Heavy Metals in Human Health and Pregnancy:

How Data Analysis, Mining, and Modeling Present a Solution

AI Health 2025, Data Mining Tools for Knowledge Discovery (DMTKD) Session- Contribution 88002

Presented by: Emma Frennborn and Khalil Rust

Biomedical Sciences PhD Students from Thomas Jefferson University

Philadelphia, Pennsylvania

United States

Jefferson

Thomas Jefferson University

HOME OF SIDNEY KIMMEL MEDICAL COLLEGE

Overview

Heavy Metals

- Importance in cellular physiology
- Toxicity and adverse health effects

Heavy Metals in Pregnancy

- Sources of heavy metals
- Heavy metal exposure during pregnancy and impact on developing fetus

Gap of Knowledge: Little is known about the **combinatory impact** of heavy metals on fetal development and neonatal health

Databases and Datasets

- Biobanks and associated databases, currently available datasets from papers

Data Mining and Modeling Approaches

Clinical Applications and Impact on Health Outcomes

Heavy Metals Play Important Roles in Many Biological Functions

Zinc (Zn)

- Zinc finger motifs
- Transcription factors

Iron (Fe)

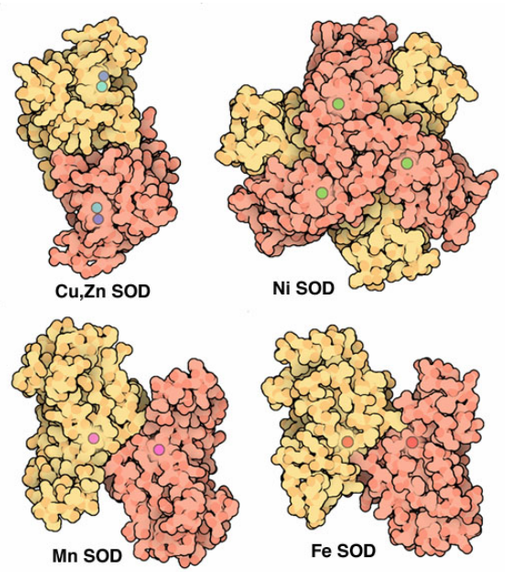
- Heme groups
- Hemoglobin, transport oxygen

Copper (Cu)

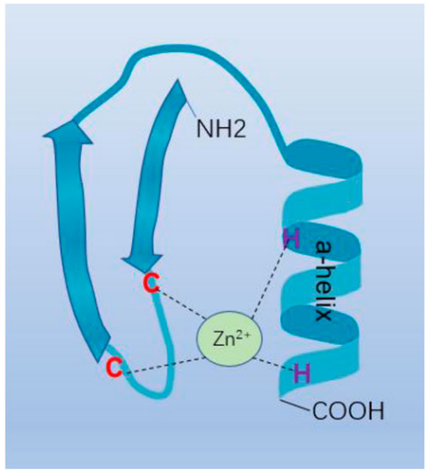
- Involved in many redox reactions (ETC)
- Cytochrome C oxidase
- Superoxide dismutase

Manganese (Mn)

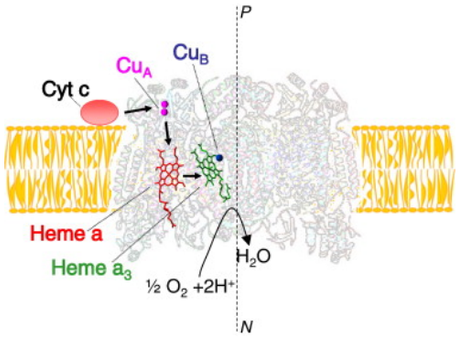
- Detoxifying reactive oxygen species (ROS)
- Manganese superoxide dismutase



https://pdb101.rcsb.org/motm/94



https://www.frontiersin.org/journals/physiology/articles/10.3389/fphys.2023.1129889/full



https://www.sciencedirect.com/science/article/pii/S000527281100212X

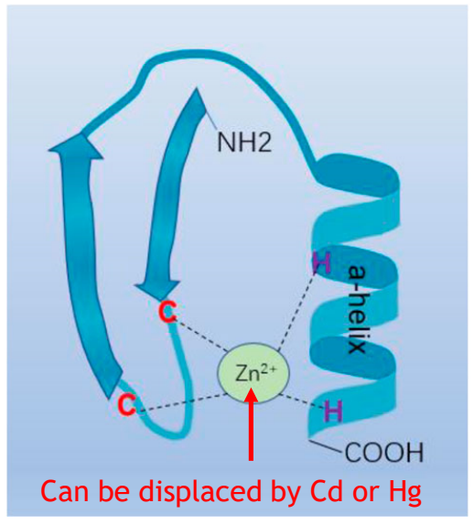
Heavy Metals Can Cause Adverse Health Effects

Examples:

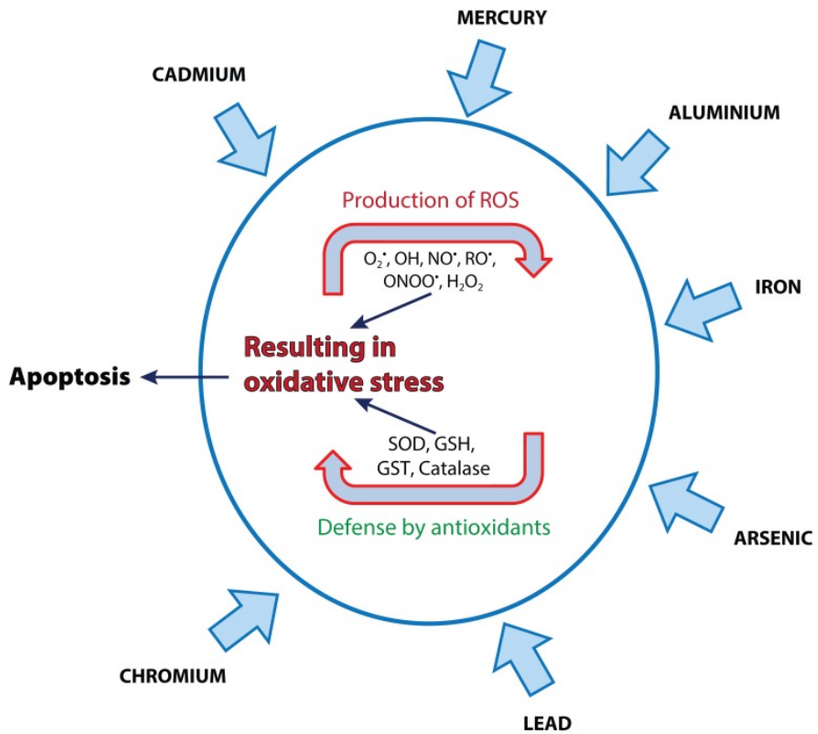
- Lead (Pb)
- Mercury (Hg)
- Arsenic (As)
- Cadmium (Cd)
- Aluminum (Al)
- Cobalt (Co)

Effects on Cells

- Increase in ROS
- Displacing essential elements in important enzymes (like transcription factors, SODs)
- Reacting with thiol groups (-SH)

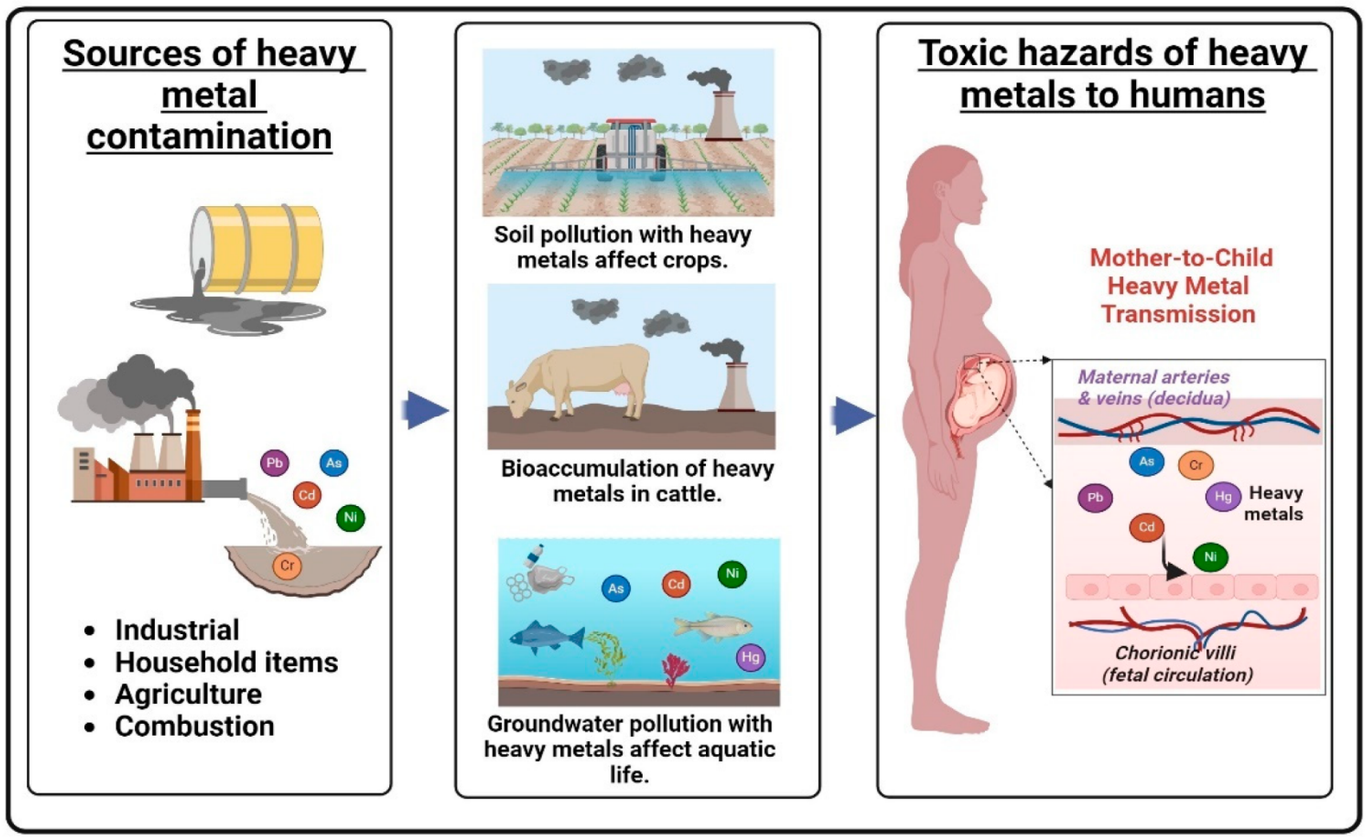


https://www.frontiersin.org/journals/physiology/articles/10.3389/fphys.2023.1129889/full



https://www.researchgate.net/figure/The-attack-of-heavy-metals-on-a-cell-and-the-balance-between-ROS-production-and-the_fig1_266560390

Heavy Metals Exposure During Pregnancy



https://www.mdpi.com/2073-4409/13/21/1775

Heavy Metals and Pregnancy

Lead

- increased risk maternal hypertension
- increased risk preterm delivery, low birth weight, small head circumference, low birth length

Mercury

- Associated with cognitive delays and motor dysfunction

Cadmium

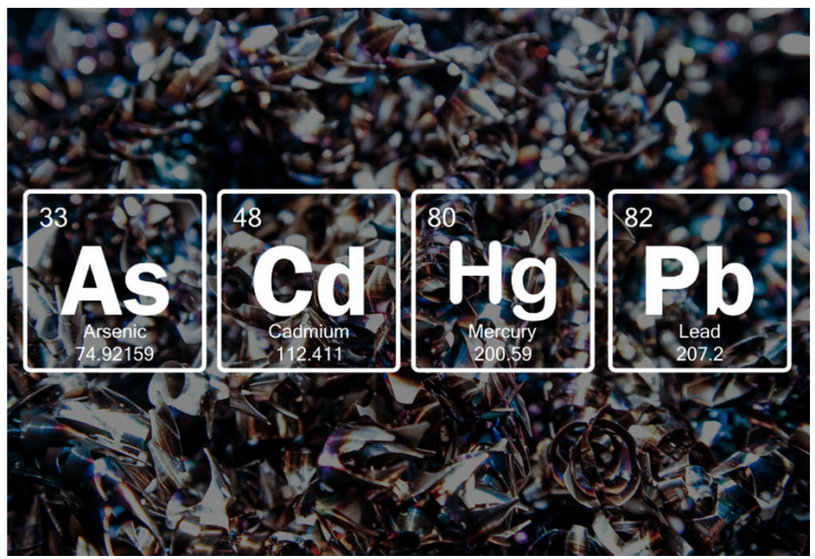
- Linked to impaired placental function and low birth weight
  - Competes with Zinc

Arsenic

- Increased risk of preterm birth or stillbirth
- Increased risk of anemia

Nickel

- Negative influence on fetal growth and birth outcomes



https://isthisnormal.littlespoon.com/heavy-metal-testing-0924/

Gap of Knowledge

Little is known about the **combinatory impact** of heavy metals on fetal development and neonatal health – most published research analyzes the effects of each metal separate from one another

Al + As → ??

Hg + Al → ??

Hg + Pb + Cd + As + Al → ??

Hg + Pb → ??

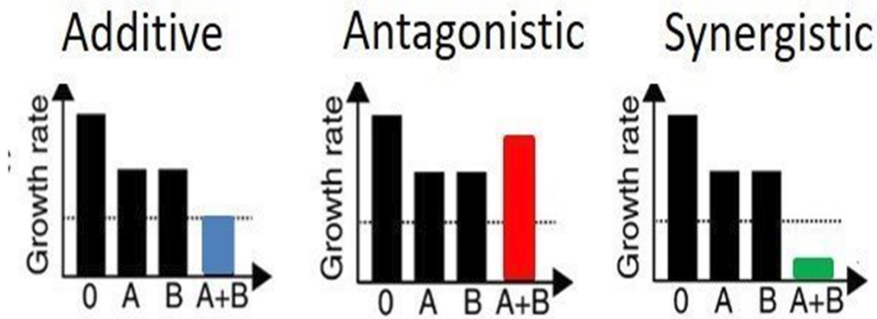
Cd + Pb → ??

Questions to Address

Are there additive, synergistic, or antagonistic interactions between heavy metals?

What databases exist to analyze the relationship between toxic element levels in blood and maternal and fetal nutritional status?

How can a computational model be utilized to prioritize data and patterns?



https://www.kuritaamerica.com/the-splash/investigating-the-effectiveness-of-antibiotic-combinations-utilized-in-fuel-ethanol-production

Biobanks and Databases

PeriBank (Baylor College of Medicine)

- Database established 2011 (only 7 other perinatal biobanks in the US)
- 2017: published findings from first 10,000 women enrolled
- Biobank of placental tissue, cord blood, maternal blood, paternal blood

MOMI (Magee Obstetric Maternal & Infant) Database and Biobank

- Established 1995
- Data from more than 220,000 pregnancies
- Maternal and fetal blood at delivery
- Longitudinally collected maternal blood

Datasets for Heavy Metal Concentrations in Maternal and Fetal Blood

1. Korea (2023)→ Pb, Cd, Hg
   - 5215 women total, 4948 sample size
2. Israel (2024) → Hg, As, Pb, Se
   - 404 women total, 378 sample size
3. Poland (2019) → Cu, Fe, Mn, Zn and Hg, Cd, Pb
   - 170 samples total: 81 placental, 22 umbilical cords
   - 83 mothers
4. Saudi Arabia (2011) → Pb, Hg, Cd
   - 1578 women total
5. Japan (2024) → Cd, Pb, Hg
   - 4683 mother-child pairs
   - Followed children through the age of 3-4 years old
6. China (2024) → 14 different metals
   - 450 mother-child pairs

Data Collection

https://www.vecteezy.com/vector-art/5187413-data-collection-flat-outline-concept-icon-showing-data-measuring-and-collection

Corresponding References

1. S. S. Zinia, K. H. Yang, E. J. Lee, M. N. Lim, J. Kim, W. J. Kim, and the Ko-CHENS Study Group, "Effects of heavy metal exposure during pregnancy on birth outcomes," *Sci. Rep.*, vol. 13, no. 1, p. 18990, Nov. 2023

2. B. Goldberg, et al., "Early pregnancy metal levels in maternal blood and pregnancy outcomes," *Sci. Rep.*, vol. 14, no. 1, p. 27866, Nov. 2024

3. K. Kot, et al., "Interactions between 14 elements in the human placenta, fetal membrane and umbilical cord," *Int. J. Environ. Res. Public Health*, vol. 16, no. 9, p. 1615, 2019.

4. Al-Saleh, N. Shinwari, A. Mashhour, G. E. D. Mohamed, A. Rabah, "Heavy metals (lead, cadmium, and mercury) in maternal, cord blood and placenta of healthy women," *Int. J. Hyg. Environ. Health*, vol. 214, no. 2, pp. 79-101, 2011.

5. T. Takatani, et al., "Association between maternal blood or cord blood metal concentrations and catch-up growth in children born small for gestational age: an analysis by the Japan environment and children's study," *Environ. Health*, vol. 23, no. 1, p. 18, Feb. 2024.

6. H. Ma, et al., "Maternal and cord blood levels of metals and fetal liver function," *Environ. Pollut.*, vol. 363, pt. 2, p. 125305, 2024.

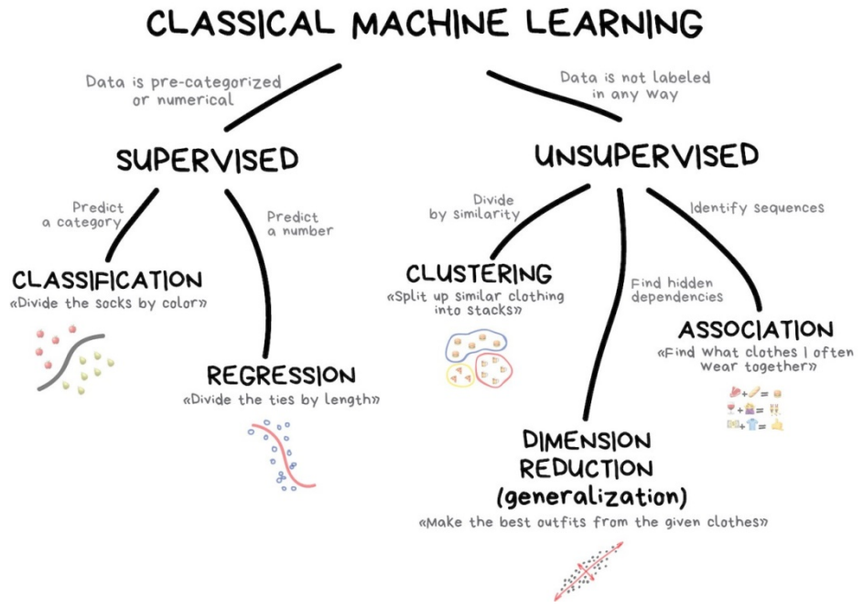
Data Mining and Modeling

Supervised Machine Learning

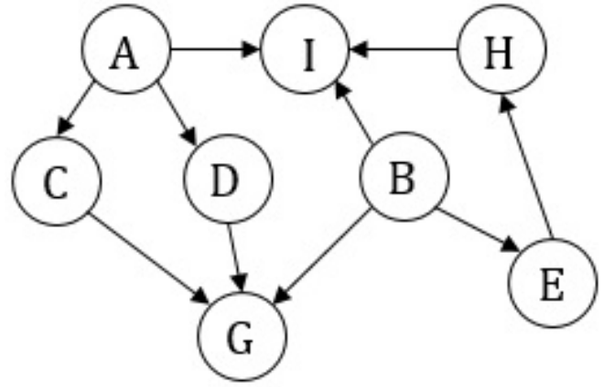
- Used to build models, desired outcome is specified
- Divide data into three subsets: training, validating, testing
- Example: Bayesian Network
  - Calculate probability of certain outcome given several interacting variables

Unsupervised Machine Learning

- Reveal patterns in data where outcome is unknown and undefined
- Data is clustered into categories
- Example: association rule-based analysis
  - Used in healthcare setting to determine associations between known disease risk factors and other variables



https://medium.com/swlh/machine-learning-basics-anyone-can-understand-episode-1-1f73401e52e0



https://mathoverflow.net/questions/228519/exploiting-conditional-independence-for-inference-in-bayesian-networks

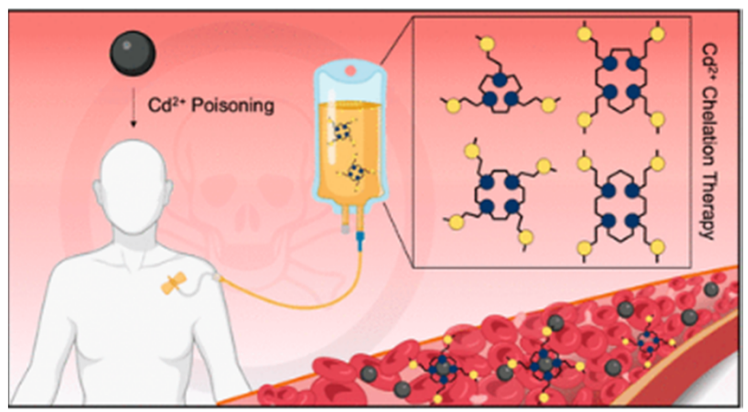
Impact on Health Outcomes

Data mining and modeling tools can be used by clinicians to:

- Estimate the likelihood of adverse pregnancy outcomes
  - Ex) Determining probability of preterm birth

Creates the opportunity to personally tailor interventions to specific cases

- Ex) Prioritization of supplementation or chelation therapy



https://pubs.acs.org/doi/full/10.1021/acs.inorgchem.4c04371

https://thewholeu.uw.edu/2014/04/24/healthy-pregnancy/

Acknowledgements

We would like to thank Dr. Les Sztandera of Thomas Jefferson University for his mentorship and guidance

We are also grateful to have received travel funding from the Jefferson Global Health Initiatives Council (GHIC) Global Office, which made presenting this work at the IARIA AI Health 2025 conference possible

References

1. P. B. Tchounwou, C. G. Yedjou, A. K. Patlolla, and D. J. Sutton, "Heavy metal toxicity and the environment," *Exp. Suppl.*, vol. 101, pp. 133-164, 2012.
2. A. Hartwig, "Zinc finger proteins as potential targets for toxic metal ions: differential effects on structure and function," *Antioxid. Redox Signal.*, vol. 3, no. 4, pp. 625-634, Aug. 2001.
3. M. Jaishankar, T. Tseten, N. Anbalagan, B. B. Mathew, and K. N. Beeregowda, "Toxicity, mechanism and health effects of some heavy metals," *Interdiscip. Toxicol.*, vol. 7, no. 2, pp. 60-72, Jun. 2014.
4. D. Witkowska, J. Słowik, and K. Chilicka, "Heavy metals and human health: Possible exposure pathways and the competition for protein binding sites," *Molecules*, vol. 26, no. 19, p. 6060, 2021.
5. S. S. Zinia, K. H. Yang, E. J. Lee, M. N. Lim, J. Kim, W. J. Kim, and the Ko-CHENS Study Group, "Effects of heavy metal exposure during pregnancy on birth outcomes," *Sci. Rep.*, vol. 13, no. 1, p. 18990, Nov. 2023
6. I. Karakis, D. Landau, M. Yitshak-Sade, et al., "Exposure to metals and congenital anomalies: a biomonitoring study of pregnant Bedouin-Arab women," *Sci. Total Environ.*, vol. 517, pp. 106-112, 2015.
7. J. M. Madrigal, V. Persky, A. Pappalardo, and M. Argos, "Association of heavy metals with measures of pulmonary function in children and youth: Results from the National Health and Nutrition Examination Survey (NHANES)," *Environ. Int.*, vol. 121, pt. 1, pp. 871-878, 2018.
8. I. Al-Saleh, N. Shinwari, A. Mashhour, and A. Rabah, "Birth outcome measures and maternal exposure to heavy metals (lead, cadmium, and mercury) in Saudi Arabian population," *Int. J. Hyg. Environ. Health*, vol. 217, no. 2-3, pp. 205-218, 2014.
9. S. F. Farzan, C. G. Howe, Y. Chen, et al., "Prenatal lead exposure and elevated blood pressure in children," *Environ. Int.*, vol. 121, pt. 2, pp. 1289-1296, 2018.
10. I. Karakis, D. Landau, R. Gat, et al., "Maternal metal concentration during gestation and pediatric morbidity in children: an exploratory analysis," *Environ. Health Prev. Med.*, vol. 26, no. 1, p. 40, 2021.
11. G. O. Arinola, A. Dutta, O. Oluwole, C. O. Olopade, "Household air pollution, levels of micronutrients and heavy metals in cord and maternal blood, and pregnancy outcomes," *Int. J. Environ. Res. Public Health*, vol. 15, no. 12, 2018.
12. X. Sun, W. Liu, B. Zhang, et al., "Maternal heavy metal exposure, thyroid hormones, and birth outcomes: A prospective cohort study," *J. Clin. Endocrinol. Metab.*, vol. 104, no. 11, pp. 5043-5052, 2019.
13. C. S. Oliveira, P. A. Nogara, D. M. P. Ardisson-Araújo, M. Aschner, J. B. T. Rocha, and J. G. Dórea, "Neurodevelopmental effects of mercury," *Adv. Neurotoxicol.*, vol. 2, pp. 27-86, 2018. doi: 10.1016/bs.ant.2018.03.005. Epub May 24, 2018.
14. J. L. Young and L. Cai, "Implications for prenatal cadmium exposure and adverse health outcomes in adulthood," *Toxicol. Appl. Pharmacol.*, vol. 403, p. 115161, Sep. 2020.
15. N. Y. Ortiz-Garcia, et al., "Maternal exposure to arsenic and its impact on maternal and fetal health: A review," *Cureus*, vol. 15, no. 11, p. e49177, Nov. 2023.
16. S. N. Caritis, "Magee obstetric maternal & infant (MOMI) database and Biobank: Magee-Womens Research Institute & Foundation," *Magee*..
17. K. M. Antony, et al., "Generation and validation of a universal perinatal database and biospecimen repository: PeriBank," *J. Perinatol.*, vol. 36, no. 11, pp. 921-929, Nov. 2016.
18. I. B. Goldberg, et al., "Early pregnancy metal levels in maternal blood and pregnancy outcomes," *Sci. Rep.*, vol. 14, no. 1, p. 27866, Nov. 2024
19. K. Kot, et al., "Interactions between 14 elements in the human placenta, fetal membrane and umbilical cord," *Int. J. Environ. Res. Public Health*, vol. 16, no. 9, p. 1615, 2019.
20. I. Al-Saleh, N. Shinwari, A. Mashhour, G. E. D. Mohamed, A. Rabah, "Heavy metals (lead, cadmium, and mercury) in maternal, cord blood and placenta of healthy women," *Int. J. Hyg. Environ. Health*, vol. 214, no. 2, pp. 79-101, 2011.
21. T. Takatani, et al., "Association between maternal blood or cord blood metal concentrations and catch-up growth in children born small for gestational age: an analysis by the Japan environment and children's study," *Environ. Health*, vol. 23, no. 1, p. 18, Feb. 2024.
22. J. Grzesik-Gąsior, J. Sawicki, A. Pieczykolan, and A. Bień, "Content of selected heavy metals in the umbilical cord blood and anthropometric data of mothers and newborns in Poland: preliminary data," *Sci. Rep.*, vol. 13, no. 1, p. 14077, Aug. 2023.
23. H. Ma, et al., "Maternal and cord blood levels of metals and fetal liver function," *Environ. Pollut.*, vol. 363, pt. 2, p. 125305, 2024.
24. W. T. Wu, Y. J. Li, A. Z. Feng, et al., "Data mining in clinical big data: the frequently used databases, steps, and methodological models," *Mil. Med. Res.*, vol. 8, p. 44, 2021.
25. J. Puga, M. Krzywinski, and N. Altman, "Bayesian networks," *Nat. Methods*, vol. 12, pp. 799–800, 2015.
26. I. Yoo, et al., "Data mining in healthcare and biomedicine: a survey of the literature," *J. Med. Syst.*, vol. 36, no. 4, pp. 2431-2448, Aug. 2012. Epub May 3, 2011.