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RESEARCH ARTICLE

Determinants affecting the blood mercury levels of preschool children in Shanghai, China: A cross-sectional study

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Abstract

Infants and children are vulnerable to mercury (Hg)-induced toxicity, which has detrimental effects on their neurological development. This study measured blood Hg levels (BMLs) and identified potential factors influencing BMLs, including demographic and socioeconomic factors, lifestyle, and daily dietary habits, among 0 to 7-year-old children in Shanghai. Our study recruited 1474 participants, comprising 784 boys and 690 girls. Basic demographic and lifestyle information were obtained and blood Hg were analyzed using the Direct Mercury Analyzer 80. The blood Hg concentrations of children in Shanghai ranged from 0.01 to 17.20 μg/L, with a median concentration of 1.34 μg/L. Older age, higher familial socioeconomic status, higher residential floors, and a higher frequency of consuming aquatic products, rice, vegetables, and formula milk were identified as risk factors. Other potential influencing factors including the mother's reproductive history (gravidity and parity), smoking (passive smoking), supplementation of fish oil and calcium need to be further investigated. These findings can be useful in establishing appropriate interventions to prevent children's high blood Hg concentrations in Shanghai and other similar metropolitan cities.

Keywords Mercury · Early childhood exposure · Dietary habits · Lifestyle · Demographic and socioeconomic factors

Introduction

Mercury (Hg), a deleterious toxic metal, is ubiquitous in the global environment due to its multiple existing forms and wide distribution (Hylander and Meili 2003). Hg can enter the human body directly through the digestive tract, respiratory tract, and skin. As Hg is not readily degraded and has a long biological half-life and low body clearance rate, it is imperative to pay attention to the health effects that arise from Hg exposure. Chronic exposure to Hg may induce a variety of symptoms in the general population, such as tremors, loss of memory, delusions, hallucinations, neurocognitive disorders, coma, or even death (Clarkson and Magos 2006; Taux et al. 2022), especially in infants or children who are vulnerable to Hg-induced toxicity (Bose-O'Reilly et al. 2010). Due to the susceptibility of infants and children during the critical developmental periods and the increased nutritional demands for growth, combined with the tendency of this population to explore the environment without adequate self-protection, they may be at a higher risk of Hg exposure than adults (Leppert et al. 2019), which is associated with neurological and developmental diseases.

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Our previous study indicated that prenatal low level Hg exposure can negatively affect neonatal neurodevelopment (Wang et al. 2019). A recent epidemiologic investigation concluded that higher hair total Hg (THg) in 9-year-old children is associated with worse scores of Child Behavior Checklist (CBCL) internalizing and total problems scales (Lozano et al. 2021).

Given the potential health risks, the United Nations Environment Programme (UNEP) has implemented the Minamata Convention on Mercury, intended to emphasize the protection of human health from Hg exposure (Bank 2020). However, in the last few decades, large quantities of Hg have been released to the environments with increased industrial developments and elevated anthropogenic activities (Milenkovic et al. 2019). Anthropogenic Hg emissions have considerably increased with the rising demand for production and manufacturing since the industrial revolution (Huang et al. 2020). Moreover, a shift in production has occurred from developed to developing countries during last few decades, especially China. It has been reported that the Hg contents in China's atmosphere far exceeds the global background average values (Cheng and Hu 2012). Therefore, it is crucial to identify possible sources of environmental exposure to Hg.

Numerous previous investigations have demonstrated that consuming aquatic products is the primary pathway for Hg exposure, especially for nonoccupational populations (Voegborlo et al. 2010). Dental amalgam, bleaching creams, and cosmetics can also contribute to high levels of Hg in the body (Al-Saleh 2016; Yin et al. 2021). However, the sources of daily exposure to Hg are often unclear in China, especially for infants and young children, who received less attention compared with fetus during the pregnancy period. Our study aimed to determine the blood Hg concentrations of 0 to 7-year-old children in Shanghai and systematically explore the potential influencing factors of blood Hg levels (BMLs), including demographic and socioeconomic factors, lifestyle, and daily dietary habits.

Materials and methods

Study population

Based on the previous project (Li et al. 2020), six prefectures in Shanghai (Jingan District, Jiading District, Chongming District, Yangpu District, Xuhui District, and Pudong New Area) were randomly selected as study areas using stratified, clustered and random sampling methods from June 2013 to July 2014, representing two urban regions, two suburban regions, and two rural areas, respectively. Overall, 1474 preschool children aged 0-7 years were recruited for this cross-sectional investigation with informed consent documentation and complete information. Prior to their participation, detailed informed consent was obtained from the children's parents. This study was approved by the Medical Ethics Committee of Xinhua Hospital, Shanghai Jiao Tong University School of Medicine.

Blood sample collection and detection

All blood samples were collected by well-trained nurses according to a standard protocol (Wu et al. 2013). A total of 3 ml of venous blood from every child was obtained in EDTA-containing blood collection tubes, immediately transported to the MOE-Shanghai Key Laboratory of Children's Environmental Health and preserved at–20°C before detection. Blood Hg concentrations of preschool children were determined by cold vapor atomic absorption spectrometry (CVAAS) using a Direct Mercury Analyzer 80 (DMA-80, Milestone, Inc., CT) according to the standard manufacture's protocol (Li et al. 2020). Control samples (Contox) purchased from the Kaulson Laboratory of United States were applied for external quality control. In addition, repeated measurements of each sample were performed, and blank samples were analyzed every 50 samples. The limit of detection (LOD) of Hg was 0.01 μg/L, and no sample fell below the LOD.

Questionnaire

The parents were required to provide basic information, including demographic and socioeconomic characteristics, lifestyle, and dietary habits. Detailed and comprehensive information was available covering almost all the aspects of potential factors associated with the BMLs of children, including the residential floor, birth mode, feeding mode, handwashing habits, reproductive history of mothers and smoking habits of caregivers. A food frequency questionnaire (FFQ) was conducted to assess the frequency of dietary ingestion. For 1 to 7-year-old children, the FFQ listed typical dietary items, including fish oil, calcium, iron, zinc supplement, drinking water, seawater food, freshwater food, shellfish, rice, vegetables, meat, and milk. Principal attention was given to formula milk consumption in infants.

Statistical methods

The normality of distribution for BMLs was assessed using the Kolmogorov-Smirnov test. As the distribution of BMLs was skewed, logarithm transformations were performed to improve normality. Descriptive statistical analyses were conducted for various essential features of the participants. ANOVA and Bonferroni tests were applied to test significant differences between groups. Multiple logistic regression analysis was further used to explore the association of lifestyle and dietary habits with BMLs adjusted by relevant demographic and socioeconomic factors. In an attempt to identify risk factors and protective factors of children's BMLs, a stepwise approach using backwards elimination with a cut point of $P < 0.10$ as the inclusion criteria was conducted to build an appropriate model with the least Akaike information criterion (AIC). All analyses were performed on SPSS software (version 22.0; SPSS Inc.) apart from the stepwise approach, which was conducted using the function stepAIC included in the *R* package MASS (Zhang 2016). The statistical significance level was set at 0.05 (two-tailed).

Results

General characteristics

The general characteristics of the preschool children participating in the study are displayed in Table 1. A total of 1474 participants aged 0 to 7 years were included, with 784 boys and 690 girls. The children were divided into 3 groups by age: <1 year (14.9%), 1-4 years (36.8%), and 4-7 years (48.3%). Regarding the participants' residence, 35.6% lived in urban areas, 29.1% in suburban areas and 35.3% in rural areas. Approximately 50% of the participating children's parents were highly educated with college or higher degrees.

Blood Hg concentrations of preschool children

The blood Hg concentrations of all 1474 preschool children in Shanghai ranged from 0.01 to 17.20 μg/L, with an arithmetic mean, geometric mean, and median of 1.62 ± 1.04 μg/L, 1.37 μg/L, and 1.34 μg/L, respectively (Table 2). 99.46% of the participants had blood Hg concentrations lower than 5.8 μg/L, which is the blood Hg concentrations equivalent to the Reference dose (RfD) (Rice et al. 2000) for MeHg.

Regarding demographic and socioeconomic factors, significant differences were found in the children's age, mode of birth, birth order, feeding mode, parents' education, parents' birth origin, parents' ethnicity, familial location, familial residence, and household income. BMLs gradually increased with age for 0 to 7-year-old children (F=26.953, $P<0.001$). Of the six study regions, those from urban cities, including Xuhui District and Jingan District, presented a high level of Hg, while that in those from suburban and rural areas were relatively low (F=14.843, $P<0.001$). However, the BMLs of children from Yangpu District and Chongming District, one of the representatives of the selected suburban area and rural areas, respectively, were significantly higher than those of children from other suburban and rural areas (Fig. 1). Compared with children who experienced cesarean section and an artificial or mixed feeding mode, children

Table 1 General characteristics of the preschool children participating in the study.

Characteristics	Mean ± SD or n (%)
Total	1474 (100)
Sex	
Male	784 (53.2)
Female	690 (46.8)
Age (years)	
≤1	220 (14.9)
1-4	543 (36.8)
4-7	711 (48.3)
Location	
Chongming District	266 (18.1)
Jiading District	254 (17.2)
Jingan District	270 (18.3)
Pudong District	222 (15.1)
Xuhui District	255 (17.3)
Yangpu District	207 (14.0)
Residence	
Urban	525 (35.6)
Suburban	429 (29.1)
Rural	520 (35.3)
Delivery mode	
Spontaneous vaginal birth	726 (49.8)
Caesarean	732 (50.2)
Feeding mode	
Breastfeeding	785 (53.7)
Artificial feeding or Mixed feeding	676 (46.3)
Mother's age (years)	30.8 ± 7.2
Mother's education level	
Primary school	516 (35.2)
Middle and high school	301 (20.5)
College or higher	649 (44.3)
Mother's birth origin	
Eastern coastal area	820 (56.4)
Central China region	510 (35.1)
Western China region	125 (8.5)
Mother's ethnicity	
Han	1425 (97.8)
Ethnic minority	32 (2.2)
Father's age (years)	32.7 ± 5.8
Father's education level	
Primary school	456 (31.1)
Middle and high school	329 (22.5)
College or higher	680 (46.4)
Yearly household income (RMB)	
≤30000	68 (4.7)
30000-50000	187 (13.3)
50000-10000	377 (26.5)
>100000	789 (55.5)

Table 2 Blood mercury concentration of the children with different demographic and lifestyle characteristics.

Characteristics	n (%)	Mean ± SD (μg/L)	Geometric mean (μg/L)	Median (μg/L)	Range (μg/L)	F (*P* value)
Total	1474 (100)	1.62 ± 1.04	1.37	1.34	0.01-17.20	
Demographic and socioeconomic factors						
Sex						
Male	784 (53.2)	1.61 ± 1.16	1.34	1.33	0.01-17.20	1.537 (0.215)
Female	690 (46.8)	1.62 ± 0.89	1.40	1.36	0.08-6.85	
Age (years)						
≤1	220 (14.9)	1.32 ± 0.94	1.06	1.01	0.10-6.55	26.953 (**<0.001**)
1-4	543 (36.8)	1.66 ± 1.04	1.36	1.33	0.01-13.00	
4-7	711 (48.3)	1.67 ± 0.95	1.49	1.51	0.06-17.20	
Location						
Chongming District	266 (18.1)	1.82 ± 0.94	1.63	1.67	0.42-6.55	45.227 (**<0.001**)
Jiading District	254 (17.2)	1.13 ± 0.53	1.00	0.96	0.14-4.43	
Jingan District	270 (18.3)	1.75 ± 1.01	1.49	1.67	0.14-6.85	
Pudong District	222 (15.1)	1.31 ± 1.32	0.98	1.16	0.01-17.20	
Xuhui District	255 (17.3)	1.77 ± 0.86	1.59	1.70	0.43-6.36	
Yangpu District	207 (14.0)	1.92 ± 1.24	1.69	1.74	0.47-13.00	
Residence						
Urban	525 (35.6)	1.76 ± 0.94	1.54	1.68	0.14-6.85	14.843 (**<0.001**)
Suburban	429 (29.1)	1.60 ± 1.32	1.28	1.33	0.01-17.20	
Rural	520 (35.3)	1.48 ± 0.84	1.29	1.31	0.14-6.55	
Delivery mode						
Spontaneous vaginal birth	726 (49.8)	1.51 ± 1.05	1.27	1.31	0.08-17.20	11.412 (**<0.001**)
Caesarean	732 (50.2)	1.72 ± 1.02	1.48	1.49	0.01-13.00	
Feeding mode						
Breastfeeding	785 (53.7)	1.55 ± 1.06	1.31	1.33	0.06-17.20	7.913 (**0.005**)
Artificial feeding or Mixed feeding	676 (46.3)	1.69 ± 1.02	1.44	1.44	0.01-13.00	
Mother’s education level						
Primary school	516 (35.2)	1.28 ± 1.02	1.05	1.16	0.01-17.20	67.198 (**<0.001**)
Middle and high school	301 (20.5)	1.53 ± 0.75	1.35	1.34	0.10-4.42	
College or higher	649 (44.3)	1.93 ± 1.09	1.70	1.73	0.20-13.00	
Mother’s birth origin						
Eastern coastal area	820 (56.4)	1.85 ± 1.04	1.61	1.72	0.10-13.00	51.222 (**<0.001**)
Central China region	510 (35.1)	1.32 ± 1.02	1.10	1.24	0.01-17.20	
Western China region	125 (8.5)	1.28 ± 0.71	1.10	1.26	0.19-5.24	
Mother’s ethnicity						
Han	1425 (97.8)	1.63 ± 1.05	1.37	1.34	0.01-17.20	8.660 (**0.003**)
Ethnic minority	32 (2.2)	1.15 ± 0.54	1.00	1.25	0.20-2.33	
Father’s education level						
Primary school	456 (31.1)	1.24 ± 1.04	1.02	1.04	0.01-17.20	71.121 (**<0.001**)
Middle and high school	329 (22.5)	1.55 ± 0.86	1.34	1.34	0.10-6.55	
College or higher	680 (46.4)	1.90 ± 1.05	1.69	1.73	0.20-13.00	
Father’s birth origin						
Eastern coastal area	883 (60.5)	1.83 ± 1.02	1.60	1.71	0.10-13.00	54.662 (**<0.001**)
Central China region	474 (32.5)	1.29 ± 1.06	1.08	1.14	0.06-17.20	
Western China region	102 (7.00)	1.27 ± 0.66	1.07	1.26	0.01-3.72	

with spontaneous vaginal delivery and breastfeeding mode had significantly lower BMLs in childhood (F=11.412, *P*<0.001; F=7.913, *P*=0.005). Intriguingly, the BMLs of children whose mothers had ever provoked an abortion or given birth were significantly higher than those in the other group (F=12.251, *P*<0.001; F=35.783, *P*<0.001). A

Table 2 (continued)

Characteristics	n (%)	Mean ± SD (μg/L)	Geometric mean (μg/L)	Median (μg/L)	Range (μg/L)	F (*P* value)
Yearly household income (RMB)						
≤30000	68 (4.7)	1.33 ± 0.93	1.03	1.04	0.01-4.19	35.210 (**<0.001**)
30000-50000	187 (13.3)	1.22 ± 0.77	1.00	1.12	0.08-6.55	
50000-10000	377 (26.5)	1.51 ± 1.00	1.27	1.33	0.06-13.00	
>100000	789 (55.5)	1.78 ± 1.10	1.55	1.67	0.16-17.20	
Gravidity of mother						
1	991 (68.1)	1.67 ± 1.10	1.42	1.37	0.08-5.82	12.251 (**<0.001**)
>1	464 (31.9)	1.49 ± 0.89	1.26	1.31	0.01-17.20	
Parity of mother						
Nulliparous	1127 (78.3)	1.69 ± 1.10	1.43	1.38	0.01-17.20	35.783 (**<0.001**)
Multiparous	313 (21.7)	1.34 ± 0.75	1.14	1.27	0.08-4.43	
Lifestyle						
Hand washing						
Always	696 (47.7)	1.58 ± 1.07	1.29	1.33	0.06-13.00	12.010 (**0.001**)
Sometimes	764 (52.3)	1.65 ± 1.02	1.44	1.35	0.01-17.20	
Makeup						
No	1253 (86.7)	1.60 ± 1.07	1.34	1.33	0.01-17.20	6.909 (**0.009**)
Yes	193 (13.3)	1.73 ± 0.85	1.52	1.70	0.06-5.49	
Kiss cheek of mother wearing makeup						
No	1147 (78.9)	1.58 ± 1.05	1.34	1.33	0.06-17.20	6.174 (**0.013**)
Yes	307 (21.1)	1.75 ± 1.03	1.47	1.51	0.01-7.92	
Residential floor						
1st floor or Bungalow	555 (38.2)	1.26 ± 0.77	1.06	1.20	0.06-7.92	163.871 (**<0.001**)
≥2nd floor	896 (61.8)	1.82 ± 1.12	1.59	1.70	0.01-17.20	
Distance of road and house						
>100m	760 (52.3)	1.60 ± 1.07	1.34	1.34	0.01-17.20	2.174 (0.141)
≤100m	693 (47.7)	1.64 ± 1.01	1.40	1.35	0.10-13.00	
Passive smoking						
Yes	224 (16.1)	1.70 ± 0.95	1.48	1.39	0.10-7.92	5.387 (**0.020**)
No	1163 (83.9)	1.59 ± 1.07	1.33	1.33	0.01-17.20	
Dietary habits						
Fish oil supplements						
Never	212 (14.7)	1.29 ± 0.67	1.11	1.26	0.12-4.43	15.736 (**<0.001**)
Once in a while	645 (44.7)	1.62 ± 1.06	1.37	1.36	0.06-17.20	
Always	586 (40.6)	1.74 ± 1.12	1.46	1.43	0.01-13.00	
Calcium supplements						
Never	206 (14.4)	1.49 ± 1.39	1.21	1.29	0.14-17.20	11.742 (**<0.001**)
Once in a while	666 (46.6)	1.56 ± 0.89	1.33	1.33	0.06-6.55	
Always	538 (39.0)	1.75 ± 1.07	1.50	1.55	0.01-13.00	
Iron supplements						
Never	811 (56.7)	1.62 ± 1.09	1.36	1.34	0.12-17.20	1.090 (0.337)
Once in a while	490 (34.3)	1.64 ± 1.01	1.42	1.35	0.10-13.00	
Always	128 (9.0)	1.59 ± 0.89	1.34	1.34	0.01-5.49	
Zinc supplements						
Never	703 (49.2)	1.59 ± 1.06	1.34	1.34	0.06-17.20	1.186 (0.306)
Once in a while	570 (39.8)	1.66 ± 1.04	1.41	1.35	0.10-13.00	
Always	158 (11.0)	1.64 ± 0.99	1.39	1.46	0.01-7.92	

Table 2 (continued)

Characteristics	n (%)	Mean ± SD (μg/L)	Geometric mean (μg/L)	Median (μg/L)	Range (μg/L)	F (*P* value)
Drinking water						
Tap water	1402(95.1)	1.62 ± 1.05	1.38	1.34	0.01-17.20	2.435 (0.088)
Ground water	10 (0.7)	1.33 ± 1.18	0.93	0.98	0.17-4.19	
Surface water	62 (4.2)	1.50 ± 0.82	1.28	1.35	0.20-3.85	
Seawater food consumption						
≤1-3 times/month	1070(72.6)	1.51 ± 0.94	1.28	1.32	0.01-13.00	25.640 **(<0.001)**
>1-3 times/month	333 (22.6)	1.87 ± 0.97	1.64	1.73	0.14-6.55	
Freshwater food consumption						
≤1-3 times/month	857 (58.1)	1.49 ± 0.97	1.25	1.31	0.10-13.00	25.416 **(<0.001)**
>1-3 times/month	504 (34.2)	1.73 ± 0.92	1.52	1.71	0.14-7.92	
Shellfish consumption						
≤1-3 times/month	1379(93.6)	1.60 ± 0.98	1.35	1.34	0.01-13.00	5.456 **(0.020)**
>1-3 times/month	95 (6.4)	1.81 ± 1.71	1.58	1.46	0.41-17.20	
Formula milk consumption						
≤1-3 times/month	84 (17.0)	1.35 ± 0.92	1.10	1.28	0.08-6.85	7.828 **(0.005)**
>1-3 times/month	411 (83.0)	1.58 ± 1.03	1.35	1.34	0.10-13.00	
Rice consumption						
≤50 grams/day	259 (20.2)	1.51 ± 1.13	1.29	1.29	0.12-13.00	9.533 **(0.002)**
>50 grams/day	1025 (79.8)	1.71 ± 1.03	1.48	1.48	0.01-17.20	
Vegetable consumption						
≤50 grams/day	637 (43.2)	1.44 ± 0.97	1.20	1.30	0.01-13.00	50.015 **(<0.001)**
>50 grams/day	837 (56.8)	1.75 ± 1.08	1.51	1.61	0.06-17.20	
Meat consumption						
<50 grams/day	691(46.9)	1.50 ± 0.97	1.25	1.32	0.01-13.00	13.224 **(<0.001)**
50-100 grams/day	586(39.8)	1.73 ± 1.13	1.49	1.45	0.06-17.20	
>100 grams/day	197(13.4)	1.69 ± 0.96	1.44	1.66	0.14-7.92	
Milk consumption						
0-100mL	518(35.1)	1.49 ± 1.06	1.24	1.32	0.01-17.20	11.198 **(<0.001)**
100-250mL	517(35.1)	1.63 ± 0.86	1.41	1.41	0.06-6.55	
>250mL	439(29.8)	1.75 ± 1.19	1.48	1.35	0.08-13.00	

[1] significance was tested by Bonferroni comparison for any two groups using log-transformed blood mercury concentration.

significant difference occurred in children's BMLs based on their parents' ethnicity and birth origin: children whose parents were born in eastern coastal cities and were of Han ethnicity had a remarkable high BMLs (F=54.662, *P*<0.001; F=8.660, *P*=0.003). Regarding socioeconomic factors, in general, the BMLs of preschool children in Shanghai were positively correlated with familial socioeconomic status (SES): the children's BLMs increased remarkably as the yearly household income and parents' education increased (F=35.210, *P*<0.001).

Regarding lifestyle associated factors, there were noticeable differences in hand washing, exposure to makeup, residential floor and passive smoking experience, while the distance between the house and the road showed no difference. Children who washed their hands before eating food had lower BMLs (F=12.010, *P*<0.001), whereas children who are exposed to cosmetics including kissing their mother's cheek wearing makeup were more likely to have higher BMLs (F=6.909, *P*=0.009; F=6.174, *P*<0.013). In addition, distinct differences were observed between the BMLs of children living on the higher residential floor and those on the first floor (F=163.871, *P*<0.001). Those who experienced passive smoking or whose caregivers had engaged in smoking habits tended to present higher BMLs (F=5.387, *P*=0.020).

Regarding dietary habits, children who consumed high quantities of fish oil, calcium, seawater food, freshwater food, shellfish, formula milk, rice, vegetables, meat, and milk were more likely to have higher BMLs than those who ingested fewer such foods.

Nevertheless, no significant association was observed between children's BMLs and sex, choice of drinking water,

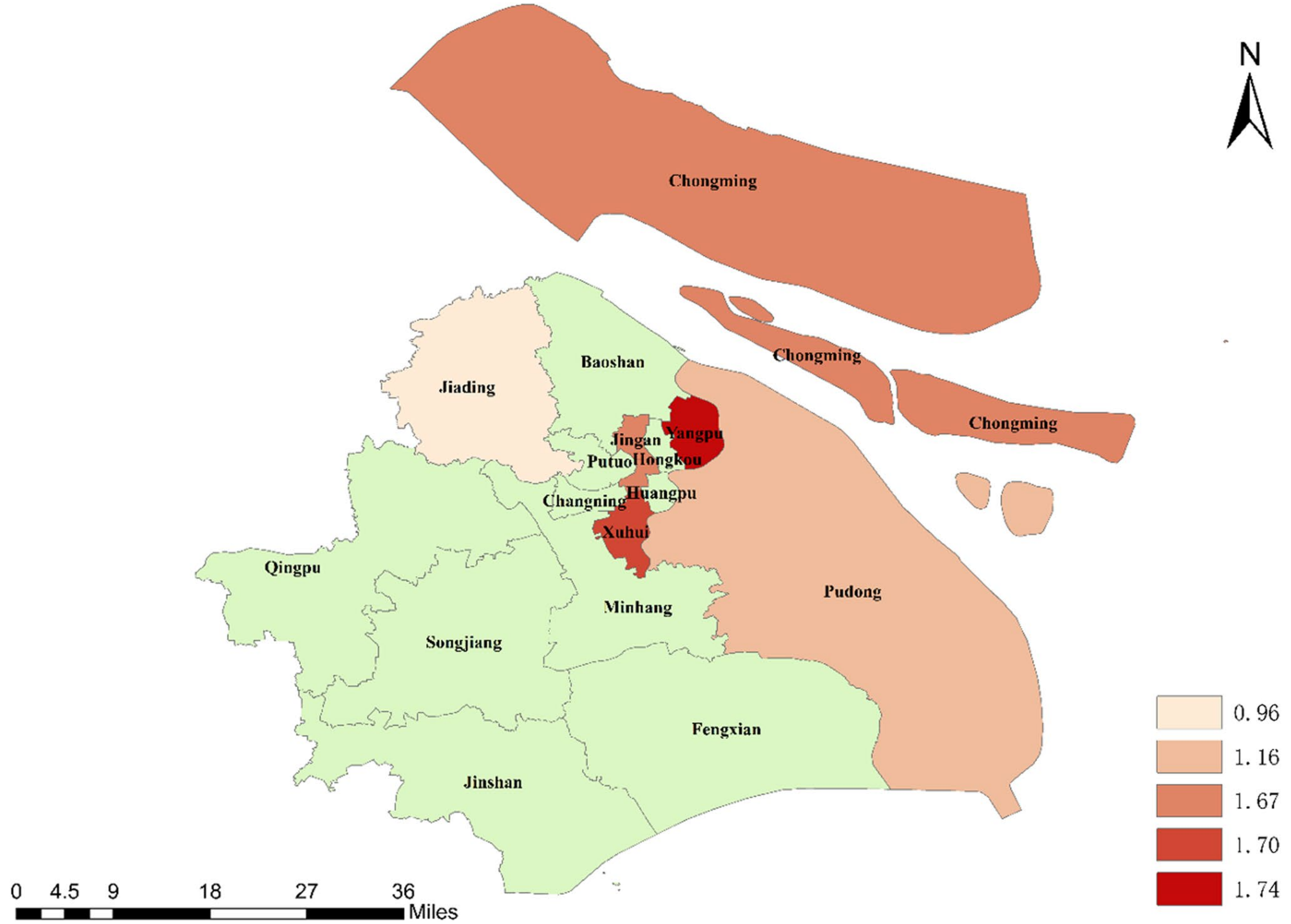

Fig. 1 Median of blood mercury concentration of preschool children in different prefectures of Shanghai.

supplementation of iron and zinc, and distance of road and house.

The relationship between lifestyle and dietary habits and blood Hg concentrations

The results of multiple logistic regression analysis using the entire sample based on the adjustment of all relevant demographic and socioeconomic factors are displayed in Table 3. Adjustment was performed for age, sex, residence, father's origin of birth, mother's origin of birth, mother's ethnicity, father's ethnicity, mother's education, father's education, yearly household income, delivery mode, and feeding mode. Living on a higher apartment floor (adjusted OR 1.81, $P<0.001$) and consuming more seawater food (adjusted OR 1.52, $P=0.0014$), freshwater food (adjusted OR 1.50, $p=0.0006$), rice (adjusted OR 1.50, $P=0.0045$) and vegetables (adjusted OR 1.56, $P=0.0004$) were associated with higher BMLs. Likewise, for infants aged 0-12 months, ingesting formula milk more frequently was related to higher BMLs (adjusted OR 1.35, $P=0.0152$).

Risk factors associated with elevated BMLs

In this final appropriate regression model (Table 4), risk factors for elevated BMLs included old age in the children and mothers (ORs of 2.64 and 1.05 respectively), father with a higher education level (OR of 2.27), living on a higher residential floor (OR of 1.74), and consuming a higher intake of formula milk (OR of 1.50), seawater food (OR of 1.31), freshwater food (OR of 1.27), and vegetables (OR of 1.38). Conversely, protective factors included the ethnicity minority mothers (OR of 0.44) and fathers' with origins in the central and western regions of China (OR of 0.55).

Discussion

Blood Hg concentrations of preschool children

Exposure to Hg continues to be a global public health concern, particularly in relation to child health. In this study, the BMLs of preschool children in Shanghai were slightly

Table 3 Multiple logistic regression analysis: lifestyle and dietary habits affecting blood mercury contents.

	Unadjusted		Adjusted[1]	
	OR (95% CI)	*P* -value	OR (95% CI)	*P* value
Lifestyle				
Hand washing				
Always	Ref		Ref	
Sometimes	0.91 (0.74,1.12)	0.365	1.00 (0.78,1.27)	0.968
Makeup				
No	Ref		Ref	
Yes	**1.46 (1.08,1.98)**	**0.014**	1.03 (0.73,1.46)	0.861
Kiss cheek of mother wearing makeup				
No	Ref		Ref	
Yes	**1.32 (1.02,1.69)**	**0.031**	1.05 (0.80,1.39)	0.722
Residential floor				
1st floor or Bungalow	Ref		Ref	
≥2nd floor	**3.57 (2.85,4.46)**	**<0.001**	**1.81 (1.38,2.38)**	**<0.001**
Passive smoking				
Yes	Ref		Ref	
No	**1.39 (1.06,1.84)**	**0.018**	1.04 (0.77,1.41)	0.783
Dietary habits				
Fish oil supplements				
Never	Ref		Ref	
Once in a while	**2.07 (1.50,2.85)**	**<0.001**	1.34 (0.94,1.92)	0.103
Always	**2.39 (1.73,3.32)**	**<0.001**	1.44 (0.99,2.10)	**0.059**
Calcium supplements				
Never	Ref		Ref	
Once in a while	1.28 (0.94,1.75)	0.118	0.88 (0.62,1.26)	0.492
Always	**1.77 (1.28,2.43)**	**<0.001**	1.01 (0.71,1.45)	0.949
Formula milk consumption				
≤1-3 times/month	Ref		Ref	
>1-3 times/month	**1.56 (1.26,1.92)**	**<0.001**	**1.35 (1.06,1.72)**	**0.015**
Rice consumption				
≤50 grams/day	Ref		Ref	
>50 grams/day	**2.09 (1.65,2.65)**	**<0.001**	**1.50 (1.13,1.99)**	**0.004**
Vegetable consumption				
≤50 grams/day	Ref		Ref	
>50 grams/day	**1.92 (1.56,2.37)**	**<0.001**	**1.56 (1.22,2.00)**	**<0.001**
Meat consumption				
≤50 grams/day	Ref		Ref	
50-100 grams/day	**1.52 (1.22,1.89)**	**<0.001**	1.21 (0.93,1.56)	0.150
>100 grams/day	**1.67 (1.22,2.30)**	**0.001**	1.19 (0.83,1.71)	0.337
Milk consumption				
0-100mL	Ref		Ref	
100-250mL	**1.49 (1.17,1.91)**	**0.001**	1.10 (0.83,1.46)	0.497
>250mL	**1.32 (1.03,1.71)**	**0.031**	1.02 (0.77,1.35)	0.896
Seawater food consumption				
≤1-3 times/month	Ref		Ref	
>1-3 times/month	**2.13 (1.68,2.69)**	**<0.001**	**1.52 (1.18,1.97)**	**0.001**
Freshwater food consumption				
≤1-3 times/month	Ref		Ref	
>1-3 times/month	**2.14 (1.73,2.64)**	**<0.001**	**1.50 (1.19,1.90)**	**<0.001**
Shellfish consumption				
≤1-3 times/month	Ref			
>1-3 times/month	**1.58 (1.04,2.42)**	**0.034**	1.27 (0.80,2.02)	0.308

[1] Adjusted model: adjusted by Age, Sex, Residence, Father's birth origin, Mother's birth origin, Mother's ethnicity, Father's ethnicity, Mother's education, Father's education, Yearly household income, Mode of birth, Feeding mode.

Table 4 Final regression model coefficients associated with the blood mercury concentration of preschool children.

Variables	Estimate	OR (95% CI)	*P* value
Age			
1-4	0.54	1.71 (1.13,2.60)	0.011
4-7	0.97	2.64 (1.51,4.62)	<0.001
Mother's ethnicity			
Ethnic minority	-0.81	0.44 (0.20,0.98)	0.044
Father's education			
Middle and high school	0.48	1.62 (1.15,2.27)	0.005
College or higher	0.82	2.27 (1.65,3.13)	<0.001
Father's birth origin			
Central China region	-0.61	0.55 (0.41,0.72)	<0.001
Western China region	-0.33	0.72 (0.44,1.16)	0.176
Residential floor			
≥2nd floor	0.55	1.74 (1.32,2.28)	<0.001
Formula milk consumption			
>1-3 times/month	0.41	1.50 (1.17,1.93)	0.001
Seawater food consumption			
>1-3 times/month	0.27	1.31 (0.97,1.77)	0.073
Freshwater food consumption			
>1-3 times/month	0.24	1.27 (0.97,1.66)	0.086
Vegetable consumption			
>50 grams/day	0.32	1.38 (1.07,1.79)	0.014
Mother's age	0.04	1.05 (1.02,1.07)	0.001

higher than those of children originating from nearby provinces and cities, such as Taizhou, Zhejiang province (2013, Taizhou, Median 1.01μg/L) and Jiangsu province (2004, Jiangsu, Median 1.26μg/L), but relatively higher than the BMLs of those residing in the 7 provinces of China (2015, Median 1.23μg/L) (Table 5). Children in the United States, Spain, and Sweden demonstrated significantly lower BMLs than those in this study, whereas those in Japan and Korea exhibited markedly higher BMLs (Table 5). These distinct differences in BMLs can be attributed to the diversity of dietary patterns and environmental exposure across different regions, with greater fish consumption in East Asian countries being a key contributing factor (Kim et al. 2017).

Determinants associated with BMLs of children

Further systematic analysis of influencing factors associated with the BMLs of children were conducted, focusing on three aspects: demographic and socioeconomic factors, lifestyle and dietary habits.

Demographic and socioeconomic factors

Age, location and familial SES Our investigation highlighted that age plays a crucial role in BMLs, consistent with the findings of several previous studies (Cho et al. 2014; Fløtre et al. 2017). A recent study conducted in New Zealand revealed a positive association between older age and higher Hg levels (2% per year of increased age) (Mannetje et al. 2021). This positive association with age can be ascribed to the process of Hg accumulation over multiple life stages, as exposure exceeds elimination. Similarly, our results on maternal age were consistent with previous investigations, suggesting that Hg exposure may increase with age (Chen et al. 2014; Hadavifar et al. 2020).

BMLs are important indicators of human exposure to environmental Hg, providing valuable guidance for regional environmental monitoring (Knobeloch et al. 2006). In this study, the BMLs of children living in urban and suburban areas are markedly higher than those in children living in rural areas. BMLs can reflect environmental exposure, such as Hg deposition fluxes (Yang et al. 2015). Shi et al. (Shi et al. 2012) reported that annual dry deposition Hg fluxes in Shanghai were higher in urban and suburban areas (9.40 and 8.70 μg/m^2, respectively) than in rural areas (7.28 μg/m^2). Nevertheless, the BMLs in Yangpu Districts, representing

Table 5 Blood mercury concentration of children from various countries and regions.

Nation	Age(years)	Sample	Sample number	Type	Mercury (μg/L)	Literature
Shanghai, China	0-7	Blood	1474	Median	1.34μg/L	This study
Taizhou, China	0-6	Blood	561	GM	1.01μg/L	(Zhou et al. 2019)
Jiangsu, China	12.08	Blood	1048	Median	1.26μg/L	(Liu et al. 2021)
China 7 provinces	0-6	Blood	14202	Median	1.23μg/L	(Gao et al. 2018)
Japan	7	hair	157	Median	2.51μg/L	(Tatsuta et al. 2017)
Korea	10-19	Blood	1585	Median	1.93μg/L	(Kim et al. 2017)
Spain	9	Hair	405	Median	0.89μg/g	(Soler-Blasco et al. 2019)
United States	12-19	Blood	2709	Mean	0.68μg/L	(Sanders et al. 2019)
Sweden	4-9	Blood	1257	Median	0.91μg/L	(Lundh et al. 2016)
Poland	7-11	Blood	30	GM	0.12μg/L	(Hrubá et al. 2012)

GM: Geometric Mean

suburban areas, even exceeded the prevailing rate in urban areas, where reasons behind are worth further exploration. It has been reported that atmospheric Hg concentrations are associated with land use types (Shi et al. 2018), where industrial areas with power plants or gas-manufactured factories had higher Hg levels in surrounding road dust (Liu et al. 2019; Wang et al. 2021). The acceleration of urbanization has led to frequent changes in land use, with areas previously used for industry or agriculture now being converted to residential areas. The higher BMLs of children in Yangpu District, known as a birthplace of modern Chinese industry, may be partly attributed to historical environmental contamination despite multiple industrial transformation efforts since the 1990s (Zhang et al. 2019). A plethora of studies have demonstrated that higher familial SES is associated with higher BMLs (Cho et al. 2014; Montazeri et al. 2019), aligns with our findings.

Birth type, feeding mode, gravidity and parity Intriguingly, our results revealed that the BMLs of children whose mothers had ever miscarried or received an abortion were lower than those of the other group in the univariate analysis. Previous study revealed that mothers who had ever undergone abortions exhibited lower BMLs (Hadavifar et al. 2020). Although the exact mechanisms remain unclear, it is plausible that Hg is expelled through vaginal bleeding during the process of reproduction or abortion, or that it is transferred to the placenta or fetus. Regarding infant feeding practices, those who were artificially fed or given mixed feeding exhibited higher BMLs. Correspondingly, infants fed formula milk over 1-3 times per month had relatively higher BMLs in the present study. This result is supported by our previous investigation regarding cord BMLs (Wu et al. 2013). It has been shown that formula milk contains higher Hg levels than breast milk (Dórea 2020). The associated health risk of Hg for infants through exposure to formula milk should not be underestimated (Dorea and Donangelo 2006).

Lifestyle and dietary habits

Lifestyles Although not statistically significant in the multivariate regression models, handwashing may be a potential protective factor. Previous studies have suggested that soil and dust could be significant sources of Hg exposure among children (Kao et al. 2022). Given the frequent hand-to-mouth activities of children, particularly those from Hg-contaminated mining regions, handwashing can effectively reduce the ingestion of Hg from soil and dust.

Exposure to cosmetics is a significant risk factor for elevated BMLs, as confirmed by numerous studies. Our results found that behaviors such as high frequency of makeup use and kiss their mother wearing cosmetics were associated with elevated BMLs (Table 3). Skin-lightening cosmetics, in particular, have been found to contain high levels of Hg, with an average of 875 ± 115 mg/kg (Podgórska et al. 2021). Thus, continuous exposure to cosmetics is a concern for Hg absorption and related health risks that warrant further evaluation.

The relationship between elevated BMLs and residential floor was mainly attributed to familial SES, where people living on the 1_{st} floor or bungalows tend to live in rural villages with lower familial SES. Maintaining good ventilation can help dilute the indoor air contaminants and improve indoor air quality (Caravati et al. 2008). However, families living on higher floors tend to ventilate their homes less frequently due to safety concerns, which may contribute to elevated BMLs.

Smoking habits and exposure to passive smoking have been controversial as risk factors for elevated BMLs. Tobacco products can contain toxic metals, including Hg (Caruso et al. 2013), leading to potential exposure (Karatela et al. 2019). Nevertheless, numerous investigations have shown a negative relationship between smoking and BMLs (Gaxiola-Robles et al. 2013; Jain 2017), where maternal smoking habits were associated with lower Hg contents in the hair of 9-year-old Spanish children (Soler-Blasco et al. 2019). Certain components of tobacco smoke may affect the metabolism of Hg, accelerating its elimination and excretion.

Dietary habits This study explored the relationship between dietary habits and BMLs in children aged 0 to 7-year-old in Shanghai. The Final regression coefficients analysis indicated that the consumption of seawater food, freshwater food, formula milk, and vegetables were risk factors for elevated BMLs (ORs of 1.31, 1.27, 1.50, and 1.38, respectively). Other potential dietary habits, such as intake of rice, fish oil, calcium supplements, shellfish, meat and milk, were also explored, but no statistical differences were observed after adjusting for covariates.

Fish consumption, whether from seawater or freshwater, is widely acknowledged as the primary route of human exposure to methylmercury (MeHg), especially for the non-occupational population (Varela et al. 2016). Evidence from studies conducted in Sweden (Almerud et al. 2021), Korea (Kim et al. 2017), and Spain (Soler-Blasco et al. 2019) has shown a significant correlation between BMLs and the consumption of large predatory and freshwater fish. In Sabzevar, where fresh seafoods are not commonly consumed, canned seafood remains the primary source of Hg exposure for fetuses and young children (Hadavifar et al. 2020). A study conducted in Shanghai demonstrated that THg concentrations in fish muscle tissues ranged from below the LOD to 60.74 μg/kg wet weight and advocated that potential health risks posed by the consumption of seawater and freshwater fish deserve more attention (Geng et al. 2015). However, our results did not suggest a significant positive association between shellfish consumption and elevated BMLs, possibly due to the homogenous dietary habits among Shanghai participants, with 93.55% consuming shellfish less than 1-3 times per month.

Long-term fish oil supplementation may raise the risk of MeHg exposure, mainly depending on the composition of the fish oil (Mozaffarian and Rimm 2006). Marine fish-derived fish oil contains higher concentrations of Hg than synthetically-produced fish oil. Our study found that children who regularly consume fish oil supplements are more likely to have elevated BMLs, although the differences were only marginally significant after adjusting for covariates, which is mainly due to the limited information on the composition of the fish oil supplements in our questionnaire.

It remains controversial whether calcium and Vitamin D supplements increase Hg body burdens. In a previous animal study, vitamin D and calcium supplementation did not affect the absorption of Hg (Jukic et al. 2020). However, a prospective cohort study conducted in 10 Canadian cities discovered that maternal calcium intake during pregnancy was negatively related to maternal blood Hg concentrations (Arbuckle et al. 2016). Conversely, high dosages of vitamin D supplementation resulted in a non-significant increase in BMLs (Arbuckle et al. 2016). The ingredients in calcium supplements may be one of the potential reasons behind. A Korean study that sought to determine the Hg contents of calcium supplements widely available on the market revealed that calcium supplements made from shark bone reached a maximum, up to 0.06mg/kg (Range: 0.01-0.12 mg/kg) (Kim 2004). Here, no significant relationship were found between calcium supplementation and higher BMLs in the adjusted model, which can be attributed to the complex composition of calcium supplements and the confounding effect of socioeconomic factors.

However, to the best of our knowledge, it remains unknown whether daily intake of vegetables and rice associated with children's BMLs in Shanghai. In inland China, rice, rather than fish, is the primary source of daily MeHg exposure (Zhang et al. 2010). Another study conducted in a Hg mining area in the southern Shannxi province of China identified a positive association between daily intake of vegetables and hair MeHg concentrations, suggesting that daily vegetables consumption may pose a health threat to local residents (Jia et al. 2018). In our study, even after adjusting the covariates, the relationship between the daily ingestion of rice and vegetables and BMLs for children aged 0-7 years in Shanghai should not be overlooked. Qing also estimated that aquatic products account for approximately 51% of the total daily dietary exposure of Hg for the population from the eastern coastal region of China, followed by 16% for cereals and 14% for vegetables (Qing et al. 2022), which coincides with results of our study.

Conclusion

The median blood Hg concentrations of preschool children aged 0-7 years in Shanghai was 1.34 μg/L, dramatically higher than that of children in Europe and the United States. Older age, higher familial socioeconomic status, higher residential floors, and higher consumption frequency of aquatic products, rice, vegetables, and formula milk were risk factors for elevated BMLs. These findings might benefit the establishment and implementation of appropriate interventions to determine and prevent high blood Hg concentrations in Shanghai and other similar metropolitan cities.

Author contributions All authors contributed to the study conception and design. Conceptualization, writing the original draft, methodology, software, and data curation were performed by Xu Xi. Methodology and review the manuscript were performed by Wang Yu-Qing, Dong Chen-Yin, Hu Chun-Ping, and Zhang Li-Na. Samples collection and detection were conducted by Gao Zhen-Yan, and Li Min-Ming. Supervision, reviewing, and editing were carried out by Wang Su-Su, and Yan Chong-Huai. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability The dataset of this study is available from the corresponding authors on reasonable request.

Declarations

Competing interests The authors have no relevant financial or non-financial interests to disclose.

Ethics approval This research was approved by the Medical Ethics Committee of Xinhua Hospital affiliated with Shanghai Jiao Tong University School of Medicine and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Consent to participate Informed consent was obtained from children's parents recruited in the study.

Consent to publish Not applicable.

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