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Original article

Occupational exposures reported by patients with leukemia and myelodysplastic syndrome in Rio de Janeiro, Brazil

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Abstract

Introduction: Little is known about occupational agents and the occurrence of leukemia and myelodysplastic syndrome in Brazil. Objective: The aim of this study was to trace the sociodemographic and occupational profiles of patients with leukemia and myelodysplastic syndrome in two hospitals in the city of Rio de Janeiro, Brazil. Methods: We carried out a study of 229 cases from the period 2000 to 2006. Interviews were conducted with patients to obtain information on family history, lifestyle risk factors, occupational history, residential history, and occupational and non-occupational exposures by using a structured questionnaire. The frequency and duration of occupational activities related to exposure among participants were estimated. Each individual's level of exposure was classified as low, moderate, high or very high. Results: The main exposures observed were to chemical cleaning and disinfectant products, followed by gasoline and lubricating oil. Most of the exposures occurred at low frequencies. However, for benzene, solvents, thinners, and coal combustion, the highest prevalence was observed for moderate exposures. Furthermore, it was observed that the exposure patterns of substances varied for each group, suggesting that the intensity of exposure was determined by specific types of substances. Conclusion: The monitoring of exposure in occupations that deal with solvents is critical, in order to reduce the incidence of leukemia. Since occupation is a preventable risk factor, strategies for primary prevention and health promotion in the workplace should be a top priority in cancer prevention policies in Brazil.

Keywords: Leukemia; Occupational Health, Myelodysplastic syndromes, Epidemiology.

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Resumo

A exposição ocupacional relatada por pacientes com leucemia e com síndrome mielodisplásica e no Rio de Janeiro, Brasil

Introdução: Pouco se sabe sobre os agentes ocupacionais e a ocorrência de leucemias e síndromes mielodisplásicas no Brasil. Objetivo: Nosso objetivo foi traçar o perfil sociodemográfico e ocupacional de pacientes com leucemia e com síndrome mielodisplásica atendidos em dois hospitais de referência na cidade do Rio de Janeiro, Brasil. Métodos: Realizamos um estudo de 229 séries de casos, selecionadas no período de 2000 a 2006. Entrevistas foram realizadas com pacientes para obter informações sobre história familiar, fatores de risco de estilo de vida, histórico residencial, histórico ocupacional e de exposições ocupacionais e não-ocupacionais, e foi utilizado um questionário estruturado. Foram calculadas a frequência e a duração das atividades ocupacionais relacionadas às exposições relatadas pelos participantes. O nível de exposição de cada indivíduo foi classificado como baixo, moderado, alto ou muito alto. Resultados: Os produtos químicos de limpeza e desinfecção, seguidos de gasolina e óleo lubrificante, foram as principais exposições observadas. A maioria das exposições ocorreu em baixas frequências. No entanto, para benzeno, solventes, diluentes e combustão de carvão, a maior prevalência foi observada para exposições moderadas. Além disso, observou-se que os padrões de exposição das substâncias variaram para cada grupo, sugerindo que a intensidade da exposição foi determinada por tipos específicos de substâncias. Conclusão: A vigilância da exposição a solventes é ainda

insipiente, como tentativa de reduzir a incidência de leucemia. Como a ocupação é um fator de risco evitável, as estratégias de prevenção primária e a promoção da saúde nos locais de trabalho devem ser uma prioridade nas políticas de prevenção do câncer no Brasil.

Descritores: Leucemia, Saúde do Trabalhador, Síndromes Mielodisplásicas, Epidemiologia.

Resumen

La exposición ocupacional relatada por pacientes con leucemia y con síndrome mielodisplásico en Río de Janeiro, Brasil

Introducción: Poco se sabe sobre los agentes ocupacionales y la ocurrencia de leucemias y síndromes mielodisplásicos en Brasil. Objetivos: Nuestro objetivo fue trazar el perfil sociodemográfico y ocupacional de pacientes con leucemia y con síndromes mielodisplásicos atendidos en dos hospitales de referencia en la ciudad de Río de Janeiro, Brasil. Métodos: Se realizó un estudio de 229 series de casos, seleccionadas del período de 2000 a 2006. Entrevistas se realizaron con pacientes para obtener informaciones sobre historia familiar, factores de riesgo de estilo de vida, histórico residencial, histórico ocupacional y de exposiciones ocupacionales y no ocupacionales usando un cuestionario estructurado. Se calcularon la frecuencia y duración de las actividades ocupacionales relacionadas con las exposiciones relatadas por los participantes. El nivel de exposición de cada individuo fue clasificado como bajo, moderado, alto o muy alto. Resultados: Los productos químicos de limpieza y desinfección, seguidos de gasolina y aceite lubricante, fueron las principales exposiciones observadas. La mayoría de las exposiciones se produjo en bajas frecuencias. Sin embargo, para benceno, disolventes, diluyentes y combustión de carbón, la mayor prevalencia se observó para exposiciones moderadas. Los patrones de exposición de las sustancias variaron para cada grupo, sugiriendo que la intensidad de la exposición se determinó por tipos específicos de sustancias. Conclusiones: La vigilancia de la exposición a disolventes sigue siendo insípida, como intento de reducir la incidencia de leucemia. Como la ocupación es un factor de riesgo evitable, las estrategias de prevención primaria en los lugares de trabajo deben ser una prioridad en las políticas de prevención del cáncer en Brasil.

Palabras clave: Leucemia, Salud Laboral, Síndromes Mielodisplásicos, Epidemiología.

Introduction

Leukemias and myelodysplastic syndromes (MDS) are considered to be heterogeneous groups of hematopoietic diseases. They are characterized by the neoplastic transformation of a certain type of hematopoietic lineage cell.

Leukemias are classified as acute or chronic, according to their latency time, and as lymphoid or myeloid according to their cellular type. They occur in individuals of all ages. In 2012, GLOBOCAN data estimated 350,000 new cases and just over 260,000 deaths from leukemia worldwide.[1] In the world ranking, they occupy the 11th place in incidence and 10th in deaths.[2] In Brazil the estimate for 2018 is around 10,800 new cases, with a predominance in men when compared with women (5,940 versus 4,860 women, with disparities in different regions).[3]

MDS are characterized by ineffective hematopoiesis, increased intramedullary apoptosis, presence of dysplasias in the bone marrow, cytopenias in one or more lineages and genetic instability with increased risk of transformation to acute myeloid leukemia (AML).[4] They occur at a rate of 4.8 cases per 100,000 people in the United States, which means about 13,000 new cases of the disease annually.[5] The number of new cases diagnosed each year seems to increase as the average age of the population rises. In Brazil, the National Cancer Institute (INCA) has no data on this type of cancer.[3]

Little is yet known about the causes of leukemia, although a variety of potential risk factors have been suggested. Among them is a wide range of occupational exposures.[5-7] Classically, the association with ionizing radiation, benzene, and treatment with cytostatic drugs has been intensely described.[5-8] Recently, other associations have been suggested, such as those with pesticides, styrene etc.[8-11]

In Brazil, cancer related to occupation remains little explored, with few available studies.[11-13] Thus, our objective is to describe the socio-demographic and occupational profile of the patients treated in tertiary hospitals located in the city of Rio de Janeiro, whose diagnoses of acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphocytic leukemia, chronic lymphocytic leukemia (CLL) and myelodysplastic syndromes were confirmed.

Methods

Study Design and Population

This is a case series study, for which new data from adult hematologic patients were selected from

2000 to 2006 in two reference public hospitals. The diagnoses of leukemias and myelodysplastic syndrome (MDS) were performed by cytohistological and complementary exams. Patients were followed up at the National Cancer Institute (INCA) and the Pedro Ernesto University Hospital (HUPE), both located in Rio de Janeiro, Brazil. This study was approved by the Ethics Committees of the INCA (084/06) and HUPE (56621716.5.0000.5259).

A total of 349 patients with leukemia and MDS diagnoses were enrolled. Exclusion criteria (non-residents of the state of Rio de Janeiro and those who refused to participate) reduced the number of eligible patients to 229.

Data collection

Face-to-face interviews were carried out with the patients to obtain information on family history, lifestyle risk factors, employment history, residential history, and occupational and non-occupational exposures by using a closed-ended questionnaire. Thus, socio-demographic data, such as age, schooling, sex, and income were collected. In addition, information was gathered that allowed the construction of a detailed occupational history. Information regarding clinical data was obtained from medical records and hospital records of cancer. The types of leukemia were classified according to the major groups differentiated in the third version of the International Classification of Oncology (ICD-O).[14]

The occupational history contained information on all occupations held by each individual during the last twenty years. Information was collected not only on the occupation and activity of participants, but also on time spent in this occupation, exposure to chemicals, and the intensity of this exposure. Based on such information, chemical substances to which participants had been exposed included the following: cleaning products, disinfectants, benzene, toluene, xylene, turpentine, thinners, removers, solvents, gasoline, kerosene, lubricating oil, wood burning, coal combustion, coke combustion, plastic firing, glues, paint, diesel engine smoke, gasoline engine smoke, metallic fumes, drugs/chemotherapeutics, and pesticides.

Data analysis

Those who answered positively the question on exposure to related substances in at least one of their occupations were considered to be exposed. Subsequently, some substances were grouped by toxicological similarity. In this way, the following groups were created: fossil fuel derivatives, composed of gasoline and kerosene; cleaning products/disinfectants; organic solvents, consisting of hydrocarbon, turpentine, thinners, removers and solvents; and organic fumes, composed of exposure to wood, coal or coke dust. It should be emphasized that an individual can have more than one exposure in the same occupation or even present different exposures during his or her working life. For each of the substances evaluated, a proxy measure of intensity of exposure was adopted. The exposure assessment considered the time in each occupational activity and the potential frequency of exposure during this time allotted in the activity. When present, the frequency was evaluated as being "daily," "weekly," "monthly," or "rare." This exposure was measured for each occupation and the total exposure (ET) consisted of the sum of the measures of exposure during the life, according to the following formula:

$$E_t = \frac{\sum I_{en} \times T_{pn}}{T_t}$$

Et =Total exposure l

Ien = Frequency of exposition during occupational activity n

Tpn = Time spent in occupational activity n

Tt = Occupational life total time

Based on the score obtained by the report of each patient in relation to the frequency of exposure, the formula was applied and the population was divided into quartiles. Each individual was classified for exposure (low, medium, high, and very high).

Variables and measures

The descriptive analysis was performed by categorizing the variables, as follows: 1 - age (young adult, 18–39; mature, 40–59; and elderly, 60 years and older); 2 - level of education was measured as years of study and placed in the classification similar to that used by DATASUS (none, 1 to 7 years, 8 to 11, 12 or above); 3 - average monthly individual income was estimated according to Brazilian minimum salary, which was around US$380.

Statistical analysis

Descriptive statistics of sociodemographic and diagnostic variables were calculated. The absolute

and relative frequencies of occupational exposures to stratified chemical substances by exposure time, as well as the prevalence of exposure by type of leukemia were also described. For the statistical analysis of the data, Pearson's $\chi 2$ test was used, being considered a level of significance of 0.05 or 5% for comparison between groups. In order to perform the analyses, the SPSS 21.0 program was used, and tables were prepared using Excel software (version 2010).

Results

Data from 229 patients were available for analysis. There was a prevalence of males (61%), whites (74%) and the greatest number of individuals was between 40 and 59 years old. Regarding the level of education, measured in study time, the characteristic was bimodal with a predominance of individuals with 12 or more years of studies (47%) followed by patients with 1 to 7 years of study (33%). Regarding the family income, there was a slight predominance of cases with income between US$423 and US$633 (23%). Table 1 summarizes these findings.

The most frequent leukemia was chronic myeloid leukemia (36%), followed by chronic B-cell lymphocytic leukemia (27%). Myelodysplastic syndrome occurred in 7% (Table 2).

With regard to occupational products and exposure accumulation, cleaning products, disinfectants, gasoline and lubricating oil were the most prevalent with 19%, 15%, 13% and 13% respectively. Within each quartile of exposure, the prevalence by substance group was evaluated. However, among those exposed to chemical substances in their occupational life, we observed that exposures to very high doses occurred mainly for thinners (26%) and high frequencies for xylene (33%), wood burning (29%) and turpentine (27%), as observed in Table 3. For the most part, the exposures occurred at low frequencies. However, for benzene, solvents, thinners and coal combustion (substances known to be myelotoxic), the highest prevalence observed was for moderate exposures. Furthermore, it was observed that the exposure pattern for certain substances was different for each group, suggesting that the intensity of exposure is determined by specific types of substances. There was no statistically significant difference between groups for benzene ($P = 0.532$), xylene ($P = 0.078$), thinners ($P = 0.230$), kerosene ($P = 0.105$), lubricating oil ($P = 0.161$), wood burning ($P = 0.387$), coke combustion ($P = 0.104$), and plastic burning ($P = 0.294$). It should be noted that the number of patients who reported use of many of these substances was small, which may have influenced the values of the descriptive statistics of the tests used. Table 3 describes the occupational products found and the accumulation of exposures during throughout the work activity of the patients.

Finally, with regard to the prevalence of chemical exposures among the types of leukemia observed, exposure to cleaning products and derivatives was more prevalent for most types of leukemias studied, with the highest percentage for acute lymphoblastic leukemia (25%). For this type of leukemia, a prevalence of 25% was also observed for organic fumes. Chronic lymphocytic leukemia showed an equal percentage for exposure to cleaning products, fossil fuels, and organic solvents (13%). However, for chronic myeloid leukemia, exposure to fossil fuels (27%) stood out from other exposures. For myelodysplastic syndrome, exposure to organic fumes was quite high (63%) among individuals with this type of leukemia (Table 4). Finally, only for organic smoke was a significant difference observed for the different types of leukemias. This occurred in a larger number of patients who reported this exposure, but who were diagnosed with myelodysplastic syndrome.

Discussion

In Brazil, occupational cancer is still poorly subject due to extensive underreporting of data. Consequently, the quality of information and the effectiveness of the Brazilian health surveillance system are jeopardized. Tabalipa and colleagues (2011) investigated the occupation and level of education in patients with different types of cancer in a mountainous region of the State of Rio de Janeiro.[13] They noted that hospital records had incomplete data in both parameters. In relation to the occupation, these data were either ignored or were unable to be classified in 44.4% of records. In another Brazilian study associating occupation profiles in patients with leukemia diagnosis, these data were found in only 52% of the medical files.[12]

In this study similarities and discrepancies became apparent when confronted with other reports. Like other studies there was a predominance of males.[2,12] Nevertheless, the white race did not match with people in this region of the country (IBGE). Another peculiarity in our sample was a predominance of people with higher education and income when compared to the rest of the Brazilian population, who have lower average schooling and lower salaries.[15]

Table 1. Characterization of leukemic people according to demographic variables (N=229)

Characteristics	Frequency	
	N	%
Sex		
Female	90	39%
Male	139	61%
Total	229	100%
Faixa Etária		
White	172	76%
Non-white	55	24%
Total	227	100%
Education time		
None	4	2%
1 - 7 years	75	33%
8 - 11 years	41	18%
≥12 years	108	47%
Total	228	100%
Family income (US$)*		
≤ 211.00	17	8%
212.00 - 422.00	37	17%
423.00 - 633.00	53	24%
634.00 - 1,055.00	39	18%
1,056.00 - 2,111.00	42	19%
2,112.00 - 4,222.00	18	8%
≥ 4,223.00	9	4%
No income	3	1%
Age		
≥18 - 39 years	71	31%
≥ 40 - 59 years	80	35%
≥ 60 years	77	34%
Total	228	100%
Total	229	100%

*dollar quotation on November 10, 2006: R$2.149

Table 2. Characterization of leukemic population according to diagnoses (N=229)

Diagnosis	N	%
Acute lymphoblastic leukemia, WOS*	20	9%
B cell Chronic lymphocytic leukemia	61	27%
Acute myeloid leukemia, WOS*	49	21%
Chronic myeloid leukemia, WOS*	83	36%
Myelodysplastic syndrome, WOS*	16	7%
Total	229	100%

*WOS: without other specification.

Table 3. Distribution of occupancy risks according to reported exposure times (weighted by working time)

Occupational exposure	Frequency										P valor**
	Low		Moderate		High		Very high		Total*		
	N	%	N	%	N	%	N	%	N	%	
Cleaning Products / disinfectants	24	42.11	17	29.82	3	5.26	2	3.45	46	20.09	<0.001
Cleaning products	20	35.09	16	28.07	5	8.77	2	3.45	43	18.78	<0.001
Disinfectants	14	24.56	10	17.54	9	15.79	1	1.72	34	14.85	0.006
Organic Solvents	24	42.11	12	21.05	8	14.04	1	1.72	45	19.65	<0.001
Benzene	2	3.51	4	7.02	2	3.51	1	1.72	9	3.93	0.532
Toluene	6	10.53	1	1.75	0	0.00	0	0.00	7	3.06	0.002
Xylenes	5	8.77	1	1.75	3	5.26	0	0.00	9	3.93	0.078
Turpentine	11	19.30	3	5.26	6	10.53	2	3.45	22	9.61	0.019
Thinner	2	3.51	4	7.02	8	14.04	5	8.62	19	8.30	0.23
Other removers	11	19.30	8	14.04	5	8.77	3	5.17	27	11.79	0.103
Other solvents	4	7.02	6	10.53	3	5.26	0	0.00	13	5.68	0.106
Fossil Fuel Derivatives	23	40.35	11	19.30	5	8.77	1	1.72	40	17.47	<0.001
Gasoline	14	24.56	7	12.28	6	10.53	3	5.17	30	13.10	0.018
Kerosene	8	14.04	6	10.53	4	7.02	1	1.72	19	8.30	0.105
Lubricant oil	19	33.33	4	7.02	6	10.53	1	1.72	30	13.10	0.161
Organic fumes (wood, coal, coke)	8	14.04	2	3.51	1	1.75	0	0.00	11	4.80	0.104
Wood burning	4	7.02	1	1.75	2	3.51	0	0.00	7	3.06	0.387
Coal combustion	1	1.75	4	7.02	1	1.75	0	0.00	6	2.62	<0.001
Coke combustion	1	1.75	0.00	0.00	0	0.00	0	0.00	1	0.44	0.104
Plastic burning	2	3.51	0.00	0.00	0	0.00	1	1.72	3	1.31	0.294
Glues	15	26.32	15	26.32	3	5.26	1	1.72	34	14.85	<0.001
Painting	14	24.56	11	19.30	3	5.26	1	1.72	29	12.66	0.003
Diesel smoke	18	31.58	2	3.51	3	5.26	1	1.72	24	10.48	<0.001
Gasoline smoke	13	22.81	9	15.79	6	10.53	1	1.72	29	12.66	0.006
Metallic fumes	10	17.54	3	5.26	2	3.51	2	3.45	17	7.42	0.009
Drug / chemotherapy	5	8.77	1	1.75	1	1.75	1	1.72	8	3.49	0.102
Pesticides	2	3.51	1	1.75	1	1.75	2	3.45	6	2.62	0.877

*WOS: without other specification.

In this study, cleaning products/ disinfectants and organic solvents had higher frequencies. They are very common substances used on a daily basis. In Australia, nearly 10.8% of cancer in males and 2.2% in females are caused by work occupation.[16] It is probable that Brazil and other developing countries may have higher levels due to the conditions of poverty to which our workers are exposed. Therefore, in order to plan prevention programs for occupational cancer, understanding the size of the problem is important. However, there is an ongoing scientific debate on the possible association of leukemia with a number of other work-related risks.[17-18]

In particular, the epidemiological evidence on the relationship between organic solvents and cancer is described in the literature. Evidence exists of increased cancer risk for continuous exposures to agents such as trichloroethylene, tetrachloroethylene, formaldehyde,

Table 4. Prevalence of exposure to chemical substances in the leukemia types observed

Chemical Substances	Diagnosis					P value*
	Acute lymphoblastic leukemia (N=20)	B cell Chronic lymphocytic leukemia (N = 61)	Acute myeloid leukemia (N = 49)	Chronic myeloid Leukemia (N = 83)	Myelodysplastic syndrome (N =16)	
Fossil fuels	10%	13%	10%	27%	25%	0.063
Cleaning and disinfectant products	25%	13%	16%	22%	25%	0.506
Organic solvent	10%	13%	12%	20%	25%	0.433
Organic fumes	25%	3%	4%	1%	63%	<0.001
Ionizing radiation	70%	61%	55%	58%	56%	0.801

*WOS: without other specification.

ethylene oxide, carbon tetrachloride, BTEX (benzene, toluene, xylenes, and ethylbenzene) etc.[17]

In general, carcinogenesis associated with benzene exposure is linked to damage of the bone marrow, resulting in a decrease in the number of circulating blood cells until aplastic anemia finally occurs. In addition, a growing effort can be observed in the literature to attempt to characterize the fine structure of the marrow and the identification of so-called "niches" that house a variety of stem cells and other cell types. Some of these "niches" may harbor cells capable of initiating leukemias. More recently, the focus of the studies has been directed to a better understanding of how benzene metabolites can alter the biology of bone marrow cells.[17,18] Many studies have been performed around the world both in developed and underdeveloped countries. [18-28]

A 28-year follow-up retrospective cohort study in China, which recruited solvent-exposed workers, demonstrated increased risk for a wide range of cancers, especially hematological ones. There was a high incidence of all myeloid disorders, with excess myelodysplastic syndrome and acute myeloid leukemia (RR = 2.7, 95% CI, 1.2-6.6) and chronic myeloid leukemia (RR = 2.5, 95% = 0.8-11), and increases in all lymphoid disorders, including lymphoid leukemia (RR = 5.4, 95% CI = 1.0 - 99).[21] In addition, a study by Stenehjem et al.[22] used data from the cancer registry to identify 112 cases of cancer diagnosed during 1999-2011 in a cohort of 24,917 Norwegian male offshore workers, many with exposure below 15 years. Dose-related risk patterns were found for cumulative exposure to acute myeloid leukemia (*P* trend = 0.052), multiple myeloma (*P* trend = 0.024), and borderline evidence for acute lymphocytic leukemia (*P* trend = 0.094).

In addition to this evidence, a study by Li et al. [27] identified genetic alterations involved in the pathogenesis of leukemia in workers exposed to benzene, even without clinical symptoms of leukemia. The results suggested that variations exist in the number of copies of chromosomes, and that the expression of leukemia-related genes may play a role in the development of leukemia in workers exposed to benzene.

It is worth adding that, despite the association strongly established in the literature, preserving data quality is fundamental for an adequate analysis. To illustrate this point, the study by Talibov et al.,[28] which analyzed approximately 15,000 incidents of acute myelogenous leukemia in Scandinavia, did not find a statistically significant increase in risk for solvent-exposed workers. However, this study was conducted through analysis by matrices of occupational exposure, and did not measure biomarkers in the workers. Although it is an extremely relevant source of data, registry databases should be used with caution, and the quality of the information contained in them must be evaluated. Still, with regard to data quality, consideration of the quality of the evidence used is important in order to make robust estimates. A recent meta-analysis that used different strategies to evaluate the quality of the studies to assess the association between occupational exposure to benzene and chronic myeloid leukemia identified an rise in the overall risk synthesized by meta-analysis with increasing study quality as well as those whose onset follow-up of the cohort occurred after the 1970s (and therefore with better measurement techniques and control of loss of follow-up).[29]

These diseases are complex but have become better understood in recent decades thanks to new laboratory techniques for detecting DNA failures produced by leukemogenic agents.[30]

Conclusion

The results of the present study indicate that patients with leukemia and MDS were exposed during their professional life to chemical agents with carcinogenic potential and that such exposure can be preventable. Of course, establishing any trace of causality is not possible by descriptive analysis. In this sense, analytical studies of the case-control type are necessary to study the association between these agents and leukemia, and thus contribute with actions that improve the health of the workers.

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References

1. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-86.
2. Miranda-Filho A, Piñeros M, Ferlay J, et al. Epidemiological patterns of leukaemia in 184 countries: a population-based study. Lancet Haematol. 2018;5(1):e14-24.
3. Brasil. Ministério da Saúde. Instituto Nacional de Câncer José Alencar Gomes da Silva. Coordenação de Prevenção e Vigilância. Estimativa 2018 Incidência de Câncer no Brasil. Rio de Janeiro: INCA; 2018. Available in: http://www.inca.gov.br/estimativa/2018/estimativa-2018.pdf. Accessed on Nov 11, 2018.
4. The American Cancer Society medical and editorial content team. https://www.cancer.org/cancer/myelodysplastic-syndrome/about/key-statistics.html. Accessed on March 25, 2019.
5. Straif K. The burden of occupational cancer. Ocupp Environ Med. 2008;65(12):787-88.
6. Khalade A, Jaakkola MS, Pukkala E, et al. Exposure to benzene at work and the risk of leukemia: a systematic review and meta-analysis. Environ Health. 2010;9:31.
7. Hoffmann W, Terschüeren C, Heimpel H, et al. Population-based research on occupational and environmental factors for leukemia and non-Hodgkin's lymphoma: the Northern Germany Leukemia and Lymphoma Study (NLL). Am J Ind Med. 2008;51(4):246-57.
8. Palmer Harris EC, Palmer KT, Cox V, et al. Trends in mortality from occupational hazards among men in England and Wales during 1979-2010. Occup Environ Med. 2016;73(6):385-93.
9. Coggon D, Ntani G, Harris EC, et al. Soft tissue sarcoma, non-Hodgkin's lymphoma and chronic lymphocytic leukaemia in workers exposed to phenoxy herbicides: extended follow-up of a UK cohort. Occup Environ Med. 2015;72(6):435-41.
10. Coggon D, Ntani G, Harris EC, et al. Risk of cancer in workers exposed to styrene at eight British companies making glass-reinforced plastics. Occup Environ Med. 2015;72(3):165-70.
11. Azevedo e Silva G, de Moura L, Curado MP, et al. The Fraction of Cancer Attributable to Ways of Life, Infections, Occupation, and Environmental Agents in Brazil in 2020. PLoS One. 2016;11(2):e0148761.
12. Moraes ES, Mello MSC, Nogueira FAM, et al. Análise de indivíduos com leucemia: limitações do sistema de vigilância de câncer. Cien Saude Colet. 2017;22:3321-32.
13. Tabalipa MM, Boccolini P, Diego SR, et al. Informação sobre ocupação em registros hospitalares de câncer no Estado do Rio de Janeiro. Cadernos Saúde Coletiva. 2011;19:278-86.
14. Organização Mundial da Saúde. CID-O Classificação Internacional de Doenças para Oncologia. 3ª Edição. Edusp – Editora da Universidade de São Paulo. São Paulo: Fundação Oncocentro de São Paulo; 2005. p.245
15. Censo Demográfico 2010. Características da população e dos domicílios: resultados do universo (PDF). Rio de Janeiro: IBGE. 2011. ISSN 0104-3145
16. Fritschi L, Driscoll T.Cancer due to occupation in Australia.Aust N Z J Public Health. 2006 Jun;30(3):213-9.
17. Polychronakis I, Dounias G, Makropoulos V, et al. Work-related leukemia: a systematic review. J Occup Med Toxicol. 2013;8(1):14.
18. Lynge E, Anttila A, Hemminki K. Organic solvents and cancer. Cancer Causes Control. 1997;8(3):406-19.
19. Snyder R. Leukemia and benzene. Int J Environ Res Public Health. 2012;9(8):2875-93.
20. Irons RD, Chen Y, Wang X, et al. Acute myeloid leukemia following exposure to benzene more closely resembles de novo than therapy related-disease. Genes Chromosomes Cancer. 2013;52(10):887-94.
21. Linet MS, Yin SN, Gilbert ES, et al. A retrospective cohort study of cause-specific mortality and incidence of hematopoietic malignancies in Chinese benzene-exposed workers. Int J Cancer. 2015;137(9):2184-97.
22. Stenehjem JS, Kjærheim K, Bråtveit M, et al. Benzene exposure and risk of lymphohaematopoietic cancers in 25 000 offshore oil industry workers. Br J Cancer. 2015;112(9):1603-12.
23. Schnatter AR, Glass DC, Tang G, et al. Myelodysplastic syndrome and benzene exposure among petroleum workers: an international pooled analysis. J Natl Cancer Inst. 2012;104(22):1724-37.
24. Collins JJ, Ireland B, Buckley CF, et al. Lymphohaematopoietic cancer mortality among workers with benzene exposure. Occup Environ Med. 2003;60:676–79.
25. Lewis RJ, Gamble JF, Jorgensen G. Mortality among three refinery/petrochemical plant cohorts. I. 1970 to 1982 active/terminated workers. J Occup Environ Med. 2000;42:721–29.
26. Koh DH, Jeon HK, Lee SG, et al. The relationship between low-level benzene exposure and blood cell counts in Korean workers. Occup Environ Med. 2015;72(6):421-27.
27. Li K, Jing Y, Yang C, et al. Increased leukemia-associated gene expression in benzene-exposed workers. Sci Rep. 2014;4:5369.
28. Talibov M, Lehtinen-Jacks S, Martinsen JI, et al. Occupational exposure to solvents and acute myeloid leukemia: a population-based, case-control study in four Nordic countries. Scand J Work Environ Health. 2014;40(5):511-17.

29. Vlaanderen J, Lan Q, Kromhout H, et al. Occupational benzene exposure and the risk of chronic myeloid leukemia: a meta-analysis of cohort studies incorporating study quality dimensions. Am J Ind Med. 2012;55(9):779-85.

30. Brown T, Rushton L. British Occupational Cancer Burden Study Group. Occupational cancer in Britain. Haematopoietic malignancies: leukaemia, multiple myeloma, non-Hodgkins lymphoma. Br J Cancer. 2012;107(Suppl 1): S41-48.