Research Paper

Investigating Bisphenol A Level Estimation and Possible Effects on Fetal Biometry

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ABSTRACT

Background: The estrogenic endocrine disruptor bisphenol A (BPA), which is used in plastics and resins, may have an impact on the fetus's growth and development and can modify postnatal development. This study aims to assess how bisphenol A affects fetal biometry.

Methods: This analytical cross-sectional study included 384 healthy Egyptian women in their third trimester during childbearing (15–44 years). They were selected from the outpatient Clinic of Obstetrics and Gynecology at Kasr El-Ainy Hospital, Cairo, Egypt. Fetal biometry was measured and urine samples were collected to estimate BPA levels.

Results: Fetal weight, centile, and corrected bisphenol A levels were significantly higher in the studied age groups ($P<0.05$). A significant positive correlation was found between BPA level and estimated fetal weight, centile, and age of the mother per year. On the other hand, no significant difference was detected with other fetal measurements in the studied groups ($P>0.05$).

Conclusion: Fetal exposure to BPA is associated with higher estimated fetal weight and centile commonly in the maternal age range 25 to 35 years.

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1. Introduction

The development and growth of the fetus depend on the mother and embryo exchanging nutrients, gases, and other necessary substrates through the placenta. The placenta has an abundant number of receptors for steroids, which makes it more liable to changes in the hormonal environment in the uterus. Meanwhile, through pregnancy, it actively synthesizes steroids. This means that the placenta is an active site that synthesizes steroids, therefore, this makes it more sensitive to be affected by the hormonal changes that occur due to bisphenols. Accordingly, the exposure of the mothers during placenta-mediated pathways to environmental toxins, which interfere with internal endocrine activity, may have an impact on the growth of the fetus [1].

Phthalates, phenols, and metals are among the most frequently detected chemicals in recent studies carried out in the United States, Canada, and Denmark that determined numerous chemicals between pregnant or planning-to-be pregnant women [2].

Plastics and resins contain the chemical bisphenol A (BPA), which has estrogenic properties and has been shown to affect embryos and alter their development postnatally [3, 4].

Bisphenols in the environment could harm both human health and the aquatic ecosystem. Bisphenol exposure may have negative results on endocrine system malfunction, including chromosomal abnormalities, enzyme activity, thyroid hormone concentration, and even cell dysfunction and gene damage [5]. Producing and accumulating harmful free radicals inhibit cells capacity to divide, repair, and operate; therefore, apoptosis is the natural outcome [6].

Intrauterine exposure to BPA affects healthy fetal growth and affect the metabolic and reproductive health of adults [7, 8].

2. Materials and Methods

Study subjects

Out of 397 pregnant women who attended the Kasr El-Ainy Obstetrics and Gynecology Clinic of Cairo University, Egypt, 13 women were excluded from the study (5 individuals declined to provide consent letters and 8 women did not meet the inclusion criteria). This analytical cross-sectional study included 384 healthy Egyptian women during their childbearing (15–44 years) and pregnant women in their third trimester with no history of chronic diseases, smoking, drug use, preeclampsia, placenta previa, congenital anomalies, multi fetal pregnancy, premature rupture membranes or intrauterine fetal death [9] from April 2021 to September 2022.

Study methods

All participants were subjected to a full history of socio-demographic details, including age, age of marriage, place of residence, educational level, and previous delivery. The obstetric and gynecological history and exposure history to bisphenol, including exposure to plastic food storage containers, household cleaners, and cosmetics (soap, shampoo, lotion, and hair sprays were also obtained).

Fetal biometry

During the third trimester of antenatal care visits, intra-uterine fetal growth was measured via abdominal ultrasound, using the fetal growth parameters as head circumference, biparietal circumference, abdominal circumference, and femoral length.

Measuring bisphenol A

Urine samples were collected once and immediately transferred to the laboratory of the Forensic Medicine and Clinical Toxicology Department, where the level of BPA was measured by high-performance liquid chromatography and isocratic system reversed-phase chromatography. Then, the total urinary BPA (conjugated and free form) was analyzed [10].

Statistical analysis

The sample size was calculated [11] and the required sample size was 384 adult pregnant females during childbearing. Microsoft Excel 2019 was used for tabulation and the statistical analysis of the results was done via the SPSS software, version 25 for Microsoft Windows 10. To compare the categorical data, the chi-square (X^2) or the Fisher exact test was performed. The Student's t-test or the Mann-Whitney U test was used for comparisons between the quantitative variables of the two groups. The one-way analysis of variance (ANOVA) or the Kruskal-Wallis test followed by a post hoc test was used to compare the 3 study groups. The statistically moderate significance was considered when the P was <0.01 and a statistically high significance was when the P was <0.001.

3. Results

Socio-demographic, obstetric, and gynaecological data between age groups

The mean age and marriage age of the studied subjects were 27.57±5.12 and 18.39±2.84 years, respectively. Most of the studied three groups were from urban areas (72.03%, 62.90%, and 62.58%, respectively), the low educational level was the most prevalent among the 3 age groups (52.45%, 46.24 % and 50.91%, respectively), and cesarean section was significantly (P<0.001) higher in all age groups, especially in individuals aged 18 to 25 years (67.13%). The 3 studied groups differed significantly in terms of age (P<0.001), age of marriage (P<0.001), place of residence (P<0.05), and previous deliveries (P<0.001); however, the educational level showed no significant difference (P>0.05) (Table 1).

Bisphenol A level and corrected bisphenol in different age groups

BPA and corrected bisphenol A levels were significantly higher in the young age group (18–25 years) compared to the older age groups (>25–35 years and>35 years, respectively; P<0.05). On the other hand, no significant difference was observed in older age groups (>35 years) (Table 2).

Fetal measurements between age groups

A significant (P<0.05) increase in head circumference was detected in age groups (>25–35 years) and (>35 years), along with a significant (P<0.05) increase in the centile in all age groups. Gestational age, bi-parietal diameter, femur length, abdominal circumference, and estimated fetal weight showed no significant difference between age groups (P>0.05) (Table 3).

Bisphenol A levels and sociodemographic data

In addition, BPA levels showed no significant relation with residence and educational level (Table 4).

Table 1. Socio-demographic and obstetric data concerning age among the studied patients

Variables	Mean±SD Age Groups (y) Group 1 18-25 (n=143)	Group 2 25-35 (n=186)	Group 3 >35 (n=55)	Total	F	P
Age (y)	22.55±1.79	30.48±2.65	38.22±1.60	27.57±5.12	738.225	<0.001*
Age of marriage	18.12±1.75	20.14±3.44	20.58±5.49	18.39±1.75	12.415	<0.001*

Variables		No. (%) Group 1 18-25 (n=143)	Group 2 25-35 (n=186)	Group 3 >35 (n=55)	Total	X^2	P
Residence	Urban	103(72.03)	117(62.90)	28(50.91)	248(64.58)	8.535	0.036*
	Rural	40(27.97)	69(37.10)	27(49.09)	136(35.42)		
Educational level	Low	75(52.45)	86(46.24)	35(63.64)	196(51.04)	7.938	0.243
	Ignorance	52(36.36)	72(38.71)	12(21.82)	136(35.42)		
	High	16(11.19)	28(15.05)	8(14.55)	52(13.54)		
Previous delivery	No	23(16.08)	9(4.84)	0(0.00)	32(8.33)	67.060	<0.001*
	CS	96(67.13)	117(62.90)	35(63.64)	248(64.58)		
	Normal	23(16.08)	16(8.60)	4(7.27)	44(11.46)		
	CS, normal	0(0.00)	44(23.66)	16(29.09)	60(15.63)		

CS: Cesarean section.

Notes: F: One-way analysis of variance test, *Significant, X^2 Chi-square test.

Table 2. Bisphenol A level and corrected bisphenol concerning different age groups

Variables	Mean±SD Age Groups (y) Group 1 18-25 (n=143)	Group 2 25-35 (n=186)	Group 3 >35 (n=55)	F	p	95% CI Lower	Upper
Bisphenol A level	0.68±0.79	0.62±0.79	0.52±0.66	0.664	0.575	0.55	0.71
	P1=0.020*, P2=0.024*, P3=0.58						
Corrected bisphenol	0.93±1.19	0.62±0.67	0.62±0.83	3.496	0.016*	0.64	0.83
	P1=0.014*, P2=0.014*, P3=1.00						

CI: Confidence interval; SD: Standard deviation.

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Notes: P1: Significance between group 1 & 2, P2: Significance bet group 2 & 3, P3: Significance bet group 1 & 3, F: One-way analysis of variance test, *Significant.

Table 3. Relation between fetal measurements and age among the studied patients

Variables	Mean±SD Age Groups (y) Group 1 18-25 (n=143)	Group 2 25-35 (n=186)	Group 3 >35 (n=55)	F	P	95% CI Lower	Upper
Gestational age/weeks	36.42±2.35	36.93±2.26	36.75±2.37	1.517	0.210	36.48	36.94
BPD	8.67±0.74	8.86±0.66	8.80±0.54	2.078	0.103	8.71	8.85
HC	31.59±1.88	32.20±1.37	31.43±2.50	4.503	0.004*	31.68	32.04
FL	6.90±0.52	7.02±0.42	6.91±0.44	2.075	0.103	6.91	7.00
AC	31.96±2.11	32.25±2.13	31.90±1.98	0.738	0.530	31.88	32.30
EFW	2802.51±452.98	2911.70±419.47	2861.36±384.07	1.801	0.147	2820.53	2906.59
Centile	43.14±24.86	44.25±26.75	54.00± 28.30	2.782	0.041*	42.65	47.97

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Abbreviations: BPD: Bi-parietal diameter; HC: Head circumference; FL: Femur length; AC: Abdominal circumference; EFW: Estimated fetal weight; CI: Confidence interval.

Notes: F: One-way analysis of variance test, *Significant.

Association between gestational age, fetal biometry, age, and BPA levels

A significant positive correlation was detected between BPA level and estimated fetal weight (r=0.144, P<0.05), centile (r=0.158, P<0.001), in addition to a significant negative correlation with age of mother per year (r=-0.101, P<0.05) (Table 5).

4. Discussion

In this study, the mean age and age of marriage were 27.57±5.12 and 18.39±2.84 years, respectively. In addition, the low educational level and urban residence were the most prevalent among the studied groups. All of the pregnant participants in this study were exposed to BPA. Also, [12] the Mean±SD age of mothers at childbirth was 30.6±3.5 years; however, having a college education or above was in most (94.0%) of the mothers. More soft drinks and canned foods, which are the main sources of exposure, were consumed by younger females.

Table 4. Bisphenol A level concerning residence and educational level

Variables		Bisphenol Level		U	P	95% CI	
		Mean±SD	Range			Lower	Upper
Residence	Urban	0.73±0.86	0.06-4.33	0.232	0.817	0.62	0.83
	Rural	0.75±1.05	0.04-4.47			0.57	0.93

Variables		Mean±SD	Range	F	P	95% CI	
						Lower	Upper
Educational level	Low	0.70±0.95	0.10-4.47	1.135	0.322	0.56	0.83
	Ignorance	0.83±0.98	0.04-4.26			0.66	0.99
	High	0.63±0.64	0.06-2.33			0.45	0.81

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CI: Confidence interval.

Notes: *Significant, U: Mann-Whitney test, F: Analysis of variance F test.

Table 5. Correlation of bisphenol A levels with gestational age, fetal biometry, and age of the studied participants

Variables	Bisphenol Level	P
	R	
Gestational age/weeks	0.0524	0.305
BPD	0.0311	0.543
HC	-0.0867	0.089
FL	-0.0336	0.511
AC	0.0640	0.211
EFW	0.144	0.004*
Centile	0.158	0.001**
Age of mother (y)	-0.101	0.04*

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Abbreviations: BPD: Bi-parietal diameter; HC: Head circumference; FL: Femur length; AC: Abdominal circumference; EFW: Estimated fetal weight.

Notes: R: Correlation coefficient, *Significant.

A previous study [13] discovered an association between increased soda and hamburger consumption and higher urinary BPA concentrations. They found no correlation between BPA exposure and eating canned fruit, which was in line with research from a Cincinnati, Ohio, regarding pregnancy cohort [14]. Another study [15] found that high levels of BPA were found in some vegetables and soups but not in canned fruit.

A study [16] that represents the first assessment of BPA exposure levels in humans living in rural and urban areas in Turkey found that BPA usage increased sharply at almost every point of daily life. BPA levels were detected in all individuals and their biological samples have their metabolites.

In this study, there was a significant difference between different age groups and corrected bisphenol (P<0.05). This is while there was no significant relation between the age groups of the studied patients and bisphenol (P=0.575). Similarly, other studies reported the dependent age of BPA levels [17-19].

The majority of studies only used one single spot urine sample to measure BPA exposure levels throughout pregnancy, which frequently results in incorrect classification of exposure. Studies [14, 20, 21] have demonstrated the significance of collecting urine samples at various times to study the BPA exposure impact on health [22].

In this study, a significant (P<0.05) increase in head circumference was in studied age groups (from 25 to 35 years) and (>35 years), and centile was significantly (P<0.05) increased in all age groups. On the other hand, gestational age, bi-parietal diameter, femur length, abdominal circumference, and estimated fetal weight showed no significant difference (P>0.05). Similarly, a cohort study [23] discovered that larger fetal head circumferences and higher weights were related to higher levels of maternal bisphenols, indicating that bisphenols exposure promotes fetal growth. Studies [24, 25] suggested that exposure to bisphenols during pregnancy affects the levels of maternal hormones, which may affect fetal growth differently depending on the time of exposure. However, a study on 125 pregnant females [26] found a negative correlation between maternal urinary BPA levels in the first trimester and fetal head circumference and abdominal circumference in the third trimester.

Moreover, maternal prenatal occupational exposure to BPA was associated with lower birth weight in a study among 587 children from which 93 fathers and 50 mothers were confirmed by personal air sampling and exposure histories exposed to occupational BPA [27]. In addition, a study conducted on 35 amniotic fluid specimens found significant differences in birth weight centiles [28]. In contrast, a prospective cohort study [29] on 845 Chinese pregnant women found that lower birth weight was associated with higher bisphenol urine concentrations.

In the current study, BPA levels did not show any significant relation with the place of residence and educational level (P>0.05). In the same line, a study [16] found no statistical significance between rural and urban areas regarding urinary BPA levels (P>0.05). These results are similar to other Chinese [30] and US [31] studies. Additionally, the majority of other studies [14, 17, 18, 32, 33] have demonstrated an inverse association, namely with lesser education exposure to BPA increases. A similar study [33] found that higher urinary BPA concentrations were associated with younger women who had a low educational level. Another study [13] discovered that Mexican-American females who lived their entire lives in the United States who were consuming more hamburgers and sodas had a higher percentage of significant dietary BPA exposure, compared to immigrant women. However, no association was found in France [19].

The median BPA concentrations in Mexican-origin pregnant women were compared to pregnant women from Mexico City. Varying BPA concentrations among populations of pregnant women may be due to diet and behavioral culture differences. The comparatively low concentrations in their Mexican/Mexican American participants and the Mexican pregnant women study [34] related to the traditional Mexican diet that prefers fresh favor foods over processed or packaged foods [35, 36].

According to this study, a positive correlation was detected between BPA level and estimated fetal weight (P<0.05), centile, and age of the mother (P<0.05). Gestational age, bi-parietal diameter, head circumference, femur length, and abdominal circumference showed no significant correlation. Similarly, many studies [21, 37, 38] found no significant associations between BPA and gestational age.

However, some studies [39, 40] found that the gestational age was decreasing. A different study discovered a connection between late-pregnancy BPA exposure and a higher risk of preterm birth [34]. However, a recent investigation discovered a connection between longer gestation and maternal unconjugated BPA at delivery [41].

High levels of BPA in the mother's urine were linked to low femur length and estimated weight growth of the fetus from 12 to 20 weeks, according to a prospective study involving 470 pregnant women [42]. Since bisphenols have brief biological half-lives, collecting multiple pools of urine is necessary to minimize measurement error [43].

In the same line, a study [44] found no mothers at the age of 35 years or older who had detectable BPA concentrations. The proportion of BPA exposure decreases from youngest to oldest age groups, possibly due to age representation. Older mothers may have lifestyles that prevent BPA-containing food storage and preparation products; meanwhile, daily variations in BPA concentrations may also explain these differences.

In contrast, a non-significant positive association was found between birth weight, head circumference, and urinary BPA concentrations in the third trimester in a study on 339 women [38]. However, a monotonic positive association with head circumference (for the second versus first tertial of exposure) and no associations with birth weight were detected in a study on 287 women [45].

5. Conclusion

Fetal exposure to BPA appears to be associated with larger fetal head circumference, higher weight and, centile. The maternal age ranged from higher than 25 years to lower than 35 years associated with higher levels of BPA. Future research in broad, large-scale studies is required. Also, there are some limitations in this study regarding the spot measurement of urinary bisphenol concentration that may not reflect the dynamics of bisphenol exposure during pregnancy, the small sample size, the limited duration, and missed data about the fetal sex.

Ethical Considerations

Compliance with ethical guidelines

The Ethics Committee and the Review Board of the Faculty of Medicine, Cairo University approved the study (Code: IRB. N: 144–2021). All study subjects offered informed consent before their participation.

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Authors' contributions

Conceptualization and supervision: Abla Abdel Meguid Attia, Reham Nafad Elbendary, Mohamed Ahmed Yehia Zakaria and Hisham Mamdouh Hamed Haggag; Sample and data collection: Sakr Mohammed Sakr and Hisham Mamdouh Hamed Haggag; Sample analysis: Sara Hamed N Taha; Writing the original draft: Howaida Saeed Mohammed and Sakr Mohammed Sakr; Review and editing: Abla Abdel Meguid Attia, Reham Nafad Elbendary and Howaida Saeed Mohammed, final approval: All authors.

Conflict of interest

The authors declared no conflict of interests.

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