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Environmental Risk Factors and the Impact of Heavy Metals on Pregnancy and Perinatal Outcomes

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Abstract. Prenatal exposure to heavy metals constitutes an important but often under-recognized environmental risk factor influencing pregnancy outcomes and perinatal health. This article reviews recent evidence (2020–2025) addressing how exposure to metals such as cadmium (Cd), lead (Pb), mercury (Hg), arsenic (As), chromium (Cr), nickel (Ni), and mixtures thereof impact maternal health, fetal growth, birth outcomes, and longer-term neonatal consequences. We discuss mechanisms of toxicity, critical windows of vulnerability, and the role of mixed exposures and environmental context. The review summarises observational and cohort studies showing associations with outcomes including preterm birth, small for gestational age (SGA), low birth weight (LBW), stillbirth, and neurodevelopmental sequelae. Findings emphasize that even relatively low exposures may exert measurable effects, and that environmental regulation, biomonitoring, and clinical awareness are required to mitigate these risks. The article concludes with recommendations for research, policy, and practice.

Keywords: heavy metals; pregnancy; perinatal outcomes; preterm birth; low birth weight; environmental exposure; cadmium; lead; mercury; mixed metal exposure

Introduction:

Maternal and fetal health are intimately influenced by the environment in which pregnancy occurs. Among the many environmental risk factors, heavy metals have emerged as critical contaminants with the potential to adversely affect reproductive outcomes. Heavy metals are generally defined as metallic elements with relatively high atomic weight and density, many of which are persistent in the environment, bioaccumulate in living organisms, and cannot be readily degraded. [3]

During pregnancy, the developing fetus is especially vulnerable to environmental insults due to rapid cell growth, differentiation, and limited capacity for detoxification. The placenta, once thought of as a more effective barrier, is now known to allow transfer of some metals or their metabolites to the fetus. [2], [3] Studies published between 2020 and 2025 have added to our understanding of how prenatal exposures to metals such as Cd, Pb, Hg, As, Cr, Ni, and combinations thereof may influence outcomes, including preterm birth, growth restriction, stillbirth, and longer-term developmental impairments. [1], [2], [3], [4]

Given the widespread presence of heavy metals from industrial, agricultural, mining, and domestic sources, and given the global burden of adverse pregnancy and perinatal outcomes, examining this relationship is of urgent public health importance. This review aims to synthesize recent evidence, identify gaps, and highlight implications for maternal-child health.

This article aims to critically review recent (2020–2025) epidemiological and mechanistic evidence on the influence of environmental exposure to heavy metals on pregnancy and perinatal outcomes. Specific objectives are:

1. To identify the heavy metals most frequently studied in relation to pregnancy/perinatal risk.
2. To summarise the associations between prenatal heavy metal exposure and adverse outcomes (preterm birth, LBW, SGA, stillbirth, neonatal/infant development).
3. To discuss proposed mechanisms by which heavy metals might disrupt pregnancy and fetal development.

4. To consider the role of mixed metal exposures, critical windows of vulnerability, and environmental/contextual risk modifiers.
5. To propose recommendations for research, public health, and clinical practice.

Materials and Methods:
A narrative (non-systematic) review was conducted of peer-reviewed articles published between January 2020 and August 2025. Searches were performed in PubMed, Embase, and Web of Science using terms including “prenatal heavy metal exposure,” “pregnancy outcomes,” “birth weight,” “preterm birth,” “mixed metals,” “cadmium,” “lead,” “mercury,” “arsenic,” “chromium,” and “nickel.” Inclusion criteria: (1) studies of pregnant women or mother–infant pairs; (2) measurement of heavy metal exposure (blood, urine, cord blood, or placenta) during pregnancy; (3) reporting of at least one perinatal outcome (e.g., birth weight, gestational age, fetal loss, neonatal health). Exclusion criteria: animal or in vitro only studies, exposures not quantified, non-pregnancy populations, or studies before 2020. Selected studies were appraised for design (cohort/case–control), exposure assessment, outcome measures, adjustment for confounders, and main findings. Key descriptive summaries are provided. Mechanistic literature was also reviewed to contextualize epidemiologic findings.

Results:
Recent studies have evaluated metals such as cadmium (Cd), lead (Pb), mercury (Hg), arsenic (As), chromium (Cr), nickel (Ni), thallium (Tl), and mixtures thereof. For example, a large differential exposure study found maternal urine levels of Cr to be strongly associated with lower birth weight and length in an Israeli cohort of 975 mother–term infant pairs. [4] Another review/meta-analysis emphasized especially cadmium’s consistent negative effect on neurodevelopment, even at low doses. [1]

Associations with pregnancy and perinatal outcomes

- Preterm birth, low birth weight, and small for gestational age (SGA): A recent study in Korea found that maternal cadmium concentrations in early and late pregnancy were significantly associated with lower birth weight ($\beta \sim -39.96$; 95% CI –63.76, –16.17) and increased odds of large for gestational age status (adjusted OR = 0.637). [5]
- Stillbirth and pregnancy loss: A 2025 study using NHANES 2011–2016 data reported that blood mercury levels were positively correlated with pregnancy loss (OR ~1.06 per unit increase; highest tertile vs lowest: 38% higher risk) while other metals (Cd, Pb, Mn, Se) were not significantly associated. [6]
- Mixed-metal exposures: Michael et al. (2022) found that in relatively low exposure settings, chromium emerged as the metal most strongly inversely associated with birth weight and infant length when considering mixtures (Cr, As, Cd, Hg, Ni, Pb, Se, Tl) in maternal urine. [4]
- Neurodevelopmental outcomes: A 2025 meta-analysis found prenatal Cd exposure significantly decreased full-scale IQ (FSIQ) among children aged 5–9 years (−0.44 point per 50% increase in Cd; 95% CI –0.67, –0.21). [1]
- Thyroid hormone disruption and birth outcomes: A 2025 Iranian cohort found that maternal urinary Pb ($\beta = -120.99$ for birth weight) and changes in maternal TSH levels mediated some associations; TSH levels were positively correlated with Pb, Cr, and Ni. [7]

Mechanisms and critical periods

Mechanistic pathways proposed include: oxidative stress and mitochondrial dysfunction induced by heavy metals; disruption of placental blood flow and nutrient transport (especially for Cd); endocrine-disrupting effects (e.g., interference with thyroid metabolism, steroidogenesis); epigenetic modifications (DNA methylation, histone modifications) in fetal and placental tissues; metal-metal interactions in mixed exposures (synergistic or antagonistic). [6], [2] Several studies emphasize that early pregnancy (first trimester) is a critical window due to organogenesis and placental development, and that even low-level exposures may matter. [5], [4]

Various studies highlight that risk is modified by maternal age, body mass index (BMI), smoking status, socioeconomic status, race/ethnicity, nutritional status (e.g., zinc, selenium levels), and environmental co-exposures (air pollution, e-waste sites). [6], [4] Contextual variation is important: for example, women living near industrial or e-waste recycling sites show higher exposures and worse outcomes. [3]

Discussions:

The evidence from 2020–2025 supports the proposition that prenatal exposure to heavy metals is an important environmental risk factor for adverse pregnancy and perinatal outcomes. Although effect sizes tend to be modest, the ubiquity of exposure and potential for population-level impact make this a public health priority.

Findings consistently link Cd and Pb with reduced birth weight and growth restriction; Hg appears particularly linked to pregnancy loss; metals like Cr, Ni, Tl are emerging as relevant in mixed exposure contexts. The neurodevelopmental impacts of prenatal metal exposures further underscore the long-term implications beyond birth. Mechanistic studies reinforce plausible biological pathways, though specific dose–response relationships and critical windows remain to be fully defined.

Challenges remain. Many studies are observational and subject to residual confounding. Exposure assessment varies (urine, blood, cord, placenta), sometimes at single time-points. Mixed exposures complicate attribution to any single metal. Critical windows and sex-specific effects (male vs female fetus) are insufficiently examined. Additionally, most data come from higher-income or specific industrialized settings; low- and middle-income countries may face higher exposures but fewer resources for monitoring.

From a policy perspective, reduction of maternal heavy metal exposure through industrial regulation, environmental clean-up, dietary advice (e.g., limit high-risk seafood for Hg, monitor Cd/lead in soils), and prenatal screening (where feasible) is indicated. Clinicians should be aware of heavy metal exposure risk, particularly in high-exposure populations (e-waste, mining, industrial zones), and consider environmental history as part of prenatal care.

Conclusion

In summary, prenatal exposure to heavy metals constitutes a tangible and preventable risk factor for adverse pregnancy and perinatal outcomes. Evidence from recent years (2020–2025) affirms associations with reduced birth weight, prematurity, fetal loss, and longer-term developmental harm. While exposure levels may be low, the cumulative and population-wide effects demand attention. Concerted efforts in surveillance, regulation, prenatal care, and targeted research (especially on mixtures, critical windows, and vulnerable populations) are needed to safeguard maternal and child health.

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