

Original Article

Screening for Distress During COVID-19 Outbreak Among Hematopoietic Stem Cell Transplantation Survivors

KOVID-19 Salgını Sırasında Hematopoietik Kök Hücre Nakli Hastalarında Distres Taraması

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ABSTRACT

Introduction: The COVID-19 pandemic has led to an increase in mental distress, such as anxiety symptoms and depression. Our objective was to evaluate the impact of COVID-19 on the anxiety and depression levels of the hematopoietic stem cell transplant (HSCT) recipients comprising a highly immunocompromised group with a greater risk of infection and prolonged isolation.

Materials and Methods: The Hospital Anxiety and Depression Scale (HADS) was administered to 203 HSCT recipients, a concurrent group of 69 hematological cancer patients receiving standard chemotherapy, and a group of 82 healthy controls.

Results: Median HADS Anxiety score was 6 (interquartile range (IQR) 2-9) for 203 HSCT patients, 7 (IQR 4-9) for 82 healthy controls, and 6 (IQR 4-8) for 69 patients with a hematological malignancy receiving chemotherapy. There was a statistically significant difference in HADS Anxiety scores between HSCT patients, chemotherapy patients, and healthy controls ($p=0.019$). The median HADS Depression score was 5 (IQR 3-8) for HSCT patients, 5 (IQR 3-8) for healthy controls, and 5 (3-8) for patients with a hematological malignancy receiving chemotherapy. There were no significant differences in HADS Depression scores in between groups ($P = 0.549$). There were no statistically significant differences in HADS Anxiety and HADS Depression scores between patients undergoing autologous and allogeneic SCT ($p=0.245$). Anxiety levels were higher in young patients ($p=0.003$), while none of the other clinical variables were associated with anxiety and depression rates.

Conclusion: Our study revealed that the COVID-19 pandemic did not have a negative impact on the levels of depression and anxiety in HSCT recipients.

Keywords: COVID-19, anxiety, depression, hematopoietic stem cell transplantation

ÖZET

Amaç: KOVID-19 salgını, anksiyete belirtileri ve depresyon gibi mental sıkıntıların artmasına neden olmuştur. Amacımız, yüksek enfeksiyon riski ve uzun süreli izolasyona sahip, ciddi düzeyde immünsüpresif bir grup olan hematopoietik kök hücre nakli (HKHN) alıcılarının anksiyete ve depresyon düzeyleri üzerine KOVID-19'un etkisini değerlendirmektir.

Gereç ve Yöntemler: Hastane Anksiyete ve Depresyon Ölçeği (HAD), 203 HKHN alıcısına, standart kemoterapi alan 69 hematolojik kanser hastasından oluşan bir gruba ve 82 sağlıklı kontrolden oluşan bir gruba uygulandı.

Bulgular: Medyan HAD Anksiyete skoru; 203 HKHN hastaları için 6 (çeyrekler arası aralık (IQR) 2-9), 82 sağlıklı kontrol için 7 (IQR 4-9) ve kemoterapi alan hematolojik malignitesi olan 69 hasta için 6 (IQR 4-8) idi. HKHN hastaları, kemoterapi hastaları ve sağlıklı kontroller arasında HAD Anksiyete skoru açısından istatistiksel olarak anlamlı bir farklılık saptandı ($p=0,019$). Medyan HAD Depresyon skoru ; HKHN hastaları için 5 (IQR 3-8), sağlıklı kontroller için 5 (IQR 3-8) ve kemoterapi alan hematolojik malignitesi olan hastalar için 5 (3-8) idi. Gruplar arasında HAD Depresyon puanları açısından anlamlı bir farklılık saptanmadı ($P = 0,549$). HAD Anksiyete ve HAD Depresyon skorları, otolog ve allojenik KHN uygulanan hastalar arasında istatistiksel olarak anlamlı değildi ($p=0,245$). Genç hastalarda anksiyete düzeyi daha yüksek iken ($p=0,003$), diğer klinik değişkenlerin hiçbirisi anksiyete ve depresyon düzeyleri ile ilişkili değildi.

Sonuç: Çalışmamız, KOVİD-19 salgınının, HKHN alıcılarının depresyon ve anksiyete seviyeleri üzerine olumsuz bir etkisi olmadığını ortaya koydu.

Anahtar Kelimeler: KOVİD-19, anksiyete, depresyon, hematopoetik kök hücre nakli

Introduction

The global Coronavirus disease 2019 (COVID-19) pandemic has drastically disrupted many aspects of life and the health-care system worldwide.

Cancer patients constitute a special population that is at high risk of acquiring SARS-CoV-2 infection [1]. As already shown, oncological patients have a higher chance of requiring an intensive level of care and mechanical ventilation, whilst the mortality rate among cancer patients with COVID-19 infection is around ten times higher than in the general population [2]. This may cause greater fear of coronavirus and further affect patients' mental health. Challenges that have been created by the COVID-19 pandemic, which include treatment interruptions, fears of contracting COVID-19, reduced access to support from healthcare providers and family, and financial hardship, have contributed to heightened distress among patients living with cancer [3,4].

Hematological cancer patients form a very vulnerable subgroup among patients with cancer due to the highly immunosuppressive status induced by their long and intensive treatment regimens. Available data supports the increased risk of COVID-19 related morbidity and mortality among adults with

hematological cancer, emphasizing the need for more specialized and tailored attention and care in this subgroup [5]. Given this vulnerability, hematological cancer patients, especially hematopoietic stem cell transplant (HSCT) recipients, being highly immunocompromised, could be at higher risk of experiencing distress during the current COVID-19 pandemic.

In this study, we intended to evaluate the impact of COVID-19 on the anxiety and depression levels of the HSCT recipients. We hypothesized that the COVID-19 pandemic would be associated with increased anxiety and depression in the HSCT population compared to other hematological cancer patients or healthy controls.

Methods

The Hospital Anxiety and Depression Scale (HADS) was administered to 203 patients who underwent HSCT after the COVID-19 pandemic declaration in Turkey (between March 2020 and October 2022). Furthermore, we included a group of 69 hematological cancer patients receiving standard chemotherapy and a group of 82 healthy controls. Eligible participants were adults aged ≥ 18 years who could read and respond to the questionnaire independently. HSCT patients who were admitted to the hospital for their

short-term controls (<3 months after discharge) and other cancer patients (who received at least one cycle of chemotherapy) who were admitted for the administration of treatment were asked by their treating physicians to participate in the study. Patients who agreed to participate signed the written informed consent and completed the study questionnaire. We excluded patients with a major psychiatric or cognitive condition precluding their adherence to study procedures. The study was approved by the local ethical committee.

We assessed distress (i.e., anxiety and depression symptoms) using the HADS, a 14-item questionnaire containing two 7-item subscales assessing anxiety (HADS-A) and depression (HADS-D) symptoms (score range, 0-21) [6]. Higher scores on the HADS-A or HADS-D subscale are indicative of higher levels of anxiety or depression symptoms, respectively. Turkish version of the HAD scale showed satisfying reliability with Cronbach's $\alpha=0.8525$ for the anxiety subscale and Cronbach's $\alpha=0.7784$ for the depression subscale. Using ROC analysis, 10 was found to be the cut-off score for anxiety and 7 for depression subscale [7].

Statistical Analysis

Statistical analysis was performed using the IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp. The normality of continuous variables was investigated by Shapiro-Wilk's test. Descriptive statistics for non-normally distributed continuous variables were presented using median and Interquartile Range. Categorical variables were expressed by using frequencies (n) and percentages (%). The Kruskal-Wallis test was used to compare more than two groups of continuous variables. Post Hoc pairwise comparisons were performed by using the Bonferroni corrected Mann-Whitney u test. The cut-off for statistical significance was set as $p<0.05$.

Results

Demographics and Patient Characteristics

The study was conducted in 203 HSCT patients, 69 hematological cancer patients receiving standard chemotherapy, and 82 healthy controls. Among HSCT patients, 146 (71.9%) underwent autologous stem cell transplantation, and 57 (28.1%) underwent allogeneic stem cell transplantation. HSCT patients' median age was 55 (43-56), and the majority of them ($n=114$, 56.2 %) were female and married ($n=163$, 80.3%). Their primary diagnosis included multiple myeloma ($n=84$, 41.4%), lymphoma ($n=67$, 33.0%), acute leukemia ($n=39$, 19.2%), and others ($n=13$, 6.4%). Further sample details are reported in Table 1 and Table 2.

Anxiety and Depression:

Median HADS Anxiety score was 6 (interquartile range (IQR) 2-9) for 203 HSCT patients, 7 (IQR 4-9) for 82 healthy controls, and 6 (IQR 4-8) for 69 patients with a hematological malignancy receiving chemotherapy. There was a statistically significant difference in HADS Anxiety scores between HSCT patients, chemotherapy patients, and healthy controls ($p=0.019$). Using a cut-off value ≥ 11 for the HADS-Anxiety score, 9.9% of HSCT patients were in an anxious state, relative to 3.4% and 6.9% in the chemotherapy and healthy groups, respectively.

The median HADS Depression score was 5 (IQR 3-8) for 203 HSCT patients, 5 (IQR 3-8) for 82 healthy controls, and 5 (3-8) for 69 patients with a hematological malignancy receiving chemotherapy. There were no significant differences in HADS Depression scores in between groups ($P = 0.549$). When considering a cut-off value ≥ 8 for the HADS-Depression score, 29.1% of HSCT patients were in a depressive state, relative to 29.4% and 31.7% in the chemotherapy and healthy group, respectively. (Table 3)

Table 1: Sample characteristics of study population

	HSCT (N=203)	Chemotherapy (N=69)	Controls (N=82)	p*
Median age, years (range)	55 (43-62)	59 (21-87)	39.5(20-76)	
Gender, n(%)				0.002
Male	114 (56%) ^a	34 (49%) ^a	62 (76%) ^b	
Female	89 (44%)	35(51%)	20 (24%)	
Social status, n(%)				0.702
Married	162 (80%)	53 (77%)	62 (76%)	
Single, divorced, widowed	41 (20%)	16 (23%)	20 (24%)	
Children, n(%)				0.003
Yes	170 (84%) ^a	53 (77%) ^{a,b}	56 (68%) ^b	
No	27 (13%)	13 (19%)	26 (32%)	
Unknown	6 (3%)	3 (4%)	-	
Education, n(%)				<0.001
Elementary school	84 (41%) ^a	12 (17%) ^b	15 (18%) ^b	
High school	48 (24%) ^a	24 (35%) ^a	23 (28%) ^a	
University	70 (34%) ^a	31 (45%) ^{a,b}	44 (54%) ^b	
Illiterate	1 (1%)	2 (3%)	-	
Employment,n(%)				<0.001
Employed	96 (47%) ^a	32(46%) ^a	77 (94%) ^b	
Unemployed	35 (17%) ^a	2 (3%) ^b	2 (2%) ^b	
Housewife	27 (13%) ^a	13 (19%) ^a	3 (4%) ^b	
Retired	40 (20%) ^a	20 (29%) ^a	0 ^b	
Student	5 (3%) ^a	2 (3%) ^a	0 ^a	

*Chi-Square test, PostHoc comparisons were performed. Different Superscripts display statistically significant difference. Bonferroni correction was applied.

Among HSCT patients, the median HADS Anxiety score was 6 (IQR 2-9) for autologous SCT patients and 5 (IQR 3-7) for allogeneic SCT patients. No statistically significant differences were found between autologous and allogeneic SCT groups ($p=0.912$). The median HADS Depression score was 5 (3-8) for autologous SCT patients and 4 (1-8) for allogeneic SCT patients. Likewise, there were no statistically significant differences between the two groups ($p=0.245$). (Table 4)

Anxiety levels were higher in young patients ($p=0.003$), where gender, transplant regimens (chemotherapy alone or TBI-based), days in the transplant unit, the interval between HSCT and study, and use of antidepressants were not associated with anxiety scores. Depression levels tended to be higher in patients given

chemotherapy-only-based conditioning regimens compared to TBI-based regimens ($p=0.099$), while none of the other clinical variables were related to depression. Among allogeneic HSCT recipients, exposure to TBI and the presence of acute GVHD were not associated with anxiety and depression score rates.

Discussion

In the present study, we assessed the impact of COVID-19 on the anxiety and depression levels of HSCT recipients. Although a few studies have described the implications of the COVID-19 pandemic for HSCT recipients, they focused on the logistic difficulties and COVID-19 complications [8-10]. However, the associations of the COVID-19 pandemic with

Table 2: Transplant-related variables of HSCT patients (n=203)

Variable	n (%)
Disease status at transplant	
Remission	182 (90%)
Relapse/Primary refractory	21 (10%)
Pretransplant therapy	
Chemotherapy	178 (88%)
Chemotherapy and radiotherapy	25 (12%)
Type of transplant	
Autologous stem cell	146 (72%)
Allogeneic stem cell	57 (28%)
Conditioning regimen prior to transplant	
Chemotherapy	184 (91%)
Total body irradiation (TBI)	19 (9%)
GVHD status	
Yes	15 (26%)
No	42 (74%)
Exposure to steroids (among allogeneic SCT recipients only)	
Yes	8 (14%)
No	49 (86%)
Use of antidepressants	
Yes	44 (22%)
No	157 (78%)
Median days in transplant unit (range)	22 (13-71)
Time elapsed since transplantation (months)	4.17 (0-20.9)

Table 3: HADS-Anxiety and HADS-Depression scores for HSCT patients, chemotherapy patients and healthy controls

HADS values, Median (range)	HSCT (n=203)	Chemotherapy (n=69)	Healthy (n=82)	p*
Anxiety	6 (2-9)	6 (4-8)	7.0 (4-9)	0.019
Depression	5 (3-8)	5 (3-8)	5 (3-8)	0.549

*Kruskal Wallis test. For HADS-A; $p=0.890$ HSCT patients vs chemotherapy patients, $p=0.016$ HSCT patients vs healthy controls, $p=0.533$ chemotherapy patients vs healthy controls.

Table 4: HADS-Anxiety and HADS- Depression scores for autologous and allogeneic SCT patients

HADS values, Median (range)	Autologous SCT (n=146)	Allogeneic SCT (n=57)	p*
Anxiety	6 (2-9)	5 (3-7)	0.912
Depression	5 (3-8)	4 (1-8)	0.245

*Kruskal Wallis test

patient-reported depression and anxiety are not well understood. Undergoing treatment for cancer and HSCT are great psychological stressors by themselves. There is ample evidence which suggests that psychological distress is frequently reported by patients who undergo HSCT. The percentage of HSCT patients with these problems, for example, depression and anxiety, varies from 5% to more than 40% [11]. Based on our clinical experience and findings from the recent literature, we expected that the anxiety, fear, and panic revolving around the current COVID-19 pandemic could make cancer patients and transplant recipients more anxious and depressive. Contrary to our hypothesis that the COVID-19 pandemic might exacerbate symptoms of depression and anxiety in HSCT recipients, we have found no increase in depression and anxiety levels in the HSCT population compared to chemotherapy patients and healthy controls. Meanwhile, the depression levels of HSCT patients (29.1%) were found to be higher than the anxiety levels (9.9%). Amonoo et al. conducted a study involving 205 patients with hematologic malignancies undergoing HSCT and assessed distress before or during the COVID-19 pandemic using HADS. Although patients in early recovery post-HSCT reported both negative and positive implications of the COVID-19 pandemic in their lives, authors found no differences in pre-HSCT distress (i.e., depression, anxiety, and posttraumatic stress disorder), fatigue, or quality of life in HSCT patients before or during the pandemic [12].

Transplantation recipients comprise an immunocompromised group at greater risk for infection and poorer outcomes, including increased risk of mortality [9]. These patients are also vulnerable due to their intense treatment regimens accompanied by prolonged hospitalizations, high risk of medical complications, and immediate and long-term medical comorbidities [12,13]. Since our

transplant patients did not have increased scores for depression and anxiety, this shows that HSCT patients are already afraid of the consequences of their life-threatening condition with a high risk of death, and the pandemic has not increased it further. In fact, the COVID-19 pandemic forced the whole world to live like HSCT recipients, which may have given HSCT recipients a psychological advantage in managing pandemic-related restrictions [14]. During their transplant experience, patients had probably acquired a certain attention to hygiene, prevention of possible infections, and use of masks that helped them to face this pandemic.

Moreover, we have found that the level of anxiety was higher in youngs while the depression level was increased in patients given chemotherapy-only-based conditioning regimens compared to TBI-based regimens. This observation stays in line with the existing studies, which show that the levels of anxiety, depression, and stress are significantly higher among young people (aged 21–40). The main reason for this seems to be that young, as key active working forces in society, are more concerned about the future consequences and economic challenges caused by the pandemic [15].

Some limitations of the current study should be noted. The levels of depression and anxiety could vary at different times of the pandemic; in our study, it was measured only once. Additionally, existing self-report measures that assess distress in the HSCT population may not possibly capture COVID-19-specific stressors.

In conclusion, our study showed that HSCT patients are already at an increased risk for adverse psychological symptoms due to their underlying disease and intense treatment regimens, and pandemic conditions did not negatively affect the depression and anxiety levels of these patient.

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