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Maternal urinary cadmium levels during pregnancy associated with risk of sex-dependent birth outcomes from an e-waste pollution site in China

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ABSTRACT

This study was to investigate whether exposure to cadmium (Cd) during pregnancy is associated with an increased risk of adverse birth outcomes in a sex-dependent manner. Cd concentrations in maternal urine (U-Cd) samples were measured in 237 subjects from Guiyu (e-waste area) and 212 subjects from Haojiang. A significance level of $p < 0.05$ was used for all analyses. The maternal U-Cd levels in Guiyu residents were significantly higher than Haojiang. We found significant inverse associations between U-Cd concentrations and birth anthropometry (birth weight, birth length, Head Circumference and Apgar scores with 1 min and 5 mins) in female neonates, but no significant associations were observed in male neonates except Apgar (1 min) score after adjustment. The association was more pronounced among female neonates than male neonates, suggesting an association between Cd and adverse birth outcomes may be sex-specific.

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1. Introduction

Electronic waste (e-waste) is defined as any end-of-life equipment which is dependent on electrical currents or electromagnetic fields in order to work properly [1]. Sources of exposure to e-waste can be classified into three sectors: informal recycling, formal recycling and exposure to hazardous e-waste compounds remaining in the environment [2]. E-waste is an emerging environmental health issue, in both developed and developing countries, because of its massive production volume and insufficient management policy [3–5]. Guiyu is one of the largest e-waste destinations and recycling areas in China. In addition, Guiyu has a decades-long history of primitive e-waste recycling activities, and nearly 70–80% of families are involved in the business of e-waste recycling [6,7]. Considering the potential chemical contamination in e-waste recycling areas, over the past decade we have been investigating the health effects of heavy metals and organic pollutants on children, as well as pregnant women. Our previous studies reported that living in an e-waste recycling site substantially increases exposure of children and pregnant women to cadmium (Cd), lead (Pb), and other organic pollutants [6,8–14], but the adverse effects of these chemicals on fetal development remain to be determined.

Cd is extensively used as important raw materials in the manufacture of electronic devices, such as rechargeable nickel-cadmium batteries, surface mount device chip resistors, infrared detectors, printer inks and toners, and many other devices [15]. Exposure to Cd has been shown to adversely affect the liver, bladder, stomach, heart, renal system, and reproductive system in adults [3,16]. The effects of Cd toxicity on fetal development have received much attention due to the observation of Cd accumulation in the placenta during gestation [17]. However, little information is available on Cd levels among pregnant women. To date, several previous studies have evaluated the association between maternal Cd concentrations and birth outcomes. These studies have reported that exposure to Cd during pregnancy significantly decreases birth

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Table 1
Descriptive statistics of pregnant women in Guiyu (exposed group) and Haojiang (reference group), China.

Characteristics	Haojiang		Guiyu		Statistic	P-value
	n	Mean ± SD or (%)	n	Mean ± SD or (%)		
Maternal characteristics						
Maternal age	207	28.52 ± 4.33	231	26.29 ± 4.27	$t = -5.438$	0.000**
Maternal weight (kg)	180	52.96 ± 8.00	197	49.27 ± 5.38	$t = -5.294$	0.000**
Maternal height (cm)	186	158.77 ± 4.63	185	158.34 ± 3.49	$t = -0.017$	0.310
BMI (Kg/m^2)	179	20.99 ± 2.88	174	19.68 ± 1.95	$t = -4.979$	0.000**
Socio-economic variables						
Education	202		225		$\chi^2 = 51.366$	0.000**
Less than primary school	3	1.49	1	0.44		
Primary school	37	18.32	68	30.22		
Junior high school	101	50.00	142	63.11		
Senior high school	37	18.32	12	5.33		
University and above	24	11.88	2	0.89		
Occupation	186		*206*		$\chi^2 = 0.550$	0.458
Farmers	30	16.13	19	9.22		
Industrial workers	34	18.28	48	23.30		
Employed participants	21	11.29	28	13.59		
Unemployed participants	101	54.30	111	53.88		
Household income (RMB)	131		86		$\chi^2 = 61.105$	0.000**
<30,000	68	51.91	6	6.98		
30,000–60,000	34	25.95	29	33.72		
60,000–90,000	16	12.21	31	36.05		
90,000–120,000	7	5.34	7	8.14		
120,000–150,000	5	3.82	7	8.14		
>150,000	1	0.76	6	6.98		

BMI: Body mass index, RMB: Renminbi (currency of China). Proportions were compared by Pearson chi-square test. Means were compared by one-way ANOVA.
** $p < 0.01$.

weight [6,18–20], birth length [21,22], and head circumference [23–25] as well as increases the risk of preterm birth[19,26,27]. Recently, Romana et al. conducted a prospective study in which sex-specific effects of Cd exposure on weight were suggested. Specifically, they observed a decrease in birth weight with increasing maternal urinary Cd among female neonates and no clear impact of Cd on fetal growth among male neonates [28]. In contrast, there are numerous others that have reported no association between maternal Cd levels and adverse birth outcomes [21,29,30].

Results can be conflicting and inconsistent because blood Cd concentrations largely reflect recent exposure [31].In the blood Cd has a half-life of 3–4 months and is later transported to other parts of the body, chiefly kidney where its half-life is 10–30 years. Cd in blood reflects recent exposure, whereas urinary Cd levels can serve

Table 2
Life style factors of pregnant women in Guiyu (exposed group) and Haojiang (reference group), China.

Characteristics	Haojiang		Guiyu		Statistic	P-value
	n	(%)	n	(%)		
Alcohol consumption					$\chi^2 = 0.06$	0.798
No	192	98.97	228	98.70		
Yes	2	1.03	3	1.30		
Smoking status					$\chi^2 = 0.55$	0.457
No	190	98.96	230	99.57		
Yes	2	1.04	1	0.43		
Food (fish, and meat) consumption (g/day)					$\chi^2 = 30.27$	0.000**
No	2	1.12	1	0.45		
100	94	52.81	157	71.36		
101–200	69	38.76	62	28.19		
>201	13	7.30	0	0.00		
House as e-waste workshop					$\chi^2 = 29.36$	0.000**
No	197	100.00	31	13.84		
Yes	0	0.00	193	86.16		
Work related to e-waste during pregnancy					$\chi^2 = 27.33$	0.000**
No	195	99.49	32	14.29		
Yes	1	0.51	192	85.71		
Distance between house and e-waste site (m)					$\chi^2 = 116.45$	0.000**
>2000	130	79.27	24	17.65		
1000–2000	18	10.98	16	11.77		
200–999	6	3.66	48	35.29		
<200	10	6.10	48	35.29		
Distance between house and highway (m)					$\chi^2 = 62.94$	0.000**
>5000	86	49.71	11	11.11		
2000–5000	33	19.08	17	11.17		
500–1999	24	13.87	10	10.10		
200–499	19	10.99	27	27.27		
<200	11	6.36	34	34.34		

Proportions were compared by Pearson chi-square test.

as a stable biomarker for assessing the lifetime body burden of Cd [32]. Further, epidemiological investigations concerning the interactions between Cd exposure during pregnancy and adverse birth outcomes in a sex-dependent manner are extremely limited. Therefore, we measured Cd concentrations in maternal urine during pregnancy, and evaluated the potential effect of maternal urinary Cd on neonate anthropometry (birth weight, birth length, head circumference, and neonatal body mass index) in a sex-specific manner.

2. Materials and methods

2.1. Study area and participants

A total of 449 subjects were recruited before birth in this study from September 2011 to June 2012. Among these, 237 mother-neonate pairs were recruited from Guiyu township (e-waste recycling area) and 212 mother-neonate pairs from Haojiang District (referenced area), China. The sampling site Guiyu is located in the southern coast of Guangdong province in China. Haojiang was selected as a reference area because of its lack of e-waste recycling activities. Haojiang is approximately 31.6 km from Guiyu and is famous for its tourism and fishing. Subjects were interviewed by using a structured questionnaire to collect information including demographic (e.g. maternal age), socioeconomic (e.g. education, occupation, and household income), and other lifestyle factors (Tables 1 and 2). Additional relevant information, such as, parity, illness during pregnancy, medical history, and family heredity history, as well as the pre-pregnancy body mass index (BMI), was recorded. The questionnaire included the factors those might influence Cd levels as working and living in the e-waste area, involvement in e-waste activities, distance between house and e-waste site and house as e-waste storage. Alcohol consumption, smoking and their dietary intake (fish and meat) were measured. All participants provided written informed consent before enrollment in this study (Fig. 1). This study procedure was approved by the Human Ethics Committee of Shantou University Medical College, Shantou, China.

2.2. Birth outcomes

As part of the birth outcomes, each neonate weight, length, BMI, and Apgar scores were measured. Birth weight was determined by an electronic neonate-weighing scale (Misaki neonate scale, Japan). Length was measured in the recumbent position using a calibration wooden length board. We also examined head circumference which is commonly used in clinical practice as a measure of head development. The Apgar score test was performed in order to evaluate a newborn's physical condition, including the neonates breathing effort, heart rate, muscle tone, reflexes, and skin color, by specially trained nurses. This test was given to babies twice; first at 1 min after birth, and again at 5 min after birth. Further, gestational age at birth was recorded using both the woman's last menstrual period (LMP) and ultrasound data.

2.3. Sample collection and analysis

Maternal urine samples were collected in the morning (7.00 a.m.–8.00 a.m.) into polypropylene conical centrifuge tubes from the hospitals on the date of delivery. To avoid contamination, we used all plastic tubes and containers for urine collection and froze the samples at −25 °C until further analysis. Urine Cd (U-Cd) concentrations were estimated by using graphite furnace atomic absorption spectrophotometry (GFAAS, Jena Zeenit 650, Germany), according to our previous publications [3,33]. Briefly, urine samples (0.2 mL volume of each subject) were digested in 3.84 mL nitric acid (65%) followed by vortexing and subsequent digestion for 10 min. Then samples were dried at different temperatures, including 90 °C, 105 °C, 120 °C, followed by ashing at 400 °C, atomization at 1100 °C, and cleaning out at 2200 °C. U-Cd was measured

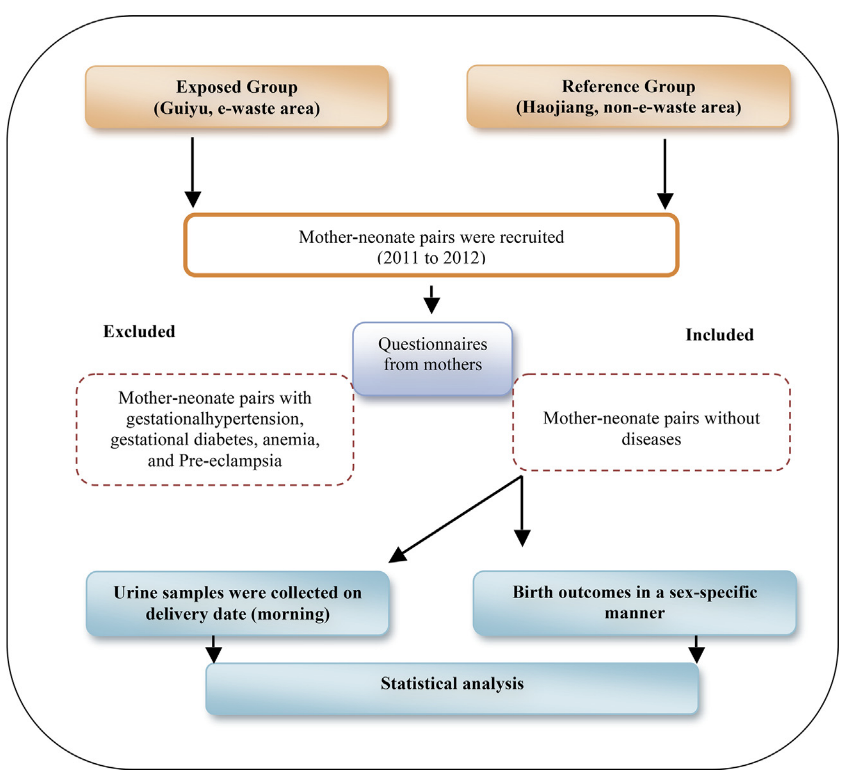

Fig. 1. Flow chart of recruitment and follow-up in this birth cohort study.

Table 3
Maternal urinary cadmium (*U-Cd*) levels *(μg/g creatinine)* from Haojiang (reference group) and Guiyu (exposed group), China.

		n	Mean ± SD	Max.	Min.	Median/25th, 75th	Z	*p*-value
Mothers with male neonates	Haojiang	111	0.75 ± 0.05	2.77	0.06	0.67/0.31,1.05	−4.217	0.000*
	Guiyu	123	1.38 ± 0.74	16.47	0.05	0.92/0.55,1.66		
Mothers with female neonates	Haojiang	101	0.76 ± 0.06	3.20	0.04	0.59/0.29,0.90	−5.779	0.000*
	Guiyu	114	1.59 ± 0.92	14.39	0.10	1.00/0.69,1.77		

* *p < 0.01*; Min: minimum; Max: maximum.

at a wavelength of 228.8 nm and the concentration of U-Cd was adjusted to urine creatinine concentration. Urine creatinine concentrations (g/L) were determined by using commercially available kits (Cayman Chemical Company, China). The concentrations of Cd in urine are expressed as μg per g (μg/g) creatinine.

2.4. Statistical analyses

Data were expressed as means ± standard deviation (SD) and frequencies (percentages). We performed all statistical analyses with SPSS statistical software (version 19.0, SPSS Inc, Chicago, IL, USA). A significance level of $p < 0.05$ was used for all analyses. Sample t-test and chi-square analyses were employed in the comparison of the difference between the two groups. Maternal U-Cd data were indicated with medians and quartiles, and compared by the Mann-Whitney *U*-test between the two groups. Spearman correlation coefficients were used to evaluate the relationship between U-Cd levels and, also a potential association with different life style factors. A linear regression model is used to evaluate the relation between maternal U-Cd levels and sex-specific adverse birth outcomes; adjustments were used for maternal factors (maternal age, height, weight, BMI and education) to assess the contributions of U-Cd concentrations to the birth outcome indices.

3. Results

The selected characteristics of the 449 mother-neonate pairs are presented in Tables 1 and 2. The pregnant women in Guiyu (exposed group) ranged from 18 to 38 years of age, with a mean average of 26.29 ± 4.27 years. Women from Haojiang averaged 28.52 ± 4.33 years of age, with the range being 18–33 years. The reference group, Haojiang had a mean maternal body weight and height of 52.96 kg and 158.77 cm whereas those in Guiyu group had a lower mean body weight and height of 49.27 kg and 158.34 cm, respectively (Table 1). Further, Guiyu mothers had a lower pre-pregnancy BMI (19.68 ± 1.95) than Haojiang group (20.99 ± 2.88). In all, the pregnant women from an e-waste area had significantly lower maternal age ($p < 0.001$), maternal weight ($p < 0.001$), and pre-pregnancy BMI ($p < 0.001$), compared to the Haojiang group. However, no significant difference was observed in maternal height between both groups of pregnant women (Table 1). An assessment of the education levels and household income showed that pregnant women from Guiyu had a lower educational level and household income than Haojiang women (Table 1). We also examined smoking status, alcohol consumption and fish and meat consumption of pregnant women in both Guiyu and Haojiang (Table 2). There were no significant differences observed in smoking status and alcohol consumption, but significant differences were observed in fish, meat consumption and maternal life styles between both groups of pregnant women ($p < 0.001$, Table 2).

Maternal urinary Cd (U-Cd) levels were significantly higher among mothers from Guiyu than mothers from Haojiang (Table 3). Interestingly, mothers with female neonates had higher Cd levels than those with male neonates (1.59 ± 0.92 vs. 1.38 ± 0.74 μg/g creatinine, $p < 0.05$, Table 3) from Guiyu. Correlation analysis revealed a significant association between maternal U-Cd levels and lifestyle factors (Table 4). Among these, residence in Guiyu while pregnant ($r_s = 0.275$; $p = 0.000$), and residing in a house near an e-waste site ($r_s = 0.137$; $p = 0.018$), and highway road ($r_s = 0.145$; $p = 0.017$) were most important variables that positively correlated with maternal U-Cd levels (Table 4).

Table 4
Spearman correlations between different factors and *U-Cd* levels.

Variables	r_s	*p*-value
Residence in Guiyu while pregnant	0.275**	0.000
House as e-waste workshop	0.070	0.152
Work related to e-waste during pregnancy	0.086	0.079
House close to e-waste site	0.137*	0.018
House close to highway	0.145*	0.017
Education	−0.089	0.066
Income	0.158*	0.020
Smoking	0.033	0.505
Alcohol consumption	−0.062	0.202
Meat and fish intake during pregnancy	−0.025	0.617

The association of maternal U-Cd concentration during pregnancy and the risk of abnormal birth outcomes, such as deviations in birth weight, birth length, head circumference, neonatal BMI, Apgar scores and gestational age were analyzed in both Guiyu and Haojiang groups (Table 5). Both male and female neonates showed a significant decrease in birth weight ($p < 0.001$), neonatal BMI ($p < 0.001$) and head circumference ($p < 0.001$), whereas birth length ($p < 0.001$) was increased in Guiyu group, compared to the Haojiang group. A significant increase in gestational age was found for male neonates in Guiyu. However, we found a significant decrease in Apgar score at 1 min in Guiyu group ($p < 0.001$), but no significant differences in Apgar score between the two groups at 5 min after birth (Table 5).

To examine the relationship between U-Cd concentrations and birth outcomes, a linear regression was used for analysis (Table 6). As shown in Table 6, maternal U-Cd concentrations were inversely associated with birth weight ($p = 0.036$), birth length ($p = 0.036$), head circumference ($p = 0.000$), Apgar (1 min) score ($p = 0.002$), and Apgar (5 min) score ($p = 0.000$) in female neonates after adjustments of maternal characteristics (age, weight, height, BMI and education). No significant associations were observed between maternal U-Cd concentrations and male newborns anthropometry, but significant association was observed only in Apgar (1 min) score ($p = 0.004$) in adjusted models (Table 6).

4. Discussion

The present study finds that increased maternal Cd concentrations in urine are associated with sex-specific differences in pregnancy outcomes. To best of our knowledge, this is the first study investigating adverse effects of urinary Cd levels on adverse birth outcomes among women of childbearing age from an e-waste recycling area. In this study, we find that women living in Guiyu have elevated urinary Cd levels when compared with Haojiang area. This concentration is greater than levels reported in pregnant women of the US-based population study, Bangladesh (0.31ug/g) [28], Japan (0.766 ug/g) [34], Washington, USA (0.29 ug/g) [35,36], Wuhan, China (0.54 ug/g) [37,38], Jiangsu

Table 5
Birth outcomes.

	Haojiang Mean ± SD	Guiyu Mean ± SD	*p*-value
Birth Weight (g)			
Male	3425.45 ± 343.07	3132.52 ± 365.75	0.000**
Female	3341.09 ± 364.1	3148.25 ± 341.17	0.000**
Birth Length (cm)			
Male	50.56 ± 1.02	51.55 ± 1.99	0.000**
Female	50.44 ± 0.99	51.25 ± 2.02	0.001**
Birth BMI			
Male	13.38 ± 1.09	11.80 ± 1.33	0.000**
Female	13.12 ± 1.25	11.98 ± 1.09	0.000**
Head Circumference (cm)			
Male	35.53 ± 1.50	34.03 ± 2.16	0.000**
Female	35.41 ± 1.64	32.47 ± 3.39	0.000**
Apgar (1 min) score			
Male	9.96 ± 0.38	9.60 ± 0.76	0.000**
Female	9.97 ± 0.30	9.55 ± 0.64	0.000**
Apgar (5 min) score			
Male	10.00 ± 0.00	9.96 ± 0.33	0.191
Female	9.97 ± 0.30	9.98 ± 0.19	0.717
Gestational Age (weeks)			
Male	39.37 ± 1.25	39.79 ± 0.79	0.003**
Female	39.77 ± 1.09	39.87 ± 0.78	0.439

Table 6
Linear Regression Analysis for urinary cadmium levels and birth outcomes.

		Unadjusted model				Adjusted model[a]			
		B	β	95%CI	*p*	B	β	95%CI	*p*
Birth Weight	Male	−18.657	−0.066	−55.327,18.013	0.317	912.811	−0.049	−49.839,24.217	0.496
	Female	−48.609	−0.204	−80.079,−17.138	0.003**	−8.792	−0.165	−75.112,−2.471	0.036*
Birth Length	Male	0.080	0.064	−0.081, 0.240	0.330	0.064	0.056	−0.104,0.232	0.453
	Female	−0.119	−0.102	−0.276, 0.038	0.137	−0.188	−0.175	−0.362,−0.013	0.036*
Birth BMI	Male	−0.112	−0.104	−0.251, 0.027	0.113	−0.084	−0.086	−0.222,0.555	0.235
	Female	−0.143	−0.168	−0.255, −0.030	0.013*	−0.078	−0.094	−0.209,0.053	0.242
Head	Male	−0.201	−0.136	−0.393, −0.010	0.039	−0.124	90.112	90.285,0.038	0.132
Circumference	Female	−0.482	−0.240	−0.746, −0.218	0.000**	90.505	−0.381	−0.704,−0.306	0.000*
Apgar(1 min)	Male	−0.074	−0.157	−0.135, −0.013	0.017*	−0.092	−0.216	−0.154,−0.031	0.004*
Score	Female	−0.076	−0.211	−0.123, −0.028	0.002**	−0.093	−0.258	−0.151,−0.034	0.002*
Apgar (5 min)	Male	−0.008	−0.048	−0.031, 0.014	0.464	−0.009	−0.049	−0.036,0.019	0.524
Score	Female	−0.049	−0.306	−0.070, −0.028	0.000**	−0.077	−0.431	−0.105,−0.050	0.000*

B: unstandardized coefficients; β: standardized coefficients; CI: confidence interval.
* $p < 0.05$.
** $p < 0.01$.
[a] Adjusted for maternal age, maternal weight, height, BMI, maternal education.

Province, China (0.62 ug/g) [36] and in the pacific north-west (0.55 ug/g) [39]. It suggests that the elevated maternal U-Cd levels are the result of environmental Cd contamination in the e-waste site of Guiyu. We examined several factors to explain this phenomenon. The relatively high U-Cd concentrations were found to correlate with mother's living in e-waste recycling area, involvement in e-waste recycling activities or residing in a house near an e-waste site. We have previously shown that women in this area have an elevated heavy metal and organic pollutant body burden, likely due to involvement in e-waste recycling and residence in e-waste area [6–9]. In this study, our results once again show that elevated Cd concentrations, in urine of pregnant women, are strongly influenced by e-waste recycling activities and residence in an e-waste area. Higher urinary Cd levels reported in Haojiang may be attributed to a high prevalence of coal mines within this long costal region.

We therefore tested whether the U-Cd concentration is associated with negative effects on pregnancy outcomes in a sex-dependent manner. We observed significant decreases in birth weight, neonatal BMI and head circumference, and an increase in birth length in both male and female neonates of Guiyu group when compared with Haojiang. Low birth weight is an important determinant of mortality, morbidity and disability in infancy, and also has a long-term impact on health outcomes in adult life [40]. Recently, Romano et al. observed a 50 g decrease in birth weight with increasing maternal U-Cd levels among female neonates only, with no clear impact observed that on birth weight of male neonates [28]. Further, this study observed maternal U-Cd is inversely associated with birth length among female neonates but not significantly associated with male neonates after adjustment. Another prospective cohort study, of 1616 pregnant women in Bangladesh, reported that each one μg/L increase in maternal U-Cd is associated with a decrease in birth weight and birth length that is limited to girls, whereas an increased trend is observed in male neonates [23]. Rollin et al. also investigated sex-related differences following Cd exposure and reported reduced birth weight, birth length and head circumference among female neonates, but no significant trend was observed for any of the three birth outcomes in male neonates [38]. The Apgar score assessments involve evaluation of the neonate heart rate, muscle tone and activity, reflex irritability, skin coloration and breathing rate. We found that both male and female neonates from Guiyu had lower Apgar scores compared to the Haojiang group. In the regression analysis, U-Cd levels were inversely associated with Apgar scores in female neonates but only Apgar (1 min) score in male neonates (Table 6). Studies have previously reported an association between cord blood Cd and 5-min Apgar scores with low birth weight [18,41]. Our previous studies also show significant decreases in Apgar scores in

Guiyu neonates with increased Cd levels in placenta [8,12]. Reduced birth head circumference has been associated with delayed neurodevelopment [42]. From the results of regression analysis, we observed a significant inverse association of birth head circumference with U-Cd levels among female neonates in both unadjusted and adjusted models whereas male neonates showed a significant association in unadjusted model. In addition, prior studies have reported an inverse association between U-Cd and head circumference among female neonates but not males [23–25,43], but other studies observe increasing head circumference with increasing U-Cd [27], and several suggest no association between U-Cd levels and head circumference [18,28]. Nevertheless, these studies have indicated that alterations in neonatal head circumference may have a detrimental effect on child motor ability and cognitive functions later in life.

In addition, similar to reduced birth weight, we report a decreasing trend in both male and female newborn BMI in the current study, which did not reach full significance. Three prior studies have assessed maternal Cd exposure during pregnancy and modification of the neonatal BMI. In contrast to our study, Romano et al. (2016) suggested that male neonates have decreased ponderal index, or BMI, with greater maternal U-Cd than females. In a cross-sectional study, Odland et al. reported a statistically insignificant increase in neonatal BMI with each μg/g increase in placental Cd [44]. Recently, another study on among Saudi Arabian Women reported that no association exists between ponderal index and maternal Cd [18].

There are various possible mechanisms by which Cd exposure during pregnancy can affect fetal growth. Sex-specific changes in adverse birth outcomes may be accomplished by Cd-induced changes to the epigenetic regulation of genes responsible for growth [45]. Dio et al. and Ooi et al. reported that Cd down-regulates gene expression of DNA methyltransferases [46,47], which are crucial for normal embryogenesis. Cd may also interfere with the insulin like growth factor axis and thereby reduce fetal growth in a sex-specific manner [48]. Another possible mechanism for our findings may be the endocrine disrupting properties of Cd, which may reduce *in utero* gene and protein expression linked to fetal growth [26]. We have also previously shown that pregnant women from an e-waste area have elevated concentrations of Cd in placental tissue, and that this metal level is inversely associated with different proteins in placenta related to mitochondria, potentially leading to persistent health problems later in life [49]. It has also been demonstrated that higher Cd levels can lead to insufficient transfer of essential nutrients to the fetus, which can retard intrauterine growth [50]. However, our study draws on several important strengths: (1) this is the first study, to the best of our knowledge, to report sex-specific differences in adverse birth outcomes among women of childbearing age from an e-waste recycling area; (2) the study populations are fairly homogeneous for prenatal-care profiles. This study also has several limitations: (1) we did not fully examine the nutritional status (calcium, zinc and iron) among the women in our population, which may affect Cd absorption as well as neonatal outcome, (2) we lacked of data on Cd concentrations at different time points during pregnancy, which would help to evaluate the critical exposure window for the effect of Cd on fetal development, (3) we were unable to explore the influence of the co-exposure to additional heavy metals and organic pollutants in this cohort. These aspects will be considered in future mechanistic studies.

5. Conclusions

We found significant inverse associations between maternal U-Cd concentrations and birth anthropometry in female neonates, but no significant associations were observed in male neonates except Apgar (1 min) score. However, associations appeared to be more apparent in female neonates with little evidence of effects in male neonates. These findings, along with previous experimental studies, suggest that there may be sex differences in both absorption and metabolism of Cd. Our findings have important implications for protecting fetal health in e-waste areas. The results of this study indicate that it is necessary to pay more attention to develop protective methods and suitable policies for e-waste recycling, and increase health education in women of reproductive age in order to help improve the quality of health. Further studies are needed to conduct well-designed studies with a larger sample size in diverse populations to further clarify the potential mechanism of Cd exposure on fetal health.

Conflicts of interest

The authors declare that they have no conflicts of interests.

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