

The Relationship of Exposure to Plastic Food and Beverage Packaging on The Severity Stadium of Endometriosis at Dr. Soetomo General Hospital Surabaya

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ABSTRACT

Introduction: Endometriosis is a gynecological problem which is one of the main causes of secondary dysmenorrhea with pathological conditions. Endometriosis is defined as a disorder characterized by the presence of tissue similar to the endometrial layer growing outside the uterus which occurs in women of reproductive age. Bisphenol A (BPA) and phthalates are two substances found in food and beverage plastics that may be endocrine disrupting chemicals (EDC). Hormonal system abnormalities are intimately linked to endometriosis. **Objectives:** This study aims to prove the relationship between exposure to food and drink plastic and the stage of endometriosis. **Methods:** The design of this research is observational analytics with a retrospective approach. The sampling technique used non-probability sampling with a consecutive sampling approach of 96 respondents. Data analysis used the chi square test. **Results:** The research results showed that 65.63% (63) of respondents experienced moderate levels of exposure to plastic food and drinks. As many as 34.38% (33) of respondents experienced stage IV (severe) endometriosis. The results of the correlation between exposure to plastic food and drinks and the stage of endometriosis showed p value = 0.042. **Conclusions:** There is a significant relationship between exposure to food and drink plastic and the stage of endometriosis at Dr. Soetomo General Hospital Surabaya

Introduction

Plastic packaging is the most commonly used packaging in everyday life. Plastic's application in food and beverage packaging is one of the most frequently employed types. This is especially true considering that food and beverages are essential needs that are inseparable from human life. Food waste makes up 40.64% of the nation's total garbage, with plastic waste coming in second at 18.08% in 2022, according to data from the Ministry of Environment and Forestry's (KLHK) National Waste Management Information System (SIPSN). Microplastics, which are very small pieces of plastic ranging from 5 mm to 1 micron, can enter the human body, including by using plastic for food and beverage packaging (Emenike *et al.*, 2023). One of the researcher from the Ecological Observation and Wetlands Conservation (ECOTON) NGO reported that none of the 40 human fecal samples from various areas in Bali and Java were free from microplastic contamination (Budiarti, 2021).

Plastic itself is a polymer compound that can be easily shaped when exposed to heat or pressure. It has properties such as being easy to form, waterproof, lightweight, flexible, and resistant to breaking, which is why it is widely used for packaging, especially for food and beverages. However, in addition to these advantages, plastic also contains and releases harmful



chemicals, Endocrine-disrupting chemicals (EDCs) are one such substance that poses a risk to human health (Cimmino et al., 2020).

A class of foreign compounds known as Endocrine Disrupting Chemicals (EDCs) has the ability to modify the endocrine system's functioning. EDCs primarily function by mimicking or blocking the receptors of the body's natural hormones. EDCs can be found in various consumer products, including kitchenware, furniture, paints, pesticides, certain medications, and plastic products (Anne and Raphael, 2021).

The EDCs that come into contact with food are phthalates and Bisphenol A (BPA). Phthalates are used to increase the flexibility of plastic and are often found in food containers and plastic wraps, while BPA is commonly used in reusable food and beverage containers, such as water bottles and food can linings. EDCs in these substances have a structure similar to endogenous steroid hormones, including estrogen (E2), and act as Selective Estrogen Receptor Modulators (SERMs), functioning as agonists. As a result, these EDCs tend to interfere with estrogen hormone activity by binding to estrogen receptors (ER) α and (ER) β (Cimmino et al., 2020).

As mentioned above, because EDCs often disrupt estrogen hormone function, they can cause abnormal reproductive system functioning. This has led EDCs to be considered one of the factors related to the occurrence of endometriosis. The symptoms of endometriosis include tissue similar to the endometrial lining growing outside the uterus, occurring in women of reproductive age (WHO, 2023). Endometriosis symptoms are often mistaken for common menstrual pain (primary dysmenorrhea) experienced by most women, as many experience pain during menstruation. However, the actual symptoms of endometriosis involve excessive menstrual pain that disrupts daily activities and may continue outside of the menstrual cycle. Endometriosis is typically also accompanied by chronic pelvic pain, pain during sex, and even infertility. It is classified as a type of secondary dysmenorrhea, which is dysmenorrhea accompanied by a pathological condition (Adnyana, 2020).

In 2023, the World Health Organization (WHO) estimated that Endometriosis affects 190 million women and girls globally who are of reproductive age, which has an incidence of about 10%. In Indonesia, the incidence of endometriosis has not been estimated due to the lack of epidemiological studies. However, data from a preliminary study showed that the number of endometriosis patient visits at the Graha Amerta Fertility Clinic of Dr. Soetomo Hospital in Surabaya was recorded at 2,484 individuals throughout 2022.

The definitive method for diagnosing endometriosis, including determining the severity/stage, is through direct visualization via surgery. Most of these visualization procedures use laparoscopy, a surgical procedure performed in the abdomen or pelvis using a small incision (0.5–1.5 cm) to insert a camera. Currently, laparoscopy is considered the gold standard in diagnostic determination and staging of endometriosis severity. Endometriosis is divided into four phases by the American Society for Reproductive Medicine (ASRM): mild (stage I), moderate (stage III), severe (stage IV), and mild (stage II). These stages depend on the location, size, depth of implants, and involvement of other organs, as determined through laparoscopy visualization (Hendarto, 2015).

Today, society's lifestyle, which heavily relies on plastic use in daily life, is considered to be at high risk of exposure to EDCs. This is especially true when it comes to food and beverages, which are essential needs. Furthermore, the use of plastic packaging, which has better advantages



compared to other types of packaging, increases the potential for exposure to EDCs, as it directly passes through the digestive system.

As previously stated, chemicals such as BPA and phthalates can induce reproductive health issues, especially in women, by raising estrogen levels since EDCs share structural similarities with estrogen (Dutta et al., 2023). Endometriosis and phthalate exposure are clearly linked, according to a 2024 study by Ribeiro et al. By binding to PPAR and ER- α , activating TGF- β , and boosting signaling cascades that control the activation of particular target genes, phthalates can particularly interfere with endometrial biological processes. This can lead to inflammation, invasion, and disruptions in cell viability and proliferation, all of which can lead to endometriosis (Ribeiro et al., 2024). In 2019, Moreira et al. conducted another assessment of the literature and came to the conclusion that phthalates lead to increased endometrial cell proliferation, invasion, cytokine alterations, and inflammation. (Moreira Fernandez et al., 2019).

While several studies have proven this, little research has been conducted on how EDC exposure affects the stage of endometriosis severity. Therefore, this is what underlies researchers' interest in identifying the severity of exposure to plastic food and beverage packaging and the severity stage of endometriosis in patients at Dr. RSUD. Soetomo Surabaya then analyzed the relationship between the two using the chi square test.

Methods

The population in this study were all female patients diagnosed with endometriosis at the Ob-gyn Outpatient Clinic at Dr. RSUD. Soetomo Surabaya throughout 2024. The sampling technique used non-probability sampling with a consecutive sampling approach of 96 respondents which is obtained from calculations using the binominal proportion formula with an infinite population. The inclusion criteria were female outpatients at the Ob-gyn Poly Outpatient Installation at Dr. RSUD. Soetomo Surabaya who was diagnosed with endometriosis by laparoscopic examination. Data was taken from medical records and consent to be a research respondent, while the exclusion criteria were endometriosis patients whose stage of endometriosis was not explained in the medical record.

The independent variable is exposure to plastic food and drinks and the dependent variable is endometriosis stage. Both primary and secondary data are used in data collection. Primary data includes an assessment of plastic exposure obtained from a questionnaire from a thesis entitled "The Relationship Between Exposure to Food Plastics and the Incidence of Dysmenorrhea in Airlangga University Midwifery Students" by (Maghrifi, 2022) which has been tested for validity. Contains 10 items to assess exposure to plastic food and beverage packaging. Secondary data, namely the stage of endometriosis, was obtained from the respondent's medical records. Then the data obtained from the questionnaire results and medical records are collected on a data collection sheet.

Before the correlation test was carried out, to assess the homogeneity of variance in stages of endometriosis severity among respondents from patients suffering from endometriosis, the Levene test was carried out with a significance level of > 0.05 . The results show a p-value of 0.373 which states that the variance between respondents is homogeneous. After that, the data was analyzed using the chi square statistical test, which seeks to determine the direction and strength of the link between variables. A 95% confidence interval (CI) was used to strengthen the reliability of the findings, with statistical significance determined at $p < 0.05$. This methodological approach provides valuable evidence regarding the impact of exposure to plastic food and beverage packaging on the severity stage of endometriosis.



Results

Table 1 Frequency Distribution of Respondent Characteristics based on Respondent Age

Respondent's Age	Frequency (n)	Percentage (%)
20-30 years	29	30,21
>30 years	67	69,79
Total	96	100

Based on Table 1, it can be concluded that the majority of respondents were >30 years old, 67 respondents (69.79%) and the remaining 29 respondents (30.21%) aged 20-30 years.

Table 2 Frequency Distribution of Respondent Characteristics based on Endometriosis Stage

Endometriosis Stage	Stage Category	Frequency (n)	Percentage (%)
Minimum	Stage I	18	18,75
Low	Stage II	20	20,83
Moderate	Stage III	25	26,04
Severe	Stage IV	33	34,38
Total		96	100

Based on Table 2 it can be concluded that the majority of respondents experienced stage IV endometriosis with 33 respondents (34.38%). Then, the next sequence is stage III with 25 respondents (26.04%).

Table 3 Frequency Distribution of Respondent Characteristics Based on Exposure to Food and Drink Plastics

Exposure of Food and Beverage Plastic	Value Category	Frequency (n)	Percentage (%)
Low	30-40	5	5,21
Moderate	20-29	63	65,63
High	10-19	28	29,17
Total		96	100

Based on Table 3 it can be concluded that the majority of respondents were exposed to plastic food and drinks with a moderate level of exposure with 63 respondents (65.63%).

Table 4 Cross Tabulation of the Relationship between Exposure to Food and Drink Plastics and Endometriosis Stage

Plastic Exposure	Endometriosis Stage								P Value	
	Stage I		Stage II		Stage III		Stage IV			Total
	N	%	N	%	N	%	N	%		



Low-Moderate	11	16,18	18	26,47	20	29,41	19	27,94	68	100	0,042
High	7	25	2	7,14	5	17,86	14	50	28	100	
Total	18		20		25		33		96		

Based on Table 4, it shows that respondents who were exposed to high plastic exposure experienced endometriosis with stage IV as many as 14 respondents out of 28 respondents or 50%, while low-medium plastic exposure experienced endometriosis with stage IV as many as 19 respondents out of 68 respondents or 27.94%. Based on these data, it can be seen that the percentage of respondents with high plastic exposure was greater in respondents who experienced stage IV endometriosis when compared to respondents who had low-medium plastic exposure.

Following an analysis of the aforementioned data using the Chi Square test at a significance level of $\alpha = 5\%$ (0.05), the statistical test yielded a p value of 0.042. The research hypothesis is approved since the p value $< \alpha$ (0.042 $<$ 0.05), indicating that there is a correlation between exposure to food and drink plastic and the stage of endometriosis in patients at the Ob-gyn Poly Outpatient Installation at Dr. Soetomo General Hospital Surabaya.

Discussion

Exposure to Plastic Food and Beverage

Plastic packaging products are widely used in everyday life. Plastic products are classified into several categories. The categories are numbers that can be seen under each product in a triangle shape. In this discussion, what will be discussed are categories number 1 and number 7. The type of plastic that contains phthalates is number one, namely polyethylene terephthalate (PET). Almost all bottled drinks fall into this category. Types of plastic that contain bisphenol A (BPA) are generally included in category number seven. This category is created for types of mixed resins that cannot be categorized into numbers one through six. Examples of this category include food containers, buckets, and other containers used for heavier tasks. However, this study did not include variables other than exposure to food and beverage (Kandaraki et al., 2011).

BPA and phthalates can be found in all areas of the environment. These two EDCs can enter living organisms through the digestive tract, respiratory tract and skin absorption, with the digestive tract being the largest source of absorption. In humans, BPA and phthalates are found in blood, urine, breast milk, amniotic fluid, and other body fluids and tissues (Ma et al., 2019).

Based on the research results, it was found that the majority of respondents were exposed to plastic food and drinks with low-medium exposure levels, namely 68 respondents (70.4%). BPA is one of the most widely produced chemicals in the world, generating more than 6 billion pounds annually. In a study that focused on the distribution of bisphenol in the urine of Flemish adolescents in the study population, it was found that the most frequently detected compound was bisphenol F (97%), followed by bisphenol A (86%) and bisphenol S (83%). Bisphenol F is the most common, but BPA has the highest concentration. BPA was most frequently detected in studies in countries such as the United States, Canada, and Brazil. BPA exposure in the United States reached 92.6% in the age group 6 years and over, with BPA detected in urine. And the level of BPA exposure in Brazil reached 90.9%. This shows that BPA is still widely used throughout the world (Gys et al., 2021).

Analysis of Exposure to Plastic Food and Beverage with Endometriosis Stage

Food packaging plastics can interact with food, leading to a diffusion process where chemical compounds transfer from the packaging into the food. This is closely linked to factors such as the



chemical properties of the plastic packaging, storage temperature, reheating (such as in a microwave), UV exposure, and product shelf life. All these characteristics can determine the amount of chemicals that may transfer, a process called migration. As a result, food has been identified as the primary route of human exposure to various chemicals related to plastics (Sessa et al., 2021).

In the assessment of plastic exposure in this study, it refers to the research by Maghrifi et al. (2021) on plastic containers for food and beverages. Participants with scores of 20-29 (71.8%) were categorized as “frequent users” of plastic products for food and drink, those with scores of 10-19 (26.2%) were “occasional users,” and those with scores of 30-40 (2.0%) were “rare users” (Maghrifi et al., 2022).

In this study, based on the analysis of the research results in Table 4, it was found that the statistical test using the chi-square test with SPSS 23 resulted in a p-value = $0.042 < \alpha = 0.05$. This indicates that there is a relationship between food and beverage plastic exposure and the severity stage of endometriosis. The cross-tabulation analysis between plastic exposure and endometriosis stage revealed a higher percentage of high plastic exposure in stage IV compared to low-to-moderate exposure levels. This indicates a dose-dependent trend, meaning that the higher the plastic exposure, the more severe the stage of endometriosis experienced.

This study aligns with research on women in Korea in 2011 that analyzed phthalate exposure in plasma. This study used an endometriosis control group (stage III and IV) and women without endometriosis. Using High Performance Liquid Chromatography (HPLC), Monoethylhexyl phthalate and di-(2-ethylhexyl) phthalate plasma levels were assessed in 169 control women and 97 women with severe endometriosis, it was found that the concentration of these phthalates was significantly higher in those with advanced endometriosis (stages III and IV) (Kim et al., 2011).

The study also aligns with research conducted on women with endometriosis in Pakistan in 2018, which showed that Diethyl hexyl phthalate (DEHP) levels increased in later stages of endometriosis (III and IV). 50 healthy, fertile women without endometriosis and 50 women with the disease, ages 20 to 40, participated in this study. The study did not include women with comorbid conditions or those under treatment. DEHP levels in serum were measured using HPLC (Nazir et al., 2018).

Moreover, this research supports findings from Peinado et al. (2020), who showed a significant difference in BPA concentrations among women with different stages of endometriosis (III/IV vs I/II). The average BPA concentration in stages I-II was 6.1 ng/ml, while in stages III-IV, it was 7.9 ng/ml. The study, using a case-control design with 124 female participants, measured urine samples before surgery to detect BPA, F, and S levels using UHPLC-MSMS (Peinado et al., 2020).

There is a significant relationship between food and beverage plastic exposure and the severity of endometriosis. Plastics used in food and beverage packaging often contain chemicals such as Bisphenol A (BPA) and phthalates, which are endocrine-disrupting chemicals (EDCs). These chemicals can leach into food or drinks, especially when plastics are exposed to heat, sunlight, or stored for extended periods. Both EDCs have structures similar to estrogen and act as Selective Estrogen Receptor Modulators (SERMs). According to the hormonal theory of endometriosis, when these EDCs enter cells, they bind to estrogen receptors (RE- α and RE- β), go into the nucleus and attach themselves to EREs (Estrogen Response Elements), thereby regulating gene transcription and affecting estrogen activity, leading to increased estrogen levels. This mechanism explains how EDCs can promote the formation and progression of endometriosis severity stages (Dutta et al., 2023).

To simplify, once these EDC chemicals enter the body, they can mimic estrogen function or disrupt other hormonal pathways, leading to increased estrogen or hyperestrogenism, which is a



key factor in the development and severity of endometriosis. Hyperestrogenism due to chemical exposure from plastics creates an environment that supports the growth and spread of endometrial tissue outside the uterus. This worsens symptoms like infertility and persistent pelvic pain, which are frequently linked to advanced stages of endometriosis, and it also raises inflammation. Research indicates that exposure to chemicals from plastics can increase endometrial cell activity, promote larger and more invasive lesions, and increase the production of pro-inflammatory cytokines, worsening the inflammatory process (Stephens and Osteen, 2021).

Furthermore, long-term exposure to chemicals in food and beverage plastics tends to be cumulative, amplifying hormonal and inflammatory impacts on the body. This explains why women with high plastic exposure are often found to have more severe endometriosis stages. Therefore, reducing plastic use in food and beverage packaging is a key preventive step in reducing the risk and severity of endometriosis (Upson et al., 2013).

Conclusion

1. The majority of endometriosis patients at Dr. Soetomo General Hospital Surabaya are exposed to moderate levels of food and beverage plastic.
2. The majority of endometriosis patients at Dr. Soetomo General Hospital Surabaya experience endometriosis at stage IV (severe).
3. From the analysis of the endometriosis stage and food and beverage plastic exposure in the respondents, it was found that there is a significant correlation between plastic exposure and the severity stage of endometriosis at Dr. Soetomo General Hospital Surabaya.

Ethics approval and consent to participate

The Dr. Soetomo General Hospital Surabaya's Health Research Ethics Committee has examined and approved this research. The ethical approval was granted under approval number 1081/KEPK/VIII/2024.

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References

- Adnyana, P. (2020). *Buku ajar Endometriosis 1*.
- Anne, B., & Raphael, R. (2021). Endocrine Disruptor Chemicals. *Journal of Occupational & Environmental Medicine*, 39(4), 358.
- Budiarti, E.C. (2021) 'Identifikasi Mikroplastik pada Feses Manusia', *Environmental Pollution Journal*, 1, pp. 87-88. Available at: <https://journalecoton.id/index.php/epj>.



- Cimmino, I., Fiory, F., Perruolo, G., Miele, C., Beguinot, F., Formisano, P., & Oriente, F. (2020). Potential Mechanisms of Bisphenol A (BPA) Contributing to Human Disease. *International Journal of Molecular Sciences* 2020, Vol. 21, Page 5761, 21(16), 5761.
- Dutta, S., Banu, S. K., & Arosh, J. A. (2023). Endocrine disruptors and endometriosis. *Reproductive Toxicology*, 115(March 2022), 56–73.
- Emenike, E.C. *et al.* (2023) 'From oceans to dinner plates: The impact of microplastics on human health', *Heliyon*, 9(10), p. e20440.
- Gys, C. *et al.* (2021) 'Determinants of exposure levels of bisphenols in flemish adolescents', *Environmental Research*, 193(December 2020), p. 110567.
- Hendarto, H. (2015). Buku Endometriosis aspek teori dan penanganan klinis. In *Airlangga University Press*.
- Kandaraki, E. *et al.* (2011) 'Endocrine disruptors and Polycystic Ovary Syndrome (PCOS): Elevated serum levels of bisphenol A in women with PCOS', *Journal of Clinical Endocrinology and Metabolism*, 96(3), pp. 1–2.
- Kim, S. H., Chun, S., Jang, J. Y., Chae, H. D., Kim, C. H., & Kang, B. M. (2011). Increased plasma levels of phthalate esters in women with advanced-stage endometriosis: A prospective case-control study. *Fertility and Sterility*, 95(1), 357–359.
- Ma, Y. *et al.* (2019) 'The adverse health effects of bisphenol A and related toxicity mechanisms', *Environmental Research*, 176(July). Available at:
- Maghrifi, D. S., Lestari, P., & Saâ€™Madi, A. (2022). Association Between Food Plastic Packaging and Dysmenorrhea in Female Adolescents. *Journal of Maternal and Child Health*, 7(1), 75–81.
- Moreira Fernandez, M. A., Cardeal, Z. L., Carneiro, M. M., & André, L. C. (2019). Study of possible association between endometriosis and phthalate and bisphenol A by biomarkers analysis. *Journal of Pharmaceutical and Biomedical Analysis*, 172, 238–242.
- Nazir, S., Usman, Z., Imran, M., Lone, K., & Ahmad, G. (2018). Women diagnosed with endometriosis show high serum levels of diethyl hexyl phthalate. *Journal of Human Reproductive Sciences*, 11(2), 131–136.
- Peinado, F. M., Lendínez, I., Sotelo, R., Iribarne-Durán, L. M., Fernández-Parra, J., Vela-Soria, F., Olea, N., Fernández, M. F., Freire, C., León, J., Pérez-Cabrera, B., Ocón-Hernández, O., & Artacho-Cordón, F. (2020). Association of urinary levels of bisphenols A, F, and S with endometriosis risk: Preliminary results of the EndEA study. *International Journal of Environmental Research and Public Health*, 17(4).
- Ribeiro, B., Mariana, M., Lorigo, M., Oliani, D., Ramalhinho, A. C., & Cairrao, E. (2024). Association between the Exposure to Phthalates and the Risk of Endometriosis: An Updated Review. *Biomedicines*, 12(8), 1–17.
- Stephens, V. R., & Osteen, K. G. (2021). *U. S. Department of Veterans Affairs*. 57–78.





Yuan, M., Chen, S., Zeng, C., Fan, Y., Ge, W., & Chen, W. (2023). Estrogenic and non-estrogenic effects of bisphenol A and its action mechanism in the zebrafish model: An overview of the past two decades of work. *Environment International*, 176(April), 107976.

