



Research article

The effect of training about environmental toxicant Bisphenol-A exposure in pregnancy on maternal urine Bisphenol-A level



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ABSTRACT

Purpose: Bisphenol A (BPA) is an environmental toxin, clearly capable of initiating epigenetic modifications, leading to the development of numerous human illnesses such as metabolic, reproductive, and behavioural abnormalities. It also causes oxidative stress, which has been shown to be alleviated by selenium supplementation. The purpose of this study was to determine the effect of training of BPA exposure during pregnancy on urine BPA levels.

Methods: This research enrolled 30 pregnant women who were in their first trimester and were free of chronic illness. Women were asked questions on their sociodemographic features, anthropometric measures, obstetric characteristics, BPA awareness level, BPA exposure and the Health Practices in Pregnancy Scale as a Pre-test and Post-Test. The initial urine samples were taken from women in their first trimester and stored in BPA-free bags. Then, training was delivered to encourage BPA exposure reduction and maternal health awareness. First-trimester face-to-face instruction and brochure distribution were followed by refresher, reminder, and follow-up trainings during the second and third trimesters. Urine samples from women in their second and third trimesters were obtained again. The levels of BPA in urine were measured using the liquid chromatography-mass spectrometry on 90 samples. Each person's urine concentration differs, thus the creatinine level in all samples was also calculated and compared to the BPA content, and the results were evaluated.

Results: Our study shown that BPA exposure may be lowered by training. It has been demonstrated that reducing BPA exposure and increasing knowledge can result in an improvement in health status. Additionally, it has been demonstrated that trainings greatly minimize exposure-causing behaviours.

Conclusion: It was discovered that while the duration of a single training does not make a meaningful effect, the continuing of reminder trainings did make a substantial difference in the urine BPA level.

1. Introduction

Different environmental toxins, such as methylmercury (MeHg), bisphenol A (BPA), formaldehyde, arsenic, nickel, and vinyl carbamate, are clearly capable of initiating epigenetic modifications, leading to the development of numerous human illnesses such as metabolic, reproductive, and behavioural abnormalities [1]. Numerous studies have established a link between chronic exposure to endocrine disrupting chemicals (EDCs) and metabolic dysfunction, reproductive system abnormalities, endocrine-related malignancies, and neurodevelopmental illnesses [2, 3]. It has been observed that the majority of these chemicals act by imitating or inhibiting the normal activities of endocrine hormones, including

estrogens, androgens, thyroid, hypothalamus, and pituitary hormones [4]. BPA, as an endocrine disrupting chemical, has an estrogenic action and is associated with detrimental health impacts, particularly given its widespread usage in industry and daily life. As a result, it has been the focus of several research and continues to maintain its appeal [5]. Early puberty, prostatic hyperplasia, impaired immunological function, alterations in the brain, sexual behaviour, decreased antioxidant enzymes, hyperactivity, elevated insulin, obesity, and osteoporosis have all been shown in animal studies [6]. Selenium (Se), an essential micronutrient and trace element, protects cells against oxidative stress (OS) via selenoproteins. Bisphenol A (BPA) is a xeno-oestrogenic chemical that disrupts spermatogenesis by causing oxidative stress [7]. Kaur, S. et al. showed Se

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supplementation significantly increased antioxidant enzyme activities and decreased the expression of stress-activated kinases, which further reduced apoptosis. As a result, Se supplementation was shown to be beneficial against BPA-induced oxidative testicular injury [7]. Similar investigations have indicated that Se supplementation reduces the impact of BPA on liver toxicity [8] and lung injury [9]. Due to its extensive usage, Bisphenol-A is regarded as a significant environmental toxicant that the public should be aware of, as it is one of the most visible EDCs and one of the pollutants with the greatest potential to threaten human and environmental health.

Studies aiming at minimizing BPA exposure may give light on a critical public health issue. The absence of a study examining the effect of training on BPA exposure in pregnant women, as well as the absence of any other literature examining how possible changes in BPA caused by training would affect pregnant women's overall health, sparked interest in this issue and formed the study's primary hypothesis.

The purpose of this study is to ascertain current exposure by evaluating the bisphenol-A (BPA) levels in pregnant women's urine samples and to assess the influence of prenatal training on the urinary BPA level. Additionally, we will analyse the association between demographic features and BPA exposure, as well as the impact of the training and any changes in the BPA level on the pregnant women's quality of life and general health.

2. Methods

2.1. Study population

The research population included volunteer pregnant women in their first trimester who registered to the Gaziantep Sahinbey Research and Application Hospital's Obstetrics and Gynecology Clinic between September 2020 and August 2021. The Hasan Kalyoncu University Faculty of Health Sciences Non-Interventional Research Ethics Committee approved the study with a decision dated 09.08.2021 and numbered 2021/92.

2.2. Questionnaire and scales

2.2.1. Bisphenol-A exposure questionnaire in pregnancy (Form-1)

In the first section, sociodemographic information (12 questions) is collected; in the second section, anthropometric measurements (2 questions) are collected; in the third section, obstetrical properties (6 questions) are collected; in the fourth section, the level of BPA in the information (6 questions) is collected; in the fifth section, the home environment from BPA exposure (31 questions) is collected; and in the sixth section, personal BPA exposure is collected (7 Questions) A total of 60 questions titled face to face interview style was used.

2.3. Health Practice Questionnaire (HPQ)

Lindgren created the Health Practice Questionnaire (HPQ) in 2005 [10], and a Turkish validity and reliability assessment of the scale was done in 2006 [11]. The Turkish version had 33 items and had a cronbach alpha coefficient of 0.74 [11]. The scale assesses the adequacy of prenatal health practices in six domains. These topics include comparing rest and exercise, quantifying safety, diet, avoiding hazardous drugs, accessing health care, and gathering information. Additionally, one article discusses prenatal health practices. High scores imply high-quality health behavior associated with considerable pregnancy benefits. The scale's lowest possible score is 33, while the greatest possible value is 165.

3. Implementation of training and sample collection

Three stages of research were conducted. The "first stage" involved administering a pre-test (Form-1) to pregnant women in their first trimester, and then collecting urine from them in appropriately sized, bags that did not contain BPA. Following that, about 30 min of face-to-

face instruction on Bisphenol A and other endocrine disrupting chemicals was provided in an appropriately equipped meeting room.

In the "second stage," pregnant women in their second trimester received reminder training between 8:00 and 12:00 a.m. on the same day and at the same time of week, prior to urine collection. Pregnant women's urine samples were collected a second time.

The "third stage" continues to provide reminder training through telephone and text messages to pregnant women in their third trimester prior to urine collection. Third urine samples were collected from pregnant women, and a post-test (Form-1) was administered. After the samples were collected, the pregnant urine was transported to the laboratory on dry ice.

3.1. Urinary BPA concentrations

BPA and BPA glucuronides (BPAG) were quantified using liquid chromatography-mass spectrometry (1200 Series 6470 triple quadrupole LC-MS/MS system). It is the preferable approach because it enables direct BPA detection by liquid chromatography (LC) without the need for derivatization. The LC-MS/MS method is more beneficial and sensitive than the gas chromatography-mass spectrometry approach. The levels of BPA in urine were measured using the liquid chromatography-mass spectrometry (LC/MS-MS) technique on 90 samples. Although several investigations have been conducted using enzyme-linked immunosorbent assay (ELISA) kits, it has been demonstrated that the ELISA approach interacts with other chemicals, including BPA-glucuronide and phytoestrogens, and is thus likely to increase BPA levels [12]. As a consequence, the mass spectrophotometer was employed to obtain accurate results in the investigation.

3.2. Preparation of urine samples

A 200 μ L sample of urine is placed in a sealed glass centrifuge tube. 25 μ L internal standard and 50 μ L Jasem Reagent E are added to it, mixed for 5 s, sealed, and kept at 37 $^{\circ}$ C for 3 h. Following that, 250 μ L of Jasem reagent-1 is added and mixed for 5 s before being centrifuged at 5000 rpm for 5 min. The supernatant collected in this step is put into the LC-MS/MS apparatus.

3.3. Analyses of urine creatinine

Urine creatinine levels were also determined in all samples, as urine concentrations might fluctuate according to an individual's water consumption. Creatinine concentrations were determined using an automated biochemical analyser (Beckman coulter AU5800, Beckman Coulter, Inc., CA, USA). After correcting for urine BPA concentrations (ng/ml) and creatinine concentrations (mg/dl), adjusted BPA (μ g/g creatinine) data for statistical analysis were examined [13, 14].

3.4. Statistical analysis

SPSS (Statistical Package for the Social Sciences) for Windows 21.0 was used to analyze the study data statistically. In descriptive statistics, categorical variables were represented by a number (n) and a percentage value (%), whereas numerical values were represented by a mean and standard deviation. The Kolmogorov Smirnov Z, Shapiro-Wilk, and kurtosis skewness tests were used to determine the normality of quantitative data. The one-way ANOVA was used to compare normally distributed quantitative variables across three groups, while the Paired Sample T test was employed to compare mean scores with descriptive characteristics. For comparisons of discrete variables, the Pearson Chi-Square Test was utilized. Pairwise comparisons were made using the Independent Samples t-Test. Testing the difference between two related percentages (McNemar chi square test in SPSS) was used to compare the qualitative data of the groups pre- and post-test [15]. All outcomes in the study were within the 95 % confidence range, and a p value of 0.05 was considered significant.

4. Results

Table 1 summarizes the characteristics of the 30 pregnant women involved in the research. According to this, the mean age of pregnant women is 32.07 ± 4.934 (min = 25; max = 41), with 36.7 % being above the age of 34. When the pregnant women's educational level was evaluated, it was discovered that 36.7 % were elementary school graduates and 13.3 % were undergraduate grads. It was discovered that 90% of participants were unemployed and 3.3% lacked health insurance. The majority of pregnant women (70%) lived in households with less than four people, 13.3 % of their spouses did not work, and 40% of employees worked. Pregnant women's first trimester BMI is 27.26 ± 4.82 (min.17.99; max.40.23), while their third trimester BMI is 30.46 ± 4.84 (min.21.80; max.44.92). 93.3 % of pregnant women gain no more than 15 kg during pregnancy. Pregnant women's mean number of pregnancies was 3.93 ± 3.38 (min = 1, max = 19), and the rate of those giving birth to three or more children was 30.0 %. 36.7 % had a history of miscarriage, and 56.7 % delivered through caesarean section.

Table 2 summarizes the results of the Health Practices in Pregnancy Scale and the BPA awareness level. According to the Health Practices in Pregnancy Scale, the mean total score in the first trimester was 102.67 ± 13.66 , and in the third trimester, it was 110.70 ± 14.40 . There was a statistically significant difference between the two averages ($p < 0.001$). As a result of BPA awareness, the BPA level in the state of hearing increased statistically significantly ($p < 0.001$). As a result of the prenatal training, all pregnant women said that they had heard of BPA prior to the last test. While the percentage of utilizing BPA-free branded items was 0 % in the pre-test, it jumped by 40 % in the post-test. In the post-test, the

Table 1. Reproductive characteristics and demographic features of pregnant women.

Characteristics	(n)	%
Age	25–29	9 30,0
Mean $\pm$ SD = $32,07 \pm 4.934$ (min = 25 max = 41)	30–33	10 33,3
	≥ 34	11 36,7
Education status	Literate	9 30,0
	Primary school	11 36,7
	High School	6 20,0
	Undergraduate	4 13,3
Working status	Unemployed	27 90,0
	Employed	3 10,0
Economic level	Low	17 56,7
	Middle	12 96,7
	High	1 3,3
Health insurance	Yes	29 96,7
	No	1 3,3
Number of people living in the house	≤ 4	21 70,0
	≥ 5	9 30,0
Spouse's employment status	unemployed	4 13,3
	Self-employment	10 33,3
	Officer	4 13,3
	Employee	12 40,0
Number of pregnancies	1–2	11 36,7
	3–4	8 26,7
	≥ 5	11 36,7
Parity (number of children)	0	4 13,3
	1	9 30,0
	2	8 26,7
	≥ 3	9 30,0
Miscarriages number	0	19 63,3
	≥ 1	11 36,7
Mode of delivery	cesarean section	17 56,7
	vaginal delivery	13 43,3
Weight gained during pregnancy (kg)	≥ 15	28 93,3
First Trimester BMI mean = 27,26	≥ 16	2 6,7
Third Trimester BMI mean = 30,46		

SD; standart deviation.

Table 2. Health Practice Questionnaire Scale and BPA awareness level.

		1.Trimester $\bar{X} \pm SD$	3.Trimester $\bar{X} \pm SD$	Test p
Health Practice Questionnaire (Mean Score)		102,67 $\pm$ 13,66	110,70 $\pm$ 14,40	t = 4.655 p<0.001
BPA awareness level		Pre-Test 1. Trimester n(%)	Post-Test 3. Trimester n(%)	Test p
The state of hearing about BPA	Yes	2 (6,7)	30 (100,0)	z = 5.292 p<0.001
	No	28 (93,3)	- (-)	
How to protect yourself from BPA?	Don't do anything.	28 (93,3)	1 (3,3)	
	Using products labeled BPA-free.	-(-)	12 (40,0)	
	Do not buy products that may contain BPA.	2(6,7)	17 (56,7)	

$\bar{X}$; Mean, SD; Standart Deviation.

percentage of not purchasing products that may contain BPA went from 6.7 % to 56.7 %.

The study examined pregnant women's BPA exposure status in the home environment using pre- and post-testing. Plastic cups, plastic electric coffee heaters, and plastic bottles, plastic buckets, spatulas, tongs, plastic/nylon bag, pickle, tomato paste, olive oil, food products such as yogurt, milk, and milk products in plastic packaging at home for storage, plastic wrap, storage bags, food cutting, plastic cutting surface, microwave oven, consume beverages in tin cans, and plastic jug, there was a statistically significant difference in frequency of use ($p < 0.05$). It was discovered that the frequency of plastic use in the home environment decreased in comparison to the previous test.

The effect of prenatal BPA awareness training on urine BPA levels is represented in Figure 1. Because the ANOVA test was found to be statistically significant in repeated measurements, a PostHoc test was performed using a double comparison with Bonferoni correction and BPA measurements taken during the third trimester were found to be statistically lower than those taken during the second and first trimesters ($p < 0.001$, $p = 0.005$ respectively).

5. Discussion

The study discovered a statistically significant difference in the HPQ average score between the first and third trimesters as a result of the training provided. Additionally, the HPQ score indicated that, despite

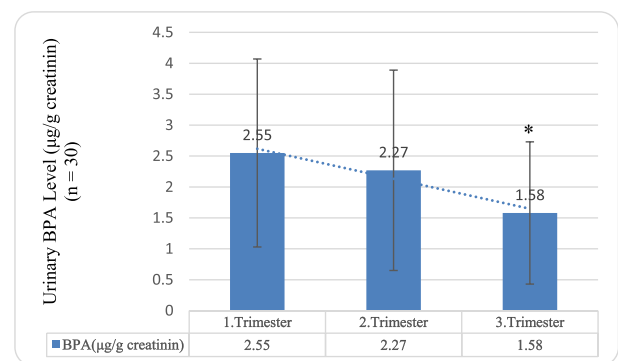


Figure 1. The effect of training on urine BPA levels *. The levels of BPA in urine were statistically lower in the third trimester than in the second and first trimesters ($p = 0.001$ and $p = 0.005$, respectively). The one-way ANOVA test and Bonferroni corrections was used.

only being taught about BPA exposure, pregnant women's general health knowledge and self-awareness about health improved. According to the findings of this study, training on BPA exposure improves quality of health.

Pregnant women's BPA knowledge increased significantly between the pre- and post-tests. There was no study discovered in the literature that included BPA training. Additionally, the effect of the training provided in our study was evaluated through pre- and post-testing, as well as through the use of direct analytical methods, mass chromatography (LC-MS/MS), which provides the most reliable results for BPA measurement, and urine BPA levels were compared before and after the training, and the training effect was evaluated. Food is the primary source of BPA exposure for the general population [16]. Polycarbonate plastics and epoxy resins are two of the most common products that come into contact with food and are made with BPA. Transparent polycarbonate plastic with low reactivity and shatter resistance. It is found in water bottles, feeding bottles, tableware, and containers for food storage [17]. Takao et al. also demonstrated that temperature has an effect on BPA migration. The study compared an unheated can to a can heated to 100 °C and discovered that BPA contents increased by 1.7–55.4 times [18]. Additionally, BPA is present in epoxy resin, which is used to cover the interiors of metal objects such as food cans [19]. The most prevalent way for humans to come into contact with BPA is through canned foods and beverages. BPA is a chemical that leaches from cans into food and beverages. Environmental factors such as high temperatures, sunlight, and acidic canned products such as tomatoes accelerate this leaching process, allowing it to get through the can liners and into the food. BPA leaching from plastics into food is also accelerated by everyday activities such as microwave cooking with plastic utensils and storing plastic beverage bottles in hot automobiles [20, 21]. As a result, the evidence cited above was considered, particularly when drafting questions concerning BPA exposure in pregnant women and giving training to limit exposure. With answers provided during the first trimester prior to the training regarding the use of numerous kitchen utensils such as storage bags and plastic storage containers that may cause BPA exposure, as well as daily consumed foods such as beverages in cans, carboy water consumption, and plastic packaged foodstuffs, and with responses provided during the third trimester following the trainings. There was a statistically significant difference between the responses. Pregnant women who consumed and used the aforementioned products or foods considerably decreased. More crucially, heat-sensitive plastic utensils, particularly plastic spoons, spatulas, and similar items. Additionally, there was a major decline in the usage of cooking utensils and plastic containers, as well as microwave ovens used to heat foodstuffs. In other words, the instruction offered served its aim, as evidenced by a decrease in the usage of products that may expose users to BPA.

As previously stated, these practices of pregnant women have altered dramatically as a result of their exposure histories and knowledge received. However, the study of the influence of these changes in healthy life practices on actual BPA levels is more critical. To this end, urine samples were tested using LC-MS/MS for the presence of BPA. Due to ongoing exposure via diet, urine BPA has been widely acknowledged as an accurate indicator of recent exposure. When determining the amount of BPA in the urine, however, variations in urine density can affect the results. As a result, urine BPA concentrations should be adjusted for specific gravity or creatinine per gram [13, 14]. As a result, creatinine levels were determined in urine samples collected for our study and statistical analysis was conducted by proportioning them to the amount of BPA. While an average of 2.55 ± 1.52 µg/g creatinine BPA was detected in our study's first trimester urine samples, this value fell to 2.27 ± 1.62 µg/g creatinine BPA in the second trimester. The mean BPA levels fell to 1.58 ± 1.15 µg/g creatinine in the third trimester. Using statistical analysis of urine BPA levels, which were observed to decrease gradually with training, it was determined that, while no significant difference existed between the first and second measurements, there was a

significant decrease between the first and third measurements, as well as between the second and third measurements.

When other research on pregnant women is investigated, it is discovered that the mean BPA levels corrected for specific gravity were 2.1 in the urine analysis (2020) of 196 pregnant women in Korea [22]. In a study examining neonatal exposure in pregnant women in Australia (2012, n = 24), the adjusted BPA concentration was determined to be an average of 1.95 µg/g creatinine [23]. In another study conducted in China (2019, n = 332), fetal development (as measured by ultrasonography) and maternal urine BPA levels were determined. BPA levels were found to be 0.95 µg/g creatinine. The study discovered a link between BPA exposure and small fetal ultrasound measurements (femur and head diameter) [24]. Similar to our study, BPA was tested in urine samples taken at the 16th, 26th, and prenatal weeks from 244 pregnant women in an area of the United States of America (Cincinnati, Ohio), where BPA exposure is assumed to be lower, and the median value of all samples was 2.2 µg/g creatinine. According to gestational week, median values of 1.7, 2.1, and 1.8 µg/g creatinine were obtained. Children were tracked up to the age of three in the same study, and it was established that BPA had an effect on the behavioural and emotional development of particularly 3-year-old girls [25]. The mean quantity of BPA corrected for urine specific gravity was 0.90 µg/L in a study of 2,000 pregnant women in Canada [26]. When studies on the measurement of BPA in pregnant women conducted in various countries are compared, it is observed that the urinary BPA levels of pregnant women without a history of exposure are very similar to the average urine levels of the pregnant women whose samples were collected in our study. Canada's metrics, which are based on a high level of training, socioeconomic status, and public welfare, were determined to be lower than our results. Although it is believed that the sample size, correction values employed in urine, or some of the testing methodologies utilized will result in a little variation, lower exposure is expected in countries that are more sensitive to natural life and environmental toxins. One of our encouraging findings from our study is that prenatal training can considerably reduce urine BPA levels. In our investigation, training had a substantial effect on the scales, which was corroborated by the decrease in BPA level. Similarly, it has been established clearly that pregnant women avoid BPA-containing products and meals as a result of training, as well as the effect this has on urine BPA levels.

Additionally, another aspect of our study that should be explored is the duration or method of training. Because the study found no significant influence of the first training on BPA in the second trimester, but a significant drop in the third trimester. These findings indicated that training should be recurrent in nature and that rather than a single training, learning should be reinforced through reminder trainings. Numerous studies have analysed findings directly, without adjusting for urine BPA levels (creatinine or specific gravity). Due to the possibility of erroneous results from these assessments of urine density, it was decided not to include research that used such measurements in the discussion.

6. Conclusion

With this study, it was discovered that raising societal awareness and knowledge about chemical protection, such as BPA, is critical. In addition, it was revealed that while the duration of a single training session did not have a significant effect, the frequency of reminder trainings had a significant impact on the urine BPA level.

Declarations

Author contribution statement

BETÜL KAPLAN: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Ortabag Tulay: Conceived and designed the experiments; Wrote the paper.

Bayramoglu Tepe Neslihan: Performed the experiments; Analyzed and interpreted the data.

Orkmez Mustafa: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Tosun Nuran: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.

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Data availability statement

The authors are unable or have chosen not to specify which data has been used.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

References

- [1] F. Khan, S. Momtaz, M. Abdollahi, The relationship between mercury exposure and epigenetic alterations regarding human health, risk assessment and diagnostic strategies, *J. Trace Elem. Med. Biol.* 52 (2019) 37–47.
- [2] X. Deng, P. Wang, H. Yuan, Epidemiology, risk factors across the spectrum of age-related metabolic diseases, *J. Trace Elem. Med. Biol.* 61 (2020), 126497.
- [3] S.-C. de Aguiar Greca, I. Kyrou, R. Pink, et al., Involvement of the endocrine-disrupting chemical bisphenol A (BPA) in human placentation, *J. Clin. Med.* 9 (2) (2020) 405.
- [4] I. Pongratz, L. Bergander, *Hormone-disruptive Chemical Contaminants in Food*, Royal Society of Chemistry, 2011.
- [5] M. Yang, S.Y. Kim, S.S. Chang, et al., Urinary concentrations of bisphenol A in relation to biomarkers of sensitivity and effect and endocrine-related health effects, *Environ. Mol. Mutagen.* 47 (8) (2006) 571–578.
- [6] K.L. Howdeshell, A.K. Hotchkiss, K.A. Thayer, et al., Exposure to bisphenol A advances puberty, *Nature* 401 (6755) (1999) 763–764.
- [7] S. Kaur, M. Saluja, A. Anika, Selenium attenuates bisphenol A incurred damage and apoptosis in mice testes by regulating mitogen-activated protein kinase signalling 53, 2021 Apr, e13975.
- [8] M.S. Ahmed Zaki, M.A. Haidara, A.M. Abdallaa, et al., Role of dietary selenium in alleviating bisphenol A toxicity of liver albino rats: Histological, ultrastructural, and biomarker assessments 45, 2021 May, e13725.
- [9] A.S. Abedelhafiez, E.A.A. El-Aziz, M.A.A. Aziz, et al., Lung injury induced by Bisphenol A: a food contaminant, is ameliorated by selenium supplementation, *Pathophysiology: The Official J International Society Pathophysiology* 24 (2) (2017 Jun) 81–89.
- [10] K. Lindgren, Testing the health practices in pregnancy questionnaire–II, *J. Obstet. Gynecol. Neonatal Nurs.* 34 (4) (2005) 465–472.
- [11] S. Er, Gebelikte Sağlık Uygulamaları Ölçeği Türkçe Formunun Geçerlilik Ve Güvenirlilik Çalışması. Ege Üniversitesi Sağlık Bilimleri Enstitüsü Kadın Sağlığı Ve Hastalıkları Hemşireliği Anabilim Dalı: Yüksek Lisans Tezi, İzmir (Tez Danışmanı: Prof. Dr. Ahsen Şirin), 2006.
- [12] H. Fukata, H. Miyagawa, N. Yamazaki, et al., Comparison of ELISA-and LC-MS-based methodologies for the exposure assessment of bisphenol A, *Toxicol. Mech. Methods* 16 (8) (2006) 427–430.
- [13] J.R. Rochester, Bisphenol A and human health: a review of the literature, *Reprod. Toxicol.* 42 (2013) 132–155.
- [14] J.L. Carwile, K.B. Michels, Urinary bisphenol A and obesity: Nhanes 2003–2006, *Environ. Res.* 111 (6) (2011) 825–830.
- [15] Büyüköztürk Ş, Sosyal bilimler için veri analizi el kitabı, Pegem Atf İndeksi. (2018) 1–214.
- [16] L.N. Vandenberg, R. Hauser, M. Marcus, et al., Human exposure to bisphenol A (BPA), *Reprod. Toxicol.* 24 (2) (2007) 139–177.
- [17] J. Michalowicz, Bisphenol A–sources, toxicity and biotransformation, *Environ. Toxicol. Pharmacol.* 37 (2) (2014) 738–758.
- [18] Y. Takao, H.C. Lee, S. Kohra, et al., Release of bisphenol A from food can lining upon heating, *J. Health Sci.* 48 (4) (2002) 331–334.
- [19] C. Monneret, What is an endocrine disruptor? *Comptes Rendus Biol.* 340 (9-10) (2017) 403–405.
- [20] E.R. Kabir, M.S. Rahman, I. Rahman, A review on endocrine disruptors and their possible impacts on human health, *Environ. Toxicol. Pharmacol.* 40 (1) (2015) 241–258.
- [21] Q.U. Ain, D. Roy, A. Ahsan, et al., Endocrine-Disrupting Chemicals: Occurrence and Exposure to the Human Being. *Endocrine Disrupting Chemicals-Induced Metabolic Disorders and Treatment Strategies*, Springer, 2021, pp. 113–123.
- [22] S. Kang, B.H. Shin, J.A. Kwon, et al., Urinary bisphenol A and its analogues and haemato-biochemical alterations of pregnant women in Korea, *Environ. Res.* 182 (2020), 109104.
- [23] A. Callan, A. Hinwood, A. Heffernan, et al., *Urinary Bisphenol A Concentrations in Pregnant Women*, 2012.
- [24] B. Zhou, P. Yang, Y.-L. Deng, et al., Prenatal exposure to bisphenol a and its analogues (bisphenol F and S) and ultrasound parameters of fetal growth, *Chemosphere* 246 (2020), 125805.
- [25] J.M. Braun, A.E. Kalkbrenner, A.M. Calafat, et al., Impact of early-life bisphenol A exposure on behavior and executive function in children, *Pediatrics* 128 (5) (2011) 873–882.
- [26] T.E. Arbuckle, K. Davis, L. Marro, et al., Phthalate and bisphenol A exposure among pregnant women in Canada—results from the MIREC study, *Environ. Int.* 68 (2014) 55–65.