

# **Mercury and cardiovascular health: exploring the association with hypertension and atherosclerosis**

## **ABSTRACT**

**Aims:** To explore the association between mercury exposure and cardiovascular health, focusing on its impact on hypertension and atherosclerosis in individuals exposed to inorganic and organic mercury forms. This study aims to review the evidence on how mercury contributes to endothelial dysfunction, oxidative stress, and inflammation, which are critical mechanisms in cardiovascular disease development.

**Study Design:** This is a literature review based on observational and epidemiological studies conducted between 2000 and 2023, which investigated the effects of mercury exposure on cardiovascular diseases.

**Place and Duration of Study:** Studies included were sourced from PUBMED, BVS, SCIELO, LILACS, and MEDLINE databases, published between 2000 and 2023.

**Methodology:** This integrative review included studies on the association between mercury exposure and cardiovascular health, focusing on hypertension and atherosclerosis. The search was conducted in the PUBMED, BVS, SCIELO, LILACS, and MEDLINE databases, covering publications from 2000 to 2023 and using specific terms with Boolean operators. Observational and experimental studies in humans were included, excluding those with significant biases, unavailable in full text, or involving only in vitro or animal models. Screening was performed in three stages, with two independent reviewers and a PRISMA flow diagram to document the process.

**Results:** The studies consistently indicated a significant association between mercury exposure and increased risk of hypertension and atherosclerosis. Individuals with higher mercury levels showed greater arterial stiffness, calcification, and an elevated risk of myocardial infarction and strokes. Observational studies in populations exposed to mercury, either occupationally or through diet, demonstrated a dose-dependent relationship between mercury exposure and cardiovascular events.

**Conclusion:** Mercury exposure, particularly in vulnerable populations like industrial workers and communities with high fish consumption, is a significant risk factor for cardiovascular

diseases. The review underscores the importance of stringent public health policies and regular monitoring of mercury levels in at-risk populations to prevent long-term cardiovascular damage.

## **INTRODUCTION**

Mercury is a heavy metal widely present in the environment, with its presence resulting from both natural sources and anthropogenic activities. The main forms of exposure include the consumption of contaminated fish and occupational exposure, such as in workers from chlorine industries and gold mining. One of the most common forms of mercury exposure for the general population occurs through the ingestion of fish and seafood contaminated with methylmercury, the most toxic organic form of mercury. In the environment, mercury is released and transformed into methylmercury by microorganisms in bodies of water. This compound bioaccumulates in the food chain, reaching higher levels in larger fish and marine predators (1,2).

Mercury can be found in the environment in two main forms: organic and inorganic. The most common organic form is methylmercury, which is mainly absorbed through the consumption of contaminated food, such as fish. This form of mercury is liposoluble, which facilitates its passage through cell membranes, including the blood-brain barrier and the placenta. Thus, methylmercury can accumulate in body tissues, particularly in the brain, where it can cause significant neurological damage over time (2). In contrast, inorganic mercury includes elemental mercury, which is often found in vapor form in industrial environments, and can be easily inhaled by workers. Although the absorption of inorganic mercury through the digestive tract is less efficient, inhalation or prolonged skin contact can still be toxic, with potential adverse effects on the kidneys and nervous system. Both forms of mercury can accumulate in the human body, especially in fatty tissues and vital organs such as the brain and kidneys, resulting in health damage, including neurological, renal, and cardiovascular dysfunctions (2).

Traditionally, mercury is widely recognized for its neurotoxicity, with severe impacts on neurological development and cognitive function. However, in recent years, attention to the cardiovascular effects of mercury exposure has grown considerably. Recent research has shown that mercury can contribute to the development of hypertension, atherosclerosis, and other heart and blood vessel-related conditions, partly due to increased oxidative stress and inflammation in cardiac tissues. These findings broaden the understanding of the dangers associated with mercury beyond classic neurotoxicity, indicating that mercury may be a critical factor in cardiovascular health, especially in populations chronically or occupationally exposed (3, 4).

The growing body of epidemiological evidence has suggested an association between mercury exposure and increased prevalence of cardiovascular diseases, including hypertension and atherosclerosis. Several observational studies indicate that mercury exposure, especially in occupational settings and through diet, may be linked to changes in blood pressure, increased arterial stiffness, and calcium deposition in the arteries, factors that directly contribute to

atherosclerosis and other cardiovascular complications. However, despite these observations, further investigation is still needed to establish a clear causality between mercury exposure and cardiovascular effects. Future studies should focus on the biological mechanisms that explain this relationship and the precise quantification of exposure to validate these epidemiological associations (3, 5).

## METHODOLOGY

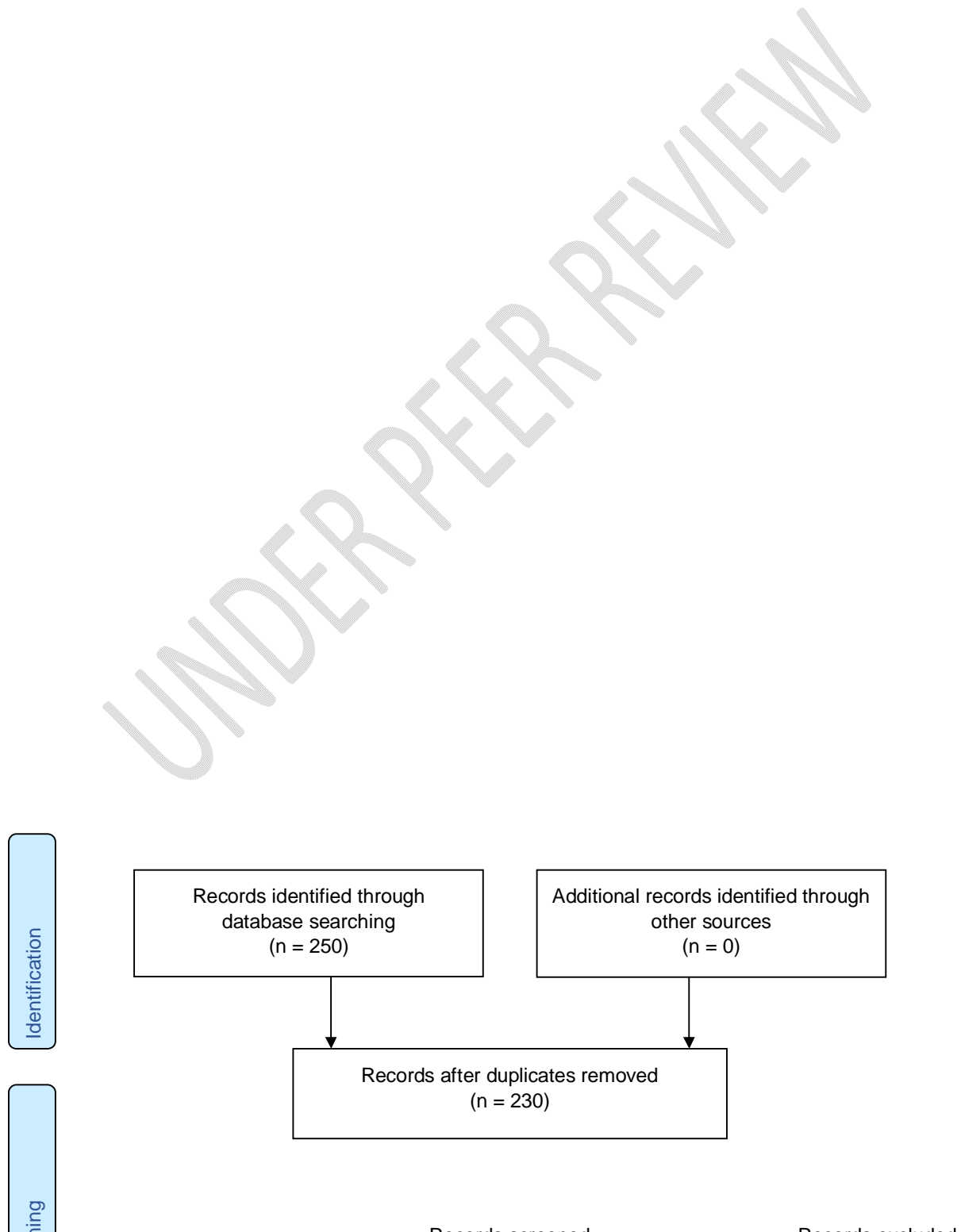


Fig 1 : Study methodology

This integrative review was developed with the aim of investigating the association between mercury exposure and cardiovascular health, focusing on conditions such as hypertension and atherosclerosis. The study gathered and analyzed epidemiological evidence and biological mechanisms from relevant research, providing a comprehensive understanding of the effects of mercury on cardiovascular health.

The sources of the new references used included the PUBMED, BVS, SCIELO, LILACS, and MEDLINE databases, covering publications from 2000 to 2023. To ensure comprehensive coverage and search precision, specific terms were used, such as "mercury exposure," "cardiovascular disease," "hypertension," "atherosclerosis," "oxidative stress," and "endothelial dysfunction," combined with Boolean operators (AND, OR). This search strategy aimed to capture high-relevance and high-quality studies, including both epidemiological analyses and experimental studies addressing the impact of mercury exposure on cardiovascular health.

Studies that directly addressed the relationship between mercury exposure and cardiovascular diseases were selected. The analysis included observational and experimental studies in humans, focusing on conditions such as hypertension and atherosclerosis, particularly in populations exposed occupationally or through diet. Studies that were not available in full text, presented significant methodological biases, or did not involve humans were excluded. Additionally, studies focusing exclusively on in vitro or animal models were not considered, in order to maintain the clinical relevance of the review.

Screening was performed in three stages: reading titles, abstracts, and finally, full texts. Two independent reviewers evaluated the studies to ensure quality and adherence to inclusion criteria, discussing any disagreements with a third reviewer for the final decision. A PRISMA flow diagram recorded the selection process, documenting the number of studies identified, excluded, and the reasons for exclusions.

This review acknowledges methodological limitations, such as the heterogeneity of the included studies, variability in mercury exposure measurements, and lack of consensus on safe exposure levels, which complicates the generalization of findings and the formulation of consistent public health guidelines.

## **RESULTS**

### **Epidemiological Evidence on the Association between Mercury and Cardiovascular Diseases**

Epidemiological studies investigating the relationship between mercury exposure and cardiovascular diseases, such as hypertension, atherosclerosis, and other cardiovascular events, point to concerning conclusions. Evidence suggests that elevated levels of mercury in the blood or hair are associated with an increased risk of developing cardiovascular diseases. For instance, in a population cohort, it was observed that mercury exposure was linked to increases in blood pressure, with individuals exposed to higher mercury levels showing a greater incidence of hypertension (6, 7, 8).

Additionally, atherosclerosis, a condition characterized by the deposition of plaques on arterial walls, was more prevalent in groups exposed to mercury. This heavy metal induces oxidative stress and damages the vascular endothelium, contributing to the development of arterial stiffness and calcification, which in turn increases the risk of myocardial infarction and strokes (CVA). Prolonged occupational exposure to mercury was particularly associated with a higher risk of vascular calcification, increasing the prevalence of events such as strokes (9, 10, 11).

Observational studies conducted in populations exposed to mercury suggest a higher incidence of severe cardiovascular events, such as myocardial infarctions, among those with higher mercury concentrations in the body. Although these studies have provided important data on the correlation between mercury and cardiovascular issues, further investigations are

still needed to understand the underlying biological mechanisms that explain this association (4, 5).

### **Pathophysiological Mechanisms**

One of the main ways mercury affects cardiovascular health is through endothelial dysfunction. The endothelium, which lines blood vessels, plays a crucial role in regulating blood pressure, primarily through the production of nitric oxide (NO), a molecule that promotes vasodilation, or the relaxation of blood vessels. Mercury directly interferes with NO bioavailability, reducing its production or increasing its degradation through heightened oxidative stress. Mercury promotes the generation of reactive oxygen species (ROS), which degrade NO, limiting its ability to mediate vasodilation, resulting in vasoconstriction and arterial stiffness (7, 12, 13).

Moreover, mercury increases the activity of enzymes such as NADPH oxidase, a major source of ROS. With the accumulation of these reactive species, NO becomes inactivated, and peroxynitrite, a highly reactive molecule, forms, contributing to oxidative damage to the endothelium and vascular tissues. This leads to a decreased ability of the vessels to dilate properly, increasing vascular resistance and, consequently, blood pressure. By elevating oxidative stress levels, mercury also triggers a chronic inflammatory response in the blood vessels. It activates inflammatory pathways, such as the NF- $\kappa$ B transcription factor, which induces the production of pro-inflammatory cytokines like IL-6 and TNF- $\alpha$ . This chronic inflammatory response is closely linked to the development of atherosclerosis, as it facilitates the deposition of lipids and the formation of atherosclerotic plaques on arterial walls. Over time, these plaques can cause the narrowing of blood vessels, further increasing the risk of myocardial infarction and strokes (CVA) (14, 15, 16).

Mercury also affects the autonomic nervous system, which controls the contraction and relaxation of blood vessels, contributing to blood pressure regulation. It increases sympathetic nervous system activity, which promotes vasoconstriction and raises blood pressure. This effect occurs mainly due to mercury's ability to enhance the sensitivity of sympathetic system receptors, exacerbating the vasoconstrictive response (3).

These interconnected mechanisms—the reduction in NO bioavailability, the increase in oxidative stress and inflammation, and the hyperactivity of the autonomic nervous system—contribute to the development of both hypertension and atherosclerosis in individuals exposed to mercury.

**Table 1 : Mechanism, Effects, and Associated Diseases**

<b>Mechanism</b>	<b>Effects</b>	<b>Associated Diseases</b>	<b>Source</b>
Endothelial Dysfunction and	Mercury reduces the bioavailability of NO,	Hypertension and Atherosclerosis	(17, 19)

Nitric Oxide (NO) Bioavailability	essential for vasodilation, leading to vasoconstriction and arterial stiffness.		
Oxidative Stress and Inflammation	Increased oxidative stress and activation of inflammatory pathways, such as NF-κB, inducing atherosclerotic plaque formation.	Atherosclerosis and Cardiovascular Diseases (MI, Stroke)	(16, 17)
Impact on the Autonomic Nervous System	Mercury stimulates the sympathetic nervous system, increasing vasoconstriction and raising blood pressure.	Hypertension	(21, 22)

Source: Authors (2024).

### Differences between Inorganic Mercury and Methylmercury

Inorganic mercury is commonly found in industrial environments, such as in chlorine production and gold mining. This form of mercury is often absorbed through inhalation or skin contact in occupational settings. The primary effects of inorganic mercury include endothelial dysfunction, with vascular damage and increased arterial resistance, leading to hypertension. However, inorganic mercury is less liposoluble than methylmercury, which limits its ability to cross cellular barriers and accumulate in tissues. On the other hand, methylmercury, an organic form of mercury, is widely found in fish and seafood, representing the largest source of exposure for the general population. Methylmercury is highly liposoluble, which facilitates its entry into cells and accumulation in adipose tissues and the central nervous system. This metal is particularly toxic due to its ability to cross barriers such as the blood-brain and placental barriers, resulting in long-term effects on the cardiovascular system (17-20).

Epidemiological studies suggest a dose-dependent relationship between methylmercury exposure and the risk of cardiovascular diseases, such as hypertension, atherosclerosis, and myocardial infarction. In populations that consume large amounts of contaminated fish, a higher prevalence of cardiovascular diseases has been observed. This occurs because methylmercury significantly contributes to increased oxidative stress and endothelial dysfunction, resulting in vasoconstriction and arterial stiffness. These effects are exacerbated in individuals with high levels of methylmercury in their blood and hair (21, 22).

**Table 2 : Forms of Mercury and Cardiovascular Effects**

Mercury Form	Cardiovascular Effects	Main Exposure Routes	Accumulation Capacity
Inorganic Mercury	Endothelial dysfunction, hypertension, vasoconstriction.	Occupational exposure (chlorine industries, gold mining).	Low tissue accumulation.
Methylmercury	Atherosclerosis, hypertension, myocardial infarction, stroke, with a dose-dependent cardiovascular risk.	Consumption of contaminated fish and seafood.	High accumulation capacity in tissues, especially in the nervous and cardiovascular systems.

Source: Authors (2024).

### **Risk Populations**

Workers in chlorine industries, gold mining, and other industrial sectors that use inorganic mercury are among the most vulnerable. These workers inhale mercury vapors, one of the most common forms of occupational exposure. Chronic exposure to inorganic mercury can result in hypertension and endothelial dysfunction, as well as increase the risk of cardiovascular diseases such as myocardial infarction and atherosclerosis. Individuals living in coastal communities or who rely on the regular consumption of fish and seafood as their primary food source are significantly exposed to methylmercury. This form of mercury accumulates in the tissues of fish, especially larger predatory fish. Prolonged exposure to methylmercury is strongly associated with increased cardiovascular risk, including hypertension and atherosclerosis. Populations that consume large quantities of fish, such as some indigenous communities or fishermen, are particularly vulnerable (8, 17, 23, 24).

In addition to workers in chlorine and mining industries, other workers who handle mercury in their daily activities, such as dentists (due to the use of mercury amalgams) and laboratory personnel where mercury is handled, are also at elevated risk of exposure. In these groups, chronic exposure, even at moderate levels, can lead to long-term cardiovascular damage (25, 26).

### **Demographic Factors Influencing Susceptibility**

- **Age:** Age is a determining factor in susceptibility to mercury's effects. Older individuals tend to be more vulnerable to the toxic effects of mercury due to greater accumulation over their lifetime and the increased fragility of the cardiovascular system. Additionally, elderly people may already have underlying diseases that are exacerbated by mercury exposure (18, 27);

- **Gender:** Studies suggest that men may be more susceptible to mercury's cardiovascular effects compared to women. However, the risk for women may increase depending on hormonal factors, such as menopause, when the drop in estrogen levels can reduce the natural protection against mercury's toxic effects, particularly in women exposed to methylmercury (27, 28, 29);
- **Genetic Characteristics:** Genetic factors also play a significant role in the response to mercury exposure. Some individuals may have genetic variations that affect the metabolism and detoxification of mercury, making them more vulnerable to its toxic effects. For example, variants in genes responsible for the production of antioxidant enzymes, such as glutathione, may influence susceptibility to mercury-induced damage, increasing the risk of cardiovascular diseases (19, 22, 29).

**Table 3: Risk Groups and Susceptibility to Mercury Exposure**

Group	Reason for Susceptibility	Cardiovascular Health Effects
Workers exposed to mercury vapors	Occupational exposure to mercury vapors in chlorine industries, mining, among others.	Hypertension, atherosclerosis, increased risk of heart attacks and stroke.
Populations with high fish consumption	Ingestion of fish and seafood contaminated with methylmercury, especially in coastal communities.	Hypertension, arterial stiffness, atherosclerosis, elevated cardiovascular risk.
Workers with indirect occupational exposure	Exposure in sectors such as dentistry and research laboratories.	Vascular damage, long-term hypertension.
Elderly	Accumulation of mercury over time, cardiovascular fragility.	Increased risk of cardiovascular diseases with age.
Post-menopausal women	Decrease in estrogen levels which may increase vulnerability to mercury, especially methylmercury.	Higher cardiovascular risk, especially after menopause.
Individuals with genetic variations	Genetic differences affecting the detoxification capacity of mercury and antioxidant response.	Greater susceptibility to mercury-induced oxidative and inflammatory damage.

Source: Authors (2024).

### Limitations and Gaps in the Literature

One of the main gaps in studies on mercury and cardiovascular health is the lack of consensus on safe exposure levels, especially regarding methylmercury found in fish and seafood. Although guidelines, such as those from the World Health Organization (WHO), establish exposure limits, studies vary widely in defining safe mercury levels in blood or hair. This inconsistency makes it difficult to compare findings and formulate consistent health policies.

Another significant limitation is the scarcity of longitudinal studies that can establish a direct causal relationship between mercury exposure and the development of cardiovascular diseases. Most of the reviewed studies are cross-sectional, which limits the ability to assess the progression of mercury exposure and the onset of diseases over time. Longitudinal studies are essential to determine whether mercury plays a direct role in the development of diseases like hypertension and atherosclerosis, or if these effects are influenced by other confounding factors.

In several studies, small sample sizes compromise the generalization of results. Studies with small or specific populations, such as workers occupationally exposed to mercury, may not reflect the effects on broader populations, like those consuming contaminated fish. Low representativity limits the application of findings to other populations, making it difficult to define public health policies that address a wider group.

The variability in methods used to measure mercury exposure is another significant limitation. Different studies use various biological markers, such as mercury levels in blood, hair, or urine, and these measurements are not always standardized. Moreover, mercury concentration can vary substantially depending on the type of exposure (dietary or occupational), making it challenging to compare results across different studies and geographic regions.

Another methodological challenge is the control of confounding factors, such as the concomitant intake of omega-3 fatty acids. Fish rich in mercury, like tuna and swordfish, are also rich sources of omega-3s, which are known to have protective effects on the cardiovascular system. This dual nature of fish consumption—simultaneously a source of toxic mercury and beneficial omega-3s—can mask mercury's adverse effects in studies, making it difficult to accurately assess its cardiovascular toxicity.

In addition to omega-3 fatty acids, many studies also struggle to control for other lifestyle factors, such as diet, smoking, physical activity, and pre-existing conditions, which can affect cardiovascular health. If these factors are not adequately adjusted in statistical models, they can introduce bias into the results, making it difficult to distinguish the direct effects of mercury from other cardiovascular risk factors.

## **DISCUSSION**

The reviewed studies indicate a strong association between mercury exposure and increased risk of hypertension and atherosclerosis. Epidemiological evidence shows that individuals with elevated mercury levels in their blood or hair are at higher risk of developing cardiovascular diseases, particularly those chronically exposed through occupational settings or the consumption of fish contaminated with methylmercury. Such exposure is associated with a higher incidence of myocardial infarctions and strokes, highlighting mercury's role in cardiovascular health. Mercury contributes to the development of these diseases through three primary mechanisms. First, it causes endothelial dysfunction by interfering with the bioavailability of nitric oxide (NO), a crucial molecule for vasodilation. Reduced NO leads to vasoconstriction and arterial stiffness, increasing vascular resistance and, consequently, blood pressure, directly contributing to atherosclerosis development (6-11).

Second, mercury exposure increases oxidative stress by promoting the generation of reactive oxygen species (ROS). These reactive species cause vascular endothelial damage and stimulate the formation of atherosclerotic plaques in arterial walls, leading to vessel narrowing and increased risk of cardiovascular events, such as heart attacks and strokes. Lastly, mercury induces chronic inflammatory responses by activating inflammatory pathways, such as the NF- $\kappa$ B transcription factor, which promotes the production of pro-inflammatory cytokines like IL-6 and TNF- $\alpha$ . This chronic inflammation facilitates lipid deposition in the arteries, promoting plaque formation and increasing the risk of cardiovascular diseases (11, 13,14-17).

Thus, these mechanisms—endothelial dysfunction, oxidative stress, and inflammation—explain how mercury can significantly increase the risk of hypertension and atherosclerosis, particularly in chronically exposed populations. The findings reviewed have important implications for both clinical practice and public health policies, particularly regarding the monitoring of cardiovascular diseases in populations exposed to mercury. The strong association between mercury exposure and increased risk of hypertension and atherosclerosis indicates the need for more rigorous hypertension screening in vulnerable groups. This includes workers in chlorine industries, gold mining, and populations that consume large amounts of contaminated fish, such as coastal and indigenous communities. Regular blood pressure screening and cardiovascular health monitoring in these groups could help in the early identification of hypertension and prevent serious complications, such as heart attacks and strokes (15, 17, 22, 23-25)

Moreover, the findings suggest the importance of regularly monitoring mercury levels in at-risk populations. Measuring mercury levels in blood or hair could be crucial to detecting exposure before irreversible cardiovascular damage occurs. This practice is especially relevant for occupationally exposed workers and individuals consuming large amounts of fish. In the field of public health policies, it is essential to educate the public about the risks of mercury exposure, particularly through the consumption of contaminated fish. Educational campaigns could guide the population on which fish species contain higher mercury levels and how to reduce consumption of these foods. Additionally, food policies that promote the consumption of

low-mercury fish would be beneficial to protect the general population's cardiovascular health (19-22, 26, 27).

In workplace settings, the findings underscore the need for stricter regulation of occupational mercury exposure. The mandatory use of personal protective equipment (PPE) and the implementation of stricter exposure limits are essential measures. Occupational health programs should also include regular monitoring of mercury levels in workers and preventive measures to mitigate the long-term effects of this exposure. Lastly, the results highlight the importance of global policies aimed at reducing mercury emissions, such as the Minamata Convention. International cooperation is crucial to limit mercury use in industrial processes and reduce environmental contamination, thus protecting vulnerable populations in different regions of the world (18, 19, 27-29).

### **Study Limitations**

This integrative review presents some important limitations that should be acknowledged for a more accurate interpretation of the findings. One of the main limitations is the heterogeneity of the included studies. Different studies used varied methods to measure mercury exposure, such as mercury levels in blood, hair, or urine. This variability in measurement methods can complicate direct comparison of results, as mercury exposure may vary depending on the type of sample collected and the environmental or occupational conditions of the participants. Additionally, some studies focused on occupationally exposed populations, while others analyzed dietary exposure, which can also introduce differences in the results.

Another relevant limitation is the potential sampling bias in the studies. Many of the works included in the review were conducted with small or specific samples, such as workers in industrial sectors or populations consuming large amounts of fish. While these groups are important for understanding the impacts of mercury exposure, the results may not be fully representative of the broader population. This limitation makes it difficult to generalize the findings to other contexts and population groups.

Additionally, there is a risk of publication bias, which is common in integrative reviews. Studies with negative or null results may have been underrepresented in the literature, as these types of research tend to be less published. This could lead to an overestimation of the relationship between mercury exposure and cardiovascular risks, potentially creating an incomplete view of the real impact of mercury on cardiovascular health.

Finally, many of the reviewed studies are observational in nature, which limits the ability to establish a direct causal relationship between mercury exposure and the development of cardiovascular diseases. Although the associations are strong, there is a lack of longitudinal studies that can confirm these relationships over time, as well as a better understanding of the biological mechanisms involved.

These limitations point to the need for additional research that uses more consistent methodologies, with larger and more representative samples, as well as better control of confounding factors such as omega-3 intake and other dietary or lifestyle variables that may influence the results.

## CONCLUSION

The main findings of this review reinforce the significant association between mercury exposure and the increased risk of developing cardiovascular diseases, such as hypertension and atherosclerosis. Epidemiological studies indicate that individuals with elevated mercury levels in their blood or hair, primarily due to occupational exposure or the consumption of fish contaminated with methylmercury, are at higher risk of cardiovascular diseases. These findings are consistent with evidence showing that mercury contributes to endothelial dysfunction, increased oxidative stress, and chronic inflammation—mechanisms underlying the development of serious heart and vascular diseases, such as myocardial infarctions and strokes (CVA).

The results show that mercury exposure is associated with an increased risk of hypertension and atherosclerosis, particularly in exposed workers and populations consuming contaminated fish. For public health, it is essential to implement strict policies to reduce this exposure, including regular screenings in vulnerable populations and educational campaigns about the risks of mercury in food. Stricter occupational regulations and the strengthening of global agreements, such as the Minamata Convention, are necessary to limit mercury emissions and protect the cardiovascular health of these populations.

Given the clear association between mercury exposure and the increased risk of cardiovascular diseases, more rigorous measures must be adopted to protect vulnerable populations. Implementing effective public policies, occupational regulations, and educational campaigns is crucial to mitigate these risks. The continued commitment of governments, international organizations, and the scientific community is essential to reduce mercury exposure and preserve cardiovascular health. Immediate and coordinated action is necessary to ensure that future generations do not suffer the devastating effects of mercury exposure (17, 18, 27 – 29).

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