Journey of the Patient with Multiple Myeloma in Brazil: An Descriptive Study

Jornada do Paciente com Mieloma Múltiplo no Brasil: Um Estudo Descritivo

Recorrido del Paciente con Mieloma Múltiple en Brasil: Un Estudio Descriptivo

RESUMO

OBJETIVO: Este estudo analisou dados sociodemográficos e o tratamento de pacientes portadores de mieloma múltiplo no Brasil, identificando impactos nos sistemas de saúde. **MÉTODOS:** Estudo descritivo por meio de questionário autopreenchido, enviado entre outubro de 2021 e janeiro de 2023 a pacientes cadastrados na Associação Brasileira de Linfoma e Leucemia (Abrale). **RESULTADOS:** Participaram 164 pacientes, dos quais 133 (81%) tinham sintomas antes do diagnóstico. A maioria (117; 71%) passou por duas ou mais consultas antes do hematologista. O tempo médio para diagnóstico foi maior no sistema público (178 dias) que no privado (128 dias), e 38% relataram dificuldades de acesso. O diagnóstico e tratamento impactaram a rotina de 138 (84%) pacientes. **CONCLUSÃO:** Os resultados reforçam a importância de mapear obstáculos para discutir melhorias no tratamento e garantir atendimento adequado a todos.

DESCRITORES: Mieloma múltiplo; Neoplasia; Integralidade em saúde; Acesso à saúde.

ABSTRACT

OBJECTIVE: This study analyzed sociodemographic data and the treatment of patients with multiple myeloma in Brazil, identifying impacts on healthcare systems. **METHODS:** A descriptive study using a self-administered questionnaire, sent between October 2021 and January 2023 to patients registered with the Brazilian Association of Lymphoma and Leukemia (Abrale). **RESULTS:** A total of 164 patients participated, of whom 133 (81%) had symptoms before diagnosis. Most (117; 71%) attended two or more consultations before seeing a hematologist. The average time to diagnosis was longer in the public system (178 days) than in the private system (128 days), and 38% reported difficulties accessing diagnosis. Diagnosis and treatment affected the daily routine of 138 (84%) patients. **CONCLUSION:** The results reinforce the importance of mapping obstacles to effectively discuss treatment improvements and ensure adequate care for all patients.

DESCRIPTORS: Multiple myeloma; Neoplasm; Comprehensive healthcare; Healthcare access.

RESUMEN

OBJETIVO: Este estudio analizó datos sociodemográficos y el tratamiento de pacientes con mieloma múltiple en Brasil, identificando impactos en los sistemas de salud. **MÉTODOS:** Estudio descriptivo mediante un cuestionario autocompletado, enviado entre octubre de 2021 y enero de 2023 a pacientes registrados en la Asociación Brasileña de Linfoma y Leucemia (Abrale). **RESULTADOS:** Participaron 164 pacientes, de los cuales 133 (81%) presentaban síntomas antes del diagnóstico. La mayoría (117; 71%) tuvo dos o más consultas antes de acudir a un hematólogo. El tiempo medio hasta el diagnóstico fue mayor en el sistema público (178 días) que en el privado (128 días), y el 38% reportó dificultades de acceso. El diagnóstico y tratamiento impactaron la rutina diaria de 138 (84%) pacientes. **CONCLUSIÓN:** Los resultados refuerzan la importancia de mapear los obstáculos para debatir mejoras en el tratamiento y garantizar una atención adecuada para todos los pacientes.

DESCRIPTORES: Mieloma múltiple; Neoplasia; Integralidad en salud; Acceso a la salud.

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INTRODUCTION

Multiple myeloma is a cancer of plasma cells that originates in the lymphoid B cell lineage, with the production of altered monoclonal protein present in the bone marrow. [1,2] This cancer represents 1% of all malignant neoplasms prevalent globally and 10 to 15% of hematologic cancers. [3,4] According to the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO), in 2020, there were around 176,000 new cases of multiple myeloma, and more than 117,000 deaths in both sexes worldwide. [5] The overall incidence was 1.8 new cases per 100,000 inhabitants, with a mortality rate of 1.1 deaths per 100,000 inhabitants. [5]

Myeloma is most common among individuals aged 65-74, but it has been diagnosed in younger people. 6 The main risk factors for multiple myeloma include age, sex, race, and family history of the disease. [4,5]

The pathophysiology of multiple myeloma is described as the proliferation of neoplastic plasma cells, which leads to a range of changes described by the acronym CRAB: **C** – elevated calcium (> 10 mg/dL), **R** – renal dysfunction (creatinine > 2 mg/dL or creatinine clearance < 40 ml/min), **A** – anemia (hemoglobin < 10 g/dL or decrease > 2 g/dL from the patient's normal) and **B** – bone disease. [4,5] Based on these changes, patients with multiple myeloma may present localized or systemic signs and symptoms, depending on the site of proliferation of the neoplasm, which may compromise their quality of life and their functional capacity in daily life. [5] Evaluation of the patient with suspected multiple myeloma includes a comprehensive clinical history with investigation of initial symptoms. 5 Common symptoms for this condition include bone pain, anemia, infections (due to leukocyte dysfunction), and changes in kidney function. [5] Additionally, neurological symptoms may also be present. [5]

The diagnosis consists of, in addition to the CRAB criteria (hypercalcemia, renal injury, anemia and osteolytic lesion), laboratory tests such as serum and/or urinary protein electrophoresis, immunofixation or serum and urinary immunoelectrophoresis, quantificatioan of free light chains in serum, myelogram, bone marrow biopsy, in addition to immunophenotyping, karyotype and cytogenetics by FISH (fluorescent in situ hybridization). [6] For prognostic evaluation, the International Staging System (ISS) is used, with assessments of serum albumin, β2-microglobulin, lactic dehydrogenase (LDH) dosage, C-reactive protein and the FISH test. [6]

For most patients, multiple myeloma is a progressive disease with no cure, but newer therapeutic approaches have significantly improved quality of life and survival, which can vary by around 10 years. [4] Drug treatment, currently composed of combinations of immunomodulators, proteasome inhibitors and immunotherapy, associated with autologous stem cell transplantation, can, in some factors, predict disease progression-free survival. [4] More advanced cases may benefit from innovative therapies such as car T cells and bispecific antibodies. [7]

When the first symptoms of a disease appear until diagnosis and treatment, the patient's journey begins. 8

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This timeline demonstrates the gradual use of health services, based on the patient's point of view and their needs, barriers, satisfactions, feelings and expectations. [8] In Brazil, there are many challenges for patients with multiple myeloma, from difficulty in accessing diagnosis and treatment to differences in treatment initiation times between services. It is important to analyze the adversities that patients with multiple myeloma suffer in the country so that progress can be made in relation to public policies and to improve the quality of life of these patients.

This study aims to describe the sociodemographic information and treatment of patients with multiple myeloma in Brazil, identifying the impacts suffered by these patients in public and/or private health services.

METHOD

A descriptive study was conducted with patients diagnosed with multiple myeloma and registered in the database of the Brazilian Association of Lymphoma and Leukemia (ABRALE - *Associação Brasileira de Linfoma e Leucemia*), using an online self-completed questionnaire. This study was approved by the Research Ethics Committee (CEP) of the Hospital Israelita Albert Einstein under opinion number 5,089,914 (CAAE: 51495321.3.0000.0071). All ethical requirements related to the study were followed, as well as confidentiality throughout the process and post-process.

The sample was constituted by convenience, as the participants voluntarily agreed to participate in the study. Patients registered with ABRALE were clearly approached and informed about the study, indicating their participation through a consent form (FICF) sent by e-mail.

The first question in the questionnaire asked whether the person responding was the patient, the caregiver or a family member. To ensure that the data were from the patient, records in the ABRALE database were checked, such as date of birth and gender. Although caregivers and family members are not the patients, they often closely follow the patient's journey and the difficulties they face.

Interviewers from the ABRALE Patient Support Department, all healthcare professionals, conducted interviews with patients who were unable to access the survey link or had difficulty opening and completing the questionnaire. In these cases, the interviewer completed the questionnaire, with the conversations previously authorized by the patient.

The study included patients with a confirmed diagnosis of multiple myeloma of both sexes, over 18 years of age, from all regions of Brazil and who had all their registration data updated and complete in the ABRALE database. The form was applied between October 2021 and January 2023.

The study variables were:

- Sociodemographic characteristics of the patient: sex; race/color; date of birth and state of residence;
- Characteristics of diagnosis and treatment: date of diagnosis; place of treatment; initial symptoms of the disease; time between symptoms and seeking medical attention; time between symptoms and confirmation of diagnosis; doctors consulted; diagnostic tests performed; treatments prescribed; satisfaction with treatment; difficulties in accessing and understanding the disease.
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The processing and descriptive analysis focused on methods to describe and summarize the data in a clear and understandable manner, using measures such as median, standard deviations and tables. The descriptive analysis was performed using Microsoft Excel 2013 and statistical software R version 4.3.0.

Some sociodemographic data were grouped, such as age group and regions of Brazil. A comparative analysis was performed between the health systems in the variables diagnosis (time between symptoms and confirmation) and treatment (start and doctors consulted). For diagnosis, the groups were divided between the public and supplementary systems. For treatment, in addition to the two systems, the "both" group was included for patients who use both the public and private systems. The sampling varied according to the self-selection of the participants.

There was no obligation to answer the questions. Since they are volunteers, the participants have no obligations. Cases in which the answers were left blank were marked with the term "ignored".

RESULTS

A total of 164 patients with multiple myeloma participated in the study, the majority of whom were women (n=97; 59%) and self-declared white skin color (n=106; 65%). The most frequent age group was between 50 and 59 years (n=56; 34%) (median=53.2; SD=11.3) (Table 1). The participants were from all regions of Brazil, with the majority from the Southeast region (n=91; 55%), followed by the Central-West (n=28; 17%), South (n=23; 14%), Northeast (n=20; 12%) and North (n=2; 1%).

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Table 1. Respondent profile

	N (164)	%
Identification		
Patient	133	81%
Caretaker	11	7%
Family member	11	7%
Ignored	9	5%
Gender		
Female	97	59%
Male	58	35%
Ignored	9	6%
Color of skin (self-declaration)		
White	106	65%
Brown	40	24%
Black	14	9%
Yellow	4	2%
Age group		
≤29 years	4	2%
30-39 years	10	6%
40-49 years	47	29%
50-59 years	56	34%
60-69 years	40	25%
≥70 years	7	4%

Patients reported that they discovered the disease through a medical consultation due to the appearance of symptoms (n=93; 57%), as well as through routine exams/consultations or emergency care (n=71; 43%) (Table 2). Of the total number of participants, a large proportion presented symptoms before receiving the diagnosis (n=133; 81%), among which bone pain (n=103; 77%), fatigue (n=64; 48%) and weakness (n=49; 37%) were the most common, understanding that each patient can select more than one symptom.

Table 2. Multiple Myeloma Diagnosis and Treatment Journey

How did you find out you had multiple myeloma?	N (164)	%
I went to a doctor to find out what the symptoms were that I was experiencing	93	57%
Randomly, during routine exams and consultations or in emergency care	71	43%
Number of doctors before being referred to a specialist		
1 medical specialist	36	22%
2 medical specialties	48	29%
3 medical specialties	24	15%

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More than 3 medical specialties	45	27%
Ignored	11	7%
Difficulties in receiving the diagnosis		
Yes	62	38%
No	98	60%
Ignored	4	2%
Where do/did you undergo your multiple myeloma treatment?		
Unified Health System (SUS)	65	40%
Supplementary health	75	46%
Both	18	11%
Ignored	6	4%
Difficulty in carrying out the first indicated treatment	N	%
Yes	22	13%
No	136	83%
Ignored	6	4%

Of the symptomatic patients (n=133) (Table 3), the majority (n=78; 60%) sought medical help one month after the onset of symptoms, with orthopedists (n=49; 37%) and general practitioners (n=45; 34%) being the most frequent specialties for the first consultation. The remaining patients indicated that they went directly to the hematologist (5%), 24% referred to other specialties.

Table 3. Time between onset of symptoms and seeing a doctor

Time to seek medical help after symptoms begin	N (133)	%
Less than 24 hours	8	6%
3 days	6	5%
3 - 7 days	8	6%
7 - 15 days	7	5%
From 15 days to 1 month	23	18%
1 - 3 months	22	17%
3 - 6 days	17	13%
From 6 months to 1 year	13	10%
More than 1 year	26	20%

It was found that, among health services, those who accessed the public system (n=33) preferred to seek out general practitioners (n=23; 73%) and orthopedists (n=6; 18%). In the private system (n=86), there was a greater variety of doctors consulted. Fourteen participants ignored this question. Most patients (n=117; 71%) had two or more medical appointments before being referred to a hematologist or oncologist, and this was the greatest difficulty reported before receiving a diagnosis (n=47; 36%).

Patients who used the public system saw more specialists (89%) than those in the private system (56%) to reach a diagnosis. The difficulty was also represented in the average time until referral to a hematologist or oncologist, which was greater in the public system (161 days) than in the private system (74 days), and in the

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average time until receiving the diagnosis, which took longer in the public system (178 days) than in the private system (128 days). Even so, both systems presented a time between consultation and diagnosis of over 30 days. Approximately 38% reported difficulties in accessing the diagnosis (Table 2).

Eighteen participants (10%) used both services (public and private), but these responses were not included in the analysis of the comparison between services for the diagnosis of multiple myeloma. Of the total number of respondents, six did not specify which health service they underwent diagnosis and treatment at.

The tests that patients who selected had the most difficulty accessing (n=19) were: bone marrow biopsy (68%), magnetic resonance imaging (68%), myelogram (53%), followed by positron emission tomography-computed tomography (PET-CT) (47%), computed tomography (CT) (37%) and the FISH test (32%), understanding that each patient can select different tests and the responses are not mutually exclusive.

After receiving the diagnosis, 15% indicated that they started their treatment after 60 days. Of the total, 13% (n=22) said they had difficulty in carrying out the first treatment and this difficulty was more frequent in the public system (n=11; 17%) than in the private sector (n=4; 5%). For those who were treated in both systems, difficulties were reported by 39% (n=7).

Some patients were able to undergo their first treatment through legal action (n=9; 41%), 14% waited for the medication to be provided by the treatment center, 9% paid their own costs, and 5% filed an administrative lawsuit at the treatment center itself. The remaining patients responded that they were able to undergo their first treatment by moving to another city/state (5%) and waiting for authorization from their health insurance plan (5%), and in 21% of cases, the method was not specified.

The first treatment indicated after the diagnosis of multiple myeloma (n=158) included dexamethasone (14%), the VCD protocol (bortezomib, cyclophosphamide, and dexamethasone) (12%), radiotherapy (12%), and cyclophosphamide (11%). In the first treatment, 25% underwent "chemotherapy," but were unable to inform which chemotherapy drug they used (Table 4). 46% (n=76) responded that they had undergone changes in treatment, with refractoriness (58%), side effects (11.8%) and medical advice (10.5%) being the most frequently mentioned reasons.

Table 4. First treatment indicated to participants.

Treatments	N	%
Chemotherapy (I don't know the name)	41	25%
Dexamethasone	23	14%
Cyclophosphamide	18	11%
VCD (bortezomib, cyclophosphamide and dexamethasone)	19	12%
Radiotherapy	19	12%
CTD (cyclophosphamide, thalidomide and dexamethasone)	6	4%
Daratumumab-VTD	5	3%
Bortezomib	5	3%
Dexamethasone and thalidomide	4	2%
Don't know	3	2%
Didn't start it yet	3	2%
Other treatments	12	6%
Ignored	6	4%
Total	164	100%

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Of the patients who needed to change treatment, 47% (n=36) underwent two lines of treatment, 30% (n=23) underwent three lines, and 21% (n=16) underwent four or more lines of treatment. One person ignored this question.

Patients in the private system receive treatment closer to their homes, since the majority (41%) live less than 10 kilometers from the treatment center, while the majority of those in the SUS (38%) live more than 50 kilometers from the location.

Bone marrow transplantation was indicated for 85% (n=139) of patients, and only 76% (n=106) underwent the transplant, 97% of which were autologous and 3% allogeneic. This treatment was not indicated for 10% of patients (n=17) and eight people did not respond.

Those who did not undergo bone marrow transplantation (n=33; 24%) reported: undergoing other treatments or changes in exams (50%); waiting list for transplantation (up until the time of participation) (16%); location that does not perform bone marrow transplantation (9%); difficulty due to the Covid-19 pandemic (6%) and lack of beds (3%). The other five indicated other reasons.

At the time the study was conducted, 48% (n=75) of patients were undergoing treatment, 27% (n=42) were in remission and approximately 25% (n=38) were being monitored. Nine people ignored this question.

The diagnosis and treatment of MM impacted and changed the routine of 84% (n=138) of patients. The majority reported that they stopped working (65%), practicing physical activity (54%), socializing (36%) and having sex (32%), in addition to changes in family/social life (36%), understanding that each patient can select different impacts/changes and the answers are not mutually exclusive (Table 5).

Table 5. Quality of life and information about the pathology

Changes in your routine due to illness and/or treatment	N (164)	%
Yes	138	84%
No	25	15%
Ignored	1	1%
Before you were diagnosed, had you heard of multiple myeloma?		
Yes	9	5%
No	154	94%
Ignored	1	1%
Do you currently consider yourself well informed about your pathology?		
Yes	129	79%
No	34	21%
Ignored	1	1%

The treatment left chronic side effects in 54% (n=88) of the patients. Considering that each patient can select different effects, the most common were peripheral neuropathy (n=73; 83%), loss of libido (n=29; 33%) and forgetfulness (n=26; 30%).

Before receiving the diagnosis, 94% (n=154) of the participants indicated that they did not know about multiple myeloma. The source of information about the disease most consulted by patients was the internet (99%), in addition to health professionals (65%), groups (34%) and patient associations (27%). Some (n=34; 21%) reported that they still feel poorly informed about the pathology. Patients did not have the opportunity to talk to their caregiver about symptoms (n=8; 12%), types of treatment (n=7; 11%), details about bone marrow transplantation (n=6; 9%) and new treatments available (n=4; 6%).

DISCUSSION

Within the sample reached, some patients (15%) started treatment after 60 days, which indicated a prevalence of treatments at an inopportune time. 9 In addition, patients also reported having difficulty accessing their first treatment, such as chemotherapy and dexamethasone.

This study also showed that many patients experienced changes in their routine due to treatment and/or complications of the disease, with an impact on their professional life, physi-

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cal activity, social, family and marital relationships.

Obtaining information about MM treatment in Brazil is still a challenge and, according to this survey, most of the interviewees did not know about the disease. Approximately one in five people in the present study still do not feel well informed about the pathology.

Patients went through many doctors before reaching a specialist hematologist and/or oncologist, and this was more observed among users of the public system than in the private system. A study [10] analyzes that this process of referral to specialties and patient turnover in the service can discourage users and can be a cause of dropouts, which impacts the time of access to diagnosis. [11]

Although most patients had to see at least two specialists before receiving a diagnosis, they reported that they had no difficulties. Another point that the present study observed was that there was great difficulty in accessing tests for diagnostic purposes. The tests mentioned by the patients are considered essential for recognizing the disease. [6,12,13]

The difficulties affect most patients, but they are more pronounced in the public health system.

Patients who receive treatment in the public system live further away from the place of treatment than those who use supplementary health care. In certain regions, the SUS still has fragmented health networks, in which there is a lack of coordination between the levels of care at its various points. 10 Therefore, this factor can be a potential challenge for the user and for the strategic health network regarding the transportation of patients to treatment clinics.

Chemotherapy is being used less and less outside the BMT environment, such as melphalan and cyclophosphamide. The most common treatment for multiple myeloma and some drugs indicated in chemotherapy regimens are dexamethasone, the VCD protocol (bortezomib, cyclophosphamide and dexamethasone) or thalidomide. [5,6,12,13] Radiotherapy has also been recommended as the initial treatment for patients due to its low cost and effectiveness in identifying bone lesions. However, this type of therapy is more appropriate for palliative treatment or for pain relief in cases of severe injuries and is rarely used as a first treatment. [14,15]

> “Therapeutic approaches often raise ethical issues when deciding how to treat patients, considering both individual health needs and reimbursement policies and treatment availability in the health service.” [16]

The Ministry of Health, through the National Commission for the Incorporation of Technologies (CONITEC), is slow to approve efficient medicines, Bortezomib took 10 years and lenalidomide is still under discussion. 5 Even the National Health Agency (ANS) is slow to incorporate oral medications, which becomes an obstacle to access for patients who need this medication.

This study had limitations. The year of initiation of treatment was not considered so that it would be possible to understand the changes in therapy over time and which new medications were adopted.

Other limitations concern the sample used, since the sample size does not allow statistical inferences and is limited to describing the results presented here. In addition, data collection was performed using a questionnaire self-completed by patients and their family members/caregivers, with the possibility of memory bias and incomplete/ignored filling out of the questionnaire, impacting the results presented.

CONCLUSION

The study identified the challenges faced by this group of patients, from the diagnosis and treatment of the disease to its impact on their daily activities. The difficulties affect most patients, but are more pronounced among users of the public health system. Despite the support and legal advances, challenging situations still persist.

The results reinforce the importance of mapping the obstacles in order to effectively find ways to act that allow for discussions on improvements in treatment and ensure adequate care for all patients in their universality.

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