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RESEARCH ARTICLE

Associations between total mercury and methyl mercury exposure and cardiovascular risk factors in US adolescents

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Abstract

Low levels of chronic heavy metal exposure are associated with a range of adverse health effects. However, whether total blood mercury (Hg) and methyl mercury (MeHg) exposure affect risk factors for cardiovascular disease (CVD) in adolescents remains unclear. The associations between CVD risk factors and total blood Hg and MeHg in adolescents were evaluated using data from the National Health and Nutrition Examination Survey (NHANES), 2011–2012. Data for 1129 adolescents (age 12–19 years) who participated in the US NHANES 2011–2012 were analyzed. A multivariate linear regression was performed to investigate the associations between CVD risk factors and blood Hg and MeHg concentrations. We identified a strong positive association between blood Hg and MeHg and total cholesterol in adolescents in adjusted model. No associations with other CVD risk factors were found in the overall population. In the gender-stratified generalized linear models, girls with the highest MeHg levels demonstrated a 4.22% (95% CI 0.80%, 7.76%) greater increase in serum total cholesterol (P for trend = 0.029) when compared with girls with the lowest MeHg levels. Our findings suggest that blood MeHg may be positively associated with total cholesterol in adolescent girls. More research is needed to verify this association and to elucidate its underlying mechanisms.

Keywords NHANES · Methylmercury compounds · Adolescent · Cholesterol

Introduction

Cardiovascular disease (CVD) is the primary cause of death among adults in developed countries. It is well known that heart attacks and stroke are the main clinical features of CVD in adulthood, and even among the elderly; however, CVD risk factors usually appear during childhood and adolescence (Raitakari et al. 2003). Reportedly, approximately 9.6 to 10.7% of persons aged 12 to 17 years who participated in the NHANES 1999 to 2006 survey had an elevated total cholesterol concentration (Ford et al. 2009). Environmental chemicals, such as polychlorinated biphenyls and polyfluoroalkyl chemicals, have been found to be positively associated with CVD risk factors (Goncharov et al. 2008; Nelson et al. 2010), suggesting that environmental chemicals may be related to CVD risk factors.

Mercury (Hg) is known as a contaminant in the global context and has recognized neurotoxicity. Different forms of Hg possess different toxicities in humans. Three subtypes of Hg, methyl mercury (MeHg), ethyl mercury (EHg), and inorganic mercury (IHg), have been found to be present in the human blood, originating from diverse exposure sources and demonstrating different toxicity characteristics. Previous scientists have suggested that Hg may be neurotoxic (Carocci et al. 2014), and Hg toxicity may be associated with hypertension and coronary heart disease in adults (Houston 2011). However, the associations between total mercury and the three subtypes mercury and CVD risk factors in adolescents remain unclear.

Yuxi Zhang and Cheng Xu contributed equally to the present study and should be regarded as joint first authors.

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In the present study, nationally representative data from the NHANES series were analyzed to evaluated the associations between low mercury exposure biomarkers and CVD risk factors (blood pressure, fasting glucose and insulin, glycohaemoglobin (HbA1c) and lipid profiles) in adolescents (in 12 to 19-year-olds).

Materials and methods

Study population

NHANES is a freely available data source that includes nationally representative data. The survey is conducted by the US National Center for Health Statistics (Centers for Disease Control and Prevention, Atlanta, GA, USA). Data for the subjects enrolled in the present study were obtained from the NHANES 2011–2012 survey, in which the participants had mercury concentrations measured and provided information regarding potential covariates. Figure 1 shows the inclusion and exclusion criteria and numbers available for each analysis that is described herein. Full details of the survey and data for scientific use are available in our previous studies (Xu et al. 2015a, b) and at http://www.cdc.gov/nchs/nhanes.htm.

Exposure variable

Total Hg, MeHg, EHg, and IHg levels were detected in serum obtained from participants. Serum specimens were obtained in collection cups at the Mobile Examination Centers and quickly frozen and shipped to a central laboratory for analysis. The methods used for MeHg, EHg, and IHg detection has been described in detail and are available in the laboratory procedure manual provided on the following website: (https://www.cdc.gov/nchs/data/nhanes/nhanes_11_12/ihgem_met_g_mercuryspecies.pdf). Briefly, blood samples were first assessed using Solid Phase Micro Extraction (SPME) fibers. Then, the samples were analyzed using gas chromatography (GC) in conjunction with inductively coupled plasma-dynamic reaction cell-mass spectrometry (ICP-DRC-MS). Similarly, total blood Hg was measured by ICP-DRC-MS. The lower detection limits were 0.16 μg/L for total Hg, 0.27 μg/L for IHg, 0.16 μg/L for EHg, and 0.12 μg/L for MeHg. When the concentration of Hg was less than the limit of detection, the value presented was the detection limit divided by the square root of two.

Outcome variables

CVD risk factors (blood pressure, fasting glucose and insulin, HbA1c, and lipid profiles) were assessed by specially assigned persons who applied a unified process. All data were collected as continuous variables.

Covariates

A wide range of sociodemographic variables such as age, gender, and ethnicity were acquired from the NHANES 2011–

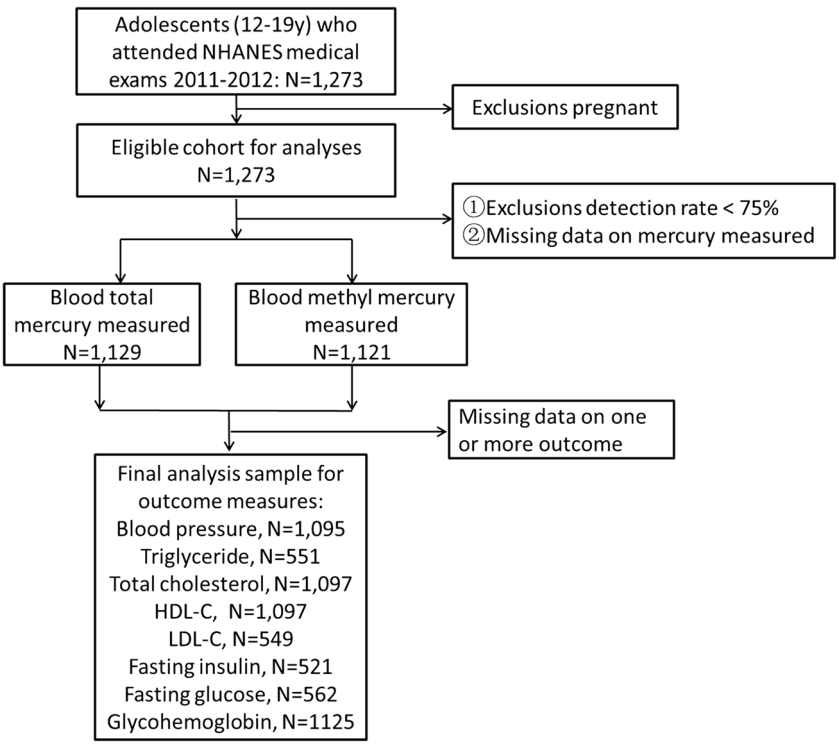

Fig. 1 Eligible participants and those included in the analyses of the associations between total and methyl mercury exposure and CVD risk factors

2012. Trained examiners measured body weight and height, and body mass index (BMI, kg/m^2) was calculated as body weight divided by height squared. The poverty to income ratio (PIR) was defined as the ratio of family income to the poverty threshold after adjusting for inflation and family size. Levels of serum cotinine, a marker of active and passive cigarette smoking exposure, were used to reflect environmental smoking exposure. Daily hours of television, video games and computer use served as a proxy for physical activity levels. Diet is the main source of cholesterol. Therefore, we considered intake of cholesterol from food as a covariate in the model.

Statistical analysis

Continuous variables are presented as the mean ± standard deviation. We identified the levels of total Hg, MeHg, EHg, and IHg in human blood, and included chemical exposure in our analysis when detection rates were greater than 75%. The blood Hg and MeHg variables underwent natural logarithmic transformation due to their skewed nature, and these variables included in the analyses as quartiles based on their distributions in the present population. To investigate the association between blood Hg and MeHg exposure and CVD risk factors, we generated age- and gender-adjusted multiple variable linear regression models and present the associations with regression coefficients (beta) and 95% confidence intervals (CIs). Multivariable linear models were used to assess the associations between interquartile ratio increases (IQ ratio = 75th/25th percentiles of Hg levels) in blood total and MeHg and total cholesterol levels. Statistical tests for linear trends were conducted by modeling quartiles as an ordinal variable using integer values. We present the magnitudes of these associations as the average percent difference in CVD risk factors within each IQ ratio group, as defined by the participants total blood Hg and MeHg variables; these magnitudes were calculated as [(IQ ratio^{beta})-1]*100. Alcohol consumption and diabetes were not included in the full adjusted models, as adjusting for these two variables separately or collectively did not change the results substantially (< 5% of change in effect estimates). The statistical analysis systems software package version 9.2 (SAS Institute, Inc.) was used for the analyses performed in this study. All *P* values are two-sided, and values less than 0.05 were considered to be statistically significant.

Results

The distributions of total Hg, MeHg, EHg, and IHg levels are presented in Supplemental Table 1. The median total Hg and MeHg levels were 0.47 and 0.33 μg/L, respectively. The total Hg and MeHg concentration variables had a wide and skewed distribution. Blood IHg was not detected in more than 75% of the population assessed. More than 95% participants were below the limit of EHg detection.

Table 1 shows the associations between mean blood total Hg and MeHg and participant characteristics. Study participants had a median age of 15.0 years, with a range of 12 to 19 years. Total blood Hg and MeHg levels were lower in 12 to 15 year old (total Hg, mean ± SD, 0.67 ± 0.85 μg/L; MeHg, mean ± SD, 0.56 ± 0.86 μg/L) than 16 to 19 year old (total Hg, mean ± SD, 0.90 ± 1.17 μg/L; MeHg, mean ± SD, 0.79 ± 1.21 μg/L) participants. Total blood Hg and MeHg concentrations were higher in subjects who were in the "other" race category, which included multiracial subjects. Higher total blood Hg and MeHg levels were identified in participants who had low levels of physical activity. Other variables, such as gender, BMI, waist circumference, PIR and serum cotinine, were not associated with Hg or MeHg levels.

The distributions of CVD risk factors within each total blood Hg and MeHg quartile are presented in Table 2. Total cholesterol levels tended to be higher in the highest total Hg and MeHg groups; however, no significant differences were identified in these two mercury exposure categories. Significant differences were not identified within the four group defined by total Hg and MeHg exposure for any of the other CVD risk factors.

Further, linear regression models were generated to explore the associations between total Hg and MeHg and CVD risk factors. Covariates were included in our model to decrease the influence of potential biases. Model 1 was adjusted for age and gender, and model 2 was adjusted for these variables plus race, serum cotinine, BMI, physical activity, and PIR (Table 3). In the age- and gender-adjusted models, blood total Hg was positively associated with total cholesterol (coefficient = 0.019, 95% CI: 0.006, 0.031), and the strength of the association increased after adjustment for other covariates (coefficient = 0.022, 95% CI: 0.009, 0.036). Similar results were observed in MeHg, which was positively associated with total cholesterol in model 1 (coefficient = 0.015, 95% CI: 0.005, 0.025) and model 2 (coefficient = 0.019, 95% CI: 0.007, 0.030), respectively. Utilizing the waist circumference variable instead of the BMI produced identical results (Supplemental Table 2).

Because total blood Hg and MeHg levels were associated with total cholesterol levels in adolescents, we subsequently used multivariable linear models to detect associations between interquartile ratio increases. Simultaneously, given that a gender difference was identified in CVD risk factors, we divided the population into boys and girls group. Total cholesterol increased with increasing quintiles of blood MeHg in girls, and the highest quintile of MeHg was significantly different from the lowest based in all four models (Table 4). Specifically, in the fully adjusted model, girls in the highest quintile had mean total cholesterol levels that were 4.22%

Table 1 Blood total mercury and methyl mercury concentration (mean ± SD) according to demographic, and lifestyle

	Total mercury (μg/L)		Methyl mercury (μg/L)	
	Participants [*n* (%)]	Mean ± SD	Participants [*n* (%)]	Mean ± SD
Overall	1129 (100%)	0.78 ± 1.02	1121 (100%)	0.67 ± 1.06
Age (years)				
12–15	572 (50.7%)	0.67 ± 0.85	570 (50.5%)	0.56 ± 0.86
16–19	557 (49.3)	0.90 ± 1.17	551 (48.8%)	0.79 ± 1.21
Gender				
Boy	582 (51.6%)	0.81 ± 1.62	576 (51.0%)	0.72 ± 1.22
Girl	547 (48.4%)	0.75 ± 0.85	545 (48.3%)	0.63 ± 0.85
Race				
Mexican American	199 (17.6%)	0.55 ± 0.66	199 (17.6%)	0.42 ± 0.66
Other Hispanic	125 (11.1%)	0.76 ± 0.72	123 (10.9%)	0.65 ± 0.76
Non-Hispanic White	251 (22.2%)	0.51 ± 0.56	250 (22.1%)	0.40 ± 0.56
Non-Hispanic Black	346 (30.6%)	0.66 ± 0.76	341 (30.2%)	0.55 ± 0.77
Other race—including multiracial	208 (18.4%)	1.54 ± 1.70	208 (18.4%)	1.46 ± 1.77
BMI (kg/m^2)[a]				
Tertile 1	375 (33.2%)	0.78 ± 1.01	373 (33.0%)	0.67 ± 1.02
Tertile 2	369 (32.7%)	0.81 ± 0.99	367 (32.5%)	0.70 ± 0.99
Tertile 3	369 (32.7%)	1.09 ± 0.77	365 (32.3%)	0.67 ± 1.16
Waist circumference (cm)[b]				
Tertile 1	371 (32.9%)	0.78 ± 1.00	368 (32.6%)	0.67 ± 1.01
Tertile 2	361 (32.0%)	0.81 ± 0.95	360 (31.9%)	0.70 ± 0.96
Tertile 3	362 (32.1%)	0.76 ± 1.12	358 (31.7%)	0.67 ± 1.22
PIR				
< 1	351 (31.1%)	0.64 ± 0.88	350 (31.0%)	0.52 ± 0.95
≥ 1	681 (60.3%)	0.83 ± 1.06	674 (59.7%)	0.74 ± 1.08
Serum cotinine (ng/mL)				
< LOD	310 (27.5%)	0.82 ± 1.19	309 (27.4%)	0.74 ± 1.27
LOD-10	680 (60.2%)	0.76 ± 0.94	676 (59.9%)	0.64 ± 0.93
> 10	108 (9.6%)	0.79 ± 0.84	108 (9.6%)	0.64 ± 0.95
Television, video game, and computer usage (hours)				
≤ 2	376 (33.3%)	0.69 ± 0.85	374 (33.1%)	0.59 ± 0.87
> 2	734 (65.05)	0.82 ± 1.10	728 (64.5%)	0.72 ± 1.14

[a] Mean values ± SD: 24.0 ± 6.2 kg/m^2 . Tertile ranges (kg/m^2): tertile 1, 14.4–20.5; tertile 2, 20.6–25.3; tertile 3, 25.4–57.1

[b] Mean values ± SD: 81.7 ± 14.9 cm. Tertile ranges (cm): tertile 1, 57.9–73.2; tertile 2, 73.3–84.5; tertile 3, 84.6–147.0

greater (95% CI: 0.80%, 7.76%) than in the lowest quintile (trend *P* value = 0.029). The relationship between MeHg and total cholesterol in girls is visualized in a scatter plot and fitted line with 95% CI (Fig. 2).

Except for age variable, we also performed stratified analysis by other covariates. We found MeHg was positively associated with total cholesterol in subjects who were aged 12–15, Mexican American, rich family, and high physical activity (Supplemental Table 3). And Hg was positively associated with total cholesterol in subjects who were aged 12–15, Mexican American, rich family, larger BMI, and high physical activity (Supplemental Table 4).

Discussion

Using data from a large population sample in the US NHANES 2011–2012 survey, we found that blood MeHg concentrations were positively associated with serum total cholesterol levels in adolescents girls but not boys. This

Table 2 Serum levels of cardiovascular disease risk factors by quartile of total mercury and methyl mercury in US adolescents 2011–2012

Characteristics	Total mercury				Methyl mercury			
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Total cholesterol (mg/dL)	154.8 ± 30.0	157.7 ± 28.1	157.7 ± 31.3	161.9 ± 31.1	155.1 ± 28.5	156.4 ± 29.3	158.7 ± 30.9	162.1 ± 31.5
LDL-cholesterol (mg/dL)	89.4 ± 28.3	88.0 ± 25.8	87.2 ± 26.0	90.8 ± 26.5	88.5 ± 27.7	87.0 ± 27.0	91.0 ± 24.8	89.8 ± 27.2
HDL-cholesterol (mg/dL)	52.3 ± 11.1	51.1 ± 10.9	51.8 ± 10.8	52.5 ± 11.5	51.8 ± 11.3	51.9 ± 10.5	51.3 ± 11.1	53.0 ± 11.3
Triglyceride (mg/dL)	85.0 ± 47.6	79.2 ± 58.5	82.05 ± 59.9	83.7 ± 58.8	89.5 ± 61.4	77.7 ± 47.5	80.7 ± 56.0	80.6 ± 57.2
Fasting glucose (mg/dL)	94.5 ± 20.3	93.9 ± 9.2	92.1 ± 9.4	93.8 ± 9.9	94.2 ± 21.2	92.3 ± 7.7	94.2 ± 10.3	93.7 ± 9.6
Glycohemoglobin (%)	5.3 ± 0.6	5.3 ± 0.6	5.3 ± 0.3	5.3 ± 0.3	5.3 ± 0.6	5.3 ± 0.3	5.3 ± 0.6	5.3 ± 0.3
Fasting insulin (uU/mL)	16.3 ± 12.3	12.8 ± 7.9	15.8 ± 15.6	15.8 ± 12.7	15.7 ± 11.6	14.8 ± 12.9	14.5 ± 12.4	15.4 ± 12.5
SBP (mmHg)	109.0 ± 10.5	109.2 ± 10.5	110.6 ± 10.5	109.4 ± 10.2	109.3 ± 10.6	108.4 ± 9.9	111.01 ± 10.8	109.6 ± 10.3
DBP (mmHg)	59.8 ± 12.4	56.3 ± 14.2	59.6 ± 13.1	59.1 ± 13.9	60.2 ± 12.6	56.3 ± 13.4	58.9 ± 13.7	59.5 ± 13.9

Mean ± SD. Total mercury (μg/L), quartile 1: < 0.26; quartile 2: 0.26–0.47; quartile 3: 0.48–0.82; quartile 4: > 0.82; methyl mercury (μg/L), quartile 1: < 0.14; quartile 2: 0.14–0.33; quartile 3: 0.34–0.68; quartile 4: > 0.69

association persisted after adjustment for age, ethnicity, serum cotinine, physical activity, BMI, PIR, and intake of cholesterol from food.

Previously, only a few studies have explored the association between blood Hg and CVD risk factors. A Korean study suggested that blood mercury was associated with metabolic syndrome in adults (Eom et al. 2014). Specifically, after adjustment for covariates, increased blood Hg levels were positively associated with elevated BMI, waist circumference, diastolic blood pressure, total cholesterol, and triglyceride. Another study from the same country suggested that there was no significant association between having metabolic syndrome or its components and blood Hg concentrations in any of their adjusted

Table 3 Multivariable associations of total mercury and methyl mercury with cardiovascular risk factors in US adolescents 2011–2012

Exposure	Risk factors	Model 1			Model 2		
		Coefficient	95% CI	*P* value	Coefficient	95% CI	*P* value
Total mercury	Total cholesterol (mg/dL)	*0.019*	*0.006, 0.031*	*0.003*	*0.022*	*0.009, 0.036*	*0.001*
	LDL-cholesterol (mg/dL)	0.014	− 0.014, 0.032	0.322	0.011	− 0.021, 0.042	0.513
	HDL-cholesterol (mg/dL)	0.009	− 0.005, 0.023	0.200	0.006	− 0.008, 0.020	0.401
	Triglyceride (mg/dL)	− 0.024	− 0.071, 0.024	0.326	− 0.006	− 0.057, 0.045	0.812
	Fasting glucose (mg/dL)	− 0.002	− 0.011, 0.008	0.747	0.003	− 0.006, 0.011	0.532
	Glycohemoglobin (%)	0.001	− 0.004, 0.006	0.631	0.001	− 0.004, 0.006	0.721
	Fasting Insulin (uU/mL)	0.012	− 0.047, 0.071	0.683	− 0.003	− 0.057, 0.051	0.906
	SBP (mmHg)	0.000	− 0.006, 0.006	0.954	− 0.001	− 0.007, 0.005	0.800
	DBP (mmHg)	− 0.007	− 0.026, 0.011	0.444	− 0.016	− 0.036, 0.004	0.119
Methyl mercury	Total cholesterol (mg/dL)	*0.015*	*0.005, 0.025*	*0.003*	*0.019*	*0.007, 0.030*	*0.001*
	LDL-cholesterol (mg/dL)	0.012	− 0.011, 0.035	0.309	0.008	− 0.018, 0.035	0.531
	HDL-cholesterol (mg/dL)	0.008	− 0.003, 0.020	0.147	0.008	− 0.003, 0.019	0.170
	Triglyceride (mg/dL)	− 0.031	− 0.070, 0.008	0.118	− 0.021	− 0.063, 0.021	0.323
	Fasting glucose (mg/dL)	0.002	− 0.006, 0.010	0.614	0.004	− 0.003, 0.021	0.223
	Glycohemoglobin (%)	0.002	− 0.002, 0.006	0.386	0.001	− 0.003, 0.006	0.528
	Fasting insulin (uU/mL)	0.014	− 0.034, 0.062	0.571	0.003	− 0.042, 0.047	0.911
	SBP (mmHg)	0.000	− 0.005, 0.004	0.913	− 0.001	− 0.006, 0.005	0.844
	DBP (mmHg)	− 0.002	− 0.017, 0.014	0.832	− 0.009	− 0.026, 0.007	0.277

Model 1: age and gender. Model 2: model 1 plus race, serum cotinine, BMI, physical activity, PIR, and dietary cholesterol (for cholesterol risk factors). Exposure variables and risk factors variables were Log-transformed in models

Table 4 Estimated percent difference (% diff) and 95% confidence intervals (95% CI) in serum total cholesterol concentrations in US adolescents 2011–2012 for each interquartile ratio (IQ ratio) increase in blood total mercury and methyl mercury levels

	Boys				Girls			
	No. of subjects	% Diff	95% CI	*P* for trend	No. of subjects	% Diff	95% CI	*P* for trend
Total mercury				0.040				0.028
Quartile 1	167	Referent			135	Referent		
Quartile 2	140	1.28%	− 1.89%, 4.38%		130	1.44%	− 1.73%, 4.88%	
Quartile 3	134	1.93%	− 1.26%, 5.38%		145	− 0.32%	− 3.44%, 3.07%	
Quartile 4	141	3.07%	− 0.16%, 6.39%		137	3.39%	− 0.16%, 6.90%	
Methyl mercury				0.052				0.029
Quartile 1	153	Referent			140	Referent		
Quartile 2	144	− 0.63%	− 3.59%, 2.58%		134	2.58%	− 0.79%, 5.89%	
Quartile 3	138	1.60%	− 1.58%, 4.88%		133	2.25%	− 1.26%, 5.72%	
Quartile 4	141	2.58%	− 0.79%, 5.89%		138	**4.22%**[a]	*0.80%, 7.76%*	

Total mercury, methyl mercury, and total cholesterol were Ln-transformed in models. Adjusted as age, race, serum cotinine, BMI, physical activity, PIR, and dietary cholesterol (for cholesterol risk factors). Percent differences = [(IQ ratio^{beta})-1]*100. Interquartile ratio = 75th/25th percentiles of serum mercury: 3.2 (total mercury), 4.9 (methyl mercury)

[a] $P < 0.05$

models (Lee and Kim 2013). Thus, seemingly conflicting results exist regarding this association. Among adolescents, the results of a case-control study (160 with metabolic syndrome and 160 healthy controls) indicated the presence of a positive relationship between blood Hg and blood pressure and metabolic syndrome in both female and male adolescents,(Poursafa et al. 2014) while our study suggest that there were no significant associations were between Hg and CVD risk factors.

The results from in vitro studies have been consistent with those of epidemiologic studies, which have suggested that MeHg may induce cardiovascular toxicity. Moreira et al. found long-term MeHg exposure to cause dyslipidemia in mice (Moreira et al. 2012). Increased plasma total cholesterol, HDL-C, and triglyceride levels were observed in Swiss and C57BL/6 mice when MeHg (40 mg/L, ad libitum) was added into tap water for 21 days

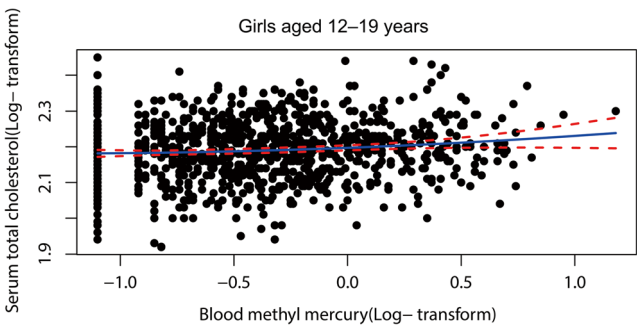

Fig. 2 A scatter plot and a fitted line with 95% CI of the relationship between blood methyl and total cholesterol in girls aged 12–19 years

when compared with control group. Maqbool et al. indicated that insulin resistance and hyperglycemia occurred when MeHg (2.5, 5, and 10 mg/kg/day, tap water) was provided to mice for 4 weeks (Maqbool et al. 2016). Moreover, glucose levels were also elevated.

MeHg is the primary organic form of Hg. In the natural environment, the mercury cycle, and namely, the fate of mercury in the oceans and fresh water is complex. In general, Hg could react with sulfate, undergo methylation and form a precipitate. Further, it may be methylated by sulfate-reducing bacteria and become MeHg (Gochfeld 2003). In addition, MeHg has been found to be produced by a variety of methylating microbes (Drevnick et al. 2007; Gilmour and Henry 1991). In fact, the vast majority of Hg detected in fish has been found to be MeHg, with previous reports indicating that this form may account for 72–100% of detected Hg (Gray et al. 2000; Storelli et al. 2002). In humans, MeHg may be ingested due to bioaccumulation in fish (Da Silva et al. 2005). Salonen et al. suggested the men who consumed more than 30 g fish per day had remarkably higher hair Hg levels than did men who consumed less than 30 g/day (Salonen et al. 1995). Thus, less consumption of Hg-polluted fish and more regulation by the government may protect persons from the adverse effects of Hg and MeHg.

In addition, the significant association between MeHg and total cholesterol was only observed in girls. Gender differences may be ascribed to the estrogenic activity of MeHg. Sukocheva et al. found that MeHg may be potential estrogen disruptors, which can activate MCF-7 cells (Sukocheva et al. 2005). More in vitro and in vivo studies

are needed to confirm the characteristics of methyl mercury. Results also showed that MeHg was significantly associated with total cholesterol in the rich family, which may be due to the widely exist of Hg in the skin whitening cream (Li and Tse 2015). Furthermore, we found that subjects aged 12–15, Mexico American, or individuals with higher physical activity were more susceptible to methyl mercury exposure, resulting in increased total cholesterol. Genetic susceptibility may be one of the reasons for the difference, that is, some people may be more susceptible to mercury toxicity due to the presence of susceptible candidate genes (Andreoli and Sprovieri 2017). More investigations are needed to explain the underlying reasons.

Although there is no clear evidence to support, we hypothesized that genetic susceptibility, that some people may be more susceptible to the toxicity of mercury, because susceptible candidate gene may be one of the reasons leading to differences (Andreoli and Sprovieri 2017). Other potential causes need more research to explain.

In this study, we were the first to find positive associations between low levels of blood MeHg and total cholesterol in adolescent girls. Our study had several strengths. A representative sample of the population was included in the analysis to avoid potential bias. Some covariates that may influence outcomes were included in our statistical models to offer more accurate and consistent results. However, our study had a few inevitable limitations. First, although we adjusted for potential confounders in the analysis, several confounders, such as accurate metrics for daily physical activity and genetic susceptibility, were not collected and adjusted for in the study. Second, due to the cross-sectional design of our study, it was not possible to determine whether MeHg affected total cholesterol or vice versa. Third, we cannot explain the gender difference identified in our results. Further studies are needed to evaluate this finding and explore potential causative mechanisms.

Author contribution statement Yuxi Zhang and Cheng Xu wrote the main manuscript text. Zhi Fu and Yaqin Shu prepared Tables 1,2,3, and 4. Changgui Lu and Jie Zhang prepared the Fig. 1 and supplemental info. Xuming Mo was responsible for the accuracy of all content in the proof. All authors reviewed the manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

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