



Full length article

Spontaneous and iatrogenic preterm birth rates among unselected women in three consecutive pregnancies[☆]



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ABSTRACT

Objective: To assess the risk of sPTB and iPTB in women with three consecutive singleton pregnancies and the impact of the outcome of the 1st and 2nd pregnancy on the (recurrent) PTB risk in the 3rd pregnancy. **Study design:** A nationwide retrospective cohort study using the population based longitudinal linked dataset of the Netherlands. We included all nulliparous women with three consecutive singleton pregnancies ending between 22 and 44 weeks of gestation between 1999 and 2009. We excluded congenital abnormalities and stillbirths. We compared the incidence of sPTB and iPTB in the three pregnancies (<37, <34 and <30 weeks). Logistic regression analysis was performed to predict PTB in the 3rd pregnancy, adjusting for maternal age, fetal gender, socio-economic status, hypertension, interpregnancy interval, artificial reproductive technology, and small for gestational age. Analyses were also performed stratified by prior PTB subtype, gestational age and combined outcome of the 1st and 2nd pregnancy.

Results: We studied 52,978 women. PTB occurred in 7.0%, 3.7% and 3.4% in the 1st, 2nd and 3rd pregnancy, respectively. The outcome of the 2nd pregnancy is more predictive for PTB in the 3rd pregnancy than the outcome of the 1st pregnancy (sPTB aOR 7.3 (95%CI 6.3–8.4) and iPTB (aOR 5.9 (95% CI 4.5–7.9) in 2nd pregnancy vs. sPTB aOR 3.0 (95% CI 2.6–3.4) and iPTB aOR 2.7 (95% CI 2.1–3.4) in the 1st pregnancy). In the prediction of sPTB in the 3rd pregnancy, sPTB in the 2nd pregnancy is most predictive (aOR 8.2 (95% CI 7.1–9.6) and for prediction iPTB in the 3rd pregnancy, iPTB in the 2nd pregnancy is most predictive (aOR 12.1 (95% CI 8.5–17.2).

Conclusion: We studied a population with three subsequent singleton deliveries within 10 year. The incidence of PTB decreased with 50% from the 1st to the 2nd pregnancy, to then stay relative stable in the 3rd pregnancy. Compared to PTB in the 1st pregnancy, PTB in the 2nd pregnancy is more predictive for the occurrence of PTB in the 3rd pregnancy.

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Introduction

Preterm birth (PTB) is the leading cause of neonatal morbidity and mortality both in well resourced and in low resourced countries. In 2010 over 10% of all children worldwide were born

preterm [1]. PTB is defined as any birth before 37 completed weeks of gestation, but often a subdivision to express the severity of PTB is used (i.e. severe PTB <30 weeks, moderate PTB 30–34 weeks and mild PTB 34–37 weeks). This subdivision is important since increasing gestational age (GA) at birth is associated with decreasing mortality, morbidity and intensity of neonatal care, and hence decreasing costs.

PTB can be subdivided in spontaneous and iatrogenic PTB. Spontaneous PTB (sPTB) is associated with an increased risk of sPTB in a subsequent pregnancy, with increasing risk with the number of prior PTBs, earlier GA at prior delivery, and with higher risk of subsequent PTB if the immediately preceding birth was

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preterm [2]. Iatrogenic PTB (iPTB) is performed for maternal or fetal reasons, for example pre-eclampsia or intra-uterine growth restriction, respectively.

Emerging data suggests that sPTB and iPTB at least partially share a pathophysiological mechanism involving placental dysfunction or inflammation of the placenta or membranes [3–7]. Improper remodelling of the uterine spiral arteries in early pregnancy and subsequent decidual changes may lead to reduced placental perfusion. This can cause PTB as well as subsequent dysfunction of the maternal vascular endothelium, leading to pre-eclampsia and subsequent iatrogenic PTB. However, our understanding of recurrent sPTB risk has mainly focused on sPTB and has not taken iPTB into consideration, and vice versa.

Here, we study the incidence of spontaneous and iatrogenic PTB rates in unselected women with three subsequent singleton pregnancies both on population and individual level. We also study the risk of (recurrent) PTB in the third pregnancy in relation to GA at delivery and type of PTB in previous pregnancies.

Material and methods

For this nationwide retrospective cohort study we used data from the Perinatal Registry in the Netherlands (PRN). The PRN consists of nationwide population-based data that contain information on pregnancies, deliveries ≥ 22 weeks of gestation and a birth weight of ≥ 500 g, and readmissions until 28 days after birth. The PRN database is obtained by a validated linkage of three different registries: the midwifery registry (LVR1), the obstetrics registry (LVR2), and the neonatology registry (LNR) of hospital admissions of newborns [8]. Longitudinal linkage of these databases has been described previously [9–11]. The PRN registry covers about 96% of all deliveries in the Netherlands. As all data were registered anonymous, separate ethical approval was not needed for this study under Dutch law. The PRN gave permission for this study (approval number 11.44).

We studied data of all women with three consecutive singleton pregnancies who gave birth between January 1, 1999, and December 31, 2009. We included women who delivered between 22–44 weeks of GA and excluded women who had any pregnancy complicated by stillbirth or congenital anomalies, leaving women with three consecutive singleton pregnancies with a live birth.

Calculation of GA was based on the women's last menstrual period and ultrasound dating. PTB was defined as delivery before 37 weeks of gestation. We made a subdivision for severity of PTB into three groups with severe PTB defined as a birth before 30 weeks of gestation, moderate PTB as a birth between 30–34 weeks and mild PTB as a birth between 34–37 weeks of gestation.

Furthermore we divided PTB in spontaneous and iatrogenic PTB, leading to a total of six subgroups. Spontaneous PTB was defined as PTB starting with a spontaneous rupture of the membranes or spontaneous contractions. Iatrogenic PTB was defined as an elective Caesarian section or induction of labour.

The overall incidences of PTB separated in the 6 subcategories are given for the 1st, 2nd and 3rd pregnancy on a population level.

Subsequently, a logistic regression analysis was performed to assess the association between pregnancy outcome of the 1st and 2nd pregnancy and the risk of (recurrent) PTB <37 weeks in the 3rd pregnancy, both for overall PTB and separated for iatrogenic and spontaneous PTB. We defined the outcome of the 1st and 2nd pregnancy as spontaneous or iatrogenic PTB and by the severity of PTB (i.e. <30, 30–34 and 34–37 weeks of gestation). In a multivariate analysis we adjusted for maternal age, fetal gender, artificial reproductive technology (ART), low social-economic-status (SES), hypertension, interpregnancy interval and small for gestational age (SGA).

Similar analyses were performed to assess the (recurrent) overall PTB risk <37 weeks in the 3rd pregnancy, in which the previous pregnancy outcomes were separated by GA per week for spontaneous and iatrogenic PTB in the 1st and 2nd pregnancy. Also, the (recurrent) PTB risk in the 3rd pregnancy,

Table 1
Baseline characteristics of the total cohort (n = 52,978) and separated by the outcome of the third pregnancy.

Characteristics	In which pregnancy	Total cohort (n = 52,978)	Separated by outcome of third pregnancy			
			No PTB (n = 51,193)	iPTB (n = 448)	sPTB (n = 1337)	
Mean maternal age at delivery (yrs, \pm SD)	1st	27.5 \pm 4.0	27.5 \pm 4.0	27.3 \pm 4.3	26.4 \pm 4.5	
	2nd	29.7 \pm 3.9	29.7 \pm 3.9	29.6 \pm 4.2	28.7 \pm 4.4	
	3rd	32.4 \pm 3.9	32.5 \pm 3.9	32.5 \pm 4.2	31.4 \pm 4.6	
Non-white European ethnicity n (%)	3rd	7,342 (13.9%)	6998 (13.7%)	76 (17.0%)	268 (20.0%)	
	Low SES n (%)	1st	11,787 (22.3%)	11,294 (22.0%)	123 (27.5%)	338 (29.0%)
		2nd	11,203 (21.2%)	10,762 (21.0%)	117 (26.1%)	379 (28.4%)
Conception by ART n (%)	3rd	10,721 (20.3%)	10,298 (20.1%)	112 (25.0%)	366 (27.3%)	
	1st	1,307 (2.5%)	1,259 (2.5%)	17 (3.8%)	37 (2.8%)	
	2nd	693 (1.3%)	658 (1.3%)	10 (2.2%)	26 (1.9%)	
Male Fetus n (%)	3rd	283 (0.5%)	263 (0.5%)	7 (1.6%)	13 (1.0%)	
	1st	27,528 (52.2%)	26,692 (52.1%)	253 (56.5%)	698 (52.2%)	
	2nd	27,362 (51.9%)	26,509 (51.8%)	253 (56.5%)	717 (53.6%)	
Mean GA at delivery (w + d \pm SD)	3rd	26,845 (50.9%)	25,955 (50.7%)	234 (52.2%)	771 (57.7%)	
	1st	39 + 2 \pm 2.2	39 + 2 \pm 2.2	37 + 5 \pm 3.6	37 + 4 \pm 3.5	
	2nd	39 + 3 \pm 1.8	39 + 3 \pm 1.7	37 + 6 \pm 3.1	37 + 3 \pm 3.3	
Birth weight (g, \pm SD)	3rd	39 + 3 \pm 1.6	39 + 4 \pm 1.2	33 + 5 \pm 3.2	34 + 3 \pm 2.7	
	1st	3385 \pm 600	3400 \pm 588	3012 \pm 848	2957 \pm 768	
	2nd	3585 \pm 555	3602 \pm 540	3162 \pm 788	3073 \pm 723	
Hypertensive disorder n (%)	3rd	3626 \pm 544	3667 \pm 491	2252 \pm 793	2530 \pm 636	
	1st	6,102 (11.6%)	5828 (11.4%)	122 (27.2%)	178 (13.3%)	
	2nd	2,798 (5.3%)	2,629 (5.1%)	92 (20.5%)	93 (7.0%)	
Mean pregnancy interval (months \pm SD)	3rd	2,621 (5.0%)	2,379 (4.7%)	141 (31.5%)	103 (7.7%)	
	1 \rightarrow 2	17.4 \pm 11.3	17.4 \pm 11.3	18.8 \pm 12.9	19.4 \pm 13.2	
	2 \rightarrow 3	23.8 \pm 14.9	23.7 \pm 14.8	26.4 \pm 17.5	24.2 \pm 16.8	

PTB = preterm birth, iPTB = iatrogenic preterm birth, sPTB = spontaneous preterm birth, SES = socio-economic status, ART = artificial reproductive technology, GA = gestational age.

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