Short Communication

Relationship between urinary bisphenol A and age at menarche among adolescent girls: A study in Sumatera Utara Province, Indonesia

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Abstract

Bisphenol A (BPA) is an endocrine-disrupting chemical widely used in various consumer products. Due to its estrogenic properties, BPA exposure is suspected to influence reproductive development, particularly the timing of menarche in adolescent girls. The aim of this study was to assess the relationship between urinary BPA levels and the age at menarche among adolescent girls in Sumatera Utara Province, Indonesia. A cross-sectional study was conducted in January 2023 involving 30 adolescent girls aged 9–14 years attending junior high school in Sumatera Utara. Data on age, body weight, height, and body mass index (BMI) were collected. Urinary BPA levels were detected using high-performance liquid chromatography (HPLC). The Mann-Whitney U test was employed to determine the association between BPA detection and age at menarche. BPA was detected in the urine of 3 out of 30 participants. The median age at menarche for girls with detectable BPA was 11 years, while those without detectable BPA had a median age of 11 (ranging from 10 to 12 years). The difference in age at menarche between the two groups was not statistically significant (p=0.646). In conclusion, this study did not find a significant association between urinary BPA levels and the timing of menarche among adolescent girls in Sumatera Utara Province. Further research with a larger sample size and consideration of additional confounding factors is recommended to better understand the potential impact of BPA on pubertal development.

Keywords: Bisphenol A, endocrine disruptor, estrogen, menarche, pollution

Introduction

Endocrine-disrupting chemicals (EDCs) interfere with the body's natural hormone systems, potentially causing long-term effects even after exposure has ceased. One of the most widely used EDCs is bisphenol A (BPA), which possesses estrogenic properties that can alter the timing of menarche in adolescents [1]. Despite its known effects, BPA is still produced on a large scale, with over 3.5 million tons manufactured annually [2]. The United States is the largest producer, accounting for more than 1 million tons per year, nearly 25% of global production [3]. Human exposure to BPA can occur through ingestion of contaminated food, dust, and water, inhalation of gases and airborne particles, as well as through skin contact.

Research in the United States, utilizing data from the National Health and Nutrition Examination Survey (NHANES), investigated the association between BPA exposure and the age

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of menarche in girls aged 12–19 years [4]. The study found that girls with moderate levels of urinary BPA experienced delayed menarche compared to those with lower levels [4]. Another study from the United States also examined the relationship between BPA and menarche timing in girls aged 12–16 years, identifying an association between BPA, 2,5-dichlorophenol, and early menarche [5]. Additionally, a recent systematic review and meta-analysis suggest that BPA exposure increases the risk of early puberty [6].

BPA and other endocrine-disrupting chemicals (EDCs) can impact reproductive development and the timing of puberty due to their estrogenic properties, which allow them to bind directly to estrogen receptors [7,8]. Additionally, these compounds may increase the activity of the aromatase enzyme, enhancing estrogen sensitivity, or indirectly boost endogenous estrogen production by influencing Gonadotropin-Releasing Hormone (GnRH) [7,8]. BPA has also been shown to increase the number of antral follicles, potentially triggering early menarche [9]. Most investigations rely on urine samples due to their non-invasive nature and advantages over blood sampling, such as lower protein and lipid content, which reduces the solubilization of unconjugated BPA, the ability to collect larger volumes, and the lack of need for sterile sampling techniques [10]. In terms of the study novelty, no research has yet been conducted on the relationship between BPA and menarche among the Indonesian population. Given the scarcity of studies reporting on the effect of BPA on the age of menarche, this study aims to assess the relationship between BPA exposure and the onset of menarche in adolescent girls.

What is also worth mentioned is that from the previous study in the United States found that household income was associated with the timing of menarche, with early menarche (<11 years) becoming more common over 50 years among girls of lower socioeconomic status [4]. Therefore, the social status of the family could also be an important confounder that could influence the result of the study.

Methods

Study design

This cross-sectional study was carried out to assess the relationship between BPA and the incidence of menarche in adolescent girls. The study was conducted in Deli Serdang District, Sumatera Utara Province, Indonesia, in January 2023. The target population was adolescent girls aged 9 years to 14 years attending a junior high school education. The sample selection was performed randomly with the assistance of Random Number Generator (RNG) software. Signed informed consent was collected from the legal guardians of the research subjects. The study protocol was approved by the Health Research Ethics Committee of the Universitas Sumatera Utara (No.1020/KEPK/USU/2022).

Eligibility criteria

Inclusion criteria are adolescent girls (aged 9–14 years) who attend Junior High School in Sumatera Utara Province, Indonesia. To be included, the participants should have experienced menarche. Both subjects and their parents were willing to participate, as indicated by the signed informed consent form. Exclusion criteria are adolescent girls with a history of kidney disease. Girls with a history of hormonal disorders like polycystic ovary syndrome (PCOS) or undergoing hormonal treatments were excluded.

Data collection

Data on age, body weight, height, and body mass index (BMI) were measured directly during the survey to ensure accuracy. BMI was calculated as weight in kilograms (kg) divided by height in meters squared (m^2). Age at menarche, along with the mother's age at menarche, was gathered through interviews with the participants. Information on the participants' school year and parental occupations, as well as parental income, was also collected through interviews.

Bisphenol A detection

Bisphenol A (BPA) detection was conducted using a high-performance liquid chromatography (HPLC) method specifically designed for detection purposes. Bisphenol A standards were obtained from Sigma-Aldrich (St. Louis, MO, USA). Urine samples were collected in sterile

containers and pre-treated by centrifugation (4°C; 10 min at 3,000 rpm), followed by dilution with HPLC-grade water and filtration through a 0.22 µm polytetrafluoroethylene membrane filter. The pre-treated samples were then analyzed using a Shimadzu LC-20AD XR HPLC system equipped with a SIL-HT auto-sampler (Shimadzu, Kyoto, Japan). The analysis utilized a Phenomenex Gemini-NX C18 analytical column (150 mm × 2.0 mm ID, 5 µm particle size) and a corresponding guard column (4 mm ID × 2.0 mm). The column was maintained at 40°C, with a total run time of 11 minutes. A gradient mobile phase system was employed, consisting of 2 mM ammonium acetate in water (pH 6.7) as solvent A and methanol as solvent B, with a flow rate set at 0.35 mL/min. The gradient began with 20% solvent B, increased to 98% by the 6th minute, held until the 9th minute, and then reverted to 20% at 9.01 minutes, holding until the 11th minute. The sample injection volume was set at 2 µL.

Data analysis

The normality of continuous variables was assessed using the Shapiro-Wilk test. Variables with a normal distribution were presented as mean ± standard deviation (SD), while non-normally distributed data were reported as median with minimum and maximum values. Categorical variables were summarized using frequencies and percentages. The Mann-Whitney U test was used to determine the difference in age at menarche between girls with and without bisphenol A detected in their urine. Statistical analysis was performed on IBM SPSS software version 26.0.

Results

Characteristics

A total of 21 subjects (70%) were grade IX children, as described in **Table 1**. The mean age of the subjects was 11.63 years. The median age of maternal menarche was 12 years, with the earliest age of menarche being 11 years and the oldest being 14 years. The median age of the child's menarche was 11 years, with the fastest age of menarche being 10 years old and the oldest being 12 years old. Weight measurements showed a median of 38.4 kg. The mean BMI was 19.96 kg/cm^2.

The most common father's occupation was teacher, totaling 10 people (33.3%), followed by private employees, as many as 11 people (36.7%). Most mothers' occupations were housewives, with 16 people (53.3%), followed by teachers with 8 people (26.7%). Based on income, most parents' income was in the range of IDR 2 million to <IDR 3 million, as many as 11 people (36.7%).

Table 1. Demographic characteristics of subjects in this study (n=30)

Demographic characteristics	n (%)
Age, mean±SD (years)	11.63±0.7
Age at menarche, median (min-max) (years)	11 (10–12)
Body weight, median (min-max) (kg)	38.4 (20–57)
Height, mean±SD (cm)	140.77±6.88
Body Mass Index (BMI), mean±SD (kg/cm^2)	19.96±5.08
Mother’s age at menarche, median (min-max) (years)	12 (11–14)
Junior high school year	
First year	2 (6.7)
Second year	7 (23.3)
Third year	21 (70)
Father's occupation	
Teacher	10 (33.3)
Private sector employee	12 (40)
Nurse	1 (3.3)
Farmer	2 (6.7)
Self-employed	5 (16.7)
Mother's occupation	
Midwife	1 (3.3)
Teacher	8 (26.7)
Housewives	16 (53.3)
Private sector employee	3 (10)
Nurse	1 (3.3)
Self-employed	1 (3.3)

Demographic characteristics	n (%)
Parental income	
<IDR 2 million	1 (3.3)
IDR 2 million to <IDR 3 million	11 (36.7)
IDR 3 million to <IDR 4 million	8 (26.7)
IDR 4 million to <IDR 5 million	6 (20)
≥IDR 5 million	4 (13.3)

Association between BPA and age at menarche

The presence of BPA was detected in three girls, while the compound was not detected in the 27 others. All the three girls who tested positive for urinary BPA had the age at menarche of 11 years old (**Figure 1**). The median age of those with negative BPA was 11 (10–12 years old). The Mann-Whitney U test revealed the absence of statistical significance on the difference of age at menarche with p=0.646.

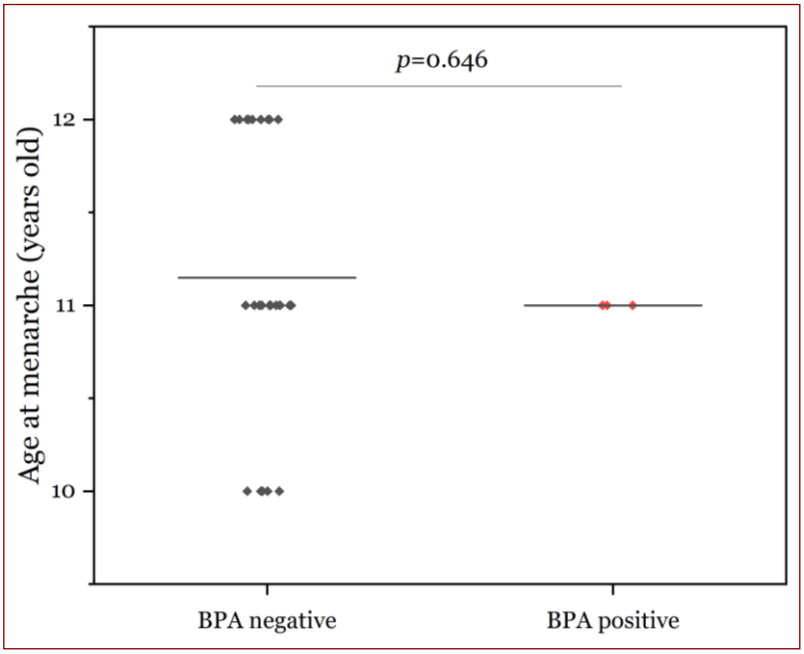

Figure 1. Age at menarche of adolescent girls with positive and negative urinary Bisphenol A (BPA).

Discussion

Herein, the average body mass index (BMI) of the participants in this study was 19.96, falling below the 95th percentile on the growth curve, categorizing them as normal weight or non-obese. Notably, all urine samples in which BPA was detected came from participants whose parents had low incomes (IDR 2 million to <IDR 3 million). This finding contrasts with a previous study which detected BPA predominantly in high-income groups [11]. A recent study in the United Kingdom over 85 years reported a decrease in menarche timing across all socioeconomic groups, suggesting that socioeconomic status alone may not fully explain shifts in menarche timing over time [12].

In this present study, three children with detectable BPA in their urine experienced normal menarche at age 11. Meanwhile, among the 27 children with no detectable BPA, the average age at menarche was 11.15 years, with the earliest at 10 years and the latest at 12 years. This result does not align with previous studies that linked earlier menarche with detectable BPA in urine [4,11]. In a study among Chinese population, girls with detectable BPA in urine tended to experience delayed menarche [13]. Adolescent girls with abnormal menarche timing are at greater risk for psychosocial and behavioral issues and are more likely to be shorter in stature and obese [14].

Menarche, the first menstruation, marks the onset of puberty and the beginning of the reproductive period in females [15]. It indicates the maturation of the sex organs, driven by hormone production initiated by the hypothalamus and conveyed to the ovaries and uterus. High serum concentrations of BPA (1.53–2.22 µg/L) in females have been shown to disturb hormonal

balance, leading to metabolic abnormalities such as precocious puberty [7]. This is due to BPA's estrogen-like activity, which can trigger a positive feedback loop, increasing the central secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). BPA also affects the hypothalamic-pituitary-gonadal axis, leading to increased gonadotropin-releasing hormone (GnRH) secretion and an estradiol-induced LH surge [7]. Several human studies have found a correlation between BPA exposure and early menarche and telarche in girls [15,16].

As there are various methods for detecting BPA in the human body, including analysis of placental tissue, urine, serum, semen, blood, amniotic fluid, breast milk, follicular fluid, and umbilical cord blood, each method provides a different limit of detection (LOD) and it could affect the sensitivity and accuracy of BPA measurement. The result of the study about the relationship between urinary BPA and age at menarche cannot directly indicate that BPA levels in human bodies are unrelated to age at menarche among adolescents.

This study is the first in Indonesia to explore the relationship between urinary BPA levels and age at menarche, offering valuable insights into this topic within the local context. However, several limitations should be noted. Firstly, BPA was only detected, not quantified, which restricts the ability to analyze dose-response relationships. Additionally, the small sample size may limit the generalizability of the findings. Furthermore, the lack of detailed assessment of exposure to other endocrine-disrupting chemicals may have introduced confounding factors that could influence the results.

Conclusion

BPA was detected in a small subset of participants, yet its presence was not found to be statistically significantly associated with the timing of menarche. Due to the limited sample size and the presence of potential confounding factors, further research with a larger cohort is necessary to conclusively determine the role of BPA in influencing pubertal development. Future studies should also consider a more comprehensive analysis of other endocrine-disrupting chemicals and environmental factors that could affect menarche timing.

Ethics approval

This study was approved by the Health Research Ethics Committee of the Universitas Sumatera Utara (No.1020/KEPK/USU/2022).

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Competing interests

The authors have no known conflict of interest in relation to the publication of this work.

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Underlying data

Data underlying this study can be requested from the corresponding authors upon reasonable request.

How to cite

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