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Association of urinary triclosan and methyl-triclosan levels with predictive indicators of cardiovascular disease and obesity in children and adolescents in 2020 (case study: Kerman, Iran)

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Abstract

Background: Exposure of children and adolescents to endocrine disrupting chemicals (EDCs) causes the development of non-communicable diseases. Triclosan (TCS) is a fat-soluble antimicrobial agent, and methyl-triclosan (MTCS) is the predominant metabolite of TCS. The increasing use of consumables TCS (toothpaste, mouthwash, personal care products) in human has raised concerns about human health.

Methods: The urinary concentrations of TCS and MTCS were measured by GC/MS. Lipid profiles (TG, TC, LDL, and HDL), anthropometric parameters (WC, BMI z-score, and BMI), FBS, SBP, and DBP tests were performed on 79 children and adolescents.

Results: Of 79 people included as the study population, 42 subjects (53.16%) were males. Most of the study population as 32 subjects (40.50%) were obese. The mean concentrations of TCS and MTCS in the obese population were 5.47 ± 2.99 and 2.32 ± 1.04 µg/L, respectively. After adjusting for possible confounding factors, the results showed that a one-unit increase in DBP caused a 0.03 units increase in TCS levels in male subjects ($P=0.01$). A one-unit increase in DBP also caused a 0.02 units increase in MTCS ($P=0.001$). There was a significant relationship between TCS and HDL (OR = 0.90, $P=0.005$), LDL (OR = 1.13, $P=0.01$), and TG (OR =1.05, $P<0.0001$). There was also a significant relationship between MTCS and HDL (OR = 0.88, P = 0.001), LDL (OR = 1.03, $P=0.009$), and TG (OR = 1.04, $P<0.0001$).

Conclusion: According to the results, there is a relationship between TCS, MTCS, and predictive indicators of cardiovascular diseases and obesity.

Keywords: Triclosan, Methyl triclosan, Cardiovascular disease, Obesity, Endocrine disrupter, Children, Adolescent

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Introduction

Childhood obesity has been known as a public health problem in the 21st century. Obesity is known as a risk factor for diseases such as cardiovascular disease and type 2 diabetes. Although the causes of obesity have been widely studied, they are not well-understood yet. Along with the development and use of more chemicals, obesity has increased. Childhood obesity may be associated with the increased exposure to various environmental pollutants in recent years (1-3).

Children due to their behavioral characteristics, weaker immune system, more respiration, are more exposed to environmental pollutants than adults. Exposure of children to environmental pollutants causes the development of non-communicable diseases such as oxidation, the onset of arteriosclerosis, insulin resistance, and diabetes (4).

Despite scientific advances in preventing chronic diseases such as cardiovascular diseases, it is also considered as a leading cause of death in adults (5). Some lifestyle habits can intensify cardiovascular risk factors.

Evidence suggests that factors such as age, sex, lifestyle (such as diet and physical activity), and environmental pollutants can exacerbate predictive indicators of cardiovascular diseases such as high blood pressure, diabetes, and hyperlipidemia (6).

Endocrine disrupting chemicals (EDCs) are used in many products such as personal care products, medicines, sunscreens, and food (7). Previous studies have shown that EDCs interfere with endocrine function such as sex hormones and thyroid hormones. Moreover, these can increase the risk of cardiovascular disease and high blood pressure (8). EDCs such as phthalates, parabens, phenols, and triclosan (TCS) are widely used as human-made chemical compounds (9).

TCS is a fat-soluble antimicrobial agent (10). TCS is used as a disinfectant, preservative in clinical settings (such as surgical scrub), toothpaste, mouthwash, personal care products (hand soap, shampoo, deodorant, detergent, and cosmetics) more than 40 years worldwide. As well, it is applied in home appliance such as cutting boards, kitchen utensils, and textiles; medical facilities such as sutures, catheters, and urethral stents; toys; and building materials (9-11).

Methyl-triclosan (MTCS) is the predominant metabolite of TCS, which is mainly produced by the degradation of TCS through microbial activity by aerobic digestion (12). Due to the high solubility of these two substances in fat, they can accumulate in plants and animals, and then, be transmitted to the human body through the food chain, which eventually causes potentially harmful effects (13). The increasing use of consumables TCS in human has raised concerns about human health (9). TCS exposure mainly occurs through swallowing and skin absorption (14,15). TCS exposure has been found to be related to the risk of asthma, obesity, and cancer in children (16).

TCS can increase the risk of obesity by altering the function of the endocrine system and gastrointestinal microbiomes (5). Several studies have shown that there is a positive relationship between urinary TCS levels and obesity (17). In vivo studies investigating the effect of TCS on liver function in mice, showed that TCS can activate PPARα nuclear receptors to act as a liver tumor stimulant. It should be noted that PPARα is one of the factors affecting lipid metabolism (18).

Many studies related to biomonitoring in human samples have been performed in Iran (19-22). But to date, no studies have been performed on the exposure to TCS and MTCS in children and adolescents in Iran. Moreover, a limited studies have been performed to investigate the association between environmental pollutants (bisphenol A, chlorophenols, and phthalates) and predictors of cardiovascular disease in children and adolescents (3,20,23-25). The present study aimed to measure the concentrations of TCS and MTCS, as well as their relationship with cardiometabolic risk factors and obesity in children and adolescents in Kerman, Iran.

Materials and Methods

Study population

This cross-sectional study was conducted on children and adolescents (aged 6 to 18 years) living in Kerman, Iran, in 2020. The inclusion criteria included age between 6 and 18 years, living in Kerman (Iran) for at least one year, having no history of chronic diseases, and no long-term drug use (3,24). As the present study was conducted in the outbreak of coronavirus disease 2019 (COVID-19), in order to be safe from being infected with this disease, the body temperature of the population was checked using a thermometer (Bukan BK8005 digital thermometer). In addition, a history of Coronavirus disease was evaluated. Thereafter, according to the health protocols and after obtaining the consent from the parents to participate in the research, a questionnaire, including demographic information and the exposure factors for TCS and MTCS was completed (24,26,27).

According to standard protocols, physical examinations included measurements of height, weight, waist circumference (WC), and blood pressure (BP) were performed. The weight of people was measured with the least dressed and barefoot using a digital scale (Horizon digital scale model 2003D). Height was measured with a meter (Ronix meter model Rh-9050) in standing position, while three points of the body (back, buttocks, and heels) were tangential to the wall. WC was measured while exhaling and from the deepest part of the waist between chest and pelvis by a meter. The ratio of weight (kg) to square height (m^2) was used for body mass index (BMI) calculation. Subsequently, according to gender and age, z-score BMI was calculated using the WHO AnthroPlus software, and the BP (in mode sitting) was measured using a digital sphygmomanometer with a suitable cuff for children from the right hand (25,28,29).

To perform biochemical experiments on children and adolescents in the fasting state, 2 mL blood samples were taken for examination of triglyceride (TG), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and fasting blood sugar (FBS) using a Hitachi 704 auto-analyzer (Tokyo, Japan) (3,24,30). 10 mL urine was also taken in glass containers; to prevent cross-contamination, the use of plastic equipment in the experiment was prohibited and glass containers were used instead, and then, stored at -24°C (31,32). The random creatinine was measured by a Hitachi 704 automatic analyzer (Tokyo, Japan) (3,24).

Sample preparation and TCS and MTCS measurement

The urine samples melted at room temperature. Subsequently, about 2 mL of hydrochloric acid was added to 5 mL of the urine sample, which was then placed in the water bath for 90 minutes at 80°C. After cooling the sample

at the lab temperature, 1 mL methyl tert-butyl ether was added, and then, placed in a shaker for 5 minutes. It was then added to the dried vial of 100 µL hexane and was extracted using dispersive liquid-liquid microextraction (33).

Afterwards, 5 µL of N-trimethylsilyl-N-methyl trifluoroacetamide derivative was added eventually, 1 µL of this solution was injected (splitless) into Gas chromatography–mass spectrometry (GC-MS). Helium gas with a purity of 99.999% and flow rate of 1 mL/min was used as the gas carrier. The source and quadruple temperatures were kept at 230 and 150°C, respectively (3,34,35).

Statistical analysis

Data were analyzed using statistical software STATA (version 12). An independent *t* test was used to compare the means of the obtained data. Univariate and multiple linear regression analyses were used to investigate the relationship among variables (age, use of cosmetics, and physical activity) and the concentrations of TCS and MTCS in the whole population. Multiple logistic regression was performed to estimate the contribution of pollutant concentrations to obesity by eliminating potential confounders.

Results

Table 1 shows demographic characteristics of the studied population. As shown in this table, in the studied population, 42 subjects were males. The most studied population were in the age range of 6 to 11 years (62.2%) and this difference was significant ($P=0.05$).

Table 2 shows the mean concentration of urinary metabolites of TCS based on the individuals' weight. The majority of the population as 32 subjects (40.50%) were obese. The mean concentration of TCS in obese subjects was 5.47 ± 2.99 µg/L. The mean concentration of

Table 3 shows the multiple linear regression analysis, the association of the analytes concentration with age, physical activity, and the use of cosmetics in male and female subjects. The level of TCS in the male subjects who were using cosmetics was 0.83 units higher than those male subjects who did not use cosmetics ($P=0.02$).

Tables 4 indicates the regression coefficient and P-value for clinical variables including lipid profiles (TG, TC, LDL, and HDL), anthropometric parameters (WC, BMI z-score, and BMI), FBS, systolic blood pressure (SBP), and diastolic blood pressure (DBP) in two crude and adjusted models. The adjustment for each variable was made by age, gender, physical activity, use of cosmetics, and other variables presented in Table 4, including WC, BMI z-score, BMI, SBP, DBP, FBS, HDL, LDL, TC, and TG.

In the adjusted model, a one-unit increase in BMI

Table 1. Distribution of variables according to gender

Variables	Male No. (%)	Female No. (%)	*P* value
Age groups (y)			
6-11	17 (40.5)	23 (62.2)	0.05
12-18	25 (59.5)	14 (37.8)	
Mean ± SD	11.82 ± 3.71	10.5 ± 3.97	0.13
Smoker family			
Non-smokers	33 (78.6)	31 (83.8)	0.55
Smokers	9 (21.4)	6 (16.2)	
Father's education			
Illiterate	6 (14.3)	5 (13.5)	
Non-academic	32 (76.2)	28 (75.7)	1.00
Academic	4 (9.5)	4 (10.8)	
Mother's education			
Illiterate	3 (7.1)	4 (10.8)	
Non-academic	31 (73.8)	24 (64.9)	0.71
Academic	8 (19.0)	9 (24.3)	
Household income (US$/month)			
≤599	24 (57.1)	23 (62.2)	0.77
≥600	18 (42.9)	14 (37.8)	
Physical activity			
Low	10 (23.8)	9 (24.3)	
Moderate	10 (23.8)	20 (54.1)	0.008
High	22 (52.4)	8 (21.6)	
Cosmetic consumption			
Yes	21 (50.0)	21 (56.8)	0.54
No	21 (50.0)	16 (43.2)	
The number of baths per week			
≤ 2	19 (45.2)	21 (56.8)	0.30
≥ 3	23 (54.8)	16 (43.2)	

Table 2. Mean concentration of triclosan urinary analytes according to weight status

Analytes concentration (µg/L)	Total (n=79)	Underweight and Normal (n=31)	Overweight (n=16)	Obese (n=32)	*P* value
TCS	4.62 ± 2.08	3.81 ± 0.54	4.46 ± 2.08	5.47 ± 2.99	<0.0001
MTCS	1.91 ± 0.88	1.42 ± 0.52	1.91 ± 0.88	2.32 ± 1.04	<0.0001

MTCS in obese subjects was 2.32 ± 1.04 µg/L.
Data are expressed as mean ± SD.

Table 3. Association between variables and concentration of urinary analytes (µg/L)

Variable	TCS (µg/L)				MTCS (µg/L)			
	Male subjects		Female subjects		Male subjects		Female subjects	
	β	*P* value	β	*P* value	β	*P* value	β	*P* value
Age (year)								
6-11	Ref	-	-	-	Ref	-	-	-
12-18	0.09	0.79	1.01	0.34	0.07	0.72	0.64	0.11
Physical activity[a]								
Low	Ref	-	-	-	Ref	-	-	-
Moderate	0.01	0.97	0.53	0.62	0.11	0.67	0.03	0.94
High	0.46	0.27	0.01	0.99	0.23	0.31	0.12	0.81
Cosmetic consumption								
No	Ref	-	-	-	Ref	-	-	-
Yes	0.83	0.02	0.10	0.91	0.23	0.24	0.28	0.44
	$R^2=0.21$		$R^2=0.09$		$R^2=0.15$		$R^2=0.15$	

[a] Physical activity: Low = less than 5 minutes, moderate = 5 to 30 minutes, high = more than 30 minutes.

Table 4. The effect of the studied variables on triclosan and methyl-triclosan

Variable	TCS (µg/L)			MTCS (µg/L)		
	Total	Female subjects	Male subjects	Total	Female subjects	Male subjects
	β	β	β	β	β	β
BMI (kg/m^2)						
Crude	0.26*	0.31*	0.17*	0.11*	0.13*	0.08*
Adjusted[a]	0.80*	1.03*	0.33*	0.22*	0.24*	0.10
BMI z-score						
Crude	0.48*	0.66*	0.23*	0.24*	0.33*	0.12*
Adjusted	-1.33*	-2.13*	-0.64*	-0.22*	-0.32*	-0.04
WC (cm)						
Crude	0.009	0.01	0.01	0.005	0.00	0.009
Adjusted	0.03*	-0.02	-0.01	-0.007	-0.02	0.003
SBP (mm Hg)						
Crude	-0.002	0.003	-0.003	0.001	-0.003	0.005
Adjusted	-0.01	0.003	-0.03	-0.01	-0.02*	0.001
DBP (mm Hg)						
Crude	-0.01	-0.02	0.003	0.005	0.009	0.005
Adjusted	0.02	0.00	0.03*	0.02*	0.04*	0.01
FBS (mg/100 mL)						
Crude	-0.03	-0.03	-0.02	-0.006	-0.008	0.004
Adjusted	0.01	-0.01	0.01	0.01	0.01	0.01
TC (mg/100 mL)						
Crude	0.003	0.006	-0.005	0.00	0.001	-0.004
Adjusted	0.006	-0.004	0.002	-0.002	-0.005	-0.004
HDL (mg/100 mL)						
Crude	-0.04*	-0.04	-0.04*	-0.02*	-0.02	-0.01
Adjusted	0.01	0.009	-0.01	0.01	0.01	0.01
LDL (mg/100 mL)						
Crude	0.03*	0.02*	0.03*	0.01*	0.01*	0.01*
Adjusted	-0.02*	0.01	0.005	-0.002	0.006	-0.005
TG (mg/100 mL)						
Crude	0.01*	0.01	0.01*	0.006*	0.01*	0.005*
Adjusted	-0.005	-0.01*	0.003	-0.001	0.001	0.001

[a] Adjusted by diastolic blood pressure (DBP), systolic blood pressure (SBP), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), total cholesterol (TC), fasting blood sugar (FBS), waist circumference (WC), body mass index (BMI), physical activity, age, and use of cosmetics.

* Statistical significant level is considered at P =0.05.

caused an increase of 0.80 units in the TCS of the study population. A one-unit increase in the WC caused an increase of 0.03 units in the TCS of the study population. A one-unit increase in DBP led to an increase of 0.03 units in the TCS levels in the male subjects. A one-unit increase in LDL caused a reduction of 0.02 in the level of TCS in the study population. A one-unit increase in TG also caused a 0.01 units reduction in the level of TCS in the female subjects. A one-unit increase in BMI caused the level of MTCS in the female subjects and in the study population to be increased by 0.24 and by 0.22 units, respectively. A one-unit increase in SBP caused a 0.02 units reduction in the level of MTCS in the female subjects. A one-unit increase in DBP caused a 0.02 units increase in the level of MTCS in the study population.

Table 5 indicates the association between the analytes and the studied variables. The results are shown based on the logistic regression (with a 95% confidence interval) in the three tertile and odds ratio (OR) in crude and adjusted forms in three models (model 1: Crude; model 2: Adjusted for age and gender; and model 3: Adjusted for age, physical activity, use of cosmetics, and other variables (DBP, SBP, LDL, HDL, TG, TC, FBS, WC, and BMI). The first tertile was considered as a reference for all analyses

In model 2, for a one-unit increase in HDL, the odds of TCS was 0.92 higher in the second tertile compared to the first tertile, and for a one-unit increase in HDL, the odds of TCS was 0.90 higher in the third tertile compared to the first tertile. Additionally, for a one-unit increase in LDL, the odds of TCS was 1.07 higher in the second tertile compared to the first tertile, and for a one-unit increase in LDL, the odds of TCS was 1.10 higher in the third tertile compared to the first tertile. In model 3, for a one-unit increase in LDL, the odds of TCS was 1.13 higher in the

Table 5. Association between a urinary concentration of analytes, and predictors of cardiovascular risk factors

Variable	TCS[a] (µg/L)		MTCS[b] (µg/L)	
	Tertile 2[c] OR (95% CI)	Tertiles 3 OR (95% CI)	Tertile 2 OR (95% CI)	Tertiles 3 OR (95% CI)
SBP (mm Hg)				
Model 1[d]	1.03 (0.97-1.08)	0.97 (0.91-1.02)	1.04 (0.98-1.10)	1.00 (0.94-1.05)
Model 2	1.03 (0.97-1.09)	0.97 (0.92-1.02)	1.04 (0.98-1.10)	1.00 (0.95-1.06)
Model 3	1.02 (0.93-1.12)	0.95 (0.84-1.07)	1.12 (0.98-1.29)	0.94 (0.83-1.07)
DBP (mm Hg)				
Model 1	1.02 (0.96-1.08)	0.96 (0.90-1.03)	1.05 (0.98-1.12)	1.02 (0.95-1.09)
Model 2	1.02 (0.96-1.09)	0.95 (0.89-1.02)	1.05 (0.98-1.12)	1.01 (0.94-1.08)
Model 3	1.00 (0.90-1.11)	0.97 (0.83-1.14)	1.06 (0.93-1.22)	1.19 (1.00-1.41)*
HDL (mg/100 mL)				
Model 1	0.93 (0.88-0.99)*	0.92 (0.87-0.98)*	0.93 (0.88-0.99)*	0.90 (0.85-0.97)*
Model 2	0.92 (0.86-0.98)*	0.90 (0.84-0.96)*	0.92 (0.85-0.98)*	0.88 (0.81-0.95)*
Model 3	0.99 (0.89-1.10)	1.02 (0.88-1.19)	0.88 (0.77-1.01)	0.99 (0.84-1.16)
LDL (mg/100 mL)				
Model 1	1.06 (1.02-1.11)*	1.09 (1.04-1.14)*	1.00 (0.97-1.03)	1.03 (1.00-1.06)
Model 2	1.07 (1.02-1.11)*	1.10 (1.05-1.15)*	1.01 (0.98-1.04)	1.03 (1.00-1.07)*
Model 3	1.04 (0.97-1.12)	1.13 (1.02-1.24)*	0.99 (0.92-1.06)	1.08 (0.99-1.18)
TG (mg/100 mL)				
Model 1	1.03 (1.00-1.05)*	1.04 (1.02-1.07)*	1.02 (1.00-1.04)*	1.03 (1.01-1.06)*
Model 2	1.03 (1.00-1.05)*	1.05 (1.02-1.07)*	1.02 (1.00-1.04)*	1.04 (1.02-1.06)*
Model 3	1.02 (0.99-1.05)	1.04 (1.00-1.08)*	0.98 (0.95-1.02)	1.03 (0.98-1.07)
TC (mg/100 mL)				
Model 1	0.99 (0.97-1.01)	1.01 (0.99-1.03)	0.99 (0.97-1.01)	0.99 (0.97-1.01)
Model 2	0.99 (0.97-1.01)	1.01 (0.99-1.03)	0.99 (0.97-1.01)	0.99 (0.97-1.01)
Model 3	0.99 (0.95-1.02)	1.05 (0.99-1.11)	1.02 (0.98-1.07)	0.97 (0.93-1.02)
FBS (mg/100 mL)				
Model 1	0.98 (0.92-1.04)	1.00 (0.99-1.00)	1.01 (0.93-1.09)	0.97 (0.90-1.05)
Model 2	0.97 (0.91-1.04)	1.00 (0.99-1.00)	1.00 (0.98-1.01)	0.98 (0.92-1.05)
Model 3	0.97 (0.88-1.07)	1.00 (0.98-1.01)	1.04 (0.93-1.17)	1.03 (0.89-1.18)

[a] The studied data were divided into three parts based on the variable TCS.
[b] The studied data were divided into three parts based on the variable MTCS.
[c] Tertile 1 is referenced.
[d] Model 1: OR (95 % CI), crude, Model 2: OR (95 % CI), age and gender-adjusted, Model 3: OR (95 % CI), multivariate-adjusted (adjusted by DBP, SBP, LDL, HDL, TG, TC, FBS, WC, BMI, age, cosmetics use, and physical activity).
*Statistical significant level is considered at $P=0.05$.

third tertile compared to the first tertile.

In model 2, for a one-unit increase in TG, the odds of TCS was 1.03 higher in the second tertile compared to the first tertile, and for a one-unit increase in TG, the odds of TCS was 1.05 higher in the third tertile compared to the first tertile.

In model 3, for a one-unit increase in TG, the odds of TCS was 1.04 higher in the third tertile compared to the first tertile. In model 3, for a one-unit increase in DBP, the odds of MTCS was 1.19 higher in the third tertile compared to the first tertile.

In model 2, for a one-unit increase in HDL, the odds of MTCS was 0.88 higher in the third tertile compared to the first tertile. In model 2, for a one-unit increase in LDL, the odds of MTCS was 1.03 higher in the third tertile compared to the first tertile. In model 2, for a one-unit increase in TG, the odds of MTCS was 1.04 higher in the third tertile compared to the first tertile.

Discussion

The present study showed that the male subjects who use cosmetics have higher levels of TCS in their urine samples than those male subjects who do not use cosmetics. Harley et al in an interventional study using TCS-free personal care products reported that if TCS-free products are used, the concentration of TCS in the urine sample would be reduced by 35.7% (36). The results of a study by Stacy et al showed that TCS levels were higher among children who used soap containing TCS than those who did not. Furthermore, the percentage of TCS increased along with the increasing number of hand washes. Additionally, the consumption of toothpaste among children was shown to have a positive association with the level of TCS (37).

In the present study, the mean concentrations of TCS and MTCS were higher in obese people ($P<0.001$). A study by Deierlein et al showed that along with increasing TCS concentrations, the rate of obesity also increases (17). Endocrine-disrupting chemicals, even at low concentrations, interfere with the body's function to produce, secrete, and transport hormones (38). Endocrine dysfunction can consequently lead to obesity, diabetes, and cardiovascular diseases. Estrogen receptors are known as one of the most important and influential parameters in glucose metabolism. EDCs attack these receptors, causing changes in glucose homeostasis and the mechanism of insulin secretion (39). TCS is structurally similar to human estrogens, because its exposure to TCS disrupts estrogen receptors and increases the risk of obesity (16,40-42).

The present study showed an association between TCS, MTCS, BMI, and BMI z-score. A study by Lankester et al showed that along with increasing urinary TCS, BMI increases (27). EDCs alter the endocrine system by altering the hemostatic mechanisms of weight control (43). Since the most EDCs such as TCS and MTCS are lipophilic (44), they may be stored in adipose tissue. In this regard, obesity and its complications can also delay metabolism or increase the lifespan of EDCs, which ultimately lead to an increase in the levels of blood and urine samples (45). Due to the high solubility of TCS and MTCS in fat, they can biologically accumulate in plants and animals, and then, be transmitted to the human beings' body through the food chain (13). TCS, as a chemical that disrupts the endocrine system, can increase the risk of obesity by disrupting the endocrine system or even by altering the gut flora (5).

The present study showed an association between TCS, MTCS, and lipid profiles (TC, TG, HDL, and LDL). EDCs disrupt the metabolism of hepatic fatty acids, which in turn can affect the lipid concentration of the circulatory profile. TCS can also activate nuclear receptors and PPARα to act as a liver tumor stimulant. Notably, PPARα affects fat metabolism (18).

The present study also showed an association between TCS, MTCS, SBP, and DBP. In the research by Liu et al on the biological monitoring of TCS in pregnant women, the results showed that TCS has a weak inverse relationship with DBP (46).

The effect of EDCs on BP can be resulted from binding to nuclear receptors, interfering with the functions of sex hormones and thyroid (46). Steroid hormones are involved in regulating an extended range of body processes, including regulating BP. Estrogen, progesterone, and testosterone receptors in blood vessels stimulate endothelium-dependent mechanisms, in order to relax blood vessels and inhibit vascular smooth muscle contraction mechanisms (47). TCS can impair the functions of sex hormone and thyroid hormones (48-50). However, it can be assumed that these chemicals may change BP levels (46).

In the present study, no significant relationship was found between TCS, MTCS, and FBS. EDCs can interfere with insulin secretion and function and other pathways that regulate glucose homeostasis (51). Several studies have shown that TCS can increase blood glucose, triglyceride, and cholesterol levels (52). Estradiol was also found to be associated with changes in body glucose homeostasis. It has recently been shown that estradiol cell failure, which was long considered as a simple sex hormone, can play an effective role in advancing prediabetes diseases to type 2 diabetes, and has a significant impact on the function of the cardiovascular system (53).

Moreover, it can play an effective role in advancing prediabetes diseases to type 2 diabetes. TCS is an EDCs, which can cause estrogen, androgen, and thyroid dysfunctions (40,52). Peripheral estrogens or xenoestrogens may also play a role in the etiology of type 2 diabetes, which can profoundly affect the normal metabolism of insulin as well as the function of beta cells. As a result, environmental estrogens or xenoestrogens may play a role in type 2 diabetes (53). However, in this

study, no significant relationship was found between TCS, MTCS, and FBS.

Study Limitations and Strengths

The limitations of the present study were its cross-sectional nature and the fact that individuals may metabolize these chemicals differently. Also, it is not clear whether a single measurement reflects the long-term exposure to these analyses. Therefore, as a result, causal relationships cannot be shown well. In this study, only TCS and MTCS were studied, while several EDCs can be effective in predicting cardiovascular diseases and obesity as well as influencing each other.

On the other hand, the present study investigated TCS and MTCS among sensitive groups (children and adolescents). To the best of our knowledge, no study has been conducted on the association between TCS, MTCS, and predictive indicators of cardiovascular diseases and obesity in children and adolescents in Iran up to now. Given the widespread use of TCS as a preservative in personal care products and detergents, this study could be considered as an alarm for stricter rules to reduce the use of TCS in consumer products in developing countries, especially in Iran.

Conclusion

The present study showed a significant relationship between urinary TCS and MTCS levels and predictive indicators of cardiovascular diseases and obesity in children and adolescents. Due to the prevalence of obesity and chronic diseases, and by considering the origin of chronic diseases from early lifetime, environmental pollution control should be considered as a health priority to prevent the spread of contagious diseases. However, due to the cross-sectional nature of this study and failure to investigate causal reasons, such findings should be reviewed in future prospective studies with a larger sample size.

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Ethical issues

All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee.

Competing interests

The authors declare that they have no conflict of interests.

Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by MH, HN, MM, and KE. The first draft of the manuscript was written by HN and all authors commented on the previous versions of the manuscript. All authors read and approved the final manuscript. Conceptualization was performed by MH and HN; Methodology by KE; Formal analysis and investigation by MM; Writing-original draft preparation by HN; Writing-review and editing by MH, MM, KE, and HN; Funding acquisition by Kerman University of Medical Sciences; Resources by HN; Supervision by MH and MM.

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