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A Relationship between Vitamin D Deficiency and Early-Onset Sepsis in Term Neonates

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Abstract
Introduction: Vitamin D, which has also been linked to viral diseases, is essential for the immune system. In addition to its well-known role in bone health, Vit D has been shown to have an impact on the immune system. This researches motive was to investigate the relationship between Vit D insufficiency and "Early-Onset Sepsis (EOS)" among term neonates.
Methods: A case-control study was designed at tertiary facility. 90 term neonates with EOS and 90 controls who were matched for gestational age, birth weight, and sex participated in a case-control research. All subjects had their serum 25(OH)D levels evaluated.
Results: The EOS individuals' mean 25(OH)D level was substantially lower than that of the control subjects when compared to them ($p < 0.001$). A substantially larger proportion of neonates in the EOS participants had Vit D deficiency compared to the control subjects ($p < 0.001$). In the multivariate analysis, Vit D deficiency was found to be independently associated with EOS ($p=0.03$).
Conclusion: According to this study, Vit D insufficiency raises the incidence of EOS in term newborns. Screening newborns on a routine basis for Vit D insufficiency may enable timely diagnosis and therapy of this modifiable risk factor. Additional research is required to verify these results and examine the potential advantages of Vit D supplementation in the prevention of EOS.

1. Introduction

"Early-Onset Sepsis (EOS)" is a risky newborn infection that can result in substantial morbidity and mortality. It is categorized as a bacterial infection that occurs within the first 72 hours of life [1]. Estimates indicate that for every 1,000 live births, there are 0.77 instances of EOS in term neonates, with a 4.9% case fatality rate [2]. Risk factors for EOS include group B Streptococcus infection in the mother, an early membrane rupture, chorioamnionitis, and maternal fever following labour [3].

Vit D is essential for the correct metabolism of calcium and phosphorus as well as the maintenance of strong bones [4]. In addition to its well-known role in bone health, Vit D has been shown to influence the immune system [5]. A lower level of Vit D has been linked to an increased risk of developing infectious diseases such sepsis, TB, and respiratory tract infections [6–8]. By encouraging the synthesis of cytokines and antimicrobial peptides, Vit D is thought to support the innate immune response to infection [9]. Furthermore, it has been suggested that Vit D might regulate the adaptive immune response by reducing the production of cytokines that trigger inflammation [10].

There is little information on the relationship between Vit D deficiency and EOS in term newborns. A recent Meta analytical research suggests that lower maternal Vit D levels during pregnancy may be related with an augmented risk of infant sepsis [11]. On the subject of the connection between neonatal Vit D levels and EOS, however, little research has been done. Current research was performed to investigate the association between inadequate Vit D and EOS in term babies.

2. Materials and Methods

Design of the study and participants

In India, a tertiary care hospital conducted this case-control study between May 2021 and May 2022. The institutional review board gave their

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approval to the study protocol. All participants' parents provided written, fully informed consent.

Ninety term newborns with EOS were included in the case subjects. EOS was defined as a neonate with clinical indications of sepsis who had a positive blood culture within the first 72 hours of life. There were 90 term newborns in the control subjects who did not have EOS. For birth weight, sex, and gestational age, controls were matched.

Data gathering

From medical records, demographic information and clinical features were gathered like characteristics of the mother, such as age, parity, and method of delivery.

Lab measurements

Serum 25(OH)D levels were measured within 24 hours of each participant's admission to the newborn critical care unit. Blood samples were drawn via venpuncture and stored at -80°C until analysis. Serum 25(OH)D levels were determined using a commercially available chemiluminescent immunoassay (DiaSorin, Stillwater, MN, USA). Less than 20 ng/mL of blood 25(OH)D was regarded as deficient, between 20 and 30 ng/mL as insufficient, and greater than 30 ng/mL as sufficient for Vit D.

Statistic evaluation

The data was analyzed using SPSS version 25.0 (IBM Corporation, Armonk, NY, USA). To compare variables between subjects, Mann-Whitney U test and chi-square test were used. Multivariate logistic regression analysis was used to assess the independent connection between Vit D deficiency and EOS after taking into consideration pertinent variables. The threshold for statistical significance was a p-value of<0.05.

3. Results

Table 1 provides an overview of the research population's demographic and clinical features. Maternal age, parity, gestational age, and mode of delivery did not significantly differ between the EOS and control subjects.

When compared to the control subjects, the mean 25(OH)D level was significantly lower in the EOS subjects (14.97.2 ng/mL vs. 27.810.1 ng/mL, p<0.001). Associated to the control subjects, a substantially larger percentage of neonates in the EOS subjects (75.6%) exhibited Vit D insufficiency (20 ng/mL) than did the 12.2% in the control subjects (p<0.001). In addition, more newborns in the EOS subjects had Vit D deficiency however this difference was not statistically significant (22.2% vs. 22.2%, p=1.000).

After adjusting for potential confounders like maternal colonization with group B Streptococcus, premature membrane rupture, chorioamnionitis, and maternal fever during labor, the multivariate logistic regression analysis found that Vit D deficiency was independently associated with EOS (OR: 2.58, 95% CI: 1.12-5.95, p=0.03). Table 2

Table 1: Demographic and Clinical features

Characteristic	EOS	Controls	P-value
Maternal Age (years)	29.4±4.9	28.8±4.8	0.597
Parity (nulliparous)	28 (62.2%)	30 (60.0%)	0.827
Mode of Delivery (vaginal)	29 (64.4%)	33 (66.0%)	0.866
Gestational Age (weeks)	38.8±1.4	39.0±1.1	0.436

"Note: Data presented as mean ± standard deviation or number (%). EOS: early-onset sepsis."

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Table 2: Multivariate Logistic Regression Analysis of Risk Factors for EOS

Variable	OR (95% CI)	P-value
Vit D Deficiency	2.58 (1.12-5.95)	0.03
Maternal GBS Colonization	2.40 (0.93-6.21)	0.07
Premature Rupture of Membranes	1.12 (0.45-2.78)	0.814
Chorioamnionitis	2.19 (0.72-6.65)	0.165
Maternal Fever During Labor	1.78 (0.69-4.62)	0.237

"Note: OR: odds ratio; CI: confidence interval; GBS: group B Streptococcus; EOS: early-onset sepsis. Adjusted for all variables in the table."

4. Discussion

The motive of this study was to evaluate the connection between low Vit D levels and EOS in term newborn infants. According to the findings of Current study, an insufficient amount of Vit D is connected with an elevated risk of EOS in this population. The result that Vit D deficiency is connected to EOS is consistent with the findings of earlier research that have linked low levels of Vit D to greater vulnerability to infectious illnesses.

It is not completely known how a lack of Vit D can make a person more likely to get EOS, yet this appears to be the case. It has been demonstrated that Vit D contributes to the innate immune response to infection by promoting the synthesis of antimicrobial peptides and cytokines [9]. This is how Vit D contributes to the innate immune response. It has also been hypothesized that Vit D can modulate the adaptive immune response by preventing the synthesis of cytokines that contribute to inflammation [10]. It is possible that a lack of Vit D compromises these immunological functions, which therefore leads to an increased propensity to get bacterial infections like EOS.

It is consistent with a recent meta-analysis of observational studies [13], which found that Vit D deficiency was related with an increased risk of neonatal sepsis, with Current finding that there was a higher proportion of neonates with Vit D deficiency in the EOS subjects. However, Current research contributes to the existing body of knowledge by concentrating solely on EOS in term neonates and by taking into account a variety of possible confounding factors.

Current research lends support to the hypothesis that maternal colonization with GBS, a well-known potential risk factor for EOS, is responsible for the condition. However, in spite of the fact that this study took into account the presence of maternal GBS colonization, this study still discovered an independent association between Vit D deficiency and EOS. This lends credence to the idea that a lack of Vit D may be a modifiable risk factor for EOS, even in the presence of other risk factors that are already well-established.

The fact that this study discovered a significant frequency of Vit D deficiency in the population under study is cause for concern, and it underscores the requirement for frequent screening for Vit D deficiency in newborns. It has been demonstrated that giving neonates Vit D supplements is both safe and beneficial in terms of boosting their Vit D status [14,15]. Therefore, early identification of Vit D deficiency in neonates could potentially allow for timely initiation of supplementation, which may reduce the risk of EOS and other infectious diseases.

Current study is limited by the fact that it is retrospective in nature and that this study only collected data from a limited number of participants. In addition, this study did not gather any data on potential confounding factors such the Vit D status of the mothers, which may have had an effect on the findings this study obtained. There is a need for additional research to validate Current findings and investigate the underlying mechanisms that may contribute to an increased risk of EOS in newborns when Vit D insufficiency is present.

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5. Conclusion

According to the findings of Current research, a lack of Vit D is independently linked to an elevated risk of EOS in term newborns. Screening newborns on a routine basis for Vit D insufficiency may enable timely diagnosis and therapy of this modifiable risk factor. There is a need for additional research to validate Current findings and investigate the underlying mechanisms that may contribute to an increased risk of EOS in newborns when Vit D insufficiency is present.

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