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RESEARCH ARTICLE

Lead exposure is associated with risk of impaired coagulation in preschool children from an e-waste recycling area

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Abstract

Environmental lead exposure leads to various deleterious effects on multiple organs and systems, including the hematopoietic system. To explore the effects of lead exposure on platelet indices in preschool children from an informal, lead-contaminated electronic waste (e-waste) recycling area, we collected venous blood samples from 466 preschool children (331 from an e-waste area (Guiyu) and 135 from a non-e-waste area (Haojiang)). Child blood lead levels (BLLs) were determined by graphite furnace atomic absorption spectrophotometry, while platelet indices were quantified using a Sysmex XT-1800i hematology analyzer. Higher blood lead levels are observed in e-waste lead-exposed preschool children. Significant relationships between high blood lead levels (exceeding current health limits) and elevated platelet count (PLT), plateletcrit (PCT), mean platelet volume (MPV), and platelet large cell ratio (P-LCR) were also uncovered. Furthermore, the median PLT and PCT levels of children from the exposed group both exceeded the respective recommended maximum reference range value, whereas the reference group did not. Location of child residence in Guiyu and BLLs were both risk factors related to platelet indices. These results suggest that high blood lead exposure from e-waste recycling may increase the risk of an amplified coagulation process through the activation of platelets in preschool children.

Keywords Blood lead · Platelet indices · Blood coagulation · Preschool children · Electronic waste (e-waste)

Introduction

Platelets are the smallest of the human blood cells (3.6 × 0.7 μm), being released from megakaryocytes in the bone marrow as anucleated fragments into the circulation. They play central roles in various pathophysiological processes including hemostasis and thrombosis, clot retraction, and vessel constriction and repair. Activated platelets participate in the initiation of the consolidation phase of the coagulation cascade (Harrison 2005; Heemskerk et al. 2002). Lead is a widely used and poisonous heavy metal that imposes adverse effects on both the environment and people. Especially in susceptible populations, such as preschool children, lead toxicity can have greater impact due to more routes of exposure, higher gastrointestinal absorption, and greater susceptibility of the neural system (Lee et al. 2006; Markowitz 2000). Lead exposure occurs mainly through the respiratory and gastrointestinal tracts and dermal contact (Fischbein and Hu 1998). Approximately 30–40% of inhaled lead is absorbed into the bloodstream (Philip and Gerson 1994), of which about 95% accumulates in the red blood cells (Goyer and Clarkson 1996). Lead exposure can result in oxidative stress and damage to the endothelium, inhibition of endothelial repair, and significantly augmented platelet adhesion and activation (Vaziri 2008).

Evidence from epidemiological research indicates that, in workers from a lead-acid battery manufacturing plant, the platelet count (PLT), plateletcrit (PCT), and mean platelet mass (MPM) are negatively associated with their blood lead

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levels (BLLs), while the platelet large cell ratio (P-LCR) is positively associated with BLLs (Barman et al. 2014). Another population-based study evaluating the relationship between BLLs and hematological parameters of painters and battery workers reported that BLLs are positively correlated with mean platelet volume (MPV) and platelet distribution width (PDW) and negatively correlated with PCT (Conterato et al. 2013). Data from animal models shows that animals exposed to chronic lead intoxication have higher levels of PLT, PDW, and MPV (Golalipour et al. 2007; Mugahi et al. 2003). However, the data are not all consistent as other investigators have observed lower levels of PLT and MPV following lead treatment (Abdel-Moneim et al. 2015; Adham et al. 2011).

Recently, platelet indices have been used routinely in the initial evaluation of thrombocytic function. PLT is frequently used as an indicator for normal coagulation capacity. The normal range of PLT for children between the ages of 1 month and 15 years is within 150–400 × 10^9/L (Hézard et al. 2003). Once the PLT exceeds 400 × 10^9/L, thrombocytosis becomes imminent. Conversely, a PLT of less than 150 × 10^9/L results in thrombocytopenia. PCT reflects the percent of volume in the blood occupied by platelets, which is an evaluation of platelet equilibrium state in the blood (Giacomini et al. 2001; Budak et al. 2016). MPV is a measure of platelet volume; alterations in which reflect a change in either platelet stimulation or rate of platelet production (Bancroft et al. 2000). This marker is a potentially useful indicator of platelet activity in the setting of cardiovascular disease (Chu et al. 2010). PDW quantitatively assesses the variability in platelet size. Elevated PDW indicates platelet anisocytosis (Vagdatli et al. 2010). P-LCR is a measure of the percentage of circulating larger platelets (> 12 fL in size), which has also been used to monitor platelet activity (Grotto and Noronha 2004; Hong et al. 2014).

Guiyu is an electronic waste (e-waste) recycling town in southeast China. Due to the primitive and uncontrolled methods employed for e-waste dismantling, substantial quantities of hazardous heavy metals and organic contaminants are released into the environment and threaten the health of the local residents (Cao et al. 2016; Heacock et al. 2015; Huo et al. 2007, 2014; Zeng et al. 2017). Lead, being one of the major heavy metals in the e-waste, occurs at high levels in the dust, soil, river sediment, surface water, and groundwater (Deng et al. 2006; Wong et al. 2007; Yekeen et al. 2016; Yu et al. 2006; Zeng et al. 2016b; Zheng et al. 2016). Our previous studies have shown that blood lead levels in Guiyu children are significantly higher than those in children from nearby non-e-waste recycling areas (Deng et al. 2006; Guo et al. 2010; Li et al. 2008; Liu et al. 2011; Xu et al. 2015a, b; Zeng et al. 2016a; Zhang et al. 2016; Zheng et al. 2008). However, there are no prior epidemiological studies concerning the relationships between lead exposure from e-waste recycling and platelet index levels in preschool children.

The aim of our present study was to identify the effects of lead exposure on the status of platelet indices in children from an informal e-waste recycling area.

Materials and methods

Study population and sample collection

This study recruited 466 native 3- to 7-year-old children in 2012. Three hundred thirty-one children, recruited from a village kindergarten located in Guiyu, constituted the lead-exposed group, and 135 children from Haojiang (an area not related to e-waste processing) served as the reference group. The population density, traffic movement patterns, residential lifestyle, cultural background, and socioeconomic status were very similar between the two areas. After informed consent was obtained from the parents or guardians of the participating children, venipuncture blood samples were collected into K3-EDTA anticoagulant tubes by well-trained nurses. Then, the blood was stored at − 20 °C until analysis. Physical examinations were performed to obtain growth parameters, including height (cm) and weight (kg), and the body mass index (BMI) was calculated, expressed as kilogram per square meter. All plastic tubes and blood containers were prewashed thoroughly, soaked with dilute nitric acid, and rinsed with deionized water before use in order to avoid contamination.

A predesigned questionnaire was utilized to survey the parents or guardians. The questionnaire collected information pertinent to child BLLs and platelet indices, including factors related to age, sex, location of child residence in Guiyu, family member smoking status, child infections in the last month, child trauma in the last month, and child drug usage in the last month. The research protocol was approved by the Human Ethics Committee of Shantou University Medical College (NSFC (21577084): SUMC-2015-19; Guangdong Province of China (2015A030313435): SUMC-26-2014). Informed consent forms had been obtained from all subjects, and the methods were carried out in accordance with the approved guidelines.

Measurement of blood lead levels

Measurement of blood lead levels by graphite furnace atomic absorption spectrophotometry was performed as previously described (Yang et al. 2013).

Measurement of platelet indices

From each child, 2 mL of venous whole blood was collected in a vacutainer tube with K3-EDTA as the anticoagulant. The platelet indices PLT, PCT, PDW, MPV, and P-LCR were quantified within 2 h of collection, using an automated

Sysmex XT-1800i hematology analyzer (Sysmex Corporation, Kobe, Japan). PCT was calculated as the product of the platelet count multiplied by MPV and divided by 10,000. MPV was calculated from a log transformation of the platelet volume distribution curve, yielding a geometric mean for this parameter. PDW reflected the standard deviation of the log-transformed PLT data (Beyan et al. 2006). Quality assurance and quality control (QA/QC) of the Sysmex XT 1800i were routinely and regularly performed during this study using 3 QC products (e-CHECK levels 1, 2, 3) to ensure accurate measurement of parameters for low, normal, and high platelet counts, before analysis of the samples.

Statistical analysis

All statistical analyses were performed using SPSS13.0 for Windows (Chicago, IL, USA). The Kolmogorov–Smirnov test was used to determine the normal distributions of data. The central tendency and spread of variables were described by the mean ± standard deviation or the median (5th to 95th percentile). Mann–Whitney U and t tests were used for two-group comparisons between continuous variables, while chi-squared tests were used for categorical variable comparisons. Spearman rank correlation analysis and multiple stepwise regression analysis were used to evaluate the relationships between peripheral blood platelet indices, BLLs, and other related factors in the questionnaire. Differences with a p value ≤ 0.05 were considered significant.

Results

Demographic characteristics of the study groups

Characteristics of the study population, including age, sex, height, weight, BMI, and other recorded factors, are presented in Table 1. The mean age of the children in the Guiyu group was slightly higher compared to that in the reference group ($p < 0.05$). Analysis of the age distribution within the groups revealed that the highest percentage of preschool children in the Guiyu group were 4 years old, as opposed to 3 years old in the reference group. However, no significant difference in the sex distribution, height, weight, and BMI was found between the Guiyu and reference groups. Family member smoking status was significantly higher in the Guiyu group, while child trauma in the last month was significantly higher in the reference group. Child infections and drug usage in the last month were not different between the groups.

Table 1 Demographic characteristics of the study population in Guiyu and the reference area

Demographic variables	Guiyu ($n = 331$)	Reference ($n = 135$)	Statistic	p value
Age (years)	4.7 ± 0.9	4.5 ± 0.9	$t = 2.267$	0.024
3	22.7%	38.9%	$\chi^2 = 14.728$	0.002
4	39.6%	26.0%		
5	33.2%	29.0%		
6–7	4.5%	6.1%		
Sex (%)			$\chi^2 = 0.190$	0.663
Male	54.1%	54.7%		
Female	45.9%	45.3%		
Height (cm)	105.26 ± 7.94	106.45 ± 7.31	$t = -1.486$	0.138
Weight (kg)	17.34 ± 3.17	17.46 ± 3.53	$t = -0.349$	0.728
BMI (kg/m^2)	15.6 ± 1.4	15.3 ± 1.7	$t = 1.762$	0.079
Family member smoking status			$\chi^2 = 31.621$	0.000
Yes	245 (76.8%)	67 (50%)		
No	74 (23.2%)	67 (50%)		
Child infections in the last month			$\chi^2 = 0.077$	0.782
Yes	126 (40.3%)	56 (41.8%)		
No	186 (59.4%)	78 (58.2%)		
Child trauma in the last month			$\chi^2 = 10.161$	0.001
Yes	38 (12.0%)	32 (23.9%)		
No	279 (88.0%)	102 (76.1%)		
Child drugs usage in the last month			$\chi^2 = 0.001$	0.969
Yes	173 (56.2%)	75 (56.0%)		
No	135 (43.8%)	59 (44.0%)		

Data are expressed as mean ± standard deviation (SD) or percentage

Blood lead levels in preschool children

BLLs and prevalence of elevated BLLs among the Guiyu children were much higher than those among the Haojiang children, even when stratified by child age ($p < 0.01$, Table 2). In the exposed group, the Guiyu children's BLLs (median, 5.64 μg/dL) were much higher than those in the reference group (median, 3.68 μg/dL) ($p < 0.01$). Importantly, 202 (61.0%) Guiyu children had high BLLs, exceeding the 5.0 μg/dL safety limit determined by the US Centers for Disease Control (Betts 2012). The percentage of children with high BLLs were only 25.2% in the reference group, significantly lower than the exposed group ($p < 0.01$). In every age range (from 3- to 7-year-olds), BLLs in the Guiyu children were significantly higher than those in the reference children (7.71 ± 6.11 vs. 4.13 ± 1.42, 6.08 ± 3.11 vs. 4.29 ± 1.60, 5.96 ± 3.11 vs. 3.50 ± 1.21, 7.39 ± 3.3 vs. 5.16 ± 1.70) ($p < 0.01$), except for the high BLLs in the 6- to 7-year-old group ($p = 0.114 > 0.05$), as were the percentages of children with high BLLs (66.2 vs. 27.5%, 62.1 vs. 32.4%, 53.8 vs. 15.8%, 78.6 vs. 25.0%).

Comparison of platelet indices between Guiyu and Haojiang preschool children

Levels of the blood platelet indices, including PLT, PCT, PDW, MPV, and P-LCR, were noticeably higher in the Guiyu group than in the reference group, whereas only the PDW levels were not significantly different between the two groups (Table 3). Although median levels of PDW, MPV, and P-LCR between the Guiyu and the reference groups were within the recommended reference range, median PLT and PCT levels of the Guiyu group both exceeded the recommended maximum reference range values of 300 (10^9/L) and 0.3%, respectively, while the values in the reference group did not. As platelet populations in children might differ from those in adulthood, we adopted a common normal range 150–400 × 10^9/L to evaluate incidence of abnormal PLT. According to these criteria, 21.8% (72/331) of children in the Guiyu group displayed abnormal PLT levels, whereas the incidence in the reference group was only 17.0% (23/135). However, no significant difference in percentage of children with abnormal PLT was observed between the two groups ($\chi^2 = 1.314$, $p = 0.252$). We also analyzed the five platelet index levels by age, stratifying between the two groups (Table 4). The results showed that the PLT, PCT, MPV, and P-LCR in 3-year-old Guiyu children were all markedly higher than those in the reference children ($p < 0.01$). As for PCT, MPV, and P-LCR of 4-year-old children and PLT and PCT of 5-year-old children, as well as MPV and P-LCR of 6- to 7-year-old children, all were noticeably higher in the Guiyu group (all $p < 0.01$ or 0.05). There were no significant differences between the two groups for PDW of 3-year-old children; PLT and PDW of 4-year-old children; PDW, MPV, and P-LCR of 5-year-old children; or PLT, PCT, and PDW of 6- to 7-year-old children (all $p > 0.05$), even though these platelet indices appeared higher in the exposed group from Guiyu than in the reference group.

Association between blood lead exposure and platelet indices

Spearman correlation between BLLs and blood platelet indices in preschool children is presented in Table 5. A positive correlation coefficient (r) was found between BLLs and PLT ($r = 0.099$, $p = 0.034$), PCT ($r = 0.124$, $p = 0.008$), PDW ($r = 0.084$, $p = 0.073$), MPV ($r = 0.109$, $p = 0.020$), and P-LCR ($r = 0.092$, $p = 0.050$). PLT was positively associated with PCT ($r = 0.888$, $p < 0.01$), but significantly inversely related to PDW ($r = -0.321$, $p < 0.01$), MPV ($r = -0.356$, $p < 0.01$), and P-LCR ($r = -0.333$, $p < 0.01$). There were strongly significant correlations between PDW, MPV, and P-LCR, and their positive correlation coefficients (r) were 0.935 (PDW vs. MPV), 0.958 (PDW vs. P-LCR), and 0.974 (MPV vs. P-LCR).

Table 2 Child BLLs (μg/dL) in Guiyu and the reference area

BLLs	Guiyu				Reference			
	n	Mean ± SD	Range	≥ 5 μg/dL n (%)	n	Mean ± SD	Range	≥ 5 μg/dL n (%)
Total	327	6.44 ± 3.96^{a}	1.51–42.19	202 (61.0)$^{a'}$	133	4.06 ± 1.49	1.54–8.87	34 (25.2)
Age (years)								
3	69	7.71 ± 6.11^{b}	1.51–42.19	47 (66.2)$^{b'}$	50	4.13 ± 1.42	2.03–7.81	14 (27.5)
4	123	6.08 ± 3.11^{c}	1.93–21.45	77 (62.1)$^{c'}$	34	4.29 ± 1.60	1.54–8.87	11 (32.4)
5	104	5.96 ± 3.11^{d}	1.94–15.94	56 (53.8)$^{d'}$	38	3.50 ± 1.21	1.57–6.53	6 (15.8)
6–7	14	7.39 ± 3.3^{e}	4.15–16.2	11 (78.6)$^{e'}$	7	5.16 ± 1.70	3.67–8.67	2 (25.0)

Compared with the reference group: ^{a} $t = 9.373$, $p < 0.01$; $^{a'}$ $\chi^2 = 49.619$, $p < 0.01$; ^{b} $t = 4.692$, $p < 0.01$; $^{b'}$ $\chi^2 = 18.674$, $p < 0.01$; ^{c} $t = 4.584$, $p < 0.01$; $^{c'}$ $\chi^2 = 9.894$, $p < 0.01$; ^{d} $t = 6.791$, $p < 0.01$; $^{d'}$ $\chi^2 = 16.386$, $p < 0.01$; ^{e} $t = 1.658$, $p = 0.114 > 0.05$; $^{e'}$ $\chi^2 = 4.947$, $p < 0.01$

Table 3 Comparison of platelet indices and BLLs between exposed and reference groups

	Guiyu			Reference			Reference range	*p* value[a]
	n	Median (P_{25}–P_{75})	Range	*n*	Median (P_{25}–P_{75})	Range		
PLT (10^9/L)	331	335.0 (286.0–392.0)	143.0–783.0	135	300.0 (251.0–352.0)	19.0–570.0	100–300	0.000
PCT (%)	330	0.34 (0.30–0.39)	0.00–0.66	133	0.28 (0.24–0.34)	0.02–0.51	0.17–0.30%	0.000
PDW (fL)	329	11.0 (10.1–12.3)	1.6–19.9	133	10.9 (10.2–11.6)	7.8–21.3	9.9–16.1	0.090
MPV (fL)	329	9.9 (9.4–10.7)	8.0–90.0	133	9.7 (9.3–10.1)	8.0–12.3	9.1–12.1	0.000
P-LCR (%)	328	24.8 (20.6–29.9)	0.0–47.1	135	23.1 (19.8–26.4)	10.5–40.8	17.5–30.0%	0.002

Data are presented as median (P_{25}–P_{75}). The reference ranges of platelet indices are from detected values recommended by the Sysmex XT-1800i hematology analyzer producer

[a] Mann–Whitney *U* test

Relationship between platelet indices and investigated factors

Multiple stepwise regression analysis was used to evaluate the relationship between investigated factors and the platelet indices in preschool children (Table 6). In this linear regression model, PLT, PCT, MPV, PDW, and P-LCR were separately set as the dependent variables. Age (years), sex, BMI, BLLs, family member smoking status, location of child residence in Guiyu, child infections in the last month, child trauma in the last month, and child drug usage in the last month were used as independent variables. The results indicated that location of child residence in Guiyu was positively correlated with all platelet indices except for PDW. BLLs contributed to PDW, while child drug usage in the last month influenced MPV. Child trauma in the last month was negatively associated with both PLT and PCT.

Discussion

Although several adverse effects of lead exposure on the hematological system have been previously reported, most of them were related to effects on hemoglobin (Fontana et al. 2004; Jacob et al. 2000; Lee et al. 2006). In addition, most of the lead exposures investigated previously resulted from the car battery industry or the automobile repair industry, and the study subjects have always been adult males (Barman et al. 2014; Fazli et al. 2014; Kianoush et al. 2013; Mugahi et al. 2003). Effects of lead exposure from an e-waste recycling area on platelets in preschool children have been less explored. Our present study, to the best of our knowledge, is the first to assess the effects of lead exposure, from a typical e-waste recycling area, on peripheral blood platelet indices in preschool children.

In the present study, we found Guiyu preschool children had a higher blood lead level than those from Haojiang (the reference area). Moreover, the incidence of BLLs ≥ 5 μg/dL was markedly higher than in the reference area and also some neighboring countries (Havens et al. 2018; Dhimal et al. 2017). These results are in agreement with a series of our previous studies conducted in Guiyu (Guo et al. 2010; Li et al. 2008; Liu et al. 2015, 2011; Xu et al. 2015a, b; Yang et al. 2013; Yu et al. 2006; Zeng et al. 2016a, b; Zhang et al. 2016; Zheng et al. 2008, 2016). Strikingly, in recent years, the BLLs in Guiyu children have been trending towards a progressive decrease when compared with our previous studies. However, in spite of the decreasing trend in Guiyu children's BLLs, these levels still exceed the latest lead poisoning safety limit of 5 μg/dL. This status remains when the BLLs are stratified by age range. Therefore, our data suggest that the children in different age groups from e-waste-polluted areas are still far more likely to suffer from a high risk of Pb exposure, and this long-term exposure may eventually cause adverse health effects.

PLT and other platelet indices, such as PCT, MPV, PDW, and P-LCR, are considered to be important indicators for disease pathophysiology (Wiwanitkit 2004). Increased and reduced platelet parameters are associated with a diversity of diseases and are generally associated with the hemostatic process (Strauß et al. 2011). In the current study, we observed higher levels of PLT, PCT, MPV, and P-LCR in Guiyu children. In addition, we found the mean age of the Guiyu children was slightly higher and the age distribution was also significantly different in comparison with the reference group. Some researchers have reported that progressively decreasing PLT occurs with age and age groups display a significant association with P-LCR (Barman et al. 2014; Biino et al. 2011). In this study, higher levels of these platelet indices were still observed in almost every age range of Guiyu children, suggesting that age was not driving a reduction in platelet indices in the Guiyu population. We also found no significant correlation between age and any platelet indices. It may be that the limited differences in age between the two groups in

Table 4 Comparison of platelet indices stratified by age (years) between the Guiyu and reference groups

Platelet indices	3 (mean ± SD)			4 (mean ± SD)			5 (mean ± SD)			6–7 (mean ± SD)		
	Guiyu ($n = 71$)	Reference ($n = 51$)	p value	Guiyu ($n = 124$)	Reference ($n = 34$)	p value	Guiyu ($n = 104$)	Reference ($n = 38$)	p value	Guiyu ($n = 14$)	Reference ($n = 8$)	p value
PLT	358.6 ± 86.5	296.2 ± 90.0	0.000	350.7 ± 88.6	333.4 ± 67.1	0.292	335.6 ± 78.3	267.1 ± 100.1	0.000	346.6 ± 70.6	300.2 ± 118.1	0.259
PCT	0.35 ± 0.10	0.28 ± 0.10	0.000	0.35 ± 0.08	0.30 ± 0.10	0.001	0.33 ± 0.07	0.26 ± 0.09	0.000	0.35 ± 0.06	0.33 ± 0.04	0.343
PDW	11.8 ± 2.2	11.1 ± 1.9	0.068	11.1 ± 1.7	10.7 ± 1.2	0.158	11.1 ± 1.7	11.3 ± 1.8	0.684	11.5 ± 1.3	10.7 ± 0.5	0.121
MPV	10.3 ± 1.0	9.8 ± 0.7	0.002	10.0 ± 0.9	9.6 ± 0.6	0.002	10.0 ± 0.8	9.9 ± 0.8	0.413	10.3 ± 0.6	9.6 ± 0.3	0.027
P-LCR	26.8 ± 8.2	23.7 ± 5.3	0.012	25.0 ± 6.9	22.2 ± 4.5	0.007	25.1 ± 5.8	24.3 ± 5.9	0.470	26.8 ± 4.9	22.0 ± 2.7	0.020

Data are expressed as mean ± standard deviation (SD). t test is used for two-group comparisons

this study (Guiyu 4.7 ± 0.9 years vs. reference 4.5 ± 0.9 years) were too small to affect platelet indices as compared with the above two studies.

Mugahi et al. (2003) reported that 12 weeks of oral lead exposure resulted in a prominent increase in PLT. Additionally, some cases of thrombocytopenia converting to thrombocytosis after lead intoxication have been reported (Sudakova et al. 1982). In this study, higher PLT and PCT levels are observed in Guiyu children with higher lead exposure. We also found a significant positive correlation of BLLs with PLT and PCT. MPV is an indicator of platelet activation. Elevated MPV is associated with other indicators of platelet activity, such as increased platelet aggregation (Park et al. 2002). In our present study, we found a positive correlation between BLLs and MPV. These results are in agreement with several studies that found higher levels of PLT and MPV in lead-exposed rats (Golalipour et al. 2007; Mugahi et al. 2003). We noticed a positive association between BLLs and P-LCR but no significant association between BLLs and PDW, which is in line with the results reported by Fazli et al. (2014) and Barman et al. (2014). Mechanistic studies on lead poisoning indicate that lead exposure results in oxidative stress and damage to the endothelium and causes reduction of NO availability via ROS-mediated NO inactivation (Vaziri 2008; Vaziri et al. 1999). Platelet adhesion and activation are potently inhibited by endothelium-derived NO, and reduced NO availability promotes platelet activation. Therefore, the higher levels of platelet indices in preschool children in the Guiyu e-waste lead-exposed area may be driven by the above mechanisms of lead exposure effects. As a result, the elevated platelets would then increase the propensity for rapid onset of the coagulation process.

Epidemiological studies have shown that chronic biomass smoke exposure activates circulating platelets and causes an increase in leukocyte-platelet aggregation, which are considered risk factors for thrombosis (Ray et al. 2006). Importantly, ongoing platelet activation is also observed in passive smokers (Raupach et al. 2006), and some infections also have active impacts on platelet counts and function (Soroceanu et al. 2008; Veneri et al. 2002). When trauma occurs, the changes in platelet populations play a critical role in the coagulation process (Rand and Kuhle 2005), and several studies indicate some drug usage in humans can affect degrees of platelet reactivity in the process of thrombosis treatment (Lau et al. 2003; Sibbing et al. 2009). In the present study, our e-waste-exposed and reference groups had significant differences related to family member smoking status and child trauma in the last month. When all the related investigated factors were considered in the multiple stepwise regression analysis (adjusted for age, sex, and BMI), our results show that location of child residence in Guiyu is a risk factor for increased PLT, PCT, MPV, and P-LCR; BLLs are a risk factor for increased PDW; and child drug usage in the last month is a

Table 5 Matrix of Spearman's correlation coefficient (*r*) between blood lead levels and platelet indices

Parameters		BLLs (μg/dL)	PLT (10^9/L)	PCT (%)	PDW (fL)	MPV (fL)	P-LCR (%)
BLLs (μg/dL)	*r*	1	–	–	–	–	–
	p	–	–	–	–	–	–
	n	460	–	–	–	–	–
PLT (10^9/L)	*r*	0.099*	1	–	–	–	–
	p	0.034	–	–	–	–	–
	n	460	466	–	–	–	–
PCT (%)	*r*	0.124**	0.888**	1	–	–	–
	p	0.008	0.000	–	–	–	–
	n	458	463	457	–	–	–
PDW (fL)	*r*	0.084	− 0.321**	− 0.050	1	–	–
	p	0.073	0.000	0.284	–	–	–
	n	457	462	462	462	–	–
MPV (fL)	*r*	0.109*	− 0.356**	− 0.037	0.935**	1	–
	p	0.020	0.000	0.422	0.000	–	–
	n	457	462	462	462	462	–
P-LCR (%)	*r*	0.092*	− 0.333**	− 0.028	0.958**	0.974**	1
	p	0.050	0.000	0.547	0.000	0.000	–
	n	457	463	461	461	461	463

*Correlation coefficient significant at $p < 0.05$; **correlation coefficient significant at $p < 0.01$

risk factor for MPV. In contrast, child trauma in the last month is a protective factor for both PLT and PCT. We did not notice any association between exposure to cigarette smoke and platelet indices, which is in agreement with Barman et al. (2014) and Suwansaksri et al. 2004.

Children who live in Guiyu may be affected by exposure to lead but also to other toxic heavy metals. Indeed, we have already analyzed the concentrations of other heavy metals, such as cadmium (Cd), in these populations but did not find significant differences in blood cadmium levels between the two groups, nor any correlations between cadmium exposure and platelet indices (data not shown). Due to restrictions in the volume of sample available from each participant, we were not able to analyze the impact of other environmental agents from this e-waste area, which is a limitation of this study.

Table 6 Multiple stepwise regression analysis of factors related to platelet indices in preschool children ($n = 466$)

Platelet indices	Investigated factors	*B*	Beta	Partial correlations	R^2	Adjusted R^2	*F*	*p*
PLT (10^9/L)					0.072	0.068	17.882	0.000
	Location of child residence in Guiyu	45.683	0.235	0.234				
	Child trauma in the last month	− 24.549	− 0.099	− 0.101				
PCT (%)					0.113	0.109	29.452	0.000
	Location of child residence in Guiyu	0.060	0.308	0.308				
	Child trauma in the last month	− 0.024	− 0.096	− 0.101				
PDW (fL)					0.010	0.008	4.695	0.031
	Blood lead levels (BLLs)	0.050	0.100	0.100				
MPV (fL)					0.038	0.034	9.269	0.000
	Location of child residence in Guiyu	0.316	0.171	0.172				
	Child drug usage in the last month	0.167	0.096	0.098				
P-LCR (%)					0.023	0.020	10.700	0.001
	Location of child residence in Guiyu	2.134	0.150	0.150				

Missing values were replaced with the mean values

B, unstandardized coefficients; *Beta*, standardized coefficients

Conclusion

In summary, this is the first study to report an association between lead exposure and platelet indices in preschool children from an informal e-waste recycling area in China. Our data show that higher BLLs are present in preschool children from the e-waste recycling town Guiyu. Significant relationships between high BLLs (exceeding current health limits) and elevated PLT, PCT, MPV, and P-LCR were uncovered in this study. Furthermore, median PLT and PCT levels of the Guiyu group both exceed the recommended maximum reference range. Location of child residence in an e-waste recycling area is a risk factor for elevated PLT, PCT, MPV, and P-LCR, while BLLs are a risk factor for increased PDW. Thus, we speculate that high blood lead exposure may increase the propensity for rapid onset of coagulation through the activation of blood platelets in preschool children. The specific mechanisms underlying lead poisoning-driven alterations in blood platelets which impact child blood coagulation cascades require further investigation.

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Compliance with ethical standards

The research protocol was approved by the Human Ethics Committee of Shantou University Medical College (NSFC (21577084): SUMC-2015-19; Guangdong Province of China (2015A030313435): SUMC-26-2014). Informed consent forms had been obtained from all subjects, and the methods were carried out in accordance with the approved guidelines.

Conflict of interest The authors declare that they have no conflict of interest.

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