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ORIGINAL ARTICLE

Anemia in Indigenous youth from an Amazonian community in Brazil exposed to mercury during a major environmental impact from gold mining activities

Anemia em jovens indígenas de comunidade da Amazônia brasileira expostos ao mercúrio durante grande impacto ambiental das atividades de mineração de ouro

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Abstract

Background: Mercury (Hg) is a highly toxic substance that can affect various body systems, including the hematopoietic system. However, information on its impact on humans remains limited. This study evaluates the potential association between anemia and Hg exposure among Indigenous children and youth from an Amazonian community in Brazil. **Objective:** To evaluate the association between anemia in indigenous children and adolescents and exposure Hg. **Method:** Secondary data analysis from a cross-sectional study comprising 95 Indigenous children and youth from an Amazonian community in Brazil. Descriptive analysis was conducted on the population's characteristics, eating habits, pathologies, and Hg concentrations in hair samples. Logistic regression was applied to assess the association between anemia and Hg exposure, adjusted for potential confounders. **Results:** Of the 95 individuals evaluated, 48.4% presented anemia, while median hair Hg levels were notably high (14.6 µg/g; IQR: 12.3–19.2 µg/g), even at the lowest recorded concentration (6.8 µg/g). A significant association was identified between anemia and Brazil nut consumption (OR=0.27; 95% CI=0.04-0.98), and between anemia and hair Hg levels ≥10 µg/g (OR=1.22; 95% CI=0.99-1.97). **Conclusion:** The prevalence of anemia in this population is severe, and elevated hair Hg levels were observed. These findings suggest a preliminary link between high Hg exposure and the developed anemia. Considering the complexity of anemia in this population and its potential long-term health impacts, further research is necessary to elucidate the role of Hg exposure in this condition.

Keywords: anemia; mercury; South American Indigenous peoples; Amazonian ecosystem.

Resumo

Introdução: O mercúrio é uma substância altamente tóxica que pode afetar qualquer Sistema, inclusive o hematopoiético. Este artigo avalia a possível associação entre anemia e exposição ao mercúrio em jovens indígenas de uma comunidade da Amazônia brasileira. **Objetivo:** Avaliar a associação entre anemia em crianças e adolescentes indígenas e exposição ao Hg. **Método:** Análise de dados secundários de estudo

Study conducted at Instituto de Estudos em Saúde Coletiva, Universidade Federal do Rio de Janeiro (UFRJ) – Rio de Janeiro (RJ), Brazil.
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transversal envolvendo 95 jovens indígenas de uma comunidade amazônica brasileira. Realizada análise descritiva das características da população e dos níveis de mercúrio no cabelo. Empregada regressão logística para avaliar a associação entre anemia e exposição ao mercúrio em modelo ajustado. **Resultados:** Dos 95 avaliados, 48.4% apresentavam anemia e a mediana dos níveis de mercúrio no cabelo estava elevada (14.6µg/g; IIQ:12.3-19.2µg/g), mesmo na menor concentração (6.8µg/g). Observada associação entre anemia e ingestão de castanha do Pará (OR = 0.27; IC 95% = 0.04-0.98), bem como entre anemia e nível de mercúrio no cabelo ≥10 µg/g (OR = 1.22, IC 95% = 0.99-1.97). **Conclusão:** A prevalência de anemia foi classificada como grave e os níveis de mercúrio no cabelo foram elevados. Evidências preliminares de possível relação entre níveis elevados de mercúrio e anemia foram estabelecidas. Uma vez que o cenário no qual anemia se desenvolve nessa população é complexo e suas consequências podem ser devastadoras, novas pesquisas que avaliem o papel da exposição ao mercúrio devem ser realizadas.

Palavras-chave: anemia; mercúrio; índios sul-americanos; ecossistema amazônico.

INTRODUCTION

Anemia is a significant public health issue, contributing to 8% of the global disease burden[1]. Children and young people are particular at risk because of critical exposure windows, with iron deficiency being the most common cause[1,2]. However, the role of chemical exposure in anemia should not be overlooked, as over 300 million individuals under the age of 20 in Latin America are exposed to a complex range of environmental hazards[3].

Mercury (Hg) is one such hazard, ranked among the ten most toxic non-radioactive substances by the World Health Organization (WHO)[4]. Mercury can disrupt organ function by inducing oxidative stress, mitochondrial damage, lipid peroxidation, protein degradation, and apoptosis[5]. Because of its high cellular proliferation and metabolic rate, the hematopoietic system is particularly vulnerable to toxic substances; however, reports on this effect in humans, especially regarding anemia, are scarce[6-8].

Its primary sources of Hg exposure are the consumption of contaminated fish and shellfish, as well as occupational settings, such as gold mining[9]. Notably, artisanal and small-scale gold mining (ASGM) is the leading anthropogenic source of Hg pollution, responsible for 37% (410 to 1400 tons/year) of global emissions into air and water. An estimated 10 to 19 million miners, including five million women and children, are directly involved with ASGM[10]. In the Amazon region, illegal ASGM has been growing stability since the 1980s, with significant environmental and human health consequences[11].

Brazil's Indigenous population comprises 305 different ethnic groups, predominantly located in the northern region (38.2%)[12]. Sai Cinza, one of the 435 Indigenous lands, is home to the Munduruku ethnic group, who reside in relatively isolation around the central Tapajós River basin, a major gold mining area in the Amazon Basin[13,14]. Their economic is based on cassava monoculture, fishing, hunting, gold mining, and a small-scale trade in wood, Brazilian nuts, and latex[14,15]. Fish is their primary protein source, and while cassava flour and Brazil nuts are common in their diet, vegetable consumption is insufficient[14].

Most Indigenous communities in the Amazon face poor sanitation and limited or no access to healthcare. Consequently, there is a high prevalence of malnutrition and infectious-parasitic diseases, characteristics of underdeveloped regions with very low average income[16].

This study reports on anemia, as determined by complete blood count (CBC), and its association with total Hg levels, measured in the hair of children and adolescents from the Sai Cinza Indigenous community in the state of Pará, Brazil, using an available dataset.

METHODS

Study design

This is an observational study with secondary data analysis from surveys conducted in the first seven days of November 1995 by the Environmental Section of the Evandro Chagas Institute (SAMAN/IEC) in the Sai Cinza Indigenous community, Munduruku Reserve, in the southwest of the state of Pará, Brazil. The selected period is relevant because it reflects the environmental impact of the continued use of mercury (Hg) in gold mining for over a decade, mainly expressed through fish contamination[15].

The procedures used in this study, conducted by SAMAN/IEC, were described in Santos et al.[14] and consisted of prior contact with the community 30 days before the field research, signing informed consent, and administering a questionnaire covering age, sex, occupation, dietary habits, and morbidity. Additionally, a medical exam was performed. For hair collection, at least 100 strands were taken from different areas of the scalp, cutting 1 cm from the scalp with non-oxidizable steel scissors, and storing them in white envelopes at room temperature until analysis at the IEC Toxicology laboratory. A validated and reliable method was used for total Hg analysis in hair[17]. This method involved homogenization, exogenous decontamination, and physical treatment of the samples, as follows: 1 to 10 mg of hair was placed in a 50 ml volumetric flask, to which 2 ml of HNO_3-$HClO_4$, 5 ml of H_2SO_4, and 1 ml of H_2O were added sequentially, and then digested at 230–250 ºC on a hot plate for 20 minutes. After cooling, the digested sample solution was made up to 50 ml with Hg-free water. Finally, an aliquot of the sample solution was introduced into the Hg-3500 mercury analyzer (Brand), consisting of a Hg vapor generation system and a flameless atomic absorption spectrometer, which completes the determination of a sample in one minute and has a detection limit of ~0.5 ng as Hg[17].

This study was approved by the Research Ethics Committees of UFRJ and IEC under CAAE protocols 84387418.7.0000.5286 and 84387418.7.3001.0019, respectively.

Description of the variables

The diagnosis of anemia (outcome variable) was made by analyzing hemoglobin concentration and was dichotomized according to reference values for sex and age as follows: children aged 6 to 59 months, <11 g/dL; 5 to 11 years, <11.5 g/dL; 12 to 14 years, <12 g/dL; non-pregnant women (≥15 years of age), <12 g/dL; pregnant women, <11 g/dL; and men (≥15 years of age), <13 g/dL[18]. The hair Hg levels—one of the biomarkers of human exposure to this metal (exposure variable)—were divided into three categories: <6.0 µg/g, 6.0–9.9 µg/g, and ≥10 µg/g. These categories correspond to the WHO's guideline, which sets a limit of 6.0 µg/g for those who consume fish regularly and states that levels of 10 µg/g or above may increase the risk of neurological defects[19]. The WHO classification for children (0 to 10 years incomplete) and adolescents (10 to 19 years) was used[20]. The variable for acute infectious diseases was based on clinical diagnosis and included cystitis, gastroenteritis, otitis, pharyngitis, pneumonia, and pyoderma. There were no reports of the flu, hepatitis, or tuberculosis. High fish consumption was defined as more than three servings per week[21]. Brazil nut consumption was considered a proxy for selenium status, as this oilseed is the largest natural source of this element. Brazil nuts from the central Amazon have the highest selenium concentration and bioavailability[22].

Statistical analysis

Categorical variables were expressed as proportion, and continuous variables were expressed as median and interquartile range (IQR), after verifying the non-normal distribution using the Kolmogorov-Smirnov test and histograms. The Chi-Squared or Fisher's exact test was used to evaluate the relationship between anemia and categorical variables, such as sex, age group, enteroparasitosis, and acute infections. The U Mann-Whitney test was used to compare median hair Hg concentrations between sex, pregnancy, age group, enteroparasitosis, acute infections, malaria, Brazil nut consumption, and anemia. A significance level of 5% ($p \leq 0.05$) was adopted for all statistical analyses. Univariable and multivariable logistic regression were used to assess the association between anemia and total hair Hg levels, controlling for gender, age group, enteroparasitosis, acute infections, malaria, and Brazil nut consumption. Odds ratios (ORs) with 95% confidence intervals (CI) are reported. The selected data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 21 (Chicago, IL, USA).

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RESULTS

Table 1 shows the sociodemographic characteristics of the 95 Indigenous individuals studied. There was a predominance of females (67.4%), with a female-to-male ratio of 2:1, and 4.2% were pregnant. The mean age was 11.4 years (SD ±3.2), with a minimum of seven years and a maximum of 19. Of these, 33.7% were children and 66.3% were adolescents. None reported using hair dyes. Regarding occupation, 80% had at least one: 61.2% were students and 16.8% were peasants.

Table 1. Sociodemographic characteristics of the children and youth Indigenous population from Sai Cinza (n=95)

Characteristics	Number	(Percentage)
Gender		
Male	64	(67.4%)
Female	31	(32.6%)
Pregnancy	4	(4.2%)
Age: years (mean)	11.4	-
Age group		
Childhood	32	33.7
Adolescence	63	66.3
Occupation	76	(80%)
Student	60	(62.1%)
Peasant	16	(16.8%)
Other occupation	51	(53.7%)
Hair Hg levels (µg/g): median (IQR)	14.6 (12.3-19.2)	-
Fish consumption	14 x / week	(100%)
Brazil nut consumption	1 to 6 x day	(80%)
Enteroparasitosis	94	(98.9%)
Acute infections	16	(16.8%)
Asthma	3	(3.2%)
Malaria	87	(91.6%)
Anemia	46	(48.4%)

All 95 individuals presented elevated hair Hg levels, with a median of 14.6 µg/g (IQR=12.3-19.2), a maximum value of 90.4 µg/g and a minimum of 6.8 µg/g. Cassava flour and fish were the staples of their diet. Vegetable consumption was considered insufficient. Brazil nut consumption was frequent, varying from one to six nuts per day among 80% of individuals. Mean fish consumption, evaluated by the weekly intake rate, was 14 times, equivalent to 1.5 kg, with a balance between carnivorous and non-carnivorous species (p=0.10). Enteroparasitosis was observed in 98.9% of the individuals, and 83.1% had polyparasitism. Only one individual (1.1%) did not undergo fecal analysis. Diarrhea was reported by 16.8%. The most common parasite groups were helminth nematodes (roundworms), represented by *Ascaris lumbricoides* (85.3%), and protozoa, represented by *Entamoeba histolytica* (75.8%).

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Clinical examination revealed three individuals with asthma (3.2%) and 16 with acute infections (16.8%). The majority (91.6%) reported at least one episode of malaria. All participants provided blood samples for complete blood count (CBC), and 48.4% were found to have anemia, of which 43.5% were children and 56.5% were adolescents (p=0.05). In the bivariate analysis of anemia's association with other variables, significant relationships were observed between anemia and Brazil nut consumption, malaria, Hg levels, and age group ($p \leq 0.05$), as shown in Table 2.

Table 2. Relationship between anemia and selected variables in the children and youth Indigenous population of Sai Cinza (n= 95)

Parameters	Anemia		
	Number (%)		
	No	Yes	*p*-value*
Hair Hg levels (µg/g)			
6.0-9.9	4 (8.2)	3 (6.5)	0.05
≥ 10.0	45 (91.8)	43 (93.5)	
Gender			
Male	12 (24.5)	19 (41.3)	0.08
Female	37 (75.5)	27 (58.7)	
Age group			
Childhood	12 (24.5)	19 (41.3)	0.05
Adolescent	37 (75.5)	26 (56.5)	
Brazil nuts consumption			
No	5 (10.2)	14 (30.4)	0.01
Yes	44 (89.8)	32 (69.6)	
Enteroparasitosis			
No	8 (16.3)	7 (15.6)	0.92
Yes	41 (83.7)	38 (84.4)	
Acute infections			
No	42 (85.7)	37 (80.4)	0.49
Yes	7 (14.3)	9 (19.6)	
Malaria			
No	1 (2.0)	7 (15.2)	0.02
Yes	48 (98.0)	39 (84.8)	
Asthma			
No	48 (98.0)	44 (95.7)	0.52
Yes	1 (2.0)	2 (4.3)	

*Chi-Squared Test

No association between hair Hg levels and other variables was observed in the bivariate analysis, as shown in Table 3. However, the median values of this biomarker in hair were consistently well above the WHO's limit for frequent fish consumers.

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Table 3. Descriptive statistics of total hair mercury levels in the children and youth Indigenous population of Sai Cinza (n= 95)

Parameters	Total hair Hg levels (µg/g)				p-value*
	Median	IQR	Minimum	Maximum	
Gender					
Male	15.5	12.3-21.3	10.2	53.3	0.06
Female	14.4	12.4-18.6	6.8	90.4	
Age range					
Childhood	14.8	12.0-18.9	9.7	38.7	0.57
Adolescence	14.5	12.5-9.3	6.8	90.4	
Brazil nut consumption					
No	13.2	11.2-15.8	10.0	30.8	0.17
Yes	15.5	12.7-19.3	6.8	90.4	
Enteroparasitosis					
No	15.8	12.3-21.8	9.7	53.3	0.90
Yes	14.5	12.3-19.2	6.8	90.4	
Acute infections					
No	14.4	12.3-17.8	6.8	90.4	0.62
Yes	18.6	13.1-27.3	10.7	53.3	
Malaria					
No	14.0	11.6-18.8	10.0	30.8	0.41
Yes	15.0	12.4-19.2	6.8	90.4	
Asthma					
No	14.5	12.3-19.2	6.8	30.8	0.62
Yes	15.9	15.0-17.5	15	90.4	
Anemia					
No	14.5	12.3-18.5	6.8	53.3	0.85
Yes	14.8	12.2-20.5	9.0	90.4	

*U Mann-Whitney test

The multivariate analysis revealed an association between anemia and Brazil nut consumption (OR=0.27; 95% CI=0.04–0.98), as well as between anemia and total hair Hg levels ≥10 µg/g (OR=1.22; 95% CI=0.99–1.97), although the latter showed borderline statistical significance (Table 4).

DISCUSSION

The prevalence of anemia (48.4%) reported in this study aligns with the findings of the First Brazilian National Survey of Indigenous People's Health and Nutrition, which recorded an overall prevalence of 51.2%, with regional differences ranging from 41.06% in the Northeast to 66.40% in the North[23]. Two other studies analyzing Brazilian data found similar results: a systematic

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Table 4. Logistic regression analysis of anemia in the children and youth Indigenous population of Sai Cinza (n= 95)

Parameters	Anemia			
	Univariate model		Multivariate model	
	OR	CI 95%	aOR*	CI 95%
Hair Hg levels (μg/g)				
6.0-9.9	1		1	
≥ 10.0	1.27	0.98-1.72	1.22	0.99-1.97
Gender				
Male	1		1	
Female	0.46	0.19-1.11	0.41	0.16-1.06
Age group				
Childhood	1		1	
Adolescence	0.42	0.18-1.01	1.27	0.33-4.93
Brazil nut consumption				
No	1		1	
Yes	0.26	0.09-0.80	0.27	0.04-0.98
Enteroparasitosis				
No	1		1	
Yes	1.06	0.35-3.20	1.24	0.36-4.23
Acute infections				
No	0.69	0.23-2.02	1.11	0.31-4.03
Yes	1		1	
Malaria				
No	1		1	
Yes	0.12	0.01-0.98	0.24	0.02-2.84
Asthma				
No	0.46	0.04-5.23	0.29	0.02-3.97
Yes	1		1	

*Adjusted model for all variables

review on the burden of anemia among Indigenous populations reported prevalence rates ranging from 86.1% among infants aged 6-24 months to 40.7% for children aged 6-120 months, while an updated meta-analysis showed prevalence rates as high as 66.5% among slum and Indigenous communities[24,25]. It is worth noting that these studies often focused on children under five years of age, which may explain the differences observed, as our study primarily included adolescents.

Nevertheless, we observed a significantly higher prevalence of anemia among the Indigenous children and youth population of Sai Cinza compared with the general young population in Brazil. The national survey that evaluated anemia in non-Indigenous children under five years of age reported a prevalence of 20.9%, with regional differences ranging from

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10.4% in the North to 25.5% in the Northeast[26]. These results are consistent with other studies worldwide, which also found marked differences in anemia prevalence between Indigenous and non-Indigenous populations[24].

Our data confirm the importance of anemia as a public health issue, as it can lead to debilitating health consequences. These include impaired physical growth and development, increased susceptibility to infections, and reduced physical capacity in children and youth. Furthermore, the persistence of anemia can impair cognitive function and reduce economic productivity in adulthood[26]. In addition, the hemoglobin levels found in this study categorize anemia as severe, given that its prevalence exceeds 40%[18].

Anemia has multifactorial causes, including both nutritional and non-nutritional factors. Iron deficiency is the most common nutritional cause worldwide, particularly among children, accounting for about half of all cases. Elevated rates of anemia in developing countries are mainly driven by socioeconomic factors related to food insecurity (malnutrition) and infections associated with poor sanitation and lack of access to safe water[16,24,27]. Enteroparasitosis and malaria are examples of infectious diseases that impose a heavy burden on children, especially in populations subject to social inequities, such as Indigenous communities, which experience significant disparities in the social determinants of health[24].

In countries where childhood anemia prevalence is high, each additional risk factor is crucial and must be addressed[27,28]. The fact that over 300 million children under 20 years of age in the Caribbean and Latin America are exposed to a complex array of environmental threats, often coexisting with other anemia risk factors, warrants further investigation[3,29]. However, few studies have addressed the combined effects of environmental and socioeconomic factors on anemia[30]. While chemicals such as benzene and lead are classically linked to anemia, a small body of evidence in humans points to an association between Hg exposure and anemia, especially with elemental and inorganic forms[6-8]. More recent studies have reported an association between anemia and methylmercury (MeHg)[29,31-33]. Two of these studies involved children and youth populations, one of which was Indigenous[29,31].

A study conducted with 83 Indigenous children under 12 years of age near an ASGM site in the Peruvian Amazon—a population very similar to ours—found median total hair Hg levels well below our results (1.18 μg/g, range: 0.06-9.70 μg/g) and an inverse association between total Hg and hemoglobin (β=–0.14 g/dL; p=0.04), providing preliminary evidence that MeHg exposure increases the likelihood of anemia in high-risk settings[29]. Another study evaluated 194 adolescents, aged 11-18 years, from two fishing communities in the Colombian Caribbean and found mean hair Hg levels below the WHO's limit (1.10 ± 0.07 μg/g), with a negative correlation between mean corpuscular hemoglobin concentration and hair Hg levels (r=–0.162; p=0.024), suggesting that blood parameters may be affected by Hg even at low levels of exposure[31].

In contrast, this study revealed a concerning pattern of Hg exposure, with a median level at least twice the WHO's limit for frequent fish consumers. The probable primary source of Hg exposure was the dietary intake of contaminated fish, due to the prolonged presence of ASGM nearby. We also found an association between anemia and total hair Hg levels ≥10 μg/g (OR=1.22, 95% CI=0.99–1.97), although this result showed borderline statistical significance. This finding emerged in a high-risk context for anemia development, within a particularly vulnerable population of Indigenous children and youth, characterized by a high prevalence of enteroparasitosis, malaria, and alarmingly elevated hair Hg levels.

There is increasing evidence that chemicals rarely act in isolation concerning toxic effects. These effects may result from interactions with other environmental factors, such as diet, nutritional status, exposure to other chemicals, genetic makeup, and the individual's developmental stage[34].

Regarding diet, we observed a negative association between anemia and Brazil nut consumption (OR=0.27; 95% CI=0.04–0.98), suggesting a protective role of selenium (Se), which has already been reported in the literature[5,13]. Brazil nut consumption serves as a proxy for Se status, as nuts are the largest natural source of this element, particularly those from the central Amazon, which have the highest Se concentration and bioavailability (mean of 58.1 ±3.0 μg

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Se/g)[22,35]. Selenium is primarily involved in metabolic pathways that regulate redox potential. It plays a biological role as an essential cofactor for proteins such as thioredoxin reductase, glutathione peroxidase, and selenoproteins. In contrast, Hg disrupts intracellular redox homeostasis by binding to the selenium site on these proteins. This interaction is a key feature of Hg toxicity, although it is complex, depending on the dose, target organ, and forms of Hg and Se. Selenium's role in reducing Hg toxicity may be multifaceted, including facilitating the demethylation of organic Hg to its inorganic form, generating an insoluble and inert inorganic Hg complex, reducing Hg absorption from the gastrointestinal tract, redistributing Hg to less sensitive target organs, replenishing Se stores, and restoring selenoprotein activity, thereby reestablishing intracellular redox homeostasis[5].

In principle, the natural occurrence of heavy metals does not pose an additional risk to ecosystems or living organisms[36]. The problem now lies in the additional burden from anthropogenic activities, such as gold mining and deforestation, which increase emissions of dioxin, lead, and Hg[37]. Additionally, another source of lead for this population may be the consumption of manioc flour, their primary carbohydrate source, which seems to be linked to environmental factors determined by local geology and soil composition, rather than by metal plates used in the roasting process[38]. This metal causes anemia, interferes with iron kinetics, and could increase the risk of anemia in the Hg exposure scenario[29].

Lastly, the current state of knowledge about genetic makeup suggests its potential involvement in an individual's susceptibility to Hg exposure, as indicated by variations in Hg levels and the resulting toxic effects[39,40]. The study of gene-environment interactions, through the analysis of polymorphisms, has been used to explain how genes involved in the glutathione metabolic pathway, which regulates the antioxidant system, can influence Hg toxicokinetics. Loss of enzyme activity (glutathione S-transferase – GST) and its association with increased Hg levels and greater susceptibility to toxic effects have been reported[40]. Moreover, chronic exposure to an agent could induce a long-term epigenetic process in susceptibility history, allowing for a transition to a chronic pathological state[39,40]. In Brazil, the frequency of the GSTM1 null genotype was reported as 26% among the Indigenous population of the state of Mato Grosso and 0% among the Munduruku villagers[41].

Finally, the developmental stage of the individual places children and youth in a particularly vulnerable position because of their critical exposure windows to toxicants. Compared to adults, they have a higher potential for adverse health effects, as they are still developing, have immature detoxification mechanisms, and are exposed to higher levels of toxicants because of differences in metabolism and behavior[2].

The role of MeHg in the development of anemia presents biological plausibility, based on reports of bone marrow hypoplasia described in the pathological analysis of Minamata disease cases and on its chemical properties, which include the induction of eryptosis due to oxidative stress, hemoglobin dysfunction related to competition for the iron-binding site, and the exacerbation of folate and vitamin B12 deficiency by inhibiting the enzyme methionine synthase[29,42].

This study has some limitations. First, both the original and current research are cross-sectional, making it impossible to infer causality. Additionally, any identified associations may be challenging to interpret, given the absence of a control group of non-exposed Indigenous individuals. Furthermore, the original study was not designed to test for a relationship between Hg and anemia, resulting in gaps such as the morphological classification of anemia (normocytic, microcytic, or macrocytic) and the hemoglobin content of red blood cells (normochromic or hypochromic), as well as an assessment of its causes. Our effect estimates could be improved by testing genetic hemoglobin disorders and measuring iron kinetics, vitamin B12, folate, and inflammatory status. Similarly, the role of other substances, such as lead, which was not evaluated, may have influenced the results. As lead interferes with iron kinetics and causes anemia, it could increase the risk of anemia in an Hg exposure setting.

This study was valuable in establishing preliminary evidence of a possible relationship between Hg exposure and anemia in a unique population, contributing to existing research[29,31-33]. Given the significantly high burden of anemia among Indigenous populations, it holds considerable public health importance, especially for children and youth, as the short- and long-term consequences can be irreversible. The context in which anemia develops in this population is complex, involving multiple coexisting risk factors. With the rapidly increasing load of toxic substances, such as Hg from areas near gold mining, along with other risk factors like inadequate diets, infectious and parasitic diseases, and chronic conditions, the situation faced by this population is highly concerning. Therefore, further research investigating the role of chemical exposure in anemia development, particularly in developing countries, is urgently needed.

AUTHOR CONTRIBUTIONS

ASV: Conceptualization, Investigation, Methodology, Formal analysis, Writing – original draft, Project administration. ASES: Methodology, Formal analysis. CIRFA: Investigation, Writing – review & editing. IRJ: Data curation, Writing - review & editing. RRL: Methodology, Formal analysis. VMC: Conceptualization, Investigation, Supervision, Writing – review & editing, Project administration.

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