

# Hematological Alterations Indicative of Benzene Exposure in a Vulnerable Southeastern Brazilian Population

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## ABSTRACT

Campos Elíseos, located in the Duque de Caxias municipality, in the state of Rio de Janeiro, Brazil accommodates the largest industrial complex in Latin America, comprising the second largest petrochemical company in the country (REDUC), a gas-chemical pole, a thermoelectric plant and approximately 50 other industries. Although this municipality registered the 6<sup>th</sup> highest Gross Domestic Product (GDP) in the national ranking and the 2<sup>nd</sup> highest in the state in 2015, its Human Development Index (HDI) was of 0.753, the 52<sup>nd</sup> in the state. In this context, the aim of the present study was to evaluate the vulnerability of Campos Elíseos residents regarding environmental exposure by chemical contaminants, through questionnaires and hematological analyses. The study group comprised of adults living in Campos Elíseos for at least 3 months, totaling 190 residents. All individuals stated no access to treated water or basic sanitation. About 98% of the participants stated they believe the region is polluted. A total of 33% of the sampled individuals presented altered hemograms, characteristic of certain pathologies. Most houses belonging to individuals exhibiting hematological alterations were located near the industrial region of the area, leading to the hypothesis that the hematological alterations observed herein, such as anemia, thrombocytopenia and leucopenia, alone or associated with neutropenia, may be indicative of chronic benzene exposure.

**Keywords:** Vulnerability in health; public health; environmental exposure; petrochemical industry.

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## INTRODUCTION

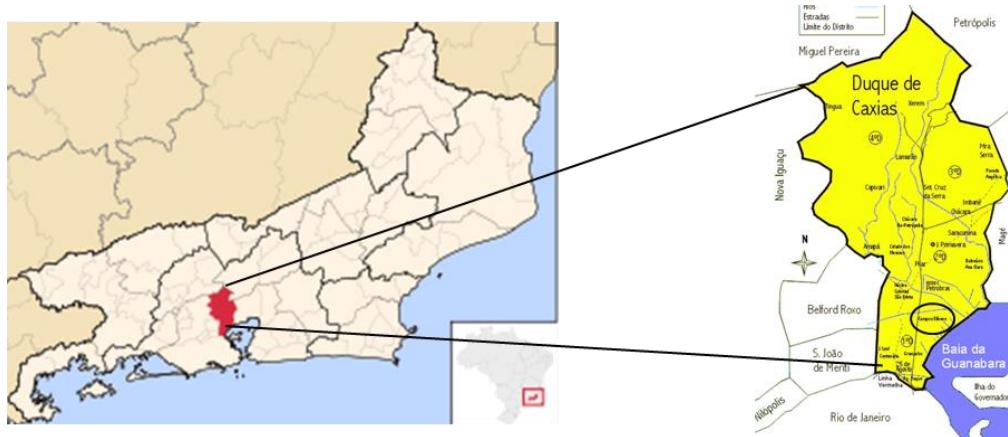
Exposure to chemicals is currently a major concern worldwide, due to the increasing number of diseases caused by these compounds in the public health system, leading to a worrying scenario regarding Public Health (Araújo, 2008).

The presence of xenobiotics in the environment is the main exposure route for the general population since these substances are present in air, food and water (Arnold et al., 2013; ATSDR, 2007; Oga, 2005).

Atmospheric contaminant concentrations vary according to their potential sources, with sites close to or surrounding different point and/or diffuse sources presenting higher contaminant concentrations (Tovalin-

Ahumada and Whitehead, 2007; Wallace, 1996; IARC, 1989). Thus, residents living or working in certain environments, such as chemical industries, gasoline stations, high-flow highways, mechanical workshops and oil exploration industries, are subject to higher environmental exposure than other population segments (Dougherty et al., 2008; Johnson et al., 2007).

The Campos Elíseos region, located in the municipality of Duque de Caxias, Baixada Fluminense, in the state of Rio de Janeiro (Figure 1), Brazil, is home to the largest industrial complex in Latin America, the Campos Elíseos Industrial Complex (PICE), comprising the second largest petrochemical company in the country (REDUC)



**Figure 1.** Representative map of the state of Rio de Janeiro, featuring the municipality of Duque de Caxias in the zoomed in map, and the Campos Elíseos region, in the circled area.

that produces naphtha and liquefied petroleum gas, among others, as fuel, in addition to a gas-chemical pole, a thermoelectric plant and about 50 other industries. The main industrial segments located in this region are the chemical, petrochemical, metallurgical, gas and plastic sectors, indicating a great diversity of products and inputs produced and consumed in the region, with benzene noteworthy as both a product and input used in several of these industries (<http://portal.baixadaon.com.br/duque-de-caxias/historia-de-duque-de-caxias-rj>). The area comprises of 26 petrochemical, transforming and thermoelectric companies, and is the second industrial center of the metropolitan region and of the State of Rio de Janeiro, accounting for 27.1% of the state production, approximately 5.2% of the companies present in the state. With costs reaching up to \$1.08 billion, the pole can produce 540 thousand tons of polyethylene annually, among other products, and its implementation has brought plastic transforming industries to the city and, consequently, the entire region (<http://portal.baixadaon.com.br/duque-de-caxias/historia-de-duque-de-caxias-rj>).

A number of chemical industries have also emerged around REDUC, several large and associated with refinery processes, such as PETROFLEX, NITRIFLEX, and other independent industries, as well as a set of medium and small companies producing resins, paints, candles, paraffin and other chemicals (<http://portal.baixadaon.com.br/duque-de-caxias/historia-de-duque-de-caxias-rj>).

Other industrial segments have also been gaining importance in the area, such as clothes production, and furniture and food industries. Thus, with the exception of the Petrobras complex, the industrial park located at Duque de Caxias is now formed by medium and small enterprises (<http://portal.baixadaon.com.br/duque-de-caxias/historia-de-duque-de-caxias-rj>).

In addition to pollution originating from the PICE,

Campos Elíseos also suffers from vehicular contamination, as it is located on the banks of the BR-040 highway, with a traffic of about 15,000 vehicles each day (Pires, 2005). According to the Awareness and Preparedness for Emergencies at Local Level (APEL-CE) Project, in case of an industrial accident at the PICE, Campos Elíseos is located within the perimeter that requires resident population displacement, i.e., an area exhibiting great vulnerability (Figure 2).

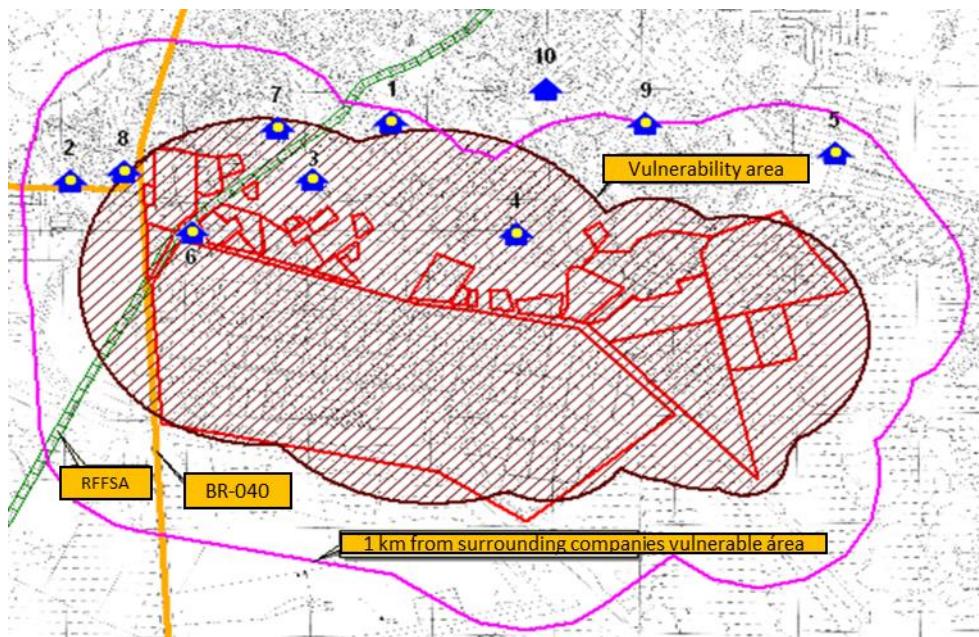
Although Duque de Caxias registered the 6<sup>th</sup> highest GDP in the national ranking and the 2<sup>nd</sup> highest of the state in 2015, it also presented an HDI of 0.753, the 52<sup>nd</sup> in the state and the 3<sup>rd</sup> worst among the neighboring municipalities, while other indicators suggest that living conditions are quite unfavorable in the entire municipality (Camaz, 2015).

Studies on population vulnerability to chemical exposure are complex and restricted, as they involve the assessment of several factors, including economic and social factors that are sometimes ignored. Published scientific studies focusing on this type of analysis at Campos Elíseos are unavailable, indicating the urgent need for the construction and definition of the actual chemical exposure scenario in the area and its effects on the health of the surrounding population.

In this context, the aim of the present study was to evaluate vulnerability to environmental chemical exposure in residents inhabiting surrounding areas and areas under the influence of the Campos Elíseos Industrial Pole, Baixada Fluminense, Rio de Janeiro, RJ, Brazil.

## METHODOLOGY

The present study was carried out at the Center for the Study of Occupational Health and Human Ecology (CESTEH), at the Oswaldo Cruz Foundations (Fiocruz). The study was approved by the ENSP Ethics Committee



**Figure 2.** Delimitation of the greatest vulnerability area and surrounding regions regarding industrial PICE accidents. 1. Marilândia; 2. Pilar; 3. Centro de Campos Elíseos; 4. Saráiva; 5. Ana Clara; 6. Vila Serafim; 7. Parque Império; 8. Nossa Senhora do Rosário; 9. Bom Retiro; 10. Parque Moderno ([http://www.apellce.com.br/mapa\\_area\\_vulneravel.php](http://www.apellce.com.br/mapa_area_vulneravel.php)).

(ENSP-no. 971.927, CAAE: 40514415.0.0000.5240), and comprised an observational descriptive exploratory study, with the description of the resident population inhabiting surrounding areas near petrochemical industries, and a convenience sampling.

The study group consisted of individuals residing up to 1,000 meters from the petrochemical complex, comprising male and female adults (age  $\geq 18$  years) from different age groups and ethnicities, living in Campos Elíseos for at least 3 months. Through an informal and individual conversation with the participants of the study, the following information was made explicit: the absence of aggregate risks in the sample collection process; the objectives and relevance of the study regarding health, and the fact that research subjects would be protected by anonymity and that the data would be treated in a confidential way. Residents who agreed to participate in the study signed a Free and Informed Consent Form, as required by the Brazilian Ministry of Health, Resolution No. 466/2012 regarding research involving humans.

A semi-structured questionnaire was applied by the researchers through individual interviews, to obtain essential information regarding chemical exposure characterization and identify of associations with minimum influence of confounding variables; define social habits throughout the day, such as food intake, air circulation inside resident homes, where residents spend most of their time; to obtain precise and quality information on relevant symptoms, for subsequent exposure-outcome association analyses, and, finally, characterize the risk to which these residents are subjected to in their home environment.

Blood samples (approximately 4 mL) were collected in vacuum tubes containing EDTA as an anticoagulant for hemogram analyses. Hemograms were performed at the Diagnostic, Teaching and Research Laboratory (LADEP) at the Germano Sinval Faria School Health Center (CSEGSF/FIOCRUZ), accredited by Joint International Commission (JCI), for hemogram analyses with Sysmex XS 1000i Analyzer.

## RESULTS AND DISCUSSION

The recruited population comprised of residents who volunteered, answered the questionnaire and provided blood samples. A total of 194 residents volunteered, but four individuals did not give satisfactory blood samples for the analysis. Therefore, the present study is comprised of a total of 190 people.

### Population profile

Women comprised the highest percentage of the sampled population (72%). Mean resident age was 55 years old, ranging from 20 to 86. Table 1 depicts the age distribution of the sampled population.

Ethnicity was self-declared during the interview. The majority (47%) of the interviewees declared themselves Brown, while about 4% did not know or did not want to fall into one of the presented categories.

Residents reported that Campos Elíseos does not have enough public schools for the entire population, and that access to vocational education is non-existent. Thus, in

**Table 1.** Population profile description.

	N=190	%
<b>Sex</b>		
Female	137	72
Male	53	28
<b>Age</b>		
Mean	54,72	
Median	56	
Minimum-Maximum (years)	20-86	
<b>Monthly Income</b>		
Mean	R\$ 1,274.08	
Median	R\$ 2.00	
Minimum-Maximum	R\$ 1- R\$ 15,000.00	
<b>Schooling</b>		
1 <sup>st</sup> to 4 <sup>th</sup> grade	40	21
5 <sup>th</sup> to 8 <sup>th</sup> grade	48	25
High school	73	38
Higher education	18	9
No schooling	10	5
<b>Employed</b>		
Yes	68	36
No	122	64
<b>Age began working</b>		
Mean	15.31	
Median	16	
Minimum-Maximum (years)	4-45	
<b>Residence time in the area</b>		
Mean	35.74	
Median	38	
Minimum-Maximum (years)	1- 78	
<b>Contact with:</b>		
Varnish/Paint		
Yes	83	44
No	68	36
Glues		
Yes	52	27

**Table 1.** Contd.

No	99	52
Cleaning products		
Yes	117	61
No	34	18
Gasoline		
Yes	35	18
No	116	61
Other solvents		
Yes	55	29
No	96	50
Smoker		
Yes	17	9
No	173	91
Passive smoker		
Yes	102	54
No	87	46
Alcohol		
Yes	131	69
No	59	31
Number of windows and doors		
Up to 3	31	16
4 to 10	147	77
Over 10	12	6
Opening frequency		
Every day	170	89
3x/week	13	7
1x/week	1	1
Less	5	3
Opening time		
0 to 4h	17	9
5 to 9h	38	20
10 to 14h	82	43
15 to 19h	18	9
20 to 24h	34	18
Electricity		
Yes	190	100
No	0	0

**Table 1.** Contd.

Water supply		
Yes	18	9
No	172	91
Garbage collection		
Yes	186	98
No	4	2
Pollution		
Yes	186	98
No	4	2
Odors		
Yes	149	78
No	38	20
Does not know	2	2
Odor characteristic		
Gases	117	61
Sewage	1	1
Not able to identify	55	29

order to obtain access to education, residents must move to other regions with vacancies or enter the private education system.

Despite this difficulty, about 38% of the respondents stated that they had attended high school, with only 6% classifying themselves as functionally illiterate or illiterate. When comparing this value to the national illiteracy percentage, Campos Elíseos presents a lower index than the general Brazilian population, of around 9% (MEC, 2017). Regarding higher education, only 9% of the interviewees had or currently have access to this degree of education, which may be related to the lack of a basic quality teaching institutions that allows students from public institutions to access universities.

Regarding occupation, about 64% of the evaluated population is unemployed, with only a small percentage retired. When questioned about their previous occupation in cases of declared unemployment, several individuals stated they worked in the petrochemical complex of the region and, due to the economic crisis, cuts in expenses and lack of qualification, lost their jobs, and until the interview, had not yet achieved a new position in the job market.

Socioeconomic conditions were evaluated by a set of variables comprising family income, home type and structural constitution, number of residents and rooms in each household.

The family income of the evaluated population was, on average, less than or equal to R\$ 1,274.00, representing two minimum wages. Most of the time, the only source of income was the retirement pay of the family patriarch/matriarch or government aid, through unemployment and social programs. The average number of residents of each household supported by such an income is four people, as reported by 33% of the study participants.

Regarding the number of rooms in each home, approximately 55% of the interviewees stated having 6 to 10 rooms, including the kitchen, bathroom, bedroom and living room. When calculating dweller density per room, the majority of households had up to 0.5 inhabitants per room, in agreement with the data from the 2010 Census for the state of Rio de Janeiro, Baixada Fluminense region and municipality of Duque de Caxias (IBGE, 2010).

Regarding home structure, 100% of the interviewees described their dwelling as masonry and 90% said they live in their own homes. Although the study area is a poor region, suffering restrictions regarding several urbanization services, no houses were built precariously with wood or cardboard remains.

Several reports regarding the performance of the public system on resident quality of life were obtained. Both electric energy and public garbage collection were

present in all residences. On the other hand, water supply by the local responsible company, CEDAE, is absent. Thus, as an alternative, the population seeks water access through the construction of artesian wells or by direct connection to pipelines that transport water intended for REDUC/PETROBRAS boiler cooling.

The source of the water consumed by Campos Elíseos inhabitants is an aggravating factor concerning population vulnerability, since boiler water and artesian wells may exhibit several physical, chemical and biological characteristics that make them unfit for human consumption (Couto, 2014; Colvara, 2009). According to Ayach et al. (2012), a serious consequence of the intake of untreated water, either through direct ingestion or when used for cooking and bathing, is a significant increase in the incidence of diseases related to the water supply that, alongside with the lack of sanitation, become a public health problem, often neglected by public authorities.

The current and previous health status of each participant was self-declared, with no need to prove the pathology. About 66% of the interviewees reported having some type of health problem, with hypertension, diabetes and thyroid changes being the most common. About 62% of the interviewees reported the absence of relevant morbidities in the previous year (2015).

A pertinent statement from participants was regarding difficulty in accessing the public health system since the district health post lacks medical care services and examination instruments according to the interviewees, and the waiting list is significant. Because of this, residents search for such services in other locations, such as Jardim Primavera. However, besides fatigue caused by population displacement and an overload in the care capacity in the regions that welcome these patients, the morbidity statistics of each district become disproportionate and may lead to a misinterpretation of the source and distribution of the disease when a health action policy is structured.

Certain social habits described in the literature as being relevant for evaluating exposure to chemical substances were questioned, such as narcotics, alcohol and tobacco consumption.

All participants reported no use of narcotic substances, with occasional alcohol consumption reported by most participants (69%). Regarding tobacco smoking, 91% of respondents said they don't smoke, but 50% reported living with or have lived with smokers in their homes.

Regarding the use of chemicals suspected of causing health damage, about 57% of the participants stated they have not made use of such substances in their home routine. However, 30% reported having presented adverse reactions after using household cleaning chemicals, in the form of contact dermatitis or more severe allergies.

Individual perception of pollution in the city was included in the study, although this is a subjective variable. However, even though this is subjective, 98% interviewees of Campos Elíseos agreed on the existence

of pollution in the area. 79% stated feeling maladies linked to the unpleasant odor present in the environment and that, in most cases, the reported pain was constantly present, similar to gases.

In an attempt to understand the exposure scenario to chemical substances present in Campos Elíseos homes, the present study addressed issues on the number of windows and doors at each house, as well as their opening frequency and how long they remain open. Such information becomes relevant regarding the knowledge of the possibility of xenobiotic circulation and concentrations in the microenvironment of each residence, increasing or decreasing the amount of inhaled toxicants (Fontes and Barros, 2009).

Around 78% of the interviewees stated having from four to 10 windows and doors in their homes, opened every day, in 90% of the homes. In most houses, doors and windows were open from 10 to 14 hours a day, closed only when the inhabitant left his/her home. Thus, high air circulation exists in most homes. This may increase exposure to toxic substances from sources outside the home, such as from the petrochemical industry, leading to high atmospheric contaminant levels. On the other hand, facilitating ventilation can minimize exposure to substances from indoor sources, such as wood-fire and cigarette smoke.

Woodstove smoke was not relevant in the present study, since 100% of the participants stated using gas only stoves. As mentioned previously, 91% of the interviewees reported not smoking, while around 50% currently or previously lived with relatives who smoked in their homes, which may contribute to chemical exposure, considering that cigarette smoking is one of the main sources of environmental exposure to toxic compounds (Tovalin-Ahumada and Whitehead, 2007).

### **Biological sample analyses**

The collected blood samples were sent to a clinical laboratory for a complete blood count, to determine the following parameters: Blood cell count, Hemoglobin, Hematocrit, MCV, MCH, MCHC (Mean Corpuscular Hemoglobin Concentration), RDW, Leukocytes, Promyelocytes, Myelocytes, Metamyelocytes, Rods, Segmented, Eosinophils, Basophils, Monocytes, Lymphocytes, Blasts and Platelets (Table 2).

Participants who presented relevant changes in blood counts were referred to medical care at the Center for Worker Health and Human Ecology (CESTEH - Fiocruz) for clinical research aiming at identifying and treating morbidities related to the detected alterations.

Approximately 33% of the interviewees presented alterations characteristic of certain pathologies. The most frequent was anemia, followed by thrombocytopenia (Table 3).

The hematological alterations observed herein can be interpreted as indicative of chronic benzene exposure, since the most frequent findings in the peripheral blood of this population, such as anemia, thrombocytopenia

**Table 2.** Description of the hematological profile of the population (N= 190).

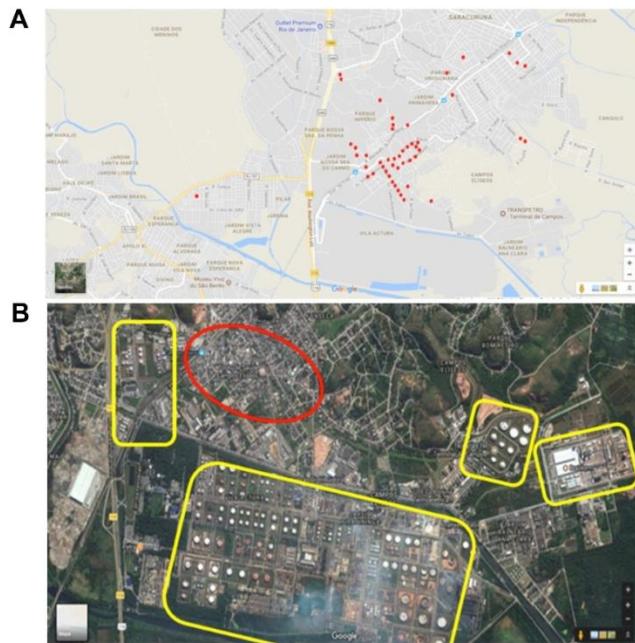
Parameters	Mean	Median	Minimum	Maximum
Blood cell count (million/mm <sup>3</sup> )	4,44	4,42	3,40	6,00
Hemoglobin (g/dL)	13,3	13,2	9,6	18,3
Hematocrit (%)	39,4	39,4	29,3	53,9
MCV (fl)	88,8	89,2	69,6	112,8
MCH (pg)	29,9	30,2	21,2	34,6
MCHC (g/dL)	33,7	33,8	25,1	36,8
RDW (%)	12,8	12,7	11,3	16,0
Leukocytes (mm <sup>3</sup> )	6298,7	6140,0	2820,0	12080,0
Promyelocytes (mm <sup>3</sup> )	0	0	0	0
Myelocytes (mm <sup>3</sup> )	0	0	0	0
Metamielocytes (mm <sup>3</sup> )	0	0	0	0
Rods (mm <sup>3</sup> )	0	0	0	0
Segmented (mm <sup>3</sup> )	3431,5	3240,0	1043,0	9420,0
Eosinophils (mm <sup>3</sup> )	219,2	154,5	0	1750,0
Basophils (mm <sup>3</sup> )	0	0	0	0
Monocytes (mm <sup>3</sup> )	418,1	402,5	157,0	4244,0
Lymphocytes (mm <sup>3</sup> )	2229,9	2214,0	881	4244,0
Blasts (mm <sup>3</sup> )	0	0	0	0
Platelets (mm <sup>3</sup> )	253826,3	235500,0	101000,0	3510000,0

**Table 3.** Hematological alterations in participants with values outside the normal range (33% of the evaluated samples), according to the Brazilian Society of Clinical Analyses.

Hematological alterations	%
Dehydration	2
Eosinophilia	13
Thrombocytopenia and Anemia	3
Anemia	41
Thrombocytopenia	17
Thrombocytopenia and Eosinophilia	2
Leukocytosis	2
Leukocytosis and Neutrophilia	3
Leucopenia	6
Leucopenia and Neutrophilia	11
<b>TOTAL</b>	<b>100</b>

and leucopenia, alone or associated to neutropenia, have been reported as the main hematological changes linked to exposure to this compounds, even at low

exposure levels (Mitri et al., 2015; Manuela et al., 2012; Wang et al., 2012; Zhang et al., 2014; Ye et al., 2015; Ruiz, 1994; D'alsacio et al., 2014). However, due to the



**Figure 4.** (A) Representative map of the addresses of participants displaying hematological alterations. (B) Satellite photo of Campos Elíseos. The region marked in red represents the locality with the highest concentration of homes belonging to inhabitants displaying hematological alterations, while regions marked in yellow indicate the existing industrial agglomerations.

multi-causal nature of these alterations, a more complete investigation of the clinical and laboratory conditions of the participants should be carried out, where a series of signs and symptoms related to intoxication by benzene;benzenism is evaluated in exposed individuals, as recommended by benzene diagnosis protocols (BMH, 2006). Any hematological change in persons exposed to benzene should be evaluated and investigated (Mitrí et al., 2015; BMH, 2006). The hematological changes observed in this study is similar to that of previous, which also reported decreases in white cell, erythrocyte and platelet counts, among other altered hematological parameters, in workers exposed to low benzene levels (1 ppm) (Lan et al., 2004; Ye et al., 2015; ATSDR, 2007; Fustinoni et al., 2012).

Eosinophilia (13%) was relevant in the present study, identified by increased eosinophils in the peripheral blood. The literature describes this hematological alteration both in individuals diagnosed with asthma and allergic diseases and in the presence of parasites, such as ascariasis. Eosinophils participate in asthma pathophysiology while fighting the parasite in ascariasis conditions (Ribeiro, 2015).

The relationship between eosinophilia and such pathologies corroborates participant statements when questioned about their health state, as the great majority complained of allergic and pulmonary diseases, such as asthma. Also, as mentioned previously, Campos Elíseos does not have access to treated water. Thus, consuming

water from sources not in accordance with microbiological quality standards for human consumption may lead to sickness caused by several types of parasites.

Participants displaying hematological alterations were selected and their addresses collected through the previously applied questionnaire. With this data, the location of each residence was plotted on a map, to ascertain whether these patients lived close to industries (Figure 3).

Certain addresses belonging to the Jardim Primavera district were also included, as they are very close to Campos Elíseos petrochemical pole (up to 1 km).

About 52% of participants displaying hematological alterations live near each other, forming an address grouping. Several large industries that both process and store petroleum products, as well as smaller industries, which, in some cases, operate illegally, are located near these homes. Thus, this is the most impacted area regarding chemical contaminants, no matter the wind direction, since the polluting source is very near, forming an industry belt. In addition, the pollution load of each industry should also be considered, which, when added up, comprises significant pollutant concentrations that may lead to deleterious health effects to the residents, as observed herein.

Several studies have evaluated population health outcomes after chemical contaminant exposure, such as hematotoxicity in the general population or in specific

populations living near petrochemical industries or in regions with a high vehicular flow or near fuel supply stations, which, theoretically, lead to higher exposure levels. However, data is still insufficient regarding the extent of the problem, and most studies evaluate biomarkers other than hematological parameters, such as Fustinoni et al. (2012).

Pelallo-Martínez et al. (2014) evaluated children residing in areas under the influence of Mexican petrochemical industries, and indicated that the distance between homes and the industries was related to changes in hemoglobin, hematocrit and blood cell counts, even at low benzene exposure levels, described as common effects in a wide range of exposure to benzene in the review carried out by Bahadar et al. (2014).

Johnson et al. (2007) compiled and evaluated several studies analyzing distinct biomarkers with a broad exposure concentration range in the general population, including not occupationally exposed children. The authors concluded that sufficient evidence exists to indicate that benzene exposure generates several health changes, including hematological alterations, from the lowest exposure level. However, the authors also indicate the need for further investigations regarding susceptibility parameters, such as metabolic polymorphisms, in order to understand how each individual generates a distinct response to the same exposure, and, thus, establish an exposure/outcome relationship for different populations.

Possible associations between the descriptive variables of the study and the results of the biological analyses were also carried out, in order to evaluate correlations between socio-environmental factors and the analyzed health outcome. However, none of the statistical analyses presented statistically significant associations, which may be justified by the small sample size.

## Conclusions

Despite the high tax revenue at Duque de Caxias, the investment policy in basic services in the district of Campos Elíseos is not prioritized in public management. Residents suffer from lack of primary resources, such as access to portable water for human consumption and primary health care. In addition, this region comprises many polluting industries, exposing the resident population to environmental contamination, resulting in several health problems.

Corroborating this statement, altered hematological profiles and homes located very near to these industries were observed herein. However, hematological alterations cannot be attributed only to exposure to chemical substances, since they are the result of the sum of several causalities, such as exposure load and genetic susceptibility.

Thus, the development of further studies that seek to understand and quantify the different variables that consolidate the relationship between chemical exposure

and different health outcomes is required. According to the present study, a *de facto* vulnerability to chemical contaminant environmental exposure at Campos Elíseos is postulated, with perceptible health problems, from the onset of disease to slight changes in non-specific clinical exams, which may be useful in establishing a direct relationship between cause and effect.

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