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Risk of Wheezing Attacks in Infants With Transient Tachypnea Newborns

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Abstract

Background: The most common reason of respiratory distress in the newborn is transient tachypnea of the newborn (TTN). There are some reports saying that TTN is associated with increased frequencies of wheezing attacks.

Objectives: The aims of this study were to determine the risk factors associated with TTN and to determine the association between TTN and the development of wheezing syndromes in early life.

Materials and Methods: In a historical cohort study, we recorded the characteristics of 70 infants born at the Shohadaye Kargar Hospital in Yazd between March 2005 and March 2009 and who were hospitalized because of TTN in the neonatal intensive-care unit. We called their parents at least four years after the infants were discharged from the hospital and asked about any wheezing attacks. Seventy other infants with no health problems during the newborn period were included in the study as the control group.

Results: The rate of wheezing attacks in newborns with TTN was more than patients with no TTN diagnosis ($P = 0.014$). TTN was found to be an independent risk factor for later wheezing attacks (relative risk [RR] = 2.8).

Conclusions: The most obvious finding of this study was that TTN was an independent risk factor for wheezing attacks. So long-term medical care is suggested for these patients who may be at risk, because TTN may not be as transient as has been previously thought.

Keywords: Asthma, Transient Tachypnea of the Newborn (TTN), Wheezing Attack

1. Introduction

The commonly reason of the respiratory distress in full-term newborns is transient tachypnea of the newborn (TTN) but with a good prognosis (1, 2). However, TTN in the rare cases cause pulmonary air leaks, hypoxia and persistent pulmonary hypertension, need to respiratory support (3, 4). Therefore, TTN is an important health problem in newborns causes complications and high frequency of occurrence of it (5). TTN in newborns cause 42.5 to 60% of non-infectious cases while respiratory distress is observed only 1% of all newborns (1, 6). TTN diagnosis is according to tachypnea (respiratory rate > 60/minutes) in the first 6 h, and last for at least 12 hours. Moreover, compromising changes (increased ventilation, vascular congestion, fluid at fissures and costophrenic angle, flattened diaphragm) should be seen in the chest x-ray and in general it should respond to 40% or less oxygen therapy (7, 8). If any problems occur, tachypnea can be resolve in three to five days (9-11).

It is believed that, after the TTN resolves, there is no risk for respiratory diseases or other long-term breathing problems (12-14). However, some studies shown that patients who had TTN in the newborn were found to have more frequent wheezing attacks and asthma than who had no respiratory problems in this period (15, 16). Thus, there is a question concerning about whether TTN is a precursor of later disease. Cakan et al. stated that TTN is a risk factor for patients' having wheezing syndrome in the future (odds ratio [OR], 2.378; $P < 0.01$) (17). In another study, it was found that the newborns with TTN, risk of having wheezing disorders in childhood were increased (adjusted hazard ratio [HR] =1.17) (18). However, more studies are needed to find that if TTN increased risk of wheezing syndrome in the infants.

2. Objectives

The purpose of this study were to determine the risk factors associated with transient tachypnea of the newborn (TTN) and whether TTN is associated with development of wheezing syndromes early in life.

3. Materials and Methods

3.1. Research Design and Setting

This was a historical cohort study. Over the four-year period from 21 March 2005 to 20 March 2009, 19,371 babies were born at the Shohadaye Kargar Hospital in Yazd, central Iran. Seventy of the babies were diagnosed with TTN.

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3.2. Sampling

To facilitate equal sampling, an equal number of healthy newborns were randomly chosen from the same hospital as the control group. We ensured that the selection was random by using of the last digit of the file number assigned in the delivery room.

3.3. Selection Criteria

3.3.1. Cases

3.3.1.1. Inclusion Criteria

All of the newborns diagnosed with TTN (70 cases) and treated in the Neonatal intensive care unit (NICU) were included in this study. The diagnosis was according to the following clinical and laboratory criteria: a) tachypnoea (respiratory rate exceeding 60/minutes) in the first 6 hours; b) tachypnea last for at least 12 hours; c) a chest radiograph in the first 24 hours that showed at least one of the these four findings, i.e., prominent central vascular markings; widened interlobar fissures of pleural fluid; symmetrical perihilar congestion; and hyperaeration as evidenced by flattening and depression of the diaphragmatic domes, an increased anteroposterior diameter, or both; d) lack of hypercapnoea (i.e., a $PaCO_2 > 6.00$ kilopascals (KPa)) and no need for assisted ventilation; and e) rule out all other known reason of respiratory distress syndrome. We explained to the parents the aim of the study, the requirements for participation, and that their participation was voluntary. Only the parents who gave their permission had their babies included in the study.

3.3.1.2. Exclusion Criteria

Patients with TTN who were treated in NICU but had accompanying hypoglycemia, hypocalcaemia, polycythemia, meconium aspiration, congenital heart disease, sepsis, or respiratory problems due to other reason were excluded from the study.

3.3.2. Controls

3.3.2.1. Inclusion Criteria

A total of 70 babies who were born at Shohadaye Kargar Hospital between 21 March 2005 and 20 March 2009 and had no health problems in the newborn included in the study as control group. We explained to the parents the aim of the study and the requirements if they chose to participate. The parents read the patient approval forms, and, if they decided to participate, the approval forms were signed by both parents and by the authors. Then, identical procedures were applied for the study group and the control group.

3.3.2.2. Exclusion Criteria

Babies were excluded from the control group based on the following decision criteria: 1) any history of a disease or diseases that could lead to respiratory distress (such as hypoglycemia, hypocalcemia, sepsis, respiratory distress syndrome, polycythemia, meconium aspiration, and congenital heart disease) and 2) the parents could not be reached by phone.

3.4. Data Collection

Appointments were arranged by contacting the parents of the 70 patients by phone for at least four year after discharge to evaluate any long-term complications associated with TTN. This was done to validate or refute the general belief that there is no increased risk for respiratory disease or other long-term sequelae after TTN resolves (2, 3). The parents of all of the patients were required to bring to the appointments at the outpatient clinic at Shohadaye Kargar Hospital the patients' immunization cards, well-baby follow-up cards, hospital files for other cases except for TTN, all prescriptions, and chest radiographs. After examination of patients who had participated in study, details related to wheezing attacks, the symptoms, and the drugs that were used during this period were explained to the parents. If the patients had a wheezing attack, the time of the first attack, the times of any recurrences, any hospitalization that was required, medications that were administered for wheezing, and any diagnosis of asthma were recorded in detail. Moreover, details was related to chronic diseases, time of weaning, house heating system, and any family history of asthma and atopic diseases were recorded. All of the children were 4 - 8 years old when visited the clinic. In our study population of children aged less than 8 years, it was impossible to confirm the diagnosis of asthma by physiological studies of airflow obstruction. The medical histories of the children in this study were obtained from the mothers of both groups by interviewing them directly to collect data. However, as a check on potential recall bias, each mother in both groups was asked to list other respiratory and non-respiratory problems in her child's medical history.

3.5. Ethical Consideration

The study was approved by the Health Research Ethics Board at the Shohadaye Kargar Hospital and the health information privacy committee of Ali-Ebne Abitaleb faculty of medicine, Islamic Azad university, Yazd branch. The aim of the study and its requirements were explained again to the parents. The patients' approval forms were signed by the parents. The provision of free medical care was considered to be an incentive for participation by the subjects of the study and by the control group. Next, the identical procedures that previously explained for the case group were used for the control group.

3.6. Statistical Analyses

SPSS version 17 (SPSS Inc., Chicago, Illinois, U.S.) was used for employing chi-squared test, Fisher's exact test (expanded) T-test, Mann-Whitney U-test, and Logistic regression. The level of significance was set at less than 0.05.

4. Results

The patients consisted of 52 males and 18 females. Sixty-four of the 70 were term, seven were small for their gestational age (SGA), 28 had normal vaginal delivery (NVD), and 42 had caesarian section (CS) delivery. The control group consisted of 24 males and 46 females. Sixty-nine of the 70 were term, four were SGA, 38 had NVD, and 32 had CS. We found statistically significant differences between two groups according to gestational age (P < 0.001), gender (P < 0.001), smoking parents (P = 0.021), and family history of asthma (P = 0.032). There were no significant differences in birth weight (P = 0.371), method of delivery (P = 0.077), maternal asthma (P = 1), heating system (P = 0.052), and nutritional status (P = 0.803) (Table 1).

Among the 70 patients in the case group, only two patients (2.8%) had asthma. Among the 70 patients in the control group, three (4.3%) had asthma. There was no significant difference between patients with TTN and patients who had asthma (RR = 1.007; P = 0.681) (Table 2). Among the 70 patients in the case group, 17 patients (24.3%) had at least one wheezing attack. Among the 70 patients in the control group, only six (8.6%) had at least one wheezing attack. The rate of wheezing attacks in the case group was significantly higher than that in the control group (P = 0.014) (Table 2). Therefore, we considered TTN as an independent risk factor for wheezing attack (RR = 2.8; P = 0.014).

Table 1. Comparison of Demographic Characteristics of the Study Group and the Control Group[a,b]

	Cases (TTN+)	Controls (TTN-)	P-Value
Birth weight, g			0.371
< 2500	7 (9.9)	4 (5.7)	
2500 - 3500	54 (77.5)	52 (74.3)	
> 3500	9 (12.7)	20 (23)	
Gestational age, weeks			< 0.01
< 37	5 (7)	1 (1.4)	
37 - 40	64 (91.5)	59 (84.3)	
> 40	1 (1.4)	10 (14.3)	
Gender			< 0.01
Male	52 (74.6)	33 (47.1)	
Female	18 (25.4)	37 (52.9)	
Method of delivery			0.077
Vaginal	28 (39.4)	38 (54.3)	
Cesarean section	42 (60.6)	32 (45.7)	
Mother's history of asthma			1
Yes	4 (5.6)	3 (4.3)	
No	66 (94.4)	67 (95.7)	
Nutritional status			0.803
Fed only breast milk (months)	52 (74.3)	50 (71.4)	
Fed only formula (months)	4 (5.7)	6 (8.6)	
Both	14 (20)	14 (20)	
Heating system (stove)	60 (85.9)	66 (94.3)	.052
Smoking parents			.021
Mother	0	1 (1.4)	
Father	25 (35.2)	12 (17.1)	
Family history of asthma			.032
Mother	4 (5.6)	3 (4.3)	
Father	3 (4.2)	0	
Siblings	0	0	

[a] Data are presented as No. (%).
[b] N = 70.

Table 2. Risk of Asthma and Wheezing Attack According to TTN Diagnosis[a,b]

	Cases (TTN+)	Controls (TTN-)	P-Value
Asthma	2 (2.8)	3 (4.3)	.681
Wheezing Attack	17 (24.3)	6 (8.6)	.014

[a]Data are presented as No. (%).
[b]N = 70.

5. Discussion

5.1. The Relationship Between a Diagnosis of TTN and the Risk of Asthma and Wheezing Attacks

The current studies shown that TTN could be a risk factor for wheezing attacks, raising the question concerning whether TTN is actually a precursor of later disease (19). We show that TTN can be a risk factor for wheezing syndrome in the future. Correlation between TTN and the progress of asthma have shown in several studies. An increased frequency of asthma and wheezing attacks among patients with TTN have shown in a study with patients followed up for 5 - 9 years (20). In another study, atopic symptoms and atopy histories had greater occurrences in first-degree relatives, recurrent wheezing attacks (two or more), and childhood asthma among patients who had TTN (21). Another study on the neonatal characteristics of pre-school children who had asthma showed that TTN is a risk factor for asthma (22).

5.2. Comparison of Demographic Characteristics of the Study Group and the Control Group

Our study identified significant differences in gestational age, gender, smoking parents, and family history of asthma between the case group and the control group. There were more diagnoses of TTN among patients who had a gestational age of 37 - 40 weeks, were males, had a father who smoked, and had a mother with a history of asthma. A study on 308 TTN patients showed that maternal asthma, birth weight greater than 4500 g, male gender, and urban location were risk factors for TTN (18). It indicated that newborns with TTN had more increased risk for wheezing disorder in childhood. In our study, there was no significant difference in diagnoses of TTN on the basis of the method of delivery, but babies delivered by cesarean section were diagnosed with TTN more often. Many researchers has been described that cesarean section is a risk factor for TTN in lack of a surge in catecholamine that is naturally released in a vaginal delivery. This surge results in a b-adrenoceptor-mediated response and subsequent Na pump absorption of the fluid in the distal airways. Patients who had TTN were treated by intravenous antibiotics for at least 72 hours before blood cultures were reported as negative. Then this may have modified the gastrointestinal flora, as a result any floraprotective influence against the progression of allergies and asthma. We believe that antibiotic treatment of children early in their lives may modify the flora of the gut, which may predispose the child to the development of allergies and asthma, as was suggested by hygiene hypothesis (9). We observed that there was no significant relationship between TTN and nutritional status; however, patients who were fed only breast milk had more diagnoses of TTN. Infants who were breast-fed had a preference of bifidobacteria and lactobacilli whiles infants who were bottle-fed develop a mixed flora with less bifidobacteria and clostridia (23). Verhulst et al. studied antibiotic use, intestinal microflora, and wheezing during the first year of life, and they understood that clostridium had a protective role against wheezing (24).

5.3. Conclusions

In this study, the ratio of wheezing attacks was found to be significantly greater in patients with TTN than it was in the control group. We established that TTN is an independent risk factor for wheezing attack. Thus, long-term medical care is suggested for newborns with TTN who could be at risk. However, a prospective study will be helpful in further establishing this relationship.

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Footnote

Authors' Contribution: All of authors contributed equally to this project and article. All of the authors read and approved the final manuscript.

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