

## Elective cesarean section versus induced vaginal delivery: Do any differences in terms of neonatal respiratory morbidities exist?

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### Ethics Committee Approval

This study was approved by İzmir Bakırçay University, Ethical Committee on Noninvasive Clinical Research. (Date: 16.01.2019, Number: 3811-5317).

All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

### Conflict of Interest

No conflict of interest was declared by the authors.

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### Abstract

**Background/Aim:** Transient tachypnea of the newborn (TTN) is mostly a benign and self-limiting common physiological disorder. Certain factors, such as elective cesarean section (CS) not preceded by spontaneous labor, delivery before 39 gestational weeks, and perinatal asphyxia, interfere with the fetal–neonatal transition. In our study, we aimed to review the results of hospitalized newborns who receive a diagnosis of TTN and investigate the possible relationship between the implementation of labor induction and the occurrence of this disorder.

**Methods:** This study used a case-control study design. We scanned the hospital records of 156 term newborns hospitalized between January 2017 and January 2018 who received a diagnosis of TTN and who did not have any additional fetal and/or maternal risk factors. Demographic features, mode of delivery, and implementation of labor induction in vaginal deliveries were recorded and compared to the data from 150 healthy term infants. Infants were then split into two groups according to their type of labor induction, and a separate subgroup analysis was performed in terms of the risk of TTN development.

**Results:** The incidence of TTN was 2.9% in vaginal deliveries and 8.5% in CSs. Differences between groups regarding gestational age, birth weights, gender, elective induction in vaginal deliveries, interventions in the delivery room, and types of intervention were found ( $P<0.05$ ). The risk of developing TTN was 2.5 times higher in the induction group compared to those who did not receive induction but still developed TTN ( $P<0.001$ ). Also, the risk was significantly higher in the induction group compared to those who did not receive induction and did not develop TTN ( $P<0.001$ ). After applying a logistic regression analysis, labor induction (odds ratio: 1.005; 95% confidence interval: 1.003–1.008,  $P<0.001$ ) was found to be an independent significant risk factor for developing TTN.

**Conclusions:** This study indicates that infants born via electively induced vaginal delivery had significantly higher rates of TTN. Therefore, elective labor induction can be added as a new risk factor for TTN development. In our opinion, labor induction without valid medical and obstetric indications should be avoided due to maternal and fetal complications.

**Keywords:** transient tachypnea of the newborn, induced vaginal delivery, elective cesarean section, fetal complications

## Introduction

Transient tachypnea of the newborn (TTN) is a benign and self-limiting common physiological disorder resulting from pulmonary edema secondary to inadequate or delayed clearance of fetal alveolar fluid [1–3]. Activation of the epithelial sodium channels after birth is the primary mechanism for formation of functional residual capacity (FRC) and prevents alveolar collapse upon expiration. Other studies have demonstrated that fetal alveolar fluid is continuously secreted during pregnancy through an epithelial chloride secretion mechanism, and the secretion rate decreases a few days before delivery [2, 4–6]. At birth, a surge in catecholamines and steroid hormones occurs, and the balance of fluid movement in the alveolus switches from chloride secretion to sodium absorption, a process that causes the resorption of intra-alveolar fluid [5, 6]. Certain factors, such as elective cesarean section (CS) not preceded by spontaneous labor, delivery before 39 gestational weeks, and perinatal asphyxia, interfere with the fetal–neonatal transition by interrupting absorption of the fetal alveolar fluid [7–9].

In elective CSs, the delivery time is determined apart from physiological mechanisms. This procedure occurs without spontaneous labor thus preventing the fetus from preparing for the transition to the neonatal period and preventing the anticipated rise of catecholamines and other hormones, a process that causes a delay in the clearance of alveolar fluid [10]. In recent years, the dramatic increase in the rate of elective induction of labor without cervical maturation is thought to cause neonatal respiratory complications with a similar mechanism of action. Joseph et al. [11] investigated the effect of CS on TTN and examined 4576 deliveries performed at their hospital. The authors determined that the relative risk of CS is 3.78 when compared with normal vaginal deliveries.

Even though one of the risk factors for developing TTN was shown to be CS versus a normal vaginal delivery, no information regarding induced vaginal delivery is available. Therefore, this study aimed to review the results of hospitalized newborns with the diagnosis of TTN and investigate the possible relationship between the implementation of labor induction and the occurrence of this disorder.

## Materials and methods

### Participants

This retrospective case-control study was conducted in the Department of Pediatrics, Division of Neonatology, Cigli Regional Training and Research Hospital. The Noninvasive Research Ethics Board of Bakırçay University approved the study protocol (16.01.2019/Number: 3811-5317). All procedures performed in the study followed the provisions of the Declaration of Helsinki (as revised in Brazil in 2013), and informed consent was obtained from the parents of all newborns involved in the study.

We scanned the hospital records of 156 term newborns hospitalized between January 1, 2017 and January 1, 2018 who had received a diagnosis of TTN and who did not have any fetal or maternal additional risk factors (such as prolonged labor, fetal distress, preeclampsia, maternal diabetes, multiparity, small or large for gestational age, prematurity, and others). All records

were scanned by a neonatologist who was blinded to the presence of TTN.

### Outcome measures

Demographic features, modes of delivery, and implementation of labor induction in vaginal deliveries were recorded and compared to the data from 150 healthy term infants. Infants were then split into two groups according to type of labor induction, and a separate subgroup analysis was performed for the risk of developing TTN.

### Sample size

Due to the study's retrospective design, post hoc power analyses were performed. The TTN ratio in both groups was used to calculate the effect size. Using the following information, the study population was 306, effect size was 0.479,  $\alpha=0.05$ , and the power of the study was determined as 100%.

### Statistical analysis

Data were analyzed using the IBM SPSS (Version 25.0. Armonk, NY: IBM Corp.) program. Normal distribution was determined using the Kolmogorov–Smirnov/Shapiro–Wilk tests and analysis of graphs. Since the variables showed a normal distribution, all analyses were performed with parametric methods. All results were presented as numbers (percentages) and mean (standard deviation). Paired sample T- and chi-squared tests were used to analyze differences in outcome measures between groups for continuous and categorical variables, respectively. Cohen's d effect size was calculated and interpreted as small ( $d=0.2$ ), medium ( $d=0.5$ ), and large ( $d=0.8$ ). A logistic regression analysis was performed to determine whether or not labor induction is a risk factor for TTN development.

## Results

In the study group involving 156 newborns with TTN, mean gestational age was 38.2 (1.4) weeks, and the mean birth weight was 3243.8 (539.6) g. Thirty-five percent of infants were born vaginally ( $n=54$ ), and 65% underwent CS ( $n=102$ ). When proportioned to the number of vaginal and CS deliveries performed in our hospital over the same time interval, the incidence of TTN was 2.9% for vaginal deliveries and 8.5% for CS. Elective labor induction was used in 74% (40/54) vaginal delivery babies who developed TTN. The rate of elective labor induction for all vaginal deliveries during that year was 53% ( $n=972$ ). Difference between groups in terms of gestational age and birth weight with a medium effect, gender, elective induction in vaginal deliveries, intervention in the delivery room with a large effect, and type of intervention were found ( $P<0.05$ ). Detailed information regarding the groups' comparison is presented in Table 1.

When the results of 40 infants who underwent induction and developed TTN were compared to those of 14 infants who did not undergo induction but developed TTN, the risk of developing TTN was 2.5 times higher in the induction group ( $P<0.001$ ). When the same comparison was applied to the infants who did not receive induction and did not develop TTN, the risk was found to be significantly higher in the induction group ( $P<0.001$ ) as shown in Table 2.

After applying a logistic regression analysis, labor induction (odds ratio [OR] 1.005; 95% confidence interval [CI]:

1.003–1.008,  $P < 0.001$ ) was an independent significant risk factor for the development of TTN.

Table 1: Demographic features and clinical findings of neonates with transient tachypnea of the newborn (TTN) and healthy controls

	TTN (n=156) mean (SD)	Control (n=150) mean (SD)	P-value	Cohen's d
Gestational age (weeks)	38.2 (1.4)	39.3 (1.6)	0.038	0.73
Birth weight (g)	3243.8 (539.6)	3581 (435.5)	0.046	0.69
Mode of delivery, n (%)	102/54 (65/35)	63/87 (42/58)	0.012	
Gender, n (%)	54/102 (35/65)	86/64 (57/43)	0.056	
Elective induction in vaginal deliveries, n (%)	40/54 (74)	46/87 (53)	<0.001	
Apgar 1'	9.0 (0.78)	9.02 (0.9)	0.542	0.02
Apgar 5'	9.37 (0.71)	9.41 (0.8)	0.641	0.05
Intervention in the delivery room	121 (77.6)	16 (10.6)	<0.001	1.90
Type of intervention, n (%)				
Aspiration	5 (4.2)	10 (62.5)	0.346	
Oxygen	58 (47.9)	6 (37.5)	<0.001	
nCPAP	58 (47.9)	0 (0)	<0.001	
CPR	0 (0)	0 (0)	0	

CS: cesarean section, nCPAP: nasal continuous positive airway pressure, CPR: cardiopulmonary resuscitation, SD: standard deviation

Table 2: Comparison of infants born vaginally in terms of developing TTN and in those who underwent labor induction

	Induction present n (%)	Induction absent n (%)	Total n (%)	P-value
TTN present, n (%)	40 (4)	14 (1.6)	54 (3)	<0.001
TTN absent, n (%)	932 (96)	848 (98.4)	1780 (97)	0.647
Total, n (%)	972 (100)	862 (100)	1834 (100)	-

TTN: transient tachypnea of the newborn

## Discussion

TTN is mostly a benign and self-limiting disorder with a good prognosis. However, it may cause severe morbidities, such as hypoxemia, respiratory failure, and air leak syndromes [12,13]. Even if no complications occur, the rate of hospitalization increases. Due to separation of the infant from the mother and prolonged hospital stay, problems regarding mother–infant attachment are experienced. It is already known that compared to normal vaginal delivery, respiratory distress, and neonatal intensive care unit (NICU) admissions are 5–7 times more prevalent in infants born via elective CS not preceded by spontaneous labor [14–17]. In the current literature, the incidence of TTN is reported as 0.3% to 3% in vaginal deliveries and 0.9% to 12% in elective CSs [3,7]. In our study, the incidence of TTN according to the mode of delivery was compatible with the upper limits reported in the literature. When compared with healthy controls, infants in the TTN group had lower gestational ages, lower birth weights, higher CS rates, and higher requirements for additional oxygen and nasal continuous positive airway pressure (nCPAP) in the delivery room.

Recently, iatrogenic stimulation of uterine contractions before the onset of spontaneous labor to achieve vaginal delivery has become a common method of labor induction [18–20]. Generally, it must be selected in case of medical and obstetric indications. Nevertheless, induction may be applied without any valid indication for logistic and psychosocial reasons and is called “elective induction” [19,21,22]. In recent years, the rate of elective induction of labor has risen dramatically throughout the world and in our country. Initiating vaginal delivery, especially before cervical maturation, has caused significant maternal and neonatal morbidity [19,23]. Although no study has investigated the effects of induced vaginal delivery on the development of TTN, one study examined the relationship between precipitous labor and TTN. Jegard et al. [24] divided the vaginal delivery

according to duration as precipitous labor (<3 h) and the reference group (>3 h). Although the TTN rate was lower in the precipitous labor group than in the reference group, this difference was not observed after adjustment for the risk factors. In our study, we demonstrated that infants born via electively-induced vaginal delivery had significantly higher rates of TTN. In such infants, the underlying mechanisms for TTN development are not fully understood. However, similar to the mechanisms in elective CS, the most probable explanation for TTN development in electively-induced vaginal deliveries is the determination of delivery time apart from physiological mechanisms and prevention of the fetus from preparing for the transition to the neonatal period; it seems that catecholamines and other hormones do not have the necessary time to increase in such infants and just as in elective CSs, epithelial sodium channels cannot be activated resulting in a delay in alveolar fluid clearance.

## Strengths and Limitations

Some study strengths and limitations should be discussed. The major strength of the study is the large sample size. Also, we scanned a short period to avoid the changes in obstetrics methods that could impact the study's homogeneity. Another strength of the study is exclusion of the cases with maternal risk factors that may have impacted perinatal outcomes. Along with the study's strength, our limitation was that we needed to evaluate long-term results. Consequently, the need the future studies with prospective and long-term designs is present.

## Conclusion

In conclusion, elective induction of labor can be added as a new risk factor for TTN development to the already known risk factors, such as elective CS, premature birth, and perinatal asphyxia. Also, considering the TTN presence results in requirements for more oxygen and nCPAP than in the control group, labor induction without valid medical and obstetric indications should be avoided due to associated maternal and fetal complications.

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