CHAPTER
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Overweight and cardiovascular risk in patients undergoing hematopoietic stem cell transplantation

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ABSTRACT
Introduction: Hematopoietic Stem Cell Transplantation (HSCT) is a therapeutic proposal for oncohematological treatment that includes the use of high-dose chemotherapy, after carrying out the conditioning regimen, and many of these classes of antineoplastic agents have cardiotoxic effects. In addition, cardiovascular diseases are among the main causes of post-HSCT morbidity and mortality. Objectives: To assess the nutritional status and cardiovascular risk of patients admitted for HSCT. Methods: Cross-sectional, retrospective study with an analytical component and a quantitative approach. Data was obtained from electronic medical records, from the years 2019 and 2020. Information was collected from the moment of admission, including age, gender, diagnosis, type of transplant, comorbidity report, biochemical tests, body weight, height, waist circumference (WC), and arm circumference. Results: The present study was carried out with 81 patients admitted for HSCT. There was a higher prevalence of Multiple Myeloma (34.6%, n=28) and autologous transplantation (64.2%, n=52). Systemic arterial hypertension (30.9%, n=25) was one of the most reported comorbidities by patients. Most patients were overweight (63%, n=51), high Low-Density Lipoprotein (57.8%, n=37), low High-Density Lipoprotein (58.46%, n=38), and cardiovascular risk assessed by WC (80.2%, n=65). Conclusion: It can be concluded that patients admitted for HSCT had a high prevalence of overweight and cardiovascular risk.

Keywords: Hematopoietic stem cell transplantation, stem cell transplantation, overweight, obesidad abdominal, cardiovascular diseases.

1 INTRODUCTION

In 2019, Brazil hosted the V Global Cardio-Oncology *Summit*, an event that brought together experts from several countries on this theme that covers the specialties of cardiology and oncology forming this subarea active in the prevention, diagnosis and early treatment of cardiovascular diseases (CVD) in cancer patients.

And it plays an essential role in the evaluation of the cardiovascular risk associated with the treatments to which patients are exposed1.

Due to the importance of this theme, we saw the need for the publication of the Update of the Brazilian Guideline (2020).

The development in this area corresponds to the high demand evidenced by the epidemiological data of cancer patients affected by CVD. Studies have demonstrated in recent years many classes of antineoplastic drugs with cardiotoxic effects2,3.

Patients with oncohematological diagnosis go through several cycles of treatment, have among the therapeutic proposals the Hematopoietic Stem Cell Transplantation (HSCT) which consists of replacing the defective bone marrow, with another of a compatible donor, called allogeneic transplantation, or even the patient himself, called autologous transplantation, after the performance of the conditioning regimen, a protocol that includes the use of high-dose chemotherapy (QT) associated or not with radiotherapy sessions[4,5].

According to data from the Brazilian Association of Organ Transplantation, in 2019 3,805 HSCTs were performed, among autologous and allogeneic[6].

Nutritional status has been shown to influence the prognosis of patients undergoing HSCT. Both protein-calorie malnutrition and obesity are risk factors for complications and increased mortality related to HSCT7,8,9,10. Being overweight is a serious public health problem according to the World Health Organization (WHO), being increasingly prevalent11,12.

According to data from the survey Surveillance of Risk and protective factors for chronic diseases by telephone survey (VIGITEL - 2019), an increase of 67.8% in the number of obese (BMI >30 kg/m²) demonstrated from 2006 to 2018 in Brazil, with a prevalence equal to 18.9% for obesity and 55.7% for overweight (BMI > 25 kg/m²) 12.

Obesity is associated with several comorbidities, mainly related to metabolic changes, such as insulin resistance and type 2 Diabetes Mellitus (DM), nonalcoholic fatty liver disease, dyslipidemias (DLP), CVDs, gastroesophageal reflux disease, lung diseases, even sleep disorders.

As it is also among the factors for the diagnosis of metabolic syndrome[13]. CVDs are among the main causes of morbidity and mortality after HSCT[14].

Thus, it is essential to monitor risk factors related to lifestyle, especially modifiable ones, so that the most prevalent profiles are elucidated due to the development of measures aimed at the conditions observed.

The present study aimed to evaluate the nutritional status and cardiovascular risk of patients admitted for HSCT.

2 METHODS

This is a cross-sectional, retrospective study, with an analytical component and a quantitative approach, carried out in a tertiary level University Hospital, a reference in bone marrow transplantation, located in the city of Fortaleza, Ceará.

The study protocol was approved by the Research Ethics Committee of the Walter Cantídio University Hospital of the Federal University of Ceará (HUWC/UFC), under opinions n° 4.767.196, n° 4.865.251, CAAE 46884821.9.0000.5045.

Data were obtained from electronic medical records from 2019 to 2020 and were collected from March to April 2021. We included 81 medical records of patients of both sexes, aged 18 years or older, admitted for HSCT.

Information was collected at the time of admission on clinical, sociodemographic, and anthropometric data, including age, gender, diagnosis, type of transplantation, report of comorbidity, biochemical tests, body weight, height, waist circumference (WC), and arm circumference (AC), and was later tabulated in Microsoft Excel® spreadsheets, version 10.

To assess nutritional status, the body mass index (BMI) was calculated and the WHO classification was used for adults and the one proposed by the Pan American Health Organization (PAHO) for the elderly (≥ 60 years)[13,16].

We also used the calculation of BC adequacy according to Blackburn and Thornton[17,18]. Cardiovascular risk was assessed by WC, according to the WHO classification (Table 1)[18].

Table 1 – Waist circumference by sex and risk of metabolic complications associated with obesity.

Risk of metabolic complications	Waist circumference (cm)	
	Female	Male
No risk	< 80	< 94
High risk	≥ 80	≥ 94

Source: Adapted from WHO, 2000.

The laboratory tests of the pre-HSCT period requested due to the follow-up to hospitalization were analyzed. The lipid profile and CRP values were evaluated by the cutoff points described in the last Update of the Brazilian Guideline on Dyslipidemias and Prevention of Atherosclerosis[19].

Glycemic changes based on the Brazilian Diabetes Guideline20. While for blood pressure levels, the reference values of the Brazilian Guideline on Hypertension were used21.

The collected data were tabulated in Microsoft Excel®. Performing descriptive analysis of the data to characterize the sample raised in the research. The variables were presented by simple frequency.

3 FINDINGS

The present study was conducted from a sample of 81 medical records of patients admitted for HSCT, most of them adults (67%, n=65) males (50.6%, n=41), with a mean age of 46 years and ranging from 18 to 69 years. Regarding the diagnosis, there was a higher prevalence of Multiple Myeloma (34.6%, n=28), which is indicated for autologous transplantation (64.2%, n=52).

In response to screening, 45.7% (n=37) of the patients reported having at least one comorbidity, with hypertension (30.9%, n=25) being the most reported (Table 2).

Table 2- Demographic and clinical characteristics of patients admitted for HSCT. Fortaleza, Brazil, 2019-2020.

Variables	N	%
Sex		
Male	41	50,6
Female	40	49,4
Age (years)		
18-59	65	67,0
≥60	32	33,0
Diagnosis		
Leukemias, Chronic	5	6,2
Acute Leukemias	19	23,5
Lymphomas	19	23,5
Myeloma, Multiple	28	34,6
Other	10	12,3
The type of Transplant indicated		
Autologous	52	64,2
Allogeneic	29	35,8
Comorbidities		
No comorbidities	44	54,3
DM	6	7,4
HAS	25	30,9
DLP	4	4,9
DCV	6	7,4
DRC	3	3,7
Other	8	9,9

Legend: SAH: Systemic Arterial Hypertension; DM: Diabetes Mellitus; DLP: Dyslipidemia; CVD: Cardiovascular Disease; CKD: chronic kidney disease.

In the assessment of nutritional status, there was variability in the prevalence of diagnoses according to the parameter used.

According to BMI, more than half of the patients were overweight, distributed between overweight (34.6%, n=28) and obesity (28.4%, n=23). As for BC, the majority presented eutrophy

(61.3%, n=38), while overweight (9.7%, n=6) and obesity (6.5%, n=4) obtained lower percentages. The cardiovascular risk assessed by WC was detected in 80.2% (n=65) of the population (Table 3).

Table 3- Nutritional status of patients admitted for HSCT. Fortaleza, Brazil, 2019-2020.

Variables	**N**	**%**
INC		
Malnutrition	3	3,7
Eutrofia	26	32,1
Overweight	28	34,6
Obesity	23	28,4
CB		
Malnutrition	14	22,6
Eutrofia	38	61,3
Overweight	6	9,7
Obesity	4	6,5
CC		
No cardiovascular risk	16	19,8
With cardiovascular risk	65	80,2

Legend: BMI: body mass index; BC: arm circumference; WC: waist circumference.

From the analysis of laboratory tests, most of them presented high LDL values (57.8%, n=37) and low HDL values (58.46%, n-38), with no change for the other findings (Table 4).

Table 4 – Laboratory tests and blood pressure levels of patients admitted for HSCT. Fortaleza, Brazil, 2019-2020.

Variables	**N**	**%**
LDL		
< 130	27	42,2
≥ 130	37	57,8
HDL		
< 40*/50**	38	58,46
≥ 40*/50**	27	41,54
TG		
< 150	38	55,9
≥ 150	30	44,1
GJ		
< 100	59	80,8
≥ 100	14	19,2
PCR		
≤ 2	59	72,8
> 2	19	23,5
≥ 10	3	3,7
STEP		
< 130	52	64,2
≥ 130	29	35,8
PAD		
< 85	58	71,6
≥ 85	23	28,4

Legend: LDL: *Low-Density Lipoprotein*; HDL: *High-Density Lipoprotein*; TG: Triglycerides; GJ: Fasting Glucose; CRP: C-reactive protein; SBP: systolic blood pressure; DBP: diastolic blood pressure; *: male; **: female.

4 DISCUSSIONS

It was possible to observe that among the patients admitted for HSCT, there was a high prevalence of overweight and cardiovascular risk. This result is similar to what can be observed in the Brazilian population, according to the last National Health Survey (PNS-2019), which showed that 60.3% of the adult population was overweight and 25.9% obese22.

Overweight and obesity have an increased risk of death from all causes and morbidity from multiple causes.

The risk of developing chronic diseases such as DM, HAS, DLP, CVDs, and most types of cancer is proportional to the increase in BMI[23].

Multiple Myeloma, the most prevalent diagnosis in the study, demonstrates this association and was added to the list recently along with seven other types, by a working group convened by the International Agency for Research on Cancer to reassess the effects of weight management on the etiology of cancer diagnoses. Regarding the conclusions about the NHL of B cells, the data were still limited 24.

Obesity is an independent risk factor for adverse outcomes and increased mortality in HSCT. Hyperglycemia and insulin resistance which are more prevalent with increasing BMI influence the occurrence of acute graft-versus-host disease (GVHD) grades II and IV.

The incidence of infections (bacterial, fungal, or viral) was also higher in these patients compared to individuals with BMI < 30 kg/m², leading to an increase in mortality unrelated to relapse of the disease. Excess weight shows a statistically significant impact for lower results only in allogeneic transplantation and not in autologous transplantation[25].

Jyan Yu et al. conducted a study with patients diagnosed with leukemia who underwent allogeneic HSCT, and it was possible to observe a reduction in overall survival and disease-free survival in overweight and obese patients compared to eutrophic and underweight patients [26].

SAH was the comorbidity most reported by the research participants and reached a prevalence equal to 30.9%, slightly higher than in the general population, which presented an equal prevalence of 24.5% among men and 27.3% among women in 2019, according to VIGITEL data27.

It is important to emphasize that data on pre-existing comorbidities were collected through self-report, but given the longitudinal clinical follow-up received by patients during treatment, with clinical evaluations and periodic examinations, the chances of not knowing about a medical condition like this when installed become minimal.

According to estimates, 35% of patients will develop hypertension during antineoplastic treatment. Many classes of antineoplastic drugs produce vascular damage by different mechanisms,

which is why hypertension is the most common cardiovascular toxicity among cancer patients and survivors28,29,30.

DM, SAH, and DLP have known risk factors for CVDs, and measures of central adiposity, especially WC, are considered superior to BMI to discriminate against them[31,32].

In a study that followed patients after HSCT, a cumulative incidence of CVD equal to 8% in 10 years was found among transplant recipients and increased to 11% in the presence of multiple risk factors14. In our study, the prevalence of multiple comorbidities in individuals was not evaluated.

Some of the limitations of this study were the sample size, which hinders more accurate inferences. Therefore, it is essential to conduct more studies involving the theme, with a larger number of participants, that can assess the incidence of these risk factors and their possible complications for HSCT.

5 CONCLUSIONS

It can be concluded that the patients admitted for HSCT had a high prevalence of overweight and cardiovascular risk. Since CVDs are one of the main causes of morbidity and mortality after HSCT, the importance of nutritional follow-up during the different phases of treatment is evidenced, aiming at reducing modifiable risk factors related to lifestyle.

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