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Paediatrics Section

Potential Sources of Exposure and Urinary Bisphenol A Concentration in Children

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ABSTRACT

Introduction: Bisphenol A (BPA) is a synthetic compound used in the plastics and epoxy resins industry for manufacturing various consumer products including plastic baby bottle, toys and protective lining of infants' food cans. Recent studies reports adverse effects of BPA on human health resulting in hormone abnormalities, obesity, asthma, cardiac, kidney and behavioral disorders.

Aim: To measure urinary concentration, estimate daily intake of BPA in children, and investigate the association between urinary BPA levels and consumption frequency of dietary sources.

Materials and Methods: The cross-sectional study included apparently healthy 292 children, aged 2-16 years. Urinary concentrations of BPA were measured using high performance liquid chromatography (HPLC). Dietary intake and frequency of consumption of probable dietary sources of BPA were recorded using structured questionaire were assessed. ANOVA test was used to show the statistical difference between the estimated levels of urinary BPA and the frequency of consumption of the dietary sources. Student's t-test was used to analyse statistical difference in daily intake of BPA amongst male and female children. p-value <0.05 was considered statistical significant.

Results: BPA was detected in 215 (73.63%) children under study. The total urinary Bisphenol A ranged from 0.3 to 18.9 ng/mL with mean 1.29+2.09 ng/mL, median 0.67 and geometric mean 0.68 ng/mL. A significant positive association was observed between urinary BPA levels and frequently used canned soft drinks (p-value=0.014) and fast food (p-value=0.05). The geometric mean of estimated daily intake was 0.015 µg/kg/day, which is much lower than the tolerable daily intake. Estimated BPA intakes showed no significant difference between males and females (p-value=0.216).

Conclusion: The consumption of canned soft drinks and fast food are the most common sources of exposure amongst children. The study reports minimal average daily intake of BPA and overall low exposure leading to the low urinary BPA concentration. However further studies are required to address other potential sources of BPA exposure in children.

Keywords: Bisphenol A, Daily intake, Egypt, Epidemiology, Paediatrics

INTRODUCTION

Bisphenol A is an industrial chemical used in the production of polycarbonate plastics and epoxy resins, used in protective coatings and linings of metal products such as food and beverage cans. [1,2].

Profound adverse health effects were thought to be associated with BPA, and consequently it was banned in production of infant related items such as feeding baby bottles [3]. Findings of recent studies provide evidence on the harmful effects of endocrine-disruptors chemical, BPA [4]. A recent review of literature enlisted the probable hazardous sources of BPA, that were a subject of research conflict however additional studies are required to confirm the association between BPA exposure and human development and metabolism disorders [5].

Various studies also report that children are more prone to adverse effects of BPA in their environment as their eating, drinking and breathing aspects are much higher in relation to per unit of their body weight [6,7]. Frequent use of BPA incorporated products and exploration of things orally also increases their exposure to BPA [8].

Dietary ingestion of BPA has been reported as the most important source of exposure in humans where it is metabolised in the liver and excreted through the urine [9]. The assessment of urinary BPA is considered as the most convenient indicator of exposure owing to the fact that BPA has a rapid metabolism and are instantly excreted through the urine [10].

Based on previous data, the objective of this study was to assess the exposure of BPA in a sample of Egyptian children, by measuring the urinary concentration and to investigate its association with frequency of consumption of potential dietary sources.

MATERIALS AND METHODS

Study Population

The observational cross-sectional study was conducted from October 2012 to October 2014, on 292 apparently healthy children of the age group 2-16 years, who were randomly selected from nearby nurseries, primary, and preparatory schools in Giza, Egypt. Previous studies revealed that BPA was detected in about 90%-100% of children and adolescents in Northern America, some European nations, Egypt, Australia, and Asian countries [6,11-20]. The rate of detection was higher in the younger age groups as in toddlers and preschoolers.

For sample size calculation, the prevalence was considered 95% in the preschool children, 93% in the primary school children and 90% in the adolescents.

Sample size was calculated using the equation published by Dawson-Saunders and Trapp, 1994: [21].

$$n = \frac{t2 \times p \times (1 - p)}{m2}$$

where n=required sample size, t=confidence level at 95% (standard value of 1.96), p=estimated prevalence of the problem in the study area, m=margin of error at 5% (standard value of 0.05). Apparently healthy children, not complaining of chronic disease were included in the study. Children with a history of liver, renal disease or thyroid disorders were excluded from the study.

Ethical Considerations

Ethical approval was obtained from The Medical Research Ethical Committee of the National Research Center (NRC) (Registration no. 16368), the Egyptian Ministry of Education and the directors of schools that participated in the research. Informed written consent were obtained from the parents and verbal consents from all the students involved in the study.

Each child and/or parent enrolled in the study was subjected to:

Filling out a structured questionnaire which included

- Assessment of frequency intake of possible BPA dietary sources: Specific food frequency questionnaires which included the monthly ingestion of canned food and beverage e.g. canned fruits, vegetables, soft drinks and fast food
- Assessment of certain hazardous habits: These included the storage of food and water in plastic boxes or jars, the usage of plastic microwave utensils, the reuse of plastic water bottles and drinking water from plastic tanks.

Physical examination: Children were subjected to measurement of weight and height and thorough clinical examination that included chest, heart, abdominal, and central nervous system examination.

Laboratory investigations: Each child gave a morning spot urine sample which stored at -70 until assays for:

Estimation of urinary BPA concentration: The concentration of total urinary BPA was determined by reverse phase HPLC, Agilent technologies 1100 series, (G131A model), according to the method described by Alkaranfilly et al., and modified by Mohsen et al., [22,23]. Serial dilutions of standards were injected onto HPLC coloumn and their peak areas were determined using florescent detector was set at 275 and 300 (excitation and emission). The concentration in samples were calculated from the standard curve constructed by plotting peak areas versus the corresponding concentrations using Agilent Chem Station software for LC and LC/MC system (Agilent Technologies). The limit of detection (LOD) was calculated with the method recommended by EPA [24]. The LODs of BPA in urine was 0.3 ng/mL.

Determination of urinary creatinine was done according to the method of Bartel, by using kinetic kit (BioMed-Creatinine, CAT NO.CRE 106120) [25]. BPA concentration was adjusted to the urinary creatinine concentration to correct for the urine dilution [26].

STATISTICAL ANALYSIS

Daily intakes of BPA were estimated by calculating: daily intake (ng/day)=urinary BPA concentration (ng/mL)×urinary output (mL/day) and daily intake (ng/kg body weight/day)=urinary BPA concentration (ng/mL)×urinary output (mL/day)/body weight (kg) [27]. For practical reasons, no 24 h urine excretion rates were collected for the children. Therefore, generic values based on age and gender was used to describe urinary output [28,29]. The daily intake was estimated for a children ≤10 years In accordance to the International Commission of Radiological Protection (ICRP) with reference value for the >12 years age group (1200 mL/day) and the ICRP value for children aged ≤11 years age group (700 mL/day).

Data analysis was performed using Statistical Package for the Social Science (SPSS) version 21 (SSPS Inc, Pennsylvania, USA). Continuous data were expressed as mean±SD, while categorical data were expressed as frequencies and percentages. ANOVA test was used to analyse the statistical difference between the estimated levels of urinary BPA and the frequency of consumption of the dietary sources. Students' t-test was used to estimate the statistical difference between male and female children as regard to daily intake of BPA. Urinary BPA and BPA/Creatinine levels were log-transformed to improve normality of the distribution. p-value was considered statistically significant at p<0.05.

RESULTS

In this study, 292 2-16 years old children were recruited (175 males represented 59.9% and 117 females represented (40.1%), and classified into three age categories [Table/Fig-1].

Characteristic	Number of individuals	Percentage
Sex		
Male	175	59.9
Female	117	40.1
Age categories		
Age 2 - <6 years	63	21.6
Age 6 - <12 years	95	32.5
Age >12 years	134	45.9

[Table/Fig-1]: Characteristics of the participants under study.
Descriptive statistics to categorise the study population into 3 age categories

The detection rate of BPA among our study subjects was 73.7%. The total urinary BPA concentration ranged from 0.3 to 18.9 ng/mL with a mean value of 1.29. The mean Log BPA/gm creatinine of males, females and of the whole sample were 2.649±0.585, 2.640±0.494 and 2.64+0.55 with no significant difference (p>0.05) [Table/Fig-2].

Parameter	Mean (SD)	Median	Geometric mean
Total BPA [ng/mL of urine]	1.29 (2.09)	0.67	0.68
Log total BPA	-0.1680 (0.47)	-0.1739	0.000
Total BPA/gm creatinine	1046.687 (2041.65)	415.14	441.45
Log BPA/gm creatinine	2.64 (0.55)	2.62	2.59

[Table/Fig-2]: Urinary BPA concentrations of children and adolescents.
Descriptive statistics of central tendency of urinary BPA concentrations [Mean, median and geometric mean]

Average daily intake of BPA was estimated based on individual urinary BPA data and individual body weight data. The mean, median and geometric mean equal 0.035, 0.014, and 0.015 (μg/kg/day) respectively as shown in [Table/Fig-3]. Estimated BPA intakes show no significant difference between males and females (p-value=0.216).

BPA daily intake (ug/kg/day)	Mean (SD)	Median	Geometric mean	p-value
Males	0.041 (0.092)	0.014	0.016	
Females	0.026 (0.035)	0.015	0.015	
Total sample	0.035 (0.073)	0.014	0.015	

[Table/Fig-3]: Average daily intake of BPA in males, females and total children and adolescents depending on the level of urinary BPA.
Students' t-test. *p<0.05 statistically significant.

The associations between the estimated level of urinary BPA and frequency of consumption of the expected dietary sources of BPA were studied. Higher consumption of canned soft drinks (once or more/week) was found to be significantly associated with the mean of urinary BPA (p-value >0.036). This association is constant even after adjustment of urinary BPA to creatinine level (p-value >0.014). The same significant association was observed with frequent consumption of fast food (p-value >0.023) but it became non-significant after adjustment for creatinine (p-value >0.059). Consumption of other types of canned food or storage of water or food in plastic utensils showed no association (p-value=0.05) with the level of urinary BPA [Table/Fig-4].

DISCUSSION

The frequent use of plastic products increases the probability of human exposure to the endocrine disrupting agent, BPA. The human exposure can be evaluated through measurement of urine concentrations, as BPA which is eliminated in urine after quick metabolism in the human body [30].

In this study the detection rate of BPA among our study subjects was 73.7%. This rate was lower than that seen among American (92.6%), Canadian (91%) and German (98.7%) populations, but was higher than the rate reported in the Chinese cohort (50%)] [6,11,15, 31].

The total urinary Bisphenol A ranged from 0.3 to 18.9 ng/mL with a mean value of 1.29 (+2.09), median 0.67 and geometric mean (GM) of 0.68 ng/mL. Our findings were similar to Nahar MS et al., study on

Potential dietary sources	Frequency of consumption	Log_{10} BPA		Log_{10} BPA/g creatinine	
		Mean±SD	p-value	Mean±SD	p-value
Fast food	Never	0.037±0.508	0.023*	2.712±0.614	0.059
	Once/month	0.041±0.509		2.840±0.533	
	2-3 times/ month	0.110±0.526		2.666±0.649	
	Once or more/week	0.290*±0.399		2.528±0.460	
Soft drink cans	Never	0.092±0.505	0.036*	2.716±0.595	0.014*
	Once/month	0.172±0.455		2.817±0.747	
	2-3 times/ month	0.106*±0.537		2.551*±0.471	
	Once or more/week	0.229*±0.438		2.975*±0.576	
Tuna cans	Never	0.135±0.507	0.834	2.672±0.616	0.864
	Once/month	0.121±0.439		2.698±0.548	
	2-3 times/ month	0.077±0.561		2.711±0.564	
	Once or more/week	0.216±0.445		2.583±0.509	
Legume cans	Never	0.143±0.474	0.742	2.656±0.536	0.872
	Once/month	0.303±0.501		2.630±0.476	
	2-3 times/ month	0.057±0.081		2.931±0.113	
	Once or more/week	0.043±0.567		2.762±0.663	
Processed meat cans	Never	0.095±0.482	0.203	2.746±0.550	0.061
	Once/month	0.266±0.360		2.535±0.390	
	2-3 times/ month	0.361±0.578		2.328±0.600	
	Once or more/week	0.236±0.390		2.465±0.440	
Jam cans	Never	0.142±0.461	0.400	2.666±0.512	0.608
	Once/month	0.283±0.374		2.610±0.556	
	2-3 times/ month	0.066±0.592		2.827±0.764	
	Once or more/week	0.263±0.714		2.458±0.638	
Vegetable or fruit cans	Never	0.190±0.450	0.173	2.610±0.516	0.062
	Once/month	0.051±0.189		2.990±0.502	
	2-3 times/ month	0.041±0.648		2.616±0.591	
	Once or more/week	0.210±0.397		2.685±0.521	
Drinking water stored in water tanks	No	0.124±0.461	0.202	2.682±0.514	0.485
	Yes	0.259±0.484		2.592±0.599	
Reused water bottles	No	0.105±0.558	0.537	2.759±0.684	0.249
	Yes	0.163±0.443		2.632±0.475	
Store food in plastic box	No	0.178±0.492	0.534	2.620±0.508	0.416
	Yes	0.129±0.452		2.695±0.544	
Use of plastic utensils in microwave	No	0.143±0.472	0.808	2.666±0.529	0.868
	Yes	0.180±0.388		2.698±0.505	

[Table/Fig-4]: The estimated level of urinary BPA and frequency of consumption of the expected dietary sources of BPA.
ANOVA test, *p<0.05 statistically significant

Egyptian girls (aged 10-13 years) with the GM 0.84 ng/mL [19]. These findings were in contrast with an Australian study on 0-15 years old children, where GM of urinary BPA was 2.57 ng/mL, i.e. more than the triple of our GM value [32]. In a larger European study on 5-12 years children recruited from six different European countries, the GM of urinary BPA was 1.97 µg/L which is also much higher than the measured GM in our study [33]. These variations in the urinary BPA concentrations between countries can be attributed to timing of urine collection, preparation of urine dilution, method of analysis, age, sex and genetic make-up of individuals. Socio-economic background and lifestyle choices including food storage and consumer product use also influence the BPA concentration [34,35]. Therefore, examining behavioral and dietary habits are essential to determine potential exposure pathways and effects of BPA on individual's health.

The frequent use of products containing BPA such as baby bottles and toys, and consumption of packaged products such as canned foods, increases the potential risk of exposure in children and adolescents. The adverse health effects of BPA exposure in young children is a major concern since they are still undergoing development [36]. In the current study, no significant difference was found in BPA concentration between females and males, which was similar to the results from several other studies [6,11,37-39]. BPA exposure did not vary significantly by sex, suggesting that the probability of exposure to BPA is highly ubiquitous among the children population. It also reflects the likelihood of multiple routes of exposure, including both food and non-food sources. Therefore, identifying the sources of BPA exposure is essential for determining the high-risk populations and for devising strategies for reducing exposure [40].

Dietary intake is considered as the predominant exposure pathway for BPA in humans [41]. Dietary exposure remains a major concern in infants, toddlers and children, who have a significantly higher intake ratio for their body weight [42]. The advancement in food technology, and use of chemicals such as bisphenol A [BPA] in food processing and packaging, leads to increased human exposure.

The frequency of consumption of soft drink and canned fast food were found to be significantly associated with urinary BPA concentrations. This result was in accordance with National Health and Nutrition Examination Survey (NHANES) data that reports association between elevated BPA levels and frequent consumption of take away meals, sodas, soft drinks and fast-food items [43-45]. In a 2013 study, Quiros-Alcala et al., reported that pregnant women who consumed higher amount of soft drinks and hamburgers showed 58% and 20% higher urinary BPA concentrations respectively, in comparison with those who did not consume either [45]. However, a cross-sectional study on US population reported a non-significant, correlation between consumption of fast food and BPA levels [46].

In the current study, there was a tendency but no significant association between consumption of canned vegetables and canned fruit and BPA. While some studies reported a significant positive association between urinary BPA concentrations and frequent consumption of canned vegetable [47,48]. This relative contribution of canned vegetables to total BPA concentration that varies depending upon the canning process, food variety, type of resin used, and frequency of consumption.

In our study, no significant association between urinary BPA concentrations and canned food such as tuna, legume, and tomato paste and processed meats was observed. These findings were similar to Fattore M et al., study that reported that bottled water and canned tuna consumption has no association to elevated urinary BPA [49]. Casas M et al., also reported that, consumption of canned food had non-significant association with urinary BPA concentration in children However, in the same study reported a significant positive association between urinary BPA concentrations and canned fish consumption in Spanish women [16].

BPA can migrate from consumer goods into food and has been detected in canned foods [50]. Both heat-sterilisation of the container and acidity levels of the contents determine the rate of BPA migration. Polycarbonate-based materials and epoxy resins that contain BPA are usually applied in the production of food packaging materials, as well as the internal coatings of food and beverage cans [51]. Furthermore, BPA migration is effected by the preservation medium used. Significantly higher BPA levels were observed in canned tuna preserved in oil as compared to tuna preserved in aqueous medium, suggesting that oil aid in BPA migration from the can lining into the food [52].

Some of the most common hazardous habits were also assessed to determine their impact on BPA levels. In our study, there was no significant association between urinary BPA concentrations between reused water bottles, food stored in plastic boxes, consumption of water drinking from tanks and use of microwave utensils was observed. Similarly, no association was observed between urinary BPA and the consumption of food stored in plastic containeror the use of plastic bottles [16,42]. But in some studies, significant positive associations was observed between urinary BPA concentrations and use of polycarbonate bottle, storage of food in plastic containers and microwave containers [53,54]. Azza A et al., also reported excessive use of plastic bottles, microwave plastic wares and consumption of canned food presented as the sources of increased exposure in high social class Egyptian children [55].

Numerous studies suggest, dietary intake as a major source of BPA exposure [42,56]. Daily intake calculations based on biomonitoring data (e.g., urine) reflect real exposure, from all the probable sources of exposure [57]. The European Food Safety Authority (EFSA) has set a Tolerable Daily Intake (TDI) for BPA of 50 μg/kg bw/day [58]. The TDI is known as "an estimate of the quantity of a chemical contaminant to which we may be exposed through environmental contamination, and which when found in food can be ingested daily over a lifetime without posing a significant risk to health". Based on new data and methodologies, EFSA has lowered the estimated TDI, to 4 μg/kg bw/day [59]. Further in 2013, the National Food Institute, Technical University of Denmark (DTU) has evaluated the EFSA opinion, and reported revised permissible TDI for BPA to be 0.7 μg/kg bw/day or lower [60]. The estimated daily intake geometric mean of BPA in our study was 0.015 (μg/kg.bw/day) (15 ng/kg bw/day), median 0.014 (μg/kg bw/day) (14 ng/kg.bw/day) which was much lower than the tolerable daily intake recommended by the guidelines established by the EFSA and DTU. This indicated that Egyptian children and adolescents are in a safe level of BPA exposure.

LIMITATION

The study provides initial information on levels of BPA and its association with probable sources of exposure. Further studies on larger sample size of both children and infants are required.

CONCLUSION

Urinary Bisphenol A concentrations and average daily intake of BPA exhibited low values in a sample of Egyptian children indicating low exposure. A positive association was found between canned soft drinks, fast food consumption and urinary BPA. These results emphasised on the need for additional studies to address other potential sources of BPA exposure, and the probable associated adverse health outcome in children.

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