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## Original Article

## Structural cardiac lesions in transient tachypnea of the newborn



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## ABSTRACT

**Background:** Transient tachypnea of the newborn (TTN) is considered a benign disorder. Given its self-limiting nature, few studies have looked for associated pathology. This study explores the association of TTN with structural cardiac lesions.

**Methods:** Over a six-month period, all inborn term and late preterm neonates with TTN (without predisposing factors) underwent 2D echocardiography within the first ten days of life, after tachypnea had subsided. Equal number of neonates born during the same period, matched for birth weight, gestational age, sex, and mode of delivery but without tachypnea, also underwent echocardiography before ten days of life. The cardiologist performing the echocardiography was blinded to the presence or absence of tachypnea.

**Results:** Thirty-six neonates with tachypnea and equal number of controls underwent echocardiography. Due to matching, there was no significant difference in birth weight, gestational age, sex, or mode of delivery between the two groups. Mean age at echocardiography also did not significantly differ. Neonates with TTN had significantly more structural cardiac lesions than those without (16 [44.44%] vs 5 [13.39%];  $p < 0.009$ ).

**Conclusion:** Significantly more neonates with TTN have associated structural cardiac lesions. All neonates with TTN should be screened for underlying structural cardiac lesions.

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## Introduction

Transient tachypnea of the newborn [TTN] is a common respiratory condition seen in term and near-term neonates

and is usually mild and self-limiting.<sup>1–3</sup> A number of studies have been conducted to predict neonates at risk for TTN with many factors like prematurity, birth asphyxia, male sex, and cesarean delivery being identified.<sup>2,4,5</sup> Some workers have looked at various serum markers in TTN<sup>1,6–9</sup> while others have

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documented cardiac functions to be different in neonates with severe TTN.<sup>10,11</sup>

The detection of structural cardiac lesions in two neonates with prolonged TTN at our center prompted us to study this possible association. We did not come across any published study dealing with the presence of otherwise asymptomatic structural cardiac lesions in neonates with TTN.

## Material and methods

This prospective study was conducted over a six-month period (May to November 2014) in a tertiary care hospital.

All inborn neonates with TTN were eligible to be considered for enrollment in the study. Inclusion or exclusion was based on the following criteria:

### Inclusion criteria

1. Birth after 34 completed weeks of gestation and birth weight > 2000 g;
2. Respiratory rate > 60/min starting within the first 6 h of birth with tachypnea persisting for at least 6 h, with or without other signs like retractions, grunting, nasal flaring, and need for supplemental oxygen;
3. Well-expanded lungs with or without increased fluid in lungs on chest radiograph.

### Exclusion criteria

1. Birth asphyxia or clinical presence of any major congenital anomaly;
2. Chorioamnionitis in the mother or features of neonatal infection including sepsis screen positivity (two features out of C-reactive protein, total leukocyte count, absolute neutrophil count, micro-ESR, and immature to total leukocyte ratio being abnormal);
3. Chest radiograph suggestive of respiratory distress syndrome due to surfactant deficiency and/or need for exogenous surfactant;
4. Clinical or radiological features of congenital heart disease;
5. Clinical, radiological, or blood gas features of meconium aspiration syndrome;
6. Metabolic or hematological disorders like hypoglycemia, hypocalcemia, and polycythemia.

The control group consisted of inborn neonates without TTN, who were not admitted to the Neonatal Intensive Care Unit. Neonates in the control group were matched with those in the study group for gestational age, sex, birth weight, and mode of delivery. All neonates with TTN were treated as per the unit protocol. Within the first ten days of life, all study subjects as well as controls underwent a 2D echocardiographic examination. In study subjects, 2D echo was done after TTN had resolved.

2D Echo for all neonates was done by the same cardiologist (RA) blinded to clinical details of the subjects. 2D Echo was done using a pediatric transducer (4–7.5 MHz; PA 122E on Esaote MyLab 30 Gold). Standard transthoracic views including

parasternal long axis, short axis, apical five-chamber, suprasternal, subcostal, and high parasternal were used. Persistent foramen ovale was diagnosed when there was an interatrial communication of <2 mm diameter with a flap-like opening with bidirectional flow and without any evidence of right ventricular volume overload. All other structural lesions were diagnosed as per standard norms.

Approval for the study was obtained from the Institutional Ethics Committee and verbal consent of parents was taken for the 2D echocardiography. All data were analyzed using a statistical software (Epi Info™ ver 7.0, CDC, Atlanta). Appropriate Chi-square tests were done for categorical variables while Student's t-test was done for continuous variables. All *p* values were two-tailed.

## Results

During the study period, a total of 36 neonates with TTN-fulfilled criteria were included in the study. Of these, four (11.11%) were near-term and 32 (88.89%) were term neonates. The control group consisted of 36 matched neonates.

The mean duration of tachypnea in the study group was 40.28 h (s.d. 28.44 h) with a median of 30 h. The shortest duration of tachypnea was 6 h and the longest was 96 h. No neonate needed any form of respiratory support other than supplemental oxygen. First-line antibiotic therapy was started for 5 (13.89%) but discontinued after 72 h on reassessment. All neonates recovered fully and were discharged home on breast feeds.

Subjects in the study group and subjects in the control group were matched for gestational age, birth weight, sex, and mode of delivery, and hence the two groups did not show any significant differences in these variables. The mean age at which 2D echocardiography was done in each group also did not show any significant difference. These variables are shown in Table 1.

The incidence of structural cardiac lesions detected by 2D echocardiography was higher in neonates with TTN as compared to the control group [*n* = 16; 44.44% in the study group vs *n* = 5; 13.89% in the control group]. This difference was statistically significant with the two-tailed *p* value <0.009 (OR 4.96; 95% CI 1.57–15.68).

The commonest cardiac lesion in both groups was atrial septal defect (ASD), detected in 14 (38.89%) in the study group and in 4 (11.11%) in the control group. In the study group, one neonate had ASD with a patent ductus arteriosus (PDA) and another had a ventricular septal defect (VSD). One neonate in the control group had a PDA. Persistent foramen ovale was found in one neonate in the study group and two in the control group. The distribution of cardiac lesions in the two groups is depicted in Table 2. The exact nature of cardiac lesions in neonates in the two groups is presented in Table 3.

The duration of tachypnea in neonates who were detected to have structural cardiac lesions was compared with that of neonates who had TTN but no cardiac lesions. The mean duration of tachypnea in neonates with cardiac lesions was 39.2 h (s.d. 30.53 h, median 24 h) while the same for those without cardiac lesions was 41.63 h (s.d. 26.52 h, median 48 h). Though neonates without cardiac lesions had longer mean

**Table 1 – Baseline characteristics and cardiac lesions in both groups.**

Variable	Study group (neonates with TTN) n = 36	Control group (neonates without TTN) n = 36	2-Tailed p value
Gestational age (days)			
Mean GA (s.d.)	269.89 (8.77)	270.8 (7.95)	0.922
Median GA	271.5	270.5	
Birth weight (g)			
Mean BW (s.d.)	3110.83 (373.86)	3125.55 (366.93)	0.8665
Median BW	3100	3180	
Sex (n & %)			
Females	11 (69.44%)	11 (69.44%)	NA
Males	25 (30.56%)	25 (30.56%)	
Mode of delivery (n & %)			
Vaginal delivery	19 (52.78%)	19 (52.78%)	NA
Cesarean delivery	17 (47.22%)	17 (47.22%)	
Age at 2D echo (hours)			
Mean age (s.d.)	41.63 (26.52)	39.2 (30.53)	p = 0.8
Median age	48	24	
Structural cardiac lesions			
Present	16 (44.44%)	05 (13.89%)	p < 0.009
Absent	20 (55.56%)	31 (86.11%)	

**Table 2 – Nature of structural cardiac lesions detected in the two groups.**

Nature of structural cardiac lesion	Study group (neonates with TTN) n = 36	Control group (neonates without TTN) n = 36
Atrial septal defect	14 (38.89%)	4 (11.11%)
Atrial septal defect with patent ductus arteriosus	01 (2.78%)	NIL
Ventricular septal defect	01 (2.78%)	NIL
Patent ductus arteriosus	NIL	01 (2.78%)
No structural cardiac lesions	20 (55.55%)	31 (86.11%)

**Table 3 – Details of abnormal echocardiography findings.**

Subject number	Group (study/control)	Birth weight (g)	GA (wks)	Sex	Mode of delivery	Echo report	Echocardiography findings
<b>CASES</b>							
01	STUDY	3105	40 <sup>+2</sup>	F	SVD	ABNORMAL	VSD 18 MM; TR
02	STUDY	2600	36 <sup>+6</sup>	F	SVD	ABNORMAL	OS ASD 2.5 MM
03	STUDY	3975	38 <sup>+6</sup>	M	SVD	ABNORMAL	OS ASD 2.4 MM; PDA 2.0 MM
04	STUDY	3335	39 <sup>+2</sup>	M	SVD	ABNORMAL	OS ASD 2.6 MM
05	STUDY	3120	40 <sup>+1</sup>	M	LSCS	ABNORMAL	OS ASD 3.0 MM
06	STUDY	2630	36 <sup>+3</sup>	M	SVD	ABNORMAL	OS ASD 2.6 MM
07	STUDY	3120	40 <sup>+1</sup>	M	SVD	ABNORMAL	OS ASD 2.4 MM
08	STUDY	2850	37 <sup>+5</sup>	M	SVD	ABNORMAL	OS ASD 2.5 MM
09	STUDY	3940	37 <sup>+3</sup>	F	LSCS	ABNORMAL	OS ASD 3.6 MM
10	STUDY	3200	36 <sup>+2</sup>	F	LSCS	ABNORMAL	OS ASD 3.0 MM
11	STUDY	3070	40 <sup>+2</sup>	M	LSCS	ABNORMAL	OS ASD 2.4 MM
12	STUDY	3005	38 <sup>+2</sup>	M	LSCS	ABNORMAL	OS ASD 2.3 MM
13	STUDY	3100	38 <sup>+6</sup>	M	SVD	ABNORMAL	OS ASD 2.6 MM
14	STUDY	3175	39 <sup>+5</sup>	M	VACU	ABNORMAL	OS ASD 4.3 MM
15	STUDY	3020	39 <sup>+1</sup>	M	SVD	ABNORMAL	OS ASD 3.0 MM
16	STUDY	3150	39 <sup>+6</sup>	M	VACU	ABNORMAL	OS ASD 4.0 MM
<b>CONTROLS</b>							
01	CONTROL	2495	37 <sup>+1</sup>	F	LSCS	ABNORMAL	OS ASD 2.6 MM
02	CONTROL	2660	36 <sup>+6</sup>	F	SVD	ABNORMAL	PDA 3.5 MM
03	CONTROL	3130	38 <sup>+4</sup>	M	SVD	ABNORMAL	OS ASD 3.7 MM
04	CONTROL	2510	37 <sup>+3</sup>	M	SVD	ABNORMAL	OS ASD 3.8 MM
05	CONTROL	3340	37 <sup>+6</sup>	M	SVD	ABNORMAL	OS ASD 2.8 MM

Abbreviations used: SVD: spontaneous vaginal delivery; LSCS: lower segment cesarean section; VACU: vacuum-assisted delivery; OS: ostium secundum; ASD: atrial septal defect; VSD: ventricular septal defect; PDA: patent ductus arteriosus.

duration of tachypnea, this difference was not statistically significant ( $p = 0.8$  by Student's  $t$ -test).

## Discussion

TTN is a commonly encountered neonatal condition. There are many studies identifying risk factors for TTN and elucidating possible pathophysiological mechanisms involved. The detection of structural cardiac lesions in two neonates with prolonged TTN at our center prompted us to review studies on this association.

Most studies on TTN have excluded neonates with congenital heart disease. In some studies, 2D echo has been done to detect and exclude neonates with cardiac anomalies<sup>12,13</sup>; one study used clinical grounds<sup>3</sup> while others mention exclusion of neonates with cardiac anomalies but do not give details of how the cardiac anomaly was detected.<sup>1,2,14</sup> We did not come across any study specifically addressing the incidence of structural heart lesions in neonates with TTN.

A couple of studies have investigated functional abnormalities of cardiac functions in neonates with TTN. Halliday et al. in 1981, reported increase in both left and right ventricular pre-ejection period in 6 neonates with severe TTN compared to isolated increase in left ventricular pre-ejection period in 19 neonates with milder TTN.<sup>10</sup> An increase in initial right ventricular systolic time intervals was reported to predict severe TTN in 7 neonates compared to milder TTN in 35 neonates.<sup>11</sup> Earlier, in 1976, Bucciarelli et al. performed cardiac catheterization in five neonates with cyanosis and tachypnea and did not find any structural lesion but noted persistent fetal circulation.<sup>15</sup> All these studies reported abnormal cardiac function in neonates with TTN but no structural cardiac lesions were reported in these studies.

This study found the presence of structural cardiac lesions to be three times more common in neonates with TTN compared to matched controls (44.44% vs 13.89%); this difference was statistically significant. There were no significant differences between the study and control groups in terms of gestational age, sex, birth weight, or mode of delivery due to matching. The age at which 2D echo was done for the two groups did not also significantly differ. Also of interest is the fact that the duration of tachypnea in neonates with structural cardiac lesions was not significantly different from that in neonates without cardiac lesions.

The findings of this study bring out the facts that structural cardiac lesions are more likely to be present in neonates with TTN and that the duration of tachypnea cannot be used to predict neonates with underlying structural cardiac lesions.

The complete recovery of all neonates with structural cardiac lesions and TTN in this study lends to the postulate that the detected cardiac lesions probably did not contribute to TTN. This assumption is strengthened by the finding that the duration of tachypnea in neonates with structural cardiac lesions is no different from that in neonates without structural cardiac lesions.

The strengths of this study include having a well-matched control group and the blinding of the cardiologist to the

presence or absence of tachypnea. The relatively small number of study subjects is a weakness of this study and this is being addressed by a larger study with sample size calculated based on the findings of this study.

Another drawback of this study is that investigations to determine the contribution of structural cardiac lesions in terms of hemodynamics to TTN were not done. This was deliberate since such investigations would have had to be done during the presence of tachypnea and would have precluded blinding of the cardiologist evaluating these neonates.

In conclusion, based on the findings of this study, screening for structural cardiac lesions by 2D echocardiography is recommended in all neonates with TTN.

## Conflicts of interest

The authors have none to declare.

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