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Leukaemia incidence in residents of municipalities in the State of Rio de Janeiro between 2006 and 2014

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This research aims to study incidence of acute leukaemia in adults living under potential environmental exposure to industrial emissions in selected cities in the state of Rio de Janeiro, Brazil. It evaluates the incidence of hospitalizations for leukaemia among residents of 19 metropolitan areas of the State of Rio de Janeiro registered in the Brazilian Health Care System (SUS) between January 2006 and March 2014, according to their residence area. Here, a comparison among the studied cities was performed taking as estimated morbidity indicator the hospitalization rate for leukaemia by residence area. Nineteen of a total of 92 municipalities in the State of Rio de Janeiro were selected for the present study. The adopted selection criteria were distance of each municipality to the City of Rio de Janeiro of less than 180 km, similar health policies, number of public health facilities, urban and rural population distribution and the amount of industries in each municipality. Thus, the selected municipalities were: Belford Roxo, Duque de Caxias, Itaboraí, Itaguaí, Japeri, Macaé, Mage, Marica, Mesquita, Nilopolis, Niterói, Nova Iguaçu, Queimados, Rio Bonito, Rio de Janeiro, São Gonçalo, São João de Meriti, Seropédica and Tanguá. The study thus revealed that among these municipalities, Macaé, Itaboraí, Queimados and Duque de Caxias showed the highest hospitalization rates for leukemia in adults (≥20 years old) for both sexes. Additionally, morbidity was about 6 times higher than the average of the reference municipalities. A common feature of these municipalities is the massive presence of potentially polluting industries, especially oil refining activities. The results presented herein strongly suggest a correlation between environmental pollution by industrial emissions and acute leukaemia in adults. It is important to note that, even in this situation, the causality can only be determined categorically through individual studies.

Key words: Leukemia, environmental contamination, epidemiology, cancer risk.

INTRODUCTION

Industrialization is a process that, over the years, have become a synonym of obtaining power and respect from those who presented technological delay. For many, it is synonym of development, In fact, development is the aim

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of every country, especially economic development, measured through the Gross Domestic Product (GDP) of each country (Maluf, 2000).

Currently, the Southeastern region of Brazil (comprising the States of São Paulo, Rio de Janeiro, Minas Gerais and Espírito Santo) generates 55.4% of the Brazilian GDP, with Rio de Janeiro State contributing with 11.2% of this total, ranked as the second contributor for the Brazilian GDP in 2011 (IBGE, 2011).

This is due to the allocation of several large investments in this area, namely automotive manufacturers in the Médio Paraíba; the Rio Polymers industry, in Duque de Caxias, aiming at the creation of a chemical-gas complex in that area; the reactivation of the naval industry; the enlargement of investments through Petrobrás and oil industries in several municipal districts such as Macaé; the installation of new oil companies in Rio de Janeiro; the creation of an oil and gas complex in Itaboraí (COMPERJ); the installation; of a metallurgical plant in the industrial district of Santa Cruz and, the development of a container port, in Itaguaí, whose project was meant to be the largest port in Latin America (Osorio and Versiani, 2013).

Alongside this exacerbated growth, harmful consequences have been linked to the environment and the human health, due to increased emissions of pollutant gases inherent to these productive processes, the inadequate discard of waste and the lack of public policies that demand manufacturer responsibility for the life cycle of their respective product (Reis et al., 2012). Proof of this environment and health relationship are the countless reports on the increasing incidence of pathologies, such as cancer, in areas of high exposure loading to chemical substances (Snyder, 2014; Koh et al., 2014; Yong et al., 2014; Loeb and Harris, 2008).

One of the most thoroughly studied cancer types in relation to exposure to carcinogenic substances alongside genetic predisposition is leukaemia (Glass et al., 2014; Boothe et al., 2014; Hoeck et al., 2014). Characterized as a clonal proliferation of hematopoietic cells present in the bone marrow, leukaemia can be classified in four subtypes: acute lymphoblastic, acute myeloid, chronic lymphoid and chronic myeloid, with the former occurring more frequently in children, while the other subtypes are more common in adults (Klepin et al., 2014; Couto, 2015).

The relationship between environmental exposure to chemicals and leukaemia has been studied. Steffen et al (2004) reported an association between acute childhood leukaemia and benzene emitting sources, while Raaschou-Nielsen et al (2016) studied the relationship between traffic-related air pollution and the risk of leukaemia in adults and found an association with the acute myeloid type but not for other subtypes. Fillipini et al. (2015) reported an association between risks for leukaemia and environmental exposure to traffic pollution, particularly benzene. Parodi et al. (2015) found a possible aetiological role of air pollution from an industrial area and the risk of leukaemia in adults in Italy. Garcia-Perez et al. (2015) reported similar results for childhood leukaemia and the proximity of industrial and urban sites. Very few scientific works have been published involving Brazilian environmental exposure and none, to the best of our knowledge have focused on exposure to industrial emissions and leukaemia in residents from surrounding regions of industrial areas.

Therefore, the purpose of the present study was to evaluate the situation of hospitalizations due to leukaemia in residents of the metropolitan area of Rio de Janeiro State registered by the Unified Health System, according to residence area from January 2006 to March 2014.

MATERIALS AND METHODS

Study design

This work refers to an epidemiological study with ecological delineation, comprehending the period between January 2006 to March 2014, using secondary data available from the Unified Health System (DATASUS) and of Brazilian Institute of Geography and Statistics (IBGE) electronic websites regarding selected municipalities in the State of Rio de Janeiro. The morbidity indicator selected was the internment rate due to leukaemia. Taking into consideration the residence areas it was possible to compare the situation in each studied district through ratio rates.

Study area

Nineteen of a total of 92 municipalities in the State of Rio de Janeiro were selected for the present study. The adopted selection criteria were distance of each municipality to the City of Rio de Janeiro of less than 180 km; similar health policies; number of public health facilities; urban and rural population distribution and; the amount of industries in each municipality. Therefore, the selected municipalities were: Belford Roxo, Duque de Caxias, Itaboraí, Itaguaí, Japeri, Macaé, Magé, Maricá, Mesquita, Nilópolis, Niterói, Nova Iguaçu, Queimados, Rio Bonito, Rio de Janeiro, São Gonçalo, São João de Meriti, Seropédica and Tanguá. The location of each study area is displayed in Figure 1.

Study groups

The studied cities were classified into two different groups: reference and cases. More than 18% of residents living in rural areas characterized the reference group. In the case group, the number of people involved in industrial activities is larger and they are, consequently, more exposed to chemical substances coming from those sources. Through these criteria, the cities of Rio Bonito and Seropédica comprised the reference group, in accordance to the data displayed in Table 1.

Morbidity indicators

The morbidity indicators were built considering the hospitalization rate due to leukaemia and the average rate of the ones classified as references, allowing for comparisons of the situations present in each evaluated municipality. Therefore, hospitalizations due to

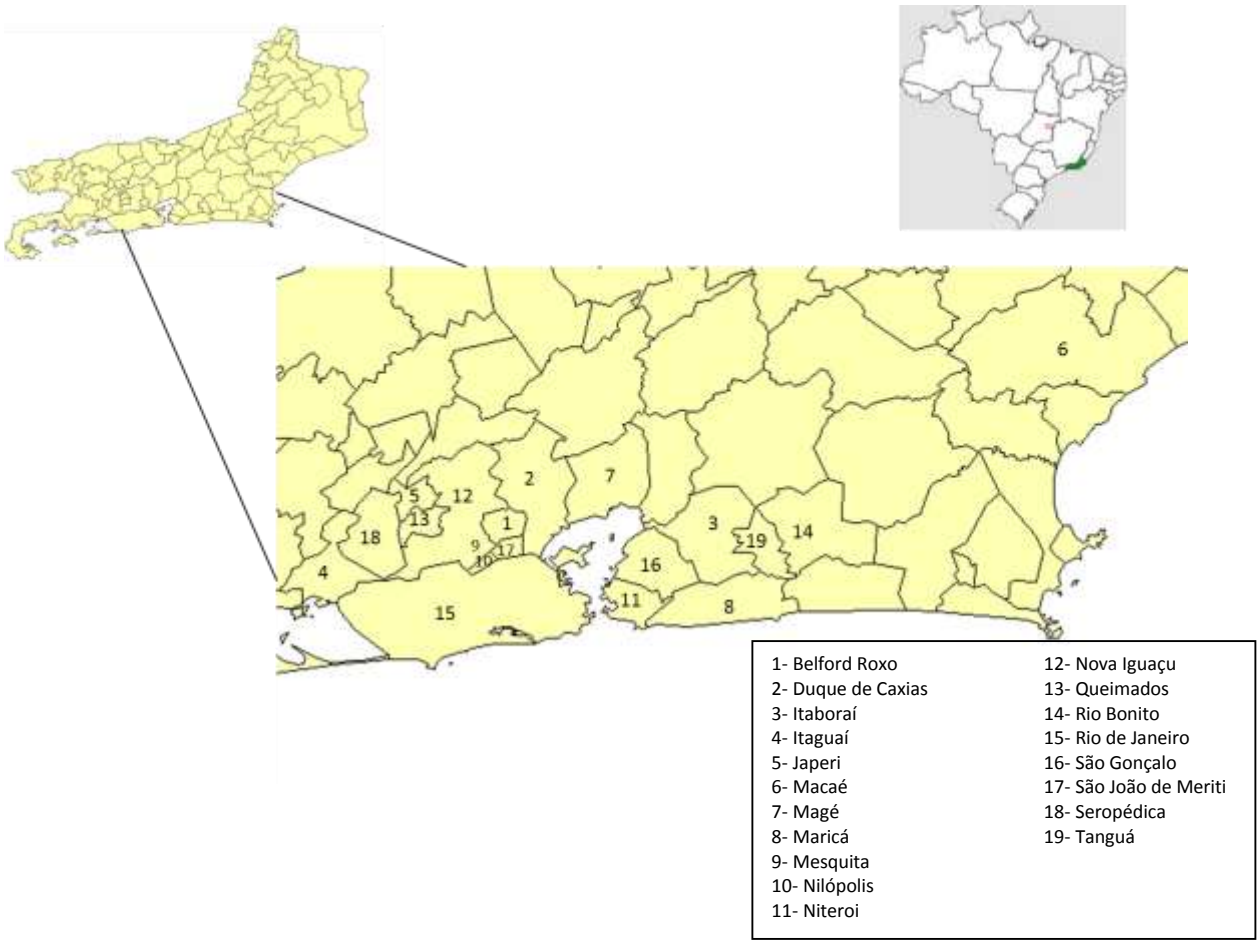

Figure 1. Representative map of Brazil and the State of Rio de Janeiro, highlighting the 19 municipalities selected for this study.

leukaemia selected in Chapter II (Neoplasms (tumours)) and the List of Morbidity (Leukaemia) of the International Classification of Diseases (ICD-10) were included in the numerators. The population at risk was used in the denominators, in other words, the population in which the cases in half of the interval of the studied period arose. Hospitalization data due to leukaemia were obtained from in the Health Information: Epidemiology and Morbidity (TABNET) database found at the electronic portal of the Unified Health System database, DATASUS. The estimates of the resident population in the studied cities were obtained from the Brazilian Institute of Geography and Statistics (IBGE, 2010).

In order to minimize interference promoted by the different age distributions, since the groups were not homogeneous, the standardization of the hospitalization rates due to leukaemia was calculated by the direct method (Pagano and Gauvreau, 2004).

The association of the measures was accomplished through the rate ratio of each municipality, obtained by dividing the rate of each one by the average of the rate of the reference group (Rio Bonito and Seropédica). The rate ratios and 95% Confidence Interval (IC95%) were calculated using the WINPEPI® version 9.3 software package.

Since this study refers to an epidemiological study with ecological delineation, using public population data applied for planning governmental actions without individual identification, there is no need of appreciation by any ethical committee.

RESULTS

The relevant information collected from the different, freely accessible, electronics databases from the selected municipalities in the State of Rio de Janeiro were compiled and are presented in Table 1.

Rio de Janeiro City has the largest population and practically its entirety lives in the urban area, followed by São Gonçalo and Duque de Caxias. Rio Bonito and Seropédica possess about 20% of their total population living in rural areas. Regarding the registration of public health facilities, the municipal districts of Rio de Janeiro and São Gonçalo lead the list, following by the population of each area.

The Human Development Index (HDI), also displayed in Table 1, is an indicator calculated from information obtained on the three basic dimensions of human development (income, education and health) of a certain population and allows for the evaluation of how the public managers of a certain area use financial resources to promote improvements in life quality of its inhabitants.

Table 1. Municipalities selected for herein and relevant information used in this study (IBGE, 2010). HDI - Human Development Index, GDP - Gross Domestic Product.

Municipalities	Total Urban population	Total Rural population	Public Health establishments	HDI	GDP (in thousands – R$)		
					Agricultural	Industrial	Services
Belford Roxo	469261	0	58	0.684	2357	996248	3184746
Duque de Caxias	852131	2915	82	0.711	7923	8403779	14918652
Itaboraí	215503	2587	62	0.693	10718	345855	1672230
Itaguaí	104292	4871	27	0.715	15332	272759	2369806
Japeri	95391	0	15	0.659	2585	86396	769042
Macaé	202873	3875	83	0.764	25649	4297335	5472995
Magé	215941	12209	78	0.709	28087	242540	1677570
Maricá	125532	1987	26	0.765	7614	498272	1073956
Mesquita	168403	0	19	0.737	365	187332	1261123
Nilópolis	157483	0	21	0.753	0	192215	1398300
Niterói	487327	0	87	0.837	15696	1800542	7935680
Nova Iguaçu	786536	8676	104	0.713	8321	1291340	7324182
Queimados	137938	0	15	0.680	2967	466375	1049380
Rio Bonito	41267	14319	35	0.710	6312	126071	654087
Rio de Janeiro	6323037	0	257	0.799	59037	22332352	125151001
São Gonçalo	999161	740	194	0.739	28491	1655305	8200147
São João de Meriti	459356	0	48	0.719	908	477505	4017426
Seropédica	64297	13886	23	0.713	11729	195298	572979
Tanguá	27426	3305	10	0.654	3864	41234	226425

The HDI has the purpose of offering development information under a different perspective from the Gross Domestic Product (GDP) per capita, another routinely applied indicator, which only considers the economical dimension of the municipal district development (PNUD, 2012).

The calculation of the internment rate was made by leukaemia adjusted by age with the data compiled on leukaemia hospitalization according to resident area registered by the Brazilian health care system (SUS) from January 2006 to March 2014 and the census data obtained from the Brazilian Institute of Geography and Statistics (IBGE) for each municipality evaluated in this study, the calculation of the internment rate was performed by leukaemia adjusted by age, as represented in Figure 2. First, the standardization of the rate was accomplished including all of population age groups, categorized only by gender, as displayed in Figure 2(a). Subsequently, only information regarding the adults (≥ 20 years old) were considered, in order to obtain data from the subtypes that occur preferentially in this age group, such as acute myeloid leukaemia, that show positive association with exposure to chemical substances, such as benzene (Keplin et al., 2014; Couto, 2015; Viacava and Bahia, 1999; Barata-Silva et al., 2014; Sahmel et al., 2013). The results obtained for this population stratum are presented in Figure 2(b).

When evaluating the rate ratio of hospitalizations due to leukaemia in adults from each city and the average rate of the reference municipalities (Rio Bonito and Seropédica - Table 2), data demonstrated that, regarding men, Macaé city presents a morbidity force by leukaemia about 6 times higher than the references, followed by Queimados (RR = 5.18; 95% CI: 2.55-10.67) and Itaboraí (RR = 4.50; 95% CI: 2.28-9.19). On the other hand, for women, Queimados presents the highest magnitude, about 7 times higher than the reference average, followed by Itaboraí (RR = 5.53; 95%CI:2.53-12.02) and Duque de Caxias (RR = 5.27; 95% CI: 2.53-11.36). These results are summarised in Figure 3.

DISCUSSION

The classification of the studied municipalities when evaluating the indicators Human Development Index (HDI) and Gross Domestic Product (GDP) per capita lead to different interpretations, indicating disparity between the economic and the human development of each area such as Duque de Caxias, which is classified as the second in the GDP rank and occupies the 12th HDI position among the 19 appraised municipalities, indicating that the revenue generated in this area is not distributed equally nor is invested in the same degree in education and health in this municipality.

An evidence of the welfare rendered by the government on behalf of the population health is the construction of

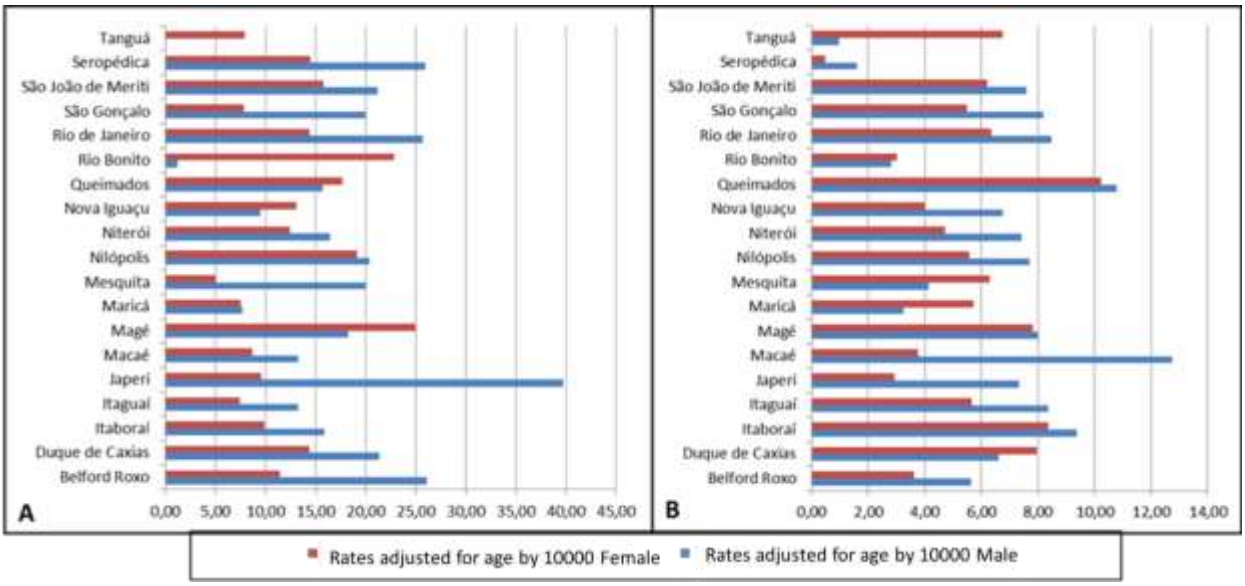

Figure 2. Age-adjusted hospitalization rates for leukaemia observed in 19 municipalities of in the State of Rio de Janeiro. (a) All ages. (b) Adults (≥20 years old).

Table 2. Rate ratio due to leukaemia hospitalization in adults registered in the municipalities of the metropolitan region of the State of Rio de Janeiro.

Municipalities	Rate Ratio (CI: 95%)	
	Male	Female
Belford Roxo	2.70 -1.39-5.50)	2.39 (1.10-5.27)
Duque de Caxias	3.18 (1.64-6.27)	5.27 (2.53-11.36)
Itaboraí	4.50 (2.28-9.19)	5.53 (2.53-12.02)
Itaguaí	4.01 (1.87-8.33)	3.74 (1.58-8.76)
Japeri	3.53 (1.62-7.65)	1.94 (0.72-5.16)
Macaé	6.12 (3.03-11.98)	2.49 (1.12-5.85)
Magé	3.85 (1.90-7.77)	5.16 (2.37-11.30)
Maricá	1.55 (0.67-3.58)	3.77 (1.63-8.60)
Mesquita	1.98 (0.94-4.41)	4.15 (1.92-9.55)
Nilópolis	3.70 (1.87-7.93)	3.69 (1.65-8.38)
Niterói	3.57 (1.78-6.90)	3.12 (1.47-6.82)
Nova Iguaçu	3.25 (1.68-6.43)	2.66 (1.27-5.84)
Queimados	5.18 (2.55-10.67)	6.77 (3.12-15.19)
Rio de Janeiro	4.07 (2.10-7.80)	4.20 (2.04-9.00)
São Gonçalo	3.93 (2.07-7.82)	3.62 (1.72-7.76)
São João de Meriti	3.64 (1.79-6.99)	4,11 (1.95-8.97)
Tanguá	0.47 (0.06-3.77)	4.46 (1.53-12.47)

Public Health Facilities, which should be geographically instituted to include the largest number of inhabitants, in other words, cities with high population density, such as Rio de Janeiro, should have a larger number of these facilities, which was confirmed herein, followed by São Gonçalo and Nova Iguaçu, respectively. However, the existence of public health facilities is not a guarantee of a general preventive and/or health promotion practice, since there is an unequal distribution of the health centres and hospitals with specialized services, privileging the central and the more developed parts of each city when compared to the suburbs, where health care is still very underdeveloped (Viacava and Bahia, 1999).

According to Figure 2a, regarding men, the city of Japeri, considered as a dormitory city, showed the

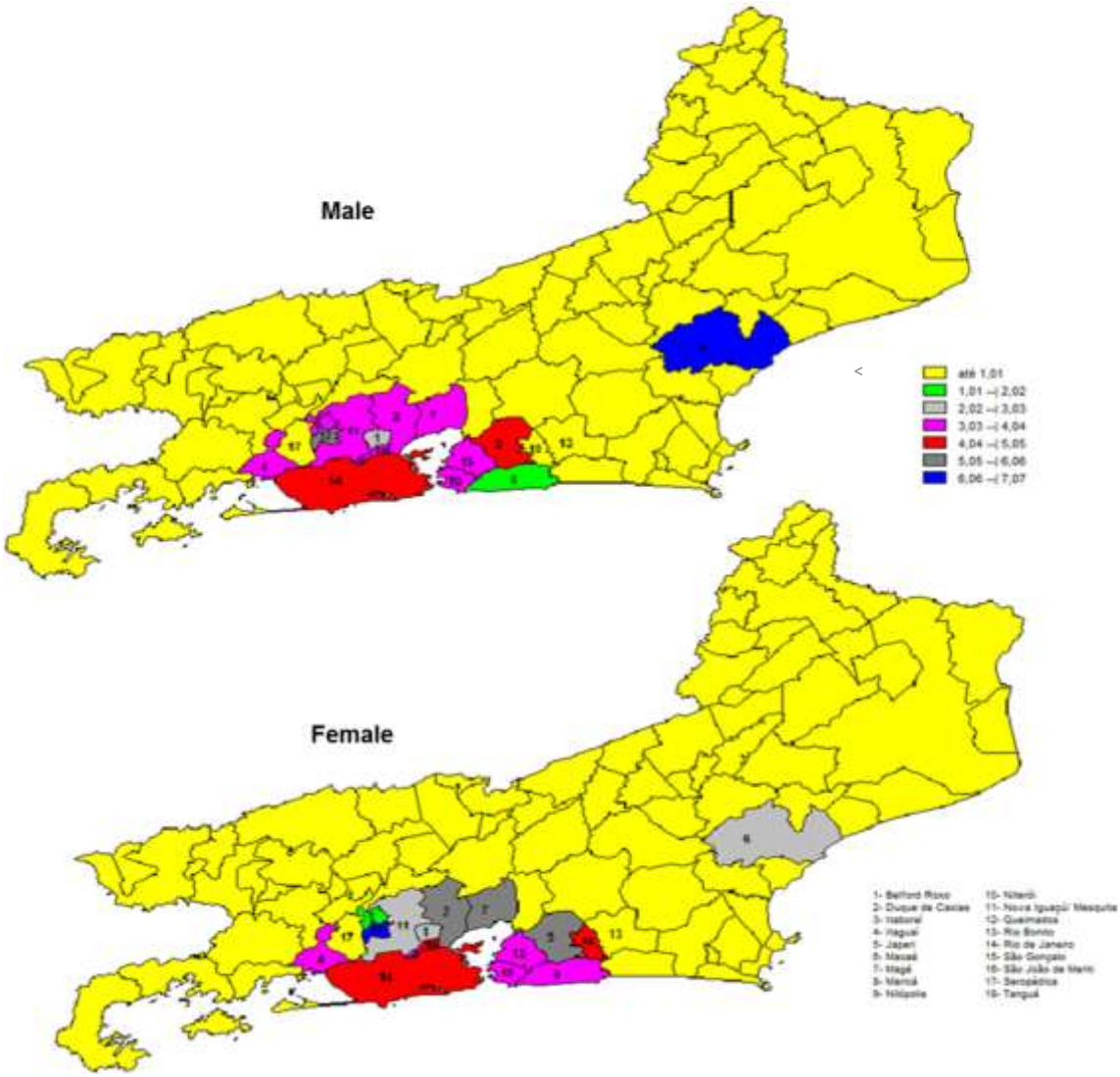

Figure 3. Map representing the leukaemia hospitalization rate ratio adjusted for age in adults of the 19 evaluated cities in the State of Rio de Janeiro, considering the Rio Bonito and Seropédica municipalities as references.

highest hospitalization rate for all types of leukaemia, followed by Rio de Janeiro and Macaé. For women, the city of Magé presented the highest rate, followed by Queimados and Duque de Caxias.

In spite of Japeri and Magé not having any significant industrial complexes, they are registered as comprising extensive agricultural areas, which consequently increases the possibility of population exposure to various pesticides (Araujo-Pinto et al., 2012). The use of pesticides has also been associated to increases in leukemia incidence, mainly Non-Hodgkin's lymphoma and multiple myeloma, in workers exposed during the preparation and application of these substances (Alavanja et al., 2014; Jones et al., 2014). In addition to the workers, their relatives and neighbours are also environmentally exposed to those xenobiotics, whether by dermal or oral or respiratory contamination (Peres et al., 2004).

The standardization of the rates considering only the adult group (≥ 20 years old) revealed a different situation. In this case, the city of Macaé showed the highest hospitalization rate standardized by age, followed by Queimados and Itaboraí, for men, while for women this occurred for the cities of Queimados, followed by Itaboraí and Duque de Caxias.

Macaé city is located in the Northern region of the state of Rio de Janeiro, known as the National Capital of Oil Production, since it holds more than 4 thousand companies linked to oil extraction activities and the production of oil and natural gas in the Campos Basin. Its

urban and economic development is linked to the installation and operation of such industries. This city receives royalties linked to oil production, resulting in significant increases in its Gross Domestic Product (GDP) in the last 15 years, leading to the highest GDP among the neighbouring cities (Neto et al., 2007).

This city currently has about 220,000 inhabitants, predominantly adults (≥20 years old), and great part develops occupational activities linked to the oil industry, either direct or indirectly. Intense population migration, responsible for population increases in the order of about 5% a year between 2000 and 2010, as a result of its high GDP, led to fast urban growth without any appropriate urban planning. Consequently, lack of basic sanitation or sewer collection is common. At the same time, increases in the occupational informality inside the productive process was observed, leading to increased occupational health risks due to lack of control of the work conditions that workers in these conditions are submitted to. In general, work opportunities are easier in places with high exposure risks to chemical substances, making the use of protection equipment necessary, which is not the main concern of any informal occupation (Carmo, 2012).

Similarly to Macaé, Duque de Caxias has its main economic activity structured around the oil industry, encompassing a complex of 26 petrochemical, processing and thermo-electrical companies. This is the second largest industrial complex in the state of Rio de Janeiro, with industries such as the Caxias Refinery (REDUC), considered the largest industrial unit of the Rio de Janeiro area, producing fuels, naphtha, and LPG (Liquefied Petroleum Gas). A series of chemical industries were built in its vicinity, some of them large-scale industries associated with oil processing, such as PETROFLEX, and NITRIFLEX, among others. In addition, a group of small and medium companies that produce resins, paints, candles, paraffin and other chemical products are also located in the area (Irigaray et al., 2013).

Recent increases in other industrial sectors, such as the manufacturing, furniture and food industries are observed in the area, in such a way, except for the REDUC complex, the industrial complex of Duque de Caxias can be considered as formed by several small and medium companies (Irigaray et al., 2013).

Queimados has a 4,000,000 m^2 industrial complex comprising about 40 companies with different activities, ranging from paint factories to recycling industries. This industrial park is located alongside the Camboatá River, which receives great part of the residual residence spilling and industrial waste (Ferreira, 2007). Additionally, environmental impacts are also generated by the Technological Centre of Dangerous Residues (CENTRES), operating since 1988 and responsible for the final destination of the toxic industrial residues of large chemical companies occupying a 70,000 m^2 area. In full operation, about 30,000 m^3 of poisonous residues stored in unidentified iron drums which were buried afterwards were registered. In 1998, the Rio de Janeiro Environment Engineering Foundation (FEEMA) suspended CENTRES activities and determined the removal of all material stocked on that area. However, the environmental liability left at the place could be detected in the soil and in groundwater even 10 years after its closure (Chagas, 2013). The adjacent district, Santo Expedito, with 2 000 inhabitants at that time, registered 21 deaths by cancer up to 2007 (Santos, 2011).

Itaboraí is a 430.374 km² municipality located in the metropolitan area of the state of Rio de Janeiro with 225.263 inhabitants. Its main economic activities are agriculture, livestock and mineral extractivism, with the Rio de Janeiro Petrochemical Complex (COMPERJ) currently being built. The construction of complex began in 2008 and foresees the operation of its first refinery in 2016. It is considered the largest Brazilian and international industrial enterprise of the last decades in the petrochemical sector, aiming at refining 165.00 barrels of oil daily (Ferreira et al., 2007).

One of the main observed impacts in this is the intense workforce migration towards participating in the construction of this Complex, occupying areas that were previously used for agricultural activities, such as fruit crops (Sanchez et al., 2009). In addition, other environmental impacts are expected to occur after this Complex begins operations, such as contamination of underground waters and soil, decreases in air quality, physiochemical and biological alterations of the local terrestrial and aquatic webs, significant increases in the population, lack of essential services for the municipal district due to high demands, irregular use and occupation of the soil (“slumization”), real estate speculation and increases in local income values (Pandeff, 2009).

In fact, the municipalities that presented higher hospitalization rates due to leukaemia during the evaluated period share in common the fact of predominantly industrial activities linked to high pollutant loads released into the environment, such as oil activities, processing and recycling of materials, production of paints and plastic and production of several industrial inputs (Koh et al., 2014; Terazaki et al., 2008; Thompson et al., 2009). In addition, a significant increase in records of other activities that use high amounts of chemical substances, such as agriculture, has also been observed (Pignati et al., 2014).

The scientific literature reports several studies that demonstrate a positive association of the xenobiotics originating from these activities with a series of environmental consequences, such as contamination of air, soil and water by volatile organic compounds, such as benzene, as well as human health concerns, like increasing incidence of several pathologies, such as cancer, alterations of abnormal chromosomes that lead to

foetus malformations and even male infertility (Koh et al., 2014; Schinatter et al., 2012; Mandani et al., 2013; Xing et al., 2010). However, the inference that environmental exposure is the main driving factor of human diseases is still fragile, since individual susceptibility is considered decisive for these events (Ross and Zhou, 2010; Norppa, 2003; Nebert et al., 2013). Therefore, the evidence should not be discarded, but instead evaluated in parallel to the identification and quantification of the environmental pollutants for a full understanding of this complex cause-effect relationship.

The results obtained herein should be cautiously analysed, since data included in information systems may somehow present typing or data aggregation flaws (inclinations of information). In addition, ecological studies, allow only for the evaluation of data obtained collectively and not from individual reports, which does not allow for the accomplishment of causal inferences.

Therefore, considering only the findings of the present study, the establishment of a cause-effect relationship between exposure to chemical substances and leukaemia occurrence is not possible due to the absence of important information at the individual level, such as exposure load, family health histories, age, previous diseases or conditions and the occupation. However, studies using the ecological methodology are still relevant in generating information on population dynamics, identifying the need for new studies.

Conclusions

The construction of the concept of economic development based on the implementation of industrial technologies that modify the scenario of certain areas may cause serious damage both to the environment and to human beings, due to the unsustainable use of natural resources and high load of contamination, which can become increasingly diversified.

Corroborating this affirmative, the present study verified that cities with higher numbers of potentially pollutant industries in the state of Rio de Janeiro registered the highest hospitalization rates due to leukaemia, for both genders, such as Macaé, Queimados and Itaboraí. However, it is not possible to only attribute exposure to chemical substances as the main factor driving the occurrence of cancer, since this is the result of the sum of several causalities, such as exposure load and genetic susceptibility.

However, the present study indicates that it is possible to presume the occurrence of a significant relationship between the productive processes of the industries located in these cities and hospitalization by leukaemia, although a verified cause-effect relationship cannot be stated with the adopted delineation. Therefore, the obtained results corroborate the need for new studies focusing on the continuous monitoring and quantification of the several variables, especially benzene and other aromatic hydrocarbons that participate in the relationship between chemical exposure and the emergence of leukaemia in adults.

Conflict of Interests

The authors have not declared any conflict of interests.

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