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Original Article

Financial toxicity and distress level in individuals undergoing hematopoietic stem cell transplantation

Toxicidade financeira e nível de distress em indivíduos submetidos ao transplante de células tronco hematopoiéticas

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ABSTRACT

Objective: to identify the financial toxicity and distress level of patients with hematological cancers undergoing Hematopoietic Stem Cell Transplantation. **Methods:** this is a descriptive, cross-sectional study, conducted with 21 patients admitted to a Bone Marrow Transplant Service. The following questionnaires were applied for data collection: sociodemographic; Comprehensive Score for Financial Toxicity; and Distress Thermometer, with descriptive statistical analysis and Spearman's correlation being performed using R software version 4.1.0 (R- Core Team 2021). **Results:** the average financial toxicity score was 24.6, indicating grade 1 and mild impact. In contrast, the distress level found was 5.3, indicating a high degree of distress (>4). There is a weak and positive correlation between financial toxicity and distress (ρ=0.45, $p<0.05$). **Conclusion:** grade 1 financial toxicity and high distress levels were identified in patients undergoing hematopoietic stem cell transplantation. **Contributions to practice:** identifying factors which may be related to patient suffering can support improvements in care.
Descriptors: Bone Marrow Transplantation; Financial Stress; Hematologic Neoplasms; Psychological Distress.

RESUMO

Objetivo: identificar a toxicidade financeira e o nível de *distress* de pacientes com cânceres hematológicos submetidos ao Transplante de Células Tronco Hematopoiéticas. **Métodos:** estudo descritivo, transversal, realizado com 21 pacientes internados em um Serviço de Transplante de Medula Óssea. Para coleta de dados, foram aplicados os seguintes questionários: sociodemográfico; *COmprehensive Score for Financial Toxicity;* e Termômetro *Distress*, sendo realizada análise estatística descritiva e correlação de Spearman através do *software* R versão 4.1.0 (*R- Core Team 2021*). **Resultados:** o escore médio de toxicidade financeira foi de 24,6, indicando grau 1 e impacto leve. Em contrapartida, o nível de *distress* encontrado foi de 5,3 indicando alto grau de sofrimento (>4). Existe correlação fraca e positiva entre a toxicidade financeira e o *distress* (ρ=0,45, $p<0,05$). **Conclusão:** identificou-se toxicidade financeira de grau 1 e alto nível de *distress* nos pacientes submetidos ao transplante de células-tronco hematopoiéticas. **Contribuições para a prática**: a identificação de fatores que podem estar relacionados ao sofrimento do paciente pode subsidiar a melhoria da assistência.
Descritores: Transplante de Medula Óssea; Estresse Financeiro; Neoplasias Hematológicas; Angústia Psicológica.

Introduction

Hematological cancers refer to those of blood origin and lymphoid organs, characterized by pathological multiplication of mature and immature blood cells that deviate from the normal functioning of the lymphohematopoietic system[1], and are composed of leukemias, lymphomas and multiple myeloma. Treatment for these neoplasms includes chemotherapy, radiotherapy, immunotherapy and hematopoietic stem cell transplantation (HSCT). A combination of one or more therapeutic modalities is necessary in certain scenarios, depending on the type of disease, stage, patient age, and bone marrow performance, among other factors[2]. HSCT is a complex procedure among such therapeutic options, with a high morbidity and mortality rate. It aims to eradicate the "sick" bone marrow and replace it with another through infusing hematopoietic progenitor cells extracted from the bone marrow, peripheral blood or umbilical cord blood, offering favorable conditions for reestablishing hematopoietic function[3].

Given the treatment aggressiveness and its adverse effects, the patient is likely to experience physical, psychological and financial repercussions[4]. Symptoms such as fatigue, mucositis, gastrointestinal dysfunction, and radiodermatitis (among others) are frequently observed. Moreover, patients are exposed to an increased risk of developing post-traumatic stress and experiencing feelings of worry, anguish, anxiety, and financial problems, which can result in social isolation[5].

In addition to the physical toxicities caused by treatment, time away from work may lead to develop or worsen financial toxicity, which is a concept that describes the financial burden and distress of patients who have difficulty paying for treatment expenses[6]. The impacts caused by financial toxicity may affect physical health[7], care neglect[8], and mental health[9] with increased anxiety and depression, which can cause emotional distress and interfere with quality of life.

In the context of psychological suffering in cancer patients, the National Comprehensive Cancer Network adopted the term distress to define the "unpleasant and multifactorial emotional experience of a psychological (cognitive, behavioral, emotional), social and/or spiritual nature that may interfere with the ability to effectively cope with cancer, its physical symptoms and its treatment"[10:5].

Considering that financial toxicity is an adverse event of cancer treatment which can influence the distress level, and that both can cause suffering for patients undergoing HSCT, this study aimed to identify the financial toxicity and distress level of patients with hematological cancers undergoing Hematopoietic Stem Cell Transplantation.

Methods

This is a descriptive, cross-sectional study which followed the guidelines of Strengthening the Reporting of Observational Studies in Epidemiology (STROBE). It was conducted at the Bone Marrow Transplant Service of a university hospital in the city of Curitiba, Paraná, Brazil, a reference for treatment in Latin America. The sector has 11 beds divided between adults and pediatrics and performs an average of 90 hematopoietic stem cell transplants per year. A patient who undergoes a transplant remains hospitalized in the sector for an average of 20 days between the conditioning period and discharge for outpatient care.

The study included adult patients diagnosed with hematologic cancer who were about to have or had undergone hematopoietic stem cell transplantation. A total of 27 patients were eligible to participate in the study during the data collection period; however, two died, two had complications that made data collection impossible, and two refused to participate. A non-probabilistic sampling process was adopted, collecting data from all adult patients admitted to the unit who were undergoing or had undergone HSCT between March and August 2024, provided they were

able to respond to the questionnaires. Patients who were admitted during the data collection period due to complications were not included. Patients with impaired cognitive ability verified in medical records or observed by the researcher were excluded.

After applying the eligibility criteria, 21 patients participated. They were approached individually in the ward where they were hospitalized by the main researcher of this study who at the time was a nursing resident and was responsible for the direct care of each of the patients, and therefore agreed on the preferred time for participation in the study. Three instruments were applied to these patients in the form of interviews, including: a sociodemographic data collection instrument, the COmprehensive Score for Financial Toxicity (COST), and the Distress Thermometer.

The instrument with sociodemographic data was developed by the researchers and contains information on age, sex, marital status, profession, family income, presence of comorbidities, physical activity, and alcohol and tobacco consumption, and has already been used in other studies on this topic[11-12].

The COST is a 12-item questionnaire that was developed by the Functional Assessment of Chronic Illness Therapy group and validated in Brazil[11] to measure the financial toxicity of cancer patients. The answers are on a five-point Likert scale and the score ranges from zero to 44, with the higher the score indicating greater financial well-being (i.e. lower financial toxicity). Question number 12 is disregarded to calculate the score, because it is a summary item. In addition, questions number two, three, four, five, eight, nine, and ten are reversed.

The Distress Thermometer version 2.2022 was developed by the National Comprehensive Cancer Network[13] and validated in Brazil[14] and aims to establish the distress level of cancer patients. It consists of two instruments: one, which analyzes the distress level, is presented as a thermometer which allows the patient to indicate their distress level starting from 0 - no distress - to 10 - extreme distress; and the other (List of Problems), contains 43 items (physical, emotional, social, practical, spiritual and/or religious concerns, and other problems) which are aimed at recognizing possible causes of distress, even if these are not associated with the diagnosis or treatment.

The data were tabulated using Microsoft Office Excel 365, and descriptive statistical analysis and Spearman's correlation (ρ) were performed to demonstrate the association between the distress level and financial toxicity, both using R software version 4.1.0 (R- Core Team 2021). A division[15] which classified the COST score into four degrees indicating greater or lesser financial toxicity was adopted to assess financial toxicity, namely: grade zero score above 26 (no impact); grade one score between 14-25 (mild impact); grade two score between one-13 (moderate impact); and grade three score zero (high impact). Thus, patients with grade two or three present financial toxicity. The distress thermometer analysis was performed according to the questionnaire guideline.

This study was assessed by the Research Ethics Committee of the Hospital de Clinics Complex of the Federal University of Paraná and approved with opinion number 6,599,780/2023 and Certificate of Presentation of Ethical Assessment.: 75736923.0.0000.0096.

Results

It was found that the majority of the sample's sociodemographic and clinical data were men, married, with a mean age of 53.5 years and a Standard Deviation of ±12.4. In addition, the majority were self-employed, had an income of 1-3 minimum monthly salaries and were undergoing oncohematological treatment for the first time.

Regarding lifestyle habits, less than half were former smokers, the majority had a habit of drinking alcohol frequently and did not practice physical activity. It was also observed that more than half reported having other types of comorbidity, and most of them used frequent medication. The prevalent diagnosis in the sample studied was acute myeloid leukemia, follo-

wed by multiple myeloma and non-Hodgkin lymphoma. Finally, it was found that autologous was the most frequent type of transplant performed, followed by haploidentical (Table 1).

Tabela 1 – Sociodemographic and clinical characteristics of patients undergoing hematopoietic stem cell transplantation (n=21). Curitiba, PR, Brazil, 2024

Variables	n (%)
Sex	
Female	5 (24.0)
Male	16 (76.0)
Civil status	
Married	13 (62.0)
Divorced	2 (9.5)
Single	2 (9.5)
Stable union	4 (19.0)
Occupation	
Retired	3 (14.2)
Self-employed	13 (62.0)
Formal employment	2 (9.5)
Public servant	3 (14.2)
Family income (minimum monthly salaries)	
No income	3 (14.2)
Up to 1	1 (4.7)
1 to 3	13 (61.9)
4 to 10	4 (19.0)
Previous cancer treatment	
Yes	2 (9.5)
No	19 (90.4)
Type of cancer being treated	
Acute myeloid leukemia	8 (38.1)
Chronic myeloid leukemia	1 (4.7)
Acute biphenotypic leukemia	1 (4.7)
Non-Hodgkin lymphoma	5 (23.8)
Hodgkin lymphoma	1 (4.)
Multiple myeloma	5 (23.8)
Diagnosis time	
3 to 6 months	5 (23.8)
7 to 12 months	8 (38.0)
> 1 year	8 (38.0)
Comorbidities	
Yes	11 (52.3)
No	10 (48)
Continuous use of medication	
Yes	17 (80.9)
No	4 (19.0)
Practice physical exercise	
Yes	5 (23.8)
No	16 (76.1)
Smoking	
Yes	10 (47.6)
No	11 (52.3)
Consume alcoholic beverages	
Yes	16 (76.1)
No	5 (23.8)
Transplant type	
Allogeneic related	3 (14.2)
Allogeneic unrelated	3 (14.2)
Haploidentical	4 (19.0)
Autologous	11 (52.3)
Transplant phase	
Pre-transplant	4 (19.0)
Day zero	1 (4.7)
Post-transplant	16 (76.2)

The average score regarding financial toxicity was 24.6, with most patients reporting that they did not have enough resources (in savings, retirement, assets, etc.) to cover treatment expenses, that medical expenses exceeded what was expected, that they were worried about employment, and that the disease caused financial difficulties. There was also a predominance of the feeling of "feeling frustrated" for not being able to work and contribute to income, and more than half were dissatisfied with their current financial situation (Figure 1).

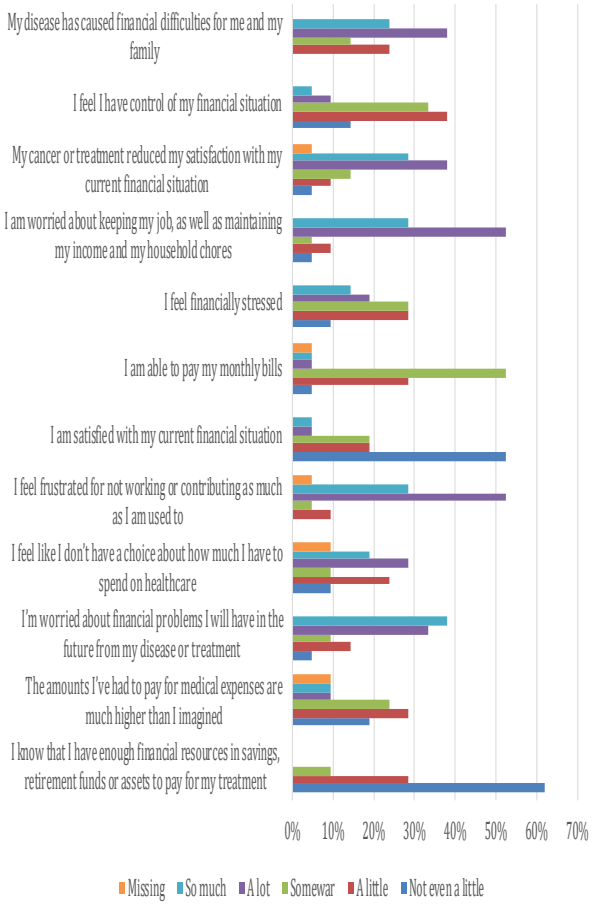

Figure 1 – Results of the Comprehensive Score for Financial Toxicity applied to patients undergoing hematopoietic stem cell transplantation (n=21). Curitiba, PR, Brazil, 2024

It was observed that the distress thermometer variables which stood out were: worry and anxiety;

change in diet; taking care of myself; relationship with spouse or partner and sense of meaning or purpose, as per Table 2. The average found regarding the distress level was 5.3, indicating a high distress level (>4).

Table 2 – Distress level and concerns associated with the anguish of patients undergoing hematopoietic stem cell transplantation (n=21). Curitiba, PR, Brazil, 2024

Variables	n (%)
Physical concerns	
Pain	11 (55.0)
Sleep	10 (50.0)
Fatigue	6 (30.0)
Smoking	0 (0)
Substance use	1 (5.0)
Memory and concentration	4 (20.0)
Sexual health	3 (15.0)
Changes in diet	12 (60.0)
Loss or changes in physical abilities	9 (45.0)
Emotional concerns	
Worry and anxiety	16 (80.0)
Sadness or depression	3 (15.0)
Loss of interest or pleasure	5 (25.0)
Sadness or loss	4 (20.0)
Fear	6 (30.0)
Loneliness	1 (5.0)
Anger	1 (15.0)
Change in appearance	8 (40.0)
Feelings of sadness	6 (30.0)
Social concerns	
Relationship with spouse or partner	6 (30.0)
Relationship with children	4 (20.0)
Relationship with family members	2 (10.0)
Relationship with friends or coworkers	2 (10.0)
Communication with medical staff	2 (10.0)
Ability to have children	3 (15.0)
Practical concerns	
Taking care of myself	9 (55.0)
Taking care of others	3 (15.0)
Work	7 (35.0)
School	0 (0)
Housing	2 (10.0)
Finances	10 (50.0)
Health insurance	0 (0)
Transportation	2 (10.0)
Having enough food	4 (20.0)
Access to medicines	9 (45.0)
Treatment decisions	6 (30.0)
Spiritual and religious concerns	
Sense of meaning or purpose	4 (20.0)
Change in faith or belief	2 (10.0)
Death, dying, or the afterlife	2 (10.0)
Conflicts between beliefs and cancer treatment	1 (5.0)
Relationship with the sacred	3 (15.0)
Need for rituals or diet	3 (15.0)

It was possible to observe a weak positive correlation for mean distress and financial toxicity (ρ=0.45, $p<0.05$) (Figure 2).

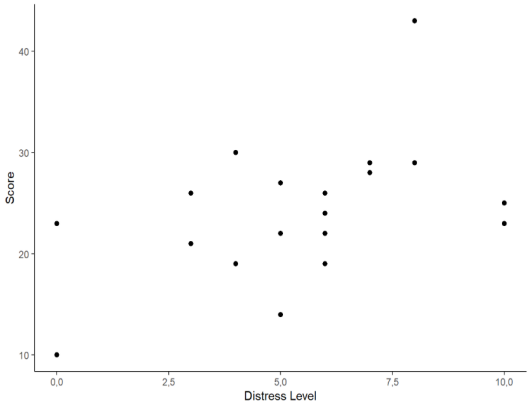

Figure 2 – Spearman's linear correlation between distress level and financial toxicity (n=21). Curitiba, PR, Brazil, 2024

Discussion

The results showed the financial toxicity and distress level of patients with hematologic cancer due to long and complex treatment, impacting several facets of the lives of the patient and their families, especially the working-age and salaried population, such as for the sample in this study.

The results regarding the gender of the participants replicated those obtained in another study conducted in a day clinic, which serves post-HSCT patients, in which 60% of the sample was composed of men[16], and similar to national data which estimated the occurrence of 11,540 new cases of leukemia for the year 2023, 6,250 of which were in men[17]. Leukemia is a malignant disease of the white blood cells caused by genetic and environmental factors. Leukemia patients present immunosuppression due to the disease or treatment which requires specific care, and at times prevents the individual from performing routine activities, including work, constituting a condition which can generate stress due to reduced family income, leading to financial difficulties[18].

The results indicated the occurrence of grade 1 financial toxicity, with a mild impact, which corroborates the findings of a study conducted in the same hospital, but in a day clinic[16], and in a study perfor-

med with 176 patients undergoing evaluation for HSCT, in which the authors identified the occurrence of mild financial toxicity in 29% and moderate-high in 23.9% of the participants[19].

This finding may be related to the care that the transplant patient receives during the treatment process, which offers financial support, housing and food. Furthermore, in addition to being 100% funded by the Unified Health System, the service has a support network which offers benefits such as housing close to the hospital and day hospital care during the first 100 days after the transplant. On another note, it is important to highlight that patients with cancer go through so many complications that they can emphasize treatment to the detriment of other needs.

Also, the financial toxicity concept has been studied in cancer patients, more specifically solid tumors, with little literature on adult transplant patients[12,18,20]. However, the findings are similar to those found by national and international authors who obtained an average COST score of 20.1 and 20, respectively[12,21].

This result suggests that although the patient receives care during treatment, this does not eliminate the presence of financial toxicity, with this result possibly being related to the resources available to meet the needs arising from the treatment. This condition was also highlighted by the review, which found some form of financial toxicity in all articles included in the sample, including loss of productivity at work, food and transportation costs, and depletion of savings[22]. An association was found between anxiety/depression and physical symptoms expressed by cancer patients undergoing chemotherapy, and financial problems were among the most cited[23].

The distress level is considered the sixth vital sign in cancer care, followed by temperature, breathing, blood pressure, heart rate and pain[24]. There are few studies which have used the distress thermometer in transplant patients; however, it is known that HSCT generates stress and psychological suffering for patients due to the complexity of the procedure, risk of death and toxicities caused by the high chemotherapy and radiotherapy doses during the conditioning period. In this scenario, the patient needs regular psychological monitoring so that they can deal with the emotions and feelings arising from the treatment, as this context makes assessment of distress essential for comprehensive care.

Distress can be measured using other tools, such as the Hospital Anxiety and Depression Scale, which assesses depression and anxiety states in the outpatient medical clinic setting, and the Short Form General Health Survey, which, although focused on quality of life, is considered an excellent instrument for measuring distress; however, both are not specific for oncology use[14].

Although not specifically related to transplant patients, clinical evidence indicates that depression and anxiety are prevalent among cancer patients and are correlated with a worse prognosis and increased mortality rates. Along these same lines, psychological distress induces cancer risk factors (including obesity, disordered circadian rhythms, and premature senescence) which indirectly promote the onset and progression of the disease[25].

The results obtained regarding the distress level indicated a high level in the sample, which suggests intervention by the care team. In turn, identifying symptoms that indicate anxiety/depression can help in structuring services for effective management of the situation[23]. Patients undergoing HSCT are separated from their families and social life for many months, have significant dietary limitations, experience the difficulty of toxicities, and need psychological support. However, this condition was not observed in this study, which may be related to the high distress level in the sample.

The use of non-pharmacological strategies to reduce psychological distress may be an accessible and possible alternative for transplant patients, as these resources have shown positive results and can

be used by nursing staff[26-27]. Finally, a weak positive correlation was observed regarding the association between financial toxicity and the distress level.

Study limitations

The limitations of this study are focused on the study type (being cross-sectional) and the sample size, which may have influenced the results, thereby not allowing generalizations. It is also worth mentioning the scarcity of studies which have used the distress thermometer among patients undergoing hematopoietic stem cell transplantation, which made it difficult to compare the findings. The lack of delimiting the treatment time for data collection may have influenced the results; however, it is believed that the findings have the potential to arouse interest among scholars of the subject.

Contributions to practice

Using the distress thermometer makes it possible to identify factors which cause distress to patients undergoing hematopoietic stem cell transplantation and can help the healthcare team develop actions that contribute to its minimization. It is believed that emotional aspects can cause physical consequences for the patient and that by dealing with these issues, the patient may have a better response to treatment. This study reinforces that patients undergoing transplantation needs to be cared for in all aspects of their life, which includes psychological support at all treatment stages.

Conclusion

Grade 1 financial toxicity and high distress levels were identified in patients undergoing hematopoietic stem cell transplantation. The combination of financial toxicity and high distress levels are considered factors which may contribute to increased emotional suffering.

Authors' contributions

Conception and design or data analysis and interpretation: Vieira JML, Vissintainer YPD, Castro GC, Nogueira LA. Writing of the manuscript or relevant critical review of intellectual content; final approval of the version to be published and responsibility for all aspects of the text to ensure the accuracy and integrity of any part of the manuscript: Vieira JML, Kalinke LP, Vissintainer YPD, Castro GC, Mantovani MF, Marcon SS, Nogueira LA.

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