HCT (auto-HCT) and 12 had allogeneic HCT (allo-HCT). Nine (75%) allo-HCT were performed from related donors and three (25%) allo-HCT were performed from unrelated donors. Nine allo-HCT were from matched donors, whereas three allo-HCT were from a haploidentical donor. At the time of COVID-19 diagnosis, six (18.7%) HCT recipients

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Table 1 Demographic and clinical characteristics of the groups.

Demographic and clinical characteristics	HCT recipients ($n = 32$)	Patients with Hematological Malignancy ($n = 465$)	Patients without cancer ($n = 497$)	p value
Gender				
Male,*n* (%)	25 (78.1%)	250 (53.8%)	269 (54.1%)	0.03[a]
Female, *n* (%)	7 (21.9%)	215 (46.2%)	228 (45.9%)	
Median age (years)	56,5 (19–74)	57 (18–93)	55 (19–87)	0.3
Comorbidity, *n* (%)				
Diabetes Mellitus	7 (21.9%)	111 (23.9%)	114 (22.9%)	0.9
Hypertension	18 (56.3%)	201 (43.2%)	200 (40.2%)	0.2
Cardiovascular diseases	5 (15.6%)	69 (14.8%)	63 (12.7%)	0.6
Respiratory system diseases	10 (31.3%)	86 (18.5%)	86 (17.3%)	0.1
Additional Treatment, *n* (%)				
Favipiravir	12 (37.5%)	131 (28.2%)	128 (25.8%)	0.3
Oseltamivir	12 (37.5%)	209 (44.9%)	222 (44.7%)	0.7
Lopinavir/ritonavir	2 (6.3%)	23 (4.9%)	12 (2.4%)	0.1
Hydroxychloroquine	24 (75%)	336 (72.3%)	352 (70.8%)	0.8
High dose vitamin C	8 (25%)	81 (17.4%)	69 (13.9%)	0.1

HCT hematopoietic cell transplantation.

[a]All hematological malignancies vs patients without cancer; $p = 0.7$.

Table 2 Outcome of COVID-19 in each group.

Factors	HCT recipients	Patients with Hematological Malignancy	Patients without cancer	p value
Hospital stay	13 days	10 days	10 days	0.2
ICU stay	12 days	6 days	7 days	0.25
ICU admission, *n* (%)	7 (21.9%)	98 (21.1%)	56 (11.3%)	0.001
MV, *n* (%)	5 (15.6%)	70 (15.1%)	36 (7.2%)	0.001
COVID-19 Severity, *n* (%)				
Severe	7 (21.9%)	78 (16.8%)	65 (13.1%)	0.001
Critical	4 (12.5%)	65 (14%)	33 (6.6%)	
CFR, *n* (%)	5 (15.6%)	55 (11.8%)	28 (5.6%)	0.001

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

were receiving immunosuppressive drugs (four patients were receiving cyclosporine and two patients were receiving tacrolimus). Among COVID-19 patients who were performed auto-HCT; there were 11 multiple myeloma (MM), 7 non-Hodgkin lymphoma (NHL) and 2 Hodgkin lymphoma (HL) patients. Among allo-HCT recipients with COVID-19, there were five acute myeloid leukemia (AML), three acute lymphoblastic leukemia (ALL), three chronic myeloid leukemia (CML) and one aplastic anemia (AA) patients. In the HM group, there were 222 NHL, 73 MM, 54 chronic lymphocytic leukemia (CLL), 38 AML, 29 CML, 25 HL, 15 ALL and 9 hairy cell leukemia (HCL) patients.

Outcome of COVID-19 in each group is given in Table 2. 21.9% of the HCT recipients had severe disease and 12.5% were critically ill. In the post hoc analysis, the rate of severe and critical disease was significantly higher in patients with HM compared with patients without cancer however there was no significant difference between patients with HM and HCT recipients regarding the rate of severe and critical disease.

The rates of MV support and ICU admission were significantly different between groups ($p = 0.001$, $p = 0.001$). 21.9% of HCT recipients were admitted to ICU during the course of COVID-19, and 15.6% of HCT recipients needed MV support during the course of COVID-19. In post-hoc analysis the rate of ICU admission and MV support was significantly higher in patients with HM compared with patients without cancer however there was no significant difference between patients with HM and HCT recipients regarding the rate of ICU admission and MV support. When

Table 3 Characteristics of deceased HCT patients.

	Gender–Age	Diagnosis–Year	Comorbidity	Antiviral	Hospitalization (days)	ICU (days)	IST
Patient one	M–31	AA-2019	–	Fa,	6	–	Cyclosporine
Patient two	M–36	CML-2019	–	Fa, H, C	6	5	Cyclosporine
Patient three	F–55	MM-2020	HT	H, L, A	9	3	–
Patient four	M–57	MM-2019	CAD, HT, DM	Fa, H, O	12	12	–
Patient five	M–57	MM-2019	COPD, CAD, HT	Fa, H, A, O	39	37	–

AA aplastic anemia, *CML* chronic myeloid leukemia, *MM* multiple myeloma, *CAD* coronary artery disease, *COPD* chronic obstructive pulmonary disease, *HT* hypertension, *DM* diabetes mellitus, *Fa* Favipiravir, *H* hydroxychloroquine, *L* lopinavir, ritonavir, *C* high dose vitamin *C*, *A* azithromycin, *O* Oseltamivir, *ICU* intensive care unit, *IST* immunosuppressive treatment.

auto-HCT recipients were compared with allo-HCT recipients, no significant difference was observed regarding rate of MV support, ICU admission and case fatality rate (CFR) (p:0.4, p:0.6 and p:0.9, respectively).

CFR was 5.6% in patients without cancer, and it was 15.6% in HCT recipients. CFR was statistically different between groups ($p = 0.001$). In post-hoc analysis, the CFR in patients with HM was higher than the patients without cancer but there was no statistical difference between patients with HM and HCT recipients regarding CFR. Among 32 HCT recipients, five patients died. The characteristics of deceased HCT recipients are given in Table 3. The CFR in HCT recipients who were not receiving immunosuppressive agents at the time of COVID-19 diagnosis was 11.5%, whereas it was 33% in HCT recipients who were receiving an immunosuppressive agent at the time of COVID-19 diagnosis.

The data about the course of COVID-19 in HCT recipients is based on case series. Huang et al. reported two post-transplant patients (transplant done for AML, 51 years old; and end-stage renal failure, 59 years old) on immunosuppressant and had stable graft function before COVID-19. The authors discontinued immunosuppressive agents and started methylprednisolone with prophylactic antibiotics. Both patients developed multiorgan failure and died [6]. Haroon et al. reported the clinical course of COVID-19 in their 11 transplant recipients aged between 11 and 60 years. Six of those patients had allo-HCT, four had auto-HCT and one patient had both allo and auto-HCT. They reported that none of the patients required MV [7]. In another case series including eight pediatric transplant recipients, researchers reported that two patients admitted to ICU and one patient died [8]. In a previous study, researchers reported the outcome of 25 patients with HM including 7 HCT recipients (5 auto-HCT, 1 allo-HCT, 1 both allo and auto-HCT). Among all HCT recipients they reported that a 65 year old, male, MM patient who had auto-HCT history died [9].

As of May 12, 213 patients have been reported from 17 countries to European Society for Blood and Marrow Transplantation. Preliminary data showed ~30% mortality in both allo and auto-HCT recipients [10].

In conclusion, our study reveals that HCT recipients, especially those receiving immunosuppressive drugs, constitute a special population of cancer patients, and physicians should effort great attention in the management of HCT recipients especially in those receiving immunosuppressive agents at the time of COVID-19 diagnosis. Due to the high infectivity of SARS-CoV-2, HCT recipients without COVID-19 should take their health services outside of the CoV pandemic hospitals. HCT centers should be isolated, and those patients' follow up should be continued with alternative ways such as teleconference systems as much as possible.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to disclose.

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