

## Risk Factors for Transient Tachypnea of the Newborn in Infants Delivered Vaginally at 37 Weeks or Later

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### Abstract

In this case-control study, we examined infants delivered vaginally at 37 weeks or later to identify factors associated with transient tachypnea of the newborn (TTN). We reviewed the obstetric records of all vaginal deliveries at the Japanese Red Cross Katsushika Maternity Hospital from 2005 through 2007. Demographic information and the characteristics of labor were extracted from patient charts. Multivariate analysis identified that the incidence of TTN was significantly associated with nulliparity; a history of infertility therapy, such as in vitro fertilization; augmentation of labor; nonreassuring fetal status; vacuum/forceps delivery; and low Apgar score (<7) at 1 and 5 minutes. In addition, a low Apgar score at 1 minute was the factor most strongly associated with the incidence of TTN (adjusted odds ratio, 20; 95% confidence intervals, 12–34;  $p < 0.001$ ). The present results indicate that the improvement of obstetric surveillance to diminish the frequency of low Apgar scores is important for preventing TTN in infants delivered vaginally at 37 weeks or later.

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**Key words:** risk factor, transient tachypnea of the newborn, vaginal delivery, term, low Apgar score

### Introduction

Transient tachypnea of the newborn (TTN) is a condition characterized by tachypnea that develops shortly after birth but resolves within 2 to 5 days<sup>1–3</sup>. Delayed resorption of pulmonary fluid has been accepted as the central problem of this condition<sup>12</sup>. TTN has been reported to occur more frequently in preterm birth, cesarean delivery, maternal sedation, perinatal asphyxia, maternal asthma, and birth of

male infants<sup>3–5</sup>. However, there have been few studies of risk factors for TTN in infants delivered vaginally at term ( $\geq 37$  weeks' gestation). In this case-control study, we examined infants vaginally delivered at 37 weeks and later to identify the factors associated with TTN.

### Patients and Methods

We reviewed the obstetric records of all vaginal deliveries at 37 weeks or later in Japanese Red

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Table 1 Relation between gestational age at delivery and incidence of transient tachypnea of newborn following vaginal delivery at 37 weeks and more

	Control	TTN	Crude OR	95% CI	P-value
Number	4,078	156			
Gestational age at delivery					
37 weeks	257 (6)	13 (8)	1.4	0.76–2.4	0.31
38 weeks	665 (16)	32 (21)	1.3	0.89–2.0	0.16
39 weeks	1,253 (31)	47 (30)	0.97	0.69–1.4	0.87
40 weeks	1,271 (31)	38 (24)	0.71	0.49–1.0	0.071
41 weeks	618 (15)	23 (15)	0.97	0.62–1.5	0.89
42 weeks	14 (0)	2 (1)	3.8	0.85–17	0.061

Cross Katsushika Maternity Hospital from 2005 through 2007. Because our institution was not a general hospital, none of the pregnant women had chronic hypertension, diabetes mellitus, or bronchial asthma. The diagnosis of TTN was established with clinical and radiology data and by excluding other causes of respiratory distress. Demographic information and the characteristics of labor were extracted from patient charts. Potential risk factors for TTN were selected according to previous studies of TTN after various deliveries<sup>3-5</sup>: maternal age, parity, gestational age at delivery, history of infertility, pregnancy-induced hypertension, premature rupture of membranes, induction or augmentation or both of labor, duration of labor, fetal status, mode of delivery, neonatal birth weight, nuchal cord entanglements, Apgar score of the neonates, and umbilical arterial pH.

Cases and controls were compared by means of the  $\chi^2$  or Fisher's exact test for categorical variables. Odds ratios (ORs) and 95% confidence intervals (CIs) were also calculated. Statistical analyses were performed with the statistical software SAS version 8.02 (SAS Institute, Cary, NC, USA), and differences with  $P < 0.05$  were considered significant. Variables used in the multivariate model were those that on univariate analysis had shown marginal significance ( $p < 0.3$  in **Table 2**) toward association with increased risk of TTN. Logistic regression was then performed to identify the factors most strongly associated with TTN in a multivariate model.

## Results

During this period, there were 4,234 infants delivered vaginally at  $\geq 37$  weeks' gestation (4,128 singleton, 16 monochorionic-diamniotic twin pregnancies, and 32 dichorionic-diamniotic twin pregnancies). Of these infants, 156 (3.7%) had TTN. The rate of TTN in vaginal deliveries was significantly lower than that with elective cesarean delivery (8.2%; 67 of 814 infants,  $p < 0.001$ ) or with emergency cesarean delivery (9.7%; 61 of 630 infants,  $p < 0.001$ ).

**Table 1** summarizes the ORs for TTN by gestational age at delivery. In this study, as shown in **Table 1**, the gestational age at delivery did not influence the incidence of TTN.

Variables, analyzed by the incidence of TTN after vaginal delivery at  $\geq 37$  weeks' gestation, are summarized as dichotomous variables in **Table 2**. **Table 3** summarizes the ORs for TTN by various types of twins. As shown in **Table 2**, the incidence of TTN was significantly greater in cases with nulliparity, a history of infertility therapy, twin pregnancy, induction or augmentation or both of labor, nonreassuring fetal status, vacuum/forceps delivery, breech delivery, neonatal birth weight of  $< 2,500$  g, Apgar score at 1 or 5 minutes or both of  $< 7$ , and umbilical arterial pH of  $< 7.0$ . In twin pregnancies (**Table 3**, the incidence of TTN did not increase significantly by any additional factors.

**Table 4** shows adjusted ORs ratios and 95% CIs for TTN using logistic multivariable regression analysis. Multivariate analysis showed that the

## TTN after Vaginal Delivery at Term

Table 2 Analysis of dichotomous variables by the incidence of transient tachypnea of newborn following vaginal delivery at 37 weeks and more

	Control	TTN	Crude OR	95% CI	P-value
Number	4,078	156			
Maternal age $\geq$ 35 years	1,037 (25)	48 (31)	1.3	0.92–1.8	0.13
$\geq$ 40 years	156 (4)	7 (5)	1.2	0.54–2.6	0.67
Nulliparous	2,019 (50)	105 (67)	2.1	1.5–3.0	$< 0.001$
History of infertility	74 (2)	13 (8)	4.9	2.7–9.1	$< 0.001$
History of IVF	46 (1)	9 (6)	5.4	2.6–11	$< 0.001$
PIH	21 (1)	0 (0)	—	—	0.37
Twins	88 (2)	8 (5)	2.5	1.2–5.2	0.014
PROM	802 (20)	39 (25)	1.4	0.94–2.0	0.10
Meconium staining	510 (13)	19 (12)	0.97	0.59–1.6	0.90
Induction of labor	562 (14)	32 (21)	1.6	1.1–2.4	0.018
Augmentation of labor	1,041 (26)	67 (43)	2.2	1.6–3.0	$< 0.001$
Duration of labor $<$ 3 hours	691 (17)	15 (10)	0.52	0.30–0.89	0.016
$\geq$ 24 hours	175 (4)	9 (6)	1.4	0.68–2.7	0.37
NRFS	82 (2)	10 (6)	3.3	1.7–6.6	$< 0.001$
Vacuum/forceps delivery	305 (8)	32 (21)	3.2	2.1–4.8	$< 0.001$
Breech delivery	24 (1)	4 (3)	4.4	1.5–13	0.0028
Neonatal birth weight $<$ 2,500 g	276 (7)	19 (12)	1.9	1.2–3.1	0.016
$\geq$ 3,500 g	464 (11)	19 (12)	1.1	0.66–1.8	0.76
Light-for-dates infant	374 (9)	9 (6)	0.61	0.31–1.2	0.15
Heavy-for-dates infant	198 (5)	11 (7)	1.5	0.79–2.8	0.21
Nuchal cord entanglements	1,179 (29)	48 (31)	1.1	0.77–1.6	0.62
Apgar score $<$ 7					
1 minute	31 (1)	24 (15)	24	14–42	$< 0.001$
5 minutes	6 (0)	4 (3)	18	5.0–64	$< 0.001$
Umbilical arterial pH $<$ 7.0	14 (0)	1 (1)	1.9	0.24–14	0.54

TTN, transient tachypnea of newborn; IVF, in vitro fertilization; PIH, pregnancy induced hypertension; PROM, premature rupture of the membrane; NRFS, non reassuring fetal status. Values are represented as number (%).

incidence of TTN was significantly associated with nulliparity; a history of infertility therapy, such as in vitro fertilization; augmentation of labor; nonreassuring fetal status; vacuum/forceps delivery; and low Apgar scores ( $<7$ ) at 1 and 5 minutes. In addition, a low Apgar score at 1 minute ( $<7$ ) was the factor most strongly associated with the incidence of TTN. The adjusted OR for TTN with this condition was 20 (95% CI, 12–34;  $p < 0.001$ ).

### Discussion

Analysis of our data confirms previously published studies showing an association between TTN and low Apgar score<sup>5,6</sup>. In vaginal deliveries at 37 weeks or later, a low Apgar score at 1 minute is the greatest risk factor for TTN. This association persisted after controlling for several variables,

including parity, history of infertility, delivery mode, and birth weight. These variables have been reported to also be associated with the increased risk of perinatal mortality<sup>7–11</sup>. Possible mechanisms for the delayed absorption of pulmonary fluid associated with a low Apgar score at 1 minute, which is a neonatal condition requiring medical attention, include dysfunctional catecholamine regulation, mild pulmonary capillary leak syndrome, and myocardial dysfunction with elevated filling pressure<sup>4,11,12</sup>.

Several limitations of our study must be kept in mind. For example, no patients had diabetes mellitus or bronchial asthma because our institution is not a general hospital. These complications have been reported to be associated with an increased incidence of TTN<sup>5,6</sup>. Thus, an additional study concerning some maternal complications may be

Table 3 Relation between twin gestation and incidence of transient tachypnea of newborn following vaginal delivery at 37 weeks and more

	Control	TTN	Crude OR	95% CI	P-value
Number	4,078	156			
Singletons	3,990 (98)	148 (95)	0.41	0.19–0.86	0.014
Twins	88 (2)	8 (5)	2.5	1.2–5.2	0.014
MD twins	29	3	2.7	0.81–9.0	0.091
DD twins	59	5	2.2	0.88–5.6	0.082
First twins	44	4	2.4	0.84–6.7	0.091
Second twins	44	4	2.4	0.84–6.7	0.091
First twin of MD	15	1	1.8	0.23–13	0.59
Second twins of MD	14	2	3.8	0.85–17	0.060
First twins of DD	29	3	2.7	0.82–9.1	0.086
Second twins of DD	30	2	1.8	0.42–7.4	0.44

MD, monochorionic-diamniotic twin; DD, dichorionic-diamniotic twin.  
Values are represented as number (%).

Table 4 Adjusted odds ratios and 95% confidence intervals for transient tachypnea of newborn using logistic multivariable regression analysis

	Adjusted OR	95% CI	P-value
Maternal age $\geq$ 35 years	1.2	0.84–1.5	0.20
Nulliparous	2.0	1.3–3.2	0.0072
History of infertility	1.9	1.0–4.4	0.029
History of IVF	2.4	1.0–5.3	0.0092
Twins	1.7	0.87–3.5	0.12
PROM	1.3	0.86–1.9	0.14
Induction of labor	1.1	0.72–1.6	0.77
Augmentation of labor	1.6	1.1–2.4	0.014
Duration of labor < 3 hours	0.72	0.55–1.10	0.18
NRFS	2.3	1.3–4.3	0.0045
Vacuum/forceps delivery	2.3	1.6–3.5	< 0.001
Breech delivery	3.0	1.2–7.5	0.048
Neonatal birth weight < 2,500 g	1.4	0.85–2.2	0.19
Light-for-dates infant	0.88	0.50–1.5	0.082
Heavy-for-dates infant	1.2	0.88–1.9	0.18
Apgar score < 7			
1 minute	20	12–34	< 0.001
5 minutes	4.2	1.9–9.1	< 0.001

IVF, in vitro fertilization; PROM, premature rupture of the membrane; NRFS, non reassuring fetal status.

needed.

The higher OR associated with a low 1-minute Apgar score than a low 5-minute Apgar score (or low pH) may suggest something probably more related to delivery than biochemical status going on as 'perinatal asphyxia'<sup>13</sup>. Thus, the present results may support a previous study suggesting that the improvement of obstetric surveillance to decrease the frequency of low Apgar scores is important for

preventing TTN in infants delivered vaginally at 37 weeks of later<sup>6</sup>.

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