J Korean Med Sci. 2024 Apr 8;39(13):e131
https://doi.org/10.3346/jkms.2024.39.e131
eISSN 1598-6357·pISSN 1011-8934

JKMS

Original Article
Obstetrics & Gynecology

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Association Between Individual Air Pollution (PM_{10}, $PM_{2.5}$) Exposure and Adverse Pregnancy Outcomes in Korea: A Multicenter Prospective Cohort, Air Pollution on Pregnancy Outcome (APPO) Study

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Received: Nov 26, 2023
Accepted: Mar 5, 2024
Published online: Apr 4, 2024

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ABSTRACT

Background: Prenatal exposure to ambient air pollution is linked to a higher risk of unfavorable pregnancy outcomes. However, the association between pregnancy complications and exposure to indoor air pollution remains unclear. The Air Pollution on Pregnancy Outcomes research is a hospital-based prospective cohort research created to look into the effects of aerodynamically exposed particulate matter $(PM)_{10}$ and $PM_{2.5}$ on pregnancy outcomes.
Methods: This prospective multicenter observational cohort study was conducted from January 2021 to June 2023. A total of 662 women with singleton pregnancies enrolled in this study. An AirguardK® air sensor was installed inside the homes of the participants to measure the individual PM_{10} and $PM_{2.5}$ levels in the living environment. The time–activity patterns and PM_{10} and $PM_{2.5}$, determined as concentrations from the time-weighted average model, were applied to determine the anticipated exposure levels to air pollution of each pregnant woman. The relationship between air pollution exposure and pregnancy outcomes was assessed using logistic and linear regression analyses.
Results: Exposure to elevated levels of PM_{10} throughout the first, second, and third trimesters as well as throughout pregnancy was strongly correlated with the risk of pregnancy problems according to multiple logistic regression models adjusted for variables. Except for in the third

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Funding
This study was supported by the National Institute of Health research project (project No. #2021-ER120801) and a research program funded by the Korea National Institute of Health (grant code# 2021-ER1208-02). This work was partly supported by the Institute of Information Communications Technology Planning Evaluation (grant funded by the Korea Government [MSIT]) (No. RS 2022 00155966 Artificial Intelligence Convergence Innovation Human Resources Development Ewha Womans University) and a Korea Evaluation Institute of Industrial Technology (KEIT) grant funded by the Korea Government (MOTIE). This research was also supported by BK21 FOUR (Fostering Outstanding Universities for Research) funded by the Ministry of Education (MOE, Korea) and National Research Foundation of Korea (NRF-5199990614253).

Disclosure
The authors have no potential conflicts of interest to disclose.

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Conceptualization: Ahn TG, Kim YJ, Kim YH, Na SH. Data curation: Ahn TG, Kim YJ, Lee G, You YA, Kim SM, Chae R, Hur YM, Park MH, Bae JG, Lee SJ, Kim YH, Na SH. Formal analysis: Ahn TG, Kim YJ, Kim YH, Na SH, Lee G. Funding acquisition: Kim YH, Na SH. Investigation: Ahn TG, Kim YJ, Kim YH, Na SH. Methodology: Ahn TG, Kim YJ, Kim YH, Na SH, You YA. Software: Ahn TG, Kim YJ, Lee G, You YA, Kim SM, Chae R, Hur YM, Park MH, Bae JG, Lee SJ. Supervision: Kim YH, Na SH. Validation: Ahn TG, Kim YJ, Kim YH, Na SH. Writing - original

trimester of pregnancy, women exposed to high levels of $PM_{2.5}$ had a high risk of pregnancy complications. During the second trimester and entire pregnancy, the risk of preterm birth (PTB) increased by 24% and 27%, respectively, for each 10 μg/m³ increase in PM_{10}. Exposure to high PM_{10} levels during the second trimester increased the risk of gestational diabetes mellitus (GDM) by 30%. The risk of GDM increased by 15% for each 5 μg/m³ increase in $PM_{2.5}$ during the second trimester and overall pregnancy, respectively. Exposure to high PM_{10} and $PM_{2.5}$ during the first trimester of pregnancy increased the risk of delivering small for gestational age (SGA) infants by 96% and 26%, respectively.
Conclusion: Exposure to high concentrations of PM_{10} and $PM_{2.5}$ is strongly correlated with the risk of adverse pregnancy outcomes. Exposure to high levels of PM_{10} and $PM_{2.5}$ during the second trimester and entire pregnancy, respectively, significantly increased the risk of PTB and GDM. Exposure to high levels of PM_{10} and $PM_{2.5}$ during the first trimester of pregnancy considerably increased the risk of having SGA infants. Our findings highlight the need to measure individual particulate levels during pregnancy and the importance of managing air quality in residential environment.

Keywords: Air Pollution; PM_{10}; $PM_{2.5}$; Pregnancy; Adverse Pregnancy Outcomes

INTRODUCTION

Air pollution is an important global environmental issue. The relationship between airborne particulate matter (PM) and human health has been widely studied.[1-3] In 2019, the World Health Organization(WHO) listed climate change and air pollution as two of the top ten global health risks and identified air pollution as the single worst environmental threat to human health.[4] Each year, 7,000,000 people die from illnesses that may be caused by both indoor and outdoor air pollution.[4] PM can have a negative impact on a pregnant woman's placenta by reducing blood flow and the fetal access to nutrients and oxygen.[5] Research in animal models showed that exposure to fine PM can cause an inflammatory response in the placental fetal tissue.[6] The inflammatory response caused by increased levels of interleukin-6, platelets, and peripheral blood mononuclear cells may alter the placental transport capacity.[7] Because they can be breathed, particles known as PM10—diameter less than 10 μm—have drawn attention. Fine particles (2.5 μm; $PM_{2.5}$) are associated with higher risks because they can penetrate deeper into the alveoli and travel via the bloodstream. $PM_{2.5}$, a heterogeneous mixture, can affect hemodynamics, oxidative stress, and systemic inflammation.[5] Numerous reviews and meta-analyses have described the significant links between PM exposure and cardiovascular mortality.[8-11]

Preterm birth (PTB), low birth weight, and other harmful health impacts are linked to maternal exposure to ambient air pollution (particularly $PM_{2.5}$) during pregnancy.[12] Additionally, a recent study combining data from 14 population-based mother-child cohort studies conducted in 12 European nations supported earlier findings showing that exposure to traffic and ambient air pollution during pregnancy was linked to constrained fetal growth.[13] However, many studies have relied on regional ambient PM_{10} data from pregnant women's homes and national birth data and do not accurately represent the level of exposure experienced by contemporary individuals in the real world who spend most of their time indoors and must cope with indoor air quality as opposed to outdoor air quality. In addition, the exposure status in relation to each person's lifestyle was not thoroughly examined. Given that most people, particularly children and pregnant women, spend most of their time draft: Ahn TG, Kim YJ, Lee G, You YA, Kim SM, Chae R, Hur YM, Park MH, Bae JG, Lee SJ. Writing - review & editing: Ahn TG, Kim YJ, Lee G, You YA, Kim SM, Chae R, Hur YM, Park MH, Bae JG, Lee SJ, Kim YH, Na SH.

indoors, exposure to environmental hazards can have a range of negative effects on humans and, in some circumstances, can be fatal to an unborn child. Thus, the purpose of this study was to investigate the association between unfavorable pregnancy outcomes and the individual exposure of mothers to PM_{10} and $PM_{2.5}$ throughout each trimester of pregnancy.

METHODS

Study area

This prospective multicenter observational cohort study was conducted between January 2021 and June 2023. Pregnant women were recruited from all outpatient clinics at the participating institutions. The six university hospitals Ewha Womans University Mokdong Hospital, Kangwon National University Hospital, Severance Hospital, Korea University Guro Hospital, Keimyung University Dongsan Medical Center, and Ewha Womans University Seoul Hospital participated in the study in 2021. Ulsan University Hospital joined this group in 2022 (**Fig. 1**). In order to find out as much as possible the nationwide impact of PM, a study was conducted targeting pregnant women across the country, and hospitals with large scale in each region were prioritized. In addition, because there is a significant difference in PM depending on the region, hospitals were classified according to specific regions to determine the impact of this on pregnancy outcomes (**Supplementary Tables 1** and **4**). To accurately represent the unique aspects of various locations, we evaluated hospitals in urban areas (Seoul), industrial complexes (Ulsan), and mountainous areas (Gangwon province). Because Seoul has a large population,

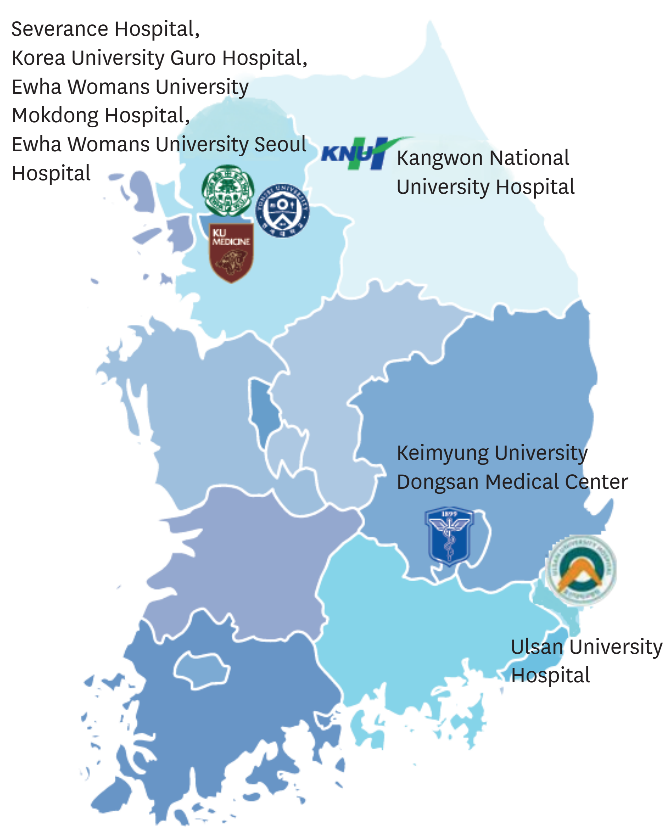

Fig. 1. Map of Korea showing regional boundaries and locations of hospitals participating in the study.

heavy traffic volume, severe air pollution, and a large number of flats, it was chosen as the key location for this study. We also selected Ulsan, South Korea's largest industrial city.

Study design and participants

We used baseline information gathered from 662 pregnant participants in the Air Pollution on Pregnancy Outcome (APPO) study, a prospective hospital-based cohort study conducted to examine the effects of exposure to PM (PM_{10} and $PM_{2.5}$) on the mother and fetus. The rationale, design, and methods of the APPO study have been described previously.[14] Pregnant women in the first and second trimesters were selected from ambulatory prenatal clinics. Women over the age of 18 years and those with singleton pregnancies without any chronic conditions such as diabetes or hypertension were included. All female participants read and signed informed consent forms. Women with multiple pregnancies or medical conditions such as cardiovascular disease, pulmonary disease, kidney disease, endocrine disorders, connective tissue diseases, hepatobiliary diseases, cancer, severe depression, epilepsy, or hereditary congenital disorders were excluded from the study.

Outcome measurements: clinical information

The database contained information on the mother's blood pressure, delivery date, gestational age, mode of delivery, PTB, gestational diabetes mellitus (GDM), hypertensive disorder of pregnancy (gestational hypertension, preeclampsia, and eclampsia), neonatal information (sex, height, weight, 1' and 5' Apgar score, meconium aspiration syndrome, and fetal asphyxia), and other information (fever and anesthetic use). Delivery before 37 weeks of gestation was considered as a PTB. Hypertensive disorders of pregnancy (including gestational hypertension, preeclampsia, and preeclampsia with severe features, eclampsia) were diagnosed based on the American College of Obstetricians and Gynecologists Practice Bulletin.[15] Fetuses classified as small for gestational age (SGA) had a weight less than the 10th percentile, while those classified as intrauterine growth retardation (IUGR) had a weight less than the 5th percentile. The INTERGROWTH tables' birth weight Z-score adjusted for gestational age was used to determine cutoff weights for analyze SGA and IUGR.[16] Except for women with a high risk of developing GDM who were examined earlier in gestation (between 24 and 28 weeks of pregnancy), most pregnant women were routinely evaluated for GDM. Laboratory results supporting a plasma glucose level of at least 200 mg/dL on the glucose challenge test or at least two plasma glucose values meeting or exceeding the following values on the 100- or 75-gram oral glucose tolerance test were used to confirm the diagnosis of GDM: fasting, 95 mg/dL; 1 hour, 180 mg/dL; 2 hours, 155 mg/dL; and 3 hours, 140 mg/dL, as previously described.[17]

Exposure assessment

Questionnaires

Using a web-based questionnaire (kopen.or.kr), we examined the present status of PM that pregnant women in Korea are exposed to indoors. And we gathered data on the sociodemographic traits, way of life, living situation, and degree of fine dust danger perception of the participants. A group of housewives created this questionnaire, and by looking at characteristics like indoor/outdoor ventilation (number of windows opened), cooking and cleaning schedules, and house occupancy—all of which can lead to indoor fine dust—it was possible to assess exposure to air pollution indirectly. Each institution's iCReaT system received and stored this data, and a representative research director integrated and oversaw the data. It was also advised that each participant complete the web-based questionnaire's time-activity log. A time-activity journal was utilized to document the data, and activity data was gathered every hour. The main activity, extra activity, transportation, indoors, and outdoors were the categories used to arrange the activities. The time activities of the participants were examined to determine the patterns of indoor and outdoor residence times. The pattern that was found was utilized to determine each person's exposure to $PM_{2.5}$ and PM_{10} both indoors and outdoors.

Outdoor air pollution concentration measurement

Outdoor PM_{10} and $PM_{2.5}$, concentrations were measured from a nearby urban air measurement network based on the residences of the pregnant study participants. The Korean Ministry of Environment's Air Korea (Air Korea) webpage (https://www.airkorea.or.kr/web) has data from the urban air monitoring stations used in this investigation. Air Korea has provided online information on the country's current air pollution levels since December 2005.[18]

Indoor air pollution concentration measurement

The concentrations of PM_{10} and $PM_{2.5}$ indoors were measured in the living rooms of each participant using a device known as a fine dust meter. AirguardK® (Kweather Co., Seoul, Korea), a very small electrically powered device, contains a sensor that measures air pollution levels using a light scattering laser photometer. The temperature, humidity, sound level, carbon dioxide, volatile organic compounds, and fine particles (PM_{10} and $PM_{2.5}$) were also measured. Every trimester, the AirguardK® was installed for at least one week to monitor the indoor air quality. The measurements were posted online every minute. The measured indoor air quality data are stored on an indoor air quality monitoring platform to prevent data loss. The measurements for each trimester of pregnancy were performed for one week, and real-time measurements of the concentration values were made using IoT and information and communication technologies.

Predicting personal exposure using a time-weighted average model

The time-weighted average model states that an individual's exposure weighted to a temporal activity pattern can be used to explain their entire exposure to all microenvironments over a 24-hour period. In cases where the concentration of air pollutants cannot be determined in all local contexts, exposure to PM_{10} and $PM_{2.5}$ can be predicted using a time log and time-weighted model.[19-21] The time-weighted model is as follows:

$$C_{\text{estimates}} = (C_{\text{household}} \times T_{\text{household}}) + (C_{\text{indoors not at home}} \times T_{\text{indoors not at home}}) + (T_{\text{outdoor}} \times C_{\text{outdoor}}) \div 24 \text{ hours}$$

$C_{\text{estimates}}$: personalized estimates of PM exposure
$C_{\text{household}}$: household PM concentration
$T_{\text{household}}$: time spent at home
$C_{\text{indoors not at home}}$: average of household PM concentration per trimester of pregnancy for all participants
$T_{\text{indoors not at home}}$: time spent indoors not at home
C_{outdoor}: outdoor PM concentration
T_{outdoor}: time spent outdoor

A time-weighted average model of temporal activity patterns and the PM_{10} and $PM_{2.5}$, both indoors and outdoors, was used to represent the expected values for individual exposure.

Statistical analysis

To examine the variations in continuous and categorical variables, independent two-sample t-test, analysis of variance, and chi-square test were applied as necessary. Logistic regression analysis was performed to determine the relationships between pregnancy outcomes and PM_{10} and $PM_{2.5}$ exposure. The results were reported using odds ratios (ORs) and 95% confidence intervals (CIs). In primary analysis, PM_{10} was modeled as a continuous variable and analyzed to explore the relationship between increased PM_{10} exposure per 10 μg/m^3 and the overall risk of pregnancy complications. In secondary analysis, we explore the relationship between increased PM_{10} exposure per 10 μg/m^3 and the risk of each pregnancy complication (PTB, GDM, hypertensive diseases of pregnancy, SGA, IUGR). The same analysis was performed for $PM_{2.5}$, and the relationship between $PM_{2.5}$ exposure increasing by 5 μg/m^3 and the risk of overall pregnancy complications and each pregnancy complication was explored. The effects of maternal age, pre-pregnancy body mass index (BMI), sex of the baby, income, educational status were adjusted. SAS 9.4 was utilized to conduct the statistical analysis (SAS Institute, Cary, NC, USA). If a comparison's two-sided probability value was less than 0.05, it was deemed statistically significant.

Ethics statement

The present study protocol was reviewed and approved by the Institutional Review Board of Kangwon National University Hospital (approval No. KNUH-B-2021-04-012). Informed consent was submitted by all subjects when they were enrolled.

RESULTS

Study population characteristics

The descriptive characteristics of the pregnant women (n = 662) enrolled in the APPO study are shown in **Table 1**. Most pregnancy study participants (43.2%) were aged 35 years or older, whereas 41.4% were aged 30 and 34 years. In terms of the pregnancy method, the natural pregnancy group accounted for the largest percentage (83.1%) and the IVF pregnancy group accounted for 15.7%. The average PM_{10} and $PM_{2.5}$, were higher in the IVF pregnancy group than in the natural pregnancy group. Women a BMI between 18.5 kg/m^2 and 22.9 kg/m^2 accounted for the largest proportion (56.7%). The group whose BMI is below 18.5 kg/m^2 showed the highest PM concentration. We found that 90.8% of women delivered at full-term (≥ 37 weeks) and 9.2% of women delivered preterm (< 37 weeks). Compared to the full-term group, the premature birth group had higher PM_{10} and $PM_{2.5}$ concentrations. When PTB, gestational hypertension, preeclampsia, GDM, IUGR, and SGA were included as pregnancy complications, the pregnancy complication group accounted for 20.8% of the total participants. The pregnancy complication group had higher concentrations of PM_{10} and $PM_{2.5}$ than did the normal group. Most women were college graduates (72%); more than 19% had completed graduate school, whereas approximately 8.6% had only completed tertiary education. Women who completed only high school education had the highest concentrations of fine dust. In terms of childbirth experience, the sample included a large number of primiparous (66.2%; n = 438) and secundiparous (28.6%; n = 189) births; the fine dust levels were similar between groups.

Average concentrations of outdoor PM_{10} and $PM_{2.5}$ (μg/m^3) according to district

Fig. 2 shows the average concentration of PM_{10} and $PM_{2.5}$ by region. The areas corresponding to the residences of the study participants were divided into Gangnam in Seoul Metropolitan City, Gangbuk in Seoul Metropolitan City, South Gyeonggi province, northern Gyeonggi province, Gyeongsang province, Incheon, Gangwon province, Chungnam and Daejeon, and Daegu, and the average PM concentrations in these areas were compared (**Fig. 3**). The average

Table 1. Characteristics of study subjects classified according to PM_{10} and $PM_{2.5}$ concentrations during pregnancy

Characteristics	No. of patients (%)	PM_{10}		$PM_{2.5}$	
Age, yr (n = 662)					
20–29	102 (15.4)	100	23.44 ± 18.71	100	12.69 ± 9.68
30–34	274 (41.4)	271	21.09 ± 14.14	271	11.43 ± 7.13
≥ 35	286 (43.2)	274	21.81 ± 14.73	274	12.06 ± 7.97
Pregnancy route (n = 662)					
Natural pregnancy	550 (83.1)	535	21.30 ± 14.39	535	11.58 ± 7.40
IUI	8 (1.2)	8	15.01 ± 2.82	8	11.58 ± 6.88
IVF-ET	104 (15.7)	102	24.66 ± 18.95	102	13.55 ± 10.41
Body mass index (n = 661)					
< 18.5	54 (8.2)		23.54 ± 20.97	54	12.64 ± 10.87
18.5–22.9	377 (56.9)		20.42 ± 14.16	377	11.16 ± 7.47
≥ 23	230 (34.7)		21.97 ± 15.74	230	12.07 ± 8.32
Infant sex (n = 661)					
Male	350 (53.0)	350	21.33 ± 17.44	350	11.50 ± 8.94
Female	311 (47.0)	311	21.13 ± 12.69	311	11.73 ± 7.04
Gestational age at delivery, wk (n = 662)					
≥ 37	601 (90.8)	599	21.02 ± 18.10	599	11.50 ± 7.90
< 37	61 (9.2)	60	23.49 ± 15.08	60	12.72 ± 9.89
Pregnancy complications[a] (n = 662)					
No	524 (79.2)	521	20.29 ± 14.53	521	11.06 ± 7.54
Yes	138 (20.8)	138	24.83 ± 17.85	138	13.71 ± 9.67
Educational status (n = 660)					
Basic	56 (8.5)	56	25.24 ± 19.71	56	14.20 ± 10.92
Secondary	478 (72.2)	477	20.72 ± 15.56	477	11.29 ± 8.01
Higher	126 (19.0)	126	21.44 ± 12.00	126	11.70 ± 6.72
Income, per mon, won (n = 420)					
< 400 (×10^4)	182 (27.5)	182	22.36 ± 18.18	182	12.20 ± 9.56
400–600 (×10^4)	139 (21.0)	139	21.81 ± 16.74	139	11.94 ± 8.50
≥ 600 (×10^4)	99 (15.0)	99	21.18 ± 14.69	99	11.54 ± 7.40
Parity (n = 662)					
0	438 (66.2)	438	20.92 ± 18.89	438	11.44 ± 7.28
1	189 (28.5)	189	20.03 ± 17.96	189	12.02 ± 9.43
≥ 2	35 (5.3)	35	20.23 ± 18.12	35	11.04 ± 9.95

Values are presented as mean ± standard deviation or number (%). Numbers are presented as sample size.
PM = particulate matter, IUI = intrauterine insemination, IVF-ET = in vitro fertilization embryo transfer.
[a]Pregnancy complications include preterm birth, gestational hypertension, preeclampsia, and gestational diabetes, intrauterine growth retardation, small for gestational age.

concentrations of PM_{10} and $PM_{2.5}$ for the entire region were 21.76 and 11.89 μg/m^3, respectively. Northern Gyeonggi province has the highest levels of PM_{10} and $PM_{2.5}$, whereas Gangwon province had the lowest concentrations. On average, the concentrations of PM_{10} and $PM_{2.5}$ were as follows from highest to lowest: northern Gyeonggi province, Incheon, Gangnam of Seoul Metropolitan City, Daegu, southern Gyeonggi province, South Chungcheong province + Daejeon, Gangbuk of Seoul Metropolitan City, Gyeongsang province, and Gangwon province. Daegu, Incheon, northern Gyeonggi province, and Gangnam showed PM_{10} and $PM_{2.5}$ concentrations that were higher than the average value for the entire region.

Comparison of indoor, outdoor and individual average concentrations of PM_{10} and $PM_{2.5}$ by pregnancy quarter

Table 2 shows the indoor/outdoor measurements and individual exposure estimates for PM_{10} and $PM_{2.5}$ during various periods of pregnancy. The mean trimester specific indoor/outdoor PM_{10} exposure was 11.54/18.10 μg/m^3 for the first trimester of pregnancy, 20.78/31.72 μg/m^3 for the second trimester, and 22.15/33.73 μg/m^3 for the third trimester. The corresponding exposure estimates for indoor/outdoor $PM_{2.5}$ exposure during these respective time periods were 6.19/15.21, 11.15/17.11, and 12.51/18.90 μg/m^3, respectively. The individual exposure

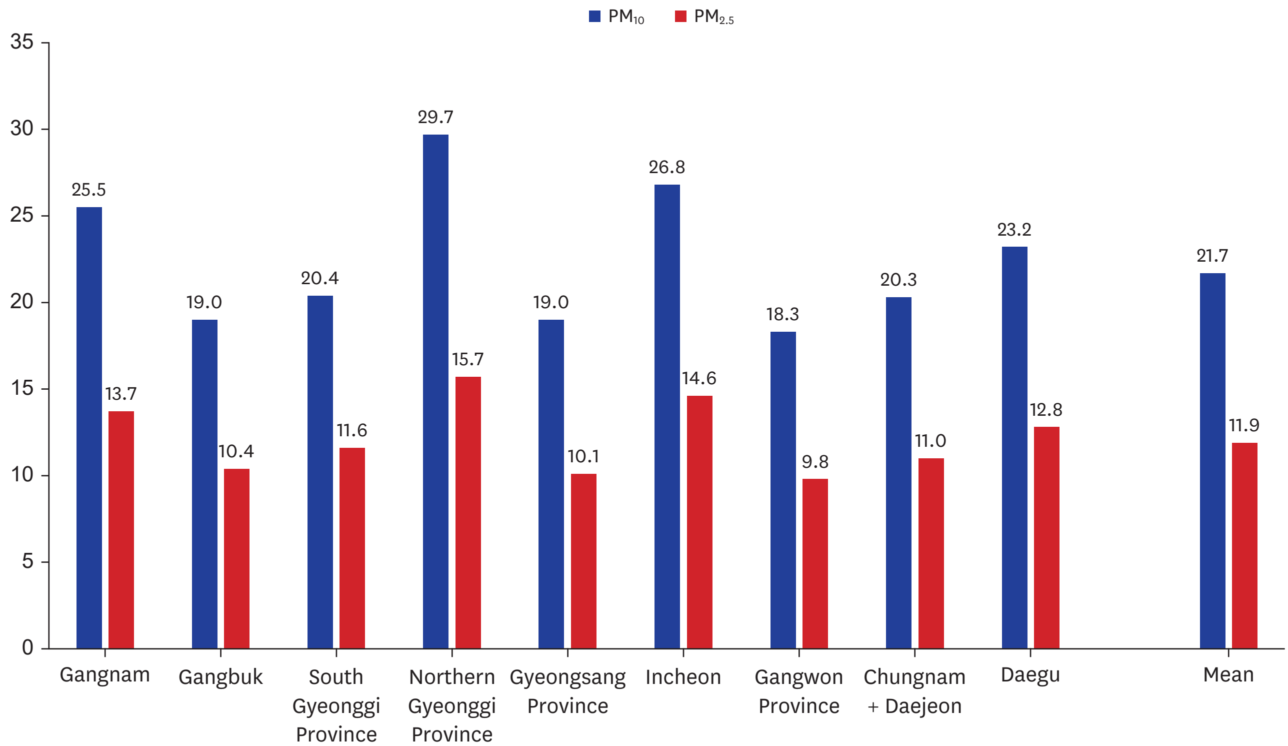

Fig. 2. Average concentrations of PM_{10}, $PM_{2.5}$ (μg/m³) according to district in South Korea.
PM = particulate matter.

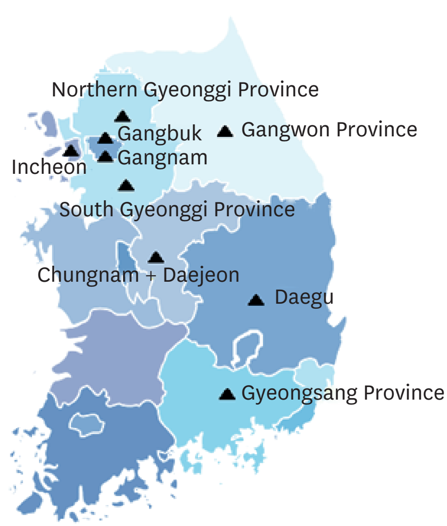

Fig. 3. Map of Korea showing locations of outdoor monitoring station.

estimates for PM_{10} and $PM_{2.5}$ were 18.77/10.01 in first trimester, 21.48/11.47 in second trimester, and 23.06/13.01 μg/m³ in third trimester. As the pregnancy progressed from the first to second and third trimesters, indoor and outdoor PM_{10} and $PM_{2.5}$ concentrations and individual exposure measurements tended to increase.

Table 2. Indoor/outdoor measurements and individual exposure estimates for PM_{10} and $PM_{2.5}$ during various periods of pregnancy

Pollutant	1st trimester		2nd trimester		3rd trimester	
PM_{10}, μg/m³						
Indoor	384	11.54 ± 19.63	640	20.78 ± 25.06	594	22.15 ± 24.18
Outdoor	384	18.10 ± 16.66	642	31.72 ± 14.72	599	33.73 ± 13.21
Individual	241	18.77 ± 18.67	621	21.48 ± 19.6	579	23.06 ± 18.97
$PM_{2.5}$, μg/m³						
Indoor	384	6.19 ± 10.42	640	11.15 ± 13.33	594	12.51 ± 12.41
Outdoor	249	15.21 ± 7.94	642	17.11 ± 8.08	596	18.90 ± 8.18
Individual	243	10.01 ± 9.91	626	11.47 ± 10.44	579	13.01 ± 9.59

Values are presented as mean ± standard deviation or number. Numbers are presented as sample size.
PM = particulate matter.

Association between pregnancy complications and individual estimates of PM_{10}

Table 3 displays the findings for the correlations between total pregnancy complications and an increase in PM_{10} exposure of 10 μg/m³, based on exposure level stratification. When pregnancy complications were defined as PTB, gestational hypertension, preeclampsia, GDM, IUGR, and SGA, the logistic regression results indicated a positive association between PM_{10} exposure and the likelihood of pregnancy complications. Multiple regression models revealed similar results. When age, pre-pregnancy BMI, newborn sex, monthly income, and education level (model 3) were considered in the PM exposure group, the adjusted odds of developing a pregnancy complication were 1.27 (95% CI, 1.09–1.48) for the entire pregnancy, 1.40 (95% CI, 1.04–1.88) for the first trimester, 1.29 (95% CI, 1.11–1.51) for the second trimester, and 1.20 (95% CI, 1.03–1.39) for the third trimester. Analysis of each pregnancy complication, particularly PTB, demonstrated a significant association between individual PM_{10} exposure and PTB during the second trimester and entire pregnancy, even after adjusting for confounding factors (**Table 4**). Similarly, the risk of developing GDM was significantly increased in groups with individual PM_{10} exposure in the second trimester of pregnancy. There was no significant association between individual PM_{10} exposure and IUGR (**Supplementary Table 2**). In contrast, individual PM_{10} exposure in the first trimester of pregnancy considerably raised the risk of SGA infants. The same results were observed after adjusting for age, pre-pregnancy BMI, newborn sex, monthly income, and education level. When a subgroup analysis was performed on primiparous, PM_{10} exposure during the first trimester of pregnancy significantly increased the risk of SGA infants. PM_{10} exposure during the second trimester of pregnancy tended to increase the risk of GDM, but this was not statistically significant (**Table 5**).

Table 3. Adjusted ORs and 95% CIs of pregnancy complications for each 10 μg/m³ increment in individual PM_{10} exposure during trimesters and the entire pregnancy

PM_{10}	Pregnancy complication[a]							
	Crude OR (95% CI)	*P* value	Model 1: adjusted OR[b] (95% CI)	*P* value	Model 2: adjusted OR[c] (95% CI)	*P* value	Model 3: adjusted OR[d] (95% CI)	*P* value
An increase in PM_{10} of 10 μg/m³								
1st trimester	1.40 (1.06–1.85)	0.017	1.38 (1.04–1.83)	0.025	1.39 (1.04–1.87)	0.025	1.40 (1.04–1.88)	0.027
2nd trimester	1.27 (1.10–1.47)	0.001	1.27 (1.10–1.47)	0.001	1.27 (1.09–1.47)	0.001	1.29 (1.11–1.51)	0.001
3rd trimester	1.20 (1.03–1.40)	0.017	1.20 (1.03–1.39)	0.021	1.20 (1.03–1.39)	0.021	1.20 (1.03–1.39)	0.021
Entire pregnancy	1.25 (1.07–1.45)	0.004	1.24 (1.07–1.44)	0.005	1.24 (1.07–1.45)	0.005	1.27 (1.09–1.48)	0.002

OR = odds ratio, CI = confidence interval, PM = particulate matter, BMI = body mass index.
[a]Pregnancy complications include preterm birth, gestational hypertension, preeclampsia, and gestational diabetes, intrauterine growth retardation, small for gestational age; [b]Logistic regression model, adjusted for maternal age and pre-pregnancy BMI; [c]Logistic regression model, adjusted for maternal age, pre-pregnancy BMI, sex of the baby; [d]Logistic regression model, adjusted for maternal age, pre-pregnancy BMI, sex of the baby, income, educational status.

Table 4. Adjusted ORs and 95% CIs of PTB, GDM, and SGA for each 10 μg/m³ increment in individual PM_{10} exposure during trimesters and the entire pregnancy

PM_{10}	PTB				GDM				SGA			
	Crude OR (95% CI)	*P* value	Adjusted OR[a] (95% CI)	*P* value	Crude OR (95% CI)	*P* value	Adjusted OR[a] (95% CI)	*P* value	Crude OR (95% CI)	*P* value	Adjusted OR[a] (95% CI)	*P* value
An increase in PM_{10} of 10 μg/m³												
1st trimester	1.15 (0.78–1.69)	0.491	1.13 (0.74–1.71)	0.572	1.15 (0.72–1.83)	0.562	1.04 (0.63–1.73)	0.874	1.75 (1.06–2.88)	0.027	1.96 (1.08–3.56)	0.026
2nd trimester	1.23 (1.00–1.50)	0.046	1.24 (1.01–1.52)	0.041	1.24 (1.02–1.52)	0.032	1.30 (1.04–1.61)	0.020	1.16 (0.85–1.53)	0.365	1.15 (0.83–1.61)	0.394
3rd trimester	1.12 (0.90–1.40)	0.309	1.11 (0.89–1.39)	0.339	1.22 (0.99–1.51)	0.061	1.20 (0.96–1.49)	0.109	1.18 (0.89–1.58)	0.256	1.18 (0.88–1.59)	0.265
Entire pregnancy	1.24 (1.01–1.53)	0.039	1.27 (1.03–1.57)	0.025	1.19 (0.97–1.47)	0.095	1.20 (0.96–1.49)	0.109	1.30 (0.97–1.75)	0.081	1.32 (0.97–1.80)	0.076

OR = odds ratio, CI = confidence interval, PTB = preterm birth, GDM = gestational diabetes mellitus, SGA = small for gestational age, PM = particulate matter.
[a]Logistic regression model, adjusted for maternal age, pre-pregnancy body mass index, sex of the baby, income, educational status.

Table 5. Adjusted ORs and 95% CIs of PTB, GDM, and SGA for each 10 μg/m³ increment in individual PM_{10} exposure during trimesters and the entire pregnancy according to the primiparous

PM_{10}	PTB				GDM				SGA			
	Crude OR (95% CI)	*P* value	Adjusted OR[a] (95% CI)	*P* value	Crude OR (95% CI)	*P* value	Adjusted OR[a] (95% CI)	*P* value	Crude OR (95% CI)	*P* value	Adjusted OR[a] (95% CI)	*P* value
An increase in PM_{10} of 10 μg/m³												
1st trimester	1.30 (0.82–2.05)	0.259	1.29 (0.70–2.39)	0.408	1.46 (0.82–2.60)	0.204	1.08 (0.43–2.73)	0.874	1.48 (0.78–2.83)	0.230	2.92 (1.01–8.44)	0.048
2nd trimester	1.04 (0.79–1.36)	0.794	1.14 (0.84–1.53)	0.398	1.22 (0.92–1.62)	0.172	1.38 (0.97–1.96)	0.074	1.01 (0.68–1.52)	0.948	0.92 (0.54–1.55)	0.743
3rd trimester	1.08 (0.82–1.42)	0.597	1.17 (0.86–1.60)	0.315	1.04 (0.75–1.43)	0.822	0.92 (0.64–1.33)	0.662	1.23 (0.89–1.70)	0.210	1.27 (0.86–1.87)	0.237
Entire pregnancy	1.14 (0.87–1.50)	0.354	1.23 (0.90–1.67)	0.192	1.09 (0.79–1.50)	0.599	1.03 (0.72–1.48)	0.873	1.27 (0.89–1.82)	0.192	1.42 (0.92–2.20)	0.112

OR = odds ratio, CI = confidence interval, PTB = preterm birth, GDM = gestational diabetes mellitus, SGA = small for gestational age, PM = particulate matter.
[a]Logistic regression model, adjusted for maternal age, pre-pregnancy body mass index, sex of the baby, income, educational status.

Association between pregnancy complications and individual estimates of $PM_{2.5}$

Table 6 displays the findings for the correlations between total pregnancy complications and an increase in $PM_{2.5}$ exposure of 5 μg/m³, based on exposure level stratification. After adjusting for important variables, the OR of pregnancy complications significantly increased in the group with $PM_{2.5}$ exposure, except for in the third trimester. Analysis of each pregnancy complication showed that the risk of developing GDM was significantly increased in groups with individual $PM_{2.5}$ exposure in the second trimester and throughout entire pregnancy. This trend was observed even after correcting for various confounding variables. Similar to the results for PM_{10} exposure, the OR of SGA infants significantly increased in the first trimester of pregnancy following $PM_{2.5}$ exposure (**Table 7**). When a subgroup analysis was performed on primiparous, $PM_{2.5}$ exposure during the second trimester of pregnancy significantly increased

Table 6. Adjusted ORs and 95% CIs of pregnancy complications for each 5 μg/m³ increment in individual $PM_{2.5}$ exposure during trimesters and the entire pregnancy

$PM_{2.5}$	Pregnancy complication[a]							
	Crude OR (95% CI)	*P* value	Model 1: adjusted OR[b] (95% CI)	*P* value	Model 2: adjusted OR[c] (95% CI)	*P* value	Model 3: adjusted OR[d] (95% CI)	*P* value
An increase in $PM_{2.5}$ of 5 μg/m³								
1st trimester	1.18 (1.01–1.37)	0.034	1.17 (1.01–1.36)	0.038	1.19 (1.02–1.38)	0.026	1.19 (1.02–1.38)	0.029
2nd trimester	1.13 (1.04–1.23)	0.004	1.13 (1.04–1.23)	0.004	1.14 (1.05–1.25)	0.002	1.13 (1.04–1.23)	0.004
3rd trimester	1.10 (1.00–1.21)	0.054	1.09 (0.99–1.21)	0.065	1.09 (0.99–1.20)	0.076	1.09 (0.99–1.20)	0.069
Entire pregnancy	1.18 (1.06–1.31)	0.002	1.18 (1.06–1.31)	0.002	1.19 (1.07–1.32)	0.001	1.19 (1.18–1.06)	0.002

OR = odds ratio, CI = confidence interval, PM = particulate matter.
[a]Pregnancy complications include preterm birth, gestational hypertension, preeclampsia, and gestational diabetes, intrauterine growth retardation, small for gestational age; [b]Logistic regression model, adjusted for maternal age and pre-pregnancy BMI; [c]Logistic regression model, adjusted for maternal age, pre-pregnancy BMI, sex of the baby; [d]Logistic regression model, adjusted for maternal age, pre-pregnancy BMI, sex of the baby, income, educational status.

Table 7. Adjusted ORs and 95% CIs of PTB, GDM, and SGA for each 5 μg/m³ increment in individual $PM_{2.5}$ exposure during trimesters and the entire pregnancy

$PM_{2.5}$	PTB				GDM				SGA			
	Crude OR (95% CI)	*P* value	Adjusted OR[a] (95% CI)	*P* value	Crude OR (95% CI)	*P* value	Adjusted OR[a] (95% CI)	*P* value	Crude OR (95% CI)	*P* value	Adjusted OR[a] (95% CI)	*P* value
An increase in $PM_{2.5}$ of 5 μg/m³												
1st trimester	1.11 (0.95–1.28)	0.190	1.10 (0.95–1.28)	0.213	1.02 (0.80–1.31)	0.880	0.98 (0.75–1.28)	0.892	1.20 (1.02–1.42)	0.027	1.25 (1.03–1.51)	0.026
2nd trimester	1.10 (1.00–1.23)	0.062	1.10 (0.99–1.22)	0.080	1.12 (1.02–1.24)	0.022	1.15 (1.03–1.28)	0.015	1.06 (0.89–1.25)	0.518	1.07 (0.89–1.28)	0.490
3rd trimester	1.08 (0.94–1.23)	0.295	1.08 (0.94–1.24)	0.288	1.15 (1.01–1.30)	0.030	1.12 (0.98–1.27)	0.095	1.09 (0.91–1.30)	0.352	1.08 (0.90–1.31)	0.393
Entire pregnancy	1.14 (0.99–1.30)	0.062	1.14 (0.99–1.30)	0.062	1.16 (1.02–1.32)	0.025	1.15 (1.00–1.33)	0.050	1.15 (0.96–1.38)	0.139	1.17 (0.96–1.42)	0.111

OR = odds ratio, CI = confidence interval, PTB = preterm birth, GDM = gestational diabetes mellitus, SGA = small for gestational age, PM = particulate matter.
[a]Logistic regression model, adjusted for maternal age, pre-pregnancy body mass index, sex of the baby, income, educational status.

Table 8. Adjusted ORs and 95% CIs of PTB, GDM, and SGA for each 5 μg/m³ increment in individual $PM_{2.5}$ exposure during trimesters and the entire pregnancy according to the of primiparous

$PM_{2.5}$	PTB				GDM				SGA			
	Crude OR (95% CI)	*P* value	Adjusted OR[a] (95% CI)	*P* value	Crude OR (95% CI)	*P* value	Adjusted OR[a] (95% CI)	*P* value	Crude OR (95% CI)	*P* value	Adjusted OR[a] (95% CI)	*P* value
An increase in $PM_{2.5}$ of 5 μg/m³												
1st trimester	1.26 (0.97–1.63)	0.085	1.29 (0.95–1.75)	0.110	1.10 (0.82–1.47)	0.520	0.97 (0.66–1.44)	0.883	1.14 (0.86–1.51)	0.373	1.3 (0.92–1.85)	0.138
2nd trimester	1.00 (0.83–1.21)	0.998	1.05 (0.88–1.27)	0.582	1.21 (1.05–1.40)	0.011	1.30 (1.08–1.56)	0.005	0.99 (0.74–1.31)	0.929	0.97 (0.68–1.37)	0.848
3rd trimester	1.06 (0.87–1.28)	0.568	1.11 (0.90–1.36)	0.322	1.06 (0.85–1.31)	0.632	0.92 (0.73–1.18)	0.518	1.16 (0.94–1.44)	0.164	1.22 (0.95–1.56)	0.128
Entire pregnancy	1.07 (0.87–1.31)	0.554	1.10 (0.89–1.38)	0.380	1.18 (0.97–1.45)	0.102	1.11 (0.88–1.41)	0.369	1.14 (0.88–1.48)	0.336	1.21 (0.89–1.65)	0.220

OR = odds ratio, CI = confidence interval, PTB = preterm birth, GDM = gestational diabetes mellitus, SGA = small for gestational age, PM = particulate matter.
[a]Logistic regression model, adjusted for maternal age, pre-pregnancy body mass index, sex of the baby, income, educational status.

the risk of GDM. $PM_{2.5}$ exposure during the first trimester of pregnancy tended to increase the risk of SGA infants, but this was not statistically significant (**Table 8**).

DISCUSSION

This study aimed to determine the relationship between unfavorable pregnancy outcomes and an individual exposure levels to PM_{10} and $PM_{2.5}$ during pregnancy. The average daily individual PM_{10} and $PM_{2.5}$ concentrations to which pregnant women were exposed during the study period were 21.76 and 11.89 μg/m3, respectively. These values exceed the 2021 WHO air quality guidelines of 15 μg/m³ for PM_{10} and 5 μg/m³ for $PM_{2.5}$.[22] We found that exposure to high PM_{10} and $PM_{2.5}$ concentrations during each trimester and entire pregnancy increased the overall risk of pregnancy complications. Additionally, exposure to high levels of PM_{10} and $PM_{2.5}$ during the second trimester and entire pregnancy, respectively, significantly elevated the risk of PTB and GDM, whereas exposure to high levels of PM_{10} and $PM_{2.5}$ during the first trimester of pregnancy considerably increased the risk of SGA, regardless of adjustment for potential confounders.

These findings are consistent with those of past research that related exposure to prenatal air pollution to PTB,[23-26] GDM,[27-29] and SGA.[30-36] We found no significant association between air pollutants and hypertensive disease of pregnancy (**Supplementary Tables 2** and **3**), although previous studies indicated that PM_{10} and $PM_{2.5}$ can increase the risk of this disease.[37-39] The discrepancy observed between our findings and prior research could perhaps be attributed to the limited sample size or differences in exposure assessments, air pollutant classification, population type, and study area, highlighting the need for additional research.

Varying findings on the association between ambient PM_{10} and PTB risk have been reported. A prospective birth cohort study in Wuhan, China showed that for every 5 μg/m^3 increase in PM_{10} exposure during pregnancy, the risk of PTB increased by nearly 2%.[23] According to a study conducted in Australia, the risk of PTB is increased by 15% for every 4.5 μg/m^3 increase in PM_{10} during the first trimester.[24] In Uruguay, researchers found that the PTB risk increased by 10% for every 10 μg/m^3 increase in PM_{10} during the third trimester.[22-25] According to a Korean study, during the first or third trimester, the risk of PTB increased by 7% for every 16.53 μg/m^3 increase in PM_{10}.[26] We found that every 10 μg/m^3 increase in the average daily PM_{10} concentration exposure during the second trimester had the strongest impact on PTB with a significantly increased risk of 27% (95% CI, 1.01–1.52), followed by exposure during the entire pregnancy with the risk of 24% (95% CI, 1.03–1.57). However, in a subgroup analysis conducted on nulliparous mothers, the effect on PTB was different from the results seen in the overall group. As shown in several previous studies, the degree of impact of PM on PTB is thought to be different in parous and nulliparous women.[23-25] Additionally, among the many risk factors for PTB, important risk factors such as previous history of premature birth, preterm labor are thought to have a greater impact on premature birth. In this regard, it is believed that more large-scale research is needed.

Our results showed that the risk of GDM increased when PM_{10} and $PM_{2.5}$ levels were high in the second trimester. This result agrees with those of other studies suggesting that $PM_{2.5}$ impacts glucose homeostasis only during the second trimester of pregnancy.[40] Fleisch et al.[41] also found that the risk of impaired glucose tolerance was 2.63-fold (95% CI, 1.15–6.01) greater in women exposed to $PM_{2.5}$ levels higher than in the first quartile (12.8–15.9 g/m^3) during the second trimester. In another study, Fleisch et al.[42] found that in the second trimester, women under the age of 20 years had 1.36 greater odds of developing GDM than did older women (95% CI, 1.08–1.70).[40] Similar results were observed in studies conducted in the northeastern United States, which revealed a positive correlation with second trimester $PM_{2.5}$ exposure.[28,42] However, in Taiwan, GDM are strongly correlated with $PM_{2.5}$ in both the first and second trimesters.[29] It remains unclear whether these variations in timing were due to real variations in the etiology of the illness rather than random fluctuations between studies, a lack of knowledge regarding the timing of GDM screening or diagnosis, variations in local medical practices, or other variations between studies.

Our results showed that the risk of SGA significantly increased when mothers were exposed to PM_{10} and $PM_{2.5}$ during the first trimester of pregnancy. During the first trimester of pregnancy, the risk of SGA increased by 96% for every 10 g/m^3 increase in exposure to PM_{10} and by 25% for every 5 g/m^3 increase in exposure to $PM_{2.5}$. Several studies have been performed to evaluate how PM_{10} affects SGA but have shown inconsistent results. Although numerous studies showed that exposure to PM_{10} during specific trimesters increases the risk of SGA,[24,30,32,33] some investigations found no correlation between SGA and PM_{10}.[43-47] In contrast, several studies demonstrated the negative effects of $PM_{2.5}$, as reported in the current study,[33,34,35,48] but did not agree that the effects were specific to each trimester. Maternal $PM_{2.5}$ exposure dramatically increases the incidence of term low birth weight from 1% to 9%.[49,50] Studies conducted in China reported higher rates, with the risk of term low birth weight ranging from 22% to 38%.[51,52] The first trimester,[53] second trimester,[33,47] third trimester,[34,53] and entire pregnancy period[36] have been described as exposure windows for $PM_{2.5}$ that influence the risk of SGA.

The discrepancies between our findings and those of earlier research could have multiple causes. First, as mentioned above, most research on the relationship between air pollution and pregnancy outcomes has been conducted in developed regions, and the lifestyles of the study populations, including their dietary habits, cooking techniques, and access to healthcare, may not be the same as those of women in South Korea. Second, we measured the mean exposure concentrations using individual measuring devices inside the home. In several studies, more precise methods were applied in residential areas to estimate individual exposure, leading to variations in exposure assessment between studies.[34,47] Third, air pollutants at the same concentration may have different compositions because of geographical heterogeneity, which may lead to drastically varying exposure levels.[54]

We found a link between exposure to PM_{10} and $PM_{2.5}$ and birth outcomes, although the precise biological mechanisms underlying these relationships are unclear. Researchers have suggested that pollutants can increase the risk of unfavorable pregnancy outcomes through processes related to inflammation, oxidative stress, endocrine disruption, impaired oxygen transport across the placenta, respiratory epithelial injury, and genetic and epigenetic changes.[55,56] Exposure to $PM_{2.5}$, which is linked to undesirable birth outcomes, is associated with decreased placental DNA methylation and increased intrauterine inflammation, both of which are related to undesirable birth outcomes.[57-59]

This study had a number of restrictions. First, we had a limited sample size. However, given that this study is ongoing, additional data will be collected, and studies that have individually measured fine dust concentrations in houses involved a large number of participants. Second, because of a lack of data, we did not assess other contaminants such as O_3, NO_x, CO, and SO_x. And in the case of nulliparous mothers, there was insufficient information about the outcome of previous pregnancies, making it difficult to completely exclude its influence on the study results. Third, the exposure estimations in this study did not account for other exposure concentrations throughout the participants' homes and various activity spaces; only the concentration in the area of the fine-dust measuring device was considered. Despite these limitations, we prospectively examined how pregnant South Korean women are affected by PM at an individual level.

Exposure to high PM_{10} and $PM_{2.5}$ concentrations during pregnancy increased the overall risk of pregnancy complications. Additionally, exposure to high levels of PM_{10} and $PM_{2.5}$ during the second trimester and entire pregnancy, respectively, significantly elevated the risk of PTB and GDM, whereas exposure to high levels of PM_{10} and $PM_{2.5}$ during the first trimester of pregnancy considerably increased the risk of SGA. Our findings highlight the need to measure individual particulate levels during each trimester of pregnancy and the importance of managing air quality in residential environments to prevent specific pregnancy complications. The findings of the APPO study will aid in the development of health management plans to protect expectant mothers from air pollution. More extensive research is required to ascertain the degree to which specific baseline pollutants, like NOx, SO2, black carbon, ozone, and pollutant combinations, in addition to PM_{10} and $PM_{2.5,}$ are causally linked to poor pregnancy outcomes, as well as to investigate their mechanisms of action.

https://doi.org/10.3346/jkms.2024.39.e131

ACKNOWLEDGMENTS

We are grateful to the APPO participants and staff at Kangwon National University Hospital, Yonsei University Hospital, Ewha Womans University Mokdong Hospital, Ewha Womans University Seoul Hospital, Korea University Guro Hospital, Keimyung University Dongsan Medical Center, and Ulsan University Hospital.

SUPPLEMENTARY MATERIALS

Supplementary Table 1

Fine dust concentration according to birth season

Supplementary Table 2

Adjusted ORs and 95% CIs of gestational HTN and IUGR for each 10 μg/m^3 increment in individual PM_{10} exposure during trimesters and the entire pregnancy

Supplementary Table 3

Adjusted ORs and 95% CIs of gestational HTN and IUGR for each 5 μg/m^3 increment in individual $PM_{2.5}$ exposure during trimesters and the entire pregnancy

Supplementary Table 4

Adjusted ORs and 95% CIs of PTB, GDM, and SGA for each 10 μg/m^3 and 5 μg/m^3 increment in individual PM_{10}, $PM_{2.5}$ exposure during trimesters and the entire pregnancy according to regions

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