ORIGINAL ARTICLE

Risk Score Predicting Spontaneous Preterm Delivery within 7 Days After Preterm Labor

Nattha Hatsabodesonton, MD[1], Monyada Pleankong, MD[1], Sinart Prommas, MD[1], Buppa Smanchat, MD[1], Kornkarn Bhamarapravatana, PhD[2], Komsun Suwannarurk, MD[3]

[1] Department of Obstetrics and Gynecology, Bhumibol Adulyadej Hospital, Royal Thai Air Force, Bangkok, Thailand; [2] Department of Preclinical Sciences, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand; [3] Department of Obstetrics and Gynecology, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand

Objective: To investigate risk factors of preterm labor (PTL) as a predictor model for preterm delivery (PTD) within seven days.

Materials and Methods: The present study was a historical cohort study conducted at Bhumibol Adulyadej Hospital, Thailand between January 2018 and December 2023. Participants were singleton pregnant women who attended antenatal care and were diagnosed with PTL with a gestational age (GA) between the 24^{+0} and the 36^{+6} weeks. Participants that delivered within and outside the seven-day mark were divided into the study and control groups. Risk factors, namely maternal age, education level, family's income, parity, history of PTD, GA at PTL, pre-pregnancy body mass index (PPBMI), nifedipine usage, preterm pre-labor rupture of membrane (PPROM), urinary tract infection (UTI), and vaginal bleeding were collected and analyzed to create predictive model of PTD within seven days (PD 7).

Results: One thousand fifty-five pregnant women were recruited. The mean age of participants was 28.8 years. Significant factors for PTD including advanced maternal age (AMA), PPBMI, nifedipine usage, multiparity, PPROM, treated UTI, vaginal bleeding and history of PTD were used to generate the predictive model for PD 7. PD 7 scores greater than 26 predicted delivery within seven days with sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratio (LR)+ and LR– of 72.7%, 78.5%, 77.9%, 73.4%, 3.4, and 0.4, respectively.

Conclusion: AMA, higher GA, multiparity, PPROM, vaginal bleeding, treated UTI, and history of PTD were significant risk factors for PD 7. The PD 7 model demonstrated good predictive performance. The model can be applied as a clinical decision-support tool to guide appropriate corticosteroid administration and timely referral, reducing unnecessary interventions. Incorporation of the PD 7 model into antenatal care practice and hospital protocols may enhance perinatal outcomes and promote standardized management of PTL.

Keywords: Prediction; Preterm; Delivery; Risk

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Preterm labor (PTL) is defined as premature regular uterine contractions before 37 weeks of gestation with cervical change. PTL may lead to preterm delivery (PTD). PTD is a delivery between the 24^{+0} and the 36^{+6} weeks of gestation[1].

In 2021, the preterm birth rate in Thailand was 12.5%[2]. It posed adverse socioeconomic effect and increased maternal and fetal morbidity and mortality in both the short and long term, these included respiratory failure, hypoglycemia, seizure, stillbirth, infant death, necrotizing enterocolitis (NEC), and intraventricular hemorrhage (IVH)[3,4].

Respiratory distress syndrome (RDS) is a significant complication of preterm birth and a leading cause of neonatal morbidity and early mortality. It occurs due to a deficiency of lung surfactant, which is essential for lung development[5]. Lung surfactant production increases with gestation age, however, preterm newborns have insufficient levels, resulting in higher susceptibility to RDS. The administration of corticosteroids during PTL has been shown to reduce the risk of short-term neonatal respiratory morbidities[6], as well as decrease the incidence of IVH and NEC. The optimal therapeutic time for antenatal corticosteroids has been demonstrated to fall within seven days after completing a full course, with the therapeutic effect significantly decreasing after seven days[5].

There are several factors associated with PTD,

Correspondence to:

Pleankong M.

Department of Obstetrics and Gynecology, Bhumibol Adulyadej Hospital, Royal Thai Air Force, Bangkok 10220, Thailand.

Phone: +66-2-5347314, +66-81-5724990

Email: monyada@gmail.com

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such as maternal demographic characteristics, socioeconomic factors, medical complications, obstetric history, tobacco use, substance use, short interpregnancy interval, low pre-pregnancy body mass index (PPBMI), obesity, lower tract genital infection, vaginal bleeding, and preterm pre-labor rupture of membrane (PPROM)[1]. A history of PTD increased the risk of PTD in a subsequent pregnancy compared to pregnant women without a history of spontaneous PTD[7]. Overweight or obese pregnant women showed a significantly increased risk of PTD, PPROM, and vaginal bleeding in the current pregnancy, and were considered relevant predictive factors for PTD[8].

Not all cases of PTL lead to PTD. There was no direct correlative risk factor for PTL and PTD. It was crucial to be able to identify PTL women who would deliver within seven days because accurately predicting PTD within seven days (PD 7) after PTL would help reduce unnecessary or premature steroid use.

The present study aimed to utilize the risk factor of PTL as a predictor model for PD 7 to prevent unnecessary administration of steroids in pregnant women with PTL.

Materials and Methods

The protocol of the present investigation was approved by the Bhumibol Adulyadej Hospital (BAH), Institutional Review Board (IRB No.42/67) in 2024. A historical cohort study was conducted at BAH, Royal Thai Air Force, using the database between January 2018 and December 2023.

Participants were singleton pregnant women who attended antenatal care and were diagnosed with PTL between gestational age (GA) of 24^{+0} and 36^{+6} weeks. Participants who delivered within seven days, and those who delivered after more than seven days after PTL diagnosis were classified as the study and the control groups, respectively. Exclusions were participants with one or more of the following, incomplete electronic medical records, indicated PTD, and evidence of congenital fetal anomaly of any organ.

Samples size was calculated by comparing two population proportion formulas. The proportion of PTD within and over seven days were 0.08 and 0.14, respectively[9]. The ratio between the two groups was 1. The alpha and beta errors were set at levels 0.05 and 0.2, respectively. The decimal was 2. The proper sample size for each group was 426 cases. A sample size of 511 cases per group was needed after the additional 20% compensation for missing data was added.

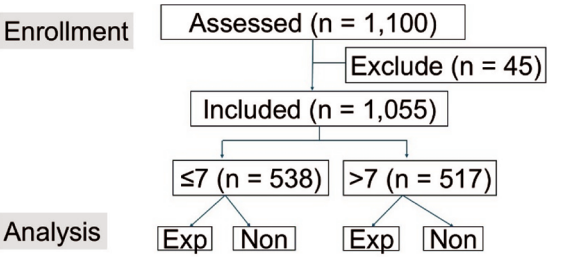

Figure 1. Flow of study.

Exp: expose to risk factor, Non: non expose to risk factor, ≤7: delivery within 7 days after preterm labor, >7: delivery more than 7 days after preterm labor, Exclude (incomplete electronic medical records 20, indicated PTD 10, and evidence of congenital fetal anomaly of any organ 15 cases)

Risk factors namely maternal age, education level, family income, number of parities, history of PTD, GA at PTL, PPBMI, nifedipine usage, PPROM, urinary tract infection (UTI), and vaginal bleeding were analyzed by uni- and multivariate analysis. The developed risk score model for PD 7 was the summation of significant factors. Diagnostic performance was analyzed by receiver operating characteristic (ROC) curve generation.

Statistical analyses were performed using PASW Statistics, version 18.0 (SPSS Inc., Chicago, IL, USA). Demographic data were investigated using frequency and percentage for categorical data. Mean, standard deviation, median and interquartile ranges were used for continuous data. Comparisons between groups was performed using independent t-test, Mann-Whitney U test, chi-square test, or Fisher's exact test as appropriate. Multivariable analysis via multiple logistic regression was used in determining independent risk factors with adjustment for potential confounders. The discrimination ability and optimal cut-off value were determined by ROC curve analysis by Youden's Index. The level of statistical significance was set at p-value of less than 0.05.

Results

One thousand fifty-five pregnant women were recruited in the present study as shown in Figure 1. The mean age of the participants was 28.8 years. The mean GA at PTL of study group was significantly higher than the control group at 34.4 versus 32.6 weeks.

Participants in the control group displayed normoweight and obesity, with a BMI of less than 23 and more than 25 kg/m^2 at percentage of 83 compared

Table 1. Demographic characters of pregnant women who delivered after preterm labor

	Delivery within (days)		p-value
	≤7 (n=538)	>7 (n=517)	
AMA; n (%)	143 (26.6)	88 (17.0)	<0.001
GAPL (weeks); mean±SD	34.36±2.2	32.61±2.6	<0.001
BMI (kg/m^2); n (%)			<0.001
Normal (≤23)	290 (53.9)	106 (20.5)	
Overweight (23 to 24.9)	82 (15.2)	88 (17)	
Obesity (≥25)	166 (30.9)	323 (62.5)	
Education; n (%)			0.094
Primary or below	96 (17.8)	66 (12.8)	
High school	271 (50.4)	261 (50.5)	
Vocational	44 (8.2)	51 (9.9)	
Bachelor or higher	127 (23.6)	139 (26.9)	
Income (USD/month); n (%)			0.477
≤438	157 (29.2)	136 (26.3)	
438.01 to 877	239 (44.4)	233 (45.1)	
877.01 to 2,920	125 (23.2)	136 (26.3)	
>2,920	17 (3.2)	12 (2.3)	
Nifedipine; n (%)	15 (2.8)	214 (41.4)	<0.001
Multiparity; n (%)	324 (60.2)	277 (53.6)	0.029
PPROM; n (%)	164 (30.5)	117 (22.6)	0.004
Treated UTI; n (%)	4 (0.7)	47 (9.1)	<0.001
Bleeding; n (%)	44 (8.2)	17 (3.3)	0.001
Hx PTD; n (%)	47 (8.7)	13 (2.5)	<0.001

AMA=advanced maternal age (≥35 years old); GAPL=gestational age at preterm labor; BMI=body mass index; PPROM=preterm prelabor rupture of the membrane; UTI=urinary tract infection; Bleeding=bloody show at labor room; Hx PTD=history of prior preterm delivery; SD=standard deviation

1 USD=34.24 Thai Baht

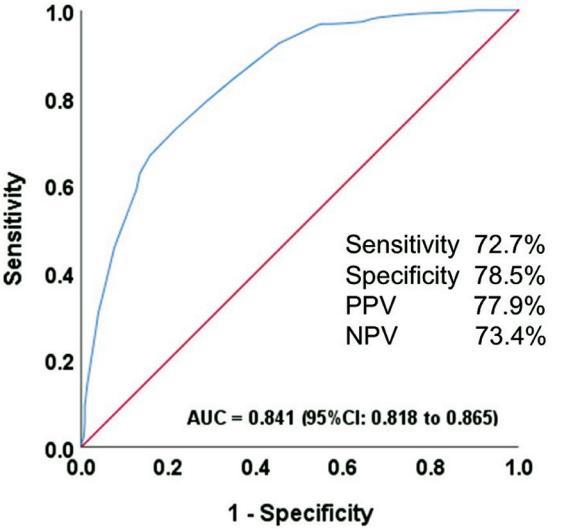

Figure 2. ROC curve of preterm labor score to predict preterm delivery within 7 days.

ROC: receiver operating characteristic curve, AUC: area under the curve, CI: confidence interval, PPV: positive predictive value, NPV: negative predictive value, Cut-off point value of PD 7 at 26

to the study group at percentage of 84.8 (p<0.001). Percentage of multiparity, PPROM, vaginal bleeding, history of PTD greater than the control group are shown in Table 1. The percentage of nifedipine usage and treated UTI occurrence of the study group was lower than the control group (p<0.001) as shown in Table 1. Monthly income and education level of both groups were comparable. Advanced maternal age, at AMA of more than 35 years old, normoweight of BMI less than 23 kg/m² to overweight of BMI of 23 to 24.9 kg/m², no nifedipine used, PPROM, treated UTI, vaginal bleeding, history of PTD were significantly prognostic factors for PTL within seven days from multivariate regression as shown in Table 2.

Model development

The influencing factors for PTD from multivariate analysis namely AMA, PPBMI, no nifedipine used, multiparity, PPROM, treated UTI, vaginal bleeding and history of PTD were used to generate the predictive model for PD 7. PD 7 was the PTD score for predicted PD 7 after PTL. The score of PD 7 consisted of summation of score from eight factors as shown in Table 3. The range of PD 7 scoring was between 0 and 42. ROC of PD 7 score and its prediction are shown in Figure 2. Area under the curve (AUC) was 84.1% (95% CI 0.818 to 0.865). Appropriate cut-off point for the PD 7 model was 26 which revealed sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratio (LR)+, and LR– at 72.7%, 78.5%, 77.9%, 73.4%, 3.4, and 0.4, respectively.

PD 7 model usage was uploaded to the website base at the URL: https://pretermdelivery-score.vercel.app and could be accessed via QR code as depicted in Figure 3.

The calibration plot demonstrated good agreement between the predicted and observed risks of delivery within seven days. The model exhibited excellent overall performance and high calibration accuracy, with a Brier scaled score of 99.6%. The discrimination ability was also strong with a C-statistic of 0.841. The E:O ratio was 1.001. The predicted number of events was nearly identical to the observed outcomes. Although the calibration slope was slightly low (0.1), it indicated a potential overfitting tendency. The calibration-in-the-large (CITL) value was 0.05, indicating minimal systematic bias as shown in Figure 4.

Table 2. Univariable and multivariable logistic regression: delivery within 7 days

	Univariate		Multivariate	
	OR (95% CI)	p-value	Adj OR (95% CI)	p-value
AMA	1.8 (1.3 to 2.4)	<0.001	2.1 (1.4 to 3.0)	<0.001
GAPL (weeks)				
≤32	Ref.	1		
>32	3.6 (2.7 to 4.9)	<0.001		
BMI (kg/m^2)				
Normal (≤23)	5.3 (4.0 to 7.1)	<0.001	5.4 (3.8, 7.6)	<0.001
Overweight (23 to 24.9)	1.8 (1.2 to 2.6)	<0.001	1.7 (1.1, 2.6)	0.014
Obesity (≥25)	Ref.	1	Ref.	1
Education				
Primary or below	1.6 (1.1 to 2.4)	0.021	1.5 (0.9, 2.4)	0.155
High school	1.1 (0.9 to 1.5)	0.395	1 (0.7, 1.5)	0.997
Vocational	0.9 (0.6 to 1.5)	0.811	0.7 (0.4, 1.2)	0.157
Primary or below	Ref.	1	Ref.	1
Income (USD/month)				
≤438	0.8 (0.4 to 1.8)	0.604		
438.01 to 877	0.7 (0.3 to 1.6)	0.405		
877.01 to 2,920	0.7 (0.3 to 1.4)	0.276		
>2,920	Ref.	1		
No nifedipine used	24.7 (14.4 to 42.5)	<0.001	22.2 (12.5 to 39.4)	<0.001
Multiparity	1.3 (1.0 to 1.7)	0.029	1.3 (0.9 to 1.7)	0.184
PPROM	1.5 (1.1 to 2.0)	0.004	1.5 (1.1 to 2.2)	0.021
Treated UTI	13.4 (4.8 to 37.3)	<0.001	8.2 (2.8 to 24.5)	<0.001
Bleeding	2.6 (1.5 to 4.7)	<0.001	2.3 (1.2 to 4.6)	0.018
Hx PTD	3.7 (2.0 to 7.0)	<0.001	2.6 (1.2 to 5.7)	0.016

AMA=advanced maternal age (age >35 years old); GAPL=gestational age at preterm labor, BMI=body mass index; PPROM=preterm prelabor rupture of the membrane; UTI=urinary tract infection; Bleeding=bloody show at labor room; Hx PTD=history of prior preterm delivery; OR=odds ratio; CI=confidence interval

1 USD=34.24 Thai Baht

Table 3. PD 7 scoring to predict PTD

	ß coefficient	Adjusted OR	95% CI	p-value	Score
AMA	0.717	2.048	1.40 to 3.00	<0.001	3
BMI <23	1.659	5.252	3.72 to 7.41	<0.001	7
BMI 23 to 24.9	0.530	1.698	1.12 to 2.58	0.013	2
NNU	3.080	21.761	12.31 to 38.48	<0.001	13
Multiparity	0.242	1.274	0.93 to 1.74	0.131	1
PPROM	0.408	1.504	1.06 to 2.13	0.022	2
Treated UTI	2.140	8.502	2.88 to 25.15	<0.001	9
Bleeding	0.824	2.281	1.15 to 4.54	0.019	3
Hx PTD	0.926	2.525	1.17 to 5.45	0.018	4

AMA=advance maternal age; BMI=body mass index; NNU=no nifedipine usage; PPROM=preterm prelabor rupture of the membrane; UTI=urinary tract infection; Bleeding=bloody show at labor room; Hx PTD=history of prior preterm delivery; OR=odds ratio; CI=confidential interval

PD 7 scoring: summation of AMA, BMI, nifedipine, multiparity, PPROM, treated UTI, bleeding, and PTD score; web-based application was cited as https://pretermdelivery-score.vercel.app/

Discussion

From the current study, AMA, higher GA, multiparity, PPROM, vaginal bleeding and history of PTD were significant risk factors for PD 7. Obesity, nifedipine usage, and treated UTI were protective factors for PD 7, as shown in Table 1. According to Su et al. from China in 2020, BMI between 23 and 30 kg/m² was a risk factor for PTL[8]. Normal

Figure 3. PD 7 score for prediction of PTD.

PTD: preterm delivery, PD 7: preterm delivery within 7 days score

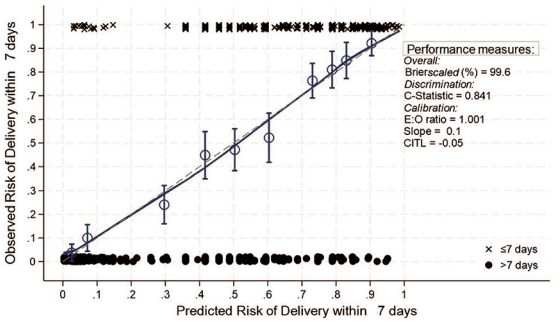

Figure 4. Calibration plot of expected and true delivery within 7 days prediction. The result of internal validation was used by the Bootstrap method (10,000 sampling times). X axis represented the predictive of delivery within 7 days by model. Y axis represented the real delivery within 7 days. The predictive model showed excellent internal validation according to the calibration plot.

to overweight in Su's study was 82.7%[8]. History of PTD, abortion and short cervical length were risk factors for PTL in China by Yan et al[4]. Another study from China by Li et al. in the year 2024 reported that multiparity and PPROM were risk factors for PTL[10]. A meta-analysis from Wang et al. in 2024 reported UTI was a risk factor for PTL[11]. Wang's population came from 11 countries in Asia, Europe, and USA[11]. Su's and Wang's studies consisted of 36,596 and 58,943 cases, respectively[8,11]. Both Wang's and Su's studies utilized big datasets. UTI and BMI were risk factors for PTL[8,11]. Talungchit et al. reported from Thailand in 2023 that UTI was associated with PTD[12]. However, UTI in the current study was a reducing risk factor. The findings from the current study were inconsistent with previous literature[11,12]. The pregnant women diagnosed with UTI were usually treated and given intensive monitoring, both as outpatient and inpatient.

Fifteen percent, two-thirds, one-fifth, and 2.8% of participants in Su's study were underweight, normoweight, overweight, and obese, respectively[8]. Yan's study consisted of 4,041 cases from upper-middle and high-income countries from France, UK, Korea, USA, Australia, Denmark, and China[4]. Yan et al. demonstrated that only the history of preterm, abortion and short cervical length were risk factors for PTD[4]. Large homogenous populations indicated that PTL was caused by multiple risk factors. The findings from the current study were in line with previous literature that PTL was affected by multiple risk factors[4,8,10,11].

Prediction of PD 7 is a useful tool for obstetricians to predict neonatal delivery. If there is high chance of delivery within seven days, dexamethasone administration for enhancing fetal lung maturation should be performed to prevent neonatal lung complications namely dyspnea, tachypnea, and respiratory failure. If there is low chance of delivery within seven days, observation without dexamethasone administration should be considered.

The PPV of the presented model (PD 7 score) demonstrated moderate precision. Only 77.9% and 73.4% of PPV and NPV were reported. Sensitivity and specificity were 72.7% and 78.5%, respectively. When the healthcare providers identified a high probability of delivery within seven days among preterm pregnant women, the model served as a guide for timely corticosteroid administration and referral to a high-performance tertiary care center. On the other hand, when the likelihood of delivery within seven days was low, they could consider and discuss the option of administering corticosteroids. A user-friendly interface and the inclusion of multiple risk factors were strengths of the present study. However, its single-center design and limited sample size were limitations of the present study.

Conclusion

In conclusion, AMA, higher GA, multiparity, PPROM, vaginal bleeding, treated UTI and history of PTD were identified as significant risk factors for the PD 7 model. The PD 7 model demonstrated sensitivity, specificity, PPV, NPV at a percentage of 72.7, 78.5, 77.9, and 73.4, respectively. The PD 7

model demonstrated good predictive performance. The model can be applied as a clinical decision-support tool to guide appropriate corticosteroid administration and timely referral, reducing unnecessary interventions. Incorporation of the PD 7 model into antenatal care practice and hospital protocols may enhance perinatal outcomes and promote standardized management of PTL.

What is already known about this topic?

PTL may lead to PTD between the 24^{+0} and the 36^{+6} weeks of gestation. Lung complications including respiratory failure, hypoglycemia, seizure, stillbirth, infant mortality, NEC, and IVH are consequences of PTD. Maternal risk factors include history of PTD, UTI, vaginal bleeding, and being overweight or obese, and were associated with PTD. PD 7 needed corticosteroid administration to promote lung maturity.

What does this study add?

AMA, longer GA, multiparity, PPROM, vaginal bleeding, treated UTI, and history of PTD are significant risk factors for PD 7. The PD 7 model was uploaded to the website base for easy access and could be used for clinical practice.

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Authors' contributions

NH and MP designed the research, collected, summarized, and analyzed the clinical data, and wrote the manuscript. MP is the corresponding author. KS and KB contributed to data collection, wrote and approved the final manuscript, and provided critical feedback. All authors read and approved of the final manuscript. Conceptualization and methodology: NH, MP, SP, and BS. Investigation: NH and MP. Formal analysis: NH, KS, and BS. Visualization and writing-original draft: NH, MP, and KS. Writing-review and editing: NH, MP, KS, and KB. Supervision: MP.

Data availability

The data supporting the findings of the present study are available upon reasonable request from the corresponding author.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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