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Original Article (Pages: 18988-18994)

# Association between Transient Tachypnea of the Newborn and Serum Vitamin D Levels in Infants and Mothers in Natural Childbirth

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***Abstract***

***Background:*** Transient Tachypnea of the Newborn (TTN) is one of the most common causes of respiratory distress, shortly after birth, and is generally a benign, self-limited condition. Meanwhile, a lot of studies have linked vitamin D (VitD) levels with probably contributing to neonatal lung development.

***Methods:*** This study aimed to assess whether the serum levels of VitD are associated with TTN in infants and mothers in natural childbirth. This descriptive-analytical research was performed on 39 infants with TTN and their mothers and 39 control infants and their mothers referred to Motazedi hospital in Kermanshah University of Medical Sciences. Serum concentrations of VitD were measured in the first 12-24 h of postnatal age in both infants and mothers.

***Results:*** In the present study, no significant difference was found between healthy and TTN groups in terms of gender, mother's education level, drug use, asthma, diabetes, 1th min Apgar score, mother's age, birth weight, and birth height. But, there was a significant difference between the two groups of control and intervention in terms of 5th min Apgar score, and birth order. The mean levels of serum VitD were significantly lower in both TTN neonate patients and mothers. The results of the Pearson correlation coefficient indicated that there is a significant relationship between serum VitD levels of mothers and term infants in both groups.

***Conclusion:*** We observed that maternal VitD levels can be preventive for the development of TTN in infants through improving respiratory distress, and potentially shortening the duration of tachypnoea in natural childbirth.

***Key Words:*** Natural childbirth, Respiratory distress, Term newborns, Transient tachypnea of the newborn, Vitamin D.

* Please cite this article as: Farshadfar S, Hosseini F, Kahrizi G, Haseli A, Brimavandi A. Association between Transient Tachypnea of the Newborn and Serum Vitamin D Levels in Infants and Mothers in Natural Childbirth. J Ped Perspect 2024; 12 (09):18988-18994. DOI: **10.22038/ijp.2024.82497.5481**

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Received date: Aug.12,2024; Accepted date:Nov.17,2024

## 1- INTRODUCTION

Neonatal Respiratory Distress Syndrome (NRDS) or surfactant deficiency disorder is one of the most common causes of morbidity and mortality rates in newborns, especially in developing countries. To decrease these rates, understanding the diagnosis, clinical presentation, pathophysiology, prevention, and management of this disorder is very vital (1).

NRDS can be caused by a benign etiology, like tachypnea. In one of the most recent definitions by Park and Khattar (2), tachypnea is defined as a breathing rate that is higher than normal, typically defined as a symptom and a focused problem within a medical evaluation particularly in born near or at term. It could arise from some causes of NRDS such as hyaline membrane disease, meconium aspiration, transient tachypnoea of the newborn (TTN) etc. (3)

TTN is the most common etiology of tachypnea in a newborn (4). TTN consists of tachypnoea, defined as a respiratory rate above 60/min that is self-limiting and usually lasts up to a couple of days (5). TTN results from the failure of the newborn to effectively clear the fetal lung fluid soon after birth (6). The incidence of this mild respiratory problem was 1-2% of all neonates with an equal sex predilection (7). Risk factors including C-section, meconium aspiration syndrome, macrosomia, asphyxia, maternal diabetes mellitus, sepsis, twin pregnancy and family history of asthma were associated with an elevated risk for persistent pulmonary hypertension of the newborn (8, 9, 10).

Our understanding of the vital role of vitamin D (VitD) has improved greatly in the last few decades, especially about the healthy relationship between infants and mothers. Recent evidence also suggests that VitD plays a significant role in the formation of pulmonary surfactants and promoting the development of fetal lung structure, thus the VitD level is an independent risk factor for NRDS in preterm infants (11). Boskabadi et al. (12) have reported that TTN in infants could be reduced via the treatment of VitD deficiency in mothers. Therefore, VitD may have a role in TTN pathogenesis.

A limited number of research studies have been done locally, many of which are not nationally representative. This study aimed to assess whether the serum levels of VitD are associated with TTN in infants and mother's natural childbirth.

## 2- MATERIALS AND METHODS

### 2-1. Design and Participants

This descriptive-analytical research was performed on 39 infants with TTN and their mothers, and 39 control infants and their mothers, referred to the Motazedi hospital in Kermanshah University of Medical Sciences from December 2021 to April 2022. Exclusion criteria included patients who were admitted with cesarean delivery, asthma, diabetes, and multiple births.

### 2-2. Procedure

Serum concentrations of VitD were measured by sampling 2 ml of venous blood in the first 12-24 h of postnatal age in both neonates and mothers using a chemiluminescence immunoassay (CLIA; Liaison, Diasorin Inc.).

All women were questioned in detail with a prepared checklist and examined thoroughly. The content of this checklist was confirmed by 5 faculty members of the pediatrics department. The women's age, birth order, mother's education level, maternal Body Mass Index (BMI), and drug use were observed. Also, neonates were evaluated for weight, height, accurate head circumference, and Apgar scores at 1th and 5th minutes.

In the current study suffering from tachypnea is defined as the presence of respiratory distress starting within 6 hours after birth. Symptoms of TTN include a respiratory rate above 60/min, classically with grunting and flaring nostrils, and grunting sounds when the baby breathes out (exhales), within the first 12 hours of life.

### 2-3. Data analysis

Frequency and percentage were used to represent data. Chi-square test and independent samples t-test were, respectively, used for comparing categorical and continuous data between the two groups. Pearson correlation test evaluated the correlation between serum VitD levels in neonates and their mothers. Statistical analysis was performed using the univariate analysis method in SPSS software (IBM Co.,NY, version 20). P-values less than 0.05 were considered statistically significant.

## 3- RESULTS

In our study, we analyzed a good sample size of singleton pregnant women using the same measurement method; and then, the clinical outcomes and laboratory results were examined. Table 1 presents the analysis of the demographics of baseline variables (infants and maternal characteristics) and situations in the two groups.

In the present study, no significant difference was found between healthy and TTN groups in terms of gender (p=0.653), mother's education level (p=0.115), drug use (p=0.556), asthma (p=0.494), diabetes (p=0.644), 1th min Apgar score (p=0.194), mother's age (p=0.979), birth weight (p=0.131), and birth height (p=0.541). But, there was a significant difference between the two groups of control and intervention in terms of 5th min Apgar score (p=0.043), and birth order (p=0.036). In other words: 1) one of the risk factors that was associated with TTN was a low 5th min Apgar score, and 2) the secondborns had worse TTN at birth (45%).

In comparison with healthy newborns, lower maternal BMI, and accurate head circumference were observed in TTN borns (p=0.001).

The mean levels of serum VitD were significantly lower in both TTN neonate patients and mothers (p>0.05). The mean levels in infants with TTN and their mothers were 18.62±10.14 and 20.45±7.47 ng/mL, respectively (p<0.001), whereas they were 39.68±11.12 and 39.71±13.9.8 ng/mL in the newborns of the control group and their mothers, respectively (p<0.001).

The results of the Pearson correlation coefficient indicated that there is a significant positive relationship between the serum VitD level of mothers and term infants in both of the study groups (Table 3; p<0.001).

## 4- DISCUSSION

Newborn diseases are quite distinctive among human disorders because (a) there is a major physiological change from fetal to neonatal life, (2) and some organs are still in their developing stage, like lungs. Structural development of the lung could be altered by several prenatal conditions, like maternal VitD deficiency. Thus, this study aimed to assess whether the serum levels of VitD are associated with TTN in infants and mothers.

The underlying mechanism leading to delayed absorption of alveolar fluid in neonates with TTN is unknown. Reduced surfactant function (13) and nitric oxide (14) have been proposed as contributing to the pathophysiology of TTN. Since these materials could play an important role in regulating pulmonary blood flow and pulmonary vasomotor tone (15).

**Table-1:** Demographics of cohort, infants and maternal characteristics and situations in healthy and transient tachypnea of the newborn (TTN) groups

| Parameters, n (%) | | Group | | P-value |
|---|---|---|---|---|
| | | Healthy | TTN | |
| Qualitative | | | | |
| Gender | Male | 21 (52.5%) | 23 (57.5%) | 0.653 |
| | Female | 19 (47.5%) | 17 (42.5%) | |
| Birth order | 1 | 21 (52.5%) | 12 (30%) | 0.036 |
| | 2 | 17 (42.5%) | 18 (45%) | |
| | 3 | 2 (5%) | 8 (20%) | |
| | 4 | 2 (5%) | 0 (0%) | |
| Mother's education level | Diploma and sub-diploma | 24 (60%) | 15 (37.5%) | 0.115 |
| | Associate | 6 (15%) | 14 (35%) | |
| | Bachelor | 9 (22.5%) | 9 (22.5%) | |
| | Master or higher | 1 (2.5%) | 2 (5%) | |
| Drug use | Yes | 1 (2.5%) | 2 (5%) | 0.556 |
| | No | 39 (97.5%) | 38 (95%) | |
| Asthma | Yes | 1 (2.5%) | 2 (5%) | 0.494 |
| | No | 0 (0%) | 38 (95%) | |
| Diabetes | Yes | 3 (7.5%) | 2 (5%) | 0.644 |
| | No | 37 (92.5%) | 2 (5%) | |
| Apgar score at 1th min | 7≤ | 8 (20.5%) | 12 (35%) | 0.194 |
| | 7< | 31 (79.5%) | 22 (65%) | |
| Apgar score at 5th min | 7≤ | 0 (0%) | 4 (12%) | 0.043 |
| | 7< | 39 (100%) | 30 (88%) | |
| Quantitative (Mean±S.D.) | | | | |
| Maternal age (y) | | 26.97±3.31 | 27±4.84 | 0.979 |
| Maternal body mass index (kg/M$^2$) | | 21.47±3.77 | 17.67±1.67 | 0.001 |
| Birth weight (kg) | | 2.95±0.35 | 2.86±0.17 | 0.131 |
| Birth height (cm) | | 49.45±2.50 | 48.08±3.51 | 0.541 |
| Head circumference (cm) | | 35±2.49 | 31.8±1.96 | 0.001 |

Qualitative results from Chi-square test, and quantitative results from independent samples t-test.

**Table-2:** Comparing maternal and neonatal vitamin D levels in healthy and transient tachypnea of the newborn (TTN) groups

| Parameter | | Group/vitamin D level (ng/mL) | | P-value |
|---|---|---|---|---|
| | | Healthy | TTN | |
| Neonates | Male | 39.22±8.77 | 18.97±12.10 | 0.001 |
| | Female | 40.15±13.47 | 18.28±8.18 | |
| Mothers | Male | 38.53±15.05 | 19.56±8.69 | 0.001 |
| | Female | 40.89±12.92 | 19.34±6.26 | |

**Table-3:** Correlations between vitamin D levels in the serum of mothers and neonates

| Parameter | | R | P-value |
|---|---|---|---|
| Groups | Healthy | 0.863 | 0.001 |
| | TTN | 0.880 | 0.001 |

TTN: Transient tachypnea of the newborn

VitD is one of the most important nutrients for our overall health. Based on the biological unity of mothers and newborns, Hollis et al. (16) demonstrated that the most significant risk factor for VitD deficiency in newborns is inadequate maternal VitD. Simply put, we know that healthy mothers mean healthier babies. Lindqvist et al. (17) reported that each increment of VitD fortification was associated with a 15% drop in stillbirths on a national level in Northern countries.

In agreement with current results, some experiments have shown that VitD deficiency is substantially more common in infants with TTN and their mothers than in healthy subjects (18, 19).

Omran et al. (20) stated that lower neonatal and maternal VitD levels were associated with TTN development in full-term infants. The optimum neonatal and maternal VitD levels suggested to enhance the clearance of lung liquid because of the role of VitD in fibroblast proliferation, surfactant synthesis, type-II pneumocyte cell maturation, and alveolarization (21, 22). Animal studies have shown that VitD may be important in lung development (23).

This can be explained by the fact that VitD can have numerous biological activities and impact neonatal morbidities (19). In this way, this vitamin may increase the rate of pulmonary fluid absorption in newborns with TTN.

Since the prenatal risk factors (C-section, maternal diabetes mellitus, sepsis, macrosomia, twin pregnancy, family history of asthma) are widespread in mothers, most newborns are at risk of developing TTN (6, 10). This disorder can lead to the need for respiratory support, maternal-infant separation, prolonged hospital stays, and extended unnecessary antibiotic therapy (6).

Although it is usually a self-limited condition, sometimes early management of TTN can be conducted through supportive care, and drug administration (24) to prevent exacerbation of respiratory distress.

In the present study, the levels of the VitD were < 20 ng/mL among all the TTN neonates. These results are similar to that reported by Kashaki et al. (25) VitD levels lower than 20 ng/mL are defined as VitD deficiency. Shahraki et al. (26) found beneficial effects of VitD supplementation for improving 25(OH) VitD levels in the neonatal and maternal populations for protecting against the harmful effects of VitD insufficiency/deficiency recommended. Thus, more local interventions to improve the VitD levels have to be implemented.

A low Apgar score in the 5th min was the risk factor most strongly associated with the incidence of TTN. In line with the current results, Takaya et al. (27) demonstrated that the improvement of obstetric surveillance to diminish the frequency of low Apgar scores is important for preventing TTN. On the contrary, Huang et al. (28) showed that the contribution of a low Apgar score for identifying the risk of short-term morbidity does not appear to be clinically significant.

Our study shows that birth order could affect neonate's health over the 6 hours after birth. The secondborns have worse TTN at birth. More well-designed perspective research is necessary to clarify the relationship between birth order and the mother's VitD levels.

## 5- CONCLUSION

Our study reveals that the monitoring of maternal serum VitD levels in clinically term neonates could play a predictive role in the occurrence of TTN during natural childbirth. Optimal concentrations of VitD may accelerate the mechanisms responsible for fetal lung fluid clearance.

### 5-1. Ethical Considerations

The study protocol was approved by the Ethics Review Committee of Medicine, Kermanshah University of Medical Science, Iran (approval no: IR.KUMS.MED.REC.1401.93). Written informed consent was obtained from study participants after receiving a study explanation form and oral explanation from the study clinicians in their native language.

## 6- ACKNOWLEDGMENTS

The authors gratefully acknowledge Dr. Ali Olfati in the Clinical Research Development Center, Motazedi Hospital, Kermanshah University of Medical Science, Kermanshah, Iran; for his helpful discussion of this study, improving the English language of the article, and providing advice during the clinical trial.

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