

# Determining the Relationship Between Maternal and Neonatal Vitamin D Serum Levels in Term Infants With and Without Sepsis

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## Abstract

**Objective:** To investigate the relationship between maternal and neonatal vitamin D serum levels in term infants with and without sepsis.

**Materials and methods:** This is a case-control study with 320 participants which include , 80 mothers and babies with neonatal sepsis and 80 control mothers and babies without neonatal sepsis that included in their quantitative vitamin D levels were compared with each other survey.

**Results:** Demographic and clinical characteristics of infants (age at admission, gender) and mothers (age, education level) were recorded. Blood samples were taken to check serum vitamin D levels of these babies along with their mothers. Vitamin D levels were classified as deficiency less than 10 ng/ml, moderate deficiency 10-30 ng/ml, mild deficiency 20-30 ng/ml and normal 100-30 ng/ml.33 (41.3%) of the infants born in the neonatal sepsis group and 45 (56.3%) of the control infants were male. Using Fisher's exact test, no significant difference was found between the two groups in terms of gender distribution,  $P=0.082$ . The median age of infants in the neonatal sepsis group was 5 (3-9) days and in the control group was 5 (4-6) days. The mean (age of mothers in the patient group was 29.6 (6.4) years and in the control group was 29.7 (5.6) years. The median range of maternal vitamin D levels in the neonatal sepsis group was 23.8 (15.0-30.0) and 28.6 (17.1-34.0) ng/ml in the control group. According to the Mann-Whitney U statistical test, the vitamin D level of mothers in the neonatal sepsis group was significantly lower than that of the group was the control ( $p=0.020$ ).

**Conclusion:** According to the result of the Mann-Whitney U test, the vitamin D level of mothers in the neonatal sepsis group was significantly lower than the control group ( $P=0.020$ ). Mother's vitamin D level maybe related to the incidence of neonatal sepsis.

**Keywords:** Vitamin D; Sepsis; Neonatal; Term Infants

## Introduction

Neonatal sepsis refers to the presence of signs and

symptoms of infection with or without the presence of bacteremia in the first month of a baby's life (1), which is one of the most important causes of mortality and morbidity of babies all over the world (2). In 2013, neonatal sepsis was the cause of 15% of

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infant deaths worldwide (3).

Neonatal sepsis is divided into two types, early (earlier than 7 days old) and late (7 days old and more) according to the age of the baby at the time of onset (4). The clinical symptoms of neonatal sepsis can be very mild or very severe to the extent of septic shock. The signs and symptoms of neonatal sepsis are non-specific and include such things as fever, restlessness, lethargy, respiratory symptoms (tachypnea, hypoxia, grunting), poor feeding, tachycardia, weak tissue perfusion and hypotension (4). Due to the non-specific nature of these symptoms, early and timely diagnosis is very important for treatment. Prematurity, low birth weight, immunodeficiency, premature rupture of the amniotic sac, PROM, prolonged labor, and perinatal asphyxia are among the most well-known risk factors of neonatal sepsis (Table 1) (4, 5).

One of the important causes in the occurrence of sepsis is the low ability of the immune system of newborns, which has various factors including vitamin D deficiency (6). Vitamin D also plays an important role in calcium metabolism and cell function and differentiation and induces Antimicrobial peptides are found in epithelial cells in immune sites such as intestines, lungs, skin, neutrophils and macrophages and lead to inhibiting the growth of Gram-negative and Gram-positive bacteria.

Vitamin D deficiency causes malfunction of macrophages and the production of pro-inflammatory cytokines, followed by an increase in the incidence of neonatal sepsis with infections such as GBS, Ecoli, group B strep (6). According to statistics published in Iran, vitamin D deficiency in the total group of women is 62% 60% has been reported in pregnant women (7).

Considering that in the past researches, the direct correlation between the vitamin D levels of the newborn and the mother's vitamin D levels has been proven (8); the use of vitamin D supplements for pregnant women is a suitable solution to increase the

vitamin D level of the newborn and its intake. It seems to reduce sepsis. (8-10) Considering that the decrease in vitamin D level is one of the factors that cause SGA and prematurity, both of which are predisposing factors for neonatal sepsis, and vitamin D is one of the factors that modulate the immune system and has a clear effect in increasing the number of lymphocytes and The occurrence of plasmacytoid dendritic cells (11-13) and considering the evidence that vitamin D level is related to the occurrence of neonatal sepsis and its faster recovery and considering that limited studies on the serum level of vitamin D and its relationship with neonatal sepsis have been conducted. We tried to study the relationship between vitamin D levels and neonatal sepsis (14-18).

### Materials and methods

This study was carried out using a case-control method on a group of newborn patients less than 28 days of term who were hospitalized at Bahrami hospital of TUMS with the diagnosis of sepsis and a group of control group of newborn patients less than 28 days of term who were hospitalized for a reason other than sepsis.

The study included 320 participant 160 mother & babies with sepsis in case group & 160 mother & their neonate without sepsis. Term infants with a gestational age of more than 37 weeks and an age of less than 28 days, who were diagnosed with sepsis or without sepsis, were admitted to the neonatal unit or neonatal intensive care unit. Exclusion criteria were congenital abnormalities, prematurity and lack of laboratory data, as well as premature rupture of membranes and maternal chorioamnionitis. After obtaining informed consent from parents, these infants were included in the study. A complete history was taken and a complete clinical examination was performed in all infants. Sepsis was defined based on at least 2 clinical and laboratory manifestations.

**Table 1:** Risk factors of neonatal sepsis

Variables	OR	95% Confidence Interval	P-value
Gender of the baby	2.0	0.98-3.9	0.056
Female			
Baby's age	4.3	1.9-9.7	< 0.001
7 days and more			
Maternal vitamin D status			
Shortage	24.6	2.8-212.2	0.004
Insufficient (moderate)	1.6	0.7-3.7	0.304
Insufficient (mild)	2.0	0.9-4.7	0.106

The ethical considerations included the following: 1) refraining from including personal characteristics in questionnaires, checklists and other measurement tools, 2) inviting participation in the study and obtaining informed consent, taking into account the objectives, methodology and potential risks, 3) explaining the methodology, objectives and potential risks to study participants, 4) ensuring that study participants know that they can withdraw their participation at any time if they so wish and that their non-participation will not limit their access to care or services, 5) ensuring that the confidentiality of study participants is maintained with respect to all data collected and its analysis, 6) making research results available to study participants and research investigators, 7) acknowledging participants' contributions to the study, and 8) ensuring that the rights of the University are respected in the presentation of research results. The study was approved by the ethics committee of Tehran University of Medical Sciences. Ethical code: IR.TUMS.MEDICINE.REC.1397.907

**Data Analysis:** The results were statistically analyzed using SPSS 24. The results were expressed as percentages for qualitative data and as mean  $\pm$  SD for quantitative data. Changes in symptom severity and patient response to treatment were analyzed. To examine the relationship between qualitative variables, the chi-square test was used. To compare quantitative variables, the T-test for independent samples and the Mann-Whitney test were used. A value of 0.05 was considered significant.

## Results

80 mothers and 80 term infants with sepsis and 80 mothers and 80 term infants hospitalized for a reason other than neonatal sepsis were evaluated, 33 (41.3%) of the infants born in the neonatal sepsis group and 45 (56.3 %) of the control infants was male. Using Fisher's exact test, no significant difference was found between the two groups in terms of gender distribution,  $P=0.082$ . The median age of infants in the neonatal sepsis group was he sama 5 (9-3) days versus control group 5 (4-6) days.

The age of 51 (63.7%) patients in the neonatal sepsis group was less than 7 days (early infection) and 29 patients (36.3%) were 7 days or more (late infection). In the control group, the number of infants less than 7 days old was 68 patients (85.0%) and the number of infants  $>7$  was 12 patients (15.0%). Using Fisher's exact test, a significant difference was found

between the two groups in terms of the frequency distribution of babies according to age group ( $p=0.003$ ). The median of vitamin D level in the neonatal sepsis group was 18.1 (12.4-24.1) and 21.2 (31-14.8) ng/ml in the control group. Using the Mann-Whitney U statistical test, the difference found between the two groups was not significant in terms of neonatal vitamin D levels ( $p=0.072$ ).

Vitamin D level was normal in 14 infants (17.5%) of neonatal sepsis patients and 27 infants (33.8%) of the control group. Vitamin D deficiency was found in 11 infants (13.8%) of the patient group and 7 infants (8.8%) of the control group. The rest of the babies had some degree of vitamin D deficiency. According to the chi-square test, there was no significant difference between the patient and control groups in terms of the classification of neonatal vitamin D levels ( $p=0.115$ ), the median of maternal vitamin D levels in the neonatal sepsis group was 23.8 and in the control group it was 28.6 ng/ml. According to the Mann-Whitney U statistical test, the vitamin D level of mothers in the neonatal sepsis group was significantly lower than that of the group was the control ( $p=0.020$ ).

Using Spearman's correlation test, we examined the relationship between mother's and infant's vitamin D levels, the level of vitamin D of mothers had a positive and significant relationship with the level of vitamin D of newborns ( $r_s=0.650$ ,  $P<0.001$ ). According to the result of the Spearman correlation test, the relationship between the level of vitamin D of newborns and the age of the newborn ( $r_s=0.128$ ,  $P=0.106$ ), baby's gender ( $r_s=-0.087$ ,  $P=0.272$ ) mother's age ( $r_s=0.141$ ,  $P=0.075$ ) and mother's education ( $r_s=0.106$ ,  $P=0.184$ ) were not significant. Maternal vitamin D level had no significant relationship with infant's gender ( $r_s=-0.032$ ,  $P=0.692$ ). (However, a weak and significant correlation was found between maternal vitamin D level and maternal age ( $r_s=0.164$ ,  $P=0.038$ ). Finally, the risk factors of neonatal sepsis were investigated using logistic regression test. After correcting the effect of the baby's age, the mother's vitamin D level was among the independent risk factors of neonatal sepsis. The probability of neonatal sepsis in infants with vitamin D deficient mothers is 24.6 times

## Discussion

According to the data collected from a total of 320 mothers and full-term babies, this study shows the effect of mother's vitamin D level on the occurrence of neonatal sepsis. Lack of vitamin D levels in the mother is associated with an increased risk of sepsis in her

baby. Although the level of vitamin D in infants with postnatal disease was lower than the level of vitamin D in infants, but it did not reach a significant level.

Due to the ease and availability of supplementary vitamins in order to reduce the serum In previous similar studies, the vitamin D level of mothers and infants with early-onset sepsis compared to the control group has been compared (19-22), but the level of vitamin D in mothers and infants with late-onset sepsis is controversial. In previous investigations, vitamin D levels in both mothers and infants of the patient group were significantly lower than the control group (23). In another study in India, the vitamin D levels of 175 infants with late-onset sepsis were compared with 50 control infants. That, like the previous study, the level of vitamin D in the patient group was significantly lower than the control group (25). In a similar study, the vitamin D level of mothers and babies with neonatal sepsis (early and late) was investigated and compared with the control group and the number of 39 people (76.5%) of the infants in the sepsis group had premature sepsis, which was a higher percentage compared to this study (63.7%), and also the vitamin D level of the mothers in the neonatal sepsis group was significantly lower than the control group. This study shows that although the level of vitamin D in infants in the sepsis group was lower than the control group, only the early sepsis group had lower vitamin D levels compared to the control group, and this result was the same for infants with late sepsis (22). In all these studies, the mother's vitamin D level had a direct and strong relationship with the baby's vitamin D level (19, 20, 22).

In the present study, the normal level of vitamin D was found in only 26% of the mothers of the patient group and 40% of the mothers of the control group. Studies conducted all over the world indicate the high prevalence of vitamin D deficiency in pregnant mothers. Higher levels of vitamin D in pregnant mothers are associated with lower rates of vaginal GBS transmission, which is one of the most common pathogens involved in neonatal sepsis (20, 21). Although it is possible to make active vitamin D in the newborn's kidneys, the level of vitamin D in the newborn is largely dependent on the vitamin D status of the mother at the time of delivery (24, 19). In another study in India, the vitamin D levels of 175 infants with late-onset sepsis were compared with 50 control infants. That, like the previous study, the level of vitamin D in the patient group was significantly lower than the control group (25).

Recent studies recommend the use of supplements and improving the mother's nutritional status during pregnancy to improve the mother's vitamin D status and the baby's health (19). In the present study, there was no significant difference in the level of mother's education in the two neonatal sepsis and control groups. However, mother's vitamin D level was directly related to mother's level of education. Thus, the level of vitamin D was higher in educated mothers. A number of other studies have mentioned the low education of the mother as one of the risk factors of vitamin D deficiency in the mother. The consumption of vitamin D supplements is higher in mothers who have a higher level of education. Therefore, the mother's low education can be considered as one of the factors that are indirectly related to neonatal sepsis (13). Another study indicated that vitamin D deficiency may increase the risk of low birth weight babies, and modifying maternal nutritional behaviour and vitamin D levels may be beneficial to pregnancy outcomes (26).

## Conclusion

It is from this study on the relationship between the level of vitamin D and then the newborn with the lowest amount, and with the consumption of vitamin D, it is able to reduce one of the risk factors of neonatal factors and, as a result, reduce mortality and costs and complications. There is a relationship between the vitamin D level of the mother and the baby, and incidence of sepsis.

## Conflict of Interests

Authors declare no conflict of interests.

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The principles of the Declaration of Helsinki were observed throughout the study.

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