Oncohematological diseases in the Vale do Paraíba, State of São Paulo: demographic aspects, prevalences and incidences

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Background: *Based on the necessity of detailed information that supports effective strategies to improve cancer outcomes in the different regions of Brazil, the aims of this study were to report demographic aspects and to calculate the prevalence and incidence rates of oncohematological diseases in the region of Vale do Paraíba.*

Methods*: This is a multicentric prospective study carried out from October 2009 to March 2010. A total of 500 over 19-year-old patients were enrolled. Data such as type of healthcare insurance, gender, age, ethnic classification, place of residence, schooling, income, body mass index, new cases and the period between the first symptoms and a definite diagnosis were collected. The prevalence and incidence rates were calculated according to an estimated number of 1,319,800 inhabitants.*

Results: *The prevalence and incidence rates per 100,000 inhabitants in the period of six months were, respectively: acute myeloid leukemia 1.5 and 0.7; acute lymphoblastic leukemia 0.5 and 0.1; chronic lymphocytic leukemia 2.4 and 0.4; chronic myeloid leukemia 6.2 and 0.8; Hodgkin´s lymphoma 2.9 and 0.9; non-Hodgkin lymphoma 9.8 and 4.3; multiple myeloma 5.7 and 0.7; myelodysplastic syndromes 2.1 and 0.2 and myeloproliferative syndromes 5.1 and 0.3.*

Conclusion: *Giving the paucity of data in this field of investigation, our data may be useful for comparisons with those of other regions of Brazil and will assist in the implementation of treatment programs of oncohematological diseases in this region.*

Keywords: *Hematological neoplasms/epidemiology; Lymphoma, non-Hodgkin; Hodgkin´s disease; Health programs and plans; Brazil/epidemiology*

Introduction

Experts from various oncological fields agree that cancer control requires comprehensive, regionalized information which reflects the characteristics and needs of the local population.[1] Therefore, the analysis of demographic characteristics and estimates of prevalence as well as the incidence of malignancies may be important for proper planning of priorities and the definition of the feasibility of treatment in a given population.

Oncohematological diseases represent a subset of all cancers, some of which require expensive treatment regimens and others are potentially lethal. Unfortunately, there are insufficient data to provide specific information on demographics, and prevalence and incidence rates of oncohematological diseases in different regions of Brazil.

The Vale do Paraíba, State of São Paulo, due to its economic and social development (population, territorial expansion, industrialization) and the formation of a multicenter research group in oncohematology, has made great strides in collecting data on patients with oncohematological diseases. Taking into consideration these factors, this study aims to report the demographic characteristics of patients and the prevalence and incidence of oncohematological diseases in the Vale do Paraíba.

Methods

This study was carried out by the Grupo de Onco-hematologia do Vale do Paraíba (GOHV). The GOHV consists of medical oncohematological representatives of the following services: Hospital Frei Galvão of Guaratinguetá, Regional Hospital of the Vale do Paraíba, located in the city of Taubaté, Oncovida - Oncohematological Treatment Center of Taubaté, Pio XII Hospital in São José dos Campos and the Hematology Service of São José dos Campos.

The services of the Hospital Frei Galvão, Regional Hospital of Taubaté and Pio XII of São José dos Campos are referral centers from the Regional Health Division XVII, composed

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of 39 municipalities in the Vale do Paraíba. These different services treat patients with oncohematological illnesses under the Brazilian National Health Service (SUS). Together, the services that comprise the GOHV attend all adult SUS oncohematological patients and more than 90 percent of adult patients from other healthcare insurers in the region.

A questionnaire was developed by the GOHV regarding demographics and diagnoses. Physicians of the different services applied the questionnaire to all patients seen during the period from October 2009 to March 2010. At the end of the period, 500 patients had been enrolled in the study.

The criteria for inclusion in the study were: 1) the patient must be over 19 years of age (the departments involved do not treat pediatric patients); 2) the patient must agree to participate in the study (the patients agreed to answer the questionnaire) and the project was authorized by the Research Ethics Committees of the hospitals involved (in hospitals that did not have an Ethics Committee the project was approved by its Technical Council); and 3) diagnostic confirmation by histopathologic examination such as corroborative exams (immunohistochemistry, immunophenotyping, bone marrow aspirate, cytochemistry, bone marrow karyotype and investigation of specific mutations). The diagnostic criteria were based on the French-American-British (FAB) classification for acute leukemias and the World Health Organization criteria for multiple myeloma, lymphomas, leukemias, chronic myeloproliferative syndromes and myelodysplasias.[2-4] The classifications of histologic types of lymphoma and subtypes of myelodysplastic syndromes were also based on criteria of the World Health Organization.[5-6]

The prevalence was defined as the total number of cases of a certain disease during the study period divided by the estimated number of population. The incidence was defined as the number of new cases of a certain disease during the study period, divided by the estimated population. Based on data from the 2000 census of the Brazilian Institute of Geography and Statistics (IBGE),[7] we estimated the population of over 19-year-old individuals in the Vale do Paraíba to be 1,319,800.

Discrete variables (demographic factors) were compared using contingency (2 x 2) tables using the Fisher exact test and the approximation of Katz. P-values of less than 0.05 were considered significant.

Results

Demographic data are presented in Table 1. A total of 82.6% of patients were treated under the Brazilian National Health Service (SUS) and there were no significant differences between the percentages of men and women. The distribution of ages showed a higher frequency of 50 to 80-year-old patients, 79.8% of patients reported being white and 92.8% lived in urban areas. The majority of participants had between one and four years of schooling. Most patients (59.6%) reported incomes either between 1 to 3 minimum wages or 3 to 6 minimum wages. The body mass index (BMI) at diagnosis was within the normal range for 63.4% of patients (values between 18.5 to 25 kg/m^2). New cases accounted for 22.4% of patients and the period between first symptoms and definitive diagnosis of the disease was less than two months in 34.6% of these cases. A low education level (less than eight years of schooling) was correlated with low wages (p-value < 0.0001; RR = 2.390) and with a period greater than two months for a diagnostic definition (p-value < 0.0001; RR = 1.955).

Table 1 - Demographic characteristics of the patients

Parameters	Percent
Health system	
State	82.6
Private	17.4
Gender	
Male	51.8
Female	48.2
Age groups (years)	
≥ 19 - 30	9.2
> 30 - 40	8.8
> 40 - 50	12.6
> 50 - 60	20.8
> 60 - 70	19.4
> 70 - 80	20.0
> 80 - 90	9.2
Ethnic classification	
White	79.8
Mulatto	12.4
Black	6.2
Asian	1.6
Place of residence	
Urban	92.8
Rural	7.2
Years of schooling	
< 1	8.0
1 - 4	27.6
4 - 8	23.2
8 - 11	22.2
> 11	19.0
Personal or family income (number of minimum wages)	
< 1	19.6
1 - 3	36.0
3 - 6	23.6
6 - 9	10.4
> 9	10.4
BMI (Kg/m^2)	
Normal (18,5 - 25)	63.4
Overweight (> 25)	23.8
Underweight (< 18,5)	12.8
Case classification	
New case	22.4
Under treatment	77.6
Time between the first symptoms and a definitive diagnosis (months)	
< 2	34.6
2 - 4	23.2
4 - 6	10.0
> 6	32.2

Table 2. Number of cases, the subtypes and the prevalence and incidence rates (per 100,000 inhabitants in a period of 6 months) of different groups of oncohematological diseases

Disease	Nº cases (%)	Prevalence	Incidence
Acute myeloid leukemia	20	1.5	0.7
M1	6 (30)		
M2	4 (20)		
M3	8 (40)		
M5	2 (10)		
Acute lymphoblastic leukemia	7	0.5	0.1
B - CALLA	1 (14.2)		
Pre - B	3 (42.9)		
T	3 (42.9)		
Hairy cell leukemia	9	0.7	0.1
Prolymphocytic leukemia	1	0.1	0.1
Chronic lymphocytic leukemia	32	2.4	0.4
B	31 (97)		
T	1 (3)		
Chronic myeloid leukemia	82	6.2	0.8
Chronic phase	59 (72)		
Accelerated phase	14 (17)		
Blast phase	9 (11)		
Hodgkin lymphoma (HL)	38	2.9	0.9
Nodular lymphocyte-predominant HL	4 (10.5)		
Lymphocyte-rich classical HL	1 (2.7)		
Nodular sclerosing HL	27 (71)		
Mixed-cellularity HL	6 (15.8)		
Non-Hodgkin lymphoma (NHL)	132	9.8	4.3
MALT NHL	4 (3)		
Mantle cell NHL	4 (3)		
Diffuse Large B cell NHL	66 (50)		
Burkitt´s NHL	1 (0.8)		
Lymphoblastic NHL	2 (1.5)		
Follicular NHL	24 (18.2)		
Low grade NHL	12 (9.1)		
CNS primary NHL	2 (1.5)		
T-Cell NHL	4 (3)		
Cutaneous NHL	9 (6.9)		
HIV-associated NHL	4 (3)		
Multiple myeloma	76	5.7	0.7
IgG	41 (53.9)		
IgA	19 (25)		
Light chain	11 (14.5)		
Non secretor	4 (5.3)		
Plasma cell leukemia	1 (1.3)		
Waldenstrom macroglobulinemia	7	0.5	0.1
Myelodisplastic syndromes	28	2.1	0.2
Refractory anemia (RA)	20 (71.5)		
RA with ringed sideroblasts	1 (3.6)		
Refractory cytopenia with multilineage dysplasia	2 (7.1)		
RA with excess blasts - 2	3 (10.7)		
5q -	2 (7.1)		
Myeloproliferative syndromes	68	5.1	0.3
Polycytemia vera	28 (41.2)		
Essential thrombocythemia	28 (41.2)		
Idiophatic myelofibrosis	9 (13.2)		
Hyperesosinophilic syndrome	1 (1.5)		
Unclassifiable	2 (2.9)		

The M3 FAB subgroup was more common among the diagnoses of acute myeloid leukemia. There were no significant differences in the proportions of other groups of acute leukemia. The B phenotype was more frequent in chronic lymphoid leukemia and the chronic phase was predominant in chronic myeloid leukemia. The morphological subtype nodular sclerosis was observed more frequently in patients with Hodgkin's lymphoma followed by those cases classified as having mixed cellularity. Non-Hodgkin large B-cell was the most common in this group followed by follicular lymphomas. In regards to the diagnosis of multiple myeloma, the predominant subgroup was immunoglobulin G (IgG) followed by immunoglobulin A (IgA). The refractory anemia subgroup was most common in cases of myelodysplastic syndrome as was polycythemia vera and essential thrombocythemia in myeloproliferative disorders. Data such as the number of cases, the subtypes and the prevalence and incidence rates per 100,000 inhabitants of different groups of oncohematological diseases are shown in Table 2.

Discussion

There were no significant differences in respect to gender even though some oncohematological diseases have different incidences for men and women. The study addressed all over 19-year-old patients however we noted that most patients were in the range from 50 to 80 years old. A possible explanation for this observation, considering São José dos Campos the largest city in the Vale do Paraíba, is the evolutionary analysis of population pyramids; the population is aging because of lower birth rates.[8] This seems to be a pattern common to other cities in this region. Another possible argument is based on the design of the study. The review group considered all types of oncohematological disorders: lymphoma, leukemia, chronic leukemias, multiple myeloma as well as myelodysplastic syndromes and myeloproliferative disorders. Many of the diseases in our study have higher rates in elderly patients, a situation reflected in our statistics.

In our analysis, the ethnic background of patients was to some extent biased due to the subjectivity of the question. This variable was studied according to the definition of each patient without any influence of the medical professional who applied the questionnaire. Thus, some patients reported being white rather than mulatto; this phenomenon was not observed for black and Asian classifications.

The Vale do Paraíba has enjoyed an industrial boom in recent decades which explains the large number of patients living in urban areas. Invariably, patients who live in rural areas have a difficult time accessing emergency care services in the period after chemotherapy and the lack of proper care during these stages can increase mortality rates. Campbell et al.,[9] showed that the distance between the residence of the patient and the treatment center was associated with lower

chances of confirmation of diagnosis before death in cases of stomach, breast, colon and rectal cancers and also showed lower survival rates for prostate and lung tumors. Jones et al.[10] observed that long distances travelled to general hospitals (not oncological centers) were associated with more advanced stages at diagnosis for breast, colon and rectal cancer, and an increased risk of death for patients with prostate cancer. These data together with those observed in our study were the basis for new treatment strategies in GOHV services aiming at supporting patients living in rural areas. These measures include special transport services between home and hospital, nighttime home support for the patient and even extending the length of hospitalization for patients with severe neutropenia after chemotherapy.

Schooling, measured by the number of years of formal education for a given population, has been used as an assessment tool. In Brazil, the mean number of years of schooling is 5.7,[11] thus less than countries such as the USA (12 years), Canada (11.6 years) and Sweden (11.4 years).[12] In the State of São Paulo the average level of schooling for the heads of households varies with the number of inhabitants in each municipality. Towns with up to 5,000 inhabitants had a mean number of years schooling of 3.5 years, those with 20,000 to 50,000 inhabitants, had an average of 4.5 years and those with more than 500,000 residents had an average of 6.7 years.[11] In our study, we observed a higher rate of patients with only one to four years of schooling, yet the proportion of patients with this level of education was not significantly different from groups with four to eight years, eight to eleven years or even over eleven years of education. In Brazil the average income is 769.00 reals and in the State of São Paulo the average is 1076.00 reals.[13] We found a wide variation in the 39 municipalities that make up the Vale do Paraíba region. The population of the town of Arapei had a mean income of 287.37 reals, while the averages of São José dos Campos and Taubaté were 972.30 and 923.29 reals, respectively. The overall average of the municipalities in our study was 714.13 reals. Our results showed similar results as the vast majority of patients were stratified in groups that earned 1 to 3 minimum wages and 3 to 6 minimum wages. Our initial expectation was that the levels of education and income would be lower, yet we observed levels comparable to state and national averages even in a sample predominantly of Brazilian National Health Service (SUS) patients. Previous studies have shown that low socioeconomic status is associated with worse survival rates related to different types of neoplasms.[14-16] Our study showed a group of patients with lower education levels (8%) and based on studies, some support measures were implemented such as social support, improvement of the language used in treatment guidelines as well as periodic evaluations to determine the degree of understanding of these patients regarding their treatment.

Considering the high number of SUS patients in this study we expected to find more patients with a low BMI and again the results were the opposite. Interestingly the BMI was high in 24% of the sample. Tarella et al.[17] found a higher risk of death in obese patients with non-Hodgkin lymphoma. Jones et al.[18] demonstrated that obesity was associated with better survival rates in patients with intermediate B-cell lymphoma. Sinicrope et al.[19] observed in patients with colon cancer that obesity was associated with higher rates of overall survival in men and that a lower BMI decreased survival in women. Given the conflicting data, the guidelines provided to our patients still rely on the proposal to maintain a BMI within the normal range.

Our comparative analysis revealed no association between education, income and BMI. On the other hand, we demonstrated that education had a positive correlation with income. Furthermore, our design allowed us to study the time elapsed between the first symptoms and a definitive diagnosis. This variable was inversely correlated with education, i.e., patients with less schooling took longer to receive a definitive diagnosis. In this field of interpretation a few hypotheses can be speculated: the patients may evaluate the symptoms and seek treatment in the SUS, yet the basic primary healthcare system does not refer patients to specialized clinics quickly enough or has not established a pattern of referrals to high complexity services. Another plausible reason is that these patients do not have adequate perception of the symptoms or their severity and therefore delay in seeking specialized care. Moreover, as we mentioned previously, factors such as distance from the centers of specialized treatment[9,10] and the socioeconomic status of patients[14-16] can directly influence the delay. In fact, we have often observed the two situations separately or together, and unfortunately, both lead to a delay in receiving a proper diagnosis which consequently worsens the chances of success of chemotherapy.

Overall, the incidence of adult acute myeloid leukemia increases with age ranging from one case in every 100,000 inhabitants per year in the fourth decade of life to ten cases per 100,000 inhabitants in over 70-year olds.[20] The occurrence of acute lymphoblastic leukemia (ALL) is rarer in adults. Unfortunately, in Brazil there is no specific regional data that allow comparisons with our findings on the prevalence and incidence. In the current series we found a higher frequency of the M3 subtype and this finding is similar to that reported for Brazilian patients.[21-24] During the study period, there were only seven reported cases of ALL, thus preventing a more detailed analysis.

Chronic lymphocytic leukemia affects 3.7 individuals per 100,000 inhabitants in the United States and represents 0.8% of all cancers and 30% of the leukemias. It is a disease that rarely affects individuals younger than 30 years of age. Neoplastic lymphocytes usually present immunophenotype B and less than 2% of cases are of the T lineage.[25] Epidemiologic data on our population were not found in the literature, however Redaelli et al.[26] reported an incidence of around 10%.

The incidence of chronic myeloid leukemia (CML) in international registries is one to two cases in 100,000 inhabitants, representing 15-20% of cases of leukemia in adults. Usually the chronic stage of the disease is more common and has better response to current treatment.[27]

Data published by the Ministry of Health estimated the incidence of chronic and acute leukemia in Brazil in 2010 to be 4.8 cases per 100,000 inhabitants and in the State of São Paulo at 5.3 per 100,000 (men and women).[1] Taking into account both acute and chronic leukemia in our study we found 2.2 cases per 100,000 inhabitants over a period of six months. If we estimate 4.4 cases per 100,000 inhabitants over one year, the incidence of leukemia in the Vale do Paraíba is similar to that estimated for Brazil.

Hodgkin´s lymphoma represents a sixth of all lymphomas and the estimates in several regions of the world vary from 0.2 to 5.7 and from 0.1 to 4.9 per 100,000 men and women, respectively.[28] In Brazil, recent data from the Ministry of Health showed an estimated 2870 new cases during 2009 with 1600 of those diagnosed being men and 1270 being women.[29] The nodular sclerosis histologic type is the one most often found in literature.[30]

The estimated incidence for non-Hodgkin lymphoma (NHL) varies widely among different countries. Data from different regions of the world show values from 1.6 to 17.1 cases per 100,000 individuals annually for men and 0.7 to 11.7 cases per 100,000 individuals annually for women.[31] In Brazil the estimated incidence for 2008 reported by the Ministry of Health was 9100 new cases; 4900 were men and 4200 were women.[32] The histological type of diffuse large B-cell is most common among non-Hodgkin lymphomas followed by follicular lymphomas.[31]

Multiple myeloma is the second most common hematologic malignancy. In the United States, 14,500 new cases are diagnosed per year and there are approximately 45,000 individuals living with multiple myeloma. In Brazil there are no precise data on the incidence and prevalence of multiple myeloma. As previously described,[33] most patients have advanced disease including cases with irreversible renal failure.

Annually in the United States, more than 10,000 new cases of myelodysplastic syndromes are diagnosed with estimated incidence rates of four cases per 100,000 inhabitants per year according to the Surveillance, Epidemiology and End Results program (SEER).[34] In Brazil there are no data to clearly show the incidence and prevalence rates in different regions in order to make a comparison with our data.

In Brazil there are no data regarding the incidence and prevalence of myeloproliferative disorders. Analyzed individually, essential thrombocythemia gained prominence in recent years due to the findings concerning the molecular changes of the JAK2 enzyme in its pathogenesis. The incidence of essential thrombocythemia in the United States and Europe ranges from 0.6 to 2.5 per 100,000 inhabitants annually[35] but there are no national data to compare. In a recent article on the diagnostic criteria and clinical aspects of myeloproliferative neoplasms, based on international case series, Chauffaille[36] described an incidence of from 0.7 to 2.5 per 100,000 population per year for polycythemia vera, 0.5 to 1.5 for myelofibrosis and 1 to 2 for essential thrombocythemia.

Finally, this study demonstrated several demographic characteristics of a group of patients with oncohematological diseases in the Vale do Paraíba and calculated prevalence and incidence rates of these diseases. We therefore believe that similar studies should be encouraged in order to establish the profiles of different regions. Such information may be relevant to the strategic planning of health managers and enable the implementation of measures to improve the services that treat patients with oncohematological diseases.

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