REVIEW ARTICLE

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Prenatal and Postnatal Heavy Metal Exposure in Relation to Neurodevelopmental Disorder and ADHD: A Systematic Review

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ABSTRACT

Background: Susceptibility to environmental insults during fetal brain development has been linked to increased risk of neurodevelopmental disorders, including Attention Deficit/Hyperactivity Disorder (ADHD). ADHD is a prevalent neurodevelopmental disorder in children, influenced not only by genetics but also by environmental factors, particularly by prenatal exposure to heavy metals. Heavy metals such as lead, mercury, cadmium, and arsenic are known neurotoxins that can disrupt fetal brain development; however, evidence regarding their role in ADHD remains inconsistent.
Objective: To determine whether prenatal and/or postnatal exposure levels are associated with increased risk or severity of ADHD in school-aged children.
Methods: : This systematic review followed PRISMA guidelines to evaluate the association between prenatal heavy metal exposure and the risk of ADHD in children. The PECO framework was used to define the population, exposure, comparator, and outcomes. A comprehensive literature search was conducted across PubMed, ScienceDirect, and ProQuest using relevant keywords. Eligible studies included human observational research (cohort, case-control, cross-sectional) between 2021 and 2025 assessing prenatal exposure to heavy metals and neurodevelopmental outcomes and ADHD.
Results: Several studies reported that elevated prenatal levels of cadmium, lead, and manganese were associated with increased ADHD symptoms or reduced cognitive performance. Findings on mercury were mixed, potentially due to confounding factors including fish intake and maternal nutrition. Selenium and copper demonstrated dual effects, being essential at low levels but harmful at high concentrations. Thallium exposure in the third trimester significantly impaired cognitive and psychomotor development. Some studies highlighted sex-specific and nonlinear dose-response effects.
Conclusion: Heavy metals affect neurodevelopment inconsistently. Some studies link prenatal cadmium and lead exposure to neurodevelopmental problems, yet others disagree. Meanwhile, prenatal and postnatal heavy metal exposure, especially cadmium, mercury, and lead, is linked to childhood ADHD.

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1. Introduction

The period of rapid brain growth and plasticity in the fetus during pregnancy, combined with distinct biological and social factors, is associated with reduced resilience to harmful environmental insults compared to adulthood.[1] This heightened vulnerability during critical developmental windows has been linked to the emergence of various neurodevelopmental disorders, including Attention-Deficit/Hyperactivity Disorder (ADHD).[2]

ADHD is one of the most common neurodevelopmental disorders among children. A recent meta-analysis reported a global prevalence of ADHD at approximately 6%–8% in children and adolescents, with a notably higher incidence in boys nearly twice that of girls.[3]

ADHD is characterized by inattention, hyperactivity, and impulsivity, all of which can disrupt academic performance and social interactions. While genetic predisposition plays a significant role, environmental exposures during the prenatal period and early life are increasingly recognized as critical risk factors for neurodevelopmental disorders, including ADHD.[4]

Environmental sources are the primary contributors to heavy metal exposure, such as lead (Pb), mercury (Hg), cadmium (Cd), arsenic (As), manganese (Mn), copper (Cu), and selenium (Se), all of which are known neurotoxins. These metals can enter the human body through contaminated air, water, soil, food, and anthropogenic sources such as industrial emissions, waste, battery recycling, and pesticides.[5]

Heavy metals have the potential to induce oxidative stress by increasing the production of reactive oxygen

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species (ROS), which in turn damages neuronal structure and function. This oxidative insult can trigger neuroinflammation and neuronal apoptosis, processes that are particularly critical during early stages of neurodevelopment.[6] Additionally, disturbances in neurotransmitter systems—especially dopaminergic and noradrenergic pathways—are recognized as key pathophysiological mechanisms contributing to core symptoms of ADHD, such as inattention and impulsivity.[7] Furthermore, prenatal exposure to heavy metals has been associated with epigenetic modifications, including DNA methylation in genes essential for neurodevelopment, which may result in long-term alterations in brain function among children.[8]

According to the World Health Organization (WHO), no level of lead exposure is considered safe; even low levels can impair children's IQ and attention capacity. Methylmercury, often found in fish and shellfish, poses a significant threat to fetal and early childhood brain development. Chronic exposure to inorganic arsenic has been linked to reductions in cognitive function, intelligence, and memory in children.[9] Globally, it is estimated that nearly one-third of children have blood lead levels of ≥5 μg/dL, which can silently damage neurological development.[10]

Several cohort studies have shown that prenatal exposure to heavy metals may adversely affect children's neurodevelopment and increase the risk of ADHD. Elevated maternal levels of lead, cadmium, and copper during pregnancy have been associated with greater behavioral symptoms resembling ADHD and reduced cognitive function in early childhood.[11,12] Additionally, children diagnosed with ADHD have been reported to exhibit higher blood mercury levels compared to neurotypical peers.[13]

However, findings across studies remain inconsistent, depending on the type of metal, exposure levels, population characteristics, and mediating factors such as maternal nutrition and socioeconomic status. Many previous investigations have assessed heavy metals in isolation, without accounting for complex mixture effects or directly linking exposures to clinically diagnosed neurological outcomes. Therefore, this study aims to investigate the association between prenatal exposure to heavy metals (including Pb, Cd, Hg, As, Mn, Cu, Se, and others) and children's neurodevelopment, with a specific focus on ADHD symptoms. The primary objective is to determine whether prenatal and/or postnatal exposure levels are associated with increased risk or severity of ADHD in school-aged children. This research seeks to address existing gaps in understanding the environmental contribution of heavy metals to ADHD and to provide an evidence-based foundation for early preventive strategies, particularly within the Indonesian context.

2. Methods

Literature Search Strategy

The literature search was conducted systematically by RHS on May 11, 2025, at 18:30, utilizing major electronic databases, including PubMed, ScienceDirect, and ProQuest. The search strategy was developed by AD using a combination of keywords and Boolean operators, including:

((ADHD) OR (Attention Deficit Hyperactivity Disorder) OR (Attention Deficit Disorder) OR (ADD) OR (Hyperkinetic Disorder) OR (MBD) OR (Attention Disorders) OR (Hyperactivity Disorder) OR (Minimal Brain Dysfunction)) AND ((Heavy metals) OR (toxic metal*) OR (trace metal) OR (dense metal) OR (contaminant metal) OR (poisonous metal) OR (hazardous metal) OR (pollutant metal) OR (environmental toxin*) OR (Cadmium) OR (Mercury) OR (Lead) OR (Arsenic) OR (Chromium)) AND ((prenatal) OR (pre-natal) OR (in utero) OR (maternal-fetal transfer) OR (fetal exposure) OR (gestational exposure) OR (Antenatal) OR (Maternal exposure)).

Research Question

The research question was formulated using the PECO framework. The population of interest included children diagnosed with ADHD. The exposure of interest is prenatal exposure to any heavy metal or trace element, irrespective of whether the metal was classified as toxic or essential. The comparison group, if available in the included studies, consisted of children with ADHD who had minimal or no exposure to these metals. The main outcomes observed were neurodevelopmental impairments such as attention deficits, hyperactivity, cognitive dysfunction, impaired adaptive behavior, or other relevant parameters.

Inclusion and Exclusion Criteria

The inclusion criteria for this review encompassed studies involving pregnant women and children, particularly those exhibiting symptoms or diagnosed with ADHD or related neurodevelopmental disorders. The studies evaluated prenatal and postnatal exposure to heavy metals such as lead, mercury, cadmium, arsenic, chromium, or any other heavy metals and assessed its association with ADHD and neurodevelopmental disorder occurrencein children. Accepted study designs included observational studies (cohort, case-control, cross-sectional), longitudinal, prospective, or retrospective studies. Only English-language articles published in the last five years (2021–2025) and available in full text were included in the analysis.

Exclusion criteria included studies involving adult or animal populations, studies not focusing on ADHD as the primary outcome, or non-scientific publications such as editorials, opinions, and review articles (except for snowballing purposes). Articles that were not in English, duplicates, or lacking sufficient data were also excluded. These criteria were established by RHS through a team discussion forum.

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Study Selection Process

The study selection was conducted in three stages. First, four researchers (ADAK, GVPH, IMR, and TAL) independently screened titles and abstracts. Second, full-text screening was conducted on articles that passed the initial screening to assess their eligibility based on the inclusion criteria, also by ADAK, GVPH, IMR, and TAL. Third, in cases of discrepancies between reviewers, a consensus discussion was held, and if necessary, a third reviewer was involved. The entire selection process was illustrated using a PRISMA flow diagram.

Data Extraction

Data from each eligible study were systematically extracted, including information on the authors, year of publication, country of study, study design, population characteristics (age, sample size, ADHD status), type and concentration of heavy metals measured, exposure assessment methods, and the reported neurodevelopmental outcomes and assessment tools.

Quality Assessment of Studies

The methodological quality of each study was assessed using ROBINS-E (Risk of Bias in Non-randomized Studies of Exposures), which was appropriate for evaluating the risk of bias in observational studies examining the relationship between exposures and outcomes.

Data Synthesis and Analysis

The data synthesis was conducted through a combination of narrative and descriptive analysis, with studies categorized according to the timing of exposure (prenatal vs. postnatal), the type of heavy metal (lead, mercury, cadmium, arsenic), and the outcome classification (general neurocognitive developmental disorders vs. Attention Deficit Hyperactivity Disorder (ADHD)). Key findings were discussed to describe the strength of evidence, the direction of the observed associations, and potential underlying neurotoxic mechanisms.

3. Results

During the treatment period, two rats from the control group (K), one rat from group P2, and one rat from group P3 dropped out due to death. Serum IL-6 levels were measured using the ELISA method

A total of 1419 studies were obtained via a comprehensive literature search, with 1408 remaining after the elimination of 11 duplicates. Following the analysis of abstracts and titles, 1392 papers were excluded for irrelevance to the issue, incorrect population, or inappropriate exposure, leaving 16 articles for full-text evaluation. A comprehensive analysis was performed, resulting in the exclusion of 2 research studies due to unavailability of full texts, whereas 14 articles were ultimately included in the study (Figure 1).

Among these studies, there are 11 cohort studies and 3 cross-sectional studies evaluating various types of heavy metals. These studies examined the impact of heavy metal exposure on neurodevelopment and the prevalence of ADHD. Of the 14 research studies, 7 examined the impact of heavy metal exposure on neurodevelopment, while the other 7 focused on ADHD.

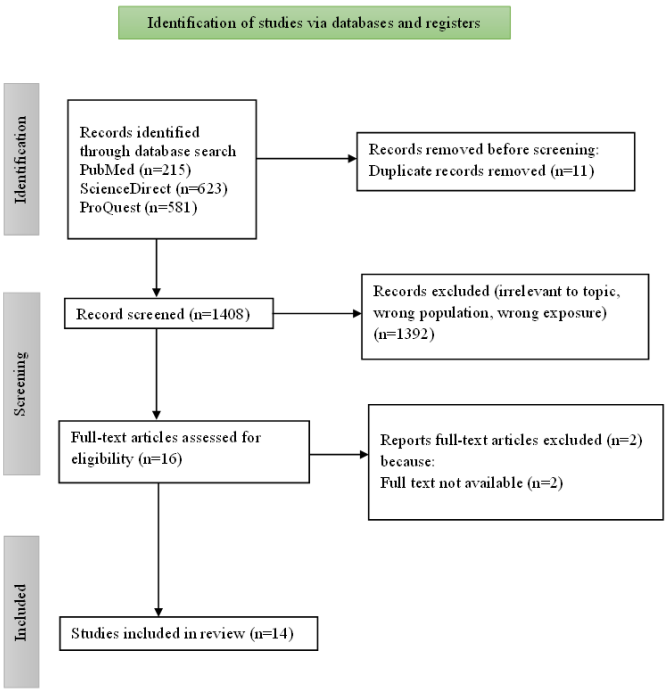

Figure 1. Study Selection

The included studies underwent a quality assessment using the ROBINS-E tool, which revealed that four articles had a low risk of bias, six had some concerns, one had a high risk of bias, and three had a very high risk of bias. Even though quality assessment results did not affect the exclusion of certain articles, it is still important to note each study's risk of bias, as seen in Figure 2.

Figure 2. ROBINS-E Quality Assessment.

Neurodevelopmental

A number of research studies have been conducted to assess the relationship between heavy metal exposure and neurodevelopmental outcomes in general. Among the seven studies reviewed, one examined the impact of prenatal cadmium exposure on neurodevelopment. It determined that with maternal blood cadmium levels at 0.76 µg/L and cord blood at 0.04 µg/L, there is no evidence correlating

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prenatal cadmium exposure with neurodevelopmental outcomes at two years of age, as assessed by the KPSD score. [14]

The impact of mercury on neurodevelopment was evaluated in two cohort studies, with divergent outcomes. Maternal hair containing 6.87 μg/g MeHg shows no significant correlation with 17 neurodevelopmental outcomes in children at 7 years of age. This outcome aligns with the previously studied cohort, wherein a maternal blood mercury level of 3.7 ng/g revealed no significant correlation with neurodevelopmental delays in infants up to 4 years, as evaluated by ASQ-3. [15,16]

Lead, as examined in two analyzed research studies, demonstrates varying outcomes. 0.64 μg/L detected in umbilical cord blood serum had no statistically significant correlations with neurodevelopment at 1 year of age, as evaluated by BSID-III. Simultaneously, another cohort examined that at maternal blood lead levels of 0.54 μg/dL, each two-fold rise in blood lead levels correlates with an increase of 0.4 points in SRS-2 scores; however, in the third trimester, the link is nonexistent, even at maternal blood lead levels of 0.49 μg/dL.[17,18]

Other studies indicated that heavy metals, including selenium and thallium, were correlated with neurodevelopmental outcomes. The heightened risk of neurodevelopmental delays in children up to 4 years of age, as evaluated by ASQ-3, was particularly significant when selenium levels in maternal blood were ≥168 ng/g. Prenatal exposure to thallium at a concentration of 0.35 μg/L in a urine sample during the third trimester of pregnancy was substantially correlated with compromised neurodevelopmental outcomes, encompassing both cognitive and psychomotor domains, in children at 2 years of age as evaluated by BSID-CR.[16,19]

A study examined three heavy metals, arsenic, strontium, and manganese, and discovered that prenatal exposure to these metals (arsenic: 1.03 μg/L; strontium: 56.3 μg/L; manganese: 2.41 μg/L), whether individually or in combinations, was significantly correlated with neurodevelopmental impairment at 1 year of age, as evaluated by BSID-CR.[18]

Copper and zinc exhibited no correlation with the cognitive composite score in both the cord blood sample (Cu: 699.2 ng/g; Zn: 2538 ng/g) and the breast milk sample (Cu: 607 ng/g; Zn: 3226 ng/g) as evaluated by BSID-III; however, a robust direct correlation was observed between Cu concentration in cord blood and the motor composite score.[20]

ADHD

Prenatal Exposure

Two studies were identified that examined ADHD outcomes associated with mercury exposure during gestation. No statistically significant association was found between mercury levels in pregnant women and ADHD diagnosis or symptom ratings in either study. The evaluation instruments employed were the ADHD-DSM-IV, SDQ, CPRS-R:S, CBCL, clinical ADHD/ASD diagnosis, Conners' Rating Scales, and ASSQ. The concentrations of mercury in maternal blood and cord blood were 0.74 μg/L and 8.22 μg/L, respectively.[12,21] A study indicated that children whose mothers possessed higher educational attainment were more predisposed to ADHD if exposed to cadmium in utero. A clinical diagnosis of ADHD/ASD was conducted with the CBCL, Conners' Rating Scales, and ASSQ for assessment of ADHD. The concentration measured was 0.17 μg/L. Prenatal exposure to cesium (1.05 μg/L) was associated with a reduced risk of ADHD, but cobalt (0.47 μg/L) was not correlated with an increased risk. A negative correlation existed between copper (1,289 μg/L) and the risk of ADHD. Lead (4.82 μg/L) exhibited a weak association, however a non-linear dose-response relationship was observed. Elevated magnesium levels (18,822 μg/L) were associated with an increased risk of ADHD in a non-linear fashion. Maternal education influenced the effects of manganese (3.31 μg/L). Selenium (128 μg/L) appeared to have no impact, however zinc (6,545 μg/L) appeared to reduce the risk of ADHD. Arsenic (0.57 μg/L) did not demonstrate a consistent significant association; nevertheless, a non-linear dose-response relationship was seen.[12]

Postnatal Exposure

Research revealed that an increase in mercury levels of 15.22 μg/L correlated with a 2.43% decrease in serine levels, whereas glycine levels increased by 4.99% and GABA levels rose by 3.09%. We employed the Conners' Rating Scale and neurobehavioral performance metrics to assess ADHD symptoms. The mean concentration of mercury in the blood was 2.47 μg/L.[22] Two research studies were identified about lead. The initial analysis revealed that hair lead concentration (0.88 μg/g) was the highest among the metals assessed. Every decile rise in all metals correlated with a decrease of −1.01 in Full Scale IQ and −1.11 in Verbal IQ, while mothers said that their children had ADHD-like behaviors and difficulties with executive function. The second investigation revealed that the mean blood lead concentration was 35.0 μg/L. A rise of 6.10 μg/L was associated with reduced levels of Glu (−8.52%), Gly (−30.06%), and GABA (−20.10%).[22,23] Two studies examined arsenic. The initial research (hair As: 0.25 μg/g) revealed a decline in IQ and behaviors akin to ADHD, similar to the effects of lead. The second research indicated that a blood As level of 4.58 μg/L was associated with an elevation of 19.37 μg/L connected to elevated glycine (+6.32%) and elevated GABA (+2.09%). Two investigations indicated that increased exposure to cadmium correlated with minor reductions in IQ and alterations in

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neurochemicals (Glu, Gly, Ser, GABA) that exacerbates ADHD symptoms. Two investigations indicated that elevated manganese levels were associated with diminished IQ, alterations in neurotransmitters, and signs of ADHD. Increased exposure to zinc (mean: 5.75 mg/L; blood: 15.58 µg/L) was associated with a rise in serine (+1.44%) but a decrease in Glu, Gly, and GABA levels. Selenium (mean: 0.19 mg/L; blood concentration: 38.75 µg/L) was associated with elevated GABA levels (+1.88%), which alleviated ADHD symptoms.[22]

Prenatal–Postnatal Exposure

Three investigations (8.9–16.12 µg/L) regarding lead yielded inconclusive outcomes: Kampouri et al. (2024) identified no significant correlation between lead exposure and cognitive function; Maitre et al. (2021) reported elevated ADHD symptomatology; and Aydin et al. (2024) saw no substantial differences between individuals with ADHD and control subjects. Kampouri et al. (2024) discovered no significant inverse correlations between cadmium levels (0.17–0.33 µg/L in maternal samples; 0.24 µg/L in serum) and ADHD scores. Maitre et al. (2021) discovered elevated ADHD scores, but Aydin et al. (2024) identified that controls exhibited greater levels. Maitre et al. (2021) and Aydin et al. (2024) discovered a correlation between elevated mercury levels (0.35–15.22 µg/L) and increased ADHD scores. Kampouri et al. (2024) did not identify any mercury-specific findings. Maitre et al. (2021) discovered a correlation between arsenic concentrations of around 1.0 µg/L and elevated ADHD scores. The other research lacked pertinent data.[11,13,24]

4. Discussion

In terms of neurodevelopment, seven studies examine different heavy metal exposures during prenatal, postnatal, or both periods and their effect on neurodevelopment. Ma, Chaochen, et al. (2021) determined that prenatal cadmium exposure is not correlated with neurodevelopmental outcomes at 2 years of age. Subsequent investigations indicated that increased prenatal cadmium exposure was markedly correlated with adverse neurodevelopmental outcomes. Data regarding the correlation between prenatal cadmium exposure and child neurodevelopment is limited and yields contradictory results. Certain investigations indicated that exposure, assessed via maternal urine cadmium levels, had a detrimental effect on children's neurodevelopment, corroborating the findings of Ma, Chaochen, et al. (2021), despite a US cohort reporting a positive correlation.[14]

This outcome on neurodevelopment corresponds with findings from earlier studies concerning the link between prenatal cadmium exposure and ADHD or behavioral issues in early childhood. Kampouri et al. (2024) discovered that lead and cadmium levels in gestational and cord blood exhibited a non-significant inverse relationship with children's cognitive capacities, but childhood erythrocyte and urine cadmium showed a non-significant association with heightened behavioral issues. Notably, although not statistically significant, all data demonstrated a constant unfavorable correlation between heavy metals and cognitive ability. Analysis of ADHD raw scores indicated that gestational erythrocyte cadmium levels were marginally but significantly elevated in children with ADHD.[24]. Additional research examining heavy metal exposure during the perinatal period corroborated this, with Skogheim et al. (2021) identifying a correlation between elevated cadmium and magnesium levels in maternal blood and an increased risk of ADHD, but copper and mercury exhibited inverse relationships with ADHD. This outcome on neurodevelopment corresponds with findings from earlier studies concerning the link between prenatal cadmium exposure and ADHD or behavioral issues in early childhood. Kampouri et al. (2024) discovered that lead and cadmium levels in gestational and cord blood exhibited a non-significant inverse relationship with children's cognitive capacities, but childhood erythrocyte and urine cadmium showed a non-significant association with heightened behavioral issues. Notably, although not statistically significant, all data demonstrated a constant unfavorable correlation between heavy metals and cognitive ability. Analysis of ADHD raw scores indicated that gestational erythrocyte cadmium levels were marginally but significantly elevated in children with ADHD.[24] Additional research examining heavy metal exposure during the perinatal period corroborated this, with Skogheim et al. (2021) identifying a correlation between elevated cadmium and magnesium levels in maternal blood and an increased risk of ADHD, but copper and mercury exhibited inverse relationships with ADHD.

Maternal consumption of substantial amounts of fish may lead to increased average methylmercury (MeHg) exposure, as demonstrated in the study by Strain, JJ., et al. (2021). This study demonstrated that MeHg exposure during and prior to pregnancy does not have a statistically significant correlation with neurodevelopmental outcomes at 7 years of age.[15] This study concurs with the research by Kobayashi, Sumitaka, et al. (2022), which indicated no significant correlation between maternal mercury exposure and the risk of neurodevelopmental delays in children up to the age of 4 years.[16] Mercury, as a heavy metal, is frequently linked to fish consumption, and its adverse correlation in prior research may be elucidated by a study conducted by Sarzo et al. (2024), which investigated total mercury levels in pregnant women concerning fish intake. This study revealed that while increased fish consumption was associated with exacerbated ADHD symptoms, intake exceeding 4.93 servings per week did not exhibit this correlation.[21,25] The advantages of a fish diet on neurodevelopment may surpass the detrimental effects of mercury, which could explain why certain research yields non-significant results. The aforementioned study by Kobayashi, Sumitaka, et al. (2022) supports the notion that

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fish eating offers nutrients, including n-3 PUFAs, which alleviate the adverse effects of mercury exposure.[16]

This, however, may not correspond with the previously mentioned study conducted by Strain, JJ., et al. (2021). This study indicated that there is no statistically significant correlation between maternal mercury exposure and certain polyunsaturated fatty acids (PUFAs) prevalent in fish (DHA and AA). However, it noted increasing trends in four outcomes related to executive function, cognition, and linguistic skills as the maternal n-6: n-3 ratio (DHA:AA ratio) rises. This finding contradicts the hypothesis posited in the study, which suggested that a higher n-6 status could elevate the previously mentioned score. However, n-6 PUFA-derived eicosanoids, such as arachidonic acid (AA), are more proinflammatory than n-3 PUFAs, like DHA, thereby diminishing protection against mercury's effects.[15]

The research by Alampi, Joshua D., et al. (2024) showed a correlation between maternal blood lead levels and autistic-like behaviors, evaluated using SRS-2 ratings. This relationship varies according to the age of gestation. During the first trimester, a two-fold increase in blood lead levels correlates with a 0.4-point rise in SRS-2 scores; however, in the third trimester, this link is nonexistent. This ultimately corresponds with other studied investigations.[17] Findings from a study conducted by Maitre et al. (2021) indicated analogous outcomes regarding ADHD, revealing that elevated exposure to lead and copper correlated with heightened Conner's rating scale and ADHD index scores. However, these results were confounded by the influences of indoor air pollution and an unhealthy diet during early childhood, thus precluding a distinct interpretation of heavy metal associations.[11] Alampi, Joshua D., et al. (2024) shown that the correlations between prenatal blood lead levels and juvenile autistic-like characteristics are more pronounced when gestational plasma total folate concentrations are diminished. This occurs because folate supplies methyl groups utilized in cellular methylation processes, including DNA methylation, essential for DNA repair and de novo nucleotide synthesis.[17]

Baribero, Fabiano, et al. (2024) demonstrated a robust direct correlation between neurodevelopment and copper levels in cord blood, as measured by the motor composite score on the BSID-III test at 18 ± 2 months of age. This indicates the critical need of copper as a trace element for children's neurodevelopment in early life, yet excessive copper can be neurotoxic. This study exclusively assessed copper as a trace element, without considering its detrimental effects. This study indicated that zinc (Zn), as a trace element, is not correlated with cognitive composite scores.[20]

Another study by Fan, Xiao Yuan, et al. (2024), utilizing PDI and MDI scores, indicates a potential correlation between copper exposure and the risk of delayed psychomotor and cognitive development in children. Positive additive interactions were seen between zinc and other evaluated metals, specifically between manganese and zinc on PDI and between iron, zirconium, zinc, and arsenic on MDI. These metals may enhance neurodevelopment in children by co-exposure, presumably via processes such as oxidative stress, immunological modulation, or metabolic function. This study indicated that iron could influence neurodevelopment through its interactions with certain metals, including copper and zinc, during absorption and metabolism.[18]

The study's findings indicated that selenium (Se) was the most significant factor in the correlation between metal combinations and newborn cognitive development, as seen by the MDI score.[18] This finding is consistent with the previously referenced work by Kobayashi, Sumitaka, et al. (2022). This study indicates that elevated selenium levels in maternal blood may correlate with a marginally heightened risk of neurodevelopmental delays, particularly in communication, gross motor skills, fine motor skills, problem-solving abilities, and personal and social skills. The escalating risk was especially significant when levels surpassed 168 ng/g in maternal blood. This correlation was more pronounced in female children and offspring of primiparous moms. Ingested selenium can be converted into selenoproteins, which are involved in the manufacture of thyroid hormones, hence influencing brain development, where thyroid hormones are crucial.[16]

Thallium, a very poisonous metal, is significantly more dangerous than previously discussed metals such as lead, mercury, and cadmium. Thallium, however, is extensively concentrated in soil and water. This ultimately presents considerable public health issues. A study by Wu, Mingyang, et al. (2024) indicated that prenatal exposure to thallium during the third trimester was significantly linked to impaired neurodevelopmental outcomes in both cognitive and psychomotor domains in children at 2 years of age, with no significant associations observed in the first or second trimester. While the mechanism is not fully elucidated, several ideas may account for thallium toxicity through mitochondrial enlargement, oxidative stress, or the induction of neurotoxic consequences via secondary excitotoxic pathways. Moreover, during late pregnancy, brain development reaches its zenith, and the fetal brain experiences accelerated growth; consequently, it is susceptible to environmental toxins such as thallium, which may interfere with the formation and maturation of the brain, resulting in delays.[19]

Other examined studies suggest the impact of heavy metal intake on ADHD. He et al. (2021) investigated the impact of postnatal heavy metal exposure on the development of ADHD and learning disabilities in early childhood, mediated by the neurotransmitter's glutamate, glycine, and GABA. While no definitive conclusions exist regarding the direct association of specific heavy metals with ADHD, it has been observed that lead, zinc, selenium, mercury, and manganese can modify neurotransmitter levels, which exhibit significant linear correlations with the impulsivity-hyperactivity index, learning disability index, and ADHD index.[22]

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Stein et al. (2022) investigated the correlation between heavy metals and ADHD development during middle childhood, revealing results consistent with prior research that indicated elevated hair metal concentrations were linked to diminished IQ scores, alongside maternal reports of ADHD-like behaviors corresponding to these assessments.[23] Nevertheless, whereas these investigations primarily utilized children as their subject samples, heavy metal exposures assessed throughout childhood may also originate from the prenatal era; thus, it is challenging to distinctly differentiate between pre- and postnatal childhood exposures.

However, the limitation of this study is the protocol for this systematic review was not registered in PROSPERO, which may increase the risk of reporting bias.

5. Conclusion

In conclusion, the result on how heavy metal exposure affects neurodevelopment is still often inconsistent. Some studies say that prenatal exposure to metals like cadmium and lead is linked to worse neurodevelopmental outcomes, while others say there is no clear association. Meanwhile, the results of mercury exposure, especially from eating fish, suggest that the health benefits of fish may outweigh the risks. However, this is still a controversial field of research. Also, the importance of trace metals like copper and selenium in brain development is emphasized, with data showing that they may have both good and bad impacts depending on how much exposure there is. Thallium is a very toxic heavy metal since there are strong links between being exposed to it before birth and having problems with cognitive and psychomotor development. In the end, both prenatal and postnatal heavy metal exposures mostly have an association with the emergence of ADHD in childhood, with results most notable for cadmium, mercury, and lead.

Ethical Approval

There is no ethical approval.

Conflicts of Interest

There is no conflict of interest between authors.

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Author Contributions

Conceptualization: GVPH, IMP, ADAK, TAL, and RHS; methodology: GVPH, IMP, ADAK; software: GVPH, IMP; validation: GVPH, IMP, ADAK, TAL, RHS, SB; formal analysis: GVPH, IMP, ADAK, TAL, and RHS; investigation, XXX; resources: GVPH, IMP, ADAK, and TAL; data curation: GVPH, IMP, ADAK, and TAL; writing—original draft preparation: GVPH, IMP, ADAK, TAL, and RHS; writing—review and editing: GVPH, IMP, ADAK, TAL, RHS, SB; visualization GVPH, IMP, ADAK, TAL, and RHS; supervision: SB; project administration: GVPH and IMP.

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