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Key Points:

- 34.3% of participants in an e-waste recycling area had a Cr concentration that exceeded World Health Organization guidelines
- Examined associations between prenatal exposure to heavy metals and birth outcomes in an area in China with e-waste
- Prenatal Cd exposure decreases the birth weight of female infants

Supporting Information:

Supporting Information may be found in the online version of this article.

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Prenatal Exposure to Heavy Metals and Adverse Birth Outcomes: Evidence From an E-Waste Area in China

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Abstract Electronic waste that has not been properly treated can lead to environmental contamination including of heavy metals, which can pose risks to human health. Infants, a sensitive group, are highly susceptible to heavy metals exposure. The aim of this study was to investigate the association between prenatal heavy metal exposure and infant birth outcomes in an e-waste recycling area in China. We analyzed cadmium (Cd), chromium (Cr), manganese (Mn), lead (Pb), copper (Cu), and arsenic (As) concentrations in 102 human milk samples collected 4 weeks after delivery. The results showed that 34.3% of participants for Cr, which exceeds the World Health Organization (WHO) guidelines, as well as the mean exposure of Cr exceeded the WHO guidelines. We collected data on the birth weight (BW) and length of infants and analyzed the association between metal concentration in human milk and birth outcomes using multivariable linear regression. We observed a significant negative association between the Cd concentration in maternal milk and BW in female infants ($\beta = -162.72$, 95% CI = −303.16, −22.25). In contrast, heavy metals did not associate with birth outcomes in male infants. In this study, we found that 34.3% of participants in an e-waste recycling area had a Cr concentration that exceeded WHO guidelines, and there was a significant negative association between prenatal exposure to the Cd and infant BW in females. These results suggest that prenatal exposure to heavy metals in e-waste recycling areas may lead to adverse birth outcomes, especially for female infants.

Plain Language Summary In this study, the concentrations of six heavy metals in human milk samples collected 4 weeks after delivery in one of the two largest e-waste recycling areas in China, that is, Taizhou, Zhejiang Province, were measured. The effects of prenatal heavy metal exposure on infant birth outcomes were analyzed. The results reveal gender differences in infant birth outcomes. For example, prenatal cadmium exposure decreases the birth weight of female infants but has no effect on male infants. We believe that our study makes a significant contribution to the literature because we provide guidance for future analyses. We suggest that the effects of metal exposure in the e-waste area on the growth and development of infants must be studied over the long term, particularly for female infants.

1. Introduction

The expansion of the electrical and electronic equipment manufacturing industry owing to globalization has led to the generation of large amounts of electronic waste (e-waste) in both developing and developed countries (Rautela et al., 2021). According to the 2022 Global E-waste Monitor, 53.6 million tons of e-waste was generated in 2019 and is expected to increase to 74.7 million tons by 2030 (Baldé et al., 2022). Furthermore, there is little regulation for electronics and e-waste exported from high-income areas to low- and middle-income countries (Bakhiyi et al., 2018). China is confronted with a double challenge with respect to the effective management of e-waste: (a) illegal foreign imports of e-waste and (b) the rapid increase in domestic e-waste over the past few decades. According to statistics, the generation of e-waste in China will increase to 2.72 and 5.16 million tons by 2030 and 2050, respectively (Zeng et al., 2020). At present, relevant industries in China do not follow standardized practices/protocols for the treatment of e-waste and rely on methods such as strong acid extraction, manual disassembly, and incineration (Chi et al., 2011). Furthermore, most of China's e-waste is handled by the informal sector, which processes it using non-scientific and crude recycling techniques, such as open burning and acid

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leaching, leading to the release of large amounts of toxic substances, such as dioxins and heavy metals, into the environment, resulting in high exposure levels for residents (Dong et al., 2020; S. S. Kim et al., 2020; Vaccari et al., 2019). These electronic wastes contain a lot of heavy metals such as lead (Pb), arsenic (As), copper (Cu), cadmium, Zine (Zn), mercury (Hg), and Argentum (Ag) (Adie et al., 2017; Houessionon et al., 2021; Shakil et al., 2022).

Even contact with trace amounts of heavy metals, such as long-term exposure to e-waste, is harmful to the human body and can cause chromosomal mutations, which are directly associated with genetic damage, bladder and lung cancer, cardiovascular disease, and other hazards (Gustin et al., 2020; Khan et al., 2020; H. Liu et al., 2018). Fetal and infant development is the most sensitive period of life (Vrijheid et al., 2016). Several toxic substances, such as Pb and Hg, can cross the placental barrier and circulate through the placenta, worsening health risks for infants (Li et al., 2019). The results of observational studies have demonstrated the negative effects of Pb, Cd, Cr, and Mn on birth outcomes, lung function, mental health, and neurodevelopment in infants (S. S. Kim et al., 2020; L. Liu et al., 2018; Zeng et al., 2021). Furthermore, associations among birth weight (BW), birth length, and head circumference were estimated in a sample of a population experiencing metal exposure in rural Bangladesh. Significant negative associations were observed between exposure to a metal mixture and birth length and head circumference (M. S. Lee et al., 2021). The results of a recent Chinese study showed that exposure to high levels of Pb, Cd, and Cr is associated with head circumference, body mass index (BMI), and ponderal index in infants (S. S. Kim et al., 2020). However, the associations of prenatal exposure to heavy metals with birth outcomes and the composition of human milk have not been studied in Chinese e-waste recycling areas.

Heavy metal concentrations in human milk are indicators of maternal exposure to heavy metals during the prenatal period (Golding, 1997). Because of organ immaturity, exposure to heavy metals in the prenatal period, which is a critical exposure window, has a significant and long-lasting effect on child development (Grandjean & Herz, 2015; Rebelo & Caldas, 2016). In summary, it is necessary to measure the metal contents in human milk in the e-waste recycling area to investigate the contamination status and possible health effects to provide a theoretical basis for e-waste management and its effects on human health.

As early as 2004, it was reported that in Taizhou, Zhejiang Province, China, almost everyone in the area was engaged in e-waste recycling in the form of family workshops (China Daily, 2004). They can dismantle 2.2 million tons of e-waste every year (Chi et al., 2014). Since the 1990s, e-waste recycling has become a major business in the region. Taizhou has become the main place for recycling transformers in China (Chan & Wong, 2013). It has been indicated that urinary Cd levels were higher in occupational and non-occupational dismantles at e-waste recycling sites than in green plantations in Taizhou (H. Wang et al., 2011). Additionally, the concentrations of Cu, Pb, and Cd in scalp hair samples collected at an e-waste recycling area were found to be higher compared to that in hair samples from Ningbo and Shaoxing, two cities engaged in general industrial activities in China (T. Wang et al., 2009). In this study, we measured concentrations of six heavy metals in human milk samples collected 4 weeks after delivery in Luqiao District, Taizhou City, Zhejiang Province, one of the two largest e-waste recycling areas in China (Ling et al., 2021), to estimate the associations between prenatal heavy metal exposure and infant birth outcomes.

2. Materials and Methods

2.1. Study Population

E-waste recycling and dismantling activities in the study area, Luqiao District, Taizhou City, started in the 1970s (Chan & Wong, 2013). Currently, Taizhou is one of the largest e-waste recycling areas in the country. In this study, 102 full-term infants born (singleton births) in 2021 were recruited as participants (preterm infants were excluded). Various aspects, such as the maternal age at delivery, BMI before delivery, lifestyle habits during pregnancy, education level, delivery times, and gestational age at delivery, may affect the birth outcomes of infants.

In addition, we collected human milk from 102 mothers (collected 4 weeks after delivery), measured the concentrations of six heavy metals in human milk (Pb, Cd, Cr, As, Cu, and Mn), collected the infant length and weight at birth, and analyzed the effects of prenatal heavy metal exposure on the physical development of the infant using post-delivery human milk heavy metal concentrations as a marker of intrauterine heavy metal exposure in infants.

All participants provided written informed consent. This study was approved by the ethics committee of Jiaxing University (JHTCM-IRB-2019).

2.2. Sample Collection and Analysis

The prenatal exposure to heavy metals was estimated by measuring the metal concentrations in human milk samples collected 4 weeks after delivery. The perinatal period is defined in diverse ways. Pertaining to the period immediately before and after birth. Depending on the definition, it starts at the 20th to 28th week of gestation and ends 1–4 weeks after birth (https://www.medicinenet.com/script/main/art.asp?articlekey=7898). This is the reason why we select this time point (4 weeks after delivery). The Pb, Cd, Cr, As, Cu, and Mn concentrations in human milk were measured using inductively coupled plasma mass spectrometry (iCAPQ, Thermo Fisher Scientific, USA). Procedures for human milk collection have been described previously (Hang et al., 2022). Briefly, 0.5 g of human milk (accurate to 0.0001 g) was aspirated after vortex shaking and then digested with 5 mL of a mixed digestion solution (HNO_3: HCl = 1:3) using a microwave digestion system (Milestone Ethos D). After the digestion, the volume was made up to 10 mL using ultrapure water. A vigorous quality control procedure was implemented throughout the analysis using a certified reference material (GBW10017). The limits of detection of Pb, Cd, Cr, As, Cu, and Mn were 0.02, 0.01, 0.06, 0.01, 1.14, and 0.02 μg/L, respectively.

2.3. Birth Outcomes

We obtained the infants' length (cm) and weight (g) at birth from their obstetric medical records.

2.4. Covariates

Personal interviews, self-administered questionnaires, and medical record transcripts were used to collect information on possible confounding variables. Maternal characteristics included the age at delivery (y) (medical records), BMI (kg/m^2) before pregnancy (medical records), smoking during pregnancy (no/yes) (questionnaires), education at recruitment (<college graduate or ≥ college student) (questionnaires), and parity (nulliparous or multiparous) (medical records). The characteristics of the children included the sex (male or female), gestational age at birth (wk), birth length (cm), and BW (g, Cathey et al., 2022; Chatzi et al., 2019; Donangelo et al., 2021; Howe et al., 2021; M. S. Lee et al., 2021). To avoid adjustments for potential intermediate factors that lie in the pathway from exposure to the outcome and lead to biased and paradoxical results (VanderWeele et al., 2012), we did not control for gestational age in our models.

2.5. Statistical Analyses

All Cr, Mn, Cu, As, and Pb concentrations in human milk were above the respective detection limits; 12 Cd measurements (12%) below the detection limit were replaced with half the detection limit. Descriptive statistics were calculated for all variables. Associations between the concentrations of each metal pair in human milk samples were examined using Pearson's correlation coefficients. The metal concentrations in human milk were right-skewed. Therefore, the concentrations were log-transformed to address the skewness in the data. All statistical analyses were performed using R software (version 4.2.1; R Foundation for Statistical Computing). The cut-off level for statistical significance was set to $p < 0.05$ for the main analyses and to $p < 0.10$ for interactions (two-tailed tests). Associations between the metals in human milk and birth outcomes were evaluated using the following multivariable linear regression:

Y_i= 〖β_0 + β〗 _1 〖As〗 _i + β_2 〖Cd〗 _i + β_3 〖Cr〗 _i+ β_4 〖Cu〗 _i + β_5 〖Mn〗 _i + β_6 〖Pb〗 _i + βZ_i + e_i,

where Y denotes the birth outcome phenotype for individual i; As, Cd, Cr, Cu, Mn, and Pb represent the standard log concentrations of As, Cd, Cr, Cu, Mn, and Pb, respectively; Z represents the covariates; and β is the regression coefficient. Point estimates are presented as changes in the infant size for each interquartile range increase in the natural log concentration of metals. The results of previous studies suggested that child sex can modify the effects of metals on birth outcomes (Chatzi et al., 2019; Howe et al., 2021; M. S. Lee et al., 2021). Therefore, the analyses were stratified according to sex.

The Bayesian kernel machine regression (BKMR) method was used to analyze the associations between mixed exposures to heavy metals and the interaction of heavy metals and birth outcomes (Bobb, 2022).

Table 1
Participant Characteristics (N = 102)

Characteristic	Mean ± SD *n* (%)	Median	Range
Maternal characteristics			
Age at delivery (y)	29.4 ± 5.4	28	16–47
BMI at enrollment (kg/m^2)	21.2 ± 2.7	20.9	16.0–30.3
Smoking during pregnancy			
Yes	3 (2.9)		
No	99 (97.1)		
Education			
<College graduate	76 (74.5)		
≥College graduate	26 (25.5)		
Parity			
Nulliparous	71 (69.6)		
Multiparous	31 (30.4)		
Neonatal characteristics			
Sex			
Male	56 (54.9)		
Female	46 (45.1)		
Gestational age at birth (wk)	38.8 ± 1.0	39.0	36.0–41.3
Birth length (cm)	50.0 ± 0.8	50.0	48–52
Birth weight (g)	3,323 ± 429	3,300	2,000–4,500

3. Results

Table 1 summarizes the characteristics of the 102 mother–infant pairs included in the analyses. The average maternal age (standard deviation) at delivery was 29.4 (5.4) years. Before pregnancy, 97.1% of mothers were nonsmokers, 25.5% had received more than a college education, and 69.6% were nulliparous. At birth, 54.9% of the children were boys. The average infant size (standard deviation) at birth was 3,323 (429) g for BW and 50.0 (0.8) cm for birth length.

Table 2 shows the distributions of heavy metal concentrations measured in human milk samples overall and stratified by sex. In general, human milk metal concentrations did not significantly differ between males and females. Girls had a slightly higher prenatal exposure to Cu, Mn, and Pb. According to the WHO, the permissible levels of heavy metals in human milk are 2–5 μg/L for Pb, <1 μg/L for Cd, 0.8–1.5 μg/L for Cr, 0.2–0.6 μg/L for As, 180–310 μg/L for Cu, and 3–4 μg/L for Mn (Parr et al., 1991), Overall, 34.3% ($n = 35$) and 2.0% ($n = 2$) of the milk samples exceeded the WHO guidelines for Cr and Mn, respectively. Meanwhile, the mean exposure of Cr exceeded the WHO guidelines (the maximum was five times above the limit). The concentrations of Cu, Pb, As, and Cd were within permissible limits set by the WHO. Moreover, Cr concentration in human milk in the e-waste recycling area was significantly higher than the WHO guidelines, while Cu, Pb, As, and Cd concentrations were significantly lower than the WHO guidelines (Table S1 in Supporting Information S1). The associations between the metals are shown in Figure S1 in Supporting Information S1. The Cr concentration was moderately associated with the Mn and Pb concentrations ($r = 0.4550$ and 0.3052, respectively; Figure S1 in Supporting Information S1).

Table 3 depicts the associations between metals and birth outcomes from multivariable linear models stratified by sex. The *P*-value for the interaction indicates whether there is a significant difference between male and female (Shih et al., 2021). No significant associations were observed between the participants or stratum. However, we found significant interactions in the associations between Cr and birth length; Mn and gestational age, birth length, and BW; and Cd and birth length. Additionally, the maternal human milk Cd concentration is inversely associated with the BW ($\beta = -162.71$; 95% CI = −303.16, −22.25; *P*-value for interaction = 0.017) of female infants, and we added a figure (Figure S2 in Supporting Information S1) with BW on the *x*-axis and the Cd level on the *y*-axis through simple linear regression analysis to visualize the relationship between BW and Cd in female infants ($r = -0.339$, $P = 0.021$). On the other hand, no significant associations were observed between education levels and heavy metals (Table S2 in Supporting Information S1).

The results of the BKMR analysis showed that in birth outcomes (male and female), each curve shifted parallel to the other metal concentrations, suggesting that the associations of mixed heavy metal exposure and birth outcomes may be additive rather than synergistic (Figures S3 and S4 in Supporting Information S1).

4. Discussion

This study analyzed the concentrations of six heavy metals in 102 human milk samples collected from pregnant women in Taizhou, an e-waste recycling area in China. In addition, 34.3% ($n = 35$) of the study participants had levels of the Cr that exceeded the WHO guideline, we also explored the associations between prenatal exposure to six heavy metals and birth outcomes, revealing a significant negative association between the Cd concentration in human milk and BW in female infants.

The BW is an essential indicator of infant growth and development. High or low BW can lead to obesity and type 2 diabetes in adulthood (Wei et al., 2003). Current research suggests that a low BW may be associated with adverse health outcomes such as intellectual disability and asthma (Gu et al., 2017; Mebrahtu et al., 2015). Low BW leads to a frequent decrease in the glomerular filtration rate (eGFR) and an increase in systolic blood pressure

Table 2
Breast Milk Metal Concentrations by Children Sex

Chromium (μg/L)	Mean ± SD	Median	IQR	Range
Overall	1.517 ± 0.849	1.410	1.229–1.532	0.598–7.453
Male	1.544 ± 0.632	1.436	1.285–1.571	0.633–3.256
Female	1.485 ± 1.062	1.376	0.974–1.518	0.598–7.453
P-value	0.729			
Manganese (μg/L)				
Overall	1.214 ± 0.830	1.043	0.817–1.369	0.438–7.040
Male	1.165 ± 0.531	1.062	0.821–1.381	0.438–3.220
Female	1.274 ± 1.093	0.988	0.776–1.323	0.506–7.040
P-value	0.513			
Copper (μg/L)				
Overall	46.64 ± 17.73	45.81	34.66–55.01	13.07–98.07
Male	44.80 ± 17.55	45.14	31.55–53.52	15.81–93.93
Female	48.89 ± 17.88	47.71	36.58–56.06	13.07–98.07
P-value	0.249			
Arsenic (μg/L)				
Overall	0.113 ± 0.086	0.089	0.048–0.151	0.012–0.440
Male	0.124 ± 0.098	0.100	0.047–0.177	0.012–0.440
Female	0.101 ± 0.068	0.086	0.044–0.132	0.019–0.278
P-value	0.179			
Cadmium (μg/L)				
Overall	0.016 ± 0.014	0.013	0.007–0.018	0.002–0.078
Male	0.017 ± 0.016	0.013	0.008–0.018	0.002–0.078
Female	0.016 ± 0.012	0.011	0.007–0.020	0.002–0.063
P-value	0.683			
Lead (μg/L)				
Overall	0.260 ± 0.385	0.176	0.137–0.262	0.050–3.449
Male	0.246 ± 0.269	0.182	0.143–0.274	0.066–2.058
Female	0.277 ± 0.494	0.161	0.130–0.248	0.050–3.449
P-value	0.690			

(Kanda et al., 2020). Furthermore, low BW is associated with later renal function and is a risk factor for the development of diabetic nephropathy (Silverwood et al., 2013). Therefore, to safeguard the health of infants, it is important to understand the risk factors of a low BW.

Cd is a toxic pollutant that is widely detected in the environment and is harmful to human health (Genchi et al., 2020). Excessive exposure to Cd can lead to liver and kidney lesions (Mezynska & Brzóska, 2018). It is also associated with delayed childhood growth patterns, especially length and weight (Geng & Wang, 2019). In this study, we evaluated the associations between prenatal heavy metal exposure and infant birth outcomes in 102 mother–infant pairs. Sex-specific associations were observed for Cd, which generally is negatively associated with the BW of female infants. Observed inverse associations suggest that female infants may be more susceptible to prenatal Cd toxicity. In a prospective cohort study of 1,616 mothers and infants in rural Bangladesh, the prenatal urinary Cd concentration was negatively associated with the BW of female infants (Kippler et al., 2012). Furthermore, in a New Hampshire birth cohort study, high levels of Cd in the placenta were associated with a decreased placenta weight and a stronger association with Cd in the placenta was observed for female infants than for male infants (Punshon et al., 2019). The Avon Longitudinal Study of Parents and Children also showed that maternal blood Cd levels are negatively associated with the BW of female infants (Taylor et al., 2016). The results of a cohort study of 408 pairs of mothers and infants in the Hubei Province, China, revealed a significant positive association between higher maternal urinary Cd levels and preterm low BW, especially in female infants (K. Huang et al., 2017). Our results are identical to those of the above-mentioned studies. In addition, in the present study, the concentration of Cd in maternal human milk was within permissible limits set by the WHO. Some studies point out that low to moderate Cd exposure adversely affects infant birth outcomes. For instance, a cross-sectional study conducted in China found that exposure to low levels of Cd in children may lead to renal tubular dysfunction and kidney damage (D. Wang et al., 2016), even though the urinary Cd level at this time was 0.12 μg/L (D. Wang et al., 2016), much lower than the urinary Cd level across all human environmental pollution surveys in Korea (0.65 μg/L) (J. W. Lee et al., 2012). Moreover, studies have shown that even short periods of exposure to low concentrations of Cd can affect the body's glomerular filtration function (M. S. Kim et al., 2018). Swedish birth cohort studies have shown that maternal prenatal exposure to low levels of Cd and Hg is inversely associated with BW and birth length (Gustin et al., 2020). Overall, the available studies indicate that fetal growth is susceptible to Cd exposure during critical periods, regardless of differences in parameters. Therefore, we need to pay continuous attention to the associations of Cd exposure with the infant birth outcomes, albeit at low concentrations.

To explore the effect of Cd exposure on sex diversity, mechanisms of sex-specific associations between prenatal Cd exposure and BW have attracted widespread attention. In previous studies, the mechanisms underlying female-specific effects, including increased Cd uptake at low iron stores and interference with insulin-like growth factors, have been identified (S. Huang et al., 2019). Other authors have reported sex-specific effects of DNA methylation patterns related to prenatal Cd exposure, presenting a potential mechanism based on which the BW might be affected by Cd exposure (Kippler et al., 2013; Mohanty et al., 2015). A cohort study of 24 pairs of mothers and infants provided evidence of a sex-specific association between placental Cd and placental genome-wide DNA methylation (Mohanty et al., 2015). Mohanty et al. (2015) reported that high Cd levels in female infants are associated with hypomethylation of siah E3 ubiquitin-protein ligase family member 3 (SIAH3), heparin sulfate (glucosamine) 3-O-sulfotransferase 4 (HS3ST4), and TP5Starget1 (TP53G1), genes associated with cellular damage response. In male infants, high Cd levels are associated with hypomethylation of the EVI1

Table 3
Adjusted Effect Estimates (β and 95% CIs) From Multivariable Linear Regression Models for Birth Outcomes in Association With IQR Increases in Log-Transformed Breast Milk Metal Concentrations[a]

Metal	Gestational age	Birth weight	Birth length
Chromium			
Overall	−0.06 (−0.47, 0.36)	101.20 (−59.04, 261.43)	0.19 (−0.13, 0.52)
Male	−0.15 (−0.78, 0.47)	95.45 (−137.35, 328.25)	−0.02 (−0.48, 0.44)
Female	0.22 (−0.42, 0.86)	164.94 (−65.91, 395.79)	0.47 (−0.02, 0.96)
P-value for interaction	0.350	0.721	**0.036**
Manganese			
Overall	−0.02 (−0.28, 0.24)	43.44 (−56.47, 143.35)	0.06 (−0.14, 0.27)
Male	0.15 (−0.27, 0.56)	116.39 (−39.52, 272.31)	0.24 (−0.07, 0.55)
Female	−0.17 (−0.53, 0.20)	8.24 (−123.15, 139.63)	−0.09 (−0.37, 0.18)
P-value for interaction	**0.071**	**0.087**	**0.042**
Copper			
Overall	−0.04 (−0.26, 0.17)	55.47 (−28.04, 138.99)	0.06 (−0.11, 0.23)
Male	0.00 (−0.32, 0.32)	65.54 (−53.61, 184.69)	0.00 (−0.23, 0.24)
Female	−0.10 (−0.42, 0.23)	28.02 (−90.92, 146.97)	0.05 (−0.21, 0.30)
P-value for interaction	0.243	0.649	0.663
Arsenic			
Overall	−0.15 (−0.49, 0.20)	−3.61 (−135.85, 128.63)	−0.04 (−0.31, 0.23)
Male	−0.11 (−0.58, 0.37)	64.60 (−112.62, 241.82)	0.06 (−0.29, 0.41)
Female	−0.25 (−0.81, 0.30)	−150.90 (−351.37, 49.56)	−0.27 (−0.69, 0.16)
P-value for interaction	0.296	0.118	0.150
Cadmium			
Overall	−0.12 (−0.38, 0.15)	−40.44 (−143.61, 62.74)	−0.09 (−0.30, 0.13)
Male	−0.09 (−0.51, 0.32)	73.48 (−81.06, 228.02)	0.10 (−0.20, 0.41)
Female	−0.05 (−0.44, 0.34)	**−162.71 (−303.16, −22.25)**	−0.27 (−0.57, 0.03)
P-value for interaction	0.960	**0.017**	**0.072**
Lead			
Overall	0.03 (−0.29, 0.35)	−77.56 (−198.92, 43.81)	−0.07 (−0.32, 0.18)
Male	0.10 (−0.33, 0.53)	−77.80 (−238.73, 83.12)	−0.13 (−0.45, 0.19)
Female	−0.13 (−0.62, 0.37)	−87.67 (−267.34, 91.99)	−0.05 (−0.44, 0.33)
P-value for interaction	0.488	0.297	0.694

Note. Bold font indicates a statistically significant difference between male and female.
[a]Models adjusted for all metals, maternal age (y), BMI at enrollment (kg/m^2), smoking during pregnancy (yes or no), education level (<college graduate or ≥ college graduate), parity (nulliparous or multiparous), and infant sex (male or female).

complex locus (MECOM) and hypermethylation of spalt-like transcription factor 1 (SALL1), genes associated with cell differentiation, angiogenesis, and organ development.

In addition to Cd, we also studied the associations of birth outcomes with prenatal exposure to five other metals. Mn is an essential trace element, which is crucial for the growth and development of children. A study conducted in Shanghai, China, on cord blood metal concentrations and birth outcomes revealed an inverse U-shaped association between the Mn concentration and BW (Chen et al., 2014). This result was supported by another study conducted in China on maternal cord blood concentration and BW (Guan et al., 2014). However, in the Infantes Salud Ambiental cohort study in Costa Rica, no association was observed between changes in the maternal blood Mn concentration and lower fetal BW (Mora et al., 2015). Similarly, no association was detected between the Mn concentration and infant birth outcomes in our study. In addition, we have not yet reached definitive conclusions regarding the associations between As concentrations and infant birth outcomes. However, a prospective cohort study reported that increased As concentrations cause lower BWs in infants (Mullin et al., 2019). In contrast, a positive association between BW and maternal As exposure was observed in a recent study (Myers et al., 2010). These results indicate that the effects of Mn and As exposure on birth outcomes remain unclear and must be confirmed in future studies.

In the current study, no association was observed between the Pb levels and birth outcomes. However, a significant negative association between high maternal blood Pb concentrations (mean = 6.81 μg/dL) and lower BW in infants was determined in a previous birth cohort study of 300 preschool children in the Guiyu e-waste recycling area in China (Zeng et al., 2019). In contrast, in another study conducted in the Guiyu e-waste recycling area, no association was observed between high Pb concentrations in the placenta (301.43 ng/g wt) and BW in 101 mother–infant pairs (Guo et al., 2010). The results of previous studies on Pb exposure revealed negative associations with birth outcomes. Therefore, the observed lack of association of birth with outcomes with Pb exposure in this study may be due to the small sample size and low levels of Pb exposure. In summary, the possibility that Pb exposure interferes with and inhibits normal growth and development in children must be further investigated.

Because Cr and Cu play important roles in human metabolism, their concentrations are also critical for infants. The results of previous studies showed that high levels of Cr and Cu are positively associated with the risk of a low BW (Bermúdez et al., 2015; Xia et al., 2016). In addition, previous data from the Spanish study INMA project showed that data from placenta samples of 327 mother-infant pairs indicated a negative association between Cr concentration and birth length (Freire et al., 2019). In our study, we found that the 34.3% of the milk samples had Cr concentrations that exceeded the WHO permissible. However, associations between the Cu and Cr levels and birth outcome were not observed in our study. Research has shown that exposure to Cr during pregnancy may increase the risk of neuroblastoma and lymphocyte damage in infants (McDermott et al., 2015). However, some studies have concluded that Cr in breast milk does not affect the health of infants (Samiee et al., 2019). The above results indicate that although the benefits of consuming breast milk may offset the potential risk of infant exposure to chromium, continuous monitoring of this pollutant is important, especially in the e-waste recycling area. This will help health authorities take measures to reduce maternal exposure to Cr during pregnancy, thereby avoiding unnecessary health risks.

In this study, we used BKMR to assess the nonlinear association and interactions among the six metals as a way to assess the association of mixed metal exposure with birth outcomes. The results show a cumulative association of mixed exposure of the six metals at low concentrations without synergistic association, which is consistent with other studies (Takatani et al., 2022).

The results of this study provide evidence for the association between prenatal metal exposure and birth outcomes. However, the current study has several limitations. First, the sample size was relatively small; our results must be validated with a larger sample size in future studies. Second, this study did not collect samples from other environmental sources, such as drinking water, food, or soil other than human milk during pregnancy or at the time of delivery, for analyzing prenatal exposure concentrations of heavy metals. Third, a cross-sectional study design was used, which means that this information may not be sufficient and might not be able to adequately explain the long-term effects of prenatal exposure to heavy metals on child health alone. Finally, to confirm the associations between heavy metal exposure and infant growth and development, it is important to conduct individualized follow-up cohort studies.

5. Conclusions

In this study, we found that 34.3% of participants in an e-waste recycling area had a Cr concentration that exceeded WHO guidelines, and there was a significant negative association between prenatal exposure to the Cd and infant BW in females. These results suggest that prenatal exposure to heavy metals in e-waste recycling areas may lead to adverse birth outcomes, particularly for female infants. In future, the associations between metal exposure in the e-waste recycling area and the growth and development of infants must be studied over the long term. Moreover, although no synergistic associations of metal exposure were found in this study, mixed exposure to metal is of interest in the future.

Conflict of Interest

The authors declare no conflicts of interest relevant to this study.

Data Availability Statement

Data is available at Sun (2023).

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References

Adie, G. U., Sun, L., Zeng, X., Zheng, L., Osibanjo, O., & Li, J. (2017). Examining the evolution of metals utilized in printed circuit boards. *Environmental Technology*, *38*(13–14), 1696–1701. https://doi.org/10.1080/09593330.2016.1237552

Bakhiyi, B., Gravel, S., Ceballos, D., Flynn, M. A., & Zayed, J. (2018). Has the question of e-waste opened a Pandora's box? An overview of unpredictable issues and challenges. *Environment International*, *110*, 173–192. https://doi.org/10.1016/j.envint.2017.10.021

Baldé, C. P., Angel, E. D., Deubzer, V. L. O., & Kuehr, R. (2022). *Global transboundary e-waste flows monitor - 2022*. United Nations Institute for Training and Research (UNITAR). Retrieved from https://ewastemonitor.info/wp-content/uploads/2022/06/Global-TBM_webversion_june_2_pages.pdf

Bermúdez, L., García-Vicent, C., López, J., Torró, M. I., & Lurbe, E. (2015). Assessment of ten trace elements in umbilical cord blood and maternal blood: Association with birth weight. *Journal of Translational Medicine*, *13*(1), 291. https://doi.org/10.1186/s12967-015-0654-2

Bobb, J. F. (2022). Package 'bkmr': Bayesian kernel machine regression. Retrieved from https://cran.r-project.org/web/packages/bkmr/bkmr.pdf

Cathey, A. L., Watkins, D. J., Rosario, Z. Y., Vélez, C., Mukherjee, B., Alshawabkeh, A. N., et al. (2022). Biomarkers of exposure to phthalate mixtures and adverse birth outcomes in a Puerto Rico birth cohort. *Environmental Health Perspectives*, *130*(3), 37009. https://doi.org/10.1289/EHP8990

Chan, J. K., & Wong, M. H. (2013). A review of environmental fate, body burdens, and human health risk assessment of PCDD/Fs at two typical electronic waste recycling sites in China. *Science of the Total Environment*, *463–464*, 1111–1123. https://doi.org/10.1016/j.scitotenv.2012.07.098

Chatzi, L., Ierodiakonou, D., Margetaki, K., Vafeiadi, M., Chalkiadaki, G., Roumeliotaki, T., et al. (2019). Associations of prenatal exposure to cadmium with child growth, obesity, and cardiometabolic traits. *American Journal of Epidemiology*, *188*(1), 141–150. https://doi.org/10.1093/aje/kwy216

Chen, L., Ding, G., Gao, Y., Wang, P., Shi, R., Huang, H., & Tian, Y. (2014). Manganese concentrations in maternal–infant blood and birth weight. *Environmental Science and Pollution Research*, *21*(9), 6170–6175. https://doi.org/10.1007/s11356-013-2465-4

Chi, X., Streicher-Porte, M., Wang, M. Y., & Reuter, M. A. (2011). Informal electronic waste recycling: A sector review with special focus on China. *Waste Management*, *31*(4), 731–742. https://doi.org/10.1016/j.wasman.2010.11.006

Chi, X., Wang, M. Y. L., & Reuter, M. A. (2014). E-waste collection channels and household recycling behaviors in Taizhou of China. *Journal of Cleaner Production*, *80*, 87–95. https://doi.org/10.1016/j.jclepro.2014.05.056

China Daily. (2004). City makes efforts to clean up in recycling business. Retrieved from http://www.china.org.cn/english/environment/98233.htm2004

Donangelo, C. M., Kerr, B. T., Queirolo, E. I., Vahter, M., Peregalli, F., Mañay, N., & Kordas, K. (2021). Lead exposure and indices of height and weight in Uruguayan urban school children, considering co-exposure to cadmium and arsenic, sex, iron status, and dairy intake. *Environmental Research*, *195*, 110799. https://doi.org/10.1016/j.envres.2021.110799

Dong, J. J., Ruan, M. C., Hang, J. G., Nakayama, S. F., Jung, C. R., Kido, T., et al. (2020). The relationship between perinatal exposure to dioxins and serum steroid hormone levels in preschool-aged children at an e-waste region in China. *International Journal of Hygiene and Environmental Health*, *229*, 113580. https://doi.org/10.1016/j.ijheh.2020.113580

Freire, G., Amaya, E., Gil, F., Murcia, M., Llop, S., Casas, M., et al. (2019). Placental metal concentrations and birth outcomes: The Environment and Childhood (INMA) project. *International Journal of Hygiene and Environmental Health*, *222*(3), 468–478. https://doi.org/10.1016/j.ijheh.2018.12.014

Genchi, G., Sinicropi, M. S., Lauria, G., Carocci, A., & Catalano, A. (2020). The effects of cadmium toxicity. *International Journal of Environmental Research and Public Health*, *17*(11), 3782. https://doi.org/10.3390/ijerph17113782

Geng, H. X., & Wang, L. (2019). Cadmium: Toxic effects on placental and embryonic development. *Environmental Toxicology and Pharmacology*, *67*, 102–107. https://doi.org/10.1016/j.etap.2019.02.006

Golding, J. (1997). Unnatural constituents of breast milk—Medication, lifestyle, pollutants, viruses. *Early Human Development*, *49*, S29–S43. https://doi.org/10.1016/s0378-3782(97)00052-2

Grandjean, P., & Herz, K. T. (2015). Trace elements as paradigms of developmental neurotoxicants: Lead, methylmercury, and arsenic. *Journal of Trace Elements in Medicine & Biology*, *31*, 130–134. https://doi.org/10.1016/j.jtemb.2014.07.023

Gu, H., Wang, L., Liu, L., Luo, X., Wang, J., Hou, F., et al. (2017). A gradient relationship between low birth weight and IQ: A meta-analysis. *Scientific Reports*, *7*(1), 18035. https://doi.org/10.1038/s41598-017-18234-9

Guan, H., Wang, M., Li, X., Piao, F., Li, Q., Xu, L., et al. (2014). Manganese concentrations in maternal and umbilical cord blood: Related to birth size and environmental factors. *The European Journal of Public Health*, *24*(1), 150–157. https://doi.org/10.1093/eurpub/ckt033

Guo, Y., Huo, X., Li, Y., Wu, K., Liu, J., Huang, J., et al. (2010). Monitoring of lead, cadmium, chromium, and nickel in placenta from an e-waste recycling town in China. *Science of the Total Environment*, *408*(16), 3113–3117. https://doi.org/10.1016/j.scitotenv.2010.04.018

Gustin, K., Barman, M., Stråvik, M., Levi, M., Englund-Ögge, L., Murray, F., et al. (2020). Low-level maternal exposure to cadmium, lead, and mercury and birth outcomes in a Swedish prospective birth-cohort. *Environmental Pollution*, *265*(Pt B), 114986. https://doi.org/10.1016/j.envpol.2020.114986

Hang, J. G., Dong, J. J., Feng, H., Huang, J. Z., Wang, Z., Shen, B., et al. (2022). Evaluating postnatal exposure to six heavy metals in a Chinese e-waste recycling area. *Chemosphere*, *308*, 13644. https://doi.org/10.1016/j.chemosphere.2022.136444

Houessionon, M. G. K., Ouendo, E. D., Bouland, C., Takyi, S. A., Kedote, N. M., Fayomi, B., et al. (2021). Environmental heavy metal contamination from electronic waste (e-waste) recycling activities worldwide: A systematic review from 2005 to 2017. *International Journal of Environmental Research and Public Health*, *18*(7), 3517. https://doi.org/10.3390/ijerph18073517

Howe, C. G., Claus Henn, B., Farzan, S. F., Habre, R., Eckel, S. P., Grubbs, B. H., et al. (2021). Prenatal metal mixtures and fetal size in mid-pregnancy in the MADRES study. *Environmental Research*, *196*, 110388. https://doi.org/10.1016/j.envres.2020.110388

Huang, K., Li, H., Zhang, B., Zheng, T., Li, Y., Zhou, A., et al. (2017). Prenatal cadmium exposure and preterm low birth weight in China. *Journal of Exposure Science and Environmental Epidemiology*, *27*(5), 491–496. https://doi.org/10.1038/jes.2016.41

Huang, S., Kuang, J., Zhou, F., Jia, Q., Lu, Q., Feng, C., et al. (2019). The association between prenatal cadmium exposure and birth weight: A systematic review and meta-analysis of available evidence. *Environmental Pollution*, *251*, 699–707. https://doi.org/10.1016/j.envpol.2019.05.039

Kanda, T., Murai-Takeda, A., Kawabe, H., & Itoh, H. (2020). Low birth weight trends: Possible impacts on the prevalences of hypertension and chronic kidney disease. *Hypertension Research*, *43*(9), 859–868. https://doi.org/10.1038/s41440-020-0451-z

Khan, K. M., Chakraborty, R., Bundschuh, J., Bhattacharya, P., & Parvez, F. (2020). Health effects of arsenic exposure in Latin America: An overview of the past eight years of research. *Science of the Total Environment*, *710*, 136071. https://doi.org/10.1016/j.scitotenv.2019.136071

Kim, M. S., Kim, S. H., Jeon, D., Kim, H. Y., Han, J. Y., Kim, B., & Lee, K. (2018). Low-dose cadmium exposure exacerbates polyhexamethylene guanidine-induced lung fibrosis in mice. *Journal of Toxicology and Environmental Health, Part A*, *81*(11), 384–396. https://doi.org/10.1080/15287394.2018.1451177

Kim, S. S., Xu, X., Zhang, Y., Zheng, X., Liu, R., Dietrich, K. N., et al. (2020). Birth outcomes associated with maternal exposure to metals from informal electronic waste recycling in Guiyu, China. *Environment International*, *137*, 105580. https://doi.org/10.1016/j.envint.2020.105580

Kippler, M., Engström, K., Mlakar, S. J., Bottai, M., Ahmed, S., Hossain, M. B., et al. (2013). Sex-specific effects of early life cadmium exposure on DNA methylation and implications for birth weight. *Epigenetics*, *8*(5), 494–503. https://doi.org/10.4161/epi.24401

Kippler, M., Tofail, F., Gardner, R., Rahman, A., Hamadani, J. D., Bottai, M., & Vahter, M. (2012). Maternal cadmium exposure during pregnancy and size at birth: A prospective cohort study. *Environmental Health Perspectives*, *120*(2), 284–289. https://doi.org/10.1289/ehp.1103711

Lee, J. W., Lee, C. K., Moon, C. S., Choi, I. J., Lee, K. J., Yi, S. M., et al. (2012). Korea national survey for environmental pollutants in the human body 2008: Heavy metals in the blood or urine of the Korean population. *International Journal of Hygiene and Environmental Health*, *215*(4), 449–457. https://doi.org/10.1016/j.ijheh.2012.01.002

Lee, M. S., Eum, K. D., Golam, M., Quamruzzaman, Q., Kile, M. L., Mazumdar, M., & Christiani, D. C. (2021). Umbilical cord blood metal mixtures and birth size in Bangladeshi children. *Environmental Health Perspectives*, *129*(5), 57006. https://doi.org/10.1289/EHP7502

Li, A., Zhuang, T., Shi, J., Liang, Y., & Song, M. (2019). Heavy metals in maternal and cord blood in Beijing and their efficiency of placental transfer. *Journal of Environmental Sciences*, *80*, 99–106. https://doi.org/10.1016/j.jes.2018.11.004

Ling, S., Lu, C., Peng, C., Zhang, W., Lin, K., & Zhou, B. (2021). Characteristics of legacy and novel brominated flame retardants in water and sediment surrounding two e-waste dismantling regions in Taizhou, eastern China. *Science of the Total Environment*, *794*, 148744. https://doi.org/10.1016/j.scitotenv.2021.148744

Liu, H., Lu, S., Zhang, B., Xia, W., Liu, W., Peng, Y., et al. (2018). Maternal arsenic exposure and birth outcomes: A birth cohort study in Wuhan, China. *Environmental Pollution*, *236*, 817–823. https://doi.org/10.1016/j.envpol.2018.02.012

Liu, L., Zhang, B., Lin, K., Zhang, Y., Xu, X., & Huo, X. (2018). Thyroid disruption and reduced mental development in children from an informal e-waste recycling area: A mediation analysis. *Chemosphere*, *193*, 498–505. https://doi.org/10.1016/j.chemosphere.2017

McDermott, S., Salzberg, D. C., Anderson, A. P., Shaw, T., & Lead, J. (2015). Systematic review of chromium and nickel exposure during pregnancy and impact on child outcomes. *Journal of Toxicology and Environmental Health, Part A*, *78*(21–22), 1348–1368. https://doi.org/10.1080/15287394.2015.1090939

Mebrahtu, T. F., Feltbower, R. G., Greenwood, D. C., & Parslow, R. C. (2015). Birth weight and childhood wheezing disorders: A systematic review and meta-analysis. *Journal of Epidemiology & Community Health*, *69*(5), 500–508. https://doi.org/10.1136/jech-2014-204783

Mezynska, M., & Brzóska, M. M. (2018). Environmental exposure to cadmium-a risk for the health of the general population in industrialized countries and preventive strategies. *Environmental Science and Pollution Research*, *25*(4), 3211–3232. https://doi.org/10.1007/s11356-017-0827-z

Mohanty, A. F., Farin, F. M., Bammler, T. K., MacDonald, J. W., Afsharinejad, Z., Burbacher, T. M., et al. (2015). Infant sex-specific placental cadmium, and DNA methylation associations. *Environmental Research*, *138*, 74–81. https://doi.org/10.1016/j.envres.2015.02.004

Mora, A. M., Wendel de Joode, B., Mergler, D., Córdoba, L., Cano, C., Quesada, R., et al. (2015). Maternal blood and hair manganese concentrations, fetal growth, and length of gestation in the ISA cohort in Costa Rica. *Environmental Research*, *136*, 47–56. https://doi.org/10.1016/j.envres.2014.10.011

Mullin, A. M., Amarasiriwardena, C., Cantoral-Preciado, A., Claus Henn, B., Leon Hsu, H. H., Sanders, A. P., et al. (2019). Maternal blood arsenic levels and associations with birth weight-for-gestational age. *Environmental Research*, *177*, 108603. https://doi.org/10.1016/j.envres.2019.108603

Myers, S. L., Lobdell, D. T., Liu, Z., Xia, Y., Ren, H., Li, Y., et al. (2010). Maternal drinking water arsenic exposure and perinatal outcomes in inner Mongolia, China. *Journal of Epidemiology & Community Health*, *64*(4), 325–329. https://doi.org/10.1136/jech.2008.084392

Parr, R. M., DeMaeyer, E. M., Iyengar, V. G., Byrne, A. R., Kirkbright, G. F., Schöch, G., et al. (1991). Minor and trace elements in human milk from Guatemala, Hungary, Nigeria, Philippines, Sweden, and Zaire. Results from a WHO/IAEA joint project. *Biological Trace Element Research*, *29*(1), 51–75. https://doi.org/10.1007/BF03032674

Punshon, T., Li, Z., Jackson, B. P., Parks, W. T., Romano, M., Conway, D., et al. (2019). Placental metal concentrations in relation to placental growth, efficiency and birth weight. *Environment International*, *126*, 533–542. https://doi.org/10.1016/j.envint.2019.01.063

Rautela, R., Arya, S., Vishwakarma, S., Lee, J., Kim, K. H., & Kumar, S. (2021). E-waste management and its effects on the environment and human health. *Science of the Total Environment*, *773*, 145623. https://doi.org/10.1016/j.scitotenv.2021

Rebelo, F. M., & Caldas, E. D. (2016). Arsenic, lead, mercury and cadmium: Toxicity, levels in breast milk and the risks for breastfed infants. *Environmental Research*, *151*, 671–688. https://doi.org/10.1016/j.envres.2016.08.027

Samiee, F., Vahidinia, A., Javad, M. T., & Leili, M. (2019). Exposure to heavy metals released to the environment through breastfeeding: A probabilistic risk estimation. *Science of the Total Environment*, *650*, 3075–3083. https://doi.org/10.1016/j.scitotenv.2018.10.059

Shakil, S., Nawaz, K., & Sadef, Y. (2022). Evaluation and environmental risk assessment of heavy metals in the soil released from e-waste management activities in Lahore, Pakistan. *Environmental Monitoring and Assessment*, *195*(1), 89. https://doi.org/10.1007/s10661-022-10701-9

Shih, Y. H., Chen, H. Y., Christensen, K., Handler, A., Turyk, M. E., & Argos, M. (2021). Prenatal exposure to multiple metals and birth outcomes: An observational study within the National Children's Study cohort. *Environment International*, *147*, 106373. https://doi.org/10.1016/j.envint.2020.106373

Silverwood, R. J., Pierce, M., Hardy, R., Sattar, N., Whincup, P., Ferro, C., et al. (2013). Low birth weight, later renal function, and the roles of adulthood blood pressure, diabetes, and obesity in a British birth cohort. *Kidney International*, *84*(6), 1262–1270. https://doi.org/10.1038/ki.2013.223

Sun, X. L. (2023). Heavy metals in human milk [Dataset]. Zenodo. https://doi.org/10.5281/zenodo.8327559

Takatani, T., Eguchi, A., Yamamoto, M., Sakurai, K., Takatani, R., Taniguchi, Y., et al. (2022). Individual and mixed metal maternal blood concentrations in relation to birth size: An analysis of the Japan Environment and Children's Study (JECS). *Environment International*, *165*, 107318. https://doi.org/10.1016/j.envint.2022.107318

Taylor, C. M., Golding, J., & Emond, A. M. (2016). Moderate prenatal cadmium exposure and adverse birth outcomes: A role for sex-specific differences? *Paediatric & Perinatal Epidemiology*, *30*(6), 603–611. https://doi.org/10.1111/ppe.12318

Vaccari, M., Vinti, G., Cesaro, A., Belgiorno, V., Salhofer, S., Dias, M. I., & Jandric, A. (2019). WEEE treatment in developing countries: Environmental pollution and health consequences—An overview. *International Journal of Environmental Research and Public Health*, *16*(9), 1595. https://doi.org/10.3390/ijerph16091595

VanderWeele, T. J., Mumford, S. L., & Schisterman, E. F. (2012). Conditioning on intermediates in perinatal epidemiology. *Epidemiology*, *23*(1), 1–9. https://doi.org/10.1097/EDE.0b013e31823aca5d

Vrijheid, M., Casas, M., Gascon, M., Valvi, D., & Nieuwenhuijsen, M. (2016). Environmental pollutants and child health—A review of recent concerns. *International Journal of Hygiene and Environmental Health*, *219*(4–5), 331–342. https://doi.org/10.1016/j.ijheh.2016.05.001

Wang, D., Sun, H., Wu, Y., Zhou, Z., Ding, Z., Chen, X., & Xu, Y. (2016). Tubular and glomerular kidney effects in the Chinese general population with low environmental cadmium exposure. *Chemosphere*, *147*, 3–8. https://doi.org/10.1016/j.chemosphere.2015.11.069

Wang, H., Han, M., Yang, S., Chen, Y., Liu, Q., & Ke, S. (2011). Urinary heavy metal levels and relevant factors among people exposed to e-waste dismantling. *Environment International*, *37*(1), 80–85. https://doi.org/10.1016/j.envint.2010.07.005

Wang, T., Fu, J., Wang, Y., Liao, C., Tao, Y., & Jiang, G. (2009). Use of scalp hair as indicator of human exposure to heavy metals in an electronic waste recycling area. *Environmental Pollution*, *157*(8–9), 2445–2451. https://doi.org/10.1016/j.envpol.2009.03.010

Wei, J. N., Sung, F. C., Li, C. Y., Chang, C. H., Lin, R. S., Lin, C. C., et al. (2003). Low birth weight and high birth weight infants are both at an increased risk to have type 2 diabetes among schoolchildren in Taiwan. *Diabetes Care*, *26*(2), 343–348. https://doi.org/10.2337/diacare.26.2.343

Xia, W., Hu, J., Zhang, B., Li, Y., Wise, J. P., Sr., Bassig, B. A., et al. (2016). A case-control study of maternal exposure to chromium and infant low birth weight in China. *Chemosphere*, *144*, 1484–1489. https://doi.org/10.1016/j.chemosphere.2015.10.006

Zeng, X., Ali, S. H., Tian, J., & Li, J. (2020). Mapping anthropogenic mineral generation in China and its implications for a circular economy. *Nature Communications*, *11*(1), 1544. https://doi.org/10.1038/s41467-020-15246-4

Zeng, X., Xu, C., Xu, X., Zhang, Y., Huang, Y., & Huo, X. (2021). Elevated lead levels in relation to low serum neuropeptide Y and adverse behavioral effects in preschool children with e-waste exposure. *Chemosphere*, *269*, 129380. https://doi.org/10.1016/j.chemosphere.2020.129380

Zeng, X., Xu, X., Qin, Q., Ye, K., Wu, W., & Huo, X. (2019). Heavy metal exposure has adverse effects on the growth and development of preschool children. *Environmental Geochemistry and Health*, *41*(1), 309–321. https://doi.org/10.1007/s10653-018-0114-z