

BMJ Open Association between uterine contractions before elective caesarean section and transient tachypnoea of the newborn: a retrospective cohort study

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ABSTRACT

Objective We evaluated the association between the presence of predelivery uterine contractions and transient tachypnoea of the newborn (TTN) in women undergoing an elective caesarean section.

Design A retrospective cohort study.

Setting National Hospital Organization Kofu National Hospital, which is a community hospital, between January 2011 and May 2019.

Participants The study included 464 women who underwent elective caesarean section. The exclusion criteria were missing data, twin pregnancy, neonatal asphyxia, general anaesthesia and elective caesarean section before term.

Primary and secondary outcome measures Patients were grouped according to the presence or absence of uterine contractions on a 40-min cardiotocogram (CTG) performed within 6 hours before caesarean delivery. We performed a multivariable logistic regression analysis to examine the association between predelivery uterine contractions and TTN.

Results The incidence of TTN was 9.9% (46/464), and 38.4% (178/464) of patients had no uterine contraction. The absence of uterine contractions was significantly associated with an increased risk of TTN (adjusted OR 2.04; 95% CI 1.09 to 3.82) after controlling for gestational diabetes mellitus, small for gestational age, male sex and caesarean section at 37 weeks.

Conclusions Accurate risk stratification using a CTG could assist in the management of infants who are at risk of developing TTN.

INTRODUCTION

Transient tachypnoea of the newborn (TTN) is a parenchymal lung disorder characterised by pulmonary oedema resulting from delayed resorption and clearance of fetal alveolar fluid.¹ Clinical characteristics appear shortly after delivery and include tachypnoea, nasal flaring and grunting.^{1–3} TTN is a common cause of respiratory distress in late preterm and term infants and is generally a benign disease treated with a brief course of oxygen.^{4–6} However, some patients develop severe respiratory distress immediately after

Strengths and limitations of this study

- We used the findings of an objective test to evaluate the risk of transient tachypnoea of the newborn, thus avoiding complicated or subjective patient examinations.
- Our study population was limited to women undergoing an elective caesarean section, and our analysis was adjusted for many known risk factors of transient tachypnoea of the newborn.
- Our study was a retrospective, single-centre study.
- Our analysis did not control for maternal asthma, which is a known risk factor of transient tachypnoea of the newborn.

birth and require invasive or non-invasive respiratory support.^{7 8}

Several studies have demonstrated that catecholamines play an important role in fetal alveolar fluid clearance,^{9–11} a process that begins before term birth and continues through labour and after delivery.¹ The spontaneous surge in catecholamine secretion caused by uterine contractions is particularly important for fetal alveolar fluid clearance,¹² and previous studies found that elective caesarean section before the onset of labour is a significant risk factor for TTN.^{3 13 14} The number of elective caesarean sections has increased in Japan over the last decades, and the caesarean section rate reached 11.5% in 2013.¹⁵ The elective caesarean section rate is expected to continue to increase due to increased maternal age,¹⁶ multiple gestations after fertility treatment¹⁷ and maternal request.¹⁸ Inevitably, the number of newborns with TTN will also increase. Therefore, it is important to completely understand the risk factors of TTN.

Many reports indicate that caesarean section before the onset of labour is a risk factor for TTN.^{3 13 14} However, another study found conflicting results.³ The problem



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appears to be the lack of consensus on the definition of labour onset between these studies and worldwide.¹⁹ Furthermore, the different definitions of labour onset are based on various features, including cervical dilatation, cervical effacement and uterine contractions.¹⁹ Therefore, these studies are still open for further consideration. Given the ambiguity surrounding the onset of labour, we examined the relationship between the presence of uterine contractions before caesarean section alone and TTN rather than considering all features of the onset of labour. Furthermore, no study to date has used the presence of uterine contractions to identify newborns at risk of developing TTN. Therefore, we aimed to examine the association between the presence of uterine contractions before an elective caesarean section and TTN.

METHODS

Study design

We performed a retrospective observational cohort study of women who underwent an elective caesarean section with spinal and epidural anaesthesia between January 2011 and May 2019 at the National Hospital Organization Kofu National Hospital, which is a community hospital. We excluded women with multiple pregnancies, missing data and those who underwent an elective caesarean section before a term delivery. In addition, we excluded cases in which the infant had neonatal asphyxia. The Human Subjects Review Committee of the National Hospital Organization Kofu National Hospital reviewed and approved the study protocol and waived the need for informed consent because of the retrospective study design. However, patients were provided the opportunity to refuse the usage of their data through the hospital's website. All procedures were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Data collection

We collected obstetric data from medical and operative records. We recorded maternal age, parity, gestational age at delivery, prepregnancy weight status and maternal weight gain. Additionally, we assessed the presence of gestational diabetes mellitus (GDM), small for gestational age (SGA), infant sex and neonatal asphyxia. These potential confounding factors have been previously described as TTN risk factors.^{13 20 21} During the study period, 523 women underwent elective caesarean section. A total of 59 (missing data, n=12; twin pregnancy, n=38; neonatal asphyxia, n=2; general anaesthesia, n=1; elective caesarean section before term delivery, n=6) were excluded. Cases of neonatal asphyxia were excluded because this diagnosis was statistically underrepresented in our study sample.

The women were grouped according to the presence or absence of uterine contractions on a 40 min cardiotocogram (CTG) obtained within 6 hours before caesarean section. CTG, which records fetal heart rate and uterine

contraction, is typically used to assess fetal well-being. In this study, CTG data were recorded using an actocardiograph (Toitu MT-516GE; Tofa Medical, Malvern, Pennsylvania). The prepregnancy body mass index (BMI) was calculated according to the WHO standard (body weight/height squared (kg/m^2)). Maternal weight gain during pregnancy was calculated by subtracting the patient's prepregnancy body weight from her body weight at the last prenatal visit before delivery. We defined SGA as a weight below the 10th percentile in each gestational week.²² The diagnosis of GDM was made if there was at least one abnormal plasma glucose value (≥ 92 , 180 and 153 mg/dL for fasting, 1-hour and 2-hour plasma glucose concentration, respectively) after a 75 g oral glucose tolerance test.²³

Neonatal asphyxia was defined as an Apgar score remaining less than 7 at 5 min after birth or as an arterial blood pH of less than 7.00.²⁴ A diagnosis of TTN, which was the outcome of interest in this study, required each of the following: respiratory rate >60 breaths/min, constant tachypnoea for ≥ 12 hours, prominent central pulmonary vessels or thickened interlobar fissures on a chest X-ray and exclusion of other causes of respiratory distress, such as surfactant deficiency, pneumonia, meconium aspiration, congenital heart disease or metabolic disorder.²⁵ A neonatologist diagnosed TTN based on the above diagnostic criteria in the first few hours after a baby was born. Moreover, when the neonatologist diagnosed TTN, all infants were treated in the neonatal intensive care unit.

Statistical analyses

The Mann-Whitney U test and χ^2 test (or Fisher's exact test when the expected frequency was <5) were used to evaluate the effects of potential confounding factors of TTN. The Mann-Whitney U test was used to analyse continuous variables such as maternal age, and the χ^2 test (or Fisher's exact test when the expected frequency was <5) was used for categorical variables such as incidence of obstetric complications. A multiple logistic regression model was used to identify the variables significantly associated with TTN. The logistic regression models were adjusted by uterine contraction, GDM, SGA infants, infant sex and gestational age at delivery. All analyses were performed using the Bell Curve for Excel (Social Survey Research Information, Tokyo, Japan) and IBM SPSS Statistics for Windows V.25. The significance level was set at $p < 0.05$.

Patient and public involvement

Patients were not invited to comment on the study design and were not consulted to develop patient-relevant outcomes or interpret the results.

RESULTS

A total of 464 women were considered eligible for inclusion in this study. The mean maternal age was 32.8 ± 5.1 years, and the mean maternal prepregnancy BMI was $21.7 \pm 3.9 \text{ kg}/\text{m}^2$, with 124 (26.7%) nulliparous women,

Table 1 Clinical characteristics of the groups with and without uterine contractions

Variable*	Uterine contraction (-) (n=178)	Uterine contraction (+) (n=286)	P value
Maternal age, years	33.0±5.2	32.7±5.0	0.49
Nulliparity	45 (25.3)	79 (27.6)	0.58
Repeat caesarean section	119 (66.9)	189 (65.0)	0.86
Prepregnancy BMI, kg/m ²	22.1±3.5	21.4±4.1	0.005
Birth weight, g	2839±320	2868±345	0.41
GDM	11 (6.2)	19 (6.6)	0.84
SGA	14 (7.9)	20 (7.0)	0.73
Male infant	90 (50.5)	144 (50.3)	0.96
TTN	25 (14.0)	21 (7.3)	0.02

Values are presented as the mean±SD or number (%).

*The Mann-Whitney U test was used to analyse continuous variables such as maternal age, and the χ^2 test (or Fisher's exact test when the expected frequency was <5) was used for categorical variables such as incidence of obstetric complications.

BMI, body mass index; GDM, gestational diabetes mellitus; SGA, small for gestational age; TTN, transient tachypnoea of the newborn.

234 male infants (50.4%), 30 GDM women (6.5%) and 34 (7.3%) SGA infants. The indications for elective caesarean sections were previous caesarean section (n=308, 66.4%), breech presentation (n=79), placenta praevia or low lying placenta (n=23), prior myomectomy (n=17), maternal disorders (n=7), cephalopelvic disproportion (n=5) and other causes (n=25).

The overall incidence of TTN was 46 (9.9%). The prepregnancy BMI was significantly higher in patients without uterine contractions, and no other significant difference was noted between the groups (table 1).

TTN occurred more frequently in women without uterine contractions (table 2), and the prevalence of TTN was significantly higher in patients without uterine contractions than in those with uterine contractions (14.0% vs 7.3%, p=0.02) (table 1).

On multivariate analyses, no uterine contraction (adjusted OR 2.04; 95% CI 1.09 to 3.82) and caesarean section at 37 weeks (adjusted OR 2.47; 95% CI 1.30 to 4.69) were associated with TTN (table 3).

Table 2 Prevalence of TTN according to number of uterine contractions before caesarean section

No of uterine contraction(s)	Prevalence of TTN*
0	25/178 (14.0)
1	4/59 (6.8)
2	8/79 (10.1)
3	1/48 (2.1)
4	1/28 (3.6)
5	2/18 (11.1)
6≥	5/54 (9.1)

*Values are presented as the number of TTN per number of women stratified according to the number of uterine contractions (percentage).

TTN, transient tachypnoea of the newborn.

DISCUSSION

In this study of women undergoing an elective caesarean section, a lack of preprocedure uterine contractions was significantly associated with TTN after adjusting for potential confounding factors. To our knowledge, this investigation is the first detailed examination of the association between uterine contractions before elective caesarean section and the incidence of TTN.

Uterine contractions during labour cause an increase in stress hormones, such as cortisol and catecholamines.⁹⁻¹¹ During late gestation, the number of functional sodium channels in the fetal lungs increases in response to increased concentrations of stress hormones.⁹⁻¹² Consequently, the mature lung epithelium switches from actively secreting chloride and liquid into the air spaces to actively reabsorbing sodium and liquid.¹¹ However, sodium channels remain inactive during elective caesarean sections because the stress hormone level is low. Thus, compared with vaginal birth, elective caesarean section more frequently results in TTN.¹¹

A previous population-based case-controlled study reported that precaesarean section labour is not protective against TTN.³ In that study, labour was defined as any indication of labour, including precipitous labour, prolonged labour, induction of labour, stimulated labour and dysfunctional labour. As in our study, the researchers grouped women based on the presence or absence of uterine contractions and examined the relationship between TTN and caesarean section. However, their study had limitations that ours did not, including its inability to distinguish between elective and emergency caesarean sections. As several other investigators have concluded, there is a well-described physiological mechanism that explains why uterine contractions could reduce the incidence of TTN.^{13 14 26}

The time before the onset of labour can be further subdivided to clarify fetal alveolar fluid clearance. For example, in Japan, the diagnosis of labour onset was

**Table 3** Crude and adjusted odds ratios of risk factors for TTN

Variable	TTN (n)	Non-TTN (n)	Crude		Adjusted	
			OR	95% CI	OR	95% CI
Uterine contraction						
Present	21	265	1.0	Reference	1.0	Reference
Absent	25	153	2.06	1.12 to 3.81	2.04	1.09 to 3.82
GDM						
No	45	389	1.0	Reference	1.0	Reference
Yes	1	29	0.29	0.04 to 2.24	0.31	0.04 to 2.39
SGA						
No	39	391	1.0	Reference	1.0	Reference
Yes	7	27	2.59	1.06 to 6.36	2.49	0.99 to 6.32
Male infant						
No	18	212	1.0	Reference	1.0	Reference
Yes	28	206	1.60	0.86 to 2.98	1.55	0.82 to 2.93
Caesarean section						
≥38 weeks	17	250	1.0	Reference	1.0	Reference
37 weeks	29	168	2.53	1.35 to 4.77	2.47	1.30 to 4.69

GDM, gestational diabetes mellitus; SGA, small for gestational age; TTN, transient tachypnoea of the newborn.

defined as six regular uterine contractions per hour.²³ Although the period without uterine contractions and that with five regular contractions per hour both occur before the onset of labour, it seems that the effect of each period on stress hormone secretion is not the same. Our results demonstrate that the frequency of TTN is higher in patients with no uterine contractions than in patients with contractions. Although several studies evaluated the association between TTN and events occurring before labour and elective caesarean section,^{3 13 14} there is no consensus on the definition of the onset of labour. For example, the onset of labour was described by Senturk *et al*²⁶ as the onset of uterine contractions with labour pain and by Derbent *et al*²⁷ as regular uterine contractions and cervix effacement with dilatation of 2 cm or more. Meanwhile, Tutdibi *et al*¹³ did not define the onset of labour in detail in their study. The diagnosis of labour onset may depend on the subjective opinion of the obstetrician or midwife. Objective indicators that can easily be determined are needed to identify TTN risk factors. This is important because recently, in Japan, relatively few institutions allow vaginal birth after caesarean section, as they are concerned about uterine rupture, with only approximately 30% of institutions allowing planned vaginal birth as an option after caesarean section.²⁸ Antepartum CTG can be routinely performed before elective caesarean section without additional cost to easily and objectively determine the presence or absence of uterine contractions. As TTN is difficult to prevent, obstetricians, paediatricians and other medical professionals involved in an elective caesarean section should be aware of the risk factors of this complication and prepared to administer treatment.

Previous reports indicate that a caesarean section at 37 weeks is a major TTN risk factor,^{29 30} and our findings support this conclusion. In our study, 16 (21.1%) of 76 women with no uterine contractions who underwent a caesarean section at 37 weeks delivered an infant who developed TTN (data not shown).

Our study has limitations. First, this was a single-centre study, and it might be difficult to extrapolate our results to the general population. Therefore, a large-scale, multi-centre, prospective cohort study is needed to confirm our results in the general population. Second, we did not evaluate some potential TTN risk factors, including maternal asthma³¹ and low infant thyroid hormone level,³² and there is the possibility that unmeasured confounders may be associated with TTN in this study. Third, the generalisability of our findings may be limited by the homogeneity of this cohort, which only included Japanese women.

In conclusion, although studies with larger sample size are required, we found that a lack of uterine contractions before an elective caesarean section was significantly associated with TTN. Accurate risk stratification using a CTG could assist in the management of infants who are at risk of developing TTN.

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