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Does exposure to PM_{10} decrease age at menarche?

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ABSTRACT

Background: There has been a consistent decrease in age at menarche in South Korea. A potential risk factor for early menarche is exposure to particulate matter (PM), because endocrine-disrupting compounds emitted into air from anthropogenic sources may be incorporated into PM. The objective of this study was to examine the association between pre-menarcheal exposure to PM ≤ 10 μm in diameter (PM_{10}) and age at menarche in adolescents of South Korea using Korea National Health and Nutrition Examination Survey (KNHANES) 2010–2012 data.

Methods: We used self-reported age at menarche of 639 girls aged 13–17 years in this study. The cut-off age for early menarche was set to 12 years. Based on each subject's address, 1-year, 2-year, and 3-year averages of annual mean PM_{10} concentrations (models 1–3) were linked to KNHANES. Models were adjusted for body mass index (BMI), city size, household income level, maternal age at menarche, and second-hand smoke exposure at home. SURVEYREG and SURVEYLOGISTIC procedures were used to address the complex survey design of KNHANES.

Results: Overall analysis showed that exposure to PM_{10} has a significant effect on decreasing age at menarche. Multiple linear regression results suggested that each 1 μg/m^3 increase in 1-year, 2-year, 3-year averages of annual mean PM_{10} concentrations accelerated age at menarche by 0.046 years (95% CI: −0.064, −0.027; p < .0001), 0.038 years (95% CI: −0.059, −0.018; p = 0.0003),and 0.031 years (95% CI: −0.047, −0.015; p = 0.0002), respectively. Adjusted ORs for a 1 μg/m^3 increase in PM_{10} concentration were 1.08 (95% CI: 1.04 −1.12) for model 1, 1.06 (95% CI: 1.02 −1.10) for model 2, and 1.05 (95% CI: 1.01 −1.09) for model 3.

Conclusion: Our findings suggest that elevated PM_{10} concentration can decrease age at menarche. This is the first study that investigates the association between exposure to PM_{10} and age at menarche using a nationally representative sample of Koreans.

1. Introduction

Several studies have shown that early menarche is associated with adverse health outcomes, including asthma, dysmenorrhea, breast cancer, type 2 diabetes, and cardiovascular diseases (Balbi et al., 2000; Canoy et al., 2015; Collaborative Group on Hormonal Factors in Breast Cancer, 2012; Janghorbani et al., 2014; Lieberoth et al., 2015). Girls who experience early menarche are more likely to commit risky sexual behaviors such as early sexual debut and unprotected sexual intercourse (Cheong et al., 2015). Furthermore, early menarche may be linked to psychological disorders including depressive symptoms, substance abuse, and eating disorders (Joinson et al., 2011; Ruuska et al., 2003; Stice et al., 2001).

Average age at menarche had declined from 14.2 years old in 1970 to 12.7 years old in 2010 in South Korea (Cho et al., 2010; Lee et al., 2016). A number of studies have suggested that socioeconomic status, life setting, nutritional status, environmental conditions, and maternal age at menarche can influence age at menarche (Ameade and Garti, 2016; Karapanou and Papadimitriou, 2010; Padez, 2003; Yermachenko and Dvornyk, 2014). However, underlying causes of early menarche remain unclear. Despite the findings showing that childhood exposure to endocrine-disrupting chemicals (EDCs) can alter pubertal timing (Parent et al., 2015), whether pre-menarcheal exposure to harmful environmental factors can affect the timing of pubertal development is

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still unclear.

Particulate matter (PM) is one of the environmental stressors that has been suggested as possible cause of the decline in age at menarche. PM is composed of diverse components, including EDCs, heavy metals, and polycyclic aromatic hydrocarbons (PAHs) (Damstra, 2002; Levy et al., 2002; Lim et al., 2010). EDCs emitted into the air from multiple sources can be absorbed into human body and then exert adverse effects on various systems, including nervous, endocrine, and reproductive systems (Rudel and Perovich, 2009). Additionally, some PAHs and heavy metals can interfere with estrogen receptor signaling pathway through estrogen mimicry (Georgescu et al., 2011; Santodonato, 1997; Sievers et al., 2013), resulting in disturbed biosynthesis of hormones and altered hormone levels. After accumulating various compounds from anthropogenic sources, PM may exhibit endocrine disrupting properties, which account for the decrease in age at menarche.

However, few studies have examined the association between PM exposure and age at menarche. Therefore, the objective of this study was to investigate the association between pre-menarcheal exposure to PM ≤ 10 μm in diameter (PM_{10}) and decrease in age at menarche among adolescents in South Korea by using data from the fifth Korea National Health and Nutrition Examination Survey (KNHANES V).

2. Methods

2.1. Study population

KNHANES V was conducted by the Division of Health and Nutrition Survey of the Korea Centers for Disease Control and Prevention between 2010 and 2012 (Korea Centers for Disease Control and Prevention, 2012). The survey employs a complex, multistage, stratified and probability cluster sampling design on a representative sample of non-institutionalized civilian Korean population (Kweon et al., 2014). It provides cross-sectional data. KNHANES V consisted of a health examination, a health interview, and a nutrition survey. Both health interview and the health examination were administered by trained health professionals in a mobile examination center (Kweon et al., 2014).

The sample population used in this study was restricted to girls aged between 13 and 17 years who already experienced menarche. Information on menstrual status and age at menarche was collected through a self-administered questionnaire by asking female participants "Are you currently experiencing menstruation?" and "How old were you when you experienced menarche?" Subjects younger than ten years old were not eligible to answer these questions, and were excluded from the study population. We also excluded subjects older than 19 years because an older population might have a higher chance to inaccurately recollect their age at menarche. Because that average age at menarche was Korea is 12.7 years (Lee et al., 2016), the cut-off age for early menarche was set to 12 years. Subjects who experienced menarche before the age of 12 were assigned into an early menarche group (< 12) and the rest was assigned into a normal menarche group (≥12). We then further excluded girls aged < 12 years because we would not know what age the subject would experience menarche. For instance, those aged 11 years without experiencing menarche at the time of the survey did not mean that they would experience menarche after the age of 12. We also excluded girls older than 17 years because 99.8% of study subjects reached menarche by the age of 16. For the purpose of the study, girls who had not reached menarche at the time of the survey and those who did not report their menarcheal age were also excluded. A total of 639 girls (86.7% response rate out of 737 girls) were eligible for analysis (Fig. 1).

2.2. Exposure assessment

PM_{10} data from January 2002 to December 2012 were obtained from Air Korea (www.airkorea.or.kr). β-ray absorption method was used to measure PM_{10}. These data were confirmed and finalized by the National Institute of Environmental Research. Air monitoring network stations were placed throughout 16 administrative divisions across South Korea. The administrative divisions consisted of nine provinces (Gyeonggi-do, Gangwon-do, Chungcheongbuk-do, Chungcheongnam-do, Jeollabuk-do, Jeollanam-do, Gyeongsangbuk-do, Gyeongsangnam-do, and Jeju-do) and seven metropolitan cities (Seoul, Busan, Daegu, Daejeon, Gwangju, Incheon, and Ulsan). PM_{10} concentration data were collected on an hourly basis. Daily PM_{10} concentration data were considered valid if hourly data met the 75% data completeness requirement.

Exposure to PM_{10} was assessed using 1-year (model 1), 2-year (model 2), and 3-year (model 3) averages of annual mean PM_{10} concentrations. Because the exact date of menarche was not identified in KNHANES, we retrospectively calculated annual mean PM_{10} concentrations over three years, based on the year when the subjects experienced menarche (Fig. 2). Since KNHANES was a cross-sectional survey (Kweon et al., 2014), follow-up data on changes in address for subjects were not available. Thus, the address provided by the subjects at the time of the survey was used under the assumption that the subject had lived in the same city over the exposure period. Considering that the average total residence duration of households in Korea was 8.8 years (Statistics Korea, 2017), we limited the time difference between the year of menarche and the time of the survey within 10 years. Models 1–3 were used as measures of exposure to ensure time difference in our study subjects. Subjects' data from KNHANES were linked to models 1–3 using an administrative division code and exposure period.

2.3. Statistical analysis

Survey analysis procedures were used to account for the complex multistage probability sampling survey design of KNHANES. Appropriate weights for pooled data were calculated and used for analysis. We included the following potential confounders identified through literature review: household income, city size(metropolitan/others), body mass index (BMI), maternal age at menarche, and second-hand smoke exposure at home (Cho et al., 2010; Karapanou and Papadimitriou, 2010; Lee et al., 2016; Yang et al., 2015).

Household income was employed as a proxy for socioeconomic status. In KNHANES, household income referred to monthly equivalized household income, which was recomputed to take household size and information about head of household such as gender and age into consideration. Household income levels were classified as lower, lower-middle, upper-middle, or upper level. City size was treated as a categorical variable: metropolitan (7 cities) and others (9 provinces). Based on the KNHANES analysis guidelines, BMI was divided into three categories: underweight (< 18.5), normal weight (≥18.5– < 25), and overweight (≥25). Maternal data could be found from KNHANES for some subjects, allowing us to obtain maternal and household information such as maternal age at menarche and second-hand smoke exposure at home. Maternal age at menarche was self-reported. Mean maternal age at menarche was calculated for the early menarche group and the normal menarche group. A question asking if there was a regular smoker at home was used to assess whether subjects were exposed to second-hand smoke at home.

Differences in basic characteristics between the two groups (early *vs.* normal menarche group) were explored using PROC SURVEYFREQ procedure (Rao-Scott Chi-square test) for categorical variables and PROC SURVEYREG procedure (Independent *t*-test) for continuous variables. PROC SURVEYREG analyses with and without covariates were conducted to evaluate the relationship between PM_{10} exposure and age at menarche. In addition, we performed PROC SURVEYLOGISTIC analysis to estimate the odds ratios (ORs) and 95% confidence intervals (CIs), which can be interpreted as the effect of a 1 μg/m^3 increase in PM_{10} concentration on the risk of early menarche. Statistical analyses were performed with SAS statistical software (SAS Institute,