



Pain, Fatigue, Nausea, and Vomiting as the Predictors of Anxiety in Patients Undergoing Hematopoietic Stem Cell Transplantation: A Prospective Cohort Study

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Abstract

The primary outcome was to assess the correlation between anxiety and pain, fatigue, nausea, and vomiting. The secondary outcome was to determine the predictive roles of pain, fatigue, nausea, and vomiting in anxiety among patients undergoing Hematopoietic Stem Cell Transplantation (HSCT). The present prospective cohort study was conducted on 200 patients treated by HSCT referred to the centers affiliated to Shiraz University of Medical Sciences. The data were collected using Spielberger Anxiety Questionnaire, Numerical Pain Scale, Brief Fatigue Inventory, and Rhodes Nausea and Vomiting Index. The data were analyzed using Spearman's test and multiple regression analysis. The means of state anxiety, trait anxiety, pain, fatigue, and nausea, vomiting, and retching were 41.67 (SD = 9.71), 43.78 (SD = 9.00), 3.79 (SD = 2.79), 4.23 (SD = 2.48), and 6.31 (SD = 7.53), respectively. The results showed that the participants with higher pain and fatigue scores had higher anxiety levels. Those with more nausea and vomiting had higher anxiety levels, as well. This indicated that fatigue, pain, severity and frequency of nausea, and type of HSCT were the predictors of trait anxiety. The results also showed the predictor role of pain, fatigue, and type of HSCT in state anxiety. The findings revealed a correlation between anxiety and pain, fatigue, nausea, and vomiting among the HSCT patients. The results also showed fatigue and pain as the predictors of anxiety among these patients. Yet, future studies are recommended to determine the other factors contributing to anxiety amongst HSCT patients.

Keywords Anxiety · Pain · Fatigue · Nausea · Vomiting · Hematopoietic stem cell transplantation

Introduction

Hematologic malignancies have been defined as the tumors that arise from bone marrow or lymphoid tissue, affect blood, bone marrow, and the lymphatic system, and are directly related to the circulatory system and the immune system [1]. Chemotherapy, target therapy, and Hematopoietic Stem Cell Transplantation (HSCT) have been commonly

used to treat hematologic malignancies [2]. Although HSCT has good clinical outcomes [3], the long course of the disease and the unpredictability of the treatment process are among its main challenges [4]. HSCT is also an invasive and complex procedure that causes many complications for patients due to the pre-bone marrow preparation regimen, which includes receiving high doses of chemotherapy drugs and whole-body radiation therapy [5].

Anxiety is one of the consequences of cancer diagnosis and treatment. It is, in fact, one of the common psychological complications [6]. The prevalence of anxiety has been found to be high in patients with hematologic malignancies treated by HSCT [7]. Before transplantation, 30% of patients experienced increased anxiety levels [8]. Patients with hematologic malignancies who were transplanted and had COVID-19 were also prone to anxiety and depression [9]. Overall, anxiety could have negative effects on cancer patients including increased complications and the related treatments, slow physical recovery, decreased quality of life, and reduced survival rate [10].

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Anxiety can also affect the sensation of pain experienced by HSCT patients [11]. Pain is the most common and debilitating symptom among HSCT patients [12]. Pain can result from the side effects of chemotherapy drugs or acute complications after HSCT [13]. Psychological distress, which is an important component of cancer pain, has increased during the COVID-19 crisis due to quarantine and social isolation [14]. Besides, anxiety can lead to fatigue in HSCT patients [15]. One study found that most HSCT survivors experienced fatigue continuously one year (62.3%), three years (68%), and six years (63.8%) after transplantation [15]. It should also be noted that patients' psychological problems before HSCT could affect the severity of their perceived fatigue [16]. Moreover, mental fatigue after HSCT could be associated with cognitive dysfunction [17].

One of the main causes of anxiety in cancer patients is nausea and vomiting [18]. Chemotherapy-induced nausea and vomiting is a global experience among HSCT patients [19]. Chemotherapy regimens before HSCT are the most common cause of nausea and vomiting within the first week after transplantation [20].

The studies performed among patients undergoing HSCT have mainly assessed the physical and psychological complications of treatment, such as anxiety [7, 8], pain [12, 21], fatigue [15, 22], and nausea and vomiting [20, 23]. However, less attention has been paid to the correlation between the complications following treatment and the predictive role of these complications in the level of anxiety among the patients undergoing HSCT. Therefore, the primary outcome of the present research was to assess the correlation between anxiety and pain, fatigue, nausea, and vomiting among the patients undergoing HSCT, and the secondary outcome was to investigate the predictive roles of pain, fatigue, nausea, and vomiting in anxiety among these patients.

Methods

Design

This prospective cohort study was conducted on adult patients undergoing HSCT. In this study, pain, fatigue, nausea, and vomiting were the exposures and anxiety was the outcome.

Setting

The data were collected in Nemazee Hospital and Motahhari Clinic affiliated to Shiraz University of Medical Sciences from September 2020 to March 2021.

Participants

The inclusion criteria were having undergone HSCT, aging 18 years and above, being oriented to time and place, and

being willing to participate in the study. The exclusion criteria were unwillingness to take part in the research and death. The participants were selected through consecutive sampling. In doing so, every HSCT patient who met the inclusion criteria was selected until the required sample size was achieved.

Measurements

The study data were collected using five questionnaires including the demographic and clinical information questionnaire, Spielberger State-Trait Anxiety Inventory (STAI), numerical pain scale, Brief Fatigue Inventory (BFI), and Index of Nausea, Vomiting, and Retching.

Demographic and clinical information questionnaire: This form included such information as age, gender, level of education, marital status, time of assessment (being in hospital/being at home), diagnosis, and type of transplant.

STAI This inventory had 40 questions. The first 20 questions were related to state anxiety and the second 20 questions were related to trait anxiety. The answer to each question was based on a four-point Likert scale, ranging from one to four. Accordingly, the scores were divided into three levels; i.e., mild (20–39), moderate (40–59), and severe (60–80) anxiety. Cronbach's alpha coefficient was reported as 0.92 for state anxiety and 0.90 for trait anxiety. Additionally, the test–retest coefficient was 0.62 for state anxiety and 0.68 for trait anxiety [24]. The content validity of the Persian version of STAI was confirmed and its reliability was reported to be 0.81 [25]. In this study, Cronbach's alpha coefficient was reported as 0.88 for state anxiety and 0.84 for trait anxiety.

Numerical Pain Scale This tool is a standard scale for measuring pain. It is a horizontal ruler divided from 0 to 10. According to this scale, scores 0, 1–3, 4–6, and 7–10 indicated no pain, mild pain, moderate pain, and severe pain, respectively. The validity of this tool was 0.80 and its reliability was 0.80 [26]. In addition, the reliability of the Persian version of the scale was 0.94 [27].

BFI This inventory was designed to measure the level of fatigue and consisted of 10 questions. The first question determined the presence or absence of unusual fatigue in the past week using a yes/no question. In questions 2 to 10, the degree of fatigue was examined by different conditions, each being measured on a scale numbered from 0 to 10, indicating no fatigue and the most severe state of fatigue, respectively. Finally, the fatigue level was determined by adding the scores of questions 2 to 10 and dividing it by 9. Accordingly, scores 0, 1–3, 4–6, and 7–10 represented no fatigue, mild fatigue, moderate fatigue, and severe fatigue,

respectively. The validity of this questionnaire was found to be 0.76 and its reliability was reported as 0.96. Overall, this inventory had the highest reliability for measuring fatigue compared to other questionnaires [28]. In the present study, the reliability of BFI was approved by the Cronbach's alpha coefficient of 0.95.

Index of Nausea, Vomiting, and Retching This index aimed at evaluating multiple objective and subjective cases of nausea, vomiting, and retching. This index contained eight questions and was scored based on a five-point Likert scale. The index included three questions about nausea (frequency, severity, and duration of nausea), three questions about vomiting (frequency, severity, and amount of vomiting), and two questions about retching (frequency and severity). These questions could be assigned zero (absence of or minimum symptoms) to four (the worst condition) scores. Thus, the total score of this index could range from 0 to 32, with higher scores representing more severe nausea and vomiting [29]. In another study, the reliability of this index was reported to be 0.88 [30]. In the current study, the reliability of the index was confirmed by Cronbach's alpha coefficient of 0.97.

Sample Size

The sample size for the primary outcome was estimated based on a pilot study on ten HSCT patients, in which the correlations between state and trait anxiety and pain, fatigue, severity and frequency of nausea, vomiting, and retching, and amount of vomiting were ≥ 0.250 . However, the correlation between state anxiety and duration of nausea was 0.227, which was the lowest correlation coefficient. Therefore, considering the power of 90%, error of 5%, and $r = 0.227$, a 200-subject sample size was determined.

$$n = \frac{(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2}{u_p^2} + 3 = 200$$

$$u_p = \frac{1}{2} \ln \frac{1+r}{1-r}$$

$$r = 0.227$$

Moreover, based on the pilot study on ten HSCT patients and the results of the multiple regression analysis ($r = 0.33$, $r^2 = 0.11$) and considering $\alpha = 0.05$, $\beta = 0.90$, and number of predictors = 10, the sample size was estimated as $197 \approx 200$ subjects. Since the sample sizes measured for the primary and secondary outcomes were similar, this study was performed on 200 HSCT patients.

Ethical Consideration

The present study was approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.

REC.1398.1329). The questionnaires were coded and the study data were collected anonymously. In addition, the patients were assured about the confidentiality of their data and the voluntary nature of the study. Written consent forms were also obtained from the patients.

Statistical Methods

Descriptive and inferential statistics were used to analyze the data. Spearman and Pearson correlation coefficients were used to determine the associations between the variables. In addition, multiple regression analysis was used to determine the predictive roles of pain, fatigue, nausea, and vomiting in anxiety. It should be noted that disease diagnosis, type of HSCT, and time passed after HSCT might be confounders in this study. Therefore, the correlations between these variables and state and trait anxiety were assessed. These variables were also added to the regression model. These data were analyzed using the SPSS 26 software, and $p < 0.05$ was considered statistically significant.

Results

Descriptive Statistics

The study sample included 200 patients who had undergone HSCT. The assessment was done after transplantation in the hospital in 51 patients (25.5%) and at home in 149 ones (74.5%). Among the patients, 112 (56%) were male and 88 (44%) were female. The participants' ages ranged from 20 to 66 years (mean = 42.78, SD = 12.57). Besides, 67% of the participants were married and 33.5% had middle school and high school degrees. Regarding the clinical characteristics, 50.7% of the participants had leukemia (acute myeloid or lymphocytic leukemia). Furthermore, 76.5% and 23.5% of the patients had undergone allogeneic and autologous transplantations, respectively. The demographic and clinical characteristics of the HSCT patients have been presented in Table 1.

The mean score of trait anxiety (43.78, SD = 9.00) was higher compared to state anxiety (41.67, SD = 9.71). The levels of state and trait anxiety have been depicted in Figs. 1 and 2. Accordingly, 53% and 63.0% of the participants had moderate state and trait anxiety levels, respectively.

The total scores of pain ranged from 0 to 10, with a mean of 3.79 (SD = 2.79). Moreover, 18.6%, 46.1%, and 35.5% of the participants had high, moderate, and low pain levels, respectively.

Based on the results, 165 patients (82.5%) had felt fatigued during the past week. The mean score of fatigue was 4.23 (SD = 2.48), and the total scores of fatigue ranged

from 0 to 9.78. Fatigue was mild in 37.5% of the participants, moderate in 42.6%, and severe in 19.9%.

The total scores of nausea, vomiting, and retching ranged from 0 to 31, with the mean score of 9.46 (SD = 8.50). According to Table 2, approximately half of the HSCT patients experienced mild to severe nausea, vomiting, and retching. Additionally, one-third of the patients reported one-four times of nausea, vomiting, and retching within the past 12 h. Moreover, 140 patients (70%) did not experience vomiting and 44% felt nausea for one-three hours.

Primary Outcome: Correlation Between Anxiety and Fatigue, Pain, Nausea, and Vomiting

The results of correlation coefficients have been presented in Table 3. Accordingly, a significant moderate correlation was found between state and trait anxiety and fatigue ($0.50 > r < 0.70$, $p < 0.001$). A significant moderate correlation was also observed between state and trait anxiety and pain ($0.50 > r < 0.70$, $p < 0.001$). In addition, there was a positive correlation between state anxiety and severity of

Table 1 Demographic and clinical characteristics of the HSCT patients (N = 200)

| Variable | n (%) |
|----------------------------|------------|
| Gender | |
| Male | 112 (56.0) |
| Female | 88 (44.0) |
| Education level | |
| Illiterate | 15 (7.5) |
| Primary school | 51 (25.5) |
| Secondary and high school | 67 (33.5) |
| Academic | 67 (33.5) |
| Marital status | |
| Single | 52 (26.0) |
| Married | 134 (67.0) |
| Divorced | 10 (5.0) |
| Widowed | 4 (2.0) |
| Time of assessment | |
| Being in hospital | 51 (25.5) |
| Being at home | 149 (74.5) |
| Disease diagnosis | |
| Multiple myeloma | 78 (39.6) |
| Acute myeloid leukemia | 41 (20.8) |
| Acute lymphocytic leukemia | 47 (23.9) |
| Lymphoma | 25 (12.7) |
| Aplastic anemia | 6 (3.0) |
| Type of HSCT | |
| Autologous | 75 (37.5) |
| Allogeneic | 125 (62.5) |

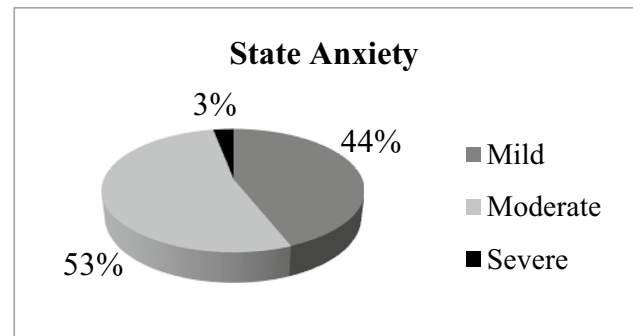


Fig. 1 The HSCT patients' state anxiety levels

nausea, vomiting, and retching ($0.30 > r < 0.50$, $p < 0.001$). Moreover, there was a negligible correlation between trait anxiety and severity of nausea and vomiting ($0.00 > r < 0.30$, $p < 0.05$) and a positive correlation between trait anxiety and severity of retching ($r = 0.33$, $p < 0.001$). Significant negligible correlations were also observed between state and trait anxiety and the frequency of nausea and vomiting, amount of vomiting, and duration of nausea ($0.00 > r < 0.30$, $p < 0.05$). Furthermore, a positive correlation was observed between state anxiety and frequency of retching ($r = 0.34$, $p < 0.001$).

According to Table 3, significant negligible correlations were found between trait anxiety and type of HSCT ($r = 0.17$, $p = 0.01$) and time of assessment ($r = 0.19$, $p = 0.007$). However, no significant correlation was observed between trait anxiety and disease diagnosis ($r = 0.06$, $p = 0.40$). The results also revealed no significant correlation between state anxiety and time of assessment, disease diagnosis, and type of HSCT ($p > 0.05$).

Secondary Outcome: Predictive Roles of Pain, Fatigue, Nausea, and Vomiting in Anxiety

The results of regression analysis have been presented in Tables 4 and 5. According to Table 4, fatigue, pain, severity and frequency of nausea, vomiting, and retching, amount of

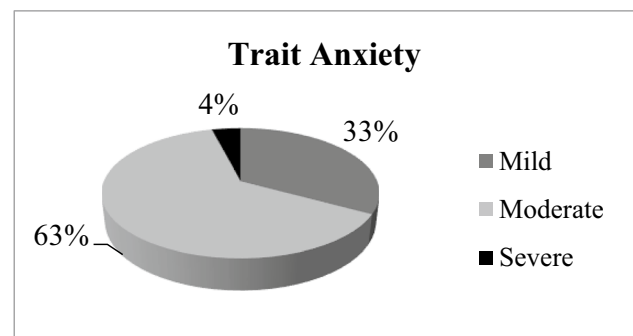


Fig. 2 The HSCT patients' trait anxiety levels

Table 2 Nausea, vomiting, and retching in the HSCT patients within the past 12 hours

| Variables | Nausea | Vomiting | Retching |
|------------------------------|------------|------------|------------|
| Severity | | | |
| No | 94 (47.0) | 119 (59.5) | 115 (57.5) |
| Mild | 48 (24.0) | 36 (18.0) | 41 (20.5) |
| Moderate | 36 (18.0) | 33 (16.5) | 27 (13.5) |
| Great | 17 (8.5) | 8 (4.0) | 11 (5.5) |
| Severe | 5 (2.5) | 4 (2.0) | 6 (3.0) |
| Frequency^a | | | |
| No | 102 (51.0) | 139 (69.5) | 108 (54.0) |
| 1–2 | 46 (23.0) | 34 (17.0) | 47 (23.5) |
| 3–4 | 29 (14.5) | 12 (6.0) | 18 (9.0) |
| 5–6 | 9 (4.5) | 7 (3.5) | 18 (9.0) |
| 7 or more | 14 (7.0) | 8 (4.0) | 9 (4.5) |
| Amount | | | |
| Very large ^b | | 5 (2.5) | |
| Large ^c | — | 7 (3.5) | — |
| Moderate ^d | | 7 (3.5) | |
| Small ^e | | 41 (20.5) | |
| None | | 140 (70.0) | |
| Time | | | |
| Not at all | 88 (44.0) | | |
| 1 h or less | 55 (27.5) | — | — |
| 2–3 h | 33 (16.5) | | |
| 4–6 h | 7 (3.5) | | |
| More than 6 h | 17 (8.5) | | |

^a times, ^b Very large (3 cups or more), ^c large (2–3 cups), ^d moderate (1/2–2 cups), ^e small (up to 1/2 cup)

Table 3 The correlation coefficient between state and trait anxiety and fatigue, pain, nausea, vomiting, and retching, time of assessment, diagnosis, and type of transplantation in the HSCT patients

| Variables | State anxiety | Trait anxiety |
|-----------------------|-------------------|--------------------|
| Fatigue | $r=0.61, P<0.001$ | $r=0.58, p<0.001$ |
| Pain | $r=0.54, p<0.001$ | $r=0.56, p<0.001$ |
| Severity of nausea | $r=0.33, p<0.001$ | $r=0.26, p<0.001$ |
| Severity of vomiting | $r=0.31, p<0.001$ | $r=0.23, p=0.001$ |
| Severity of retching | $r=0.41, p<0.001$ | $r=0.33, p<0.001$ |
| Frequency of nausea | $r=0.29, p<0.001$ | $r=0.18, p=0.008$ |
| Frequency of vomiting | $r=0.28, p<0.001$ | $r=0.25, p<0.001$ |
| Frequency of retching | $r=0.34, p<0.001$ | $r=0.27, p<0.001$ |
| Amount of vomiting | $r=0.27, p<0.001$ | $r=0.22, p=0.001$ |
| Duration of nausea | $r=0.26, p<0.001$ | $r=0.22, p=0.002$ |
| Time of assessment | $r=-0.13, p=0.06$ | $r=-0.19, p=0.007$ |
| Disease diagnosis | $r=0.01, p=0.79$ | $r=0.06, p=0.40$ |
| Type of HSCT | $r=0.13, p=0.05$ | $r=0.17, p=0.01$ |

vomiting, time of assessment, disease diagnosis, and type of HSCT predicted 51% of the variance in HSCT patients' state anxiety ($R=0.71, R^2=0.51, \text{ADJ. } R^2=0.47$). These results revealed the predictor roles of pain ($p<0.001$), fatigue ($p<0.001$), acute myeloid leukemia diagnosis ($p=0.01$), and type of HSCT ($p=0.03$) in state anxiety. According to Table 5, the above-mentioned variables also predicted 50% of the variance in HSCT patients' trait anxiety ($R=0.71, R^2=0.50, \text{ADJ. } R^2=0.46$). Thus, pain, fatigue, severity and frequency of nausea, and type of HSCT predicted the HSCT patients' trait anxiety.

Discussion

In this study, all HSCT patients showed mild to severe anxiety and 53% and 63% of the participants had moderate state and trait anxiety, respectively. It was reported that HSCT patients had moderate anxiety levels during the COVID-19 pandemic [31].

In the present study, the mean score of pain was 3.79, and 64.7% of the participants had moderate and high levels of pain. Similarly, another study reported moderate to severe pain intensity among the patients undergoing HSCT [12]. Another study also indicated that the pain burden could be potentially high in the hematology patients, especially those treated by HSCT [32]. In fact, excessive bone marrow activity in the patients undergoing HSCT may lead to bone pain in these patients.

Based on the present study findings, the mean score of fatigue was 4.23, and 82.5% of the patients had mild to severe fatigue. Moreover, 42.6% and 19.9% of the participants reported moderate and severe fatigue levels, respectively. It was previously observed that the HSCT patients experienced high fatigue levels during their treatment period [33]. In another study evaluating fatigue in allogeneic stem cell transplant recipients, patients reported 68% fatigue on the day of transplantation, 90% in the first month, and 81% on day 100 after transplantation [34].

In the present study, the mean score of nausea, vomiting, and retching was 6.31. In another study, the mean score of nausea and vomiting was 7.2 (SD=8.7) in patients undergoing chemotherapy [35]. Overall, 70–80% of the patients undergoing chemotherapy experienced nausea and vomiting, which could be both acute (36%) and delayed (59%) [36].

The present study investigated the correlation between anxiety and pain, fatigue, nausea, and vomiting in the patients treated by HSCT. The results demonstrated that state and trait anxiety and fatigue were moderately correlated with each other. In another research, patients undergoing chemotherapy with moderate to severe fatigue had higher anxiety scores and showed significantly more anxiety symptoms [37]. Another research also revealed a moderate

Table 4 The results of regression analysis for determining the predictive roles of pain, fatigue, nausea, and vomiting in the HSCT patients' state anxiety (n = 200)

| | Unstandardized coefficients | | Standardized coefficients | t | P-value | 95% CI ^a |
|--------------------------------------|-----------------------------|------------|---------------------------|-------|---------|---------------------|
| | B | Std. Error | | | | |
| 1 (constant) | 27.25 | 3.07 | | 8.85 | <0.001 | 21.17, 33.32 |
| Fatigue | 1.56 | 0.28 | 0.40 | 5.56 | <0.001 | 1.01, 2.11 |
| Pain | 0.78 | 0.25 | 0.22 | 3.07 | 0.002 | 0.28, 1.29 |
| Severity of nausea | 1.41 | 1.03 | 0.16 | 1.36 | 0.17 | -0.62, 3.45 |
| Severity of vomiting | -0.54 | 1.30 | -0.05 | -0.41 | 0.67 | -3.10, 2.02 |
| Severity of retching | 2.29 | 1.20 | 0.25 | 1.91 | 0.05 | -0.07, 4.67 |
| Frequency of nausea | -0.69 | 0.83 | -0.08 | -0.83 | 0.40 | -2.34, 0.94 |
| Frequency of vomiting | 0.26 | 0.97 | 0.02 | 0.27 | 0.78 | -1.65, 2.18 |
| Frequency of retching | -0.35 | 0.79 | -0.04 | -0.44 | 0.65 | -1.91, 1.21 |
| Amount of vomiting | -1.07 | 0.96 | -0.10 | -1.11 | 0.26 | -2.98, 0.83 |
| Duration of nausea | -1.10 | 0.76 | -0.14 | -1.45 | 0.14 | -2.60, 0.39 |
| Time of assessment | 0.10 | 1.33 | 0.005 | 0.07 | 0.93 | -2.53, 2.74 |
| Acute myeloid leukemia diagnosis | -4.58 | 1.75 | -0.19 | -2.61 | 0.01 | -8.04, -1.12 |
| Acute lymphocytic leukemia diagnosis | 0.51 | 1.68 | 0.02 | 0.30 | 0.75 | -2.80, 3.83 |
| Lymphoma diagnosis | 3.12 | 1.71 | 0.10 | 1.82 | 0.07 | -0.26, 6.50 |
| Aplastic anemia diagnosis | -3.92 | 3.32 | -0.06 | -1.18 | 0.23 | -10.47, 2.63 |
| Type of HSCT | 3.03 | 1.45 | 0.15 | 2.09 | 0.03 | 0.17, 5.90 |

Multiple myeloma diagnosis was excluded
a, 95.0% confidence interval for B

correlation between anxiety and fatigue, such a way that anxiety could be continuously correlated to fatigue [38].

In the present study, state and trait anxiety were moderately correlated to pain. In another study also, there was a positive correlation between anxiety and pain among cancer patients [39]. Anxiety was also directly related to pain in cancer patients during the COVID-19 pandemic, such a way that increase in pain might increase the anxiety level [40].

In the current study, nausea, vomiting, and retching were correlated to state and trait anxiety. Researchers have indicated that nausea and vomiting could be one of the main causes of anxiety in cancer patients. In other words, the presence of nausea and vomiting might lead to several mental problems, such as anxiety and depression among these patients [18]. Hence, controlling nausea and vomiting during and after the HSCT could significantly prevent or reduce the physical and psychological effects of transplantation, such as fatigue and anxiety. It could improve the patients' quality of life, as well [19].

The results of regression test in the present study demonstrated that the most important factors that predicted the participants' state and trait anxiety were fatigue and pain. Moreover, severity and frequency of nausea and type of HSCT were the predictors of trait anxiety in the study participants. A prior study disclosed that anxiety and depression were positively correlated to psychological distress in HSCT patients, and fatigue might play a positive predictive role in anxiety among these patients [41]. Furthermore, anxiety was significantly

associated with pain in cancer patients, and pain intensity might predict anxiety in these patients [11].

Although the assessment time was determined as "being in hospital" and "being at home" in the present study, the exact time of assessment could not be identified. Therefore, future studies are recommended to take this possible confounder into account. In addition, etiological studies are suggested to be performed in this field so as to determine the other factors associated with anxiety during the COVID-19 pandemic. Considering generalizability also, further studies are required to be conducted in this area.

Conclusion

The result related to the primary outcome showed a moderate correlation between state and trait anxiety and pain and fatigue. Moreover, a positive correlation was reported between state anxiety and the severity of nausea and vomiting. These variables also had negligible correlations with trait anxiety. In addition, a positive correlation was observed between state and trait anxiety and retching among the HSCT patients.

The results related to the secondary outcome revealed the predictor roles of pain, fatigue, and type of HSCT in state anxiety. Moreover, pain, fatigue, severity and frequency of nausea, and type of HSCT predicted the HSCT patients' trait anxiety. Considering the moderate correlation between

Table 5 Multiple linear regression analysis predicting the HSCT patients' trait anxiety (n = 200)

| Factors | Unstandardized coefficients | | Standardized Beta | t | 95% CI ^a | P-value |
|--------------------------------------|-----------------------------|------------|-------------------|-------|---------------------|--------------|
| | B | Std. Error | | | | |
| 1 (constant) | 32.32 | 2.87 | | 11.23 | <0.001 | 26.64, 38.00 |
| Fatigue | 1.11 | 0.26 | 0.30 | 4.25 | <0.001 | 0.60, 1.63 |
| Pain | 0.79 | 0.23 | 0.24 | 3.31 | 0.001 | 0.32, 1.26 |
| Severity of nausea | 3.05 | 0.96 | 0.37 | 3.16 | 0.002 | 1.15, 4.96 |
| Severity of vomiting | -2.00 | 1.21 | -0.22 | -1.64 | 0.10 | -4.39, 0.39 |
| Severity of retching | 2.31 | 1.12 | 0.27 | 2.05 | 0.04 | 0.09, 4.53 |
| Frequency of nausea | -0.87 | 0.78 | -0.11 | -1.11 | 0.26 | -2.41, 0.66 |
| Frequency of vomiting | 1.08 | 0.91 | 0.12 | 1.18 | 0.23 | -0.71, 2.87 |
| Frequency of retching | -0.10 | 0.74 | -0.01 | -0.13 | 0.89 | -1.56, 1.36 |
| Amount of vomiting | -1.67 | 0.90 | -0.17 | -1.85 | 0.06 | -3.45, 0.10 |
| duration of nausea | -1.21 | 0.71 | -0.16 | -1.71 | 0.08 | -2.62, .185 |
| Time of assessment | -1.02 | 1.25 | -0.05 | -0.82 | 0.41 | -3.49, 1.43 |
| Acute myeloid leukemia diagnosis | -1.71 | 1.64 | -0.07 | -1.04 | 0.29 | -4.95, 1.51 |
| Acute lymphocytic leukemia diagnosis | 0.70 | 1.57 | 0.03 | 0.44 | 0.65 | -2.39, 3.80 |
| Lymphoma diagnosis | 2.39 | 1.60 | 0.09 | 1.49 | 0.13 | -0.77, 5.55 |
| Aplastic anemia diagnosis | -4.32 | 3.10 | -0.08 | -1.39 | 0.16 | -10.44, 1.80 |
| Type of HSCT | 2.86 | 1.35 | 0.15 | 2.11 | 0.03 | 0.18, 5.54 |

a, 95.0% confidence interval for B

physical complications such as pain and fatigue and mental complications such as anxiety among the HSCT patients, healthcare workers are recommended to evaluate these patients in terms of both physical and mental problems and control and manage these complications by complementary and integrative interventions.

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Data Availability The data transparency was approved by FZ, NP, and MR. Data are available by MR, NP, and FZ in form of an SPSS file.

Data would be available on request based on the privacy and ethical limitations.

Code Availability Not applicable.

Declarations

Ethics Approval The present study was approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1398.1329).

Consent to Participate Written consent forms were obtained from the patients. The questionnaires were coded and the study data were collected anonymously. In addition, the patients were assured about the confidentiality of their data and the voluntary nature of the study.

Consent for Publication The data were published anonymously.

Conflicts of Interest/Competing interests None declared.

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