**RESEARCH ARTICLE** 



# Association of urinary triclosan, methyl triclosan, triclocarban, and 2,4-dichlorophenol levels with anthropometric and demographic parameters in children and adolescents in 2020 (case study: Kerman, Iran)

Habibeh Nasab<sup>1,2</sup> · Saeed Rajabi<sup>1,3</sup> · Moghaddameh Mirzaee<sup>4</sup> · Majid Hashemi<sup>1,2</sup>

Received: 11 November 2021 / Accepted: 29 December 2021 / Published online: 7 January 2022 © The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2022

#### Abstract

Endocrine-disrupting chemicals (EDCs) can be a major risk factor for noncommunicable illnesses, especially when children are exposed to them. The purpose of this study was to assess the urine concentrations of triclosan (TCS), methyl triclosan (MTCS), triclocarban (TCC), and 2,4-dichlorophenol (2,4-DCP) and its association with anthropometric and demographic parameters in children and adolescents aged 6–18 living in Kerman, Iran, in 2020. A GC/MS instrument was used to measure the concentrations of the analytes. TCS, MTCS, TCC, and 2,4-DCP geometric mean concentrations ( $\mu g/L$ ) were  $4.32 \pm 2.08$ ,  $1.73 \pm 0.88$ ,  $4.66 \pm 10.25$ , and  $0.19 \pm 0.14$ , respectively. TCS, MTCS, TCC, and 2,4-DCP were shown to have a positive and significant association with BMI *z*-score and BMI (*p*-value < 0.01). TCS and MTCS have a positive, strong, and substantial association (*p*-value < 0.01, *r*=0.74). There was no significant association between the waist circumference (WC) and the analytes studied. In addition, there was a close association between analyte concentration and demographic parameters (smoking, education, income, etc.) overall. In Kerman, Iran, the current study was the first to look into the association between TCS, MTCS, TCC, 2,4-DCP, and anthropometric parameters in children and adolescents are shown to have a significant association in this study. However, because the current study is cross-sectional and it is uncertain if a single experiment accurately reflects long-term exposure to these analytes, more research is needed to determine the impact of these analyses on the health of children and adolescents.

Keywords Endocrine-disrupting chemicals · Obesity · Body mass index · Children · Adolescent · Demographic factors

Responsible Editor: Lotfi Aleya

Majid Hashemi mhashemi120@gmail.com; ma.hashemi@kmu.ac.ir

- <sup>1</sup> Environmental Health Engineering Research Center, Kerman University of Medical Sciences, Kerman, Iran
- <sup>2</sup> Department of Environmental Health Engineering, Faculty of Public Health, Kerman University of Medical Sciences, Kerman, Iran
- <sup>3</sup> Department of Environmental Health Engineering, School of Health, Shiraz University of Medical Sciences, Shiraz, Iran
- <sup>4</sup> Modeling in Health Research Center, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran

## Introduction

Obesity is characterized as abnormal or excessive fat accumulation in adipose tissue (Martens et al. 2017). Obesity indices include body mass index (BMI) and waist-to-hip ratio (WHR) (Yousefi et al. 2018, 2019). The global prevalence of juvenile obesity has risen considerably (Friedemann et al. 2012; Skinner et al. 2015), and a global trend has been noticed, prompting greater worry in this age range (Martens et al. 2017). Approximately 4% of children and adolescents (2 to 19 years old) were extremely obese between 1999 and 2004. In 2011–2012, this amount grew by 6% (Skinner et al. 2015; Amin et al. 2018b). To put it another way, one out of every six children and adolescents is presently fat. Although obesity has a hereditary component, current epidemics cannot be attributed to genetic alterations in the population since the human genome has not altered in such a short period. Environmental contaminants, without a doubt, are a major contributor to the rise in obesity as a risk factor for noncommunicable illnesses (Zarean and Poursafa 2019; Amin et al. 2019b).

Today, the concerns of human societies regarding the types of diseases related to environmental factors are increasing. Environmental risk factors such as pollution, water, air, soil, exposure to chemicals are involved in causing a variety of diseases (Yousefi et al. 2018). Environmental chemicals may be a major motivator for a variety of illnesses, especially in children, and these compounds may interact with genetic and epigenetic systems, affecting the body's natural growth (Zarean and Poursafa 2019; Amin et al. 2018d). EDCs are substances that affect endocrine function and are among these pollutants (Kolšek et al. 2015; Vela-Soria et al. 2014).

EDCs have the potential to alter the body's normal hormones. The effects of these substances on steroid and thyroid hormone function, as well as the activation of peroxisome proliferator-activated receptors (PPARs), are important in fat cell differentiation and energy storage and can be used as biological mechanisms for the association between obesity and EDCs (Amin et al. 2018c; Wang and Tian 2015; Hashemi et al. 2021). Triclocarban (TCC), 2,4-dichlorophenol (2,4-DCP), and triclosan (TCS) and its metabolites, such as methyl triclosan (MTCS), are examples of EDCs (Baumann et al. 2010; Karzi et al. 2018; Lv et al. 2013; Zhang et al. 2020).

TCS (2,4,4-trichloro-2-hydroxy diphenyl ether) and TCC (3,4,4-trichlorocarbanilide) are used as antimicrobials and preservatives in a variety of personal care products, including soaps, detergents, shampoos, hair conditioners, shaving creams, kinds of toothpaste, mouthwashes, deodorants and antiperspirants, cosmetics, laundry detergents, fabric softeners, acne medications, and trash cans (Dhillon et al. 2015; Giuliano and Rybak 2015; Karzi et al. 2018; Li et al. 2015; Montaseri and Forbes 2016; Yueh and Tukey 2016). TCC is a common ingredient in antibacterial soaps (Hinther et al. 2011). MTCS, a triclosan metabolite, is mostly generated when the hydroxyl group in triclosan is replaced with methoxy (Li et al. 2020; Wang et al. 2019).

2,4-DCP is a lipophilic chlorinated phenol from the phenoxy acetic acid herbicide family that is frequently utilized in the production of herbicides and insecticides (Exon et al. 1984; Magnoli et al. 2020; Zhang et al. 2018). Excessive doses of herbicides are frequently employed due to weed resistance, resulting in biological buildup even with shortterm exposure (Magnoli et al. 2020).

2,4-DCP can be generated by the deformation of pesticides, primarily phenoxy herbicides like 2,4-dichlorophenoxyacetic acid, as well as antibacterial and antifungal chemicals like triclosan, which is also a byproduct of municipal drinking water and industrial effluent chlorination (Bukowska et al. 2016; Ye et al. 2014). Because of these chemicals' lipophilic characteristics, if they reach the environment, they can accumulate in the bodies of plants and animals, eventually entering the food chain and endangering health (Ding et al. 2020; Exon et al. 1984; Yueh and Tukey 2016; Parastar et al. 2018).

TCS has a detrimental influence on the endocrine system's functioning, such as thyroid and sex hormone balance, according to in vivo research and also exposure to it has been associated with childhood asthma, cancer risk, and obesity (Iyer et al. 2018). TCS and BMI have been found to have a positive association, according to research (Lankester et al. 2013). MTCS can significantly alter the transcription of HepG2 hepatocytes (Baumann et al. 2010).

TCC has been shown to affect the function of sex hormones and the thyroid in studies and also has an effect on glycolipid metabolism in the rat liver (Dong et al. 2019; Schultz et al. 2012; Wang et al. 2013). Pesticides have a variety of negative consequences for a child's development, including neurological and metabolic issues including diabetes and obesity (Buser et al. 2014). 2,4-DCP has the potential to produce genetic activity, mutagenicity, function as a cancer promoter, and alter estrogen receptor expression (Exon et al. 1984; Ma et al. 2012). These chemicals enter the body by ingesting and skin adsorption, and traces of them have been found in urine and blood. As a result, urine is an essential biomonitoring technique for determining and evaluating EDC exposure (Braun 2017; Giuliano and Rybak 2015; Park et al. 2019).

Some Iranian research, such as Hashemi et al. (Amin et al. 2019a) and Amin et al. (Amin et al. 2018c) looked at the association between environmental contaminants (phthalate, bisphenol A) and anthropometric characteristics. The research's results revealed a significant association between bisphenol A and phthalate concentrations and gender, BMI *z*-score, BMI, WC, and age. However, no research on TCS, MTCS, TCC, or 2,4-DCP exposure in Iranian children and adolescents has been conducted, too, yet. The goal of this study was to determine the concentrations of TCS, MTCS, TCC, and 2,4-DCP in children and adolescents in Kerman, Iran, as well as their association to anthropometric parameters and demographic factors.

## **Materials and methods**

### **Study population**

The current study, a cross-sectional questionnaire, was performed in 2020 on 79 children and adolescents (6–18 years old) residing in Kerman, Iran. Kerman University of Medical Sciences' ethical committee has authorized this study (IR. KMU.REC.1399.258). Children and adolescents (6–18 years old) were sampled in Kerman-based labs. The participants had to be between the ages of 6 and 18, have no chronic disease or coronavirus (COVID-19), and have resided in Kerman for at least a year. Noncooperation at all phases of the project was a criterion for exclusion.

The parents first notified the children and adolescents about the research's goals, after which, they filled the consent form. The level of exposure to TCS, MTCS, TCC, and 2,4-DCP should be assessed in the participants using a structured questionnaire comprising demographic information, lifestyle factors such as the use of various personal care products, the number of baths per week, and the amount of physical activity of children and adolescents throughout the week completed by parents.

Anthropometric data such as height and weight and WC were measured tangential to the wall using a shoeless meter; weight was computed using the Seka digital scale when the individual was least clothed and barefoot; WC (cm) was measured using an expiratory meter, and the distance between the chest and the pelvis was measured from the deepest portion, and BMI was calculated using the formula of weight (kg) divided by square height (m<sup>2</sup>). The WHO AnthroPlus software was used to compute the BMI z-score for children and adolescents based on their age and gender. The BMI z-score is used to compare BMI under the same conditions and to determine how much a data point deviates from the average in terms of your criteria. Based on the growth charts provided by the Centers for Disease Control and Prevention (CDC) for children and adolescents, the BMI status of this age group from the percentiles used by this committee includes the following: underweight < 5th percentile; normal or healthy weight: 5th percentile to less than the 85th percentile; overweight: 85th to less than the 95th percentile; and obese: 95th percentile or greater (Amin et al. 2018b).

#### **Sample preparation**

Researchers mentioned the process of analyzing urine samples in a prior study, and it is briefly detailed here (Nasab et al. 2021). Urine samples were kept at -20 °C in sealed 15-mL Falcon glass vials until the experiment. The Jaffe technique and a Hitachi 704 auto-analyzer were used to quantify random creatinine.

Five milliliters of urine was extracted using the dispersive liquid–liquid microextraction (DLLME) technique to assess TCS, MTCS, TCC, and 2,4-DCP concentrations. After that, the extracted material was transferred to a dedicated gas chromatography (GC) vial, where  $5 \,\mu$ L of MSTFA derivative was added. It was then heated for 1 h at 50 °C before being injected into an Agilent (USA) Model 7890 gas chromatography-mass system fitted with an MS Detector Model 5975

in Split/Spitless mode. According to Table 1, the selected ions with the greatest frequency were chosen to enhance the sensitivity of the device and provide a more accurate analysis of the analytes using the selected ion monitoring (SIM) mode (Amin et al. 2018a).

The carrier gas was 99.99% pure helium with a flow rate of 1 mL/min. Various temperature schemes for the column and carrier gas intake velocities were utilized to achieve the optimum separation and segregation between the acquired chromatogram peaks.

#### Statistical analysis

For statistical evaluation of the data, concentrations below the detection limit (LOD) were considered half of the LOD (Amin et al. 2018b). SPSS software was used to analyze the data. The means were compared using an independent *t*-test. The association between TCS, MTCS, 2,4-DCP, and TCC and the examined factors was investigated using univariate and multiple linear regression analysis. By reducing possible confounders, linear and multivariate regression analyses were performed to evaluate various TCS, MTCS, 2,4-DCP, and TCC with anthropometric and demographic parameters.

## Results

According to the descriptive data in Table 2, 42 of the 79 children and adolescents evaluated were boys. The majority of the participants in the research were youngsters aged 6 to 11 (50.6%). Boys were more physically active than girls, with a significant difference (*p*-value = 0.008), according to the findings.

Table 3 investigates the association between analyte concentrations ( $\mu$ g/L) and demographic variables in both girls and boys. According to the findings, the MTCS rate in girls exposed to secondhand smoke was 0.98 higher than that of nonexposed girls, while the TCS rate in boys whose parents had a college degree was 1.80 and 2.27 points higher than that of other boys. Furthermore, the TCC rate in boys with greater family income was 1.42 points lower than in boys with low income.

 Table 1
 Selection of main ions for the quantitative analysis of analytes

Analyte	Quantification ion $(m/z)$
3,4,4-Trichlorocarbanilide	302, 253, 219, 198, 174, 161
2,4-Dichlorophenol	
Triclosan	
Methyl triclosan	

Table 2 I	Distribution	of variables	according to	gender
-----------	--------------	--------------	--------------	--------

Variables	Boys <i>n</i> (%)	Girls $n$ (%)	All $n$ (%)	<i>p</i> -value
Age groups				
6-11 years	17 (40.5)	23 (62.2)	40 (50.6)	0.05
12-18 years	25 (59.5)	14 (37.8)	39 (49.4)	
Smoker family				
Nonsmokers	33 (78.6)	31 (83.8)	64 (81.0)	0.55
Smokers	9 (21.4)	6 (16.2)	15 (19.0)	
Father's educat	ion			
Illiterate	6 (14.3)	5 (13.5)	11 (13.9)	1.00
Nonacademic	32 (76.2)	28 (75.7)	60 (75.9)	
Academic	4 (9.5)	4 (10.8)	8 (10.1)	
Mother's education	n			
Illiterate	3 (7.1)	4 (10.8)	7 (8.9)	0.71
Nonacademic	31 (73.8)	24 (64.9)	55 (69.6)	
Academic	8 (19.0)	9 (24.3)	17 (21.5)	
Household income	e (US \$/month)	1		
≥ 599	24 (57.1)	23 (62.2)	47 (59.5)	0.77
$\leq 600$	18 (42.9)	14 (37.8)	32 (40.5)	
Physical activity <sup>1</sup>				
Low	10 (23.8)	9 (24.3)	19 (24.1)	0.008
Moderate	10 (23.8)	20 (54.1)	30 (38.0)	
High	22 (52.4)	8 (21.6)	30 (38.0)	

<sup>1</sup>Physical activity: low=less than 5 min, moderate=5 to 30 min, high=more than 30 min

The geometric mean concentrations of urine analytes TCS, MTCS, TCC, and 2,4-DCP in the two age groups of 6–11 and 12–18 years, with and without creatinine adjustment, are shown in Table 4. The geometric mean concentration of triclosan ( $\mu$ g/g.cr) in girls aged 6–11 years (6.86 ± 5.37) was greater than girls aged 12–18 years (4.21 ± 1.09) (*p*-value = 0.03), whereas the geometric mean concentration of triclosan ( $\mu$ g/g.cr) in boys aged 12–18 years (4.36 ± 1.02) was higher than boys aged 6–11 years (3.95 ± 1.43) (*p*-value = 0.03). In addition, boys and girls aged 6–11 years had a higher mean BMI *z*-score than boys aged 12–18 years (4.21–18 years (*p*-value = 0.02). All of the participants had TCS, MTCS, TCC, and 2,4-DCP pollutants.

Table 5 displays the results of correlations between the analytes ( $\mu g/L$ ) and other factors (age, sex, WC, BMI, and BMI *z*-score). The association between TCS and MTCS and BMI was found to be significant. Between TCC and 2,4-DCP and BMI, there was a moderate mean positive association. There was also a positive and significant association (*p*-value = 0.01) between all analytes, which was with the highest correlation (*p*-value = 0.01, *r*=0.74) between TCS and MTCS.

The association between the concentration of analytes ( $\mu$ g/L) examined with the BMI *z*-score and WC is shown in Table 6. This association was investigated using

univariate and multivariate regression models (adjusted for gender, age, and physical activity). According to Table 6 in model 2 (adjusted for age, gender, and physical activity), a unit increase in BMI *z*-score raises the TCS by 0.58 units, the MTCS by 0.28 units, the TCC by 0.49 units (*p*-value < 0.0001), and the 2,4-DCP by 0.02 units (*p*-value = 0.01). Analytes and WC, on the other hand, were shown to have no significant relationship.

The results of Table 7 show the mean concentrations of TCS, TCC, MTCS, and 2,4-DCP ( $\mu$ g/L) according to the weight status of individuals. The number of obese people was more than other people studied (n=32). The mean concentration of all analytes was higher in obese people than other people, and this value was  $5.47 \pm 2.99$  for TCS and  $5.50 \pm 2.20$  for TCC,  $2.32 \pm 1.04$  for MTCS, and  $0.29 \pm 0.13$  for 2,4-DCP.

#### Discussion

EDCs have an impact on the onset and progression of obesity. These substances, known as environmental fatteners, disrupt lipid metabolism and cause the body to accumulate fat inefficiently. By activating nuclear receptors, environmental fatteners promote fat cell development from stem cells. They can attach to particular receptors in the target cell and inhibit cell signaling by blocking signals in the body, similar to the body's endogenous hormones, such as sex and thyroid hormones in the human body (Buser et al. 2014; Kabir et al. 2015; Chavoshani et al. 2020a).

Because most EDCs are highly lipophilic and may be stored in adipose tissue, increased levels of these chemicals may imply an association between obesity and their accumulation in the body. Obesity and associated consequences have also been associated with a delay in the metabolism of endocrine-disrupting substances, as well as an increase in their half-life and blood or urine levels (Ribeiro et al. 2020). By altering the endocrine system, these drugs also induce alterations in hemostatic systems (such as adrenal glands, hypothalamus, and pituitary gland) of weight regulation (Grün and Blumberg 2009). TCS may potentially raise the risk of obesity by changing gut flora or causing endocrine disruption (Kalloo et al. 2018a).

The urinary TCS, MTCS, TCC, and 2,4-DCP levels were 4.32, 1.73, 4.27, and 0.19 ( $\mu$ g/L), respectively, as indicated in Table 4. The investigation on the association between anthropometric parameters such as BMI *z*-score and WC (cm) with pollutant concentrations discovered that there is a significant relationship between TCS, MTCS, TCC, and 2,4-DCP ( $\mu$ g/L) concentrations and BMI *z*-score but no significant relationship between WC and pollutant concentrations (Table 6). So, when the association between demographic factors and pollutant levels was evaluated, it was shown that

Table 3	Association	between o	demographic	factors and	concentration	of urinary	y analytes (µ	g/L)
---------	-------------	-----------	-------------	-------------	---------------	------------	---------------	------

Variable	TCS (µg	g/L)		MTCS (µ	g/L)		TCC (µĮ	g/L)		2,4-DCP	(µg/L)	
	Total	Girls	rls Boys	Total	Girls	Boys	Total	Girls	Boys	Total	Girls	Boys
	β	β	β	β	β	β	β	β	β	β	β	β
Age groups												
6-11 years	Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
12-18 years	-0.40	-0.84	0.12	-0.34	-0.65	-0.02	-0.32	-0.39	-0.35	-0.05	-0.05	-0.04
Smoker family												
Nonsmokers	Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
Smokers	-0.72	-1.35	-0.20	-0.45	0.98*	-0.05	-0.30	-1.54	0.54	-0.03	-0.07	0.007
Father's education												
Illiterate	Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
Nonacademic	0.88	0.37	1.30*	0.02	-0.14	0.15	0.06	0.19	-0.04	0.01	-0.04	0.05
Academic	1.10	0.27	1.80*	0.21	0.02	0.36	0.17	0.66	-0.27	0.003	-0.09	0.08
Mother's education	n											
Illiterate	Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
Nonacademic	0.41	-0.48	1.54*	-0.15	-0.38	0.15	-0.70	-0.26	-1.33	-0.01	-0.07	0.08
Academic	2.03*	1.96	2.27*	0.25	0.24	0.30	0.007	0.51	-0.66	-0.03	-0.15	0.11
Household income	e (US \$/mc	onth)										
≥599	Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
$\leq 600$	0.17	0.42	-0.05	-0.007	-0.06	0.01	-0.74	0.13	-1.42*	-0.009	-0.05	0.02
Physical activity <sup>a</sup>												
Low	Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
Moderate	0.58	0.74	0.15	0.03	0.12	-0.09	-0.48	-0.48	-0.49	-0.03	-0.07	0.02
High	0.27	0.23	0.34	-0.01	0.43	-0.20	-0.45	-0.71	-0.36	-0.02	-0.06	-0.03

<sup>a</sup>Physical activity: low = less than 5 min, moderate = 5 to 30 min, high = more than 30 min

\*p-value  $\leq 0.05$ 

there is a strong relationship between MTCS concentration in girls and smoking in the family. In addition, a substantial association was discovered between the boys' parents' educational level and TCS, as well as a positive relationship between parents' academic level and TCS concentration. On the other hand, there was a substantial negative association between boys' parents' income level and TCC but no significant association between other demographic factors and pollutant concentrations (Table 3).

According to the findings, the volume of urine excreted during sampling had no influence on the concentration of this; and therefore, instant sampling can be used to monitor the urinary levels of TCS and TCC, that these findings are comparable to those of Iyer et al. study (Iyer et al. 2018).

Chlorophenols, on the other hand, are compounds that are employed in pesticides or as intermediates in medicines and dyes, the most prevalent of which are dichlorophenols. The conversion of TCS to dichlorophenols is the cause of this contaminant in the urine of children and adolescents, and as a result, there is a significant relationship between the concentration levels of triclosan and dichlorophenols, indicating that triclosan is the main source of dichlorophenols. TCS and 2,4-DCP concentrations were 8.26 and 2.60 ( $\mu$ g/L), respectively, in research on Brazilian children done by Rocha et al., which is higher than the concentration reported in this study and might suggest reduced exposure of children and adolescents in Kerman, Iran, with products such as toothpaste, detergents, soaps, and personal care products are the primary sources of these pollutants (Rocha et al. 2018; Iyer et al. 2018). 2,4-DCP is less harmful than TCS in terms of toxicity (Surampalli et al. n.d.).

Han et al. investigated the association between TCS and TCC concentrations in schoolchildren's obesity and overweight. These youngsters had TCS and TCC concentrations of 0.32 and 0.33 µg/L, respectively. Furthermore, the findings of this study revealed that there is a substantial positive association between these pollutants' concentrations and obesity and overweight. Lankester et al. found a significant association between urinary TCS and BMI in the sample population (r=0.3) in cross-sectional descriptive research by the National Health and Nutrition Examination Survey (NHANES) (Lankester et al. 2013). In a study of children and adolescents aged 6 to 19, Buser et al. discovered a linear

Analytes	Total	Boys		<i>p</i> -value	Girls		<i>p</i> -value
		6–11 years	12-18 years		6–11 years	12-18 years	
	Geometric mean $\pm$ SD ( $\mu$ g/L)			Geometric mean			
TCS	$4.32 \pm 2.08$	$3.95 \pm 1.43$	$4.36 \pm 1.02$	0.96	$4.65 \pm 3.41$	$4.21 \pm 1.09$	0.42
MTCS	$1.73 \pm 0.88$	$1.71 \pm 0.63$	$1.67 \pm 0.64$	0.90	$2.01 \pm 1.23$	$1.44 \pm 0.72$	0.07
TCC	$4.27 \pm 1.93$	$4.49 \pm 2.13$	$4.26 \pm 1.75$	0.58	$4.26 \pm 2.22$	$4.05 \pm 1.66$	0.55
2,4-DCP	$0.19 \pm 0.14$	$0.21 \pm 0.12$	$0.16 \pm 0.10$	0.19	$0.22 \pm 0.19$	$0.17 \pm 0.13$	0.51
	Geometric mear	$h \pm SD (\mu g/g.cr)$			Geometric mean	$\pm$ SD (µg/g.cr)	
TCS	$5.05 \pm 3.41$	$3.24 \pm 2.69$	$4.98 \pm 1.13$	0.03	$6.86 \pm 5.37$	$5.32 \pm 1.64$	0.03
MTCS	$2.19 \pm 1.30$	$2.19 \pm 0.80$	$1.97 \pm 0.76$	0.39	$2.74 \pm 1.88$	$1.83 \pm 1.06$	0.07
TCC	$4.94 \pm 2.94$	$3.58 \pm 4.27$	$4.87 \pm 1.86$	0.16	$6.26 \pm 3.00$	$5.12 \pm 2.28$	0.14
2,4-DCP	$0.26 \pm 0.20$	$0.28 \pm 0.17$	$0.23 \pm 0.14$	0.41	$0.30 \pm 0.26$	$0.22 \pm 0.18$	0.60
Anthropometric parameter and creatinine concentration	$Mean \pm SD$						
Age (years)	$11.36 \pm 3.81$	$8.27 \pm 1.88$	$14.39 \pm 2.03$	< 0.0001	$7.90 \pm 1.71$	$14.93 \pm 2.33$	< 0.0001
BMI (kg/m <sup>2</sup> )	$22.76 \pm 5.69$	$21.36 \pm 4.91$	$22.75 \pm 4.45$	0.28	$24.21 \pm 7.41$	$21.92 \pm 5.38$	0.34
BMI z-score	$1.38 \pm 2.09$	$1.97 \pm 2.21$	$0.70 \pm 1.35$	0.02	$2.48 \pm 2.31$	$0.14 \pm 1.71$	0.002
WC (cm)	$68.30 \pm 12.71$	$60.13 \pm 11.30$	$75.84 \pm 11.60$	< 0.0001	$63.27 \pm 10.90$	$71.76 \pm 10.42$	0.02
Creatinine (µg/mL)	$0.77 \pm 0.12$	$0.70 \pm 0.0$	$0.88 \pm 0.12$	< 0.0001	$0.69 \pm 0.07$	$0.79 \pm 0.11$	0.001

Table 4 The geometric mean concentration of urinary metabolites of TCS and MTCS with and without modulation by creatinine and mean age, creatinine level, and anthropometric parameters

Table 5 Correlation between analytes with age, sex, BMI, and WC

Variables	The correlation coefficient $(\beta)$							
	TCS (µg/L)	MTCS (µg/L)	TCC (µg/L)	2,4-DCP (µg/L)				
Age (years)	0.002	-0.08	-0.06	-0.14				
WC (cm)	0.08	0.11	0.06	0.01				
BMI (kg/m <sup>2</sup> )	0.78*	0.67*	0.47*	0.43*				
BMI z-score	0.62*	0.56*	0.42*	0.41*				
TCS (µg/L)	1	0.74*	0.60*	0.49*				
MTCS (µg/L)		1	0.30*	0.49*				
TCC (µg/L)			1	0.35*				
2,4-DCP (µg/L)			0.51*	1				

connection between 2,4-DCP levels and BMI z-score, WC, and obesity (Buser et al. 2014). TCS and MTCS were shown to have a significant positive

association (r = 0.74, p-value < 0.0001) in this study. This might be since MTCS is the most common metabolite of triclosan, which is made by replacing the hydroxyl group with methoxy. Methoxy triclosan loses its antibacterial capabilities when the hydroxyl group is replaced with methoxy, but it has better fat solubility, bioaccumulation, and stability than triclosan (Li et al. 2019, 2020; Wang et al. 2019). MTCS is another type of triclosan that comes from triclosan methylation. Because MTCS is more lipophilic than its parent compound, it has a strong resistance to breakdown and can accumulate in human and animal adipose tissue (Surampalli

\**p*-value  $\leq 0.05$ 

Table 6 The effect of the BMI z-score and WC on TCS, MTCS, TCC, and 2,4-DCP  $(\mu g/L)$ 

Variable	TCS (µ	g/L)	MTCS	$TCS (\mu g/L)  TCC (\mu g/L)$		µg/L)	2,4-DCP (µg	
	β	<i>p</i> -value	β	<i>p</i> -value	β	<i>p</i> -value	β	<i>p</i> -value
BMI z-score								
Model 1	0.48	< 0.0001	0.24	< 0.0001	0.38	< 0.0001	0.02	0.004
Model 2	0.58	< 0.0001	0.28	< 0.0001	0.49	< 0.0001	0.02	0.01
WC (cm)								
Model 1	0.009	0.62	0.005	0.56	0.01	0.56	0.001	0.68
Model 2	0.01	0.46	0.01	0.15	0.02	0.19	0.003	0.06

Model 1: crude

Model 2: adjusted by age, gender, and physical activity

Table 7 Mean concentration analytes (µg/L) according to weight status

Analyte concen-	Mean ± SD						
tration (µg/L)	$\overline{\text{Total}(n=79)}$	Underweight and normal $(n=31)$	Overweight $(n=16)$	Obese $(n=32)$			
TCS	$4.62 \pm 2.08$	$3.81 \pm 0.54$	$4.46 \pm 2.08$	$5.47 \pm 2.99$	< 0.0001		
TCC	$4.47 \pm 2.02$	$4.06 \pm 1.78$	$4.66 \pm 1.64$	$5.50 \pm 2.20$	0.016		
MTCS	$1.91 \pm 0.88$	$1.42 \pm 0.52$	$1.91 \pm 0.88$	$2.32 \pm 1.04$	< 0.0001		

 $0.22 \pm 0.19$ 

 $0.17 \pm 0.10$ 

et al. n.d.). Because triclosan is the major ingredient of MTCS, there has been no research on MTCS biomonitoring so far, but this study supported the relationship assessment of MTCS concentration (Chavoshani et al. 2020b).

λ 2,4-DCP

 $0.23 \pm 0.14$ 

Physical inactivity is widely acknowledged as one of the key factors that contribute to childhood obesity and overweight, which is a major problem nowadays (Owen et al. 2010). Other variables that influence obesity and overweight children include heredity, a high-calorie diet, and exposure to chemical compounds such as triclosan and its derivative. The term "physical inactivity" refers to activities that the kid engages in for an extended period, such as watching TV, playing computer games, or sleeping excessively (Kalloo et al. 2018b). Excessive physical activity has been shown in certain studies to lower the amounts of pollutants that disturb the endocrine glands, preventing them from accumulating in the body (Arya et al. 2020). The current study's findings revealed that there is no significant association between EDC concentrations and physical activity. Nassan et al. published another study in which they found that there was no significant association between TCS concentration and physical activity in males, which likely relies on the individual's employment, the intensity of physical activity, and the length of it (Nassan et al. 2019). There was no association observed in this study because the youngsters did not participate in severe physical exercise.

It is difficult to compare concentrations owing to changes in age, sex, race, and pollution exposure, and people's metabolisms may differ in various areas and depending on climatic conditions (Seo et al. 2020). However, when compared to previous research, the geometric mean of the analytes investigated in the current study (Kerman children and adolescents) is approximately low that of other areas. The concentration of these pollutants was greater in the age groups of 6–11 years than the age groups of 12–18 years, according to a finding reported in Table 4. In terms of gender, the concentration of pollutants was greater in the sexual group of girls than in the sexual group of boys, suggesting that girls and children aged 6 to 11 are more exposed to products containing these pollutants. Similar results were found in Iyer et al. and Rocha et al. investigations, as well as the current study's findings (Iyer et al. 2018; Rocha et al. 2018).

It is worth noting that while the effects of one type of endocrine-disrupting compound may be minor, exposure to several combinations of these compounds might have substantial consequences. Simultaneous exposure to numerous endocrine disruptive compounds, on the other hand, may not simply enhance the effects compared to a single endocrinedisrupting compound, as the effects of these compounds may be distinct or even opposing (Ribeiro et al. 2020).

 $0.29 \pm 0.13$ 

0.003

## Study strengths and limitations

One of the strengths of the study was that the effect of several EDCs on anthropometric parameters was investigated simultaneously. The present study showed a good relationship between TCS, MTCS, 2, 4-DCP, and TCC with anthropometric parameters in children and adolescents. And that yet the relationship between TCS, MTCS, 2, 4-DCP, and TCC with anthropometric parameters among children and adolescents in Iran has not been studied. And more studies are needed on the impact of using EDCs in developing countries. One of the limitations of the present study is that it is cross-sectional, which does not show causal relationships well and only shows the relationship between the analyses and anthropometric parameters in children and adolescents. As a result, cohort studies need to be conducted in this field. Some information was collected through a questionnaire, and there is a possibility of error in collecting this information, but this error in the questionnaires is inevitable due to the self-reported nature of the questionnaire.

## Conclusion

The findings revealed that the analytes were found in the majority of the samples, indicating that the vast majority of children and adolescents were exposed to these pollutants and that the current study has a strong positive correlation between BMI z-score and BMI, and there was a strong association between analyte concentration and demographic variables. TCS, MTCS, and 2,4-DCP are the major indicators of overweight and obesity in children and adolescents; thus, the pathways of exposure to these analytes must be limited.

Given that this is a cross-sectional study and that individual people may metabolize these chemical compounds differently, as well as the fact that it is unclear whether a single measurement reflects long-term exposure to these analytes, more research into the effects of TCS, MTCS, TCC, and 2,4-DCP on the health of children and adolescents is necessary.

Acknowledgements The authors wish to thank the Vice Chancellor for Research of Kerman University of Medical Sciences for providing the financial support of this study. The research was approved by the Ethics Committee of Kerman University of Medical Sciences (Project code: 98001219; Ethical code: IR.KMU.REC.1399.258).

Author contribution All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by MH, HN, MM, and SR. 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 HN, MH, and SR; Formal analysis and investigation by MM; writing-original draft preparation by HN; writing-review and editing by MH, MM, SR, and HN; funding acquisition by Kerman University of Medical Sciences; resources by HN; and supervision by MH and MM.

**Funding** This research was financially supported by the Kerman University of Medical Sciences (Grant No. 98001219), and it was conducted as a student thesis (Master of Sciences in Environmental Health and Engineering) by Habibeh Nasab.

**Availability of data and materials** The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

#### Declarations

Ethics approval and consent to participate All procedures performed in studies involving human participants were by the ethical standards of the institutional and/or national research committee. The study was approved by the Bioethics Committee of the Medical University of Kerman. The Ethics Approval Code is IR.KMU.REC.1399.258. Written informed consent was obtained from the parents.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

## References

- Amin MM, Ebrahimpour K, Parastar S, Shoshtari-Yeganeh B, Hashemi M (2018a) Method development of di-(2-ethylhexyl) phthalate metabolites detection by dispersive liquid–liquid microextraction gas chromatography–mass spectrometry from urine. Int J Environ Health Eng 7:4
- Amin MM, Ebrahimpour K, Parastar S, Shoshtari-Yeganeh B, Hashemi M, Mansourian M, Poursafa P, Fallah Z, Rafiei N, Kelishadi R (2018b) Association of urinary concentrations of phthalate metabolites with cardiometabolic risk factors and obesity in children and adolescents. Chemosphere 211:547–556
- Amin MM, Parastar S, Ebrahimpour K, Shoshtari-Yeganeh B, Hashemi M, Mansourian M, Kelishadi R (2018c) Association

of urinary phthalate metabolites concentrations with body mass index and waist circumference. Environ Sci Pollut Res 25:11143–11151

- Amin MM, Rafiei N, Poursafa P, Ebrahimpour K, Mozafarian N, Shoshtari-Yeganeh B, Hashemi M, Kelishadi R (2018d) Association of benzene exposure with insulin resistance, SOD, and MDA as markers of oxidative stress in children and adolescents. Environ Sci Pollut Res 25:34046–34052
- Amin MM, Ebrahim K, Hashemi M, Shoshtari-Yeganeh B, Rafiei N, Mansourian M, Kelishadi R (2019a) Association of exposure to bisphenol A with obesity and cardiometabolic risk factors in children and adolescents. Int J Environ Health Res 29:94–106
- Amin MM, Tabatabaeian M, Chavoshani A, Amjadi E, Hashemi M, Ebrahimpour K, Klishadi R, Khazaei S, Mansourian M (2019b) Paraben content in adjacent normal-malignant breast tissues from women with breast cancer. Biomed Environ Sci 32:893–904
- Arya S, Dwivedi AK, Alvarado L, Kupesic-Plavsic S (2020) Exposure of US population to endocrine disruptive chemicals (parabens, benzophenone-3, bisphenol-A and triclosan) and their associations with female infertility. Environ Pollut 265:114763
- Baumann A, Lohmann W, Rose T, Ahn K, Hammock B, Karst U, Schebb NH (2010) Electrochemistry-mass spectrometry unveils the formation of reactive triclocarban metabolites. Drug Metab Dispos 38:2130–2138
- Braun JM (2017) Early-life exposure to EDCs: role in childhood obesity and neurodevelopment. Nat Rev Endocrinol 13:161
- Bukowska B, Wieteska P, Kwiatkowska M, Sicińska P, Michalowicz J (2016) Evaluation of the effect of 2, 4-dichlorophenol on oxidative parameters and viability of human blood mononuclear cells (in vitro). Hum Exp Toxicol 35:775–784
- Buser MC, Murray HE, Scinicariello F (2014) Association of urinary phenols with increased body weight measures and obesity in children and adolescents. J Pediatr 165:744–749
- Chavoshani A, Hashemi M, Amin MM, Ameta SC (2020a) Personal care products as an endocrine disrupting compound in the aquatic environment. Micropollutants and challenges: emerging in the aquatic environments and treatment processes, p91
- Chavoshani A, Hashemi M, Amin MM, Ameta SC (2020b) Risks and challenges of pesticides in aquatic environments. Micropollutants and challenges: emerging in the aquatic environments and treatment processes, p179
- Dhillon GS, Kaur S, Pulicharla R, Brar SK, Cledón M, Verma M, Surampalli RY (2015) Triclosan: current status, occurrence, environmental risks and bioaccumulation potential. Int J Environ Res Public Health 12:5657–5684
- Ding Z-M, Ahmad MJ, Meng F, Chen F, Wang Y-S, Zhao X-Z, Zhang S-X, Miao Y-L, Xiong J-J Huo L-J (2020) Triclocarban exposure affects mouse oocyte in vitro maturation through inducing mitochondrial dysfunction and oxidative stress. Environ Pollut 114271
- Dong M, Xu X, Huang Q, Lei H, Xu G, Ma J, Hatzakis E, Wang X, Zhang L (2019) Dose-dependent effects of triclocarban exposure on lipid homeostasis in rats. Chem Res Toxicol 32:2320–2328
- Exon JH, Henningsen GM, Osborne CA, Koller LD (1984) Toxicologic, pathologic, and immunotoxic effects of 2, 4-dichlorophenol in rats. J Toxicol Environ Health Part A 14:723–730
- Friedemann C, Heneghan C, Mahtani K, Thompson M, Perera R, Ward AM (2012) Cardiovascular disease risk in healthy children and its association with body mass index: systematic review and metaanalysis. Bmj 345:e4759
- Giuliano CA, Rybak MJ (2015) Efficacy of triclosan as an antimicrobial hand soap and its potential impact on antimicrobial resistance: a focused review. Pharmacotherapy 35:328–336
- Grün F, Blumberg B (2009) Endocrine disrupters as obesogens. Mol Cell Endocrinol 304:19–29
- Hashemi M, Amin MM, Chavoshani A, Rafiei N, Ebrahimpour K, Kelishadi R (2021) Relationship of urinary phthalate metabolites

with cardiometabolic risk factors and oxidative stress markers in children and adolescents. J Environ Public Health 2021

- Hinther A, Bromba CM, Wulff JE, Helbing CC (2011) Effects of triclocarban, triclosan, and methyl triclosan on thyroid hormone action and stress in frog and mammalian culture systems. Environ Sci Technol 45:5395–5402
- Iyer AP, Xue J, Honda M, Robinson M, Kumosani TA, Abulnaja K, Kannan K (2018) Urinary levels of triclosan and triclocarban in several Asian countries, Greece and the USA: association with oxidative stress. Environ Res 160:91–96
- Kabir ER, Rahman MS, Rahman I (2015) A review on endocrine disruptors and their possible impacts on human health. Environ Toxicol Pharmacol 40:241–258
- Kalloo G, Calafat AM, Chen A, Yolton K, Lanphear BP, Braun JM (2018a) Early life triclosan exposure and child adiposity at 8 years of age: a prospective cohort study. Environ Health 17:24
- Kalloo G, Calafat AM, Chen A, Yolton K, Lanphear BP, Braun JM (2018b) Early life triclosan exposure and child adiposity at 8 years of age: a prospective cohort study. Environ Health 17:1–10
- Karzi V, Tzatzarakis MN, Vakonaki E, Alegakis T, Katsikantami I, Sifakis S, Rizos A, Tsatsakis AM (2018) Biomonitoring of bisphenol A, triclosan and perfluorooctanoic acid in hair samples of children and adults. J Appl Toxicol 38:1144–1152
- Kolšek K, Gobec M, Raščan IM, Dolenc MS (2015) Screening of bisphenol A, triclosan and paraben analogues as modulators of the glucocorticoid and androgen receptor activities. Toxicol in Vitro 29:8–15
- Lankester J, Patel C, Cullen MR, Ley C, Parsonnet J (2013) Urinary triclosan is associated with elevated body mass index in NHANES. PloS one 8:e80057
- Li S, Zhao J, Wang G, Zhu Y, Rabito F, Krousel-Wood M, Chen W, Whelton PK (2015) Urinary triclosan concentrations are inversely associated with body mass index and waist circumference in the US general population: experience in NHANES 2003–2010. Int J Hyg Environ Health 218:401–406
- Li X, An J, Li H, Qiu X, Wei Y, Shang Y (2019) The methyl-triclosan induced caspase-dependent mitochondrial apoptosis in HepG2 cells mediated through oxidative stress. Ecotoxicol Environ Saf 182:109391
- Li X, Shang Y, Yao W, Li Y, Tang N, An J, Wei Y (2020) Comparison of transcriptomics changes induced by TCS and MTCS exposure in human hepatoma HepG2 cells. ACS Omega
- Lv W, Chen Y, Li D, Chen X, Leszczynski J (2013) Methyl-triclosan binding to human serum albumin: multi-spectroscopic study and visualized molecular simulation. Chemosphere 93:1125–1130
- Ma Y, Han J, Guo Y, Lam PK, Wu RS, Giesy JP, Zhang X, Zhou B (2012) Disruption of endocrine function in in vitro H295R cellbased and in in vivo assay in zebrafish by 2, 4-dichlorophenol. Aquat Toxicol 106:173–181
- Magnoli K, Carranza CS, Aluffi ME, Magnoli CE, Barberis CL (2020) Herbicides based on 2, 4-D: its behavior in agricultural environments and microbial biodegradation aspects. A review. Environ Sci Pollut Res 1–12
- Martens L, de Smet S, Yusof M, Rajasekharan S (2017) Association between overweight/obesity and periodontal disease in children and adolescents: a systematic review and meta-analysis. Eur Arch Paediatr Dent 18:69–82
- Montaseri H, Forbes PB (2016) A review of monitoring methods for triclosan and its occurrence in aquatic environments. TrAC, Trends Anal Chem 85:221–231
- Nasab H, Mirzaee M, Ebrahimpour K, Hashemi M (2021) 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). Environ Health Eng Manag J

- Nassan FL, Mínguez-Alarcón L, Williams PL, Dadd R, Petrozza JC, Ford JB, Calafat AM, Hauser R, Team ES (2019) Urinary triclosan concentrations and semen quality among men from a fertility clinic. Environ Res 177:108633
- Owen C, Nightingale C, Rudnicka A, Sattar N, Cook D, Ekelund U, Whincup P (2010) Physical activity, obesity and cardiometabolic risk factors in 9-to 10-year-old UK children of white European, South Asian and black African-Caribbean origin: the Child Heart And health Study in England (CHASE). Diabetologia 53:1620–1630
- Parastar S, Ebrahimpour K, Hashemi M, Maracy MR, Ebrahimi A, Poursafa P, Kelishadi R (2018) Association of urinary concentrations of four chlorophenol pesticides with cardiometabolic risk factors and obesity in children and adolescents. Environ Sci Pollut Res 25:4516–4523
- Park M, Kim S, Kim Y, Ryoo J-H, Lim S (2019) Relationship between personal care products usage and triclosan exposure: the second Korean National Environmental Health Survey (KoNEHS 2012– 2014). Ann Occup Environ Med 31:2
- Ribeiro CM, Beserra BTS, Silva NG, Lima CL, Rocha PRS, Coelho MS, Neves FDAR, Amato AA (2020) Exposure to endocrinedisrupting chemicals and anthropometric measures of obesity: a systematic review and meta-analysis. BMJ open 10:e033509
- Rocha BA, Asimakopoulos AG, Honda M, da Costa NL, Barbosa RM, BARBOSA JR, F. & KANNAN, K. (2018) Advanced data mining approaches in the assessment of urinary concentrations of bisphenols, chlorophenols, parabens and benzophenones in Brazilian children and their association to DNA damage. Environ Int 116:269–277
- Schultz MM, Bartell SE, Schoenfuss HL (2012) Effects of triclosan and triclocarban, two ubiquitous environmental contaminants, on anatomy, physiology, and behavior of the fathead minnow (Pimephales promelas). Arch Environ Contam Toxicol 63:114–124
- Seo MY, Choi MH, Hong Y, Kim S-H, Park MJ (2020) Association of urinary chlorophenols with central obesity in Korean girls. Environ Sci Pollut Res 1–7
- Skinner AC, Perrin EM, Moss LA, Skelton JA (2015) Cardiometabolic risks and severity of obesity in children and young adults. N Engl J Med 373:1307–1317
- Surampalli R, Olaniyan WL, Thomas O, Dupont V, Bedoux G (n.d.) A review on occurrence, fate and toxicity of triclosan
- Vela-Soria F, Ballesteros O, Zafra-Gómez A, Ballesteros L, Navalón A (2014) A multiclass method for the analysis of endocrine disrupting chemicals in human urine samples. Sample treatment by dispersive liquid–liquid microextraction. Talanta 129:209–218
- Wang C-F, Tian Y (2015) Reproductive endocrine-disrupting effects of triclosan: population exposure, present evidence and potential mechanisms. Environ Pollut 206:195–201
- Wang Y, Li P, Liu Y, Chen B, Li J, Wang X (2013) Determination of triclocarban, triclosan and methyl-triclosan in environmental water by silicon dioxide/polystyrene composite microspheres solid-phase extraction combined with HPLC-ESI-MS. J Geosci Environ Protect 1:13
- Wang L, Mao B, He H, Shang Y, Zhong Y, Yu Z, Yang Y, Li H, An J (2019) Comparison of hepatotoxicity and mechanisms induced by triclosan (TCS) and methyl-triclosan (MTCS) in human liver hepatocellular HepG2 cells. Toxicology Research 8:38–45
- Ye X, Wong L-Y, Zhou X, Calafat AM (2014) Urinary concentrations of 2, 4-dichlorophenol and 2, 5-dichlorophenol in the US population (National Health and Nutrition Examination Survey, 2003–2010): trends and predictors. Environ Health Perspect 122:351–355
- Yousefi M, Yaseri M, Nabizadeh R, Hooshmand E, Jalilzadeh M, Mahvi AH, Mohammadi AA (2018) Association of hypertension, body mass index, and waist circumference with fluoride intake;

water drinking in residents of fluoride endemic areas, Iran. Biol Trace Elem Res 185:282–288

- Yousefi M, Saleh HN, Yaseri M, Jalilzadeh M, Mohammadi AA (2019) Association of consumption of excess hard water, body mass index and waist circumference with risk of hypertension in individuals living in hard and soft water areas. Environ Geochem Health 41:1213–1221
- Yueh M-F, Tukey RH (2016) Triclosan: a widespread environmental toxicant with many biological effects. Annu Rev Pharmacol Toxicol 56:251–272
- Zarean M, Poursafa P (2019) The role of environmental disruptor chemicals in the development of non communicable disease. Primordial prevention of non communicable disease. Springer
- Zhang Y, Liu M, Liu J, Wang X, Wang C, Ai W, Chen S, Wang H (2018) Combined toxicity of triclosan, 2, 4-dichlorophenol and 2, 4, 6-trichlorophenol to zebrafish (Danio rerio). Environ Toxicol Pharmacol 57:9–18
- Zhang C, Li D, Ge T, Han J, Qi Y, Huang D (2020) 2, 4-Dichlorophenol induces feminization of zebrafish (Danio rerio) via DNA methylation. Sci Total Environ 708:135084

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.