

Epidemiological Profile of Patients with Hematological Neoplasms in an Oncological Hospital of Mato Grosso

Perfil Epidemiológico de Pacientes com Neoplasia Hematológica em um Hospital Oncológico de Mato Grosso

Claudia da Fonseca Granjeiro^a; Alex Semenoff-Segundo^b; Alessandra Nogueira Porto^a; Natalino Francisco da Silva^c; Álvaro Henrique Borges^{a*}; Tereza Aparecida Delle Vedove Semenoff^b

^aUniversidade de Cuiabá, Programa de Pós-Graduação Stricto Sensu em Ciências Odontológicas Integradas. MT, Brasil.

^bFaculdade de Ciências Sociais Aplicadas do Vale do São Lourenço MT, Brasil.

^cUniversidade de Cuiabá. MT, Programa de Pós-Graduação Stricto Sensu em Biociência Animal. MT, Brasil.

*E-mail: alvarohborges@gmail.com.

Recebido em: 09/10/2019

Aprovado em: 06/12/2018

Abstract

The objective of this study was to analyze the epidemiological aspects of adult patients diagnosed with hematologic neoplasia, from 2004 to 2014, at a Cancer Hospital in Mato Grosso. Data collection was performed through the search and analysis of 590 patient records. Among the patients, 335 (56.8%) were male ($p < 0.05$). The majority was older than 50 years ($p < 0.05$), with a mean age of 53.97 ± 14.95 years. Regarding origin, 257 patients came from the metropolitan region of Cuiabá (43.6%) and 333 (56.4%) from other sites ($p < 0.05$). The majority was non-white patients ($p < 0.05$) and unmarried 342 (58%) ($p < 0.05$). About treatment, 537 (91%) patients used chemotherapy ($p < 0.05$), 57 (9.7%) used radiotherapy ($p < 0.05$). Fifty-four (9.2%) patients used both therapies in an associated way ($p < 0.05$) and 50 patients (8.4%) did not use either radiotherapy or chemotherapy at any time of their treatment. Regarding the types of neoplasia, the diagnoses most found in the analysis were: chronic myelogenous leukemia 131 (22.2%); non Hodgkin lymphoma 119 (20.2%); multiple myeloma 93 (15.8%); essential thrombocythemia 49 (8.3%); Hodgkin's lymphoma 39 (6.6%); chronic lymphocytic leukemia 38 (6.4%); policitemia vera 34 (5.8%); acute myeloid leukemia 27 (4.6%); myelodysplastic syndrome 21 (3.6); acute lymphocytic leukemia 13 (2.2%) and myeloproliferative syndrome 10 (1.7%) ($p < 0.05$). From the results of this study, it can be concluded that, in general, the most affected patients by hematological malignancies were older than 50 years, were men from the interior of the State, non-white and unmarried.

Keywords: Hematologic Diseases. Epidemiology. Hodgkin Lymphoma. Leukemia.

Resumo

O objetivo do estudo foi analisar os aspectos epidemiológicos de pacientes adultos com diagnóstico de neoplasia hematológica, no período de 2004 a 2014, em um Hospital Oncológico em Mato Grosso. A coleta de dados foi realizada através de busca e análise de 590 prontuários. Entre os pacientes, 335 (56,8%) eram do sexo masculino ($p < 0,05$). A maioria possuía mais de 50 anos ($p < 0,05$), com idade média de $53,97 \pm 14,95$ anos. Quanto ao local de procedência, 257 pacientes eram provenientes da região metropolitana de Cuiabá (43,6%) e 333 (56,4%) de outros locais ($p < 0,05$). A maioria eram pacientes não brancos ($p < 0,05$) e solteiros 342 (58%) ($p < 0,05$). Em relação ao tratamento, 537 (91%) pacientes utilizavam quimioterapia ($p < 0,05$), 57 (9,7%) fizeram uso da radioterapia ($p < 0,05$). Cinquenta e quatro (9,2%) pacientes fizeram uso de ambas as terapias de forma associada ($p < 0,05$) e 50 pacientes (8,4%) não fizeram uso de radioterapia e nem de quimioterapia. Referente aos tipos de neoplasia, os diagnósticos mais encontrados na análise foram de: leucemia mielóide crônica 131 (22,2%); linfoma não Hodgkin 119 (20,2%); mieloma múltiplo 93 (15,8%); trombocitemia essencial 49 (8,3%); linfoma de Hodgkin 39 (6,6%); leucemia linfocítica crônica 38 (6,4%); policitemia vera 34 (5,8%); leucemia mielóide aguda 27 (4,6%); síndrome mielodisplásica 21 (3,6); leucemia linfocítica aguda 13 (2,2%) e síndrome mieloproliferativa 10 (1,7%) ($p < 0,05$). A partir dos resultados deste estudo, pode-se concluir que, em geral, os pacientes mais acometidos pelas neoplasias hematológicas tinham mais de 50 anos, eram homens, provenientes do interior do Estado, não brancos e solteiros.

Palavras-chave: Doenças Hematológicas. Epidemiologia. Leucemia.

1 Introduction

In Brazil, it is estimated approximately 590,000 diagnoses of neoplasms per year, having been registered 189,454 deaths in just one year arising from these. So, these pathological processes are the second leading cause of death in the country, surpassing the total number of deaths by external causes, and leaving behind only of circulatory system diseases¹⁻³.

Data from the National Institute of Cancer (INCA, report that non-melanoma skin cancer is the most prevalent in Brazil with 174,000 cases affecting men and women. Then are:

prostate cancer with 61,200 cases, breast cancer with 57,960 cases and cancers of the colon and rectum with 34,000 cases. It is noteworthy that, if the hematological neoplasms were analyzed as a single group of pathologies, they would occupy the fourth place of the proportional distribution of neoplasms in the country with approximately 40,000 cases⁴.

The hematological neoplasms are a group of malignant diseases affecting the hematopoietic precursors, affecting mainly the blood, bone marrow, lymph nodes, spleen and liver^{5,6}. The most common types of hematological neoplasm are: leukemia, which is subdivided according to the speed

of evolution and of cell types involved: acute myeloid leukemia - AML, chronic myeloid leukemia - CML, acute lymphocytic leukemia - Lymphoblastic Leukemia or chronic lymphocytic leukemia - LLC; the lymphomas can be grouped into: Hodgkin's lymphomas - LH when there is presence of atypical cell of *Reed-Sternberg* and non-Hodgkin lymphoma - NHL when there is the absence of the same; and the multiple myeloma - MM that depending on the immunoglobulins increased in the body, are subdivided into different types^{7,8}.

Generally, the hematological neoplasms affect approximately 136,000 individuals per year in the United States of America^{2,8}. According to estimates by the National Institute of Cancer (INCA, approximately 23,000 individuals were affected by some type of lymphoma or leukemia in Brazil in 2016⁴. In addition, some estimates indicate that 7,600 diagnoses of multiple myelomas^{9,10} and 10,000 diagnoses of some type of myeloproliferative or myelodysplastic syndromes¹¹ in Brazil.

The incidence rates of lymphomas showed a steady increase during the years 1970 and 1980, stabilized in 1990, and started a slight decline until the end of the decade¹². Currently, the incidence rates of lymphoma, in general, have decreased slightly (0.3% per year) since 2001 in females and males since 2004. For the state of Mato Grosso, it is estimated that 100 non-Hodgkin lymphomas and 20 cases of Hodgkin's lymphomas were diagnosed in 2016^{2,4}.

Regarding the leukemia, epidemiological data indicate that in 2012, 352 000 people were affected by this disease, being responsible for 265 000 deaths worldwide. In 2016 10,070 diagnoses were performed throughout Brazil, being that 110 of these diagnoses occurred in the state of Mato Grosso^{2,4}.

However, the population affected by this group of illness is little known regarding its epidemiological characteristics. Undoubtedly, these data are fundamental to the public bodies responsible for the health of the population may have clarity of demand of patients, being capable of providing early diagnosis and therefore, a more effective treatment and a more favorable prognosis.

The objective of this study was to analyze the epidemiological aspects of adult patients diagnosed with hematologic neoplasia, from 2004 to 2014, at a Cancer Hospital in Mato Grosso.

2 Material and Methods

After the research project approval by the ethics committee (CAAE: 53895116900005165 and Legal Opinion: 1526355) a technical visit was performed to the Cancer Hospital of Mato Grosso (HCAN), with the aim to verify what data were routinely recorded in the medical records of adult patients and establish the work flowchart. After the analysis of 10 medical records obtained at random in the archive of the institution, it was possible to structure an annotation sheet of the data catalogued.

Then, a single examiner performed the survey of all the patients' medical records treated between 2004 to 2014 and collected the information recorded.

As inclusion criterion, it was stipulated that the records analyzed should be patients aged more than 17 years old and who made treatment and/or monitoring of hematological neoplasias in the Cancer Hospital of Mato Grosso - HCAN, in the period from 2004 to 2014.

In addition, the records should be filled out with the following data: gender, age, place of residence, ethnicity, marital status, type of hematological neoplasm diagnosed, type and duration of treatments used, the evolution of the case.

For the annotation of the diagnosis of neoplasia, the pathologist's record, attached to the patient's medical records, was consulted. For the determination of deaths, deaths certificates of HCAN and also of the information of the data basis of vital records from the Ministry of Health, through the National Mortality Information System – SIM of the Informatics Department of the Single Health System³.

The exclusion criteria were: medical records completed incorrectly; Medical records not found.

Data were recorded in the printed sheets and then tabulated in Microsoft Office Excel 2010 and exported to the IBM SPSS - Statistical Package for the Social Sciences, version 20.0.

The chi-square statistical test ($p < 0.05$) was used for comparison of frequencies of variables of the study. In addition, the dependent variables - hematological neoplasias, were subjected to the test of estimated relative risk ($p < 0.05$) for the following independent variables: gender (male and female), age (less than 50 years; over 50 years), place of origin (metropolitan region of Cuiabá; other cities), ethnicity (white and non-white), marital status (single; kingdom someone) and evolution of the event (death confirmed; no data on deaths).

3 Results and Discussion

Of the 783 medical records of patients treated at Cancer Hospital of Mato Grosso, between 2004 to 2014, 193 were excluded because they did not meet the inclusion criteria, of which 590 were statistically analyzed.

Among the 335 patients (56.8%) were male and 255 (43.3%) were female ($p < 0.05$). The mean age of the patients was 53.97 ± 16.55 years, being the minimum age of 17 years and maximum of 91 years.

When the ages were stratified into categories, it is perceived that 57 patients (9.7%) were with 29 years or less, 166 (28.1%) were aged between 30-49 years, 254 (43.1%) between 50-69 years and 113 (19.2%) were with 70 years or more, thus there was is statistical difference among all the groups ($p < 0.05$).

Regarding to the place of origin of the patients, it is perceived that 257 patients came from the metropolitan region of Cuiabá (43.6%) and 333 (56.4%) of other sites ($p < 0.05$).

In the classification regarding ethnicity, the majority was

brown with 415 (70.3%) patients, the white ones totaled 139 (23.6%), Black ones totaled 20 (3.4%) patients and the yellow ones accounted for 16 (2.7%) patients, there is statistical difference among all groups (p<0.05).

Concerning marital status, 342 (58%) patients were single, 200 (33.9%) were married, 40 (6.8%) reported being in Common Law Marriage, 6 (1%) were widowed, 2 (0.3%) were divorced, no statistical difference among all groups (p<0.05).

In relation to the treatment, 537 (91%) patients used chemotherapy and 53 (9%) did not use this therapy (p<0.05), 57 patients (9.7%) made use of radiotherapy and 533 (90.3%)

did not (p<0.05). By observing the quantity of patients who were subjected to two combined therapies, 54 (9.2%) patients went through this process and 536 (90.8%) did not used them in association (p<0.05). On the other hand, 50 patients (8.4%) did not use neither radiotherapy nor chemotherapy in any moment of their treatment.

As analysis of medical records proposed, 82 (13.9%) of the patients evolved to death and 508 (86.1%) continued in treatment, under follow-up, in the process of healing or evolved to death, but there was no record (p<0.05). The results are shown in Table 1.

Table 1 - Frequency (N) and percentage (%) of the data found in the categories of the study

Categories	Subcategories			N	%	Value p
	AVG	±	(min/max)			
Age	53.97	16.55	7 91			
	≤ 29 years			57a	9.7	0.001
	30-49 years			166b	28.1	
	50-69 years			254c	43.1	
	≥70 years old			113d	19.2	
Sex	Male			335a	56.8	0.001
	Female			255b	43.2	
Location	Metropolitan region of Cuiaba			257a	43.6	0.002
	Other cities			333b	56.4	
Ethnicity	White			139a	23.6	0.001
	Black			20b	3.4	
	Brown			415c	70.3	
	Yellow			16b	2.7	
Marital Status	Single			342a	58	0.001
	Married			200b	33.9	
	Common Law Marriage			40c	6.8	
	Divorced			2d	0.3	
	Widowed			6d	1.0	
Use of Chemotherapy	Yes			537a	91	0.001
	No			53b	9.0	
Use of Radiotherapy	Yes			57a	9.7	0.001
	No			533b	90.3	
Radiotherapy and chemotherapy	Yes			54a	9.2	0.001
	No			536b	90.8	
Deaths	Yes			82a	13.9	0.001
	No			508b	86.1	

Different letters show no statistical difference among the subcategories of the study. Chi-square statistical test (p<0.05).

Source: Research data.

Regarding the types of neoplasia, the most commonly found diagnosis in the analysis were: Chronic myeloid leukemia (CML) 131 (22.2%); Non-Hodking lymphoma (NHL) 119 (20.2%); multiple myeloma (MM) 93 (15.8%); Essential thrombocytosis (TE) 49 (8.3%); lymphoma of Hodking (LH) 39 (6.6%); chronic lymphocytic leukemia (LLC) 38 (6.4%); polycythemia vera(PV) 34 (5.8%); acute myeloid leukemia (AML) 27 (4.6%); Myelodysplastic syndrome (SMD) 21 (3.6); acute lymphocytic leukemia (LLA)

13 (2.2%), and myeloproliferative syndrome (SMP) 10 (1.7%) (p<0.05) (Table 2). Sixteen neoplasias(2.7%) were grouped as other hematological neoplasias, namely: undifferentiated acute leukemia (LAI) 4 (0.7%), myelofibrosis (MF) 3 (0.5%), unclassified lymphoproliferative disease (DLPNC) 2 (0.3%),Hairy cell leukemia (TL) 2 (0.3%), Waldestron's Macroglobulinemia 1 (0.2%), lymphoblastic lymphoma 11 (0.2%), B-cells lymphoma 1 (0.2%), plasma cells leukemia 1 (0.2%), follicular lymphoma 1 (0.2%) (Table 2).

Table 2 - Frequency (N) and percentage (%) of the types of hematological neoplasms present in the study

Hematological neoplasms	N	%
Chronic myeloid leukemia	131a	22.2
Non- Hodgking lymphoma	119ab	20.2
Multiple Myeloma	93b	15.8
Essential thrombocythemia	49c	8.3
Hodking lymphoma	39cd	6.6
Chronic Lymphocytic Leukemia	38cd	6.4
Polycythemia vera	34cde	5.8
Acute Myeloid Leukemia	27de	4.6
Myelodysplastic syndrome	21ef	3.6
Acute Lymphocytic Leukemia	13f	2.2
Myeloproliferative Syndrome	10f	1.6
Other hematological neoplasias	16	2.7
Total	590	100

Small Case Letters in different column represent a statistically significant difference (Chi-square $p < 0.05$).

Source: Research data.

Regarding the analysis of estimated risk, it should be noted a correlation for the following categories: multiple myeloma and males (1.641 1,030-2,615); myeloproliferative syndrome and age less than 50 years 3.932 (1.006-15.265). In addition, the myeloproliferative syndrome 4.489 (1,238-16,278); acute myeloid leukemia (5.922 2,659-13,191) and acute lymphocytic leukemia (8,935-189 41.169.697) were associated with death (Table 3).

Table 3 - Contingency demonstrating relative risk estimated between the neoplasias described and the variables of the study. Number of valid cases (590)

Neoplasia	Variable	Categories	N	Value	Confidence interval of 95%	
					Inferior	Superior
Multiple Myeloma	Sex	Male	62	1.641	1.030	2.615
		Female	31			
Myeloproliferative Syndrome	Age	< 50 years old	7	3.932	1.006	15.365
		≥ 50 years	3			
Myeloproliferative Syndrome	Evolution	Death Yes	4	4.489	1.238	16.278
		Death No	6			
Acute Myeloid Leukemia	Evolution	Death Yes	15	5.922	2.659	13.191
		Death No	12			
Acute Lymphocytic Leukemia	Evolution	Death Yes	11	41.169	8.935	189.697
		Death No	2			

Source: Research data.

The hematological neoplasias are serious diseases and that certainly negatively impact on patients' lives and social groups and family in which the same is inserted¹³. The evolution of cases varies according to numerous factors such as the stage of the disease at the time of diagnosis, severity or aggressiveness of neoplasia, organic and emotional conditions of patients and time to access to adequate treatment^{1,5,14}.

The results of this study show that in general, the most

affected patients were more than 50 years old, were men, in their majority, coming from the interior of the State, non-white and single. There were 13.9% of deaths in the occurrence of the disease. The most prevalent hematological neoplasias in the study were chronic myeloid leukemia, lymphoma, non Hodgking and multiple myeloma.

Regarding the risk analysis, the results showed that men were more likely to develop multiple myeloma than women. Individuals aged less than 50 years showed a higher estimated risk to develop myeloproliferative syndrome and patients with a diagnosis of myeloproliferative syndrome, acute myeloid leukemia or Acute Lymphocytic Leukemia showed higher estimated risks of death that the other patients in the study.

The findings concerning the patients' gender are consistent with data from a study conducted in France, whose results show that 19,400 men and 15,600 women have developed some kind of hematological neoplasias between the years of 1980 and 2012¹⁵. A fact corroborated by other studies^{4,16}.

Patients aged more than 50 years were the most affected and this information corroborates other studies that point to a growth in the incidence of neoplastic lesions with the longevity^{6,7,8}. Concerning ethnicity observed in this study most patients was of non-white. This fact is observed in some studies^{17,18}.

The use of chemotherapy, radiotherapy and associated therapies vary according to the diagnosis, symptoms and location of the present pathologies^{19,20}.

Concerning the prevalence of neoplasms analyzed in the present study, there is a concordance with other authors^{21,22} who also point to high rates of incidence of chronic myeloid leukemia and non- Hodgkin lymphomas.

The inferential statistical analysis is of great importance in clinical practice²³. Therefore, it was sought to infer whether there was any correlation among the variables analyzed. Despite the relatively small sample and the limitations of the study, it was possible to observe the association of multiple myeloma with males, a fact widely observed in the literature^{8,24,25}.

The myeloproliferative syndrome presented in this study, greater relative risk for patients with less than 50 years, a fact corroborated by Tefferi et al.²⁶. In addition, as well as the acute myeloid leukemia and acute lymphocytic leukemia, this syndrome, also presented a higher relative risk of death for patients analyzed. Although the literature supports this information²⁷⁻²⁹, it must be emphasized that the notification of deaths of patients was the most fragile of the study. This fact occurred in part by the difficulty of contact with the patient's hospital when he or she returned to his or her home town and there was a notification of the same when there was death and in part by the disclosure of information in the database of the national mortality information system of the Ministry of Health³ which still presented inaccurate information at the time of this study.

It is believed that despite the limitations the work is

relevant and can contribute to a better understanding of the hematological neoplasias and assist the professionals involved in this area of knowledge.

4 Conclusion

From the results of this study, it can be concluded that, in general, the most affected patients by hematological malignancies were older than 50 years, were men from the interior of the State, non-white and unmarried. There were 13.9% of deaths in the occurrence of the disease.

There was a higher relative risk of male patients to develop multiple myeloma, individuals with less than 50 years develop myeloproliferative syndrome, and patients with a diagnosis of acute myeloid leukemia, acute lymphocytic leukemia or myeloproliferative syndrome evolve to death.

References

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 2015;136(5):E359-86. doi: 10.1002/ijc.29210.
2. WHO (World Health Organization). Global cancer rates could increase by 50% to 15 million by 2020. [acesso em 12 dez 2017]. Disponível em <http://www.who.int/mediacentre/releases/2003/pr27/en>.
3. Brasil. Ministério da Saúde. Sistema de informações sobre mortalidade. [acesso em 13 dez 2017]. Disponível em <http://tabnet.datasus.gov.br/cgi/sim/obtmmap.htm>.
4. Brasil. Ministério da Saúde. Estimativa 2016: incidência de câncer no Brasil / Instituto Nacional de Câncer José Alencar Gomes da Silva. Rio de Janeiro: INCA; 2015.
5. Smith A, Howell D, Patmore R, Jack A, Roman E. Incidence of haematological malignancy by sub-type: a report from the haematological malignancy research network. *Brit J Cancer* 2011;105:1684-92.
6. Da Silva FC, Araújo LS, Frizzo MN. Neoplasias hematológicas no idoso: uma revisão. *Rev Saúde Int* 2015;8(15-16):1-12.
7. Boing AF, Vargas SAL, Boing AC. A carga das neoplasias no Brasil: mortalidade e morbidade hospitalar entre 2002-2004. *Rev Assoc Med Bras* 2007;53(4):317-22.
8. Teras LR, DeSantis CE, Cerhan JR, Morton LM, A Jemal, CR Flowers. 2016 US lymphoid malignancy statistics by world health organization subtypes. *CA Cancer J Clin* 2016;66(6):443-59. doi: 10.3322/caac.21357.
9. Kaya H, Peressini B, Jawed I, Martincic D, Elaimy AL, Lamoreaux WT, Fairbanks RK, Weeks KA, Lee CM. Impact of age, race and decade of treatment on overall survival in a critical population analysis of 40,000 multiple myeloma patients. *Int J Hematol* 2012;95(1):64-70.
10. Silva ROP, Faria RMD, Côrtes MCJW, Clementino NCD, Faria JR, Moraes TEC. et al. Mieloma múltiplo: verificação do conhecimento da doença em médicos que atuam na atenção primária à saúde. *Rev Bras Hematol Hemoter* 2008;30(6):437-444.
11. Ferreira-Júnior MA, Ivo ML, Pontes ERCJ. Survival and leukemic evolution of patients with myelodysplastic Syndromes. *Cad Saúde Colet* 2013;21(2):154-9.
12. Wang SS, Vajdic CM, Linet MS, Slager SL, Voutsinas J, Nieters A. et al. Associations of non-Hodgkin Lymphoma (NHL) risk with autoimmune conditions according to putative NHL loci. *Am J Epidemiol* 2015;15(6):406-21. doi: 10.1093/aje/kwu290.
13. Yoo H, Shin DW, Jeong A, Kim SY, Yang HK, Kim JS, et al. Perceived social support and its impact on depression and health-related quality of life: a comparison between cancer patients and general population. *Jpn J Clin Oncol* 2017; 20:1-7. doi: 10.1093/jjco/hyx064.
14. Percival MEM, Tao L, Medeiros BC, Clarke CA. Improvements in the early death rate in 9,380 acute myeloid leukemia patients following initial therapy: a SEER database analysis. *Cancer* 2015;121(12):2004-12. doi: 10.1002/cncr.29319.
15. Le Guyader-Peyrou S, Belot A, Maynadié M, Binder-Foucard F, Remontet L, Troussard X, et al. French network of cancer registries (Francim). Cancer incidence in France over the 1980-2012 period: Hematological malignancies. *Rev Epidemiol Sante Publique* 2016;64(2):103-12. doi: 10.1016/j.respe.2015.12.017.
16. Smith A, Crouch S, Lax S, Li J, Painter D, Howell D et al. Lymphoma incidence, survival and prevalence 2004-2014: sub-type analyses from the UK's haematological malignancy research network. *Br J Cancer* 2015;112, 1575-84. doi: 10.1038/bjc.2015.94.
17. Li Y, Wang Y, Wang Z, Yi D, Ma S. Racial differences in three major NHL subtypes: descriptive epidemiology. *Cancer Epidemiol* 2015;39(1):8-13. doi: 10.1016/j.canep.2014.12.001.
18. Van Valkenburg ME, Pruitt GI, Brill IK, Costa L, Ehtsham M, Justement IT, et al. Family history of hematologic malignancies and risk of multiple myeloma: differences by race and clinical features. *Cancer Causes Control* 2016;27(1):81-91. doi: 10.1007/s10552-015-0685-2.
19. Chihara D, Nastoupil LJ, Williams JN, Lee P, Koff JL, Flowers, CR. New insights into the epidemiology of non-Hodgkin lymphoma and implications for therapy. *Expert Rev Anticancer Ther* 2015;15(5):531-44. doi: 10.1586/14737140.2015.1023712.
20. Greenberg PL, Attar E, Bennett JM, Bloomfield CD, Castro CM, Joachim DH, et al. Myelodysplastic syndromes: clinical practice guidelines in oncology. *J Natl Compr Canc Netw* 2013;11(7):838-874.
21. Feurstein S, Drazer MW, Godley LA. Genetic predisposition to leukemia and other hematologic malignancies. *Semin Oncol* 2016;43(5):598-608. doi: 10.1053/j.seminoncol.2016.10.003.
22. Alexander DD, Mink PJ, Adami HO, Chang ET, Cole P, Mandel JS et al. The non-Hodgkin lymphomas: a review of the epidemiologic literature. *Int J Cancer* 2007;120(Supl 12):1-39.
23. Sim J, Reid N. Statistical inference by confidence intervals: issues of interpretation and utilization. *Phys Ther* 1999;79(2):186-95.
24. Silva ROP, Brandão KMA, Pinto PVM, Faria RMD, Clementino NCD, Silva CMF et al. Mieloma múltiplo: características clínicas e laboratoriais ao diagnóstico e estudo prognóstico. *Rev Bras Hematol Hemoter* 2009;31(2):63-8.
25. Greipp PR, San Miguel J, Durie BG, Crowley JJ, Barlogie B, Bladé J et al. International staging system for multiple myeloma. *J Clin Oncol* 2005;23(15):3412-20.
26. Tefferi A, Thiele J, Vardiman JW. The 2008 World Health

- Organization Classification System for Myeloproliferative Neoplasms. *Order Out of Chaos. Cancer* 2009;115(17):3842-47.
27. Maurillo L, Buccisano F, Principe MID, Sarlo C, Caprio LD, Ditto C et al. Treatment of acute myeloid leukemia with 20-30% bone marrow blasts. *Mediterr J Hematol Infect Dis* 2013;5(1):e2013032.
28. Chen Y, Yang T, Zheng X, Yang X, Zheng Z, Zheng J, et al. The outcome and prognostic factors of 248 elderly patients with acute myeloid leukemia treated with standard-dose or low-intensity induction therapy. *Medicine* 2016;95(30):e4182. doi: 10.1097/MD.0000000000004182.
29. Sultan S, Irfan SM, Parveen S, Mustafa S. Acute lymphoblastic leukemia in adults: an analysis of 51 cases from a tertiary care center in pakistan. *Asian Pac J Cancer Prev* 2016;17(4):2307-9.