Upper respiratory infection and seasonal variations in the occurrence of in South Korea

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Abstract

The aim of this study was to examine the effect of seasonal changes on the incidence of preeclampsia in Asian regions and populations, and to evaluate the relationship between upper respiratory infection during pregnancy and the development of preeclampsia. This was a cohort study of women who delivered singletons between 2012 and 2018 in South Korea. A total of 548080 first singleton births were included for analysis. A total of 9,311 patients (1.70%) were diagnosed with preeclampsia. Multivariate analysis showed that older age (≥ 30 years old), low income, residing in the southern area of Korea, history of smoking, history of heavy drinking, higher body mass index, hypertension, or diabetes mellitus were risk factors for PE. Univariate analysis showed that upper respiratory infection was associated with the incidence of preeclampsia ($P=0.0294$). However, this association was not maintained in the multivariate analysis (aOR, 1.01; 95% CI, 0.95 - 1.07). After adjusting for confounding variables, the occurrence of PE was the highest in December (aOR, 1.21; 95%CI, 1.10-1.34) and lowest in July and August. This study demonstrated that there are seasonal variations in the occurrence of preeclampsia in Korea. Moreover, upper respiratory infection may be associated with the development of PE.

1. Introduction

Preeclampsia (PE) is a disorder of pregnancy affecting 5–7% of all pregnant women and is characterized by new-onset hypertension (HTN) and proteinuria after 20 weeks of gestation. PE adversely affects various organs, such as the liver, kidney, brain, and lungs. In addition, severe PE can lead to multiple organ dysfunction, which is responsible for over 70,000 maternal deaths and 500,000 fetal deaths every year¹. The definitive treatment for PE is delivery of the placenta and the baby. However, despite the serious adverse effects of PE on maternal and fetal health, its cause and pathogenesis have yet to be elucidated.

Several researchers have indicated that environmental factors, such as the socioeconomic status of the mother, maternal obesity, and cigarette smoking during pregnancy, have potential roles in the development of PE^{2–4}. In addition to various maternal demographic factors, seasonal changes are known risk factors for the development of PE. In Norway, the prevalence of PE is the highest in the winter months and the lowest in August⁵. Similarly, in Sweden, the prevalence of PE is lower in summer than in winter⁶. The prevalence of PE increases during the dry season and decreases during the rainy season in Zimbabwe⁷. In addition to seasonal variations, ethnic differences associated with the monthly variations of PE incidence have been reported⁸. However, although previous studies on PE have been conducted in various regions and populations, there is little data on the incidence of PE in Asian populations and regions.

The cause of seasonal variations in the occurrence of PE remains unknown. In our previous study, we conducted transcriptome analysis using cell-free RNA in amniotic fluid extracted from patients predicted to develop PE⁹. KEGG pathway analysis showed that various immune pathways, such as those of asthma, antigen processing and presentation, and *Staphylococcus aureus* infection, were dysregulated in patients with PE. Generally, seasonal variations are observed for common cold or upper respiratory infection (URI). Considering the findings of our previous study and the seasonal variations in the occurrence of PE, we hypothesized that URI during pregnancy affects the development of PE. Therefore, we performed this study to examine the effect of seasonal changes on the development of PE in Asian regions and populations, and to evaluate the relationship between URI during pregnancy and the development of PE.

2. Results

A total of 2,354,219 births were recorded in Korea between 2012 and 2018 (Fig. 1). Of these, 1,282,507 were the first deliveries of the mothers. We excluded twin pregnancies (N=16,988), women who did not undergo National Health Screening Examination (NHSE) within 2 years before their delivery (N=696,562), those with missing variables (N=20,813)

in the NHSE, and those who were covered by medical aid (N=694). Therefore, a total of 548,080 singleton deliveries recorded between 2012 and 2018 were included in this study, and PE was diagnosed in 9,311 (1.70%) women.

The maternal characteristics of the participants are described in Table 1. In univariate the analysis, age, income, residential area, smoking, physical activity, body mass index (BMI), HTN, diabetes mellitus (DM), and URI were associated with the incidence of PE. In the multivariate logistic regression analysis, all demographic variables were adjusted as possible confounders. The results showed that older age (≥ 30 years old), low income, residing in the southern area of Korea, history of smoking, history of heavy drinking, higher BMI, HTN, and DM were risk factors for PE. In addition, physical activity was associated with the incidence of PE, whereas heavy drinking was not observed in the univariate analysis. However, heavy drinking was associated with the incidence of PE in the multivariate analysis, whereas physical activity was not. URI was associated with the development of PE in the univariate analysis ($P = 0.0294$); however, multivariate analysis showed that there was no relationship between URI and the prevalence of PE (aOR, 1.01; 95% CI, 0.95-1.07; $P = 0.7806$). Women aged ≥ 40 years, who were obese, had a history of HTN, or had DM had substantially higher risks for PE ([age ≥ 40 years old: aOR, 1.56; 95% CI, 1.42-1.72] [obesity: aOR, 3.52; 95% CI, 3.35-3.69] [HTN: aOR, 5.67; 95% CI, 5.16-6.24] [DM: aOR, 2.56; 95% CI, 2.13-3.08]).

Table 1
Demographic data of the participants

Variables	Total	Preeclampsia				
	N (%)	No (N, %)	Yes (N, %)	<i>P</i>	aOR (95% CI)	<i>P</i>
Age at the time of delivery				<0.0001		
Under 25	12,497 (2.3)	12,282 (98.3)	215 (1.7)		1.12 (0.97 – 1.29)	0.1221
25-29	138,807 (25.3)	136,839 (98.6)	1,968 (1.4)		1.0	
30-34	290,598 (53.0)	286,117 (98.5)	4,481 (1.5)		1.07 (1.01 – 1.12)	0.023
35-39	85,663 (15.6)	83,653 (97.7)	2,010 (2.4)		1.45 (1.36 – 1.54)	<0.0001
40 or older	20,515 (3.7)	19,878 (96.9)	67 (3.1)		1.56 (1.42 – 1.72)	<0.0001
Income status				<0.0001		
1st quartile	65,671 (12.0)	64,394 (98.1)	1,277 (1.9)		1.0	
2nd quartile	161,029 (29.4)	158,051 (98.2)	2,978 (1.9)		1.01 (0.95 – 1.08)	0.7072
3rd quartile	226,536 (41.3)	222,926 (98.4)	3,610 (1.6)		0.93 (0.87 – 0.99)	0.0271
4th quartile	94,844 (17.3)	93,398 (98.5)	1,446 (1.5)		0.90 (0.83 – 0.97)	0.0065
Residential area				0.0002		
Central	362,046 (66.1)	356,064 (98.4)	5,982 (1.7)		1.00	
Southern	186,034 (33.9)	182,705 (98.2)	3,329 (1.8)		1.08 (1.03 – 1.12)	0.0010
Smoker				<0.0001		
No	530,431 (96.8)	521,550 (98.3)	8,881 (1.7)		1.00	
Yes	17,649 (3.2)	17,219 (97.6)	430 (2.4)		1.24 (1.12 – 1.38)	<0.0001
Heavy drinker				0.1092		
No	445,903 (81.4)	438,388 (98.3)	7,515 (1.7)		1.00	
Yes	102,177 (18.6)	100,381 (98.2)	1,796 (1.8)		1.07 (1.01 – 1.13)	0.0134
Physically active				0.0445		

BMI, body mass index; HTN, hypertension; GDM, gestational diabetes mellitus; URI, common cold.

Variables	Total	Preeclampsia			
No	344,318 (62.8)	338,562 (98.3)	5,756 (1.7)	1.00 (0.96 – 1.04)	0.9669
Yes	203,762 (37.2)	200,207 (98.3)	3,555 (1.7)	1.00	
BMI				<0.0001	
Underweight	69,326 (12.7)	68,760 (99.2)	566 (0.8)	0.70 (0.64 – 0.76)	<0.0001
Normal	337,373 (61.6)	333,331 (98.8)	4,042 (1.2)	1.00	
Overweight	70,968 (13.0)	69,511 (98.0)	1,457 (2.1)	1.66 (1.56 – 1.76)	<0.0001
Obese	70,413 (12.9)	67,167 (95.4)	3,246 (4.6)	3.52 (3.35 – 3.69)	<0.0001
History of HTN				<0.0001	
No	543,382 (99.1)	534,656 (98.4)	8,726 (1.6)	1.00	
Yes	4,698 (0.9)	4,113 (87.6)	585 (12.5)	5.67 (5.16 – 6.24)	<0.0001
History of DM				<0.0001	
No	461,062 (84.1)	453,727 (98.4)	7,335 (1.6)	1.00	
Yes	1,355 (0.3)	1,193 (88.0)	162 (12.0)	2.56 (2.13 – 3.08)	<0.0001
GDM	85,663 (15.6)	83,849 (97.9)	1,814 (2.1)		<0.0001
URI during pregnancy				0.0294	
No	476,485 (86.9)	468,461 (98.3)	8,024 (1.7)	1.00	0.7806
Yes	71595 (13.1)	70,308 (98.2)	1,287 (1.8)	1.01 (0.95 - 1.07)	
BMI, body mass index; HTN, hypertension; GDM, gestational diabetes mellitus; URI, common cold.					

The prevalence of PE was the highest (1.88%) in December and lowest (1.56%) in July and August (Table 2, Fig. 2). After adjusting for confounding variables, the occurrence of PE was still the highest in December (aOR, 1.21; 95% CI, 1.10-1.34) and lowest in July and August. Fig. 3 shows the monthly variations in the occurrence of PE. When stratified according to the season of delivery before adjusting for confounding variables, the prevalence of PE was the lowest in the summer, increased gradually in the fall, and was highest in the spring. Adjustment for demographic variables did not alter seasonal trends in the development of PE. The prevalence ratios of PE were as follows: winter, 1.10 (95% CI, 1.04-1.17); spring, 1.12 (95% CI, 1.06-1.19); and fall, 1.06 (95% CI, 1.00-1.13). The prevalence of PE in spring and winter did not differ.

Table 2

Prevalence rates and ratios of preeclampsia according to the month of delivery, with August as the reference month

Month of delivery	Total N (%)	Preeclampsia		Prevalence	P	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
		No (N, %)	Yes (N, %)						
January	46,397 (8.5)	45,616 (98.3)	781 (1.7)	1.68	0.0002	1.08 (0.98 – 1.20)	0.1257	1.03 (0.93 – 1.14)	0.5640
February	41,351 (7.5)	40,621 (98.2)	730 (1.8)	1.77		1.14 (1.02 – 1.26)	0.0149	1.10 (1.00 – 1.22)	0.0609
March	45,053(8.2)	44,235 (98.2)	818 (1.8)	1.82		1.17 (1.06 – 1.29)	0.0022	1.15 (1.04 – 1.27)	0.0064
April	42,954 (7.8)	42,172 (98.2)	782 (1.8)	1.82		1.17 (1.06 - 1.30)	0.0020	1.17 (1.06 – 1.30)	0.0020
May	42,194 (7.7)	41,489 (98.3)	705 (1.7)	1.67		1.07 (0.97 – 1.19)	0.1775	1.08 (0.97 – 1.19)	0.1656
June	41,859 (7.6)	41,162 (98.3)	697 (1.7)	1.67		1.07 (0.97 – 1.19)	0.2012	1.06 (0.96 – 1.18)	0.2405
July	45,716 (8.3)	45,004 (98.4)	712 (1.6)	1.56		1.00 (0.90 – 1.11)	0.9927	0.98 (0.88 – 1.09)	0.6766
August	49,160 (9.0)	48,394 (98.4)	766 (1.6)	1.56		1.00		1.00	
September	51,203 (9.3)	50,402 (98.4)	801 (1.6)	1.56		1.00 (0.91 – 1.11)	0.9371	1.01 (0.91 – 1.12)	0.8553
October	49,505 (9.0)	48,664 (98.3)	841 (1.7)	1.70		1.09 (0.99 – 1.21)	0.0811	1.10 (0.99 – 1.21)	0.0670
November	46,683 (8.5)	45,869 (98.3)	814 (1.7)	1.74		1.12 (1.01 – 1.24)	0.0243	1.13 (1.02 – 1.25)	0.0185
December	46,005 (8.4)	45,141 (98.1)	864 (1.9)	1.88		1.21 (1.10 – 1.33)	0.0001	1.21 (1.10 – 1.34)	0.0001
Delivery season					0.0002				
Spring	130,201 (23.8)	127,896 (98.2)		1.77		1.12 (1.05 – 1.18)	0.0003	1.12 (1.06 – 1.19)	0.0002

Adjusted for age at the time of delivery, income status, residential area, smoking status, drinking, physical activity, body mass index, history of hypertension before pregnancy, diabetes mellitus, and upper respiratory infection during pregnancy

Month of delivery	Total N (%)	Preeclampsia		Prevalence	<i>P</i>	Unadjusted OR (95% CI)	<i>P</i>	Adjusted OR (95% CI)	<i>P</i>
		No (N, %)	Yes (N, %)						
Summer	136,735 (25.0)	134,560 (98.4)		1.59		1.00		1.00	
Fall	147,391 (26.9)	144,935 (98.3)		1.67		1.05 (0.99 – 1.11)	0.1116	1.06 (1.00 – 1.13)	0.0407
Winter	133,753 (24.4)	131,378 (98.2)		1.78		1.12 (1.06 – 1.19)	0.0002	1.10 (1.04 – 1.17)	0.0015
Adjusted for age at the time of delivery, income status, residential area, smoking status, drinking, physical activity, body mass index, history of hypertension before pregnancy, diabetes mellitus, and upper respiratory infection during pregnancy									

3. Discussion

In this study, we analyzed the effects of seasonal variations on the incidence of PE in South Korea, and evaluated the relationship between URI during pregnancy and the development of PE. The results showed that several patient demographic factors, including age, socioeconomic status, residential area, behavioral habits, BMI, HTN, and DM were associated with the risk for PE. We also observed seasonal variations in the occurrence of PE in Korea. In this study cohort, the incidence of PE was the lowest in August but increased steadily from August to December, thus reaching its nadir in spring. In addition, this seasonal trend was maintained after maternal characteristics were adjusted as potential confounders. Furthermore, the results indicated that URI was associated with the occurrence of PE. However, the association between the development of PE and URI was not maintained in the multivariate analysis.

In the retrospective cohort study of Magnus et al., which included 1,869,388 recorded deliveries in Norway for over 30 years (1967 to 1998), the risk for PE was the lowest in August and highest in the winter months⁵. Since this study by Magnus et al. was published, several researchers have also noted seasonal trends in the occurrence of PE. Ros et al. reported that the risk for PE was the lowest in the summer and among women who delivered outside Nordic countries⁶. Phillips et al. reported that in Vermont, United States, the incidence of PE in the summer was decreased compared to that in spring¹⁰. In Texas, although minimal seasonal variation was reported, the prevalence of PE was the lowest in the fall and highest in the winter¹¹. This observation was maintained after adjusting for several confounders. Korea is located in East Asia and has a temperate climate with four distinct seasons. The mean temperature of Seoul, which is the capital of Korea, is -4°C in January and 24.0°C in August (Fig. 4). Although there were some differences depending on the region, the seasonal variations in PE occurrence in the present study are consistent with those of previous studies conducted in various regions.

Differences between the monthly variations in the incidence of PE among white and black women has been reported. Bodnar et al. stated that the incidence of PE among white women in the United States decreased during summer⁸. However, this seasonal pattern was not noted in black women. The Republic of Korea is an ethnically homogenous country. Approximately 96% of the total population are of Korean ethnicity and Asian; even half of the immigrants in Korea are from China¹². Therefore, our data, which represents the Asian population, demonstrates that the incidence of PE in Asian women varies according to seasons, as in white women.

The prevalence of PE may vary according to seasons. Some researchers have proposed that cold temperatures may cause peripheral vasoconstriction, which increases placental vascular resistance, thus resulting in placental insufficiency and PE. However, there are several limitations to the hypothesis of the relationship between seasonal variation and PE. Seasonal variation in PE exists in regions where there is no winter season⁷. In addition, ethnic differences in the monthly variations of the incidence of PE have been reported⁸. These observations suggest that environmental exposures related to monthly changes in lifestyle patterns, such as acute infection, dietary intake, and sunlight exposure, may contribute to the pathogenesis of PE. Of these environmental factors, infection plays a crucial role in the initiation and aggravation of uteroplacental insufficiency¹³. Various infectious diseases activate systemic inflammatory responses and endothelial injury, which may lead to uteroplacental atherosclerosis and placental hypoxia. These responses to inflammation result in an increased risk of PE. Several studies have demonstrated that urinary tract infection and periodontal disease are also potential risk factors for PE^{14–17}. Among other infections, those related to URI vary with seasons. We hypothesized that the immune response associated with URI during pregnancy affects the development of PE. Although multivariate analysis did not show a statistically significant association between the development of PE and URI, univariate analysis demonstrated that URI was associated with an increased prevalence of PE. Thus, the data of the present study show a potential association between URI and PE. In addition, a correlation between URI caused by viral infection and increased odds of PE was observed in a prospective study of pregnant women with asthma¹⁸. Furthermore, Romanyuk et al. observed a statistically significant association between pneumonia and severe PE in their population-based study¹⁹. However, the results of some studies do not suggest an association between URI and the development of PE. Minassian et al. conducted a population-based case-control study of 1,533 patients with PE and 14,236 randomly selected controls to assess the effect of URI on the risk of PE. The authors excluded any non-specific URI from the analysis, such as acute respiratory infection and respiratory tract infection, but did not observe any association between URI and PE¹⁶. The conflicting results of these studies might be a result of the varying definitions of URI and PE and the heterogeneity of the study populations. Therefore, further studies with larger populations and more stringent definitions of URI are required.

The present study has several limitations. First, we could not determine exact pregnancy dates, which is important to distinguish the subtypes of PE and estimate the month of conception. PE is divided into two subtypes according to disease onset: early (<34 gestational weeks) and late ($\geq$ 34 gestational weeks). The pathophysiology of these two subtypes differs. Therefore, as we could not determine the subtypes of PE in this study, the effect of seasonal changes on the development of PE according to its subtypes could not be elucidated. Second, we did not analyze PE in relation to the timing of conception. Phillips et al. suggested that the timing of conception is more strongly related to the seasonal variations in the incidence of PE than the season of delivery¹⁰. Lastly, the timing of infection during pregnancy may affect pregnancy outcomes related to PE. Placental development is complete by the end of the first trimester of pregnancy. Development of URI during this critical period may have a greater impact on the development of PE. However, we could not evaluate the association between the development of PE and the timing of URI during pregnancy because we had limited data on pregnancy dates.

This study also has several strengths. To the best of our knowledge, there is little data on the association between seasonal variations and the incidence of PE in Asian populations and regions. Therefore, the present study makes a considerable contribution to the existing research. Another strength is the use of a national database. Considering that we examined all recorded births between 2012 and 2018 in Korea, the study data provides more reliable information. Moreover, we investigated the relationship between URI and PE development. Several studies have been conducted to evaluate the association between the development of PE and urinary tract infection. However, few studies have been conducted to investigate the relationship between URI and PE.

In summary, the present study demonstrated that there are seasonal variations in the occurrence of PE in Korea. In this study cohort, the incidence of PE was the lowest in August but gradually increased from August to December, thus

reaching its nadir in spring. In addition, univariate analysis showed that URI was associated with the occurrence of PE. Further studies regarding the association between seasonal variations and the development of PE, with data on exact pregnancy dates, are required to evaluate the factors involved in the seasonal trends of PE development. Clarifying the biological mechanisms by which seasonal variations affect the development of PE is also necessary to elucidate the pathogenesis of PE.

4. Methods

This was a retrospective cohort study conducted using National Health Insurance Service (NHIS) claims data, which were collected from January 2012 to December 2018. The government of South Korea provides universal healthcare coverage for 97% of the population residing in Korea through the NHIS. The remaining 3% are covered by medical aid to protect them from the financial burden of excessive medical expenditure. As part of the NHIS healthcare program, beneficiaries are invited to participate in a NHSE program biannually. The NHSE consists of health examinations and interviews, including questions regarding patients' demographic, socioeconomic, and lifestyle characteristics. The results of the NHSE are stored in the NHIS database. To facilitate the evaluation of pre-pregnancy characteristics, only women who underwent an NHSE at least 2 years before their first delivery were included in the analysis. Those with missing data in the database were excluded. This study complies with the Declaration of Helsinki. The Institutional Review Board of the National Health Insurance Service (NHIS) Ilsan Hospital approved this study (NHIMC 2020). All methods were performed in accordance with the relevant guidelines and regulations. Written informed consent was waived by the Institutional Review Board of the National Health Insurance Service Ilsan Hospital because of the large number of participants in the cohort and the retrospective nature of the study.

Given that the pathophysiology of HTN during pregnancy differs between parous and nulliparous women, only nulliparous women were included in the present study. The women included were identified using International Classification of Diseases, 10th revision (ICD-10) codes O11, O14, and O15 to identify cases of PE. The Korean Society of Obstetrics and Gynecology recommends that PE be diagnosed if gestational HTN and proteinuria are present. Gestational HTN was defined as ≥ 2 systolic blood pressure measurements ≥ 140 mmHg and/or a diastolic blood pressure ≥ 90 mmHg, which was observed for the first time in antenatal care. Proteinuria was defined as a 1+ result on two random urine dipstick tests or a 2+ result on one urine dipstick test.

We examined known demographic risk factors for PE, including maternal age, income status, history of smoking, physical activity, heavy drinking, BMI, and medical history of HTN, DM, or URI during pregnancy. The women were stratified into four groups (quartiles) according to their economic status and according to BMI: underweight ($\text{BMI} < 18.5 \text{ kg/m}^2$), normal ($18.5\text{--}24.9 \text{ kg/m}^2$), overweight ($25\text{--}29.9 \text{ kg/m}^2$), obese ($\geq 30 \text{ kg/m}^2$). Regarding alcohol consumption habits, the included women were categorized as non-heavy or heavy drinkers. Heavy drinkers were defined as those with an alcohol consumption status that needed correction, those who consume alcohol more than four times per week, or those who have more than four drinks at a time. This definition is based on the criteria outlined by the National Institute on Alcohol Abuse and Alcoholism and revised by the Ministry of Health and Welfare (MOHW) in consideration of the alcohol consumption scenario in Korea. Regarding smoking status, the participants were categorized as current or non-smokers based on their NHSE results. For physical activity, the MOHW has presented a physical activity guide for Koreans based on the physical activity guidelines published by the US Department of Health and Human Services. According to the guidelines, physical activity is defined as more than three episodes of high-intensity workouts per week or more than five episodes of intermediate workouts per week.

Korea has four distinct seasons: spring (March–May), summer (June–August), fall (September–November), and winter (December–February). Winter temperatures are higher along the southern coast (southern region) and considerably lower in the mountainous interior (central region). Therefore, we classified the participants' areas of residence into southern or

central regions. Regarding URI during pregnancy, the following ICD-10 codes were used to define/identify URI: R05, cough; R04, hemorrhage from respiratory passage; A37, whooping cough; J00-J06, acute upper respiratory infection; J10, influenza due to other identified influenza virus; and B34, viral infection of unspecified site.

4.1. Statistical analysis

The demographic characteristics of the PE and control groups were compared using the chi-square test for categorical variables. The prevalence of births complicated by PE in each month and season was calculated. The relative risks for PE according to the month and season of delivery were estimated as adjusted prevalence odds ratios (aORs) using the month with the lowest risk as the reference. To adjust for possible confounding variables, multiple logistic regression was used to analyze the relative risk for PE using the other variables as ORs. The exact delivery date of each woman was identified using the NHIS claims data. The monthly prevalence of PE was calculated by dividing the number of women with PE in a month by the number of deliveries in that month. Statistical analyses were performed using SAS software (version 9.4; SAS Institute, Inc.; Cary, NC, USA).

Declarations

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Author contributions

EK: Conceived and designed the study, collected data,

SAL: Collected and analyzed the data,

SM: Collected data

YWJ: Conceived and designed the study, wrote the manuscript

All authors contributed to data interpretation

Conflicts of interest

There are no conflicts of interest to declare.

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Highlight

There is a seasonality of preeclampsia incidence in South Korea

References

1. Kuklina, E. V., Ayala, C. & Callaghan, W. M. Hypertensive disorders and severe obstetric morbidity in the United States. *Obstet Gynecol* **113**, 1299–1306, doi:10.1097/AOG.0b013e3181a45b25 (2009).
2. Conde-Agudelo, A., Althabe, F., Belizan, J. M. & Kafury-Goeta, A. C. Cigarette smoking during pregnancy and risk of preeclampsia: a systematic review. *Am J Obstet Gynecol* **181**, 1026–1035, doi:10.1016/s0002-9378(99)70341-8 (1999).
3. Shao, Y. *et al.* Pre-pregnancy BMI, gestational weight gain and risk of preeclampsia: a birth cohort study in Lanzhou, China. *BMC Pregnancy Childbirth* **17**, 400, doi:10.1186/s12884-017-1567-2 (2017).
4. Silva, L. M. *et al.* Low socioeconomic status is a risk factor for preeclampsia: the Generation R Study. *J Hypertens* **26**, 1200–1208, doi:10.1097/HJH.0b013e3282fcc36e (2008).
5. Magnus, P. & Eskild, A. Seasonal variation in the occurrence of pre-eclampsia. *BJOG* **108**, 1116–1119, doi:10.1111/j.1471-0528.2003.00273.x (2001).
6. Ros, H. S., Cnattingius, S. & Lipworth, L. Comparison of risk factors for preeclampsia and gestational hypertension in a population-based cohort study. *Am J Epidemiol* **147**, 1062–1070, doi:10.1093/oxfordjournals.aje.a009400 (1998).
7. Wacker, J. *et al.* Seasonal change in the incidence of preeclampsia in Zimbabwe. *Acta Obstet Gynecol Scand* **77**, 712–716 (1998).
8. Bodnar, L. M., Catov, J. M. & Roberts, J. M. Racial/ethnic differences in the monthly variation of preeclampsia incidence. *Am J Obstet Gynecol* **196**, 324 e321–325, doi:10.1016/j.ajog.2006.11.028 (2007).
9. Jung, Y. W. *et al.* Global gene expression analysis of cell-free RNA in amniotic fluid from women destined to develop preeclampsia. *Medicine (Baltimore)* **98**, e13971, doi:10.1097/MD.00000000000013971 (2019).
10. Phillips, J. K., Bernstein, I. M., Mongeon, J. A. & Badger, G. J. Seasonal variation in preeclampsia based on timing of conception. *Obstet Gynecol* **104**, 1015–1020, doi:10.1097/01.AOG.0000143306.88438.cf (2004).
11. Wellington, K. & Mulla, Z. D. Seasonal trend in the occurrence of preeclampsia and eclampsia in Texas. *Am J Hypertens* **25**, 115–119, doi:10.1038/ajh.2011.173 (2012).
12. Worldatlas. <<https://www.worldatlas.com/articles/ethnic-minorities-and-immigrants-in-south-korea.html>> (
13. Kim, C. J., Romero, R., Chaemsaithong, P. & Kim, J. S. Chronic inflammation of the placenta: definition, classification, pathogenesis, and clinical significance. *Am J Obstet Gynecol* **213**, S53–69, doi:10.1016/j.ajog.2015.08.041 (2015).
14. Easter, S. R. *et al.* Urinary tract infection during pregnancy, angiogenic factor profiles, and risk of preeclampsia. *Am J Obstet Gynecol* **214**, 387 e381–387, doi:10.1016/j.ajog.2015.09.101 (2016).
15. Khalighinejad, N., Aminoshariae, A., Kulild, J. C. & Mickel, A. Apical Periodontitis, a Predictor Variable for Preeclampsia: A Case-control Study. *J Endod* **43**, 1611–1614, doi:10.1016/j.joen.2017.05.021 (2017).
16. Minassian, C., Thomas, S. L., Williams, D. J., Campbell, O. & Smeeth, L. Acute maternal infection and risk of pre-eclampsia: a population-based case-control study. *PLoS One* **8**, e73047, doi:10.1371/journal.pone.0073047 (2013).
17. Mazor-Dray, E., Levy, A., Schlaeffer, F. & Sheiner, E. Maternal urinary tract infection: is it independently associated with adverse pregnancy outcome? *J Matern Fetal Neonatal Med* **22**, 124–128, doi:10.1080/14767050802488246 (2009).
18. Murphy, V. E., Powell, H., Wark, P. A. B. & Gibson, P. G. A prospective study of respiratory viral infection in pregnant women with and without asthma. *Chest* **144**, 420–427, doi:10.1378/chest.12-1956 (2013).
19. Romanyuk, V., Raichel, L., Sergienko, R. & Sheiner, E. Pneumonia during pregnancy: radiological characteristics, predisposing factors and pregnancy outcomes. *J Matern Fetal Neonatal Med* **24**, 113–117, doi:10.3109/14767051003678275 (2011).

Figures

Figure 1

Flowchart of the study

Figure 2

Prevalence of preeclampsia according to the month of delivery

Figure 3

Association between the month of delivery and preeclampsia

*Adjusted for age at the time of delivery, income status, residential area, smoking status, drinking status, physical activity, body mass index, history of hypertension before pregnancy, diabetes mellitus, and upper respiratory infection during pregnancy.

Figure 4

Climate chart of South Korea