Seasonal Variation in the Prevalence of Preeclampsia

Supakorn Pitakkarnkul MD*,
Chadakarn Phaloprakarn MD*, Budsaba Wiriyasirivaj MD*,
Sumonmal Manusirivithaya MD*, Siriwan Tangjitgamol MD*

** Department of Obstetrics and Gynecology, Faculty of Medicine, Vajira Hospital,
University of Bangkok Metropolis, Bangkok, Thailand*

Objective: *To determine whether there is a seasonal impact on the prevalence of preeclampsia in the tropical climate of Bangkok.*

Material and Method: *Medical records of all singleton pregnant women who delivered in the authors' institution between 2008 and 2009 were reviewed. The meteorological variables during the study period were obtained from database of the Thai Meteorological Department. The period of study was then divided into two main seasons: monsoon and dry seasons. The rates of preeclampsia occurring in the two seasons, based on the date of conception and date of delivery, were compared.*

Results: *Data of 7,013 gravidas were included for analysis. Of these, 327 (4.7%) developed preeclampsia. The monsoon season had lower mean maximum temperature (37.0°C vs. 38.1°C, $p = 0.114$), was more humid (77.0% vs. 68.7%, $p < 0.001$) and had higher daily rainfall (196.5 mm vs. 37.0 mm, $p < 0.001$) than dry season. Women who conceived in the dry season were at greater risk to develop preeclampsia than those who conceived in the monsoon season (5.3% vs. 3.7%, adjusted OR 1.51; 95% CI 1.18-1.93). The preeclampsia rates of women who delivered in both seasons were not significantly different: 5.0% in the dry season vs. 4.3% in the monsoon, $p = 0.178$.*

Conclusion: *There is a seasonal impact on the prevalence of preeclampsia based on the time of conception, but not the time of delivery. The rate of preeclampsia is significantly higher when conception occurs in the dry season.*

Keywords: *Seasonal variation, Preeclampsia, Tropical climate, Date of delivery, Date of conception*

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Preeclampsia is a common complication in pregnancy throughout the world[1-3]. One recent study demonstrated that over eight million gravidas worldwide were affected by this hypertensive disorder in each year, resulting in approximately 60,000 maternal deaths[4]. Aside from being an important cause of mortality, the disease can result in many short and long-term sequels, such as, preterm delivery, intra-uterine growth restriction, abruptio placentae, or an increased risk of future cardiovascular disease[2,5]. Despite its major impact on global social and economic burden, there has been no proven effective therapy other than termination of pregnancy.

Although the precise etiologic factor of preeclampsia remains elusive, many proposed a multifactorial theory with attempts to link pre-eclampsia to several conditions including genetic, immunological, inflammatory, nutritional, angiogenic, and environmental factors[6,7].

Meteorological factor or climate is one among various environmental factors that has been extensively studied. The rational for the association of seasons and the prevalence of preeclampsia is that the climate can affect the physiology of blood vessels or plasma volume[8,9]. Many studies found an association of meteorological factors, such as, ambient temperature, humidity, or rainfall and the prevalence of preeclampsia or eclampsia[8-14]. However, the results from these studies reported controversial data. Most studies reported a higher rate of preeclampsia in cool weather, winter, or with increased humidity or rainfall[9-12] while others demonstrated higher association with high temperatures or summer[8,13]. Another difference among these studies is the period of reference being studied in association with preeclampsia. Although most studies used the date of delivery as a point of reference, few studies applied the date of conception to evaluate a relationship

Correspondence to:
Pitakkarnkul S, Department of Obstetrics and Gynecology, Faculty of Medicine, Vajira Hospital, University of Bangkok Metropolis, Bangkok 10300, Thailand.
Phone: 0-2244-3422, Fax: 0-2243-7907
E-mail: supakorn_dr@hotmail.com

between season and the risk of hypertensive disorder[14,15].

The present study aimed to evaluate the rates of preeclampsia according to the seasons in which the women had conceived or delivered.

Material and Method

This retrospective study was conducted after an approval of the Bangkok Metropolitan Administration Ethics Committee for Researches Involving Human Subjects (Registered Number 080.53). Eligibility criteria were all singleton pregnant women residing in the area of Bangkok and its vicinity. The women must attend the antenatal clinic of the authors' institution, must be certain of her last menstrual period (LMP) to obtain an accurate gestational age, which was also confirmed by ultrasound in early gestation, and delivered in the authors' institution between January 1, 2008 and December 31, 2009. Exclusion criteria were those who had known risk factors for preeclampsia (*i.e.*, chronic hypertension, overt diabetes, renal or collagen vascular disease, or hyperthyroidism), history of irregular menstrual period within the past three months, or incomplete clinical data.

Data collected were maternal age, parity, body mass index (BMI) at first visit, pre-pregnancy weight, weight gain during pregnancy, current smoking status during pregnancy, the presence or absence of gestational diabetes mellitus (GDM) and preeclampsia, meteorological parameters (maximum daily temperature, morning humidity and daily rainfall), seasonal period of conception, diagnosis of preeclampsia, and delivery (monsoon or dry seasons). Maternal age was assigned in the whole number of years at the time of initial booking. Date of conception was defined as two weeks after the onset of LMP. Preeclampsia was diagnosed using the criteria of the International Society for the Study of Hypertension in Pregnancy[16]. Meteorological data were obtained from records of the Thai Meteorological Department.

The season in Thailand is divided into three seasons of summer, winter, and rainy season based on the conventional classification of the Thai Meteorological Department. However, data from the Meteorological database (http://www.tmd.go.th/climate/climate.php) revealed that the meteorological variables in Bangkok are relatively uniform throughout the year, except in the rainy season, which begins from May 16 to October 15. Hence, the authors regrouped the climate condition in the present study into two main seasons as monsoon or rainy season and dry season according to the Meteorological information.

Statistical analysis was performed with the SPSS software package version 11.5 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean with standard deviation (SD) and categorical variables as number with percentage. The Student t-test was used to compare continuous variables and χ^2-square test was used to compare categorical variables. Odds ratios (ORs) with 95% confidence intervals (95% CIs) for a development of preeclampsia in the two seasons based on periods of conception and delivery were examined using logistic regression with adjustment for potential confounders. P-value < 0.05 was considered statistically significant.

Results

During the study period, 7,013 gravidas were included in the present study. Of these, 6,900 (98.4%) were Thai and the remaining (1.6%) were other Southeast Asians. Three hundred and twenty seven (4.7%) developed preeclampsia. The majority of the present study population conceived (n = 4,173; 59.5%) and delivered (n = 3,907; 55.7%) in the dry season. Both groups of women who conceived in the monsoon and dry seasons had similar proportions of teenage- or advanced-age pregnancies, rates of nullipara, GDM, and smoking, percentages of overweight or obesity, and mean weight gain during pregnancy. Likewise, these clinical characteristics were also comparable between women who delivered in the monsoon and dry periods except for mean weight gain, which was found to be significantly higher in individuals delivering in the dry season. Details of the characteristic features of the present study population based on periods of conception and delivery are presented in Table 1 and Table 2, respectively.

Over the two-year period of the present study, the monsoon weather was significantly more humid with higher daily rainfall than the dry season (Table 3). Although the mean maximum daily temperature in the monsoon season was lower than that in the dry season, it did not reach statistical significance.

The risks of preeclampsia between the two seasons, based on the periods of conception and delivery, were determined by univariable and multivariable analyses (Table 4). There was a seasonal variation in the risk of preeclampsia based on a conception period. Women who conceived in the dry season had a greater risk of preeclampsia than those who conceived in the monsoon season (5.3% vs. 3.7%

Table 1. Characteristic features of the study population based on periods of conception (n = 7,013)

	Conception period		p-value
	Monsoon season (n = 2,840)	Dry season (n = 4,173)	
Age (years), n (%)			0.44
< 20	380 (13.4)	603 (14.4)	
20-34	2,094 (73.7)	3,033 (72.7)	
≥ 35	366 (12.9)	537 (12.9)	
Nullipara, n (%)	1,366 (48.1)	2,071 (49.6)	0.21
First-visit body mass index (kg/m^2), n (%)			0.15
< 20.0	1,068 (37.6)	1,661 (39.8)	
20.0-24.9	1,293 (45.5)	1,799 (43.1)	
25.0-29.9	351 (12.4)	540 (12.9)	
≥ 30.0	128 (4.5)	173 (4.2)	
Prepregnancy weight, mean (SD)	53.8 (10.7)	53.6 (10.6)	0.48
Weight gain during pregnancy, mean (SD)	13.3 (5.2)	13.1 (5.2)	0.14
Gestational diabetes mellitus, n (%)	96 (3.4)	148 (3.5)	0.71
Current smoking, n (%)	53 (1.9)	78 (1.9)	0.99

Table 2. Characteristic features of the study population based on periods of delivery (n = 7,013)

	Delivery period		p-value
	Monsoon season (n = 3,106)	Dry season (n = 3,907)	
Age (years), n (%)			0.83
< 20	440 (14.2)	543 (13.9)	
20-34	2,274 (73.2)	2,853 (73.0)	
≥ 35	392 (12.6)	511 (13.1)	
Nullipara, n (%)	1,564 (50.4)	1,873 (47.9)	0.05
First-visit body mass index (kg/m^2), n (%)			0.09
< 20.0	1,249 (40.2)	1,480 (37.9)	
20.0-24.9	1,353 (43.6)	1,739 (44.5)	
25.0-29.9	367 (11.8)	524 (13.4)	
≥ 30.0	137 (4.4)	164 (4.2)	
Prepregnancy weight, mean (SD)	53.4 (10.5)	53.9 (10.7)	0.05
Weight gain during pregnancy, mean (SD)	13.0 (5.2)	13.3 (5.2)	0.01
Gestational diabetes mellitus, n (%)	109 (3.5)	135 (3.5)	0.90
Current smoking, n (%)	49 (1.6)	82 (2.1)	0.11

Table 3. Comparison of meteorological parameters between monsoon and dry season during the study period

	Monsoon season	Dry season	p-value
Maximum daily temperature (°C), mean (SD)	37.0 (0.7)	38.1 (2.0)	0.144
Morning humidity (%), mean (SD)	77.0 (1.9)	68.7 (2.6)	<0.001
Daily rainfall (mm), mean (SD)	196.5 (46.1)	37.0 (42.2)	<0.001

Table 4. Univariable and multivariable analyses to determine the risks of preeclampsia between the monsoon and dry seasons based on both timing of delivery and conception

	Preeclampsia (n = 327)	No preeclampsia (n = 6,686)	Crude OR (95% CI)	Adjusted OR* (95% CI)
Timing of conception				
Monsoon, n (%)	106 (3.7)	2,734 (96.3)	1.00	1.00
Dry season, n (%)	221 (5.3)	3,952 (94.7)	1.44 (1.14-1.82)	1.51 (1.18-1.93)
Timing of delivery				
Monsoon, n (%)	133 (4.3)	2,973 (95.7)	1.00	1.00
Dry season, n (%)	194 (5.0)	3,713 (95.0)	1.17 (0.93-1.46)	1.15 (0.91-1.45)

* Adjusted for maternal age, parity, body mass index, weight gain during pregnancy, gestational diabetes mellitus and smoking status

OR = odds ratio; CI = confidence interval

respectively, adjusted OR 1.51; 95% CI 1.18-1.93). However, there was no significant relationship of preeclampsia and the season of delivery.

Discussion

Previous studies from the Western countries divided the climate conditions into three or four characteristic seasons according to their Meteorological background(9,11,14,15). The geographic location of Bangkok is at 13° 45' degrees north latitude and at sea level. Although the seasonal patterns are formally divided into three, it has been observed that the ambient temperatures are generally warm to hot throughout the year. For instance, the respective mean daily temperatures in 2009 of summer, rainy season, and winter were 28.5°C, 28.2°C, and 25.8°C. This is not observed with the humidity and level of daily rainfall when the climate in the rainy season is considered as "wet" compared to the "dry" summer and winter. The average humidity of summer and winter compared to the rainy season were 70.8% and 67.3% vs. 77.2% with the average daily rainfall of 60.3 mm and 10.6 mm vs. 193.7 mm, respectively. Per this observation, it appears that the actual weather circumstances in Bangkok can be classified into two distinct features: warm wet and warm dry seasons. Hence, to provide an insight into the potential influence of seasonal factor as the risk for preeclampsia, the authors separated these climate conditions into two- rather than the usual three seasons.

In the present study, the authors found an association of conception date with the risk of preeclampsia in the tropical climate of Bangkok. This finding was in agreement with two previous studies of Rudra and Williams[14] and Phillips et al[15] who identified a similar relationship in the temperate climate of Washington and Vermont States in the US. Although many different aspects of the present study and those two studies were observed *i.e.* geographic locations, climate patterns, as well as population backgrounds; the results were in the same direction that the risk of preeclampsia was significantly increased when conception occurred in the warm dry season. These data should alert the physicians to be aware of the environmental impact on such hypertensive disorder aside from the other well-known factors.

The mechanism by which the warm dry ambiance during conception affects the pathogenesis of preeclampsia is still unknown. Several hypotheses have been proposed. One possible mechanism is a direct effect of climate on body fluid balance[8]. Evidence suggests that the warm dry climate causes significant sweating and insensible fluid loss, resulting in a decrease in plasma volume[17]. This subnormal plasma volume could, in turn, lead to a reduction in utero-placental perfusion[18], causing placental ischemia/hypoxia and consequent cytokines or oxidative stress release[19]; these elements have been widely regarded as the key steps in the pathophysiology of preeclampsia[19,20]. Additional data to support this concept were the findings of higher preeclampsia rates in the warm tropical regions (4.2% in India[10], 4.7% in the present study [Thailand] and 5.5% in Singapore[8]) than the cold weather areas in Western countries (1.8% or 3.4% in the US[12,15] and 2.8% in Norway[11]). Nevertheless, intrauterine growth restriction (IUGR), another pregnancy complication that is believed to share the same underlying pathogenesis with preeclampsia, has not been reported to be more prevalent in the tropical areas compared to the cold climate regions. This may be because IUGR has multifactorial etiologies *e.g.* decreased uteroplacental blood flow, reduced plasma volume, decreased oxygen carrying capacity, poor nutritional status, teratogens, and miscellaneous causes[21]. Another potential mechanism is a seasonal impact on the prevalence of infections and inflammatory process[1] which are involved in the etiology of preeclampsia[19,20]. Lastly, some authors hypothesized that various dietary intakes in different seasons might also play a role for preeclampsia via an influence of antioxidants obtained from food[22,23]. Unfortunately, the authors were unable to prove the latter two hypotheses since the data about infection or nutrient intake were not available due to the retrospective nature of the present study. Future researches are needed to explore the possible mechanisms involved.

The present study could not demonstrate any significant impact of delivery date on the prevalence of preeclampsia. Other reports showed conflicting results on this issue even the studies, which were conducted in similar climate regions[8-14]. For example, the study of Tan and Salmon in the tropical climate of Singapore[8] found a significantly increased rate of preeclampsia in women who delivered during the warm dry season while the study of Subramaniam in Mumbai, India[10] did not identify such a relationship. The authors made some observations that might be responsible for these variable results. Births during any given period could be spontaneous delivery or induction of labor due to any obstetric or medical indications. The numbers of indicative delivery will certainly affect the authors' outcome of interest.

There were some other limitations of the present study. Some past history which may have an impact on the prevalence of preeclampsia, *i.e.*, pre-eclampsia in previous pregnancy, ambient temperature or the environment where the pregnant women lived (and where conception had taken place), etc. were not known. However, the authors adjusted for known potential confounders for preeclampsia by using multivariable analysis. Another possible limitation was an uncommon incidence of eclampsia in the study population did not allow the authors to determine a seasonal variation in the risk of such a complication.

Based on the present results, the authors agreed with the other studies that the environmental factor has an impact on the prevalence of preeclampsia. Knowing this additional risk factor may improve a holistic patient care of a pregnant woman at risk. This may also serve as a basic foundation to develop further knowledge of a pathogenesis of preeclampsia.

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Potential conflicts of interest

None.

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ความชุกของภาวะครรภ์เป็นพิษแยกตามฤดูกาล

ศุภกร พิทักษ์การกุล, ชาดากานต์ ผโลประการ, บุษบา วิริยะสิริเวช, สุมนมาลย์ มนัสศิริวิทยา, ศิริวรรณ ตั้งจิตกมล

วัตถุประสงค์*: เพื่อศึกษาว่าฤดูกาลในพื้นที่เขตร้อนอย่างกรุงเทพมหานครมีอิทธิพลต่อความชุกของภาวะครรภ์เป็นพิษหรือไม่*

วัสดุและวิธีการ*: เก็บข้อมูลจากเวชระเบียนของสตรีตั้งครรภ์เดี่ยวทุกรายที่มาคลอดที่คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยกรุงเทพมหานครในปี พ.ศ. 2551-2552 และข้อมูลสภาพภูมิอากาศในกรุงเทพมหานครจากฐานข้อมูลของกรมอุตุนิยมวิทยา ภูมิอากาศในช่วงเวลาที่ศึกษาแบ่งเป็นสองฤดูกาลคือฤดูฝนหรือมรสุมกับฤดูแล้ง ทำการเปรียบเทียบความชุกของภาวะครรภ์เป็นพิษระหว่างฤดูกาลทั้งสองฤดู โดยอ้างอิงตามช่วงเวลาที่มีการปฏิสนธิ และตามช่วงเวลาที่คลอดบุตร*

ผลการศึกษา*: จากข้อมูลของสตรีตั้งครรภ์ 7,013 ราย ที่รวบรวมได้พบว่า 327 ราย (ร้อยละ 4.7) เกิดภาวะครรภ์เป็นพิษ สภาพภูมิอากาศในช่วงของการศึกษาพบว่าฤดูมรสุมมีค่าเฉลี่ยอุณหภูมิสูงสุด (37.0 องศาเซลเซียส ต่อ 38.1 องศาเซลเซียส, $p = 0.114$) ต่ำกว่าแต่มีความชื้น (ร้อยละ 77.0 ต่อร้อยละ 68.7, $p < 0.001$) และปริมาณน้ำฝน (196.5 มิลลิเมตร ต่อ 37.0 มิลลิเมตร, $p < 0.001$) สูงกว่าฤดูแล้ง การศึกษาอิทธิพลของฤดูกาลต่อความชุกของครรภ์เป็นพิษ พบว่าสตรีที่มีการปฏิสนธิในฤดูแล้งจะมีความเสี่ยงต่อการเกิดภาวะครรภ์เป็นพิษมากกว่า สตรีที่มีการปฏิสนธิในฤดูมรสุมอย่างมีนัยสำคัญทางสถิติ (ร้อยละ 5.3 ต่อ ร้อยละ 3.7, ค่าความเสี่ยงสัมพัทธ์ 1.51 เท่า; ช่วงความเชื่อมั่นร้อยละ 95 เท่ากับ 1.18-1.93) ในขณะที่ไม่พบความแตกต่างของอัตราการเกิดครรภ์เป็นพิษระหว่างสตรีที่คลอดทั้งสองฤดู (ร้อยละ 5.0 ในฤดูแล้ง ต่อ ร้อยละ 4.3 ในฤดูมรสุม, $p = 0.178$)*

สรุป*: ฤดูกาลมีอิทธิพลต่อความชุกของภาวะครรภ์เป็นพิษโดยมีผลในช่วงของการปฏิสนธิ แต่ไม่มีผลในช่วงของการคลอดบุตรของสตรีตั้งครรภ์ ภาวะครรภ์เป็นพิษมีความชุกเพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติในสตรีที่มีการปฏิสนธิในฤดูแล้ง*