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ORIGINAL ARTICLE

Medicine Science International Medical Journal

Medicine Science 2025;14(3):657-61

Recurrent preterm birth across three consecutive pregnancies: A retrospective cohort study in a tertiary care center

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Received 18 June 2025; Accepted 02 July 2025
Available online 18 August 2025 with doi: 10.5455/medscience.2025.06.158

Abstract

Preterm birth (PTB) remains a leading cause of neonatal morbidity and mortality globally. A prior PTB is a recognized predictor of recurrence; nonetheless, most existing studies have limited their focus to the first two pregnancies. We aimed to evaluate the risk of recurrent PTB across three consecutive singleton pregnancies. This retrospective cohort study analyzed data from 97,854 women with singleton pregnancies. Participants were stratified based on the gestational age at their first delivery, and PTB outcomes in subsequent pregnancies were assessed. Additionally, a sub-analysis of 11,760 women with three consecutive deliveries was conducted to assess the cumulative risk of recurrent PTB. The adjusted relative risk (aRR) for PTB was estimated using multivariable models. Among the study population, 12.3% (n=12,036) experienced PTB in their first pregnancy, of which 10.1% were spontaneous and 2.2% were medically indicated. The risk of PTB in the second pregnancy demonstrated an inverse relationship with gestational age at the first delivery: 8.6% for term, 19% for 34–36^6 weeks, 25.9% for 32–33^6 weeks, and 29.3% for deliveries under 32 weeks. The aRR for PTBs in the second pregnancy were 3.72 (34–36^6 weeks), 5.65 (32–33^6 weeks) and 6.21 (<32 weeks) compared with term births. The risk of PTB in the third pregnancy was lowest among women with two prior term births (4.8%) and increased progressively with each prior PTB: 15.6% (aRR=3.38) with preterm/term, 19.1% (aRR=5.34) with term/preterm, and 29.7% (aRR=9.87) with two prior PTBs. The likelihood of recurrent PTB rises with the number of previous preterm deliveries, being highest among women with two consecutive PTBs. A term delivery, especially as the most recent pregnancy, has a protective effect. By extending risk assessment to third pregnancies, this study provides novel insights that may guide targeted prevention strategies and improve counseling for women at elevated risk.

Keywords: Gestational age, pregnancy outcomes, preterm birth, recurrent preterm birth, protective factors

Introduction

Defined as delivery before 37 weeks of gestation, preterm birth (PTB) constitutes more than 10% of births globally and continues to be a major contributor to neonatal morbidity and mortality [1]. PTB ranks as the second leading cause of mortality in children under five, surpassed only by pneumonia [2]. Beyond its immediate effects on neonatal survival, PTB is linked to numerous long-term complications, such as neurodevelopmental delays, cognitive impairments, sensory deficits—including vision and hearing loss—and a heightened risk of chronic diseases in later life [3]. The probability of adverse outcomes decreases with increasing gestational age, with the highest rates of morbidity and mortality observed among extremely preterm neonates—those born before 28 weeks of gestation [4].

The underlying causes of PTB are diverse and involve multiple contributing factors. Clinically, PTB is generally classified into two main subtypes: medically indicated PTB, which is initiated by healthcare providers in response to maternal or fetal

CITATION
Balkas G, Erturk Aksakal S, Alan V, et al. Recurrent preterm birth across three consecutive pregnancies: A retrospective cohort study in a tertiary care center. Med Science. 2025;14(3):657-61.

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DOI: 10.5455/medscience.2025.06.158

compromise, and spontaneous PTB, triggered by spontaneous labor, either in the presence or absence of premature membrane rupture. Spontaneous PTB is often triggered by underlying pathophysiological processes, such as intrauterine infection, systemic or local inflammation, uteroplacental ischemia, maternal stress, cervical insufficiency, or hormonal dysregulation [5-7].

Of all established predictors of PTB, a prior history of PTB is considered the most reliable and significant indicator of recurrence [8]. The Preterm Prediction Study demonstrated that women with a prior PTB have a 2.5-fold higher likelihood of delivering before 37 weeks in a subsequent pregnancy compared to those without such a history [9]. This risk is influenced by several factors, such as the underlying etiology of the prior PTB, the gestational age at which it occurred, and the number of prior PTBs [10]. Although PTB recurrence is well-established, population-level data evaluating recurrence risk across multiple successive pregnancies remain limited.

In addition, racial and ethnic disparities in PTB rates have been well-documented [11]. Population-based studies have identified Black race as an independent risk factor for recurrent PTB, although these disparities remain under-explored in many international contexts [12]. According to data from the Turkish Ministry of Health, Türkiye's national PTB rate was 12.9% in 2022. Nevertheless, no official data are currently available on the incidence or risk factors associated with recurrent PTB in the Turkish population.

Accurate estimation of PTB recurrence is essential for delivering individualized, patient-centered antenatal care. Such estimations should be grounded in population-specific data and consider relevant clinical patterns. Accordingly, the primary aim of this study is to assess the occurrence and recurrence of PTB across successive pregnancies in the Turkish population.

While most large-scale epidemiological studies have focused primarily on recurrence between the first and second pregnancies, limited attention has been given to the sequence, gestational timing, and cumulative effect of prior PTBs. This gap hinders a comprehensive understanding of recurrence dynamics across multiple pregnancies. Notably, data on PTB risk in third pregnancies remain limited. In line with this, the secondary objective of the research is to evaluate the frequency of PTB in third gestations and examine how recurrence varies with the number, timing, and sequence of prior preterm deliveries.

Material and Methods

The study was carried out in compliance with the ethical principles of the Declaration of Helsinki and was approved by the Ethics Committee of Etlik Zübeyde Hanım Gynecology Training and Research Hospital (date: 21.12.2020, approval no: 18/25). Due to the retrospective design of the study, the Ethics Committee waived the requirement for informed consent. Women with singleton pregnancies of at least 20 weeks' gestation who delivered between January 2015 and December 2022 were included in this retrospective cohort study. The dataset was derived from electronic medical records and archived patient files maintained by the hospital. Pregnancies involving multiple gestations were excluded to ensure the analysis was limited to independent obstetric events.

Participants were classified based on the gestational age at their first delivery, categorized as either term (≥37 weeks) or preterm (<37 weeks). PTBs were further stratified into three groups—34–36^6 weeks, 32–33^6 weeks, and less than 32 weeks—and classified as either spontaneous or medically indicated. The recurrence of PTB was initially evaluated by comparing outcomes between the first and second pregnancies. The study population was then divided into four subgroups: (1) women who had term births in both pregnancies; (2) those with a preterm first birth and a subsequent term birth; (3) those with a term first birth and a subsequent PTB; and (4) women who experienced PTBs in both pregnancies. The outcomes of the third pregnancy were analysed in relation to the delivery outcomes of the previous two pregnancies. Gestational age was determined using the last menstrual period and validated by an ultrasound assessment of fetal crown–rump length performed between 11 and 14 weeks' gestation. Data on maternal characteristics—including age, smoking, and body mass index (BMI)—along with obstetric outcomes such as gestational age at delivery and PTB recurrence, were documented.

Data Analysis

Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequencies and percentages. Comparisons of categorical variables between groups were performed using the Chi-square test or Fisher's exact test. Relative risks (RRs) and their corresponding 95% confidence intervals (CIs) were calculated to assess the association between gestational age at first and second deliveries and the risk of subsequent preterm birth. Both unadjusted and adjusted RRs were reported. Multivariate analyses were conducted using log-binomial regression models adjusted for maternal age, smoking status, and BMI. In cases where model convergence was not achieved, Poisson regression with robust error variance was used as an alternative. Although p-values were calculated during analysis, they were not reported in the final tables, in line with the descriptive and comparative focus of the study.

Results

The study included a total of 97,854 women with singleton pregnancies. Maternal characteristics were analyzed among women with a term (≥37 weeks) or preterm (<37 weeks, spontaneous, or medically indicated) first birth, as presented in Table 1. Of these, 85,818 (87.7%) had a term birth, and 12,036 (12.3%) had a PTB, comprising 9,869 (10.1%) spontaneous and 2,167 (2.2%) medically indicated PTBs.

DOI: 10.5455/medscience.2025.06.158

Table 1. Maternal demographic characteristics of the study population in the first pregnancy

	Term birth ≥37 weeks (n=85818)	Preterm birth <37 weeks	
		Spontaneous (n=9869)	Medically indicated (n=2167)
Maternal age, n (%)			
≤19	7552 (8.8)	1816 (18.4)	238 (11)
20-34	69513 (81)	7106 (72)	1593 (73.5)
≥35	8753 (10.2)	947 (9.6)	336 (15.5)
Smoking status, n (%)	4291 (5)	730 (7.4)	169 (7.8)
BMI (kg/m²), n (%)			
<20	14589 (17)	2862 (29)	347 (16)
20-29	56125 (65.4)	5724 (58)	1365 (63)
≥30	15104 (17.6)	1283 (13)	455 (21)

BMI: body mass index

As shown in Table 2, gestational age at delivery in the second pregnancy was categorized by gestational age at first delivery. Among women with a term first birth, 91.4% delivered at term, and 8.6% had a PTB. Among women with a preterm first birth, the PTB rate in the second pregnancy was 19.0% for those with a first delivery at 34–36⁶ weeks, 25.9% for those at 32–33⁶ weeks, and 29.3% for those at <32 weeks.

Table 2. Distribution of gestational age at second delivery by gestational age at first delivery

Gestational age at delivery in the first pregnancy	Total n (%)	Gestational age at delivery in the second pregnancy (%)			
		≥37	34-36⁶	32-33⁶	<32
≥37 weeks	85818 (87.7)	78438 (91.4)	5750 (6.7)	1030 (1.2)	600 (0.7)
34-36⁶ weeks	9688 (9.9)	7847 (81)	1240 (12.8)	320 (3.3)	281 (2.9)
32-33⁶ weeks	1311 (1.3)	971 (74.1)	218 (16.6)	68 (5.2)	54 (4.1)
<32 weeks	1076 (1.1)	761 (70.7)	198 (18.4)	60 (5.6)	57 (5.3)

Table 3 presents adjusted relative risk (aRR) estimates for recurrent PTB in the second delivery. Compared with women who delivered at term in their first pregnancy (reference group; aRR=1.00), those with a first delivery at 34–36⁶ weeks had an aRR of 3.72 (95% CI: 3.284.05). The risk increased with decreasing gestational age: aRR=5.65 (95% CI: 4.63–6.25) for deliveries at 32–33⁶ weeks and aRR=6.21 (95% CI: 4.71–7.47) for deliveries at <32 weeks. Following adjustment for maternal demographic factors, including age, smoking and BMI, the aRRs remained significant, albeit slightly attenuated.

Table 3. The risk of preterm birth in the second pregnancy according to gestational age at first delivery

Gestational age at first delivery	Total n (%)	Preterm delivery in the second pregnancy	Preterm delivery <37 weeks in the second pregnancy	
			Unadjusted RR (95% CI)	Adjusted RR* (95% CI)
≥37	85818 (87.7)	7380 (8.6)	Referent	Referent
34-36⁶ weeks	6245 (6.4)	1187 (19)	3.96 (3.43-4.32)	3.72 (3.28-4.05)
32-33⁶ weeks	1311 (1.3)	340 (26)	5.934 (4.95-6.95)	5.65 (4.63-6.25)
<32 weeks	1076 (1.1)	315 (29.2)	6.32 (4.85-7.65)	6.21 (4.71-7.47)

RR: relative risk, CI: confidence interval, Models were adjusted for maternal age, body mass index and smoking status; *Relative risks and 95% confidence intervals were calculated using log-binomial regression models

As shown in Table 4, the analysis of PTB risk in the third pregnancy was conducted among 11,760 participants with three successive births, categorized by the outcomes of their first and second births. Women who delivered at term in both initial pregnancies (n=9,420, 80.1%) had a 4.8% rate of PTB in the third pregnancy and were used as the reference group (aRR=1.00). Among those with a PTB in the first delivery followed by a term second birth (n=1,032, 8.8%), 15.6% (aRR=3.38; 95% CI: 2.36–3.98) experienced a PTB in the third pregnancy. Women with a term birth in the first delivery and a PTB in the second (n=961, 8.2%) had a 19.1% rate of PTB in the third pregnancy (aRR=5.34; 95% CI: 4.23–6.32). The highest rate was observed among women with PTBs in both previous pregnancies (n=341, 2.9%), 29.7% of whom had a preterm third birth (aRR=9.87; 95% CI: 8.55-11.42).

DOI: 10.5455/medscience.2025.06.158

Table 4. Risk of preterm birth in the third pregnancy based on outcomes of the first and second deliveries

First delivery/second delivery	Total n (%)	Preterm in third birth, n (%)	Unadjusted RR (95% CI)	Adjusted RR* (95% CI)
Term birth/term birth	9420 (80.1)	452 (4.8)	Referent	Referent
Preterm birth/term birth	1032 (8.8)	161 (15.6)	3.42 (2.38-4.15)	3.38 (2.36-3.98)
Term birth/preterm birth	961 (8.2)	184 (19.1)	5.48 (4.71-6.21)	5.34 (4.23-6.32)
Preterm birth/preterm birth	341 (2.9)	101 (29.7)	10.12 (9.85-11.51)	9.87 (8.55-11.42)

RR: relative risk, CI: confidence interval, Models were adjusted for maternal age, body mass index and smoking status; *Relative risks and 95% confidence intervals were calculated using log-binomial regression models

Discussion

PTB remains a significant global public health issue, affecting approximately 13.4 million births globally in 2020 [12]. Complications related to PTB are the primary cause of mortality in children under five, contributing to an around 900,000 deaths in 2019 [13]. Importantly, three-quarters of these deaths are considered preventable through the use of currently available, cost-effective interventions. Beyond mortality, PTB is a leading contributor to neonatal morbidity and places a substantial economic burden on healthcare systems. Moreover, women with a prior history of PTB face a higher likelihood of experiencing anxiety in later pregnancies—an independent factor linked to an elevated risk of PTB and other adverse perinatal outcomes. These combined clinical, psychological, and economic consequences underscore the critical need to recognize high-risk women and implement targeted prevention strategies.

This retrospective cohort study provides robust evidence of a strong association between the timing of the first delivery and the risk of PTB in subsequent pregnancies. The findings indicate that women with earlier gestational ages at their first delivery had a significantly higher likelihood of PTB in their second pregnancy. The rate of PTB increased from 8.6% among women with a term first birth to 29.3% among those whose first delivery occurred before 32 weeks. Furthermore, our analysis of third pregnancies revealed a stepwise increase in PTB risk with each prior PTB. Women who had experienced PTBs in both their first and second pregnancies were found to be at the highest risk, with approximately a ten-fold increased likelihood of preterm delivery in the third pregnancy than those with two previous term births. Conversely, having at least one prior term birth was linked to a decreased risk of preterm delivery in the third pregnancy, with the most pronounced protective effect observed when the most recent pregnancy resulted in a term birth.

These findings are consistent with previous research that identified a prior PTB as the most reliable indicator of recurrence. Mercer et al. [9] reported that individuals who had previously experienced a spontaneous PTB faced a significantly increased risk of recurrence, particularly when the initial PTB occurred at an earlier gestational age. Their analysis showed that those with a prior spontaneous PTB had a 2.5-fold higher recurrence risk compared to those with no such history (21.7% vs. 8.8%). Ananth et al. [14] similarly demonstrated a three- to seven-fold increased risk of recurrent PTB, regardless of whether the initial PTB was spontaneous or medically indicated. Moreover, their findings indicated that women with a previous medically indicated preterm delivery were at risk not only for another medically indicated preterm delivery but also for subsequent spontaneous preterm delivery. Laughon et al. [15] further demonstrated that a history of spontaneous PTB conferred a RR of 5.64 for experiencing another spontaneous PTB, and an RR of 1.61 for a subsequent medically indicated PTB, highlighting overlapping etiological pathways. A history of indicated PTB also conferred a strong recurrence risk for the same subtype and an elevated risk for spontaneous PTB. These findings support the hypothesis that PTB phenotypes share common pathophysiological mechanisms and underscore the clinical importance of monitoring recurrence risk, including in women with medically indicated or spontaneous initial PTBs.

Unlike most previous studies, which have primarily focused on the first two pregnancies, our research also included outcomes from third births, offering a more comprehensive understanding of PTB recurrence patterns. This study observed a significantly increased risk of preterm delivery in the third pregnancy among women with one or more previous PTBs, with the highest PTB rate (29.7%) in those with PTBs in both previous pregnancies. Our findings are in agreement with those reported by McManemy et al. [16], who observed a 42% recurrence risk of PTB in the third pregnancy among women with PTBs in both prior pregnancies, with recurrence rates ranging from 38% to 57% based on gestational age at prior deliveries. McManemy et al. [16] further reported that third pregnancy PTB risk varied by pregnancy sequence, women whose second pregnancy resulted in a PTB were more likely to experience a third PTB (21%) than those whose first delivery was preterm but second was term (13%). Correspondingly, this study observed third pregnancy PTB rates of 19.1% among women whose first birth was at term followed by a PTB, and 15.6% among those with a preterm first birth followed by a term birth, consistent with the sequence-based findings of McManemy et al. [16]. However, a study by Ouh et al. [17] found no statistical evidence of a difference in PTB risk in the third pregnancy between women with a single PTB in the second pregnancy and those with two consecutive PTBs. The authors suggested that short interpregnancy intervals following a PTB, more common among women with recurrent PTB, may impair uterine recovery, particularly in terms of resolving inflammation and restoring normal uterine function, thus increasing recurrence risk.

DOI: 10.5455/medscience.2025.06.158

Several limitations of this study should be taken into account when interpreting the results. Firstly, the retrospective nature of the study may have introduced certain biases, including potential misclassification or incomplete data, particularly regarding gestational age and obstetric history. Second, although adjustments were made for several maternal characteristics (e.g., age, BMI, and smoking status), residual confounding from unmeasured variables – such as cervical length, interpregnancy interval, socio-economic status, or prior obstetric interventions (e.g., progesterone therapy or cerclage) – may influence the observed associations. Third, the inability to differentiate between spontaneous and medically indicated PTBs limits the ability to draw conclusions about the underlying pathophysiological mechanisms, which likely differ by subtype. These two forms of PTB have distinct etiologies, clinical trajectories, and implications for recurrence. Fourth, factors such as the quality of antenatal care, infection status, or maternal comorbidities (e.g., hypertensive disorders or diabetes) were not assessed, though they may significantly affect PTB risk. Fifth, the study population was drawn from a national database of a single institution, potentially restricting the applicability of the findings to populations with differing demographic profiles, healthcare systems, or obstetric practices.

Despite these limitations, the large sample size and detailed evaluation of PTB recurrence across three consecutive pregnancies offer meaningful insights into risk stratification and clinical decision-making for women with a history of PTB. The findings support the development of individualized surveillance protocols and targeted preventive strategies in subsequent pregnancies. Notably, the inclusion of third-pregnancy outcomes represents a novel contribution to the existing body of the literature, which has largely concentrated on earlier parities. Based on the available literature, this appears to be the first study conducted in Türkiye to evaluate the recurrence of PTB across three consecutive pregnancies, thereby providing a valuable foundation for enhancing long-term maternal and neonatal health outcomes.

Conclusion

This study demonstrates a stepwise increase in the risk of PTB with each prior preterm delivery, with the greatest risk observed in women with two consecutive PTBs. Having a previous term birth—especially as the most recent delivery—was linked to a reduced risk of recurrent PTB. Given that PTB remains the primary cause of neonatal morbidity and mortality, these findings provide important guidance for risk stratification and patient counseling. By including third-pregnancy outcomes, this study offers a novel contribution to the literature and may inform targeted interventions in high-risk populations.

Conflict of Interests
The authors declare that there is no conflict of interest in the study.

Financial Disclosure
The authors declare that they have received no financial support for the study.

Ethical Approval
This study received ethical approval from the Ethics Committee of Etlik Zübeyde Hanım Gynecology Training and Research Hospital (approval date: 21/12/2020, approval no: 18/25).

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