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A Case-Control Study of Preterm Delivery Risk Factors According to Clinical Subtypes and Severity

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Abstract

Aims—To examine risk factors of preterm delivery (PTD) among Thai women.

Methods—Our case-control study included 467 term controls and 467 PTD cases. PTD was studied in aggregate and in subgroups (i.e., spontaneous preterm labor and delivery [SPTD], preterm premature rupture of membrane [PPROM], medically indicated preterm delivery [MIPTD], moderate preterm delivery [32–36 weeks], and very preterm delivery [<32 weeks]). We used multivariable logistic regression procedures to estimate odds ratio (OR) and 95% confidence intervals (CI) of potential PTD risk factors.

Results—Advanced maternal age (≥ 35 years) was associated with a 2.27-fold increased PTD risk overall (95%CI: 1.40, 3.68); and with a 3.79-fold increased risk of MIPTD (95%CI: 1.89, 7.59). Young maternal age (<20 years) was associated with a 2.07-fold increased risk of SPTD (95%CI: 1.19, 3.61). Prior history of PTD was associated with a 3.64-fold increased PTD risk overall (95%CI: 1.87, 7.09), and with a 5.69-fold increased risk of MIPTD (95%CI: 2.44, 13.24). No prenatal care was associated with all PTD subtypes. Lean women ($\text{BMI} < 18.5 \text{ kg/m}^2$), compared with normal weight women ($18.5\text{--}24.9 \text{ kg/m}^2$), had a 1.70-fold increased risk of PTD (95%CI: 1.21, 2.39). Risk of SPTD (OR=2.16, 95%CI: 1.44, 3.24) and very PTD (OR=2.45, 95%CI: 1.35, 4.45) were also elevated in lean women.

Conclusions—Maternal age, pre-pregnancy body mass index, prior history of PTD and no utilization of prenatal care were covariates identified in this study as risk factors for PTD. Our findings also suggest heterogeneity in risk factors for clinical subtypes of PTD.

Keywords

Epidemiology; Preterm Delivery; Pregnancy; Risk Factors; Gestational Length

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Introduction

Preterm delivery (PTD), delivery before the completion of 37 weeks gestation, is the leading cause of perinatal morbidity and mortality in both developed and developing countries.¹ Putative PTD risk factors include low maternal socioeconomic status, maternal African-American race/ethnicity, nulliparity, grand-multiparity, a prior history of PTD, pre-gestational hypertension or diabetes, psychiatric disorders, antepartum hemorrhage, vaginal infections, psychosocial stress, and lifestyle habits such as smoking, alcohol and illicit drug use during pregnancy.^{2–5} The strength of the association of each identified risk factor has been shown to vary.^{1, 6} Women with a prior history of preterm delivery carry the highest risk of recurrence, estimated to be between 15 to >50%, dependent on the number and gestational age of previous deliveries.^{1, 6} Low maternal pre-pregnancy BMI, psychosocial stress and cigarette smoking during pregnancy were also associated with approximately 2-fold increase in risk of PTD.^{1, 7} Despite intensive research efforts, the underlying causes of PTD remain elusive. Moreover, although the risk factors for PTD have been widely studied in North American and European populations, they have not been as extensively characterized in Thai women, an understudied Southeast Asian population. We, therefore, sought to evaluate risk of PTD in relation of maternal socio-demographic, behavioral, and medical characteristics among Thai women.

Materials and Methods

Study population and selection of cases and controls

A case-control study using one control for each case of preterm delivery was conducted among women who delivered singleton live born infants without malformations at King Chulalongkorn Memorial Hospital, Rajavithi Hospital, and Police General Hospital, Bangkok, Thailand between July 2006 and November 2007. Cases were women who delivered before completed 37 weeks of gestation (22–36 weeks of gestation). Preterm delivery cases were identified by daily monitoring of all new deliveries at postpartum wards of participating hospitals. Of the 478 eligible cases approached, 467 (97.7%) agreed to participate in the study. Controls were women who delivered at term (≥ 37 weeks of gestation) and were selected from the same hospital of delivery. An eligible control, delivering immediately after a case patient, was approached and recruited for the study. Of the 482 eligible controls approached, 467 (96.9%) agreed to participate in the study.

All participants provided informed consent and the research protocol was reviewed and approved by ethical committees of the Faculty of Medicine, Chulalongkorn University, Rajavithi Hospital, Police General Hospital and the Institutional Review Boards, Division of Human Subjects Research, University of Washington.

Data collection

Participants were invited to participate in a 45-minute in-person interview in which trained research personnel used a structured questionnaire to elicit information regarding maternal socio-demographic, lifestyle, medical and reproductive characteristics. Participants' labor and delivery medical records and prenatal medical records were also reviewed by trained obstetric research nurses who used a standardized abstraction form. Information abstracted from medical records included participants' pre-pregnancy weight, height, blood pressure, pregnancy complications and condition of the newborn.

Analytical variable specification

Preterm delivery—The diagnosis of preterm delivery was made using American College of Obstetricians and Gynecologists (ACOG) guidelines.⁸ Gestational age was based on the

last menstrual period (LMP) or ultrasound examination. If both LMP and ultrasound dating (before 20 weeks gestation) were available and the two agreed within 14 days, we used the former to assign gestational age. If the two dates differed by more than 14 days, we used the ultrasound date. In order to account for the possible heterogeneity in the etiology of preterm delivery, we categorized preterm delivery cases according to the three pathophysiological groups previously described (i.e., spontaneous preterm labor and delivery [SPTD], preterm premature rupture of membranes [PPROM], and medically indicated preterm delivery [MIPTD]).^{9, 10} Spontaneous preterm labor and delivery cases were comprised of women whose medical records indicated a physician diagnosis of spontaneous labor onset (with intact fetal membranes) and delivery prior to the completion of 37 weeks gestation. Preterm premature rupture of membranes cases were comprised of women whose medical records indicated a physician diagnosis of rupture of fetal membranes (prior to the onset of labor) and delivery prior to the completion of 37 weeks gestation. Women who delivered prior to 37 completed weeks of gestation as a result of medical intervention comprised the medically indicated preterm delivery group. We also categorized preterm delivery cases according to gestational age at delivery (i.e., very preterm delivery, defined as delivery prior to the completion of 32 weeks gestation; and moderate preterm delivery, defined as delivery between 32 and 36 weeks).

Other covariates—Covariates considered in this analysis included maternal socio-demographic and behavioral characteristics including maternal age, marital status, educational attainment, employment status, cigarette smoking and alcohol consumption during pregnancy. Also considered were maternal reproductive and medical histories including parity, prior history of preterm delivery, history of abortion, maternal height, weight and infant gender. Parity was reported as the number of previous pregnancies lasting more than 22 weeks gestation. Pre-pregnancy body mass index (BMI) was calculated as weight (in kilograms) divided by the square of height (in meters).

Statistical analysis

Multivariable logistic regression procedures were employed to calculate odd ratios (OR) of potential risk factors associated with preterm delivery. Confidence intervals, at the 95% level were also reported for each unadjusted and adjusted OR. Confounding was assessed by entering potential cofounders into a logistic regression model one at a time, and by comparing the adjusted and unadjusted ORs. Final logistic regression models included covariates that altered unadjusted ORs by at least 10%.^{11, 12} We considered the following covariates as possible confounders in these analyses: maternal age, parity, marital status, and maternal educational attainment. Backward logistic regression modeling procedures combined with the change-in-estimate approach to select the final models reported in this manuscript. Variables of *a priori* interest (e.g., age, parity, infant gender, and pre-pregnancy body mass index) were forced into final models. These analytical procedures were also used in stratified analyses designed to assess risk of sub-types of preterm delivery (i.e., spontaneous preterm labor and delivery, preterm premature rupture of membranes, medically indicated preterm delivery, very preterm delivery, moderate preterm delivery and very preterm delivery). All analyses were completed using SPSS, version 16.0 statistical software (SPSS Inc., Chicago, IL).

Results

Table 1 displays selected maternal socio-demographic and behavioral characteristics of preterm cases and term controls. We observed evidence of a U-shaped relationship of PTD risk in relation to maternal age. Women who were <20 years of age, compared to those who were 25–29 years old, had a 1.69-fold increased risk of PTD (95% CI: 1.12, 2.56).

Advanced maternal age was associated with a 1.75-fold increased risk of PTD (OR=1.75, 95% CI: 1.11, 2.76). Maternal educational attainment, marital status, smoking, alcohol consumption, employment, and participation in leisure-time physical activity during pregnancy were not statistically significantly associated with PTD risk.

Nulliparous, compared with parous women with no history of preterm delivery had a 51% increased risk of PTD (OR=1.51, 95% CI: 1.15, 1.98) (Table 2). Parous women with a prior history of PTD, when compared with their parous counterparts who had no prior history of preterm delivery, had a 4.21 fold increased risk of PTD in the current pregnancy (95% CI: 2.22, 7.97). Maternal history of abortions and family history of hypertension were not statistically significant risk factors for PTD. As seen in Table 3, low pre-pregnancy body mass index was associated with an increased risk of PTD (OR=1.75, 95% CI: 1.26, 2.42). Women without prenatal care during the index pregnancy had a 4.28-fold increased risk of PTD (OR=4.28, 95% CI: 2.17, 8.41).

Because results from prior studies suggest that there may be some heterogeneity in the epidemiology of preterm delivery according to pathophysiology and gestational age of delivery,^{9, 10} we repeated analyses allowing for this possibility. As seen in Table 4, young maternal age (< 20 years) was associated with a 2.73-fold (95% CI: 1.68, 4.44) and a 2.76-fold (95% CI: 1.31, 5.83) increased risk of SPTD and very PTD, respectively. On the other hand, advanced maternal age was associated with an increased risk of very and moderate PTD. Women ≥35 years of age were 3.27-times more likely to have a pregnancy complicated by MIPTD than women 25–29 years of age (OR=3.27, 95% CI: 1.75, 6.10). Marital status was associated with SPTD risk. Women who were separated, as compared to married women, had a 2.50-fold increase in risk of SPTD (OR=2.50, 95% CI: 1.23, 5.04). Association of similar magnitudes was observed for very PTD. However, this association did not reach statistical significance (OR=2.15, 95% CI: 0.80, 5.79). Maternal educational attainment, alcohol consumption, employment status, and leisure time physical activity during pregnancy were not statistically significant risk factors for any of the PTD subtypes.

Nulliparous women, compared with parous women with no prior history of PTD, were more likely to have a pregnancy complicated by PPROM (OR=3.02, 95% CI: 1.89, 4.80) (Table 5). Prior history of PTD was associated with all PTD subtypes. As seen in Table 6, low maternal pre-pregnancy BMI was associated with a 2.28-fold increased risk of SPTD (OR=2.28, 95% CI: 1.56, 3.33). Low maternal pre-pregnancy BMI was also associated with an approximate doubling in risk of very PTD (OR=2.42, 95% CI: 1.38, 4.26). Overweight (OR=2.12, 95% CI: 1.18, 3.83) and obese women (OR=2.39, 95% CI: 0.93, 6.14) had an approximate doubling in risk of MIPTD, as compared with women with a pre-pregnancy BMI of 18.5–24.9 kg/m². No prenatal care was associated with all PTD subtypes. Notably women who received no prenatal care, as compared to those who initiated prenatal care in the first trimester, had a 5.71-fold increased risk of SPTD (95% CI: 2.66, 12.27). The corresponding ORs for very PTD were 4.57 (95% CI: 1.72, 12.14).

Results from multivariable logistic regression models for PTD in aggregate and clinical subtypes of PTD (after adjusted for all other covariates in the models) are summarized in Table 7. Overall, advanced maternal age, nulliparity, prior history of preterm delivery, low pre-pregnancy BMI, and no prenatal care were statistically significant risk factors of PTD. Maternal smoking during pregnancy and infant gender were not statistically significant risk factors for PTD overall. The relationships of these risk factors varied across the clinical subtypes of PTD. For example, young maternal age was a risk factor of SPTD (OR=2.07, 95% CI: 1.19, 3.61) and not a risk factor of PPROM (OR=0.85, 95% CI: 0.42, 1.73) or MIPTD (OR=0.43, 95% CI: 0.15, 1.22). However, increased maternal age (30–34 years) and advanced maternal age (≥35 years) were statistically significantly associated with MIPTD.

Other evidence of heterogeneity in risk factors of PTD clinical subtypes were noted for maternal pre-pregnancy BMI. =Low maternal pre-pregnancy BMI was associated with an increased risk of SPTD (OR=2.16, 95% CI: 1.44, 3.24), moderate PTD (OR=1.60, 95% CI: 1.12, 2.29), and very PTD (OR=2.45, 95% CI: 1.35, 4.45), but was weakly, and non-statistically significantly associated with PPRM (OR=1.37, 95% CI: 0.81, 2.32) and MIPTD (OR=1.12, 95% CI 0.60, 2.08). Conversely, pre-pregnancy obesity status was associated with increased risks of PPRM and MIPTD, though these associations did not reach statistical significance. In addition, we observed a linear decrease in risk of SPTD with increasing levels of pre-pregnancy BMI (p-value for linear trend <0.001). No similar patterns of linear trends were observed for PPRM and MIPTD (p-values for linear trend were > 0.05, respectively). Finally, no prenatal care was uniformly associated with all clinical PTD subtypes.

Discussion

Young and advanced maternal age, a prior history of PTD, low and high maternal pre-pregnancy body mass indices, and underutilization of prenatal care were identified as risk factors of PTD on our study of Thai women residing in metropolitan Bangkok. Our findings are consistent with the hypothesized complex multifactorial etiology of PTD;² and are also consistent with other studies that provide some evidence suggestive of heterogeneity of risk factors for clinical subtypes of PTD.^{9, 10, 13–18} Consistent with previous reports,^{17, 19} young and advanced maternal age, respectively, were associated with PTD risk overall. Furthermore, we noted that young maternal age was strongly associated with SPTD, whilst advanced maternal age was strongly associated with MIPTD. This pattern in risk is consistent with observations made by previous investigators. For instance, Meis et al. reported that adolescent mothers (<18 years) had a 2-fold increase in risk of SPTD (95% CI: 1.43, 2.81) compared with mothers aged 20–34 years.²⁰ Advanced maternal age was not associated with an increased risk of SPTD (OR=1.05, 95% CI: 0.75, 1.47), however, it was associated with a 1.83-fold increased risk of MIPTD (95% CI: 1.31, 2.55). Our findings and those of Meis et al differ, however, from those reported by Berkowitz et al.¹⁵ In their cohort of African American, Hispanic, and White women in New York, Berkowitz et al, found only a modest association between young maternal age (<20 years) and spontaneous preterm labor (OR=1.5, 95% CI: 1.3, 1.9); and a statistically significant increased risk of PPRM with advanced maternal age (≥ 35 years) (OR=1.5, 95% CI: 1.3, 1.8). The authors did not find advanced maternal age to be a statistically significant risk factor of MIPTD (OR=1.2, 95% CI: 0.9, 1.5).

We noted that lean women, as compared with normal weight women, had a 2.16-fold increased risk of SPTD and a 2.45-fold increased risk of very PTD. Maternal underweight status was not strongly associated with other PTD subtypes. However, maternal pre-pregnancy overweight and obesity status were positively associated with risk of MITPD. This finding, suggestive of heterogeneity with regards to the direction and magnitude of associations of selected PTD clinical subtypes with maternal body habitus, has been reported by several other investigators.^{13, 16, 18, 21, 22} Consistent with our findings, Smith et al.,²² in their cohort of Scottish women, reported that underweight women (early pregnancy BMI < 20.0 kg/m²) had a 1.46-fold increased risk of SPTD as compared with women with a normal BMI (20.0–24.9 kg/m²) (95% CI: 1.32, 1.62). Overweight and obese women, however, had no increase risk of SPTD, but statistically significant increases in risk of MIPTD. Specifically, the authors reported that overweight women had a 1.52-fold increased risk of MIPTD (95% CI: 1.31, 1.77), as compared with normal weight women. The corresponding OR for obese women was 2.13 (95% CI: 1.75, 2.58).

We noted that Thai women with a prior history of PTD, as compared with those parous women who had no such history, had a 3.64-fold increase in risk of PTD in the current pregnancy. This observation of high relative risk given prior history of PTD has been consistently reported by several investigators.^{15, 17, 23–25} For example, in their cohort study of Vietnamese women, Nguyen et al. reported that parous women with a prior history of PTD had a 5.2-fold increased risk of PTD (95% CI: 2.3, 11.5) when compared with parous women who did not have a history of PTD.²⁵

Like other investigators, we found that the risk of PTD was greatly elevated among women who did not use prenatal care.^{15, 25–27} However, in contrast with many prior studies,^{10, 28–30} we did not observe a statistically significant association of PTD risk with maternal smoking during pregnancy. Overall, maternal smoking was associated with a 55% increased risk of PTD overall (95% CI: 0.57, 4.21). Additionally, we observed evidence suggestive of a particularly strong association of maternal smoking with risk of very PTD (OR=3.31, 95% CI: 0.74, 14.75). The overall low frequency of maternal cigarette smoking among Thai women in our study prohibited more precise estimates of relative risks. In populations where the frequency of maternal smoking is considerably higher (e.g., $\geq 15\%$), investigators have reported that maternal smoking during pregnancy is associated with a 1.53-fold increase in risk of PTD.²⁹

Our study has several strengths, including the relatively large sample of preterm delivery cases and controls, the fact that we were able to assess risk factors of clinical subtypes of PTD, and that we used well trained personnel to collect information from all participants. All interviewers were blinded to participants' case-control status and a well-structured questionnaire was used to systematically collect risk factor information. The high participation rates for cases and controls (97.7 and 96.9%) also served to attenuate concerns about selection bias. Several limitations, however, should be considered when interpreting results from our study. Firstly, our cross-sectional study may be limited by recall bias since mothers were interviewed after delivery. The overall consistency of our findings with those from prospective cohort studies, however, serves to attenuate some concerns about recall bias. Secondly, information pertaining to several risk factors previously reported to influence PTD risk, such as maternal genitourinary tract infections during pregnancy, psychiatric diagnoses and psychosocial stressors, were not available for study. Thirdly, the analyses of relationships between several covariates and PTD risk in aggregate and in subgroups by necessity involved multiple tests of significance. Thus, type 1 error could exist. Lastly, findings from our study of women residing in metropolitan Bangkok are not likely to be generalizable to all Thai women.

PTD, a devastating obstetrical outcome with far-reaching implications for infants, parents, and communities at large, continues to be one of the most significant unsolved problems of public health and perinatology.^{2, 31} Infants born preterm, as compared with those born at term, are at greater risk for mortality and a wide range of medical and developmental complications. Findings from our present study are consistent with increasing evidence that PTD is a complex cluster of problems with a set of overlapping factors and influences. Further studies, preferably prospective cohort studies that include evaluation of individual-level behavioral and psychological factors, environmental exposures, medical conditions, biological factors, and genetics and epigenetic characteristics are needed to identify and characterize the underlying causes of preterm delivery in Thailand and elsewhere. Such studies should avoid treating PTD as a single entity. Rather, future studies should be designed to evaluate common pathophysiological pathways that may lead to PTD (e.g., chronic systematic inflammation, endothelial dysfunction, oxidative stress, placental ischemia and neuro-endocrine alterations). PTD is a global obstetric challenge that requires

more integrative comprehensive research approaches that include genetic factors to more fully understand its multi-factorial etiology.

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Table 1

Odds ratios (OR) and 95% confidence intervals (CI) for socio-demographic and behavioral characteristics of preterm cases and term controls, Bangkok, Thailand, 2006–2007.

Covariates	Controls (n = 467)		Preterm Cases (n = 467)		Unadjusted OR (95% CI)
	n	%	n	%	
Maternal age (years)					
<20	63	13.5	81	17.3	1.69 (1.12, 2.56)
20–24	130	27.8	129	27.6	1.31 (0.92, 1.85)
25–29	145	31.0	110	23.6	1.00 (Reference)
30–34	83	17.8	86	18.4	1.37 (0.92, 2.02)
≥35	46	9.9	61	13.1	1.75 (1.11, 2.76)
Maternal education (years)					
≤6	153	32.8	155	33.2	0.95 (0.56, 1.62)
7–12	282	60.4	278	59.5	0.93 (0.56, 1.55)
>12	32	6.9	34	7.3	1.00 (Reference)
Marital status					
Married	231	49.5	229	49.0	1.00 (Reference)
Unmarried	219	46.9	208	44.5	0.96 (0.74, 1.25)
Separated	17	3.6	30	6.4	1.78 (0.96, 3.32)
Smoked during pregnancy					
No	459	98.3	455	97.4	1.00 (Reference)
Yes	8	1.7	12	2.6	1.51 (0.61, 3.74)
Alcohol use in pregnancy					
No	445	95.3	451	96.6	1.00 (Reference)
Yes	22	4.7	16	3.4	0.72 (0.37, 1.38)
Employed during pregnancy					
No	178	38.1	171	36.6	0.94 (0.72, 1.22)
Yes	289	61.9	296	63.4	1.00 (Reference)
Leisure-time physical activity during pregnancy					
No	371	82.3	372	81.9	1.00 (Reference)
Yes	80	17.7	82	18.1	1.02 (0.73, 1.44)

Odds ratios (OR) and 95% confidence intervals (CI) for reproductive and medical characteristics of preterm cases and term controls, Bangkok, Thailand, 2006–2007.

Table 2

Covariates	Controls (n = 467)		Preterm Cases (n = 467)		Unadjusted OR (95% CI)
	n	%	n	%	
Parity					
Nulliparous	249	53.3	275	58.9	1.25 (0.97, 1.62)
Multiparous	218	46.7	192	41.1	1.00 (Reference)
Prior history of PTD					
Nulliparous	249	53.3	275	58.9	1.51 (1.15, 1.98)
Parous-no prior PTD	204	43.7	149	31.9	1.00 (Reference)
Parous-prior PTD	14	3.0	43	9.2	4.21 (2.22, 7.97)
Number of previous abortion					
0	369	79.0	375	80.3	1.00 (Reference)
1	82	17.6	79	16.9	0.95 (0.67, 1.33)
≥2	16	3.4	13	2.8	0.80 (0.38, 1.69)
Family history of hypertension					
No	413	88.4	405	86.7	1.00 (Reference)
Yes	51	10.9	59	12.6	1.18 (0.79, 1.76)
Missing	3	0.6	3	0.6	

Odds ratios (OR) and 95% confidence intervals (CI) for current pregnancy characteristics of preterm cases and term controls, Bangkok, Thailand, 2006–2007.

Table 3

Covariates	Controls (n = 467)		Preterm Cases (n = 467)		Unadjusted OR (95% CI)
	n	%	n	%	
Pre-pregnancy BMI (kg/m ²)					
<18.5	80	17.1	119	25.5	1.75 (1.26, 2.42)
18.5–24.9	315	67.5	268	57.4	1.00 (Reference)
25–29.9	45	9.6	38	8.1	0.99 (0.63, 1.57)
≥30.0	14	3.0	18	3.9	1.51 (0.74, 3.10)
Missing	13	2.8	24	5.1	
Maternal height (m)					
Low stature (≤145 cm)	16	3.4	16	3.4	1.00 (0.49, 2.02)
Normal (>145 cm)	448	95.9	450	96.4	1.00 (Reference)
Missing	3	0.6	1	0.2	
Prenatal care onset					
Care initiated in 1 st trimester	199	42.6	159	34.0	1.00 (Reference)
Care initiated after 1 st trimester	256	54.8	267	57.2	1.31 (1.00, 1.71)
No prenatal care	12	2.6	41	8.8	4.28 (2.17, 8.41)
Infant gender					
Female	232	49.7	211	45.4	1.00 (Reference)
Male	235	50.3	254	54.6	1.19 (0.92, 1.54)

Table 4

Odds ratios (OR) and 95% confidence intervals (CI) for socio-demographic and behavioral characteristics of preterm cases (categorized according to clinical subtype and severity) and term controls, Bangkok, Thailand, 2006–2007.

Covariates	Controls (n = 467)		PTD by Clinical Subtype						PTD by Severity			
			SPTD (n = 230)		PPROM (n = 120)		MIPTD (n = 117)		Moderate PTD (n = 389)		Very PTD (n = 78)	
	n	OR (95% CI)	n	OR (95% CI)	n	OR (95% CI)	n	OR (95% CI)	n	OR (95% CI)	n	OR (95% CI)
Maternal age (years)												
<20	63	57	2.73 (1.68, 4.44)	19	1.25 (0.66, 2.35)	5	0.43 (0.16, 1.16)	63	1.53 (0.99, 2.36)	18	2.76 (1.31, 5.83)	
20–24	130	73	1.70 (1.10, 2.62)	30	0.96 (0.56, 1.64)	26	1.07 (0.60, 1.93)	110	1.29 (0.90, 1.86)	19	1.41 (0.69, 2.89)	
25–29	145	48	1.00 (Reference)	35	1.00 (Reference)	27	1.00 (Reference)	95	1.00 (Reference)	15	1.00 (Reference)	
30–34	83	31	1.13 (0.67, 1.91)	24	1.20 (0.67, 2.15)	31	2.01 (1.12, 3.59)	71	1.31 (0.87, 1.97)	15	1.75 (0.81, 3.75)	
≥35	46	21	1.38 (0.75, 2.54)	12	1.08 (0.52, 2.25)	28	3.27 (1.75, 6.10)	50	1.66 (1.03, 2.67)	11	2.31 (0.99, 5.39)	
Maternal education (years)												
≤6	153	77	1.79 (0.81, 3.94)	35	0.52 (0.25, 1.08)	43	0.82 (0.38, 1.76)	126	0.98 (0.56, 1.72)	29	0.87 (0.35, 2.15)	
7–12	282	144	1.82 (0.84, 3.91)	71	0.58 (0.29, 1.14)	63	0.65 (0.31, 1.36)	236	0.99 (0.58, 1.70)	42	0.68 (0.28, 1.64)	
>12	32	9	1.00 (Reference)	14	1.00 (Reference)	11	1.00 (Reference)	27	1.00 (Reference)	7	1.00 (Reference)	
Marital status												
Married	231	98	1.00 (Reference)	61	1.00 (Reference)	70	1.00 (Reference)	191	1.00 (Reference)	38	1.00 (Reference)	
Unmarried	219	114	1.23 (0.88, 1.70)	53	0.92 (0.61, 1.38)	41	0.62 (0.40, 0.95)	174	0.96 (0.73, 1.27)	34	0.94 (0.57, 1.55)	
Separated	17	18	2.50 (1.23, 5.04)	6	1.34 (0.51, 3.53)	6	1.16 (0.44, 3.07)	24	1.71 (0.89, 3.27)	6	2.15 (0.80, 5.79)	
Smoked during pregnancy												
No	459	223	1.00 (Reference)	117	1.00 (Reference)	115	1.00 (Reference)	380	1.00 (Reference)	75	1.00 (Reference)	
Yes	8	7	1.80 (0.64, 5.03)	3	1.47 (0.38, 5.63)	2	1.00 (0.21, 4.76)	9	1.36 (0.52, 3.56)	3	2.30 (0.60, 8.85)	
Alcohol use in pregnancy												
No	445	220	1.00 (Reference)	116	1.00 (Reference)	115	1.00 (Reference)	374	1.00 (Reference)	77	1.00 (Reference)	
Yes	22	10	0.92 (0.43, 1.98)	4	0.70 (0.24, 2.06)	2	0.35 (0.08, 1.52)	15	0.81 (0.41, 1.59)	1	0.26 (0.03, 1.98)	
Employed during pregnancy												
No	178	103	1.32 (0.96, 1.81)	38	0.75 (0.49, 1.15)	30	0.56 (0.36, 0.88)	146	0.98 (0.74, 1.29)	25	0.77 (0.46, 1.28)	
Yes	289	127	1.00 (Reference)	82	1.00 (Reference)	87	1.00 (Reference)	243	1.00 (Reference)	53	1.00 (Reference)	
Leisure-time physical activity during pregnancy												
No	371	183	1.00 (Reference)	95	1.00 (Reference)	94	1.00 (Reference)	315	1.00 (Reference)	57	1.00 (Reference)	
Yes	80	41	1.04 (0.69, 1.58)	21	1.03 (0.60, 1.74)	20	0.99 (0.58, 1.69)	64	0.94 (0.66, 1.35)	18	1.46 (0.82, 2.62)	

Table 5

Odds ratios (OR) and 95% confidence intervals (CI) for reproductive and medical characteristics of preterm cases (categorized according to clinical subtype and severity) term controls, Bangkok, Thailand, 2006–2007.

Covariates	Controls (n = 467)			PTD by Clinical Subtype						PTD by Severity			
	SPTD (n = 230)			PPROM (n = 120)			MIPTD (n = 117)			Moderate PTD (n = 389)		Very PTD (n = 78)	
	n	OR (95% CI)	n	OR (95% CI)	n	OR (95% CI)	n	OR (95% CI)	n	OR (95% CI)	n	OR (95% CI)	n
Parity													
Nulliparous	249	1.31	1.16 (0.84, 1.59)	93	3.02 (1.89, 4.80)	51	0.68 (0.45, 1.02)	227	1.23 (0.94, 1.61)	48	1.40 (0.86, 2.29)		
Multiparous	218	99	1.00 (Reference)	27	1.00 (Reference)	66	1.00 (Reference)	162	1.00 (Reference)	30	1.00 (Reference)		
Prior history of PTD													
Nulliparous	249	131	1.34 (0.96, 1.87)	93	3.46 (2.10, 5.71)	51	0.89 (0.57, 1.38)	127	1.46 (1.10, 1.95)	22	1.79 (1.04, 3.06)		
Parous-no prior PTD	204	80	1.00 (Reference)	22	1.00 (Reference)	47	1.00 (Reference)	227	1.00 (Reference)	48	1.00 (Reference)		
Parous-prior PTD	14	19	3.46 (1.66, 7.23)	5	3.31 (1.09, 10.07)	19	5.89 (2.76, 12.59)	35	4.02 (2.08, 7.76)	8	5.30 (2.00, 14.03)		
Number of previous abortion													
0	369	194	1.00 (Reference)	94	1.00 (Reference)	87	1.00 (Reference)	312	1.00 (Reference)	63	1.00 (Reference)		
1	82	30	0.70 (0.44, 1.09)	21	1.01 (0.59, 1.71)	28	1.45 (0.89, 2.36)	66	0.95 (0.67, 1.36)	13	0.93 (0.49, 1.77)		
≥2	16	6	0.71 (0.27, 1.85)	5	1.23 (0.44, 3.43)	2	0.53 (0.12, 2.35)	11	0.81 (0.37, 1.78)	2	0.73 (0.16, 3.26)		
Family history of hypertension													
No	413	205	1.00 (Reference)	106	1.00 (Reference)	94	1.00 (Reference)	336	1.00 (Reference)	69	1.00 (Reference)		
Yes	51	25	0.99 (0.59, 1.64)	13	0.99 (0.52, 1.89)	21	1.81 (1.04, 3.15)	50	1.21 (0.80, 1.83)	9	1.06 (0.50, 2.24)		
Missing	3	0		1		2		3		0			

Table 6

Odds ratios (OR) and 95% confidence intervals (CI) for current pregnancy characteristics of preterm cases (categorized according to clinical subtype and severity) and term controls, Bangkok, Thailand, 2006–2007.

Covariates	Controls (n = 467)			PTD by Clinical Subtype				PTD by Severity			
				SPTD (n = 230)		PPROM (n = 120)		MIPTD (n = 117)		Moderate PTD (n = 389)	
	n	n	n	OR (95% CI)	n	OR (95% CI)	n	OR (95% CI)	n	OR (95% CI)	Very PTD (n = 78)
Pre-pregnancy BMI (kg/m²)											
<18.5	80	73	28	2.28 (1.56, 3.33)	28	1.45 (0.88, 2.39)	18	1.07 (0.60, 1.91)	95	1.63 (1.16, 2.3)	24
18.5–24.9	315	126	76	1.00 (Reference)	76	1.00 (Reference)	66	1.00 (Reference)	229	1.00 (Reference)	39
25–29.9	45	12	6	0.67 (0.34, 1.30)	6	0.55 (0.23, 1.34)	20	2.12 (1.18, 3.83)	31	0.95 (0.58, 1.54)	7
≥30.0	14	5	6	0.89 (0.32, 2.53)	6	1.78 (0.66, 4.77)	7	2.39 (0.93, 6.14)	17	1.67 (0.81, 3.46)	1
Missing	13	14	4		4		6		17		7
Maternal height (m)											
Low stature (≤1.45 m)	16	5	5	0.62 (0.23, 1.72)	5	1.23 (0.44, 3.42)	6	1.51 (0.58, 3.96)	13	0.97 (0.46, 2.04)	3
Normal (>1.45 m)	448	225	114	1.00 (Reference)	114	1.00 (Reference)	111	1.00 (Reference)	375	1.00 (Reference)	75
Missing	3	0	1		1		0		1		0
Prenatal care onset											
Care initiated in 1 st trimester	199	61	54	1.00 (Reference)	54	1.00 (Reference)	44	1.00 (Reference)	130	1.00 (Reference)	29
Care initiated after 1 st trimester	256	148	54	1.89 (1.33, 2.68)	54	0.78 (0.51, 1.18)	65	1.15 (0.75, 1.76)	226	1.35 (1.02, 1.80)	41
No prenatal care	12	21	12	5.71 (2.66, 12.27)	12	3.69 (1.57, 8.66)	8	3.02 (1.16, 7.81)	33	4.21 (2.10, 8.45)	8
Infant gender											
Female	232	108	52	1.00 (Reference)	52	1.00 (Reference)	51	1.00 (Reference)	175	1.00 (Reference)	36
Male	235	120	68	1.10 (0.80, 1.51)	68	1.29 (0.86, 1.93)	66	1.28 (0.85, 1.92)	212	1.20 (0.91, 1.57)	42

Table 7

Adjusted odds ratios (OR) and 95% confidence intervals (CI) according to selected factors, Bangkok, Thailand, 2006–2007.

Covariates	PTD by Clinical Subtype			PTD by Severity		
	All PTD (n = 467)	SPTD (n = 230)	PPROM (n = 120)	MIPTD (n = 117)	Moderate PTD (n = 389)	Very PTD (n = 78)
	OR [†] (95% CI)	OR [†] (95% CI)	OR [†] (95% CI)	OR [†] (95% CI)	OR [†] (95% CI)	OR [†] (95% CI)
Maternal age (years)						
<20	1.27 (0.80, 2.01)	2.07 (1.19, 3.61)	0.85 (0.42, 1.73)	0.43 (0.15, 1.22)	1.21 (0.75, 1.96)	2.13 (0.91, 5.01)
20–24	1.10 (0.76, 1.60)	1.37 (0.85, 2.20)	0.70 (0.39, 1.25)	1.00 (0.53, 1.90)	1.08 (0.73, 1.59)	1.20 (0.55, 2.61)
25–29	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
30–34	1.53 (1.00, 2.34)	1.08 (0.61, 1.92)	1.75 (0.91, 3.34)	2.00 (1.02, 3.90)	1.47 (0.95, 2.28)	2.07 (0.86, 4.98)
≥35	2.27 (1.40, 3.68)	1.60 (0.83, 3.09)	1.67 (0.76, 3.68)	3.79 (1.89, 7.59)	2.11 (1.28, 3.49)	3.64 (1.44, 9.16)
<i>Trend test p-value</i>	0.025	0.189	0.016	<0.001	0.038	0.263
Maternal education (years)						
≥6	-	1.50 (0.65, 3.49)	-	-	-	-
7–12	-	1.33 (0.59, 2.99)	-	-	-	-
>12	-	1.00 (Reference)	-	-	-	-
Smoke during pregnancy						
No	1.00 (Reference)	1.00 (Reference)	-	-	-	1.00 (Reference)
Yes	1.55 (0.57, 4.21)	1.93 (0.60, 6.19)	-	-	-	3.31 (0.74, 14.75)
Prior history of PTD						
Nulliparous	1.60 (1.15, 2.21)	1.00 (0.65, 1.53)	3.99 (2.27, 7.02)	1.66 (0.97, 2.85)	1.54 (1.10, 2.16)	1.79 (0.91, 3.53)
Parous-no prior PTD	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Parous-prior PTD	3.64 (1.87, 7.09)	2.92 (1.32, 6.48)	2.62 (0.80, 8.56)	5.69 (2.44, 13.24)	3.57 (1.80, 7.08)	4.38 (1.49, 12.89)
Family history of hypertension						
No	-	-	-	1.00 (Reference)	-	-
Yes	-	-	-	1.71 (0.94, 3.14)	-	-
Pre-pregnancy BMI (kg/m²)						
<18.5	1.70 (1.21, 2.39)	2.16 (1.44, 3.24)	1.37 (0.81, 2.32)	1.12 (0.60, 2.08)	1.60 (1.12, 2.29)	2.45 (1.35, 4.45)
18.5–24.9	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
25–29.9	1.05 (0.65, 1.71)	0.66 (0.33, 1.33)	0.74 (0.29, 1.88)	1.83 (0.95, 3.52)	1.03 (0.62, 1.71)	1.26 (0.51, 3.15)
≥30.0	1.59 (0.76, 3.35)	0.89 (0.30, 2.63)	2.31 (0.78, 6.86)	2.35 (0.85, 6.50)	1.78 (0.83, 3.78)	0.52 (0.06, 4.51)

Covariates	PTD by Clinical Subtype				PTD by Severity	
	All PTD (n = 467)	SPTD (n = 230)	PPROM (n = 120)	MIPTD (n = 117)	Moderate PTD (n = 389)	Very PTD (n = 78)
	OR [†] (95% CI)	OR [†] (95% CI)	OR [†] (95% CI)	OR [†] (95% CI)	OR [†] (95% CI)	OR [†] (95% CI)
<i>Trend test p-value</i>	0.154	<0.001	0.783	0.087	0.352	0.020
Prenatal care onset						
Care initiated in 1 st trimester	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Care initiated after 1 st trimester	1.29 (0.97, 1.72)	1.62 (1.11, 2.37)	0.88 (0.56, 1.39)	1.31 (0.82, 2.11)	1.33 (0.98, 1.80)	1.10 (0.62, 1.94)
No prenatal care	4.34 (1.96, 9.61)	4.92 (2.00, 12.11)	5.53 (1.90, 16.06)	4.87 (1.56, 15.23)	4.46 (1.97, 10.08)	4.92 (1.46, 16.54)
Infant gender						
Female	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
Male	1.24 (0.94, 1.63)	1.09 (0.77, 1.54)	1.40 (0.91, 2.16)	1.45 (0.92, 2.27)	1.28 (0.96, 1.70)	1.18 (0.70, 1.99)

[†]Each column represents a different logistic regression model. Covariates not included in final models are indicated as (-). Each OR and 95% CI is adjusted for all other covariates listed in the model.