Mercury levels and neurological clinical presentations in the exposed population of Chocó-Colombia

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Resumen

Título: Niveles de mercurio y presentaciones clínicas neurológicas en la población expuesta del Chocó- Colombia*.

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Palabras clave: Mercurio, ambiental, paraocupacional, neurotóxico, Colombia

Descripción

Introducción: El mercurio (Hg) es un elemento altamente tóxico que representa un importante problema de salud pública, ya que afecta los ecosistemas y la salud humana. Entre las condiciones más destacadas se encuentran las alteraciones del sistema nervioso. El diagnóstico a través de laboratorios es costoso y de difícil acceso. El objetivo fue estimar la asociación entre los niveles de Hg en cabello y las presentaciones clínicas neurológicas más prevalentes.

Materiales y métodos: Se realizó un estudio transversal en Chocó, Colombia. Se midieron niveles de Hg en cabello proximal, se realizó cuestionario y valoración médico neurológica. Se utilizó lógica difusa para transformar los signos/síntomas según el grado de severidad y realizar agrupaciones sindromáticas. Se utilizó la regresión de Poisson de varianza robusta para explorar las posibles asociaciones entre los síndromes y los niveles de Hg. Se utilizó el software estadístico STATA versión 14.

Resultados: Para este estudio se incluyeron 167 participantes, el 85,63% son mujeres, con una mediana de edad de 47 años y el 41,10% son analfabetos. En el análisis múltiple de cinco síntomas, memoria(D), concentración(B), visual(G), vértigo(E) debilidad para realizar actividades(J), conformaron tres cuadros clínicos estadísticamente significativos: DEG RP=1.13 (IC95% 1,04-1,24), BDE PR=1,08 (IC95% 1,05-1,23), DGJ PR=1,08 (IC95% 1,01-1,17).

Conclusión: Este estudio identifica tres síndromes sintomáticos que se observan en individuos que forman parte de un grupo poblacional con exposición moderada y baja. Estos resultados dependen del contexto sociocultural de la región y funcionan como un sistema de vigilancia de salud pública basado en la comunidad.

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Abstract

Title: Mercury levels and neurological clinical presentations in the exposed population of Chocó-Colombia*.

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Keywords: Mercury, environmental, paraoccupational, neurotoxic, Colombia.

Description

Introduction: Mercury (Hg) is a highly toxic element that represents a major public health problem, since it affects ecosystems and human health. Among the most prominent conditions are alterations of the nervous system. Diagnosis through laboratories is expensive and difficult to access. The objective was estimate the association between Hg levels in hair and the most prevalent neurological clinical presentations.

Materials and methods: A cross-sectional study was carried out in Chocó, Colombia. Hg levels were measured in proximal hair, a questionnaire and neurological medical evaluation were carried out. Fuzzy logic was used to transform the signs/symptoms according to the degree of severity, and to make syndromatic groupings. Robust variance Poisson regression was used to explore possible associations between syndromes and Hg levels. The statistical software STATA version 14 was used.

Results: For this study, 167 participants were included, 85.63% are women, with a median age of 47 years and 41.10% are illiterate. In the multiple analysis of five symptoms, there was memory(D), concentration(B), visual(G), vertigo(E) weakness to perform activities(J), they formed three statistically significant clinical pictures: DEG RP=1.13 (95%CI 1.04-1.24), BDE PR=1.08 (95%CI 1.05-1.23), DGJ PR=1.08 (95%CI 1.01-1.17).

Conclusion: This study identifies three symptom syndromes that are observed in individuals who are part of a population group with moderate and low exposure. These results are dependent on the sociocultural context of the region and works as a community-based public health surveillance system.

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Introduction

Mercury (Hg) is an element of the periodic table that can be highly toxic; it is in the group of heavy metals. It is found in elemental (Hg^0), organic and inorganic form (Hg^{2++} and Hg^{2+}) which causes various interactions in the environment (Syversen y Kaur, 2012; Risher y DeWoskin 1999). It is usually in liquid form and is highly volatile at room temperature; these vapors are dangerous for humans since the main route of absorption is respiratory. Hg crosses most cell membranes and can cause poisoning with different severity levels (Syversen y Kaur, 2012; Risher y DeWoskin 1999; Clarkson, 2002)

Toxicodynamics and toxicokinetics of Hg vary according to its form of presentation, and this determines the different alterations in health (Syversen y Kaur, 2012). The adverse effect will depend on the routes of exposure, the length of time, the amount of Hg, time of exposure onset, and individual factors (Bose-O'Reilly, et. al., 2017). Inorganic Hg can cause gastrointestinal, renal, and autoimmune disorders (Syversen y Kaur, 2012). Organic Hg, especially methylmercury, has been studied for its effects on human health, mainly neurological alterations, since in this form it has a great affinity for the cells of central nervous system (Syversen y Kaur, 2012). In general, Hg has adverse effects on nervous, dermatological, renal, and gastrointestinal systems (Risher y DeWoskin 1999; Bose-O'Reilly, et. al., 2017).

In the world, Hg has generated massive poisonings derived from industrial activities. The most known was reported in Minamata, Japan, in 1956, where mercury was poured into the sea, which caused bioaccumulation and biomagnification in the aquatic food chain ending in the ingestion of methylmercury by humans, other mammals and birds. This caused health alterations such as: ataxic gait, instability in the hands, blurred vision, olfactory and gustatory alterations, hearing impairment, dysarthria, somatosensory alterations, and psychiatric disorders. This type of clinical manifestation received the name of “Minamata disease” (Minamata, Sakai y Okabe, 1975). Another major secondary Hg poisoning was reported in Iraq from 1971 to 1972 following consumption of homemade wheat bread contaminated with a methylmercury fungicide, resulting in multiple poisonings and deaths in several regions of the country (Epstein, et al. 1969).

In Latin America, exposure to Hg represents a major public health problem, mainly because of mining, that uses this element as an amalgamator for gold extraction (inorganic mercury). This can cause health problems among those who use this element in their work activities, and the population environmentally exposed to water, fish consumption, food grown in the region and atmospheric exposure (organic mercury) (Junior, et al., 2017).

In the history of Colombia there are two important environmental health events related with Hg exposure. The first one occurred in the only Hg extraction mine that existed in the country. "La Esperanza" mine located in Aránzazu, Caldas, active between 1948 and 1974 when it was closed due to financial and health problems among workers (Valencia, David y Soto, 2016). Second, the Hg spill in the bay of Cartagena discovered in 1975, which exposed concentrations higher than allowed; fortunately, the conditions of the sea floor did not allow the conversion of elemental to organic mercury. This prevented the biochemical processes that lead to inclusion in the food chain and thus avoided a possible environmental catastrophe (Ministerio de Minas y Energía - Unidad de Planeación Minero Energético, Universidad de Córdoba, 2014).

1. Approach to the proble

Currently, and from some decades before, the Hg used in Colombian gold mining comes mainly from Mexico and Peru; its commercialization is illegal, which makes it difficult to control (Rubiano, 2018; Boris, 2020). This fact explains why chronic exposure continues to occur in occupational and environmental contexts related with gold mining (Rubiano, 2018; Boris, 2020). During decades, Colombian laws related to the import and use of Hg have been poorly regulation, and government strategies to mitigate the impacts caused by the use of Hg were insufficient. However, in recent years actions have emerged to reduce the impact on ecosystems and the health of the population (Casas, et. al., 2015). In this context, the Santander´s population has become involved in socio-environmental conflicts derived from the planned mining activities in the Santurbán wasteland, which has generated debate on government strategies (El Espectador, 2020; Ministerio de Ambiente y Desarrollo Sostenible, s.f.).

However, the departments that mainly continue to use Hg for the extraction of precious metals are Antioquia, Chocó, Córdoba, Bolívar, Guainía, Cauca, Amazonas and Santander. These departments generate the greatest release of Hg in the ecosystems and place Colombia as the third country with the most Hg contamination after China and Indonesia. This highlights an important environmental and health problem associated with this metal (Epstein, et al. 1969; Casas, et. al., 2015; Tirado, et. al., 2020; Mesquidaz, Negrete y Hernández, 2013; Olivero, Mendonza y Mestre, 1995; Mireya, et. al., 2018). The department of Antioquia is the largest contributor to Hg concentrations in air, especially in the municipalities of Segovia, Remedios, Zaragoza, El Bagre and Nechí (Cordy P, et al., 2011). Currently, in Colombia the use of Hg mining is prohibited in accordance with the law 1658 od 2013, with the aim of reducing Hg levels in ecosystems and exposures in populations (Ley 1658, 2013).

Studies carried out at the national level show the problems caused by Hg use, due to the pollution of different ecosystems and health problems among the exposed population, which have been reported in accordance with what has been evidenced in other populations. These include the mining population of Bolivar, where symptoms such as nausea, headache, mouth lesions, metallic taste, memory loss and irritability were reported (Olivero, Mendonza y Mestre, 1995). In Antioquia tremors were reported in hands, eyelids, tongue and lips, memory and sleep loss, headache, kidney damage, nasal irritation, severe depression, anxiety, insomnia, decreased visual acuity, and neuropsychological alterations (Tirado, et. al., 2020; Muñoz-Vallejo y García-Ardila, 2012). In Guainía they identified physical fatigue, memory impairment, decreased labor productivity, tremor and insomnia (Idrovo, et al., 2001).

In the department of Santander, one of the most representative studies on neurotoxicity was carried out in the 1990s in a chronically exposed population on Caratá River, whose main economic activity was gold mining. Greater prevalence of epilepsy, extrapyramidal diseases, peripheral neuropathies and cognitive disorders was found. Therefore, epilepsy, peripheral neuropathies and migraine may be related to Hg exposure; extrapyramidal diseases, especially tremors seem to be the most associated with chronic intoxication (Pradilla, et al., 1992). Likewise, other cases have been shown as irregularities in the menstrual cycle associated with Hg; without being found, alterations such as: abortion (Rodríguez-Villamizar, et. al., 2015), kidney damage (Rodríguez, et. al., 2016) or autoimmune disease (Sánchez, et. al., 2015), contrary to what was reported in another research.

In relation to the above problem, Chocó is one of the main departments with use of Hg in mining. Being also one of the richest in natural resources in Colombia and whose population, composed predominantly of Afro-Colombians, has as one of its main economic activities the mining of precious metals, each year up to 24,500 kg of gold is extracted in this department (Gutiérrez-Mosquera, et al., 2018). Consequently, this population has been studied to determine the impact on ecosystems and human health. Symptoms such as headache, memory loss, tremors; less often hand hardening, mood swings, hemopathies, joint pain and insomnia have been described (Gutiérrez-Mosquera, et al., 2018). Given this problem, the present study will explore the association between Hg levels and neurological clinical presentation in a population exposed to environmental and occupational Hg in Chocó, Colombia.

2. Research Question

Is there an association between the levels of Hg in hair and the neurological clinical presentations identified in the Colombian population of Chocó?

Is it possible to group, from medical semiology, the neurological syndromes derived from chronic Hg poisoning?

3. Study hypothesis

The levels of Hg found in hair are associated with the neurological clinical presentations of the population of Chocó. Colombia

From semiology, neurological signs and symptoms derived from chronic Hg intoxication can be associated with neurological syndromes.

4. Justification

Hg is a highly toxic element that can become a major problem for ecosystems and human health. Despite policies focused on decreasing the use of this element, it is still used in mining for gold extraction worldwide (Salazar-Camacho, 2017). In Latin America, Hg has been used for the extraction of precious metals since the 16th century till present (Nriagu, 1994). It is believed that the use of Hg began by Europeans after their arrival on the continent, since studies carried out on pre-Columbian samples describe levels below the level of detection in hair samples (Idrovo, et. al., 2002). Since then, these levels have been reported to increase in the environment, mainly in the last two centuries; this coincides with the "gold rush" period that the region has had, especially in Brazilian Amazon (Nriagu, 1994). Currently, the techniques used by ancestral mining continue to be used by the most vulnerable communities.

On the other hand, mining areas have become one of the main economic sources for various regions and the economic development of Colombia. Likewise, various sectors have been encouraged to continue this practice for the extraction of gold given the economic benefits generated by its high cost at the international level (Boris, 2020; Ramírez, 2015). However, mining continues to use Hg for gold extraction due to the low price and its high profitability. Currently, the main difficulty to control the use of this metal is the illegal traffic by groups outside the law (Ministerio de Minas y Energía - Unidad de Planeación Minero Energético, Universidad de Córdoba, 2014; Rubiano, 2018 ; Boris, 2020; Ramírez, 2015).

Research carried out in the national territory has shown high levels in biological, human and animal samples; also health problems, both in those exposed at the occupational level and in the inhabitants who present environmental exposure (Tirado, et. al., 2020; Mesquidaz, Negrete y Hernández, 2013; Olivero, Mendonza y Mestre, 1995; Mireya, et. al., 2018; Gutiérrez-Mosquera, et al., 2018). Among the health problems reported by exposure to Hg, both in mining workers and the population living in the mining area, the alterations in the nervous system stand out. Neurological and neuropsychological impairment is described, caused mainly by occupational exposure to Hg vapors, among the symptoms reported are: headache; alterations of visual-spatial, thinking, sleep and concentration; loss of memory, attention, motor coordination, fatigue; and behavioral disorders such as irritability, depression and anxiety (Tirado, et. al., 2020; Mesquidaz, Negrete y Hernández, 2013; Olivero, Mendonza y Mestre, 1995). This symptomatology has been found more frequently among mining workers and fishermen, the latter perhaps explained by exposure to contaminated water sources and the consumption of fish with high Hg concentrations.

The health effects generated by exposure to Hg in these mining regions of Colombia have been addressed from various approaches. However, despite that there have been multiple studies on this subject, few reports of adverse health effects focused on neurological signs and symptoms beyond the description of these in exposed populations exist. Therefore, this study evaluated the possible association between Hg levels in biological samples and neurological clinical presentations of the population exposed to Hg in the department of Chocó, Colombia, seeking to identify from semiology the neurological syndromes derived from chronic Hg poisoning.

5. Objectives

5.1 General objective

Estimate the association between Hg levels in hair and the most prevalent neurological clinical presentations in the population of Chocó, Colombia.

5.2. Specific objectives

Demographically describe the population participating in the study.

Describe the type of Hg exposure of the participating population.

Identify neurological clinical conditions in the population exposed to Hg.

Estimate the prevalence of neurological clinical presentations.

Characterize from the semiology the neurological signs and symptoms of the population under study.

6. Theoretical framework

6.1 Context of Hg in mining

Gold mining using Hg as an amalgam is a 3,000-year-old technique (Global Mercury Partnership, s.f.); however, apparently not used on the American continent until the 16th century when European colonizers used it for the extraction of precious metals (Gutiérrez-Mosquera, et al., 2018; Malm, 1998). Globally, Hg pollution has increased mainly since industrialization, causing concentrations in the environment to increase by two to five times in the last two centuries.

Currently, Hg is used for gold extraction, due to its profitability, despite the environmental, social and public health problems that this entails (Olivero, Mendonza y Mestre, 1995; Mireya, et. al., 2018). This element is used to extract approximately 15% to 20% of gold worldwide (PlanetGOLD, s.f.; Global Mercury Partnership, s.f.), and generates more than 2000 tons of Hg each year, which are mostly released into the environment, causing pollution in ecosystems and health alterations in living beings among humans (Global Mercury Partnership, s.f.).

Hg mining is carried out in about 76 countries around the world, being more frequent in Latin America, Africa and Asia (OMS, 2017). By 2010, Latin America emitted 15% of Hg globally, finding that gold mining with Hg is practiced in at least 12 countries in the region, mainly in the Andean and Amazonian countries. By 2010 the region emitted 263 tons of Hg, of which 90% was emitted in South American countries, and whose artisanal or small-scale mining activity accounts for 71% of the total emission in the region (OMS, 2017; America y Region, s.f.).

In the same context, what was found in Colombia describes that historically mining departments present difficulties for control, given the illegality of the use of mercury, the economy, violence, groups outside the law, and exacerbated by the lack of regulations and planning (Casas, et. al., 2015). These populations have been described as immersed in vulnerable situations such as: poverty, location in remote or rural areas, few work alternatives, low educational level configuring themselves as factors that predispose to continue the use of Hg in gold mining. Compounding this problem is the fact that most of these activities are carried out informally, with limited use of mechanical tools and personal protection elements (OMS, 2017).

Consequently, the populations of the mining areas are exposed to different forms of Hg, on the one hand, miners are exposed to elemental Hg via respiratory airways in the process of extraction of precious metals (Syversen y Kaur, 2012); while the general community more frequently to organic Hg; as a result of the biomethylation of elemental Hg, discarded in water sources during mining activities and introduced to the food chain by means of fish and marine mammals until reaching the human being. (Syversen y Kaur, 2012; Myers, 2000; Clarkson, Magos y Myers, 2003). That is why some people, such as mining workers, can present double exposure, occupational with elemental Hg and environmental with organic Hg as inhabitants of these sites.

6.2. Mining and use of Hg

In the gold mining process with Hg the following steps are employed: extraction of the minerals, processing, crushing, amalgamation, burning and refining. In this order of ideas, the Hg is used in the last three steps. First, in amalgamation the elemental Hg forms an alloy with gold, which requires between 3 to 50 units of Hg for each unit of gold that is recovered from this process.

Second, the amalgam is subjected to high temperatures so that the Hg evaporates and separates from the gold, this process is usually carried out in the open without actions for its adequate elimination. Third, in the refinement the gold obtained from the previous step is porous, whereby it is heated again to remove impurities and remove Hg residues that are still adhered (OMS, 2017; Myers, 2000; Programa de las Naciones Unidas para el Medio Ambiente, 2015; Esdaile y Chalker, 2018 Palacios-Torres, Caballero-Gallardo y Olivero-Verbel, 2018).

6.3 Clinical Manifestations

Clinical manifestations derived from Hg intoxication mainly compromise the nervous, renal, reproductive, immunological, gastrointestinal and dermatological systems (Rodríguez-Villamizar, et. al., 2015; Bernhoft, 2012; Cordier, Deplan, Mandereau y Hemon, 1991). However, these manifestations are varied and depend on multiple factors, among which stand out: the forms of Hg (organic or elemental), the time of exposure (acute or chronic) or concentrations (high, moderate or low) (Malm, 1998). Given the interest of this research, these factors and their clinical manifestations are described below, but emphasis is placed on neurological alterations, as they are the objective of this research.

6.4 Hg classification

6.4.1 Elemental

The main route of entry into the body, in this form, is given by the inhalation of Hg vapors (Syversen y Kaur, 2012); they are retained in the body up to 74% and the average purification times can vary from 1.7 days in the lungs to 64 days in the kidney (Hursh, et. al., 1976). Once in the body, it can cross the blood-brain barrier and brain Hg levels will depend in part on glutathione levels (Syversen y Kaur, 2012). In the context of mining, exposure to these vapors occurs in the process of burning the amalgam, which together with improper use or non-use of personal protective equipment, generates a direct exposure for the inhalation of these vapors.

In acute poisonings with high concentrations, the main symptoms recorded are respiratory, such as respiratory distress, given by the inhalation of this element. While in chronic conditions, alterations in the nervous system prevail; the main signs and symptoms described are: irritation (56.6%), insomnia (59.2%), tremors of the hands and feet (70.4%), fatigue (59.2%) and exhaustion (69.7%) (Kishi, et. al., 1993; Kishi, et. al., 1994), as well as more complex clinical conditions such as memory impairment, neurocognitive and psychiatric disorders (Syversen y Kaur, 2012; Noble, Decker y Zane 2016; Gasca, 2000).

6.4.2 Organic

The main routes of entry into the body of organic Hg can be by inhalation of particles with absorption up to 80% or orally whose absorption can be up to 100% (Syversen y Kaur, 2012). The latter, given by the consumption of foods containing high concentrations of Hg in organic form, derived from the consumption of animals, such as fish and marine mammals, with high levels of Hg (Myers, 2000)

Consequently, Hg in this form, has great affinity for the cells of the nervous system and concentrations in the brain can be up to six times higher compared to those reported in blood (Syversen y Kaur, 2012) causing significant alterations in this system. Within the clinical conditions described, there is Minamata disease, which consists of ataxic gait, instability in the hands, olfactory and gustatory alterations, blurred vision, somatosensory disorders, hearing impairment and blurred vision. Concordant with what was found in the poisoning of Iraq (Minamata, Sakai y Okabe, 1975; Epstein, et al. 1969). Similarly, studies measuring total Hg concentrations found: tremors (34.8%), pain in the extremities (52.2%), muscle weakness (27.5%) and paresthesias (54.3%) (Junior, et al., 2017).

6.4.3 According to the intensity and time of exposure

It has been found that mild exposures, but lasting over time, months and years, present nonspecific symptoms such as weakness, fatigue, weight loss, memory and renal impairments; while moderate exposures, of weeks, describe sialorrhea, insomnia, behavioral and personality alterations; on the other hand, intense exposures, of hours and days, report respiratory problems, lung damage, excitability, tremors and renal failure (Mesa, et. al., 2016).

Currently, all the possible effects generated by the intensity and time of exposure to Hg are still unknown; even in recent years, cases such as the one documented in Santander have been reported in the literature, in which a patient with high levels of Hg in a biological sample and without other apparent causes, presented hydrocephalus and symptoms similar to those described above (Silva, Díaz, Ardila y García, 2012).

6.5 Biomarkers and toxicity levels from exposure to Hg

Hg can be quantified using biological samples such as blood, urine, and hair. Blood quantification is mainly used for acute exposures between three and five days (Bernhoft, 2012); this method is mainly used for the quantification of methylmercury that reaches maximum blood levels between 4 and 14 hours, and its half-life can reach up to 50 days (Raimann, Rodríguez, Chávez y Torrejón, 2014). In hair, Hg correlates with concentrations found in blood and is used to quantify levels of chronic Hg exposure, taking into account the rate of hair growth, approximately 1 cm /month. (Bernhoft, 2012; Raimann, Rodríguez, Chávez y Torrejón, 2014).

Currently, the World Health Organization (WHO) has established toxicity cutoffs in biological samples that vary between environmental and occupational exposures. The toxicity values established for environmental exposures are: in blood values above 5 μg/L, in urine 7 μg/L and in hair 1 μg/g; while in occupational exposures they are: in blood values above 15 μg/L, in urine 25 μg/L and in hair and 2 μg/g. (OMS, s.f.). In relation to the above, a study carried out in Colombia found high levels of Hg in biological samples, hair, urine and blood, from inhabitants exposed in an occupational and environmental context in the Mojana region (Tirado, et. al., 2020). In turn, other studies carried out in the country described elevated levels of Hg in urine and hair among mining workers and fishermen (Mesquidaz, Negrete y Hernández, 2013; Olivero, Mendonza y Mestre, 1995; Salazar-Camacho, 2017).

6.6 Organization of clinical manifestations

Classically, the signs and symptoms found in populations exposed to Hg are presented individually with an emphasis on their prevalences. Few studies have proposed groupings of signs and symptoms as more complex clinical conditions. Minamata disease is an example of these structures, which seek to go beyond the description of isolated signs and symptoms. Therefore, it is important to approach these alterations from the perspective of semiology. (Scadding, 1988).

J G Scadding, in 1988, proposed characteristics to define diseases from philosophical concepts and taking into account medical knowledge (Scadding, 1988). The diseases that we currently know, have been refined over time, identifying anatomical, physiological alterations or even their etiology. However, in many of them, initially only shared signs and/or symptoms were known in a group of patients, which refers to the definition of disease as a syndrome. Today the definition of syndrome is still used in some disciplines such as psychiatry.

In the context of this research, we seek to identify the possible neurological clinical conditions found in populations exposed to Hg, beyond their individual prevalence. Evoking the organization of signs and symptoms recognizable from semiology, which lead to improving clinical presentations and identify knowledge about the prognosis of said disease from the description of syndromes (Scadding, 1988); and identify its possible relationship with either Hg type and exposure time.

7. Methodology

7.1 Study design

Observational, analytical cross-sectional study. This study is a secondary analysis of the data from the project entitled: “Epidemiological evaluation of health effects due to occupational and environmental exposure to mercury in the department of Chocó, Colombia” carried out by researchers from the Colombian National Institute of Health. Permission was given by the authors to use this data for the purpose of this research.

7.2 Study population

The population of the study is made up of inhabitants of the municipalities of Quibdó, Condoto, Rio Quito, Canton, Istmina of the department of Chocó, with environmental and occupational exposure to Hg.

7.3 Selection criteria

According to the study protocol: "Epidemiological evaluation of health effects due to occupational and environmental exposure to mercury in the department of Chocó, Colombia", criteria for the selection of participants were established. In section, these criteria are taken up, since, since this research was a secondary data study implicitly the participating population had to meet these criteria, which is important to contextualize the future findings found. The selection criteria are described below.

7.3.1 Inclusion Criteria

1. Men and women with environmental and/or occupational exposure to Hg
2. Have resided in the area for at least six months.

7.3.2 Exclusion Criteria

1- Participants diagnosed with a neurological disease such as:

Epilepsy

Parkinson's disease.

Vascular brain event

Mental disorders (schizophrenia or bipolar disorders).

History of severe trauma with loss of consciousness.

7.4 Sample

In the project from which this research derives, a convenience sampling was carried out for participant selection. The reason a convenience sample was carried out was because the number of people engaged in this line of work was unknown since this practice tends to be carried out informally. As well as the logistical limitations inherent in field work in these populations far from large urban centers. Using the aforementioned selection criteria, a total of 167 participants met the study requirements and had hair samples taken for Hg quantification levels

7.5 Study Variables

7.5.1 Independent variable of interest (exposure)

Hg concentration: Hg level reported in biological sample of proximal hair of participants. Since hair growth is approximately 1 cm per month, under usual conditions (Bernhoft, 2012), this measurement is understood as corresponding to the month prior to sampling. We will call this measurement “immediate chronicle.”

7.5.2 Outcome variables

The outcome variables will be analyzed by phases, starting from the isolated signs and symptoms; then diades, triads and other possible combinations found will be built, taking into account the findings in the truth tables. The information on how this will be performed is detailed in the statistical analysis section.

The signs and symptoms that will be analyzed in the first phase are: Headache; vertigo; irritation; insomnia; general weakness; weakness for the development of activities; muscle strength; paresthesias; hearing loss; blurred vision; campimetry; ataxia; rigidity; dysmetry; adiadokinesia; general tremors in distal, eyelid, tongue, and lips; memory, concentration and sensitivity alterations; Babinski, Hoffman, Tricipital, Bicipital, Aquilian and mentolabial reflexes, and heel-knee test

Table 1.

Operationalization of the variables.

Variable Name	Operational definition.	Options	Variable Type/ Measurement Scale
Hair Hg Levels	Levels found in biological sample in µg/g hair. Hair samples were obtained from the occipital area of the head (scissored from the hair root), including at least 20 strands of hair. The sample is taped so that the root part of the hair can be identified, and the sample is placed in polyethylene bags stored at room temperature. For further processing in the laboratory.	Reported values µg/g	Continuous Quantitative Ratio
Headache	Asked in the questionnaire as: Do you get headaches?	1=Never 2=At least once a month 3=At least once a week 4=At least once a day	Ordinal qualitative
Vertigo	Asked in the questionnaire as: Do you notice that things around you move(vertigo)?	1=Never 2=Sometimes 3=Always 4=NS/NR	Ordinal qualitative

Variable Name	Operational definition.	Options	Variable Type/ Measurement Scale
Irritation	Asked in the questionnaire as: Do you get irritated easily?	1=Never 2=Sometimes 3=Always 4=NS/NR	Ordinal qualitative
Insomnia	Asked in the questionnaire as: How do you feel after a usual night of sleep?	1=Ok 2=Medium 3=Bad	Ordinal qualitative
Overall weakness	Asked in the questionnaire as: Do you feel weak?	1=Same as usual 2=Worse than normal 3=Much worse than usual	Ordinal qualitative
Weakness for development of activity	Asked in the questionnaire as: Can you start things without difficulties, but get weak as you go on?	1=Same as usual 2=Worse than normal 3=Much worse than usual	Ordinal qualitative
Muscle strength	Asked in the questionnaire as: Do you have less muscle strength?	1=Same as usual 2=Worse than normal 3=Much worse than usual	Ordinal qualitative
Tremors (general)	Asked in the questionnaire as: Have you had any problems with tremors (shaking)?	1= I have not had tremors or tremors do not interfered with my job 2= I can work, but I need to be more careful than the average person 3=I am able to do everything, but with errors; poorer than usual performance because of tremors	Ordinal Qualitative

Variable Name	Operational definition.	Options	Variable Type/ Measurement Scale
		4= I am unable to do a regular job, I may have changed to a different job. due to tremors; it limits some housework, such as ironing 5= I am unable to do any outside job; housework very limited	
Distal tremor	Asked in the questionnaire as: Do your fingers tremble (Distal tremor)?	1=Never 2=Sometimes 3=Always 4=NS/NR	Ordinal qualitative
Eyelid tremor	Asked in the questionnaire as: Do your eyelids tremor?	1=Never 2=At least once a month 3=At least once a week 4=At least once a day	Ordinal qualitative
Paresthesias	Asked in questionnaire as: Have you felt numbness, tingling, pain mainly around the mouth and in the hands?	1=Never 2=At least once a month 3=At least once a week 4=At least once a day	Ordinal qualitative
Concentration	Asked in the questionnaire as: Do you have problems concentrating?	1=Same as Usual 2=Worse than Normal 3=Much worse than usual	Ordinal qualitative
	Asked in the questionnaire as: Do you need to write down the things you need to do during the day?	1=Never 2=Sometimes 3=Always 4=NS/NR	Ordinal qualitative

Variable Name	**Operational definition.**	**Options**	**Variable Type/ Measurement Scale**
Memory	Asked in questionnaire as: Do you often have to check things you have already done, such as closing the door, gas, etc.?	1=Never 2=Sometimes 3=Always 4=NS/NR	Ordinal qualitative
	Asked in the questionnaire as: Do your family/friends tell you that you have a bad memory?	1=Never 2=Sometimes 3=Always 4=NS/NR	Ordinal qualitative
Hearing loss.	Asked in the questionnaire as: Have you had hearing loss in the last year?	1=Yes 2=No	Qualitative dichotomous nominal
Blurred vision.	Asked in the questionnaire as: In the last year have you had blurred vision?	1=Yes 2=No	Qualitative dichotomous nominal
Campimetry*	In the physical examination the visual fields are evaluated.	1=Normal. 2= Altered	Qualitative dichotomous nominal
Ataxia*	Different levels of affectedness: **Absent:** no alterations **Slight** Only visible when walking without visual aid. **Moderate:** Visible when walking. Normal gait, but difficulty walking with one foot behind the other.	1=Absent 2= Slight 3=Moderate 4=Marked 5=Severe 6=Most severe (bedridden)	Ordinal qualitative

Variable Name	Operational definition.	Options	Variable Type/ Measurement Scale
	Marked: Increased lift range, shaky gait, inability to walk in line. **Severe:** Inability to walk without support, limited to wheelchair. **Most severe:** Bedridden.		
Rigidity of gait*	Observed gait, swing of arms, general posture It is classified as: Normal Mild diminution in swing while the patient is walking Obvious diminution in swing suggesting shoulder rigidity Stiff gait with little or no arm swinging noticeable Rigid gait with arms slightly pronated; this would also include stopped-shuffling gait with propulsion and retropulsion	1=Normal 2=Mild 3=Obvius diminution 4= Siff gait 5= Rigid gait	Ordinal qualitative
Dysmetria*	**Finger nose test.** Examiner indicates to the patient, positioned with their legs together, arms outstretched, and eyes closed, to alternate between touching the examiner´s index finger	1=Normal 2=Moderate to pathological 3=Severely pathological	Ordinal qualitative

Variable Name	Operational definition.	Options	Variable Type/ Measurement Scale
	and their own nose using their own index finger.		
Dysdiadochokinesia*	Alternating movements of wrists. Slight=Minimal decrease in the alternation of movements Moderate=Marked decrease in alternation of movements Severe = Severe irregularity to alternate movements	1=Absent 2=Light 3=Moderate 4=Severe	Ordinal qualitative
Eye lid tremor*	Physical exam with eyes closed	1=None 2=Slight 3=Marked	Ordinal qualitative
Tongue	To the physical examination	1=None 2=Doubtful 3=Present	Ordinal qualitative
Lips	To the physical examination	1=Absent 2=Present	Qualitative dichotomous nominal
Sensory disturbances *	Sensory disturbances identified during physical examination	1=Absent 2=Present	Qualitative dichotomous nominal
Babinski reflex*	Consists of firmly rubbing the sole of the foot. The first toe (Hallux) moves upward or toward the top of the	1=Absent 2=Present.	Qualitative dichotomous nominal

Variable Name	Operational definition.	Options	Variable Type/ Measurement Scale
	foot. The other fingers fan out.		
Hoffman reflex *	Sign of pyramidal pathway involvement affecting upper limbs. It is explored by tapping the nail of the second, third or fourth finger of the hand. In response, the stimulated finger bends, including the thumb. It shall be classified as: **Absent** **Present** **Altered:** Hyporeflexia, hyperreflexia or clonus	1=Absent. 2=Present. 3=Altered.	Ordinal qualitative
Tricipital reflex *	It consists of hanging the forearm and striking the triceps tendon located on the elbow, in the olecranon. It is classified as: **Absent** **Present** **Altered**: Hyporeflexia hyperreflexia or clonus.	1=Absent. 2=Present. 3=Altered.	Ordinal qualitative
Bizeps brachii reflex*	On the inner face of the elbow, at the level of the biceps tendon in its distal insertion on the forearm or flexure of the elbow impacting on the thumb placed above said insertion	1=Absent. 2=Present. 3=Altered.	Ordinal qualitative

Variable Name	Operational definition.	Options	Variable Type/ Measurement Scale
	It is classified as: **Absent** **Present** **Altered**: Hyporeflexia, hyperreflexia or clonus.		
Ankle jerk reflex*	It consists of the seated participant hanging the lower limb on the edge of the chair, slightly lifting the foot with his hand and with the other striking the Achilles tendon. It is classified as: Absent Present Altered:(Hyponeflexia, hyperreflexia or clonus)	1=Absent. 2=Present. 3=Altered.	Ordinal qualitative
Mentolabial reflex*	On physical examination by evaluator, it is classified into: Absent Present Altered:(Hyporeflexia, hyperreflexia or clonus)	1=Absent. 2=Present. 3=Altered.	Ordinal qualitative
Heel-to-shin test*	The patient is asked to touch the knee of the other leg and slide the heel along the pretibial region of the leg. Absent Mild (Terminal mild tremor and hypermetry,	1=Absent 2=Slight 3=Moderate 4=Marked 5=Severe 6=Most severe	Ordinal qualitative

Variable Name	Operational definition.	Options	Variable Type/ Measurement Scale
	i.e. the heel does not reach right to the knee) Moderate (Terminal Tremor and Marked Hypermetry) Marking (Balancing marked throughout the movement) Severe (Strong kinetic tremor that interferes with daily life) More severe (Maximum form of kinetic tremor that prevents testing)		
Gender	Biological sex referred by participants.	1=Male 2=Female	Qualitative dichotomous Nominal
Age	Years of age provided by the participants at the time of the interview.	Age to-date	Quantitative discrete
Schooling	Level of education completed by participants.	1=Illiterate 2=Incomplete primary 3= Complete primary 4=Incomplete high school 5=Complete high school 6= Incomplete technical 7= Complete technical 8= Incomplete university 9= Complete university 10= Specialist 11= Pre-Kindergarten 12=Other	Ordinal Qualitative

Variable Name	Operational definition.	Options	Variable Type/ Measurement Scale
Place of residence	Municipality of residence referred by the participants, in which they have lived in the last 6 months without interruption.	Name of the municipality in which you reside	Nominal qualitative
Distance	Distance between home and the nearest buying and selling site of Hg	<50 meters 50-100 meters 100-300 meters >300 meters	Ordinal qualitative
Burning amalgam at home	Amalgam (gold-Hg) burning procedure is performed at home	1=Yes 2=No	Qualitative Nominal Dichotomous
Store Hg at home	Store Hg at home	1=Yes 2=No	Qualitative Nominal Dichotomous
Tobacco smoking	Cigarette smoking	1=Yes 2=No	Qualitative Nominal Dichotomous
Alcohol	Alcohol consumption	1=Yes 2=No	Qualitative Nominal Dichotomous
Strawberry consumption	Frequency of strawberries consumption	1= Never 2=Monthly 3=Weekly 4=Daily	Ordinal Qualitative
Consumption of red paprika	Frequency of red paprika consumption	1= Never 2=Monthly 3=Weekly 4=daily	Ordinal Qualitative

Variable Name	Operational definition.	Options	Variable Type/ Measurement Scale
Whole-wheat flour	Frequency of whole wheat flour consumption	1= Never 2=Monthly 3=Weekly 4=daily	Ordinal Qualitative
Yeast extract	Frequency of yeast extract consumption	1= Never 2=Monthly 3=Weekly 4=daily	Ordinal Qualitative
Canned tuna	Frequency of canned tuna consumption	1= Never 2=Monthly 3=Weekly 4=daily	Ordinal Qualitative
Fish from the river	Frequency of river fish consumption	1= Never 2=Monthly 3=Weekly 4=Daily	Ordinal Qualitative
Brazil nuts	Frequency of Brazil nuts consumption	1= Never 2=Monthly 3=Weekly 4=Daily	Ordinal Qualitative
Sunflower seed	Frequency of sunflower seed consumption	1= Never 2=Monthly 3=Weekly 4=Daily	Ordinal Qualitative

* Evaluation performed by a doctor trained in neurological evaluation.

7.7 Collection of information.

In the project from which this research is derived, the places with mining population exposed to Hg by gold extraction in the department of Chocó were selected. This selection was made with the support of the Instituto de Investigaciones Ambientales del Pacifico (IIAP) and the Corporación Autónoma Regional para el Desarrollo Sostenible del Chocó (CODECHOCO).

Two formats adapted from the Global Mercury Project health assessment tool (Mesquidaz, Negrete y Hernández, 2013) were applied to all selected individuals, exposed occupationally or environmentally, seeking to identify symptoms related to mercury toxicity. Medical assessment focused on neurological signs and symptoms associated with mercury neurotoxicity and application of neuropsychological tests. The professionals in charge were previously trained to carry out this phase. Hg levels were measured in biological samples of hair, urine, and blood in humans; also, Hg levels were measured in samples of water, fish, sediment and air.

7.8 Potential biases

7.8.1 Selection bias

Since the sampling was carried out by convenience, this research may present a selection bias generated by non-random differences between the participants and other individuals with environmental exposure. Other possible sources of bias were considered, such as the social conditions in the region that may cause residents with more serious clinical presentations, due to this exposure, to not be present in these sites, since they require special care and periodic assessments by specialty. The inclusion of only those who had lived 6 months or more in the region, was to avoid the possible migration bias.

7.8.2 Information bias

In the medical evaluation, prior to performing the anamnesis and physical examination, the exposure to Hg is investigated. This can cause an information bias, since the evaluators (doctors) may become more repetitive in the questionnaire and physical examination of the participants who report being exposed.

7.8.3 Confunding bias

The possible confounding variables that can be presented in this research are: age, given that, the older the exposure, the longer the exposure time and the higher the prevalence of neurological clinical conditions. Sex, it has been described that men are the ones who most often perform activities in which the exposure is presented directly, such as post-amalgam burning for the extraction of precious metals. Diet, the consumption of fish in these regions can cause an elevation of Hg levels, due to the elimination of inorganic Hg residues in water sources that subsequently undergoes transformation to organic Hg and is introduced into the food chain, mainly affecting larger animals or humans by the highest concentrations as it advances in the food chain, these variables have been described in the literature as potential confounders. Another potential confounding variable is the place of residence, as it is related to the concentrations of Hg and to the symptoms given by the sociocultural context of the region. Additionally, since this research is a secondary analysis, it is possible that residual confusion exists, even when the analyses are performed by multiple regressions.

7.9. Statistical analysis

7.9.1 Univariate analysis

The categorical variables will be described with percentages and the continuous variables with measures of central tendency and dispersion, considering the distribution of the variables described above. The assessment of normality shall be made by the Shapiro-Wilk test. In this way, the sociodemographic variables age, sex, education, place of residence and occupation will be analyzed first according to the nature of the variables. Second, given the interest in neurological signs and symptoms, a description of their frequency will be made in the participants.

The clinical signs and symptoms were transformed for their analysis using fuzzy logic, because in their measurement there were intermediate categories, between total absence and full presence of each one (see table 2). Fuzzy logic is a mathematical technique used to model problems involving uncertainty and subjectivity. It was developed by mathematician Lotfi Zadeh in the 1960s. Instead of classifying data into precise categories, such as true or false, the fuzzy method uses fuzzy sets that allow data to be classified into different degrees of category membership, i.e., it is an extension of Boolean logic (Zadeh, 1965). In this way, fuzzy logic for linguistic variables allowed having continuous values between zero (no sign/symptom) and one (sign/symptom) (Kacprzyk, Massad y Ortega, 2008).

Among the areas in which it has been used are engineering, systems control, artificial intelligence for decision making and data analysis; likewise, in recent years it has been used in healthcare because in medical care one of the common characteristics is uncertainty, as well as the information is often incomplete and inaccurate (Zadeh, 1965; Kacprzyk, Massad y Ortega, 2008; Sizilio, Leite, Guerreiro y Neto, 2012; Thukral y Rana V. 2019). That is why fuzzy logic has been used for the evaluation of symptoms, diagnoses, and as an aid in decision making, it has been even used in cancer to combine results of diagnostic tests (Sizilio, Leite, Guerreiro y Neto, 2012). It has been used for the analysis of chronic diseases such as diabetes, Parkinson, brain tumor, etc. (Thukral y Rana V. 2019). Considering the above mentioned, fuzzy logic was considered since it allows us to model the uncertainty and subjectivity of the information, as well as to have different degrees in the presentation of signs and symptoms.

The formula used for the transformation of the categories is explained below: the absence of alteration was considered as zero and for the different degrees of alterations whole numbers were assigned starting at one up to the maximum category. Lastly, divided by the total number of categories to obtain a value greater than zero and equal to one for the maximum possible alteration. For example, absent ataxia was assigned as value 0, likewise, some degree of alteration has five categories. That is, 1/5=0.2, so in order of severity the values were assigned as follows: discrete 0.2, moderate 0.4, marked 0.6, severe 0.8 and very severe, which is the maximum possible alteration, 1. This exercise was performed with each of the signs and symptoms evaluated. Likewise, the crude prevalence ratio and 95% confidence interval (95% CI) between each of the clinical presentations and the Hg levels in hair were calculated.

Table 2.

Fuzzy transformation of signs and symptoms.

symptoms	Categories	Fuzzy Calibration
How do you feel after a usual night of sleep?	Ok	0
	Medium	0.5
	Bad	1
Do you get headaches?	Never	0
	At least once a month	0.33
	At least once a week	0.67
	At least once a day	1
Have you felt numbness, tingling, pain mainly around the mouth and in the hands?	Never	0
	At least once a month	0.33
	At least once a week	0.67
	At least once a day	1
Do you have problems concentrating?	Same as Usual	0
	Worse than Normal	0.5
	Much worse than usual	1
Do you need to write down the things you need to do during the day?	Never	0
	Sometimes	0.5
	Always	1
	NS/NR	0
Do you often have to check things you've already done, such as closing the door, checking the gas line, etc?	Never	0
	Sometimes	0.5
	Always	1
	NS/NR	0
Do your family/friends tell you that you have a bad memory?	Never	0
	Sometimes	0.5
	Always	1
	NS/NR	0
Do you notice that things around you move(vertigo)?	Never	0
	Sometimes	0.5
	Always	1
	NS/NR	0
Do your fingers tremble (Distal tremor)?	Never	0
	Sometimes	0.5
	Always	1
	NS/NR	0

symptoms	**Categories**	**Fuzzy Calibration**
If you have tremors, do they prevent you from writing, buttoning your buttons, etc?	Never	0
	Sometimes	0.5
	Always	1
	NS/NR	0
Do your eyelids tremble?	Never	0
	Sometimes	0.5
	Always	1
	NS/NR	0
Do you feel sad?	Never	0
	At least once a month	0.33
	At least once a week	0.67
	At least once a day	1
Are you easily irritated?	Never	0
	Sometimes	0.5
	Always	1
	NS/NR	0
Have you had hearing loss in the last year?	Yes	1
	NO	0
	NS/NR	0
In the last year have you had blurred vision?	Yes	1
	NO	0
	NS/NR	0
Do you have less muscle strength?	Same as usual	0
	Worse than normal	0.5
	Much worse than usual	1
Do you feel weak?	Same as usual	0
	Worse than normal	0.5
	Much worse than usual	1
Can you start things without difficulties, but get weak as you go on?	Same as usual	0
	Worse than normal	0.5
	Much worse than usual	1
Have you had any problems with tremors (shaking)?	I have not had tremors or tremors do not interfered with my job	0
	I can work, but I need to be more careful than the average person	0.25

symptoms	Categories	Fuzzy Calibration
	I am able to do everything, but with errors; poorer than usual performance because of tremors	0.5
	I am unable to do a regular job, I may have changed to a different job. due to tremors; it limits some housework, such as ironing	0.75
	I am unable to do any outside job; housework very limited	1

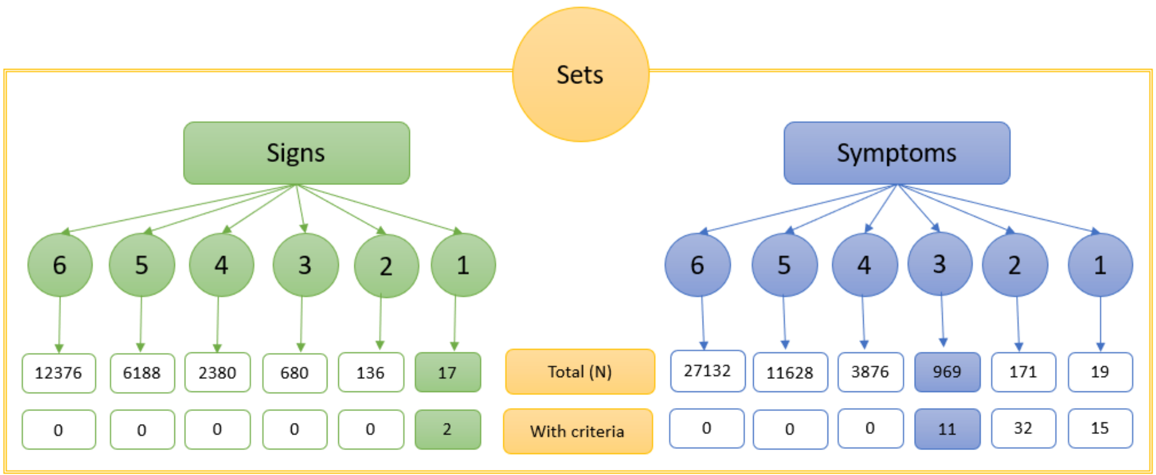
Signs	Categories	Fuzzy Calibration
Ataxia and gait	Absent	0
	Slight	0.2
	Moderate	0.4
	Marked	0.6
	Severe	0.8
	Most severe (Bedridden)	1
Posture	None	0
	Light to moderate	0.33
	Evident	0.66
	Severe	1
Dysmetria	Normal	0
	Moderate to Pathological	0.5
	Severely Pathological	1
Dysdiadochikinesia	Absent	0
	Lightweight	0.33
	Moderate	0.66
	Severe	1
Eye lid tremor.	None	0
	Slight	0.5
	Marked	1
Tongue tremor	None	0
	Doubtful	0.5
	Present	1
Tremor in the lips	None	0
	Doubtful	0.5

Signs	Categories	Fuzzy Calibration
	Present	1
Mentolabial reflex*	Absent	0
	Present	0
	Altered	1
Suction reflex	Absent	0
	Present	1
	Altered	1
Babinski reflex	Absent	0
	Present	1
	Altered	1
Hoffman reflex	Absent	0
	Present	1
Tricipital reflex	Absent	1
	Present and Symmetrical	0
Bizeps brachii reflex	Absent	1
	Present and Symmetrical	0
Ankle jerk reflex*	Absent	1
	Present and Symmetrical	0
Heel-to-shin test	Absent	0
	Slight	0.2
	Moderate	0.4
	Marked	0.6
	Severe	0.8
	Most severe	1
Sensory disturbances	Absent	0
	Present	1
Rigidity of gait (walking)	Normal	0
	Mild diminution in swing while the patient is walking	0.25
	Obvious diminution in swing suggesting shoulder rigidity	0.5
	Stiff gait with little or no arm swinging noticeable	0.75
	Rigid gait with arms slightly pronated; this would also include stopped-shuffling gait with propulsion and retropulsion	1

The conformation of the syndromes was carried out with the signs and symptoms forming sets of six, five, four, three and two (figure 1). The following inclusion criteria were evaluated for further analysis: compliance with all the clinical manifestations that compose it with a value p≤0.20 and a minimum number of 30 participants who comply with syndrome.

Figure 1.

Grouping of signs and symptoms and the eligible sets



The figure describes the possible sets that can be formed from the signs and symptoms. For the analysis, the groups with the greatest number of attributes were included, in the symptoms three sets and in the signs, it was not possible to generate a set, since it did not meet the inclusion criteria.

7.9.2 Bivariate analysis

In this sense, the crude association between the dependent variable, Hg concentrations, and the following signs and symptoms were evaluated: Headache; vertigo; irritation; insomnia; general weakness; weakness for the development of activities; muscle strength; paresthesias; hearing loss; blurred vision; campimetry; ataxia; rigidity; dysmetry; adiadokinesia; general tremors in distal, eyelid, tongue, and lips; memory, concentration and sensitivity alterations; Babinski, Hoffman, Tricipital, Bicipital, Aquilian and mentolabial reflexes, and heel-knee test.

Then, the crude association between the dependent variable, Hg concentrations, with the presence/absence of diades, triads and most prevalent clinical conditions, found in the univariate analysis, were evaluated; with the aim of determining the clinical tables that were included in the final model. Additionally, the association between the dependent variable and the sociodemographic characteristics and exposure to Hg were explored.

For statistical analysis, the normality of the independent variable (Hg concentration in hair) was evaluated with the Shapiro-Wilk test, in case of normality, the use of t-student was planned for dichotomous variables and ANOVA for polytomous variables. In case of non-normality, the Mann-Whitney U non-parametric test was used for dichotomous and Kruskal Wallis for polytomous. Statistical significance was considered at alpha values below 0.05.

7.9.3 Multiple analysis

Given the cross-sectional design of the study and the interest in comparing exposure levels, and the dependent neurological variables, the Poisson regression with robust variance was used;

in this way, good approximations to the prevalence ratios are achieved (Barros y Hirakata, 2003), the natural measure of the prevalence studies. For the use of regression, the following assumptions were verified: 1) The observations are independent of each other, 2) The response variable is a count per unit of space or time, 3) The mean is equal to its variance and 4) There is linearity. The variables included in the final model, as previously indicated, were those in which a crude association in the bivariate analysis was identified; likewise, the confounding variables were included in the final model.

8. Ethical considerations

This research derives from the project entitled “Epidemiological evaluation of health effects due to occupational and environmental exposure to Hg in the department of Chocó, Colombia” carried out by the, Grupo factores de riesgo ambiental (DVARSP) led by the Director of Research of the Instituto Nacional de Salud (INS) and endorsed by the ethics committee of the INS on May 31, 2016 with CTIN 36-2015 and considered of minimum risk. **(See Annex 1)**

Consequently, for the conduct of this research, the database of the participants in the study were requested from the PI research of INS, after the endorsement of the ethics committee of the Universidad Industrial de Santander (UIS). The database will be requested anonymously, with a consecutive code that is not related to the participants. In case of discovery of any key finding, for which it is required to inform a participant about any condition, this will be notified to the research director of INS, without breaking the confidentiality of the data. The treatment of personal data adheres to the regulations of the Statutory Law 1581 of 2012, Decree 1377 of 2013 and Resolution 1227 of August 2013, seeking to protect the data of the participants in the study.

In relation to this topic, this research adheres to the ethical standards elaborated in the Declaration of Helsinki, modified Brazil 2013, and the report of Belmont taking into account the bioethical principles of charity, justice and respect for others (Asamblea general Fortaleza Brasil, 2013; Departamento de Salud, Educación y Bienestar de los Estados Unidos, 1979). The principle of Beneficence is fulfilled by respecting the decisions of the research subjects and protecting it from potential harm, so this research seeks to do no harm and maximize the benefits of the participants. Respect for the person is given through the autonomy of the participants and the protection of people with diminished autonomy. The benefits of the results of this research will be used for decision-making focused on improving the living conditions and health of the population under study.

Likewise, this research adheres to the guidelines indicated by the Council of International Organizations of Medical Sciences (CIOMS) and emphasizes the following guidelines: guideline one, social and scientific value and respect for rights; guideline two, research in an environment of scarce resources, since as previously indicated the research is carried out in municipalities with poverty and social problems; guideline six, attention to the health needs of the participants; guideline nine, people who have the ability to give informed consent; guideline ten, modification and dispensations of informed consent; guideline eleven, collection, storage and use of biological materials and related data, this part was mainly applied to the taking of biological samples for the measurement of Hg levels in blood, urine and hair; and guideline twelve, collection, storage and use of data in a health-related research (Organización Panamericana de la Salud y Consejo de Organizaciones Internacionales de las Ciencias Médica, 2016).

In the Colombian context, according to article 11 paragraph A of resolution 008430 of 1993 “for research with human beings of the Ministry of Health and Social Protection of Colombia”, research with minimal risk is considered (Asamblea general Fortaleza Brasil, 2013). In addition, it is supported in the fifth article of the same resolution: "by which in any research in which the human being will be studied , the criterion of respect for his dignity, the protection of his rights and his well-being must prevail" and article 6 numeral G by which it mentions that: "it will be carried out when the authorization of the legal representative of the research institution and of the institution where the research is carried out and the subsequent approval of the project by the research ethics committee of the institution is obtained" (Resolución 008430, 1993).

Finally, the master's student in Epidemiology Edgar Fabián Manrique Hernández and the director of this proposal, Dr. Álvaro Javier Idrovo, do not have conflicts of interest for carrying out the research. Likewise, the results found in this process will be communicated to the research director of the INS and will be presented at academic events required by the student to opt for the master's degree in Epidemiology.

9. Results

A total of 167 people participated in the study voluntarily and met the inclusion criteria, the characteristics of the participants are in Table 1. The largest proportion of participants were female (85.63 per cent), subsidized security (75.45 per cent), illiterate (40.12 per cent) and married (35.76 per cent). Among the toxicological history the most frequent was alcohol consumption

(41.92%), followed by smoking (30.54%), the burning and storage of Hg at home was 7.18% and 4.79% respectively. Among the foods evaluated with the highest daily consumption is red paprika (12.57%), followed by river fish (7.78%), in contrast to sunflower seeds or Brazil nuts (0.59%) that report the lowest daily consumption.

When comparing the characteristics of the participants in relation to Hg levels, differences were observed in marital status (p=0.007) and municipality of residence (p<0.001). Likewise, among people with a history of smoking (p=0.029), amalgam burning (p=0.003) and Hg storage at home (p=0.05). Among the foods, differences were found with consumption of river fish (p=0.004), yeast extract (p=0.013) and Brazil nuts (p=0.019). **Table 1.**

Table 3.

Some characteristics of participants and mercury concentrations (n=167)

				Hg concentrations (μg/g)			
Variable		**n**	**%**	**Min**	**Q50**	**Max**	**P value**
Sex	Woman	143	85.63	0.01	0.37	6.19	0.312[a]
	Man	24	14.37	0.009	0.41	3.16	
Social security	Contributive	25	14.97	0.04	0.25	3.6	0.125[b]
	Subsidized	126	75.45	0.01	0.36	6.19	
	Not affiliated	7	4.19	0.01	0.56	4.38	
	Special	1	0.6	1.58	1.58	1.58	
	No data	8	4.79	0.02	1.7	4.33	
Age	<10 years	8	4.79	0.36	0.58	1.31	0.380[b]
	10-20 years	10	5.99	0.02	0.32	0.90	
	20-30 years	18	10.78	0.01	0.32	3.16	
	30-40 years	34	20.36	0.01	0.31	5.31	
	40-50 years	22	13.17	0.02	0.26	1.66	
	50-60 years	35	20.96	0.01	0.21	6.19	
	60-70 years	24	14.37	0.02	0.40	3.60	
	70-80 years	10	5.99	0.09	0.65	4.38	
	80-90 years	4	2.40	0.57	0.82	1.45	
	>90 years	2	1.20	0.60	0.86	1.14	

Variable		n	%	Hg concentrations (µg/g) Min	Q50	Max	P value
Education	Illiterate	67	40.12	0.01	0.48	4.38	0.310[b]
	Incomplete elementary	12	7.19	0.02	0.38	6.19	
	Complete elementary	11	6.59	0.02	0.13	5.31	
	Incomplete secondary	28	16.77	0.01	0.21	3.16	
	Complete secondary	10	5.99	0.03	0.16	1.03	
	Incomplete technical	7	4.19	0.02	0.29	1.35	
	Complete technical	9	5.39	0.04	0.23	3.6	
	Incomplete university	15	8.98	0.06	0.37	1.67	
	Complete university	4	2.4	0.33	0.44	0.98	
Civil status	Married	59	35.76	0.01	0.25	5.31	0.008[b]
	Divorced	14	8.38	0.02	0.51	4.38	
	Widowed	53	31.74	0.01	0.31	6.19	
	Single	20	11.98	0.02	0.41	1.77	
	No date	21	12.57	0.05	0.9	4.33	
Municipality	Condoto	41	24.55	0.07	0.97	6.19	<0.001[b]
	Canton	20	11.98	0.03	0.38	1.65	
	Quibdó	31	18.56	0.01	0.15	3.60	
	Isthmina	49	29.34	0.01	0.21	1.76	
	Rio Quito	26	15.57	0.01	0.76	4.38	
Tobacco consumption	Not	116	69.46	0.009	0.355	5.31	0.229[a]
	Yes	51	30.54	0.02	0.54	6.19	
Alcohol consumption	Not	97	58.08	0.01	0.45	6.19	0.029[a]
	Yes	70	41.92	0.01	0.30	5.31	
Fish consumption	No	23	13.77	0.01	0.84	5.31	0.001[b]
	Omnivores	90	53.89	0.01	0.47	6.19	
	Herbivores	54	32.34	0.01	0.17	3.6	
Burn amalgam at home	Not	155	92.81	0.24	0.93	1.65	0.003[a]
	Yes	12	7.19	0.29	0.91	4.33	

Variable		n	%	Hg concentrations (μg/g)			
				Min	Q50	Max	P value
Store Hg at home	Not	159	95.21	0.01	0.36	6.19	0.055[a]
	Yes	8	4.79	0.25	0.94	1.65	
Distance between the house and the nearest mercury place	<50 m	36	21.56	0.01	0.25	4.38	0.541[b]
	50-100 m	12	7.19	0.06	0.17	1.67	
	100-300 m	7	4.19	0.19	0.37	1.02	
	>3000 m	112	67.07	0.01	0.42	6.19	
Strawberry consumption	Never	67	40.12	0.01	0.47	5.31	0.437[b]
	Monthly	35	20.96	0.02	0.42	2.86	
	Weekly	32	19.16	0.01	0.42	6.19	
	Daily	2	1.2	0.48	1.08	1.67	
Red paprika consumption	Never	57	34.13	0.01	0.45	6.19	0.092[b]
	Monthly	30	17.96	0.01	0.43	2.86	
	Weekly	28	16.77	0.07	0.88	1.64	
	Daily	21	12.57	0.02	0.16	4.38	
Whole wheat flour consumption	Never	57	34.13	0.01	0.82	5.31	0.030[b]
	Monthly	34	20.36	0.01	0.38	1.3	
	Weekly	37	22.16	0.01	0.39	6.19	
	Daily	8	4.79	0.02	0.46	1.1	
Yeast extract consumption	Never	68	40.72	0.02	0.68	6.19	0.013[b]
	Monthly	33	19.76	0.01	0.39	1.29	
	Weekly	28	16.77	0.01	0.37	1.67	
	Daily	7	4.19	0.02	0.13	1.02	
Canned tuna consumption	Never	34	20.36	0.02	0.54	5.31	0.406[b]
	Monthly	55	32.93	0.01	0.47	3.16	
	Weekly	44	26.35	0.02	0.39	6.19	
	Daily	3	1.8	0.01	0.58	1.67	
River fish consumption	Never	26	15.57	0.01	0.82	5.31	0.004[b]
	Monthly	65	38.92	0.01	0.22	2.86	
	Weekly	63	37.72	0.01	0.43	3.6	
	Daily	13	7.78	0.07	0.48	6.19	
Sunflower seeds consumption	Never	131	78.44	0.01	0.47	6.19	0.335[b]
	Monthly	3	1.8	0.08	0.21	1.32	
	Weekly	2	1.2	0.02	0.16	0.29	
	Daily	0	0	0	0	0	
	Never	123	73.65	0.01	0.47	6.19	0.019[b]

Variable		n	%	Hg concentrations (μg/g)			
				Min	**Q50**	**Max**	**P value**
Nuts consumption	Monthly	7	4.19	0.01	0.06	0.79	
	Weekly	5	2.99	0.02	1.03	1.67	
	Daily	1	0.6	0.58	0.58	0.58	

a= Mann-Whitney U test, b= Kruskal Wallis test

Table 4.

Prevalence of signs and symptoms in population and PR (Hg concentrations (µg/g) environmental exposure.

NEUROTOXIC SYMPTOMS						NEUROTOXIC SIGNS				
	Abbreviation	**n**	**%**	**PR***	**95% CI**		**n**	**%**	**PR***	**95% CI**
Memory (self-perception)	D	93	55.7	1.1	(1.04 - 1.26)	Reflex				
Irritability	F	91	54.5	1	(0.89 - 1.17)	Hoffman	49	29.3	0.86	(0.6 - 1.23)
Vision	G	81	48.5	1.1	(1.02 - 1.27)	Babinski	23	13.8	1.11	(0.83 - 1.5)
Vertigo	E	71	42.5	1.2	(1.02 - 1.31)	Suction	20	12	1.15	(0.84 - 1.57)
Insomnia	A	69	41.3	1	(0.77 - 1.18)	Sensory distrurbances	15	8.98	0.54	(0.25 - 1.17)
Concentration difficulty that requires taking notes	C	66	39.5	1	(0.82 - 1.22)	Tricipital	8	4.79	1.32	(0.75 - 2.32)
Muscle strength	H	66	39.5	1	(0.82 - 1.22)	Ankle jerk	6	3.59	0.48	(0.07 - 3.43)
Overall Concentration	B	65	38.9	1.1	(0.9 - 1.25)	Bizeps brachii	3	1.8	0	(0 - 6.84)
Weakness (self-perception)	I	60	35.9	1.2	(1.02 - 1.32)	Heel-to-shin test	1	0.6	1.41	(1.18 - 1.68)
Weakness in daily activities	J	60	35.9	1.1	(0.97 - 1.3)	Mentolabial	0	0	0	0
Memory evidenced by others	K	57	34.1	1.2	(1.02 - 1.33)	Tremor				
Hearing	L	49	29.3	1.1	(0.92 - 1.34)	Eyes closed	45	27	1.1	(0.91 - 1.34)
Headache	M	44	26.4	1	(0.89 - 1.19)	Tongue	16	9.58	1	(0.71 - 1.42)
Tremor in eyelids	N	42	25.2	1	(0.8 - 1.36)	Lip	5	2.99	1.01	(0.54 - 1.89)
Distal tremor	O	35	21	1	(0.78 - 1.36)	Rigidity of gait	5	2.99	1.23	(0.75 - 2.03)
Paresthesias	P	26	15.6	1	(0.84 - 1.23)	Dysdiadochokinesia	5	2.99	1.39	(1.23 - 1.57)
Fine tremor	Q	18	10.8	1.2	(0.83 - 1.65)	Ataxia	1	0.6	0.93	(0.51 - 1.72)
Sadness	R	13	7.78	0.9	(0.76 - 1.15)	Posture	1	0.6	1.13	(0.78 - 1.65)
General tremor	S	4	2.4	1	(0.66 - 1.58)	Dysmetria	1	0.6	1.39	(1.22 - 1.6)

*Unadjusted prevalence ratio, Reference category ‘not occurrence of signs or symptoms’.

We found 11 possible syndromes with three symptoms in which the established criteria were met, value p≤0.20 and a minimum number of 30 participants who comply with syndrome. The highest prevalence was recorded for HIJ (28.14%), followed by FHI (24.55) and DFG (23.95%). Raw association was found between hair Hg levels, DGJ, DEG, BDE, DFG, EFG and CDG syndromes **(See table 3).** No possible sign syndromes were found. We explored the conformation of sets with the selected symptom syndromes plus each of the signs, but these did not meet the selection criteria.

Table 5.

Bivariate analysis of symptom syndromes and sociodemographic, toxicological and eating habits.

Variables		**HIJ**	**FHI**	**DFG**	**CDF**	**DEG**	**DFH**	**DGJ**	**EFG**	**BDE**	**ADF**	**CDG**
Characteristics of syndromes	n	47	41	40	37	36	34	34	32	31	31	30
	%	28.14	24.55	23.95	22.16	21.56	20.36	20.36	19.16	18.56	18.56	17.96
	95% CI	21.47 - 35.61	18.23 - 31.8	17.7 - 31.16	16.11 - 29.22	15.58 - 28.57	14.53 - 27.27	14.53 - 27.27	13.49 - 25.96	12.97 - 25.3	12.97 - 25.3	12.46 - 24.64
BIVARIATE ANALYSIS												
Hg	1 µg/g	1.1 (0.95 - 1.26)	1.06 (0.94 - 1.18)	1.11 (1.02 - 1.2)	1.07 (1 - 1.14)	1.14 (1.05 - 1.24)	1.07 (0.98 - 1.16)	1.14 (1.05 - 1.23)	1.11 (1.02 - 1.21)	1.13 (1.04 - 1.22)	1.05 (0.96 - 1.15)	1.11 (1.04 - 1.19)
Gender (Ref. woman)	Man	0.8 (0.45 - 1.41)	0.79 (0.5 - 1.24)	0.7 (0.5 - 0.99)	0.84 (0.57 - 1.24)	0.57 (0.37 - 0.89)	0.72 (0.49 - 1.08)	0.7 (0.46 - 1.06)	0.63 (0.45 - 0.88)	0.58 (0.37 - 0.91)	0.76 (0.52 - 1.1)	0.75 (0.5 - 1.13)
Age	1 year	1.01 (1 - 1.02)	1.01 (1 - 1.01)	1.02 (1.01 - 1.02)	1.01 (1 - 1.01)	1.02 (1.01 - 1.02)	1.01 (1 - 1.01)	1.02 (1.01 - 1.02)	1.02 (1.01 - 1.02)	1.01 (1.01 - 1.02)	1.01 (1 - 1.01)	1.02 (1.01 - 1.02)

Variables		HIJ	FHI	DFG	CDF	DEG	DFH	DGJ	EFG	BDE	ADF	CDG
Alcohol (Ref. not)	Yes consumption	1.12 (0.78 - 1.61)	1.11 (0.85 - 1.46)	0.95 (0.76 - 1.18)	0.91 (0.72 - 1.14)	0.92 (0.73 - 1.17)	1.05 (0.85 - 1.3)	0.94 (0.73 - 1.2)	0.95 (0.75 - 1.19)	0.89 (0.69 - 1.13)	0.89 (0.72 - 1.1)	0.89 (0.5 - 1.13)
Smoking (Ref. not)	Yes smoking	1.29 (0.9 - 1.86)	1.21 (0.91 - 1.6)	1.29 (1.04 - 1.58)	1.21 (0.97 - 1.49)	1.42 (1.14 - 1.78)	1.23 (1 - 1.51)	1.34 (1.06 - 1.7)	1.29 (1.03 - 1.61)	1.56 (1.25 - 1.95)	1.31 (1.08 - 1.59)	1.34 (1.08 - 1.67)
Municipality (Ref. Quibdó)	Canton	0.57 (0.32 - 1.02)	0.46 (0.27 - 0.8)	0.81 (0.58 - 1.14)	0.59 (0.36 - 0.97)	0.99 (0.71 - 1.39)	0.59 (0.4 - 0.89)	0.94 (0.65 - 1.36)	0.79 (0.57 - 1.1)	0.98 (0.67 - 1.43)	0.68 (0.48 - 0.95)	0.92 (0.64 - 1.32)
	Condoto	0.47 (0.27 - 0.84)	0.64 (0.46 - 0.89)	1.07 (0.84 - 1.37)	1.17 (0.94 - 1.46)	1.15 (0.85 - 1.55)	0.89 (0.7 - 1.13)	0.98 (0.73 - 1.33)	1.04 (0.79 - 1.36)	1.11 (0.81 - 1.52)	0.98 (0.77 - 1.24)	1.23 (0.93 - 1.64)
	Isthmina	0.5 (0.33 - 0.76)	0.45 (0.32 - 0.63)	0.46 (0.33 - 0.64)	0.57 (0.43 - 0.76)	0.55 (0.39 - 0.79)	0.53 (0.4 - 0.71)	0.5 (0.35 - 0.72)	0.44 (0.31 - 0.62)	0.72 (0.5 - 1.02)	0.61 (0.46 - 0.82)	0.57 (0.42 - 0.79)
	Rio Quito	0.38 (0.19 - 0.76)	0.45 (0.29 - 0.69)	0.88 (0.66 - 1.17)	0.66 (0.46 - 0.94)	0.97 (0.69 - 1.36)	0.64 (0.46 - 0.91)	0.87 (0.62 - 1.23)	0.81 (0.6 - 1.1)	0.9 (0.61 - 1.34)	0.74 (0.52 - 1.05)	0.89 (0.63 - 1.24)
Fish consumption (Ref. non-consumption)	herbivore	0.83 (0.51 - 1.32)	0.76 (0.54 – 1.06)	1.4 (0.92 - 2.14)	0.95 (0.68 - 1.33)	1.67 (0.96 - 2.88)	0.98 (0.71 - 1.36)	1.62 (0.98 - 2.70)	1.2 (0.81 - 1.82)	1.19 (0.76 - 1.88)	1.37 (0.93 - 2.00)	1.4 (0.96 – 2.33)
	Omnivorous	0.68 (0.39 - 1.17)	0.72 (0.50 – 1.04)	1.52 (0.99 – 2.34)	1.22 (0.68 – 1.71)	1.81 (1.03 - 3.15)	1.07 (0.77 - 1.48)	1.67 (0.99 - 2.77)	1.3 (0.89 - 2.06)	1.44 (0.91 - 2.26)	1.66 (1.12 - 2.44)	1.66 (1.05 – 2.62)
Marital Status (Ref. Married)	Separated	1.04 (0.58 - 1.85)	0.78 (0.45 - 1.36)	1.4 (1.12 - 1.76)	0.96 (0.69 - 1.35)	1.63 (1.28 - 2.07)	0.99 (0.76 - 1.28)	1.64 (1.29 - 2.09)	1.49 (1.14 - 1.95)	1.62 (1.22 - 2.14)	1.08 (0.81 - 1.43)	1.37 (1.09 - 1.72)
	Widowed	0.95	0.89	0.83	0.69	0.83	0.77	0.86	0.89	0.83	0.84	0.77

Variables		**HIJ**	**FHI**	**DFG**	**CDF**	**DEG**	**DFH**	**DGJ**	**EFG**	**BDE**	**ADF**	**CDG**
		(0.6 - 1.51)	(0.63 - 1.24)	(0.63 - 1.09)	(0.52 - 0.92)	(0.62 - 1.11)	(0.57 - 1.02)	(0.63 - 1.17)	(0.67 - 1.19)	(0.61 - 1.12)	(0.65 - 1.09)	(0.58 - 1.02)
	Single	0.86 (0.43 - 1.71)	0.93 (0.58 - 1.5)	0.86 (0.57 - 1.3)	0.8 (0.53 - 1.21)	0.82 (0.51 - 1.31)	0.86 (0.59 - 1.25)	0.81 (0.5 - 1.32)	0.93 (0.61 - 1.4)	0.75 (0.46 - 1.23)	0.86 (0.56 - 1.31)	0.75 (0.45 - 1.25)
	Not responding	1.34 (0.8 - 2.24)	1.14 (0.77 - 1.69)	0.91 (0.65 - 1.29)	0.88 (0.66 - 1.19)	1.02 (0.68 - 1.51)	1.06 (0.79 - 1.43)	0.99 (0.67 - 1.48)	0.99 (0.68 - 1.45)	1.01 (0.71 - 1.44)	1.03 (0.77 - 1.39)	0.83 (0.58 - 1.18)
Burning amalgam at home (Ref. not)	Yes	1.13 (0.4 - 2.27)	1.3 (0.25 - 1.9)	1.13 (0.19 - 1.56)	1.16 (0.19 - 1.6)	1.1 (0.26 - 1.76)	1.16 (0.22 - 1.69)	1.02 (0.27 - 1.71)	1.3 (0.21 - 1.78)	1.2 (0.27 - 1.86)	1.25 (0.18 - 1.65)	0.99 (0.19 - 1.44)
Store Hg at home (Ref. not)	Yes	0.89 (0.43 - 2.28)	1.15 (0.28 - 1.87)	1.28 (0.25 - 1.89)	1.33 (0.25 - 1.91)	1.01 (0.26 - 1.68)	1.07 (0.21 - 1.57)	1.13 (0.3 - 1.9)	1.22 (0.27 - 1.88)	0.97 (0.22 - 1.52)	1.21 (0.22 - 1.73)	1.24 (0.26 - 1.86)
Whole wheat flour (Ref. Never)	Monthly	0.97 (0.6 - 1.56)	0.84 (0.57 - 1.25)	0.89 (0.65 - 1.23)	0.71 (0.5 - 1.01)	1.02 (0.73 - 1.43)	0.87 (0.63 - 1.21)	0.98 (0.7 - 1.38)	0.94 (0.67 - 1.32)	0.93 (0.64 - 1.36)	0.81 (0.58 - 1.12)	0.89 (0.64 - 1.23)
	Weekly	0.86 (0.53 - 1.39)	0.71 (0.48 - 1.06)	0.91 (0.68 - 1.22)	0.84 (0.63 - 1.14)	1.01 (0.74 - 1.38)	0.76 (0.56 - 1.03)	1.03 (0.74 - 1.44)	0.95 (0.71 - 1.27)	1.03 (0.75 - 1.42)	0.81 (0.62 - 1.05)	1 (0.75 - 1.35)
	Daily	1.02 (0.47 - 2.22)	0.93 (0.54 - 1.6)	0.41 (0.19 - 0.88)	0.8 (0.42 - 1.5)	0.4 (0.18 - 0.88)	0.69 (0.38 - 1.25)	0.4 (0.18 - 0.89)	0.45 (0.21 - 0.97)	0.63 (0.29 - 1.36)	0.51 (0.24 - 1.09)	0.6 (0.31 - 1.2)
Yeast extract (Ref. Never)	Monthly	0.64 (0.38 - 1.07)	0.66 (0.44 - 0.98)	0.82 (0.6 - 1.12)	0.7 (0.49 - 1)	0.91 (0.66 - 1.25)	0.79 (0.57 - 1.1)	0.82 (0.58 - 1.17)	0.84 (0.61 - 1.14)	0.84 (0.58 - 1.23)	0.81 (0.58 - 1.13)	0.79 (0.56 - 1.1)
	Weekly	0.77	0.63	0.82	0.9	0.89	0.75	0.94	0.76	0.99	0.81	0.98

Variables		HIJ	FHI	DFG	CDF	DEG	DFH	DGJ	EFG	BDE	ADF	CDG
		(0.47 - 1.26)	(0.4 - 0.99)	(0.59 - 1.13)	(0.65 - 1.24)	(0.63 - 1.26)	(0.54 - 1.04)	(0.66 - 1.33)	(0.54 - 1.08)	(0.71 - 1.38)	(0.6 - 1.07)	(0.74 - 1.31)
	Daily	0.51 (0.15 - 1.75)	0.54 (0.2 - 1.45)	0.33 (0.13 - 0.83)	0.55 (0.23 - 1.32)	0.36 (0.14 - 0.91)	0.43 (0.14 - 1.26)	0.29 (0.09 - 0.95)	0.41 (0.17 - 1)	0.5 (0.17 - 1.47)	0.42 (0.17 - 1.07)	0.44 (0.21 - 0.94)
Brazilian walnuts (Ref. Never)	Monthly	0.12 (0.02 - 0.74)	0.1 (0.02 - 0.65)	0.5 (0.22 - 1.12)	0.62 (0.3 - 1.29)	0.61 (0.29 - 1.29)	0.48 (0.23 - 1.01)	0.55 (0.2 - 1.46)	0.38 (0.18 - 0.79)	0.86 (0.38 - 1.96)	0.66 (0.3 - 1.48)	0.56 (0.25 - 1.25)
	Weekly	1.16 (0.48 - 2.78)	0.73 (0.33 - 1.62)	0.7 (0.36 - 1.35)	1.3 (0.88 - 1.92)	0.96 (0.5 - 1.87)	0.94 (0.56 - 1.58)	0.98 (0.6 - 1.62)	0.63 (0.27 - 1.5)	1.36 (0.75 - 2.45)	1.06 (0.67 - 1.68)	1.12 (0.82 - 1.52)
	Daily	2.48 (2.04 - 3.02)	1.46 (1.25 - 1.7)	1.5 (1.32 - 1.71)	0.72 (0.63 - 0.83)	2.14 (1.86 - 2.46)	1.34 (1.18 - 1.53)	2.19 (1.89 - 2.53)	1.58 (1.39 - 1.8)	2.26 (1.96 - 2.62)	1.33 (1.17 - 1.51)	1.68 (1.47 - 1.92)
River fish (Ref. Never)	Monthly	0.59 (0.35 - 1)	0.41 (0.41 - 0.89)	1.19 (0.77 - 1.83)	0.88 (0.62 - 1.24)	1.48 (0.84 - 2.58)	0.88 (0.62 - 1.25)	1.32 (0.79 - 2.2)	1.02 (0.67 - 1.56)	1.16 (0.72 - 1.85)	1.19 (0.81 - 1.74)	1.29 (0.82 - 2.02)
	Weekly	1.05 (0.66 - 1.67)	0.7 (0.7 - 1.34)	1.81 (1.22 - 2.69)	1.28 (0.94 - 1.75)	2.26 (1.32 - 3.87)	1.2 (0.88 - 1.63)	2.12 (1.3 - 3.44)	1.71 (1.17 - 2.51)	1.65 (1.06 - 2.57)	1.64 (1.16 - 2.33)	2.02 (1.32 - 3.1)
	Daily	0.63 (0.27 - 1.47)	0.34 (0.34 - 1.1)	1.81 (1.16 - 2.83)	1.01 (0.69 - 1.5)	2.41 (1.35 - 4.33)	0.99 (0.67 - 1.46)	2.13 (1.29 - 3.53)	1.61 (0.98 - 2.65)	1.7 (1 - 2.89)	1.83 (1.19 - 2.81)	1.94 (1.23 - 3.05)

A multiple regression model was performed with the syndromes and the independent variables of interest. The six syndromes in which a crude association with Hg levels was found were used. The final models were built following the principle of parsimony. Table 4.

Table 6.

Multivariate analysis using a Poisson regression with robust variance model.

Síndrome	PR	95% CI	Valor p
DEG[1]	1.13	(1.04 - 1.24)	0.005
BDE[2]	1.08	(1.05-1.23)	0.001
DGJ[3]	1.08	(1.01 - 1.17)	0.026
CDG[4]	1.08	(0.99 - 18)	0.057
EFG[5]	1.06	(0.97 - 1.17)	0.168
DFG[6]	1.03	(0.95 - 1.19)	0.435

*Note***:** Adjusted by **1**=Age, smoking, alcohol consumption, Brazil nuts, fish consumption (omnivore/herbivore), **2**= age, smoking, marital status, Brazil nuts ¥= age, smoking, alcohol consumption, municipality, Brazil nuts, river fish consumption. **3**= Age, smoking, alcohol consumption, municipality, Brazil nuts, consumption of river fish. **4** =Age, smoking, alcohol consumption, municipality, Brazil nuts, river fish consumption, **5**=Age, smoking, municipality, Brazil nuts, river fish consumption, whole wheat flour.

Of the six syndromes evaluated, three were statistically significant DEG, BDE and DGJ. Symptom D (Memory (self-perception)) was present in all of them, while symptoms E and G were present in two of them. Among the confounding variables found in the three final models were Brazil nuts, age, and smoking. Similarly, in the DEG and DGJ syndromes, alcoholism and fish consumption were present within the adjustment variables.

10. Discussion

The key findings described in this study suggest an association between three possible syndromes with the highest levels of Hg in hair samples. These were: 1) Alteration in memory, visual and weakness for the performance of activities (DGJ), 2) Alteration in memory, vision, vertigo (DEG) and 3) Alteration in concentration, memory, and vertigo (BDE). Likewise, no association was found in this population with the signs observed during the medical evaluation. This fact is interesting, because the scientific literature is clear in showing that clinical signs tend to be more evident when there is high exposure to methyl mercury or inorganic mercury.

One of the hypotheses is that, given that the exposures are moderate or low, the occurrence of signs is lower compared to high exposures populations such as in miners. Likewise, this research for the evaluation of signs and symptoms follows the guidelines indicated in the Global Mercury Project, which focuses mainly on symptoms. In cases of lower concentrations, only symptoms manifest themselves, but they are not considered as signs of intoxication because they are usually non-specific. Therefore, the three syndromes identified, based on the presence of symptoms, are an important step to support the diagnosis of possible cases of mercury poisoning, without the need for laboratory tests.

However, the fact that the syndromes are based on symptoms forces us to overcome the biomedical vision, hegemonic in modern medicine, and resort to the knowledge of medical anthropology. For this discipline it is clear that the symptoms are cultural manifestations dependent on specific social and political contexts (Hernáez, 1998). Symptoms require a proper interpretation in which the experience of each individual is considered, without the need to be confirmed by any test that seeks the appearance of a sign. Non-acceptance of the symptom as it is expressed by individuals can cause an inadequate translation by the doctor, which changes the essence of its meaning (Wardrope y Reuber, 2022). For this reason, it is important to apply some of the relevant principles in hermeneutics such as the interpretation (perception) that is given to the symptoms; the prefigured and prejudice, that is, the historical and social context that conditions our interpretation, given that perception is the result of constructive processes. The incompleteness of interpretation cannot be clearly determined, and the hermeneutic circle given that interpretation is an iterative process where our interests and expectations, our interpretations and consequent interpretations meet. Likewise, depending on the context in which the symptoms occur, they can change their function and therefore the actions they trigger (Wardrope y Reuber, 2022).

Therefore, the symptomatic clinical presentations that were observed in this population are not only defined by subjective "complaints and/or ailments", but by a construction in which different topics are involved, among which environmental and occupational exposure to Hg stands out, but of equal importance is the social, cultural, and political construction of one of the regions with the greatest inequality, poverty and social problems in Colombia (Geoportal DANE, s.f.). That is why these clinical presentations should not be generalized to the different populations, but deepened from social for the confrontation of a problem that transcends medicine and public health.

In the same sense, it is worth highlighting the context in which these alterations are evidenced, the participants are mostly women with environmental and occupational exposure compatible with what was reported in Brazil and in Colombian Orinoquia (Idrovo, et al., 2001; Junior, et al., 2017) where there was a greater proportion of young women living in areas exposed to Hg. This is because men are generally considered to be exposed to occupational exposure and in which case this activity corresponds to the main forms of employment and livelihood for their households (Ministerio de Minas y Energía - Unidad de Planeación Minero Energético, Universidad de Córdoba, 2014 ; Rubiano, 2018 ; Boris, 2020 Idrovo, et al., 2001 ; Ramírez, 2015).

Under this context and further aggravating the situation, the population of this area is Afro-Colombian, predominantly illiterate, poor and consume alcohol and smoke, as well as consume fish obtained from water sources contaminated by mining activities, compatible with what is reported in the literature (Epstein, et al. 1969; Tirado, et. al., 2020). In the same way, in these places there is evidence of dominance from groups outside the law, forced displacement and few work alternatives (Casas, et. al., 2015 ; OMS, 2017).

A proper interpretation of the results of this study should consider some methodological limitations. It was not feasible to have differential measurements of organic and inorganic Hg, which would have made it easier to identify clinical presentations. However, given the participating population, exposure to methyl mercury via food was more likely to be significant due to the environmental exposure. Another limitation is the selection of participants, Since the sampling was performed for convenience, this research may present a selection bias generated by non-random differences between the participants and other individuals with environmental exposure. However, since there is no general information available about the population, the presence of bias cannot be determined. Furthermore, a of the possible limitations found was the exclusion of neurological diseases in the population, even though this criterion was described in the protocol, it was not taken into account for the exclusion of the participants since none presented these diseases, which avoided the presence of a possible selection bias.

Other possible sources of bias were considered, such as possibility that the residents with more serious clinical presentations, due to this exposure, to not be present in these sites. However, it is considered that these are exceptional cases since the population targeted by this research is environmentally exposed populations with lower concentrations of Hg, hence lower severity in their clinical pictures. Among the possible confounding variables was the place of residence, explained by the levels of exposure (independent variable), that can be related to the place of residence and likewise the symptoms (dependent variable), related to cultural constructs typical of the place of residence. Therefore, the models were adjusted for this potential confounding variable, as well as for sex, age, and food consumption that have been described in the literature as potential confounding variables. Likewise, this study may present residual confounding.

Finally, for this research, fuzzy logic was implemented instead of factorial analysis for the formation of syndromes, as fuzzy logic is used to make decisions when the boundaries between categories are ambiguous or when there is uncertainty. Fuzzy logic not only allows us to group signs or symptoms, reduce the dimensionality of data, or search for underlying relationships between variables, but it also enables us to evaluate and classify the severity of symptoms or risk factors on a continuous spectrum instead of categories.

11. Conclusions

In conclusion, this study identified clusters of symptoms that were observed in individuals with higher concentrations of mercury, which were part of a population group with low and medium exposure. Given the sociocultural dependence on the manifestation of symptoms, it is a finding that cannot be extrapolated to other populations. However, for the participating population there is a list of symptoms that, when presented together, can serve as a rapid screening to identify cases of possible mercury poisoning. It is believed that such approaches can be used in contexts where laboratory tests used to identify poisonings are not readily available, which may be part of a community-based public health surveillance system. These types of tools allow communities to empower themselves over their issues and to better address their environmental health problems.

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