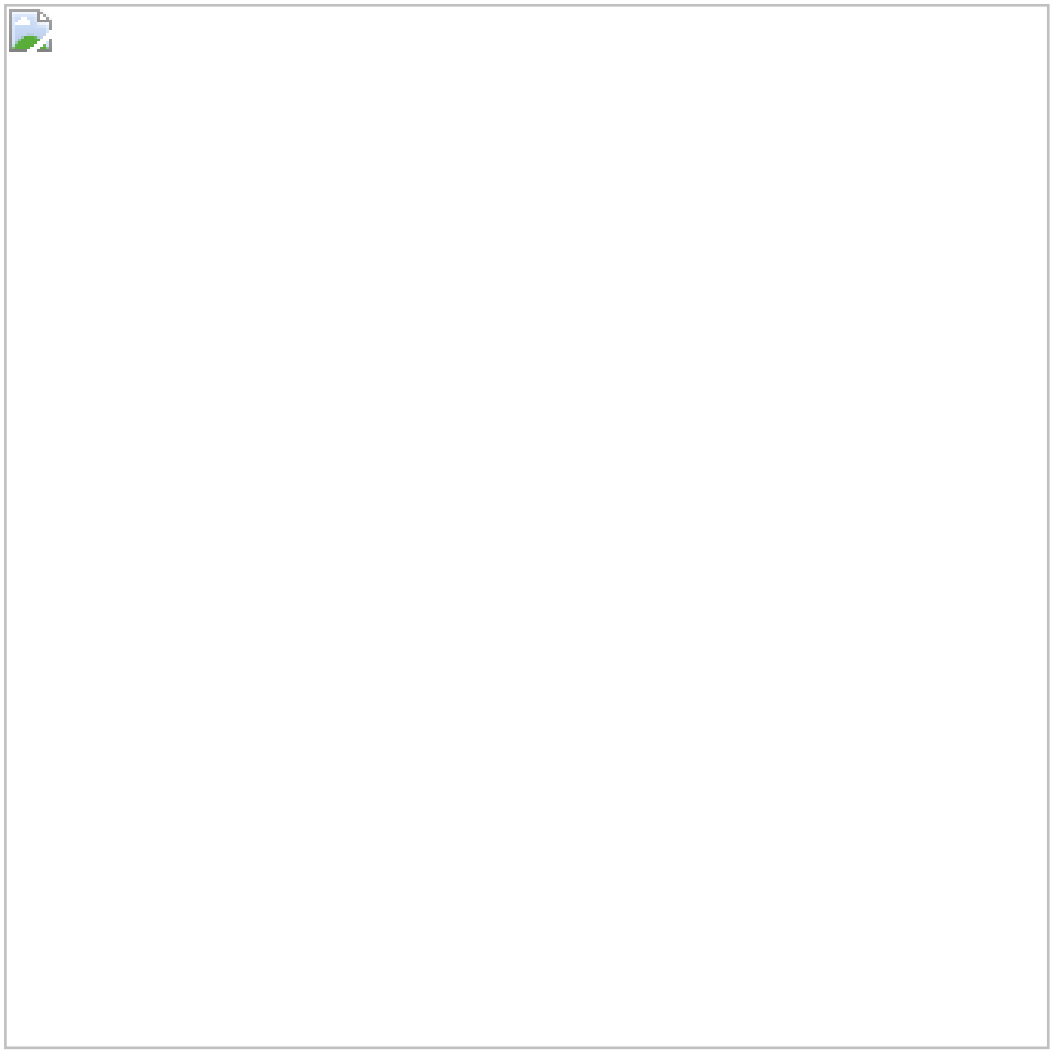

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Authors: Dehdashti, Bahare, Nikaeen, Mahnaz, Amin, Mohammad Mehdi, and Mohammadi, Farzaneh

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Health Risk Assessment of Exposure to Bisphenol A in Polymeric Baby Bottles

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Bahare Dehdashti[1,2,3], Mahnaz Nikaeen[1], Mohammad Mehdi Amin[1,3] and Farzaneh Mohammadi[1]

[1]Department of Environmental Health Engineering, School of Health, Isfahan University of Medical Sciences, Isfahan, Iran. [2]Student Research Committee, School of Health, Isfahan University of Medical Sciences, Isfahan, Iran. [3]Environment Research Center, Research Institute for Primordial Prevention of Non-communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran.

ABSTRACT: In recent decades, paying attention to bisphenol A (BPA), as one of the endocrine disruptor compounds, has increased due to its harmful effects. Although, scattered studies have been conducted in order to measure BPA concentration migrated into polymeric baby bottles in different countries of the world, there are no review studies and evaluation with a global perspective in the field of BPA risk. Some of these studies indicated the potential risks and estrogenic effects associated with BPA in babies' daily intake. For this purpose, we reviewed the information on the migration levels of BPA into baby bottles has been reported in 10 countries. The potential risks associated with BPA through the daily intake as well as the estrogenic effect on 3 age groups of babies which include 0 to 6, 6 to 12, and 12 to 24 months were analyzed using the Monte Carlo simulation. Also, kinetic models were applied to predict the kinetics of the migration process of BPA. The median daily intake for 3 age groups was obtained as 191.1, 161.37, and 153.76 µg/kg/day, respectively; which indicated Hazard Index (HI) > 1. The median estrogenic effect for the 3 groups was estimated to be 0.021 ngE_2/L. The kinetics of contaminant transfer with Polynomial model at 2 temperatures of 24°C and 40°C showed a better fit with $R^2 = 0.99$ and 0.91, respectively. Based on the risk assessment analysis conducted in the present study, the BPA migration in baby bottles appeared to be a health concern for babies. Therefore, it is needed to increase the safety level of bottles for babies as they are sensitive and vulnerable members of every society. Furthermore, in this study, only the investigation of the global situation of BPA in polymeric baby bottles was stated; therefore, more investigation about another potential sources of BPA in food chain is needed.

KEYWORDS: Baby bottle, bisphenol A, daily intakes, estrogenic effects, risk assessment

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CORRESPONDING AUTHOR: Farzaneh Mohammadi, Department of Environmental Health Engineering, School of Health, Isfahan University of Medical Sciences and Health Services, Hezar Jerib Street, Isfahan 81746-73461, Iran. Email: fm_1363@hlth.mui.ac.ir

Introduction

Bisphenol A, as an endocrine disruptor, has received widespread attention due to its harmful effects.[1] BPA is a crystalline solid of diphenylmethane derivatives, which is soluble in natural solvents, and it was commercialized for the first time in 1957.[2] This colorless substance with a low solubility level in water is composed of 2 phenolic rings linked to methyl functional groups.[3] BPA is used in manufacturing plastic products such as water bottles, baby bottles, food containers, automotive spare parts,[2] and epoxy resin to be used in metal cans.[1] In this regard, ingestion is the first route of exposure to BPA.[4] Still, its presence in soil, dust, air, water, and medical supplies suggests other ways of its transmission, such as skin and respiratory absorptions.[5] Babies are mostly exposed to this contaminant through plastic baby bottles usage. Studies have previously shown the BPA rate in the urine samples of adults and babies as 95% and 93%, respectively.[3] Moreover, various human and animal studies have emphasized the effect of BPA on estrogenic function due to its early exposure, especially during infancy. Accordingly, some of the health effects are autism, hyperactivity, and neurological problems. Hormonal and reproductive disorders, breast and prostate cancers, delayed maturation in women, and infertility in men have also been reported which resulted from exposure to BPA.[6,7] For example in the study of Fonseca et al,[8] the increased risk of adult cardiovascular diseases and gestational hypertension disorders by exposure to BPA caused through intracellular processes, inhibition of main ion routs, changes in Ca^{2+} movement, induction of oxidative stress, and epigenetic changes.

The US environmental protection agency (USEPA) has proposed a reference dose of 50 µg/kg body weight/day through oral exposure.[9] The specific level of migration of BPA in food was also reported as 600 µg/kg.[6] Since the migration of chemicals, especially plastic compounds, to food is done through chemical reactions in very low concentrations, chronic toxicity is caused by the accumulation of low concentrations of contaminants over time. In addition, the use of general health risk assessment techniques to estimate EDCs risks is common throughout the world.[10]

The increased use of BPA, as well as its toxic, teratogenic, carcinogenic, and estrogenic effects and potential health risk associated with exposure to it, especially in the childhood period,[9] highlights the need for more investigations on the risk of the exposure to BPA through baby containers.

Risk assessment as an important and systematic method has had a wide managerial role since the past. So its importance is significant in the fields of exposure to material with potential health concern.[11]

Improving the level of safety, risk management and preparedness in emergency situations, as well as increasing public mindfulness due to the development of various chemical processes in the production of compounds and the creation of probable risks, has increased the importance of the science of risk assessment.[12]

Monte Carlo is a simulation based probabilistic method, by estimating an empirical distribution similar to the risk distribution in the whole population, reduces the unsolved computation of the distribution density.[13,14] Exposure to chemicals in foods, both acute and chronic, is evaluated by probabilistic methods using the Monte Carlo Risk Model.[15] Given 10 000 simulations in this simulator, 10 000 probable outcomes have been investigated with finally a distribution for estimated risk and population exposure.[14]

Since the possible adverse effects of BPA have been confirmed on human health, various studies have investigated the concentration of BPA in baby bottles. In addition, the storage and maintenance conditions that were effective in the migration of BPA to baby bottles were also taken into consideration. However, global assessment of the BPA migration status in baby bottles is not yet obvious. It is noteworthy that the most of the studies were cross-sectional. Due to the exposure of babies to plastic bottles during long-term period, it seems that mathematical models have a great ability to predict the migration of BPA to baby bottles in different storage conditions with using a simple and effective way. Therefore, this study was designed to evaluate the health risk, estrogenic activity and migration kinetics associated with BPA in baby bottles based on the concentrations reported in various studies performed worldwide.

Materials and Methods

Data sources

Data collection was performed by searching some international databases, including web of science, Scopus, and Google scholar, using the following keywords: "bisphenol A," "baby bottles," and "polycarbonate bottles" between 2000 and 2021. Finally, 23 articles from 16 countries were found, and eventually, 10 original articles were selected to be included in this study.

Different concentrations of BPA (part per billion, ppb) migration from various brands of polycarbonate plastic baby bottles into beverages (milk, water, apple juice) have been reported under various application conditions (Table 1).

Migration kinetics of BPA from plastic baby bottles to beverages

To describe the migration process of BPA from plastic baby bottles into baby beverages, kinetic models were made considering storage time and temperature. For this purpose, the information reported in the study by Li et al[18,23] was analyzed with different linear, exponential, polynomial, logarithmic, and power models (Table 2).

Health risk assessment

The survey on the possibility of adverse health effects associated with the exposure to a contaminant over a specified period of life and on a specific population, is called human health risk assessment, which includes hazard identification, toxicity evaluation, exposure assessment, and risk characterization.[7,24] In the current study, the risk assessment analysis was performed using R Studio Version 1.3.959 software, Environmental Probabilistic Risk Assessment Tools (EnviroPRA), and Monte Carlo packages.

Hazard identification. Health risk associated with BPA ingestion by using plastic baby bottles in the 3 age groups 0 to 6, 6 to 12, and 12 to 24 months was estimated according to the data collected from several previously-performed studies (Table 1).

Exposure assessment. Oral exposure to BPA using polymer bottles in 3 age groups was obtained by equation (6).[13]

$$EDI_{ing} = \frac{C_{BPA} \times IR}{BW} \quad (6)$$

Where EDI_{ing} is the estimated daily intake through ingestion (μg/kg/day), C_{BPA} is the concentration of BPA (μg/L) released from baby bottles into beverages (including water, milk, fruit juices, etc.) or emigration concentration. IR is beverage ingestion rate (mL/day), and BW is body weight (kg).[13] In this study, for baby bottles in which the concentration of BPA has been reported either as not detectable (ND) or as the lower limit of detection (<LOD), the concentration of BPA was considered to be half of the limit of detection (LOD).[24] Furthermore, the data reported in the study in Egypt in 2018 (1) were not entered into the model of this study due to having a wide range of values, which were considerably different from other concentrations reported in the other studies.

Dose response and risk characterization. HI was used to evaluate the non-carcinogenic effects of BPA due to its oral exposure. Where $HI < 1$ indicates safety levels and $HI > 1$ indicates potential risk. The HI value was calculated using equation (7).

$$HI = \frac{EDI}{RFD} \quad (7)$$

BPA reference dose (RFD) based on the oral exposure route was considered as 50 μg/kg/day using the USEPA Integrated Risk Information System (IRIS) database.[9]

In risk assessment, the possibility of uncertainties in data increases by assigning a single value to variables. Therefore, in this study, Monte Carlo simulation was used to decrease the uncertainties of input variables. More effective variables in risk assessment were also determined by sensitivity analysis.[13] The parameters used in our study are presented in Table 3.

Table 1. Minimum and maximum levels of migration concentration of BPA (μg/L) from baby bottles.

COUNTRY	YEAR	BPA MIGRATION CONCENTRATION (μG/L)	BABY BOTTLE APPLICATION CONDITION	REFERENCE
Jordan	2019	Min = 0.35 Max = 5.2	A random selection of 15 free/safe/clear (of BPA) polycarbonate plastic (PC) baby bottles with 30 times brush, filled with milk	Ali et al[3]
		Min = 0.68 Max = 5.6	A random selection of 15 free/safe/clear (of BPA) polycarbonate plastic (PC) baby bottles with 60 times brush, filled with milk	
Egypt	2018	Min = 4.6 Max = 123.53	Selection of different brands (3A and 3B), PC, filled baby bottles with anise, milk, water for 1 h	Osman et al[1]
		Min = 38.04 Max = 222.9	New brands of A, B, C of 9 PC baby bottles at 25°C, 60°C, and 90°C filled with milk	
		Min = 132.54 Max = 623.81	50 times used brands A, B, C of 9, PC baby bottles at 25°C, 60°C, and 90°C filled with milk	
		Min = 405.01 Max = 1046.79	100 times used brands A,B,C of 9, PC baby bottles at 25, 60, and 90°C filled with milk	
Iran	2015	Min = 0.49 Max = 13.58	7 new brands of PC baby bottles with the first and second tests filled with water	Moghadam et al[6]
		Min = 0.63 Max = 2.47	8 times used brands of PC baby bottles filled with water	
India	2015	Min = 3.05 Max = 3.82	6 brands of PC baby bottles filled with water, milk, and apple juice at room temperature	Johnson et al[16]
		Min = 3.16 Max = 46.05	6 brands of PC baby bottles filled with boiled water, milk, and sterilization water at 95°C	
India	2014	Min = 17 Max = 22	3 brands of PC baby bottles filled with water	Shrinithivihahshini et al[17]
China	2010	Min = 0.0375 Max = 18.75	4 brands of PC baby bottles filled with water within 1 day (24 h) at 24°C, 40°C, and 100°C	Li et al[18]
		Min = 0.0079 Max = 0.98	4 brands of PC baby bottles filled with water within 3 days at 24°C and 40°C	
		Min = 0.0458 Max = 1.058	4 brands of PC baby bottles filled with water within 5 days at 24°C and 40°C	
		Min = 0.00416 Max = 0.67	4 brands of PC baby bottles filled with water within 7 days at 24°C and 40°C	
Greece	2008	Min = 2.4 Max = 14.3	6 brands A, B, C, D, E, and F of PC baby bottles filled with water	Maragou et al[19]
Netherland	2008	Min ⩽ 0.1 Max = 0.49	18 brands of PC baby bottles filled with water after microwave heating cycle (the First cycle)	Ehlert et al[20]
		Min ⩽ 0.1 Max = 0.73	18 brands of PC baby bottles filled with water after microwave heating cycle (the Second cycle)	
		Min ⩽ 0.1 Max = 0.3	18 brands of PC baby bottles filled with water after microwave heating cycle (the Third cycle)	

(Continued)

Table 1. (Continued)

COUNTRY	YEAR	BPA MIGRATION CONCENTRATION (μG/L)	BABY BOTTLE APPLICATION CONDITION	REFERENCE
Norway	2003	Min = 0.11	12 new brands of PC baby bottles filled with water	Brede et al[21]
		Max = 0.43		
		Min = 3.7	12 brands of PC baby bottles filled with water and 51 days usage	
		Max = 16.7		
		Min = 2.54	12 brands of PC baby bottles filled with water and 169 days usage	
		Max = 15.2		
Japan	2000	Min = 0.13	PC and glass baby bottles filled with water used for 4 sequences?? (the first, second, third, and fourth). All glass samples were not detected.	Sun et al[22]
		Max = 0.75		

Table 2. Migration kinetics of BPA.

MODELS	EQUATIONS	EQUATION NUMBER
Linear	$C = a_1 + b_1 \times t$	(1)
Exponential	$C = a_2 \times EXP(b_2 \times t)$	(2)
Polynomial	$C = a_3 + b_3 \times t + c_3 \times t^2$	(3)
Logarithmic	$C = b_4 \times \ln(t) + a_4$	(4)
Power	$C = a_5 \times t^{b_5}$	(5)

a_1, b_1, the constants of linear model; a_2, b_2, the constants of exponential model; a_3, b_3, and c_3, the constants of polynomial model; a_4, b_4, the constants of logarithmic model; a_5, b_5, the constants of power model; C, BPA concentration; t, storage time.

Table 3. Parameters used in the study.

PARAMETERS	UNIT	SYMBOL	PROBABILITY DISTRIBUTION	REFERENCE
BPA concentration	μg/L	C	Weibull $a = 2.332$, $b = 0.648$, $c = 0$	This study
Drinking beverage ingestion rate	mL/day	IR		
0-6 (months)			Uniform (609.04, 1116.76)	US EPA National Center for Environmental Assessment WDEA and RCG[25]
6-12 (months)			Uniform (866.04, 1415.75)	
12-24 (months)			Uniform (1117.03, 1578.79)	
Body weight	kg	BW		
0-6 (months)			Uniform (3.3, 8.9)	US EPA National Center for Environmental Assessment WDEA and RCG[25]
6-12 (months)			Uniform (7.5, 11.2)	
12-24 (months)			Uniform (9.2, 14)	
Reference dose	(μg/kg/day)	RFD	Constant = 50	Notardonato et al[9]
Estrogenic potency	(μg/kg/day)	EP	Constant = 0.0000160	Wang et al[26]

Table 4. Kinetic models on migration of BPA from plastic baby bottles.

MODEL	TEMPERATURE (°C)	EQUATION	R^2
Linear	24	$C = -0.0061 \times t + 1.0356$	0.70
	40	$C = -0.0214 \times t + 3.7581$	0.67
Polynomial	24	$C = 9 \times 10^{-5} \times t^2 - 0.0235 \times t + 1.6114$	0.99
	40	$C = 0.0003 \times t - 0.0784 \times t + 5.6402$	0.914
Power	24	$C = 24.281 \times t^{-0.992}$	0.87
	40	$C = 62.234 \times t^{-0.891}$	0.91
Exponential	24	$C = 1.063E - 0.012 \times t$	0.71
	40	$C = 3.8146E - 0.011 \times t$	0.76
Logarithmic	24	$C = -0.502 \ln \times t + 2.634$	0.90
	40	$C = -1.776 \ln \times t + 9.4179$	0.87

Estrogenic activity assessment

BPA was shown to have a weak estrogenic activity compared to natural estrogens. However, its high concentrations in baby bottles may cause a considerable estrogenic potency.[27] Due to the estrogenic activity of BPA, the estrogen equivalence (EEQ) was calculated using equation (8).[24,26]

$$EEQ\_ = EP \times C \quad (8)$$

Where EP represents the estrogenic potency of BPA and C is BPA concentration in the baby bottles (μg/L). Of note, the unit of EEQ_ is μgE_2/L. As the selected standard compound, 17β-estradiol (E_2) was indicated to have the most vigorous estrogenic activity; therefore, the EP of this compound was considered as 1. When the EP of a compound is lower than 1, its estrogenic activity is weaker than E_2.

Results and Discussion

Effective factors in BPA migration from polymeric baby bottles

There are 2 different processes in the migration of BPA from polycarbonate bottles into liquids. (1) The diffusion of BPA occurs due to its residues from the production process, (2) through the consumption process such as, contact of liquid food with polycarbonate, hydrolysis of bottles, and the catalysis of its polymers by hydroxide groups (OH^-). In the case of dry food, diffusion is the main way of BPA transmission.

Effective parameters for BPA release are temperature, contact time, washing method, food pH, detergent type, kind of food, mineral contents of food, and duration of using plastic bottles,[28] which some of them are listed in Table 1.

In a study, 50% ethanol in water or 3% acetic acid was used to simulate milk and fruit juice, respectively. An 8% to 50% increase in ethanol level in liquid solutions after 10 days at 65°C increased the BPA level from 0.87 to 5.9 mg/L.[28] BPA concentration of 1 mg/L was also obtained in tap water and distilled water after 10 days at 65°C.[28]

According to the reports by Cao and Corriveau,[29] BPA migration was found to be directly related to the temperature, which increases over time, so that for 6 days at 70°C, the BPA concentration in water varied from 228 to 521 μg/L and showed a rising trend. On the other hand, Li et al in their study examined the trend of BPA concentration changes after 1, 3, 5, and 7 days in different brands and at various temperatures. A decrease in BPA concentration was observed over time.[18]

Maragou et al in their study have emphasized the temperature in baby bottles as an essential factor in the transfer of BPA to water. Accordingly, the concentrations ranged from 2.4 to 14.3 μg/kg in boiling water.[19]

In another study, Brede et al[21] analyzed the number of times of baby bottle's washing, and reported an average BPA concentration of 0.23 ± 0.12 μg/L in new bottles, as well as 8.4 ± 4 and 6.7 ± 4 μg/L for 51 and 169 times of washings, respectively. However, some release monitoring has stated low BPA values after washing. Increasing the pH up to more than 8 during the food production process, which is sometimes due to the presence of minerals in food, is another effective parameter in increasing the BPA release.[28] Age of baby bottles also plays an influential role in BPA migration.[28]

Kinetics analysis

To investigate the kinetics of BPA migration into the contents of the baby bottles, the trend of BPA concentration changes at 24, 72, 120, and 168 hours at 24°C and 40°C was considered and then analyzed using the equations of the models reported in Table 2.[18] The results summarized in Table 4 show that at 24°C and 40°C, the polynomial model had the best fit for the

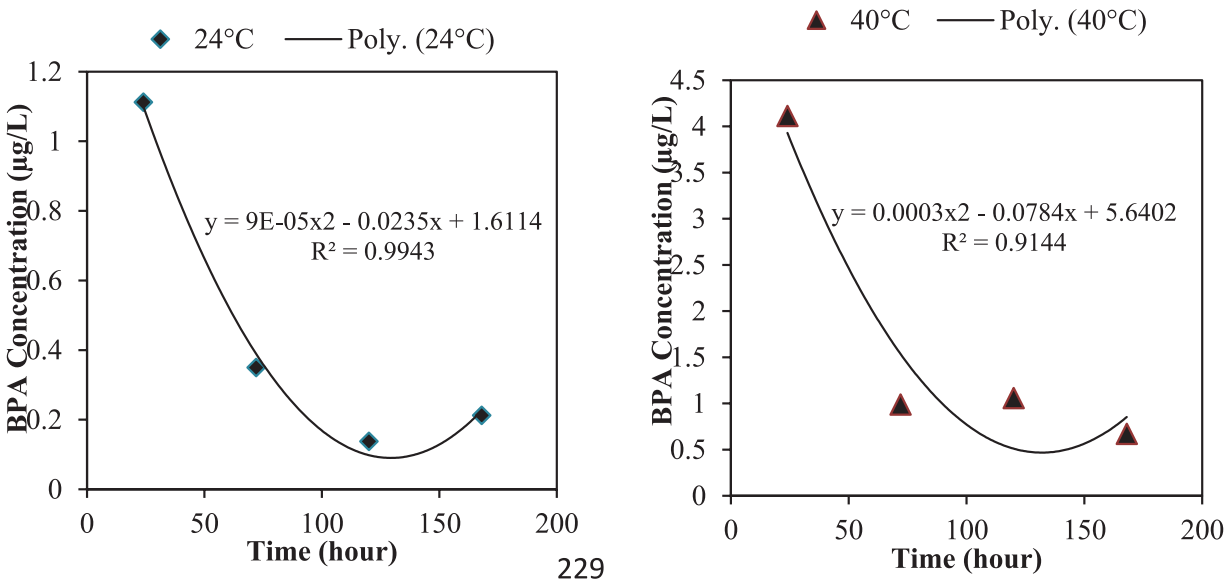

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Figure 1. The trend of changes in the concentration of migrated BPA in plastic baby bottles at different storage time at 2 temperatures, 24°C and 40°C.[18]

variation of BPA concentration over time with R^2 equal to 0.99 and 0.91, respectively. The trend of concentration variation over time at the 2 investigated temperatures is illustrated in Figure 1.

Figure 1 shows that the rate of BPA release during initial storage (normal temperature) is the highest, which decreases with increasing time. In addition, the level of BPA released from 24˚C to 40˚C risen from 1.1 to 4.1 µg/L in the early days of storage. Therefore, a positive and significant relationship was observed between the temperature increase and the increased release of BPA. Luo et al[24] assessed the potential risk of free phthalate compounds in plastic water bottles in 21 countries using various kinetic models, in order to describe and predict the migration process of phthalates. The exponential model revealed more appropriate fit and showed that low storage temperature had a significant effect in reducing the migration of phthalates into water.[24]

Risk assessment of BPA in polymeric baby bottles

Since BPA released from bottles and plastic packaging is a significant health concern because of its toxicity and disruptive effects, USEPA has recommended the tolerable daily intake of BPA as 50 µg/kg of body weight/day 30.

EDI for the 3 age groups was calculated (equation (6)) as 191.1, 161.37, and 153.76 µg/kg/day, respectively. The estimated EDI of BPA in babies was generally higher than the standard level for all age groups (50 µg/kg of bodyweight/day). In this regard, the HI (equation (7)), as a non-carcinogenic index, was obtained as 3.82, 3.22, and 3.07 in the age groups of 0 to 6, 6 to 12, and 12 to 24 months, respectively, which is higher than 1. The results indicate that exposure to BPA through the use of baby bottles is a risk to babies health. In contrast, Farooq et al[30] has previously reported the daily exposure dose (DED) of BPA in milk samples as 1.42 to 2.67 and

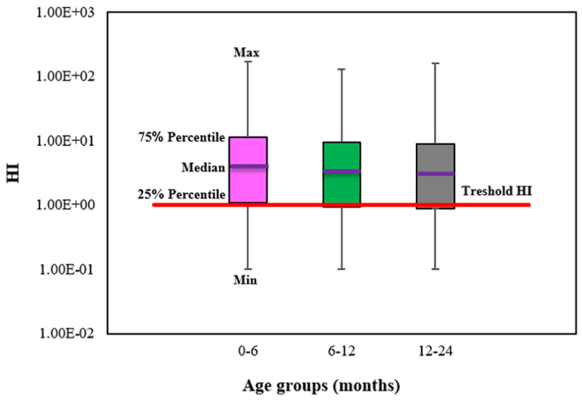

Figure 2. Comparison of calculated risk in 3 age groups.

5.58 to 10 µg/kg, which was lower than 50 µg of BPA/kg of body weight standard limit.

Abdi Moghadam et al[6] reported that, the exposure of babies aged less than 1 year with BPA using plastic baby bottles in Isfahan city was about 0.1 to 0.3 µg/kg body weight/day with a Hazard Quotient (HQ) < 1, indicating a low risk. Figure 2 compares the risk estimated in this study and the reference level. The limitation of this study was the lack of available studies on BPA concentrations in polymeric baby bottles in all countries. On the other hand, there were several potential sources of BPA in baby bottles, including drinking water sources, milk powder, food packaging, baby food, dairy products, fruit juices, and baby products.[27,31-37] For example, despite having a short half-life of 2.5 to 5 days, BPA is commonly found in surface waters. The scale of BPA detection for river water was in the range of ng/L, but in the USA, Japan, Spain, China, and the Netherlands, it was reported to be more than 1 µg/L. Immersed and discarded plastics in the river, including pipes, glasses, and drinking bottles, as well as discharging agricultural and industrial wastewater, are the other possible dissemination ways of BPA to the river or municipal sewage system.[26]

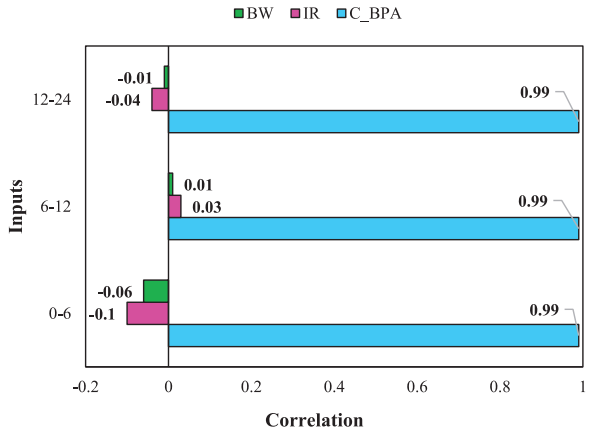

Figure 3. Sensitivity analysis of HI model for BPA in different age groups.

The BPA concentration of water in 3 geographical regions of the United States, Ghana, and Jamaica with different economic levels, was determined in the study of Karalius et al. In their study, the concentrations of BPA in the river, drinking, and bottled water in the United States were obtained as 0.12, 0.01, and 0.003 ng/mL, respectively. Additionally, the average concentration of BPA in drinking water in Ghana was 0.008 ng/mL, and in Jamaica the concentrations of 0.003, 0.016, and 0.008 ng/mL were reported for drinking, surface, and bottled water, respectively.[32]

BPA compounds due to their lipophilic properties, are also found in high-fat, high-protein animal foods. Contamination of baby milk powder has been found to be likely through plastic packaging, so Cai et al[38] have identified 0.8 to 14 g/kg BPA in 35 samples of baby milk powder.

In another study, Lee et al[36] examined the level of BPA in the diet of babies aged less than 2 years old. They have reported an average of 5.09 and 0.47 ng/g for BPA concentrations in the diet of 15 months-old babies and 9 or 12 months-old babies, respectively.[36]

Santonicola et al[39] have also analyzed BPA in 72 cow milk samples and reported average concentrations of 0.757, 0.580, and 0.797 µg/L for the samples of manual, mechanical, and cooling tanks, respectively. Lee et al[36] and Gallo et al[37] have also evaluated the amount of BPA in fruit juices, and reported its concentration in a range of 0.5 to 2.58 ng/mL.

Sensitivity analysis

Sensitivity analysis was done to determine the most influential variables in calculating risk assessment. Figure 3 shows the results of the sensitivity analysis for the 3 age groups of babies exposed to BPA through baby bottles. Correspondingly, the results showed that the concentration of BPA was the most influential parameter in calculating HI for all groups. The reported concentrations of BPA migrated into baby bottles according to the relevant available studies are as the mean ± SD of 3.185 ± 4.99 µg/L and the median of 1.33 with 1.27 and 1.38 µg/L as low and high limits, respectively. Farooq et al[30] determined the level of leachate containing BPA caused by milk plastic packaging as 0.17 to 0.32 and 0.77 to 1.59 mg/kg, in winter and summer, respectively. Wang et al also calculated the average amount of BPA as 20.8 and 1394.3 ng/L in both PET and PC bottles, respectively. In addition, Abdi Moghadam et al have reported the concentration of BPA in baby bottles by considering new and old bottles in the age group of 6 to 12 months. The average concentration for both new and old bottles was obtained as 1.57 µg/L and the average concentration of BPA in conventional plastic bottles was estimated as 2.7 µg/L. The maximum amount of free BPA calculated in the used bottles under boiling conditions was 14 µg/L.[6]

In the age group of 6 to 12 months, the daily ingestion rate (IR) was the second influential parameter with a positive effect on HI, and body weight had a small effect in this regard. However, IR and BW in the age groups of 0 to 6 and 12 to 24 months showed a negative relationship with HI with a very low effect. Therefore, reducing the concentration of migrant BPA in baby bottles is one of the ways to reduce non-carcinogenic risks. Chang et al in their study by examining the 4-nonyl phenol and BPA compounds in food, have stated that the concentration of contaminant (C) is the most effective parameter for creating risk in the age range of 0 to 3 years. Then the daily consumption (IR) was found to be important.[40]

Potential estrogenic effect of BPA

The evaluation of the potential estrogenic activity of BPA based on equation (3) was done for the 3 age groups, the statistical distribution shows in Table 3.

In the study, the mean and median EEQ values for 3 age groups were obtained as 0.05 ± 0.079 and 0.021 ngE_2/L, respectively which showed no high risk of estrogenic effect. The EEQ level of BPA in the water through ingestion was estimated to be 0.019 and 0.15 ng/L/day for babies and adults, respectively.[41] Therefore, EEQ is slightly higher for babies in this study compared to the results mentioned above. BPA in the body at high concentrations behaves similar to natural estrogen, 17β-estradiol. Also, small amounts (pico and nanomolar) were shown to cause multidirectional effects on the physiological function of cells and tissues by binding to receptors outside the cell.[41]

In contrast to our results, the study by Wang et al[26] on the evaluation of BPA in drinking water bottles, the average and maximum EEQ level in PC bottles were obtained as 2.71 and 12.54 ngE_2/L. respectively, which has shown high estrogen equivalence values

Implications to Safety of Baby Bottles

According to Ali et al[3] many countries, including the United States, Sweden, China, and Malaysia, have banned the use of BPA in manufacturing products. Despite using the term "BPA

free" on the labels of some baby bottles, there is still uncertainty about the use of BPA in production of baby bottles. Ali et al have shown that BPA release is possible under certain conditions, and baby bottles are not 100% BPA free. Therefore, it is necessary to perform further tests and present clear information on the possible amount of BPA in baby bottles. It is also recommended that parents replace glass bottles with plastic ones. Additionally, they should change the old bottles and replace them with new ones, and the use of suitable detergents is also recommended.[3]

BPA and BPS (bisphenol S) might not be the only problematic chemicals in plastic materials. For instance, phthalates are chemicals widely used to make plastic flexible. Močnik et al[42] stated that BPA, phthalates, perfluorinated alkyl substances, and persistent organic pollutants are the most effective substances in the development of obesity in children.

Fonseca et al[8] also confirmed the effect of BPA on increase the risk of cardiovascular diseases and recommended storing food in glass containers and reducing plastic containers in order to improve lifestyle and decrease exposure to BPA. In addition, plastic bottles have a weaker structure than glass and are more difficult to clean.[43] Trasande et al[44] also stated the use of stainless steel and glass as another option to reduce exposure to the chemical compounds.

Conclusion

In the present study, a comprehensive picture of BPA concentration in baby bottle liquids around the world along with its health risk assessment as well as the level of estrogenic effect in the 3 age groups of 0 to 6, 6 to 12, and 12 to 24 months based on the amount of daily intake was provided. The kinetics of BPA release from the bottles using Polynomial model indicated better fit and predicted the highest rate of transferring this contaminant into the bottle liquids at early hours and a normal temperature between 24°C and 40°C. The risk analysis showed HI values greater than one, demonstrates the problematic release of this compound in baby's bottles. In addition, the result showed that the daily intake for 3 age groups was high, but estrogenic activity was negligible. The sensitivity analysis presented that the concentration of BPA was the most critical parameter in assessing BPA risk in baby bottles.

Therefore, it is essential for the public health departments to test the toxicity of chemicals before presentation the product to the market. Finally, it is recommended to ban the use of this compound in the structure of baby bottles and then replace it with safe substances such as stainless steel and glass.

Authors Contributions

Bahare Dehdashti: Data collection and curation, original draft. Mahnaz Nikaeen: Conceptualization, supervision, review & editing. Mohammad Mehdi Amin: Conceptualization, review & editing. Farzaneh Mohammadi: Methodology, data analysis, Software.

Consent for Publication

Not applicable.

Data Availability Statement

All data analyzed during this study are included in this published article, and the datasets used during the current study are available from the corresponding author on reasonable request.

Ethics Approval

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ORCID iD

Farzaneh Mohammadi https://orcid.org/0000-0002-8248-3629

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