A comparative study of cadmium levels in blood from exposed populations in an industrial area of the Amazon, Brazil

Karytta Sousa Naka, Lorena de Cássia dos Santos Mendes, Thaís Karolina Lisboa de Queiroz, Brenda Natasha Souza Costa, Iracina Maura de Jesus, Volney de Magalhães Câmara, Marcelo de Oliveira Lima

HIGHLIGHTS
• This was the first study to show there is greater exposure to Cd in populations living near industrial areas in the Amazon.
• Blood levels of Cd showed that adults are more exposed to this contaminant in industrial areas in the Amazon.
• Human exposure to Cd was evident for individuals residing close to industrial areas in the Amazon for 2 years or more.

ABSTRACT
Chemical pollution from industrial sources is one of the main problems affecting the environment. In urban areas, the emission of toxic gases and particulates to the atmosphere can damage human health. Cadmium (Cd) is one of the most ecotoxic metals among these pollutants, even at low concentrations. In this study, environmental exposure to Cd was evaluated from the Cd blood levels (CdB) of the human populations living in two Amazonian districts. The first was Bairro Industrial (BIN), which is located next to the industrial complex in Barcarena City, while the second was Vila do Beja (VBJ), a control group located in the farthest area from industrial activities in Abaetetuba City. Sectional and comparative studies were applied for both districts. Sampling (N = 469) occurred in 2012 and 2013. Gender, age, residence time, drinking water source, alcohol consumption, and smoking were used as independent variables. CdB levels were analyzed by induced coupled plasma mass spectrometry (ICP-MS). In BIN, geometric mean and median CdB levels were 0.27 and 0.43 μg·L⁻¹, respectively (range: ≤0.03 – 17.49 μg·L⁻¹), while in VBJ these were 0.19 and 0.23 μg·L⁻¹ (range: ≤0.03 – 2.38 μg·L⁻¹). The higher CdB concentration in the blood of people from BIN was similar to levels previously found in people living near other industrial areas, and showed that the BIN residents were more exposed to Cd pollution. The studies showed the need for surveillance actions to evaluate possible routes of exposure, avoiding the future worsening of the health of the population living next to industrial areas in the Amazon.

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Keywords:
Environmental exposure
Cadmium
Toxicology
Public health
1. Introduction

Losses from or inefficiencies of industrial processes result in the emission of atmospheric pollutants or the production of hazardous wastes. Depending on the physical and chemical characteristics and mobilization capacity of these contaminants, occupational or environmental exposure of humans to them may occur (Kira, 2014). In the 1980s, large multinationals began industrial production activities in Barcarena City, Brazil, and were responsible for the release of pollutants, including toxic metals, and numerous environmental disasters in the area, such as contamination of surface and underground water bodies by kaolin processing effluents; fish death; excessive soot from industrial chimneys; rupture of ducts with acid effluents, reaching rivers; tailings leak from kaolin and bauxite processes (Nascimento and Hazeu, 2015; Lima et al., 2011). These changes modified the ecosystems and increased the health risk for the urban and traditional human populations (riverine, quilombolas, and indigenous) living in this region (Nascimento and Hazeu, 2015).

Cadmium (Cd) is a toxic and biologically non-essential metal, which is widely distributed in the Earth’s crust at trace levels (~0.1–0.5 mg kg\(^{-1}\)). This element is generally emitted into the environment (soil, water, air) from anthropogenic activities, as mining and industrial processing of ferrous and non-ferrous metals; manufacture and application of phosphate fertilizers; fossil fuel combustion, and incineration and waste disposal (Agency for Toxic Substances and Disease Registry (ATSDR), 2012). In addition, this metal tends to bioaccumulate along the food chain and may cause damage aquatic and terrestrial organisms and human health (Agency for Toxic Substances and Disease Registry (ATSDR), 2012; Kira et al., 2016). Gastrointestinal absorption is the main route of human exposure to Cd for nonsmokers, and is usually associated with the consumption of contaminated food and water, such as meat, rice, fish, shellfish, fruits, and vegetables (Kira et al., 2016; Ahn et al., 2017). Cd-containing compounds can bioaccumulate and biomagnify through the food chain. Inhalation of air in industrial environments and cigarette smoke are the main forms of lung exposure to Cd (Agency for Toxic Substances and Disease Registry (ATSDR), 2012; Ahn et al., 2017). In smoking members of the population, cigarettes represent the main route of exposure, since tobacco leaves naturally contain high Cd concentrations. Studies have shown that Cd absorption is greater by the pulmonary route compared to that by the gastrointestinal route, since about 10 to 50% of the inhaled fraction is absorbed (Centers for Disease Control and Prevention (CDC), 2012).

Cd is classified as a human carcinogen (Group 1) by the International Agency for Research on Cancer (IARC) (Kira, 2014; Kim et al., 2017). Exposure to cadmium: a major public health concern preventing disease through healthy environments, 2010). It is identified by the National Program of American Toxicology (NTP) as a carcinogenic substance, and by the United States Environmental Protection Agency (USEPA) as a probable inhalation carcinogen (Group B1) (Agency for Toxic Substances and Disease Registry (ATSDR), 2012; Centers for Disease Control and Prevention (CDC), 2012). The probable inhalation and absorption of Cd is associated with the development of lung cancer in both animals and humans (Kira, 2014; Agency for Toxic Substances and Disease Registry (ATSDR), 2012; Kim et al., 2017). Exposure to cadmium: a major public health concern preventing disease through healthy environments, 2010). Recent epidemiological studies have provided evidence that even low-level environmental exposure to this toxic metal is a risk for human health (Kira, 2014; Agency for Toxic Substances and Disease Registry (ATSDR), 2012). Low lifetime exposure may lead to renal, hepatic, skeletal, and cardiovascular damage, as well as contribute to the development of lung, breast, prostate, pancreatic, bladder, and nasopharyngeal forms of cancer (Agency for Toxic Substances and Disease Registry (ATSDR), 2012).

In the Amazon region of Brazil, few studies have assessed and demonstrated the environmental exposure of the population to Cd and its effects on the health of people living in potentially contaminated areas. The ineffectiveness of public health policies in relation to industrial activities and the diversity of interests around this issue hinder environmental management, increasing the damage to communities by contamination (Almeida et al., 2017; Lima, 2016).

Studies on the relative health of populations potentially exposed to environmental contaminants are key tools for decision-making and the implementation of strategies to promote and protect health and improve social and living conditions (Kim et al., 2017). Obtaining toxicological information associated with the epidemiological data for an exposed population is important for future health mitigation and protection actions by the public sector to avoid risks to human health. In this context, the objective of this study was to evaluate the environmental exposure of residents in the two districts in the cities of Barcarena and Abaetetuba, in Pará State, Brazilian Amazon, to Cd using human blood as biomarker. This study also assessed the associations and correlations between toxicological information and sociodemographic and lifestyle factors in these populations.

2. Materials and methods

2.1. Study design

A sectional and comparative study was carried out to evaluate human exposure to Cd from the blood levels (CdB) of people living in the Bairro Industrial (BIN) and Vila de Beja (VBJ) districts, with the latter of these being used as a control group. These areas are located within the cities of Barcarena and Abaetetuba, respectively, in northern Brazil (Fig. 1). Sampling took place between May 2012 and February 2013. This study was submitted to and approved by the Research Ethics Committee of the Evandro Chagas Institute (approval no. 0010/2009), and was carried out while following all ethical research procedures as foreseen in the Declaration of Helsinki and Brazilian legislation.

2.2. Study areas

Barcarena is a small city (1310 km\(^2\)) located in Pará State, Amazon Region, which has an estimated current population of 121,190 people and an industrial sector that integrates the aluminum and kaolin productive chains (Instituto Brasileiro de Geografia e Estatística (IBGE), 2010). Within its territory, the transformation of bauxite into alumina and alumina into aluminum ingot occur, as well as the processing of kaolin (Nascimento and Hazeu, 2015). These activities, among others, have made Barcarena the city with the highest economic growth in the region over the last decades, with a per capita income of R$ 47,864.37. Abaetetuba is a city located next to Barcarena. When compared with Barcarena, it covers a slightly larger territory (1610 km\(^2\)) and has a larger population (153,380), but its per capita income is 6 times lower (R$ 7960.05) (Instituto Brasileiro de Geografia e Estatística (IBGE), 2010).

The selection of these study areas was motivated by geopolitical factors and previous reports of human health risks from consumption of water contaminated by toxic metals and inhalation of particulate matter (soot) emitted by industries (Instituto Evandro Chagas (IEC), 2003; Instituto Evandro Chagas (IEC), 2007; Instituto Evandro Chagas (IEC), 2010). The population that lives in BIN is located next to (within ~30 m of) the location where industrial kaolin processing occurs (Instituto Brasileiro de Geografia e Estatística (IBGE), 2010). There have been previous reports about BIN that indicated that there is atmospheric particulate emission from boiler chimneys and possible contamination of groundwater used for human consumption from decantation basins of liquid effluents from the kaolin processing in this district. In contrast, the people living in VBJ were selected as a control group because this district is relatively distant (~10 km) from where these anthropogenic activities occur (Instituto Brasileiro de Geografia e Estatística (IBGE), 2010). At the time of this study, there were no
previous reports indicating that VBJ is an exposed population. It is also important to know that the wind direction in BIN is northeast, contrary to VBJ, located southeast of the district (Companhia Docas do Pará (CDP), 2016). In both districts occurs drinking water is available from two sources: 1) distribution network with groundwater abstraction; 2) artesian or.amazon type wells.

2.3. Epidemiology

The participants included in this study were individuals of both sexes, who had lived in BIN or VBJ for a period equal to or longer than 2 years. This study involved the application of epidemiological inquiry and biological material (blood) sampling. Participation was voluntary, and after all individuals signed the Free Consent Form (TCLE) an epidemiological form was applied to the sociodemographic and lifestyle data obtained.

2.4. Blood sampling and analysis of Cd

Intravenous blood samples (5 mL) were collected, stored in tubes with anticoagulant, and frozen. The determination of Cd was performed in a clean room environment (classification 1000) by induced coupled plasma mass spectrometry (ICP-MS).

After thawing and homogenization, the blood samples were diluted 1:20 with nitric acid 65% (HNO₃) (TEDIA), Triton X-100 solution 10% (SIGMA-ALDRICH) and internal standard solution of 100 ppb (FLUKA). A blood aliquot of 200 μL was inserted together with 200 μL of 0.1% (v/v) Triton X-100 solution and 1% (v/v) HNO₃ into a 15 mL polytetrafluoroethylene (PFA) tube. The solution was then shaken using a microprocessed Vortex tube stirrer (QUIMIS), and then after resting for 5 min, 200 μL of an internal standard solution of 100 ppb (Au and Y) was added. The solution was then homogenized again and adjusted to a final volume of 4 mL with 1% (v/v) HNO₃ solution. Subsequently, the solution was homogenized and centrifugated for 10 min. After centrifugation, the supernatant was removed and transferred to a polypropylene tube to be analyzed, following methods adapted from the Kira, Sakuma, and Gouveia method (Kira et al., 2014).

All blood samples were analyzed in duplicate, with five readings taken per sample. The limit of quantification (LOQ) was 0.063 μg·L⁻¹, and the limit of detection (LOD) was 0.019 μg·L⁻¹ for Cd. For quality control, the analytical determination method for Cd was validated using the Seronorm® Trace Elements in Whole Blood Lyophilized Level 1 and Level 2 (SERO) Certified Reference Materials (Kuno et al., 2013).

2.5. Statistical analyses

Cd concentrations below the LOQ were adjusted to half of the LOQ (LOQ/2) to perform statistical analyses (Kira et al., 2016). The distribution of blood metal content data was not normal according to the Kolmogorov-Smirnov test. The Grubbs test was applied to verify the presence of outliers. The arithmetic mean (AM), geometric mean (GM), median, and amplitude of Cd concentrations were therefore the descriptive values used in analyses of metal levels.

Non-parametric Mann-Whitney and Kruskal-Wallis tests were used to compare Cd concentrations between two groups and three or more
3. Results

Study participants included 484 subjects, but 15 blood samples did not have sufficient volume at the time of analysis. In addition, 2 samples with CdB levels of 19.43 μg L⁻¹ (G = 8.48, p < 0.001) and 6.65 μg L⁻¹ (G = 10.06, p < 0.001) were found in BIN and VBJ, respectively, which were identified as outliers and thus excluded from statistical analyses.

Table 1 shows the descriptive characteristics of the study population. This population was comprised of 469 individuals, 181 living in BIN and 288 in VBJ. The majority were female (54.2%), belonged to the age group between 20 and 59 years old (48.2%), had residence times of ≥10 years (58.2%), had a general network as their source of drinking water (56.3%), did not consume alcoholic beverages (67.0%), and did not smoke (84.4%). Comparing the distributions of these characteristics between the districts, statistically significant differences were observed between districts in their age group (p = 0.049), residence time (p < 0.001), and alcohol consumption (p < 0.001).

The results of statistical analyses correlating Cd blood levels and epidemiological variables are presented in Table 2. For people living in the BIN district, the geometric mean (GM) and median CdB were 0.27 and 0.43 μg L⁻¹, respectively (range: ≤0.03–17.49 μg L⁻¹), while for those in the VBJ district these were 0.19 and 0.23 μg L⁻¹ (range: ≤0.03–2.38 μg L⁻¹), respectively. When comparing the median levels of CdB between the two districts, it was observed that the values found in BIN were twice as high as those found in the VBJ population (control), with this difference being statistically significant (U = 22,746.5, p = 0.010). The highest levels of CdB were observed in BIN (17.49 μg L⁻¹), and these were approximately eight times higher than the maximum value found in VBJ (2.38 μg L⁻¹).

The GM value of the CdB concentrations, as well as the median and amplitude, was higher in the BIN population for all of the exposure variables studied compared to those in the VBJ population (control). Fig. 2 shows the median levels of CdB distributed according to the different levels of these variables.

Regarding gender, in BIN the median level of CdB was higher in females (0.46 μg L⁻¹; range: ≤0.03–5.61 μg L⁻¹) compared to that in males (0.38 μg L⁻¹; range: ≤0.03–17.49 μg L⁻¹), whereas in VBJ these
values were similar for men and women (0.24 and 0.22 μg·L⁻¹, respectively) (Table 2).

For age, the highest median levels of CdB were found in adults (20 to 59 years old) in comparison to the other age groups, with adults presenting levels of 0.47 μg·L⁻¹ (range: ≤0.03–9.33 μg·L⁻¹) in BIN and 0.25 μg·L⁻¹ (range: ≤0.03–2.38 μg·L⁻¹) in VBJ. The values found in BIN adults were significantly different from those observed in VBJ adults, with median levels in BIN being almost twice as high as those in VBJ (U = 5016.0, p = 0.012).

For those individuals with residence times in the study area between 6 and 9 years, median CdB levels were significantly different between the two districts (U = 893.5, p = 0.025), with BIN residents having an approximately three times greater CdB than VBJ residents.

Regarding the source of drinking water, in BIN there was a significant association between CdB levels and drinking water source (U = 2477.5, p = 0.001), with there being an almost 3 times greater CdB in those individuals consuming water from the general network compared to those who consumed well water. In VBJ, there was also a significant association between CdB levels and drinking water source (U = 8050.0, p < 0.001), with individuals who consumed well water having CdB levels approximately 1.5 times greater than those that consumed water from the general network.

Regarding lifestyle, higher median levels of CdB were significantly associated with individuals that did not consume alcohol (U = 10,241.0, p = 0.008), with the difference in these levels being higher in the BIN population (0.46 μg·L⁻¹; range: ≤0.03–9.33 μg·L⁻¹) than in the VBJ one. For smoking, CdB levels in BIN smokers were almost twice as high as those of smokers in VBJ (U = 441.5, p = 0.043). This statistically significant difference between districts was also observed among nonsmokers (U = 16,805.5, p = 0.040) (Table 2). It was also observed that a greater proportion of adults were smokers in the studied districts, with 75.0% (N = 18/24) and 51.0% (N = 25/49) of adults being smokers in BIN and VBJ, respectively, while 45.2% (N = 71/157) and 46.9% (N = 112/239) of adults were nonsmokers (Fig. 3A–B).

Fig. 2. Median levels of Cd in the blood (μg·L⁻¹) of the resident population in Bairro Industrial and Vila de Beja according to (A) gender, (B) age group, (C) residence time, (D) source of drinking water, (E) alcohol consumption, and (F) smoking habit.
Further, when considering CdB levels both smokers and nonsmokers in BIN presented higher levels compared to those in VBJ (Fig. 3C–D). Fig. 4 shows the comparison of CdB levels between adults (≥18 years old) according to their smoking habit in the studied districts, as well as in the adult populations of other countries.

The Spearman correlations between CdB levels and age and residence time for BIN residents were weak and non-significant (rho = 0.063, p = 0.395 and rho = −0.020, p = 0.792, respectively). In VBJ, age and the length of residence also showed weak and non-significant correlations (rho = −0.046, p = 0.435 and rho = −0.081, p = 0.172, respectively) with CdB levels.

4. Discussion

The Cd concentration in blood is a widely accepted index used for environmental biomonitoring of exposure to toxic metals, which indicates recent exposure to this toxicant (Agency for Toxic Substances and Disease Registry (ATSDR), 2012; Sun et al., 2016). Population studies in several countries have stated that metal concentrations in the general population tend to be more significant when there are known sources of exposure, such as in populations residing near industrial or contaminated areas (Agency for Toxic Substances and Disease Registry (ATSDR), 2012; United Nations Environment Programme (UNEP), 2013; Environmental Protection Agency (EPA), 2013). In the present study, the evaluation of Cd concentrations in blood was reported for the first time in a general population living next to an industrial area in the State of Pará, in the northern Amazon Region of Brazil. When compared to previous studies of populations not exposed to Cd in other countries, the levels found herein in the BIN (N = 181, GM = 0.27 μg·L⁻¹) and VBJ (N = 288, GM = 0.19 μg·L⁻¹) districts were low, as they were below those found in Canada (GM = 0.35 μg·L⁻¹) (Canada and Health Canada, 2010), the United States (GM = 0.38 μg·L⁻¹) (Centers for Disease Control and Prevention (CDC), 2015), and Italy (GM = 0.53 μg·L⁻¹) (Forte et al., 2011). This suggests that the population of the present study has low Cd exposure compared to no exposed populations in other countries (Table 3).

In a previous study involving 1125 adult blood donors in five Brazilian states, including the State of Pará, the AM CdB of the general population evaluated was 0.40 μg·L⁻¹ (Nunes et al., 2010), and presented CdB levels similar to those found in VBJ (AM = 0.43 μg·L⁻¹) and about half of those found in BIN (AM = 0.81 μg·L⁻¹). The GM of CdB levels in the BIN district (N = 181, GM = 0.27 μg·L⁻¹) was higher than that observed in a general population exposed to Cd in the State of Pará.
of São Paulo (N = 1324, GM = 0.19 μg L−1) (Kira et al., 2016), whereas in VBJ (N = 288, GM = 0.19 μg L−1) the GM of CdB levels was 3 times higher than that found in a previous study of an adult population in the State of Paraná (N = 889, GM = 0.06 μg L−1) (Lopes et al., 2017). This comparison suggests that the population of VBJ, which is located relatively far away (~10 km) from the industrial area in BIN, present levels of CdB similar to those found in other Brazilian populations that are not exposed to industrial pollutants, but quite different from those in BIN, whose Cd levels suggest a pattern of increased environmental exposure to contamination associated with closer proximity to industrial areas. In the Amazon, the results of a previous study of an adult population in the State of Acre (Freire et al., 2015) (N = 1183; GM = 0.09 μg L−1, median = 0.18 μg L−1, AM = 0.30 μg L−1) were well below those found in BIN in this study (N = 181, GM = 0.27 μg L−1, median = 0.43 μg L−1, AM = 0.81 μg L−1), and slightly lower than those observed in the VBJ district (N = 288, GM = 0.19 μg L−1, median = 0.23 μg L−1, AM = 0.43 μg L−1). Although the population examined in the present study covered all age groups, the BIN district again showed much higher levels of CdB when compared to the results of other studies in the same region.

The area of residence was significantly associated with CdB levels in the present study (p = 0.009) because higher levels of cadmium in the blood were recorded in the BIN population than in the VBJ one. This shows that residents in the vicinity of industrial enterprises are more exposed to Cd, which may be related to either geographical differences, sources of exposure, or both. For more than two decades, industrial kaolin processing activities have been conducted in Barcarena. The presence of these activities generated major environmental disasters both in BIN and in other districts of the city, resulting in considerable contamination by industrial pollutants in rivers, drinking water, and soils, as well as the discharge of soot, contributing to increased CdB (Medeiros et al., 2016). A study conducted in China (Li et al., 2014) also showed that individuals residing near industrial areas had elevated levels of CdB.

In BIN, mean levels of CdB were higher in males, which was similar to findings previously reported in China (Li et al., 2014) and Brazil (Kira et al., 2016). When comparing the districts, a significant difference was observed between median CdB levels in males in VBJ and those in BIN (p = 0.029). Compared to other studies of men exposed to industrial pollutants, CdB levels in men in BIN (GM = 0.28 μg L−1) were lower than those observed in Korean men (GM = 1.14 μg L−1) (Hong et al., 2014) and two-fold higher than those of men exposed to Cd contamination in São Paulo (GM = 0.15 μg L−1) (Kira et al., 2016). The differences in Cd concentration from men in this study to Korean men may be related to occupational activity, dwelling time in the exposed area, and differences in age ratio. In addition, studies report high Cd concentration in rice, the staple diet of Asian populations, including Koreans (Eunha et al., 2006; Moon et al., 1995). Comparing with the São Paulo study, the differences may be caused by the fact that BIN men consume more cigarettes and alcohol (in this study, in BIN, 58.3% of smokers and 63.4% of alcohol consumers were men), contributing to increased levels of Cd (Lopes et al., 2017; Lee et al., 2016; Gan et al., 2008).

Children constitute a more vulnerable group to environmental pollutants due to the characteristics of body development (Kira et al., 2016). In this study, children considered exposed (in BIN) presented slightly higher levels of CdB than non-exposed ones (in VBJ), similarly to findings of a study carried out in industrial areas of China (exposed children: GM = 1.93 μg L−1; non-exposed children: GM = 1.07 μg L−1) (Pan et al., 2018). In another study conducted in the Chinese population, median levels of CdB in children (<12 years of age) were 0.19 μg L−1 (United Nations Environment Programme (UNEP), 2013), which is equal to the values found in this study. In adolescents, the values found in this study were higher than those reported in São Paulo (Kira et al., 2016) (GM = 0.30 versus 0.17 μg L−1, respectively). In Brazil, Kira et al. (Kira et al., 2016) derived reference values (RV) for children (0.2 μg L−1) and adolescents (0.6 μg L−1) from São Paulo. Compared with the levels of Cd in the present study, 48.1% (N = 38) and 35.8% (N = 39) of children and adolescents, respectively, were above these RVs. In adults, GM and median CdB values (0.30 and 0.47 μg L−1, respectively) were three and two times higher than the values reported by Freire et al. (Freire et al., 2015) in an adult population of Acre, Brazil (0.09 and 0.18 μg L−1, respectively).

Cd tends to accumulate in the blood with age, resulting in a higher blood Cd concentration in the elderly (Kira et al., 2016). However, in the present study, CdB levels in the elderly did not increase with age. CdB levels in BIN elderly (GM = 0.23 μg L−1) were lower than values obtained in elderly exposed in Korea (GM = 1.26 μg L−1) (Hong et al., 2014). This difference may be related to the proportion of participants and longer residence time in Korea (>20 years) than in the present study. Comparing with RVs reported in Italy (GM = 0.56 μg L−1) (Forte et al., 2011), BIN values were also lower, as compared to a study in Greece (GM = 0.68 μg L−1) (Sakellari et al., 2016). According to Alfvén et al. (Alfvén et al., 2002), the elderly have an approximately 3 times higher risk of bone mineral density loss when the levels of CdB are above 1.1 μg L−1. In the present study, 6 elderly patients presented levels above 1.1 μg L−1.

Herein, it was observed that after only 2 years of living in the area, Cd was found in the blood of the population and remained present over time, providing evidence of chronic human exposure to Cd, but at low concentrations. Although residence times in BIN tended to be longer than those in VBJ (Table 1), in the latter district the exposure to metal is lower due to the absence of sources of exposure in its vicinity. It was shown that residing in the BIN district for between 6 and 9 years resulted in CdB levels significantly higher than those in VBJ (p = 0.0251), but there was a decline in metal levels in individuals residing in BIN for 10 years or more, which contrasts with other studies reporting increasing levels of metal over time (Forte et al., 2011). These results corroborate the use of blood as a biomarker sensitive to recent exposure, since the highest levels were found in individuals resident in the area for

### Table 3

<table>
<thead>
<tr>
<th>Country, year</th>
<th>N</th>
<th>Population</th>
<th>AM</th>
<th>GM</th>
<th>Median</th>
<th>Reference</th>
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</table>

AM: Arithmetic mean; GM: geometric mean; NR: not reported.
In this study, the source of drinking water was significantly associated with blood levels of Cd in both BIN \((p \leq 0.001)\) and VBJ \((p \leq 0.001)\). In BIN, residents who consumed water from the general grid showed higher levels of CdB. This fact can be explained by the fact that the population’s water supply comes from two community wells \((-50 \text{ m deep})\) located next to the kaolin processing industrial plant, and built by the company itself in agreement with the Federal Public Ministry, which is characterized as a system of groundwater pumping without any treatment. In addition, groundwater analyzed in previous years in Barcarena already presented values of CdB higher than that recommended by Brazilian legislation \((\text{Instituto Evandro Chagas (IEC), 2007})\). This suggests that residents of BIN may be experiencing chronic exposure to CdB by consuming water contaminated with CdB due to flaws in conventional industrial waste treatment processes. It should be noted that the consumption of contaminated water with low levels of CdB over a long period can cause renal damage and bone fragility \((\text{Agency for Toxic Substances and Disease Registry (ATSDR), 2012})\).

In VBJ, a significant association between CdB levels and well water consumption was observed, even though this area is considered one with no evidence of anthropogenic sources of CdB. This indicates that the population is exposed to some environmental source of CdB in the region, which should be investigated through further monitoring and studies evaluating the water quality in the area.

In the present study, median CdB levels in those who did not drink alcohol were higher in BIN than in the VBJ district \((0.46 \text{ versus } 0.20 \mu g \cdot L^{-1}, \text{respectively})\), demonstrating that CdB levels did not appear to be influenced by alcohol consumption, which is consistent with results from studies observed in Italy \((\text{Forte et al., 2011})\) and China \((\text{Chen et al., 2019})\). This result may be explained by the prevalence of non-alcoholic drinkers being higher in BIN than in the control area, and by reports that alcohol consumption may reduce CdB body load by inhibiting CdB absorption and increasing urinary excretion \((\text{Grasmick et al., 1985})\), influencing the highest total blood levels of metal in this group. Comparing with studies from other countries, the BIN results found in alcohol drinkers were different from exposure studies conducted in South Korea \((\text{Lee et al., 2016})\), as south koreans who drank alcoholic beverages had higher CdB levels than those who did not consumed.

When considering smoking, it is known that the CdB levels in smokers are 2 to 3 times higher than those in individuals who do not smoke \((\text{Freire et al., 2015}; \text{Faro et al., 2014})\). According to our findings, BIN and VBJ smokers had CdB levels almost 2 times higher than non-smokers, similar to the results of other studies \((\text{Sun et al., 2016}; \text{Faro et al., 2015}; \text{Sakellari et al., 2016}; \text{Batáriová et al., 2006}; \text{Seo et al., 2015}; \text{Moberg et al., 2017})\). These results confirm smoking as a factor that increases CdB body contamination and are consistent with those reported in national \((\text{Takeda et al., 2017})\) and international \((\text{Pan et al., 2018}; \text{Chen et al., 2019}; \text{Choi and Park, 2017})\) studies.

Comparing the districts, the median levels of CdB in the smokers of BIN were significantly higher than those in the smokers of VBJ \((p = 0.043)\). This difference was also found among nonsmokers from both districts \((p = 0.040)\). According to the RV derivatives for adult \((\geq 20 \text{ years old})\) smokers and nonsmokers in the city of São Paulo \((\text{GM: 0.8 and 0.4 } g/L^{-1}, \text{respectively})\) \((\text{Kira et al., 2016})\), 25.0\% \((N = 6)\) of the adult smokers \((N = 24)\) and 39.0\% \((N = 77)\) of the nonsmokers \((N = 157)\) were above the RV in this study, indicating a potential health risk. In addition, CdB levels in adult smokers and nonsmokers showed lower levels of BIN than in exposed populations in Korea \((\text{Hong et al., 2014})\), but these may increase over the years, while in VBJ levels remained well below the values reported in studies of non-exposed populations. This suggests that the exposure of adult smokers to CdB in the VBJ area is well below that in other countries \((\text{Fig. 4})\).

CdB levels found in residents of industrial areas were higher than the control group and may increase over time of exposure. In the medium and long term these results can have public health impacts in the region. Thus, public health policy should address the effects of these exposures, as there is evidence that long-term exposure to CdB can cause kidney damage, cardiovascular, hematological, skeletal changes, and cancers \((\text{Agency for Toxic Substances and Disease Registry (ATSDR), 2012}; \text{Kim et al., 2017}; \text{Centers for Disease Control and Prevention (CDC), 2015}; \text{Seo et al., 2015}; \text{Maruzeni et al., 2014}; \text{Mezynska and Brzóska, 2018})\).

The limitations of this study were the relative scarcity of data on blood cadmium levels in relation to some of the characteristics of the study population, and that information on dietary habits was not included in the analyses but may influence the concentrations of CdB in the blood \((\text{Takeda et al., 2017})\). However, the strengths of this study were that it used blood, in which CdB has a half-life of 3–4 months making it the most valid biomarker for recent exposure to cadmium \((\text{Lee et al., 2016})\), and the rigor and quality of the analytical procedures used.

5. Conclusions

This study provided data on the levels of CdB in a Brazilian general population residing in the Amazonian region and evaluated possible sources of human exposure. The levels of CdB were significantly higher in residents of the industrial area compared to those in the control area. In addition, greater exposure to CdB was observed in adults, in individuals residing in the area for 2 years or longer, in those whose source of drinking water was the general network, and in the vicinity of industrial areas. These results show that such factors increase the risks of adverse effects on human health and should not be neglected in the study of contaminant exposure.

In conclusion, the metal concentration remained relatively low in both studied areas herein compared with those reported in other studies. The results of this study provide relevant toxicological information on the levels of this toxic metal in the Amazon and will contribute to future comparisons in epidemiological studies of human exposure to CdB in Brazil and other countries. In Brazil, there are no known levels of environmental exposure to metals, and there would be a need for surveillance actions that include systematic monitoring and control, especially in populations located in industrial production areas, has emerged. Further studies should be performed to evaluate cadmium exposure, including potential environmental sources of exposure such as drinking water, soil and atmospheric air and other population groups living near industrial areas such as children, women of childbearing age, pregnant women and elderly whose data are very limited.

CRediT authorship contribution statement


Declaration of competing interest

The authors declare no conflict of interest.

Acknowledgments

The authors thank the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brazil (CAPES), the Term of Adjustment of Conduct (TAC-Barcarena), and the Evandro Chagas Institute for funding and laboratory support for the research.
Financial support

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brazil (CAPES) - Finance Code 001.

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