Biomonitoring of Bromine-Containing Trihalomethanes in the Pregnant Women: Urinary Levels and Association with Lifestyle Factors

Bahare Dehdashti

Isfahan University of Medical Sciences

Awat Feizi

Isfahan University of Medical Sciences

Mohammad Mehdi Amin (✉ mohammadmehdia@gmail.com)

Isfahan University of Medical Sciences <https://orcid.org/0000-0001-5758-7277>

Nasrin Bagheri

Isfahan University of Medical Sciences

Seyede Shahrbanoo Daniali

Isfahan University of Medical Sciences

Roya Kelishadi

Isfahan University of Medical Sciences

Research Article

Keywords: Br-THMs, DBCM, BDCM, TBM, Pregnancy, Biomonitoring, Urine

Posted Date: August 17th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-773379/v1>

License: This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

Trihalomethanes containing bromine (Br-THMs) are compounds formed from the reaction of organic and inorganic substances in drinking water with chlorine as a common disinfectant. Epidemiological evidence indicated various outcomes as a result of long-term exposure to these compounds.

This study aims to investigate the concentration of urinary Br-THMs in a sample of third-trimester pregnant women and to determine its correlation with lifestyle factors.

This cross-sectional study was conducted among 118 pregnant women in Isfahan, Iran. The third-trimester urine Br-THMs including dibromochloromethane (DBCM), bromodichloromethane (BDCM), and bromoform (TBM) were measured using solid-phase micro-extraction gas chromatography. The distribution of urinary Br-THMs concentration was positively skewed then these variables were subjected to logarithmic transformation. Spearman ranks correlation coefficient, and two independent samples t-test were used to assess the association of urinary Br-THMs concentration with its demographic and lifestyle determinants.

The findings showed that the mean (SD) concentrations of DBCM, BDCM, TBM and brominated THMs were 14.76 (27.17), 10.25 (11.37), 4.96 (3.21) and 30.17 (40.80) ng/L, respectively. In addition, significant inverse correlation was found between the use of water storage tanks and Br-THMs (DBCM, BDCM, TBM and brominated THMs, P-value = 0.005, 0.019, >0.001 and 0.007 < 0.05, respectively).

In this study, among the quantitative and qualitative variables, the use of storage tanks had an inverse correlation with Br-THMs. In addition, the status of urinary concentration of Br-THMs in pregnant women was less than in the other countries in the same area. Improving water quality and using modern methods to eliminate disinfection by-products as well as improving lifestyle patterns are efficient methods to reduce exposure to these contaminants.

1. Introduction

Public health has been enhanced by disinfecting drinking water to prevent waterborne infections. Followed by disinfection by-products (DBPs) are created from the natural reaction of chlorine as the most popular disinfectant of drinking water with organic and inorganic substances in water. So that chlorination processes have produced more than 700 types of DBPs up to now (Deng *et al.*, 2019).

Among these, 4 groups of trihalomethanes (THMs), haloacetic acids (HAAs), halo ketones (HKs), and halonitromethanes (HNMs) are the main by-products of disinfection (Mosaferi *et al.*, 2020). In drinking water, THMs and HAAs form 66 and 27% of DBPs, respectively. Chloroform (CHCl_3 : TCM), bromoform (CHBr_3 : TBM), bromodichloromethane (CHCl_2Br : BDCM), and chlorodibromomethane (CHClBr_2 : DBCM) are chemicals produced from chlorination of water, refer to THMs. The amount of total THMs (TTHMs), is the sum of TCM, TBM, BDCM, and DBCM that varies between tens to hundreds $\mu\text{g/L}$ (Batterman *et al.*, 2002). Brominated trihalomethanes are the sum of TBM, BDCM, and DBCM (Chen *et al.*, 2019). Experiments have shown that brominated-DBPs have more carcinogenic effects than chlorinated (Liu, 2014).

Water ingestion or other activities such as swimming, showering, and bathing are the routes of exposure to THMs, through ingestion and non-ingestion, respectively (Andra *et al.*, 2015). Also, adult women can be exposed to non-ingestion THMs by cleaning the house, such as washing dishes, cleaning surfaces, and toilets (Andra *et al.*, 2015). Around 60 days accumulation of 100 mg/kg/day TCM, TBM, and BDCM and 400 mg/kg/day for TTHMs in mature rats caused neurotoxicity (Chen *et al.*, 2019). Moreover, reproductive disorders in rodents have also been found based

on exposure to high levels of DBPs according to toxicological evidence. For example, respiratory and oral exposure to THMs has resulted in low birth weight infants in rodents (Deng *et al.*, 2019). Also, the carcinogenic and mutagenic effects of Br-THMs have been reported in rodents (Stayner *et al.*, 2014).

Followed by cancer and reproductive implications in humans, including length of pregnancy, sperm quality, menstrual cycle, and pregnancy outcomes such as fetal growth, fetal loss, preterm delivery, and congenital anomaly, on epidemiological evidence, are the consequences of long-term exposure to THMs (Villanueva *et al.*, 2011). How to use water in bathing, showering, and swimming, also water consumption pattern displays the degree of external exposure to THMs through tap water. Internal exposure to THMs can be assessed by measuring blood and urine biomarkers (Charisiadis *et al.*, 2014). Different routes of exposure to THMs biomarkers are evaluated by measuring it in the urine and using lifestyle questionnaires. The remaining THMs in the kidneys and greater than in the liver are metabolized through the interaction of cytochrome (CY) P450 and the enzymatic system in two phases. The production of reactive oxygen types in the liver and kidneys by CYP2E1, followed by combination with glutathione in phase II, determines the biological activation of THMs (Gängler *et al.*, 2018).

Researchers have evaluated the concentration of THMs in tap water in different cities of the world and Iran (Mohammadi *et al.*, 2016). Mohammadi *et al.* in 2016 measured the concentration of THMs in the drinking water distribution network in the 30 points of this study area that the mean (SD) of THMs was 37.98 (2.56) µg/L (Mohammadi *et al.*, 2016, Mosaferi *et al.*, 2020). The use of urinary biomarkers to assess exposure increases the reliability of risk assessment studies by reducing exposure classification errors (Mosaferi *et al.*, 2020).

Therefore, according to the available evidence based on the presence of these contaminants in the drinking water distribution system, this study aimed to investigate the concentration of urinary Br-THMs among third-trimester pregnant women in Isfahan as a sensitive and vulnerable group and their correlation with lifestyles such as how to consume drinking water and washing and bathing activities.

2. Materials And Methods

2.1. Study population

This cross-sectional study was conducted to measure the concentration of urinary Br-THMs. The target group consisted of 118 pregnant women in the third trimester, who participated in the PERSIAN Birth Cohort and lived in different parts of Isfahan city, Iran (Ref: DOI: <https://doi.org/10.1332/175795920X16062247639874>).

The locations of living areas of participants are given in Fig. 1. The informed consent form was provided to participants regarding the type of study, purpose, and method of urine sampling. Also, all stages of this study were performed after the approval of the ethics committee of Isfahan University of Medical Sciences. Inclusion criteria in this study for participants include living in Isfahan for at least one year or more, the third trimester of pregnancy, and no history of chronic diseases. Subsequently, smoking and alcohol consumption were considered exclusion criteria.

2.2. Questionnaire

To determine the correlation between the concentration of urinary Br-THMs with lifestyle factors and demographic characteristics such as age, education, and BMI the prepared questionnaires in the birth cohort were used that its validity and reliability had been confirmed.

In addition, all the questions of the questionnaire were asked under face-to-face interviews by the trained questioner. Personal information of pregnant women including age and occupation and their physical characteristics such as

height, the third-trimester weight of each month, and body mass index regularly during prenatal care according to appointments scheduled was requested by a trained health expert and was measured using calibrated instruments and recorded electronically. BMI is equivalent to weight divided by height squared. (Kang *et al.*, 2016). Education level was also classified into 5 groups: primary school, junior school, high school, and academic. In addition, study participants were selected from different areas of Isfahan. Moreover, information on how to use drinking water daily or weekly or related activities were collected in the form of questions such as drinking water source, amount of water used per day, consumption of boiled water, use of refrigerator, frequency and duration of washing dishes, clothes and baths.

2.3. Urine Sampling and Analysis

In this study, morning spot urine samples of 118 pregnant women in the third trimester were randomly collected in the referral hospitals of Isfahan University of Medical Sciences, Isfahan, Iran. Urine sampling was performed by sterile polypropylene containers by the individual and finally, the samples were transferred to the laboratory of the Health school under cold conditions and kept at -20°C until use.

2.3.1. Extraction method

The solid-phase microextraction method was used to extract species from urine tissue. The used fiber was PDMS-CAR with a thickness of 75 µm. 0.5 mL of the urine sample was poured into a 12 mL glass container with a septum lid. 1.2 g of sodium chloride with a magnet was added to the container and the lid was closed and equilibrated at room temperature at 1250 rpm. After 5 min of equilibrium time, the fiber was exposed through the septum to the upper space of the sample and the extraction was performed for 15 min. Decoding was performed at 240°C for 45 sec inside a gas chromatographic injection chamber.

2.3.2. Chromatographic method and device conditions

Gas chromatography-mass spectrometer was used to isolate and measure the species. The gas chromatograph used was the FISIONS-8000 (8060) and the mass spectrometer used was the Hewlett Packard-5972. Supelco column (SLB-5 MS) with a length of 30 m and a static phase thickness of 0.25 µm and a diameter of 0.25 mm was used for separation. Oven temperature programming: 45°C for 5 min – increase the temperature to 100 ° C with a slope of 20 ° per minute and stay at 100°C for 1 min. Limit of detection (LOD) for DCBM, CDBM, and TBM was calculated 5, 6, and 3 ng/L, respectively. The terms of the mass spectrometer can be seen in Table 1.

Table 1
The terms of the mass spectrometer used in this study.

Compound	Ions	Time (min)
BDCM	83 and 85 (200 milliseconds in total)	1.5
CDBM	127 and 129 (220 milliseconds in total)	0.4
TBM	171 and 173 (240 milliseconds in total)	0.6

2.4. Statistical analysis

In this study, the obtained data were analyzed using SPSS software (SPSS Inc. Released 2007. SPSS for Windows, Version 16.0 Chicago, SPSS Inc.). Quantitative continuous data were reported as mean (SD) or geometric mean and

minimum and maximum. Qualitative variables were also reported as frequency and percentage. The normality of urinary Br-THMs concentration was evaluated using the Kolmogorov-Smirnov test and Q-Q plot. The distribution of urinary Br-THMs concentration was positively skewed. Then these variables were subjected to logarithmic transformation. Person or Spearman ranks correlation coefficients were used to assess the association of urinary Br-THMs concentration with demographic and lifestyle-related variables of study participants. Two independent samples t-test was used for comparing urinary Br-THMs concentration between categories of qualitative lifestyle-related variables.

3. Results

3.1. Characteristics of the study population

The demographic and lifestyle characteristics of 118 pregnant women in the present study are shown in Table 2. Mean (SD) of maternal age, BMI, and weight in the third trimester of pregnancy was 30.41 (5.79) years old, 28.21 (4.36) Kg/m², and 73.63 (12.34) Kg, respectively. Regarding water use and related activities, the mean consumption of tapping water and other sources were 1785 (750) and 380 (960) mL/day, respectively. Pregnant mothers in this study used refrigerator water with an average of 1567.5 (865) mL/day. Also, their tea consumption was expressed with a mean of 455 (410) mL/day.

Table 2
Demographic and lifestyle characteristics of study pregnant women.

Variables	Mean	SD	Geometric mean	Range	
				Min	Max
Maternal weight (kg) (Total third Trimester)	73.63	12.34	72.69	50.17	130.33
7 (months)	71.79	12.35	70.83	49.50	130
8	73.55	12.33	72.61	50	130
9	75.54	12.43	74.60	51	131
Maternal age (years)	30.41	5.79	29.91	19	62
Maternal BMI (Total third Trimester) (Kg/m ²)	28.21	4.36	27.89	19.60	44.94
Water consumption (mL/day)					
Tap water	1785	750	0	0	5000
Others	380	960	0	0	5000
Use refrigerator water (mL/day)	1567.5	865	0	0	5000
Use of tea (mL/day)	455	410	0	0	2500
Washing dishes					
Frequency of washing the dishes (per day)	2.94	1.10	2.75	1	10
Time of Washing dishes by hand (min)	27.71	15.94	0	0	90
Washing clothes					
Frequency of washing clothes (Per week)	2.11	1.57	1.79	0.5	14
Time washing clothes by hand (min)	7.84	26.25	0	0	210
Showering/bathing					
Frequency of showering/bathing (per week)	3.35	1.38	3.1	1	7
Time of Showering/bathing (min)	51.22	26.65	45.36	15	210
Time of cleaning Bath and toilet (min/week)	6.42	10.29	0	0	60
Time of cleaning house (surfaces, glass, etc.) (min/week)	111.40	180.71	0	0	1260

Other information about washing dishes and clothes, as well as cleaning the house, including the number of times (per day or week) and duration (min), is given in Table 2.

3.2. Maternal urine Br-THMs concentrations

Table 3 shows the distribution of Br-THMs concentration in the urine of pregnant women. The mean (SD) concentrations of DCBM, BDCM, TBM, and brominated THMs without creatinine adjustment were 14.76 (27.17), 10.25 (11.37), 4.96 (3.21), and 30.17 (40.80) ng/L, respectively. Their medians were calculated as 4, 6, 4, and 14 ng/L, respectively. Concentration distributions in 25th, 50th, 75th, and 95th percentiles of DCBM, BDCM, TBM, and

brominated THMs were (4, 4, 12.5, and 79.4), (6, 6, 6 and 32), (4, 4, 4 and 12) and (14, 14, 24 and 116.9) ng/L, respectively.

Table 3												
Urinary concentrations of Br-THMs during third trimester of pregnancy in the present study (ng/L) ^a (n = 118).												
Br-THMs categories ^b	Mean	SD	Median	Range		Percentile						
				Min	Max	2.5th	5th	25th	50th	75th	95th	97.5th
DCBM	14.76	27.17	4	4	168	4	4	4	4	12.5	79.4	128.6
BDCM	10.25	11.73	6	3	78	6	6	6	6	6	32	62
TBM	4.96	3.21	4	2	29	4	4	4	4	4	12	16
Brominated THMs	30.17	40.80	14	14	247	14	14	14	14	24	116.9	209.02
^a Limit of detection (LOD) for DCBM, CDBM, and TBM were calculated 5, 6 and 3 ng/L respectively.												
^b Brominated-THMs: Sum of DCBM, CDBM, and TBM.												

3.3. Urinary concentration of Br-THMs and related factors

No significant dose-response relationship was observed through correlation coefficient (r_s) between all of the variables (P-value > 0.05) in Table 4. The variables were age, education, weight, BMI, water, and tea consumption, and frequency and time of washing clothes, dishes, and bathing.

Table 4 Spearman or Pearson correlation analysis between unadjusted urinary of Br-THMs and demographic and lifestyle parameters

Variables	Br-THMs categories			
	DCBM	BDCM	TBM	Brominated THMs
	r_s	r_s	r_s	r_s
Age (Year)	0.055	0.082	0.112	0.088
Education	-0.119	-0.117	-0.150	-0.131
Third trimester weight (Kg)	0.120	0.024	-0.043	0.061
7(months)	0.116	0.031	-0.030	0.062
8	0.123	0.030	-0.042	0.061
9	0.124	0.017	-0.060	0.059
BMI (Kg/m ²)	0.041	-0.034	-0.101	0.006
Water consumption (mL/day)				
Tap water	0.106	0.007	-0.073	0.069
Others	0.051	0.094	-0.069	-0.017
Use refrigerator water (mL/day)	-0.009	-0.078	-0.132	-0.029
Use of tea (mL/day)	0.040	0.014	0.016	-0.005
Washing dishes				
Frequency of washing the dishes (per day)	-0.084	-0.086	-0.148	-0.108
Time of Washing dishes by hand (min)	-0.006	0.016	0.053	-0.004
Washing clothes				
Frequency of washing clothes (Per week)	-0.044	-0.086	-0.103	-0.062
Time washing clothes by hand (min)	0.013	0.028	-0.081	0.117
Showering/bathing				
Frequency of showering/bathing (per week)	-0.108	-0.155	-0.058	-0.008
Time of Showering/bathing (min)	0.090	0.065	0.077	0.04
Time of cleaning Bath and toilet (min/week)	-0.123	-0.099	-0.076	-0.118
Time of cleaning house (surfaces, glass, etc.) (min/week)	-0.006	-0.016	-0.040	-0.049

Table 5 reports the concentrations of DBCM, BDCM, TBM, and brominated THMs concerning qualitative variables. According to the results, use of water that was stored in the storage tank showed the mean (SD) concentration of DBCM, BDCM, TBM, and brominated THMs in the urine of pregnant women, 12.38 (24.6), 9.17 (10.40), 4.72 (3.2) and 46.9 (53.37) ng/L, respectively. However, their concentration in participants who did not use the storage tank was 25.66 (35.35), 15.19 (15.91), 6.04 (3.02), and 26.47 (36.8) ng/L, respectively, which have higher averages than users. The effect of the storage tank on the concentration of three contaminants has shown a significant relationship (P-value < 0.05). Other parameters in Table 5, such as boiling water, level of education, use of dishwasher, and gloves did not show a significant relationship with the concentration of all three contaminants (P-value > 0.05).

Table 5
Relationship between unadjusted urinary Br-THMs concentrations and qualitative parameters

Variables	Br-THMs categories (ng/L)							
	DCBM		BDCM		TBM		Brominated THMs	
	Mean ± SD	Geometric mean	Mean ± SD	Geometric mean	Mean ± SD	Geometric mean	Mean ± SD	Geometric mean
Use of water storage tank								
Yes	12.38 ± 24.62	6.63	9.17 ± 10.40	7.36	4.72 ± 3.21	4.35	46.90 ± 53.37	30.23
NO	25.66 ± 35.35	12.51	15.19 ± 15.91	10.61	6.04 ± 3.02	5.50	26.47 ± 36.80	19.29
P- value	0.005*		0.019*		< 0.001*		0.007*	
Use of water purifier								
Yes	24.5 ± 46.37	9.04	13.07 ± 16.17	8.93	5 ± 3.46	4.5	42.57 ± 65.61	24
NO	13.44 ± 23.46	7.24	9.87 ± 11.04	7.72	4.99 ± 3.19	4.57	28.47 ± 36.29	20.53
P- value	0.656		0.311		0.647		0.42	
Use of boiled water								
Yes	18.09 ± 24.40	9.42	11.63 ± 10.05	9.15	4.81 ± 1.60	4.63	34.54 ± 35.29	24.56
NO	14.52 ± 27.63	7.29	10.18 ± 11.96	7.81	5 ± 3.34	4.56	29.71 ± 41.46	20.58
P-value	0.535		0.135		0.487		0.42	
Maternal education								
Primary School	19.40 ± 28.52	9.73	10.60 ± 10.28	8.22	4 ± 0.0	4	34 ± 38.74	23.66
Junior school	7.88 ± 9.62	5.59	7.55 ± 4.66	6.85	4.22 ± 0.66	4.18	19.66 ± 14.88	17.09
High School	13.30 ± 26.89	6.92	9.20 ± 9.68	7.43	4.68 ± 2.51	4.35	27.24 ± 38.12	19.65
* In bold are the statistically significant associations and p-values < 0.05.								

Variables	Br-THMs categories (ng/L)							
	DCBM		BDCM		TBM		Brominated THMs	
	Mean ± SD	Geometric mean	Mean ± SD	Geometric mean	Mean ± SD	Geometric mean	Mean ± SD	Geometric mean
Academic	16.81 ± 29.48	8.10	11.62 ± 14.18	8.42	5.45 ± 4.05	4.84	34.30 ± 46.31	22.69
P-value	0.576		0.569		0.106		0.57	
Use of gloves/ washed clothes								
Yes	13.50 ± 25.55	7.10	9.69 ± 10.75	7.64	4.93 ± 3.24	4.51	47.90 ± 60.07	28.66
NO	27 ± 39.09	11.48	15.63 ± 18.67	10.32	5.27 ± 2.96	4.79	28.31 ± 38.17	20.25
P-value	0.327		0.243		0.882		0.11	
Use of dish washer								
Yes	21.33 ± 29.71	10.59	11.66 ± 10.13	9.19	4.5 ± 0.83	4.44	37.5 ± 40.65	25.79
NO	14.41 ± 27.12	7.29	10.18 ± 11.85	7.79	4.99 ± 3.29	4.54	29.77 ± 40.96	20.69
P-value	0.216		0.455		0.670		0.45	
Use of gloves/ washing dishes								
Yes	14.65 ± 26.27	7.66	10.15 ± 11.19	7.89	4.96 ± 3.37	4.51	31.10 ± 48.59	19.54
NO	15.36 ± 32.21	6.37	10.78 ± 14.57	7.69	4.94 ± 2.27	4.64	29.98 ± 39.39	21.21
P-value	0.216		0.455		0.670		0.64	
Use of chlorinated detergent								
Yes	10.40 ± 13.62	6.70	8.37 ± 5.91	7.27	4.91 ± 3.60	4.44	23.95 ± 20.89	19.43

* In bold are the statistically significant associations and p-values < 0.05.

Variables	Br-THMs categories (ng/L)							
	DCBM		BDCM		TBM		Brominated THMs	
	Mean $\pm$ SD	Geometric mean	Mean $\pm$ SD	Geometric mean	Mean $\pm$ SD	Geometric mean	Mean $\pm$ SD	Geometric mean
NO	19.51 $\pm$ 36.20	8.32	12.30 $\pm$ 15.62	8.55	5.01 $\pm$ 2.75	4.63	36.83 $\pm$ 54.09	22.66
P-value	0.329		0.246		0.220		0.23	
* In bold are the statistically significant associations and p-values < 0.05.								

4. Discussion

An area of present cross-sectional research about investigating the concentration of Br-THMs in urine as a biomarker of exposure to drinking water disinfection by-products, in pregnant women was done in Isfahan, Iran, as the first study.

In the previous studies, the concentration of total trihalomethanes (TTHMs) has been identified in the water of Isfahan city (Mohammadi *et al.*, 2016, Ali Dehnavi, 2018, Bijan Bina, 2012). In spite of this issue, TCM was not detected in the urine of pregnant women in this study, but DBCM, BDCM, TBM, and also brominated THMs were measurable. Researchers have attributed this, to the low volatility of Br-THMs (Gängler *et al.*, 2017). Although the ingestion is the main route of exposure to DBPs (Liu, 2014) in a study by Gangler *et al.*, the non-ingestion route, especially through the air, was more important in predicting TCM levels (Gängler *et al.*, 2017).

The lifestyle habits of the participants in this study, such as using suitable ventilation or cool water during washing and bathing, have an effective role in limitation and its exit from the environment. Liu research revealed that hot water tanks are effective in degradation DBPs and have increased THMs (Liu, 2014).

According to Fig. 2, in addition to this study, the amount of Br-THMs in women's urine has been reported in three other countries. The urinary concentration levels of this group of contaminants in this study were dramatically different compared to Kuwait and Cyprus (Charisiadis *et al.*, 2013, Gängler *et al.*, 2017). This is due to personal habits and characteristics such as water consumption patterns and genetics and physiological features that have affected the metabolism of THMs (Rivera-Núñez *et al.*, 2012). But, the same as Cyprus, mean urinary DBCM and BDCM were higher than compared to TBM; the reason is perhaps the increase in hydrophilicity of the compounds in the following order (TBM < DBCM < BDCM < TCM) (Rivera-Núñez *et al.*, 2012). On the other hand, measurement in the blood compared to urine has been shown lower concentrations, which is in contrast to urine analysis. The amount of TBM was higher than DBCM and BDCM because of the lipophilicity of TBM compared to the other compounds (Rivera-Núñez *et al.*, 2012).

Figure 2 Comparison of Br-THMs concentrations in global studies (Charisiadis *et al.*, 2013, Zeng *et al.*, 2016, Cao *et al.*, 2016, Gängler *et al.*, 2017, Wang *et al.*, 2019, Chen *et al.*, 2019, Sun *et al.*, 2020, Liu *et al.*, 2020).

In our study, according to statistical reports, the effective source of receiving Br-THMs in pregnant women in Isfahan was the use of a water storage tank ($p < 0.05$) (Tables 5). That showed a significant negative correlation with the concentration of urinary Br-THMs in the participants.

Using a tank is a common way for storage of water in the residential house. In this study, the use of water tanks, which are usually made of plastic, with a negative correlation, reduced the amount of DCBM, BDCM, and TBM. Scientific research by Cao *et al.* showed that the application of polyethylene pipes has been effective on water quality over time by sorption contaminants, especially THMs (Cao *et al.*, 2020). Also, according to the study of Slavik *et al.*, increasing the volume of the storage tank has reduced the amount of disinfection residual, thus affecting the formation of disinfection by-products (Slavik *et al.*, 2020).

In Table 2, in addition to tap water, participants have used other sources, such as bottled water, for drinking; but most of them had a higher average consumption of tap water than other sources. According to the analysis of Charisiadis *et al.*, the amount of THMs in water bottles against tap water was non-detectable (Charisiadis *et al.*, 2013).

Although there was an excessive daily intake of drinking water with an average of 7.14 glasses per day, urinary levels of THMs were reduced because of dilution of the THMs mass (Charisiadis *et al.*, 2013). As a result, according to Table 4, there is no significant relationship between the urinary concentration of these contaminants and water intake ($p > 0.05$).

Also, Table 4 revealed no significant relationship between other demographic and lifestyle parameters (age, education, weight, BMI, frequency, and time duration of washing dishes, clothes, as well as bathing and cleaning the house) with the concentrations of unadjusted urinary Br-THMs. Charisiadis *et al.* reported a significant relationship between the concentration of THMs in toilet cleaning and hand washing dishes (Charisiadis *et al.*, 2013). In contrast, Chen *et al.*, similar to the findings of this study, did not report a significant relationship between the concentrations of maternal blood THMs with the parameters of age, BMI, education, drinking water source, and showering (Chen *et al.*, 2019).

In another evaluation, participants' tea consumption did not have a significant correlation with brominated THMs. According to Fakour *et al.*, the use of boiling water and preserving the water temperature at 100°C for a long time, as well as more use of teapot instead of the flask as tea containers, reduces chlorine by 5–19% via better output evaporated volatile compounds into the atmosphere (Fakour and Lo, 2019). In Iran, based on the culture, tea is consumed as a common beverage during the day and for a long time, and also using teapot is usual but our data in this study did not agree with the findings of this researcher (25).

In Table 5, for other qualitative parameters, we did not observe a significant relationship between the concentration of Br-THMs and the use of household water purifiers, boiled water, dishwasher, gloves, and finally the type of detergent.

Carrasco-Turigas *et al.* stated that the use of household reverse osmosis filters affect the removal of THMs containing bromine as non-volatile compounds, moreover boiling through conventional heating such as electric kettles by creating big bubbles and equally energy had a significant influence on the chloroform removal (Carrasco-Turigas *et al.*, 2013).

Study strengths and limitations

The strengths of this study include the population-based design, high-quality urinary Br-THMs assays.

One of the strong limitations of this study was the small statistical population. According to previous studies, despite long-term sampling, increased the identification of THMs compounds, especially chloroform, which has high volatility (Gängler *et al.*, 2017), but the agreement of the participants to attend in this study depended on the short sampling time. In addition, the majority of participants have not much contribution in household tasks due to being in the third trimester of pregnancy.

The spot urine sampling may not be the best biomarker of maternal Br-THMs exposure and does not control the effect of other pollution during pregnancy.

5. Conclusion

Among the participants of this study, the use of storage tanks inversely showed a significant correlation. There was no evidence of significance between other quantitative and qualitative parameters. Comparison of Br-THMs concentrations in global studies showed that the amount of Br-THMs in women's urine in this study was dramatically less than some Asian and Asian-European countries in urine samples and was more than some American and other Asian countries in blood samples. Lifestyle and the way of consuming water between different countries have created different external and internal exposures.

Our findings show that information extracted from a combination of external and internal exposure can be effective in identifying and managing the health outcomes of environmental exposure. Furthermore, larger sample size is necessary to more suitably and significantly correlate the concentration of contaminants with lifestyle factors.

Declarations

Authors' contributions

BD contributed in the concept, conducting the study, and drafting the manuscript. AF conducted the statistical analysis and revision of the manuscript. MA contributed in the concept, conducting the study, and revising the manuscript. NB contributed in conducting the study and revising the manuscript. ShD contributed in conducting the study and revising the manuscript. RK contributed in the concept, conducting the study, and revising the manuscript.

All authors approved the final draft of the manuscript for submission, and accept the responsibility of its content.

Data availability All data generated and analyzed during this study are available from the corresponding author on reasonable request.

Compliance with ethical standards

Ethics approval and Consent to Participate IR.MUI.RESEARCH.REC.1398.631

Consent for Publication Not applicable

Competing interest The authors declare that they have no competing interest.

Funding Sources

This research was supported by Isfahan University of Medical Sciences as project # 298145. The main cohort study is funded by the Ministry of Health as the project number 194354 (IR.MUI.REC.1394.1.354)

Funding information Isfahan University of Medical Sciences (Research Project No.: 298145)

References

1. DEHNAVI, A, Azimi, GH, SARAJI, M, RABIEI-RAD, MH, 2018. Determination of Trihalomethanes Concentrations in the Drinking Water Distribution Network of Isfahan City, Iran, during the Years 2015-2016. Health Serv. Res 14:

314-320.

2. ANDRA, SS, CHARISIADIS, P, KARAKITSIOS, S, SARIGIANNIS, DA & MAKRIS, KC 2015. Passive exposures of children to volatile trihalomethanes during domestic cleaning activities of their parents. *Environ. Res* 136: 187-195.
3. BATTERMAN, S, ZHANG, L, WANG, S & FRANZBLAU, A 2002. Partition coefficients for the trihalomethanes among blood, urine, water, milk and air. *Sci. Total Environ* 284: 237-247.
4. BINA, B, Mohammadi, A, EBRAHIMI, A, AMIN, MM, POURZAMANI, HR NEMATI MANSOR, S 2012. Survey of chloroform concentration in the water distribution system of Isfahan, Iran, and zoning by GIS. *Health Serv. Res* 204-213.
5. CAO, G, HUANG, K, WHELTON, AJ & SHAH, AD 2020. Formation and sorption of trihalomethanes from cross-linked polyethylene pipes following chlorinated water exposure. *Environmental Science: Water Research & Technology* 6: 2479-2491.
6. CAO, W-C, ZENG, Q, LUO, Y, CHEN, H-X, MIAO, D-Y, LI, L, CHENG, Y-H, LI, M, WANG, F, YOU, L, WANG, Y.-X, YANG, P & LU, W.-Q 2016. Blood Biomarkers of Late Pregnancy Exposure to Trihalomethanes in Drinking Water and Fetal Growth Measures and Gestational Age in a Chinese Cohort. *Environ. Health Perspect* 124: 536-541.
7. CARRASCO-TURIGAS, G, VILLANUEVA, C. M, GOñI, F, RANTAKOKKO, P & NIEUWENHUIJSEN, M. J 2013. The effect of different boiling and filtering devices on the concentration of disinfection by-products in tap water. *J Environ Public Health* 2013.
8. CHARISIADIS, P, ANDRA, S, MAKRIS, K, CHRISTODOULOU, M, CHRISTOPHI, C, KARGAKI, S & STEPHANOU, E 2014. Household cleaning activities as noningestion exposure determinants of urinary trihalomethanes. *Environ. Sci. Technol* 48: 770-780.
9. CHARISIADIS, P, ANDRA, SS, MAKRIS, KC, CHRISTODOULOU, M, CHRISTOPHI, CA, KARGAKI, S & STEPHANOU, E G 2013. Household Cleaning Activities as Noningestion Exposure Determinants of Urinary Trihalomethanes. *Environ. Sci. Technol* 48: 770-780.
10. CHEN, Y-J, LIU, C, HUANG, L-L, AI, S-H, SUN, L, HUANG, Z, LI, J, LEI, H-S, LIU, J, LIU, Y-A, WANG, X, LIU, X-Y, CHENG, Y-H, WANG, Y-X, PAN, A & LU, W-Q 2019. First-trimester blood concentrations of drinking water trihalomethanes and neonatal neurobehavioral development in a Chinese birth cohort. *J. Hazard. Mater* 362: 451-457.
11. DENG, Y-L, YANG, P, CAO, W-C, WANG, Y-X, LIU, C, CHEN, Y-J, HUANG, L-L, LU, W-Q, WANG, L-Q & ZENG, Q 2019. Urinary biomarker of late pregnancy exposure to drinking water disinfection by-products and ultrasound measures of fetal growth in Wuhan, China. *Environ. Res* 170: 128-133.
12. FAKOUR, H & LO, S-L 2019. Formation and risk assessment of trihalomethanes through different tea brewing habits. *Int J Hyg Environ Health* 222: 117-124.
13. GÄNGLER, S, MAKRIS, KC, BOUHAMRA, W & DOCKERY, DW 2017. Coupling external with internal exposure metrics of trihalomethanes in young females from Kuwait and Cyprus. *J Expo Sci Environ Epidemiol* 28:140-146.
14. GÄNGLER, S, MAKRIS, KC, BOUHAMRA, W & DOCKERY, DW 2018. Coupling external with internal exposure metrics of trihalomethanes in young females from Kuwait and Cyprus. *J Expo Sci Environ Epidemiol* 28: 140-146.
15. KANG, H-S, KYUNG, M-S, KO, A, PARK, J-H, HWANG, M-S, KWON, J-E, SUH, J-H, LEE, H-S, IM MOON, G & HONG, J-H 2016. Urinary concentrations of parabens and their association with demographic factors: A population-based cross-sectional study. *Environ. Res* 146:245-251.
16. LIU, B 2014. Impact of water heating on disinfection byproducts concentration.
17. LIU, C, WANG, Y-X, CHEN, Y-J, SUN, Y, HUANG, L-L, CHENG, Y-H, LIU, E-N, LU, W-Q & MESSERLIAN, C 2020. Blood and urinary biomarkers of prenatal exposure to disinfection byproducts and oxidative stress: A repeated

measurement analysis. *Environ. Int* 137: 105518.

18. MOHAMMADI, A, MIRI, M, EBRAHIMI, A, KHORSANDI, H & NEMAT, S 2016. Monitoring of THMs concentration in Isfahan water distribution system and zoning by GIS, a case study in the center of Iran. *Iranian journal of health, safety and environment* 3: 421-427.
19. MOSAFERI, M, ASADI, M, ASLANI, H, MOHAMMADI, A, ABEDI, S, MANSOUR, SN & MALEKI, S 2020. Temporospatial variation and health risk assessment of trihalomethanes (THMs) in drinking water (northwest Iran). *Environ. Sci. Pollut. Res* 1-13.
20. RIVERA-NÚÑEZ, Z, WRIGHT, JM, BLOUNT, BC, SILVA, LK, JONES, E, CHAN, R L, PEGRAM, R A, SINGER, PC & SAVITZ, DA 2012. Comparison of trihalomethanes in tap water and blood: a case study in the United States. *Environ. Health Perspect* 120: 661-667.
21. SLAVIK, I, OLIVEIRA, KR, CHEUNG, PB & UHL, W 2020. Water quality aspects related to domestic drinking water storage tanks and consideration in current standards and guidelines throughout the world—a review. *J Water Health* 18: 439-463.
22. STAYNER, L T, PEDERSEN, M, PATELARO, E, DECORDER, I, VANDE LOOCK, K, CHATZI, L, ESPINOSA, A, FTHENOU, E, NIEUWENHUIJSEN, MJ, GRACIA-LAVEDAN, E, STEPHANO, EG, KIRSCH-VOLDERS, M & KOGEVINAS, M 2014. Exposure to Brominated Trihalomethanes in Water During Pregnancy and Micronuclei Frequency in Maternal and Cord Blood Lymphocytes. *Environ. Health Perspect* 122: 100-106.
23. SUN, Y, WANG, Y-X, LIU, C, CHEN, Y-J, LU, W-Q & MESSERLIAN, C 2020. Trimester-Specific Blood Trihalomethane and Urinary Haloacetic Acid Concentrations and Adverse Birth Outcomes: Identifying Windows of Vulnerability during Pregnancy. *Environ. Health Perspect* 128:107001.
24. VILLANUEVA, CM, GRACIA-LAVEDÁN, E, IBARLUZEA, J, SANTA MARINA, L, BALLESTER, F, LLOP, S, TARDÓN, A, FERNÁNDEZ, M F, FREIRE, C & GOÑI, F 2011. Exposure to trihalomethanes through different water uses and birth weight, small for gestational age, and preterm delivery in Spain. *Environ. Health Perspect* 119: 1824-1830.
25. WANG, Y-X, LIU, C, CHEN, Y-J, DUAN, P, WANG, Q, CHEN, C, SUN, Y, HUANG, L-L, WANG, L & CHEN, C 2019. Profiles, variability and predictors of concentrations of blood trihalomethanes and urinary haloacetic acids along pregnancy among 1760 Chinese women. *Environ. Res* 172: 665-674.
26. ZENG, Q, CAO, W-C, ZHOU, B, YANG, P, WANG, Y-X, HUANG, Z, LI, J & LU, W-Q 2016. Predictors of Third Trimester Blood Trihalomethanes and Urinary Trichloroacetic Acid Concentrations among Pregnant Women. *Environ. Sci. Technol* 50: 5278-5285.

Figures

Figure 1

The locations of living areas of participants

Figure 2

Comparison of Br-THMs concentrations in global studies (Charisiadis et al., 2013, Zeng et al., 2016, Cao et al., 2016, Gängler et al., 2017, Wang et al., 2019, Chen et al., 2019, Sun et al., 2020, Liu et al., 2020). *M: Mean; GM: Geometric Mean; Med: Median;