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Maternal Bisphenol a Levels in Patients Diagnosed with Preeclampsia: A Case-Control Study

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Abstract: This study aims to assess Bisphenol-A levels in serum samples from preeclampsia patients and determine potential distinctions by comparing them against samples from healthy pregnant women. This single-center prospective case-control study aimed to investigate the potential differences in serum Bisphenol-A (BPA) levels between pregnant patients diagnosed with preeclampsia and healthy pregnant women. The study encompassed two distinct groups: the study group consisted of 30 pregnant patients diagnosed with preeclampsia, while the control group included 30 healthy pregnant women matched in terms of gestational weeks and demographic characteristics, maintaining a 1:1 ratio. Serum samples were subjected to analysis using a BPA ELISA kit. The study encompassed a total of 60 patients, who were categorized into two groups: preeclampsia (n=30) and control (n=30). Upon comparison of the BPA values between the two groups, no statistically significant difference was detected (p=0.579). Clear-cut scientific evidence establishing a conclusive causal link between BPA and preeclampsia is still lacking. Further research is needed in this area..

Keywords: Bisphenol A; Preeclampsia; Pregnancy.

1. Introduction

Preeclampsia is a progressive and multisystem disorder that usually occurs after the 20th week of pregnancy or postpartum, with hypertension and proteinuria, or with the significant end-organ-damaging dysfunction of hypertension [1, 2].

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Bisphenol A (BPA) is a synthetic organic compound with the formula (CH3)2C(C6H4OH)2. It is studied under diphenylmethanes and bisphenols [3]. Although BPA dissolves in organic solvents, it is only slightly soluble in water. It has been determined that BPA has an estrogenic effect with hormone-like activity [4, 5]. In addition, different studies have supported it because it causes cancer development by causing epigenetic changes in the tissue [6]. Its abnormal proliferative effect is not only limited to cancer diseases, but it has been shown in the literature that it has a toxic effect on trophoblastic cells. It may cause placentation defects due to aberrant proliferation [7]. Similarly, there are studies showing that it causes placental disorders that mimic hypertensive diseases of pregnancy in animal models [8]. No relation could be established between urinary Bisphenol-A levels in early pregnancy and increased risk of hypertensive disease in advanced gestational patients. Still, it was thought that placental dysfunction could be due to the accumulation of toxic effects [9].

In this study, it was aimed to measure Bisphenol-A levels in serum samples of patients with preeclampsia and to show the possible difference by comparing them with healthy pregnant women.

2. Material and Methods

This single-center prospective case-control study was conducted at a tertiary center from May to July 2023. The study protocol received approval from the Local Ethics Committee and was designed in accordance with the principles of the Declaration of Helsinki.

The study was divided into two groups: the study group comprised pregnant patients diagnosed with preeclampsia, and the control group consisted of healthy pregnant women at similar gestational weeks with comparable demographic characteristics, maintaining a 1:1 ratio. Patients aged 18-45 years, referred to us due to the diagnosis of preeclampsia according to the results of clinical laboratory evaluation, were included in the study. Patients with additional comorbid diseases were excluded from the study. Healthy pregnant patients without a diagnosis of placentation anomaly, gestational hypertension, preeclampsia, and eclampsia were determined as the control group. Blood samples were collected, centrifuged, and stored at -80 degrees Celsius in the laboratory. Control group samples were handled similarly, and after completion of the study groups, thawed samples were analyzed in the laboratory.

The sample number and power analysis required for the research were calculated using G*Power 3.1 software. The study's minimum sample size was 52 when the effect size was 0.5, the alpha error probability was 0.05, the power was 0.8, and the number of groups was 2. The total number of patients was determined as 52 out of 26 cases per group, but considering possible data losses, it was decided to conduct the study with 30 patients per group and a total of 60 cases.

Venous blood samples taken from the patients after 8-12 hours of fasting were centrifuged at 3000 rpm/min for 10 minutes. Serum samples separated into Eppendorfs were stored at -80°C until the study day. BPA level was studied in a Biotek (Elx 800, USA) device using the Sun Red brand, catalog numbered Enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions. Optical density was read at 450 nm. The threshold value was calculated according to the manufacturer's instructions. Measurement values were recorded as pg/mL.

2.1. Statistical Analysis

Data analysis was conducted utilizing SPSS software (version 26.0; SPSS Inc., Chicago, IL, USA). Descriptive statistics were presented as either mean ± standard deviation or median±range. Normal distribution of data was assessed through Skewness and Kurtosis analysis. Non-parametric variables were compared using the Mann-Whitney U test. A significance level of $p<0.05$ was adopted for all statistical evaluations.

3. Results

Sixty patients were included in the study. The patients were evaluated in 2 groups: preeclampsia, Group I (n=30) and control Group II (n=30). Demographic data and symptoms of the patients are shown in Table 1. The BPA values of the two groups were compared (p=0.579), and no significant difference was observed (Table 2).

4. Discussion

The potential effects of BPA on human health have caused concern among some researchers and health professionals because of its endocrine-disrupting properties [10]. It was thought that BPA might affect hormonal regulation and thus cause pregnancy complications, especially conditions such as preeclampsia [11]. However, there is a lack of conclusive scientific evidence about a definitive causal relationship between BPA and preeclampsia [12]. In our study, in order to explain this relationship, no relationship was found in the results examined.

Dagdeviren et al.'s investigation accentuated the correlation between elevated maternal serum BPA concentrations and the occurrence of preeclampsia. Notably, the preeclampsia group displayed notably higher median BPA levels in comparison to the control group. Intriguingly, an inverse trend was observed, with serum BPA levels showing notable reductions in individuals who underwent delivery at or beyond the 37-week mark, in contrast to those who experienced delivery before 34 weeks due to severe preeclampsia [13]. The absence of a statistically significant contrast in our study may be attributed to certain factors.

Table 1: Demographic and clinical characteristics.

		Group 1 (n=30) Mean (%)	Group 2 (n=30) Mean (%)
	Age(years)	31.8	28.6
BMI			
	Before pregnancy	28.48±5.11	25.42±5.17
	During pregnancy	32.87±5.05	28.91± 5.08
Gravidity			
	Nulligravida	14	10
	Multigravida	11	11
Smoking			
	Yes	6 (20%)	4 (12%)
	No	24 (80%)	26 (78%)
Folic acid			
	Yes	20 (66.7%)	23 (76.7%)
	No	10 (33.3%)	7 (23.3%)
Clinical symptoms			
	None	15 (50%)	30 (100%)
	Vision problems	5 (16.7%)	0
	Severe headaches	5 (16.7%)	0
	Edema	1 (3.3%)	0
	Multiple systemic symptoms	4 (13.3%)	0

Table 2: The relationship of the BPA levels between the groups.

	Group 1 (n=30) Mean	Group 2 (n=30) Mean
BPA Levels	29,25	31,75
	P = 0.579 (p>0,05) Z = -0.554 *	

*Mann Whitney u Tests.

Notably, categorizing preeclampsia severity and its classification based on gestational weeks was not undertaken. Additionally, disparities might arise from the utilization of differing measurement kits. These factors collectively underscore the need for further research to elucidate the intricacies of the observed outcomes.

In the research conducted by Leclerc et al. they explored the concentrations of BPA in a cohort of 58 pregnancies, encompassing 35 normotensive women and 23 women diagnosed with preeclampsia. They employed the advanced technique of high-sensitivity gas chromatography-mass spectrometry (GC-MS) for their assessments. Their findings unveiled the presence of BPA in maternal and fetal blood and within the placental tissue. Remarkably, a substantial aggregation of BPA was detected in the placentas of women afflicted with preeclampsia, particularly when contrasted with the levels found in normotensive women. This study stands as a pioneering endeavor, highlighting a noteworthy link between preeclampsia and the heightened accumulation of BPA within the placental environment [14]. However, it's essential to note that our study, in contrast to Leclerc et al. focused solely on maternal blood serum samples using an ELISA kit and did not encompass the examination of placental tissue. Delving into placental tissue samples might offer further insightful revelations in this domain.

BPA, a chemical widely used in producing polycarbonate plastic found in food and beverage containers, air, and soil, poses risks to human health as it accumulates in various tissues. With hormone-like properties, BPA can bind to estrogen receptors, affecting tumor development. BPA's effects involve numerous transcription factors related to factors such as fat and liver balance, cardiovascular health, and cancer. Lastly, epigenetic changes like DNA methylation, histone modifications, and alterations in microRNA expression contribute to its pathological effects [3]. Considering the increasing rates of plastic use today, more studies can be conducted on the relationship between BPA and hormone-related cancers.

5. Conclusions

In conclusion, the potential impact of BPA on human health, especially its endocrine-disrupting properties, has deserved attention and discussion among researchers and healthcare professionals. The hypothesis that BPA may disrupt hormonal regulation and potentially contribute to pregnancy complications such as preeclampsia has been of interest. However, the current scientific evidence for a definitive causal relationship between BPA and preeclampsia is inconclusive. Our research aimed to shed light on this relationship, but our results did not reveal a significant link.

Limitations of the Study

A larger sample size of the study, including placental tissues, and new studies that will be evaluated by subgrouping according to preeclampsia severity and gestational weeks may provide strong scientific evidence for a possible causal relationship between BPA and preeclampsia.

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Conflict of Interests

None.

Financial Support

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Author Contributions

MAT; Conception, Writer, FE; Data collection, IG; Analysis, GS; Literature Review, IP; Design, NCK; Supervision.

Ethical Approval

Local Ethics Committee, approval number is 2022.05.175.

Data sharing statement

None.

Consent to participate

Consent was obtained from the patient and control groups participating in the study.

Informed Statement

Available.

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