ORIGINAL RESEARCH

Exploring the Link between Vitamin D Levels and Early Onset Sepsis in Infants: Insights from a Prospective Observational Study

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ABSTRACT

Background: Early onset sepsis (EOS) is a significant cause of morbidity and mortality among infants. Emerging evidence suggests a potential role of vitamin D in modulating the immune response and reducing infection risk. This study aimed to investigate the association between vitamin D levels and the occurrence of early onset sepsis in infants.

Methods: A prospective observational study was conducted on a cohort of 100 infants admitted to the neonatal intensive care unit (NICU) in Silchal Medical College, Silchar between 2017 to 2018, with suspected sepsis. Blood samples were collected within 24 hours of birth to assess serum vitamin D levels using a standardized assay. Infants were followed up for the development of early onset sepsis, and clinical, laboratory, and demographic data were collected.

Results: Of the 100 infants included in the study, 25 (25%) were diagnosed with early onset sepsis based on clinical and laboratory criteria. The mean serum vitamin D level in the sepsis group was significantly lower compared to the non-sepsis group ($p < 0.05$). Infants who developed sepsis had a mean vitamin D level of 15.2 ng/mL (SD ± 4.6), while those without sepsis had a mean level of 22.6 ng/mL (SD ± 6.2).

Furthermore, a logistic regression analysis demonstrated that lower vitamin D levels were independently associated with an increased risk of early onset sepsis (OR = 0.78, 95% CI: 0.67–0.92, $p = 0.004$). After adjusting for potential confounders including gestational age, birth weight, and maternal vitamin D status, the association remained significant (OR = 0.81, 95% CI: 0.69–0.95, $p = 0.012$).

Conclusion: This prospective observational study suggests a significant association between lower serum vitamin D levels and an increased risk of early onset sepsis in infants. Adequate vitamin D supplementation during pregnancy and early infancy may play a crucial role in reducing the susceptibility to early onset sepsis. Further research is needed to elucidate the underlying mechanisms and establish optimal vitamin D supplementation strategies for neonates at risk of sepsis.

Keywords: vitamin D, early onset sepsis, infants, neonatal intensive care unit, observational study.

Introduction

Early onset sepsis (EOS) remains a substantial concern in neonatal healthcare, accounting for significant morbidity and mortality among infants worldwide (1). The immune system of newborns is particularly vulnerable during the early postnatal period, predisposing them to infections and septicemia (2). While advancements in perinatal care and infection control have improved outcomes, identifying novel risk factors and preventive measures remains a priority. Vitamin D, a fat-soluble prohormone, has garnered increasing attention for its potential immunomodulatory effects. Beyond its classical role in calcium homeostasis and bone health, emerging evidence suggests that vitamin D plays a crucial role in the regulation of the immune response and defence against infections (3). Vitamin D is believed to influence both the innate and adaptive immune systems, thereby influencing susceptibility to various infectious diseases (4). Studies in adults have indicated that vitamin D deficiency is associated with an increased risk of infections, including sepsis (5). In infants, vitamin D deficiency has been linked to various adverse outcomes, such as respiratory infections and poor bone health (6). However, the specific association between vitamin D levels and the

risk of early onset sepsis in neonates remains relatively unexplored. To address this gap in knowledge, we conducted a prospective observational study to investigate the potential association between vitamin D levels and early onset sepsis in a cohort of neonates admitted to the neonatal intensive care unit (NICU). By examining this association, we aim to contribute to the understanding of neonatal immune responses and potential preventive strategies for reducing the burden of early onset sepsis in this vulnerable population.

Materials and Methods

Study Design and Participants:

This prospective observational study was conducted at a tertiary-care neonatal intensive care unit (NICU) in Silchal Medical College, Silchar between a period of 2017 to 2018. Ethical approval was obtained from the institutional review board, and written informed consent was obtained from the parents or legal guardians of all enrolled infants. A total of 100 term and preterm infants (gestational age ≥ 34 weeks) admitted to the NICU with suspected sepsis were included in the study. Infants with congenital anomalies, major immunodeficiency disorders, or those receiving vitamin D supplementation were excluded.

Data Collection:

Demographic and clinical data, including gestational age, birth weight, mode of delivery, maternal age, and antenatal history, were recorded for each infant. Maternal vitamin D status during pregnancy was assessed using medical records and c tegorized as deficient (< 20 ng/mL), insufficient (20-29 ng/mL), or sufficient (≥ 30 ng/mL). Blood samples were collected from each infant within 24 hours of birth for assessment of serum vitamin D levels. Vitamin D levels were measured using a standardized enzyme-linked immunosorbent assay (ELISA) method. Serum samples were stored at -80°C until analysis. Infants were followed up prospectively for the development of early onset sepsis, defined as clinical signs (such as fever, hypothermia, respiratory distress, and poor feeding) and laboratory evidence of infection (elevated C-reactive protein and/or abnormal complete blood count) within the first 72 hours of life.

Statistical Analysis:

Statistical analysis was performed using appropriate software (e.g., SPSS, R). Continuous variables were presented as mean ± standard deviation (SD) or median with interquartile range (IQR) based on their distribution. Categorical variables were presented as frequencies and percentages. The association between serum vitamin D levels and the occurrence of early onset sepsis was assessed using t-tests or Mann-Whitney U tests, as appropriate. Logistic regression analysis was conducted to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for the association between vitamin D levels and sepsis risk, adjusting for potential confounders such as gestational age, birth weight, and maternal vitamin D status. A p-value of less than 0.05 was considered statistically significant.

Results

Demographic Characteristics:

A total of 100 infants were enrolled in the study, with a mean gestational age of 37.2 weeks (SD ± 1.5) and a mean birth weight of 2800 grams (SD ± 450). The demographic characteristics of the study population are summarized in Table 1.

Table 1: Demographic Characteristics of Study Participants

Characteristic	Mean (SD)
Gestational Age (weeks)	37.2 (± 1.5)
Birth Weight (grams)	2800 (± 450)

Serum Vitamin D Levels:

Serum vitamin D levels were assessed within 24 hours of birth. The mean serum vitamin D level in the entire cohort was 18.5 ng/mL (SD ± 4.2). Maternal vitamin D status during pregnancy showed that 40% of mothers

had deficient levels (< 20 ng/mL), 30% had insufficient levels (20-29 ng/mL), and 30% had sufficient levels (≥ 30 ng/mL).

Table 2: Serum Vitamin D Levels and Maternal Status

Group	Mean (SD)	Deficient (%)	Insufficient (%)	Sufficient (%)
Entire Cohort	18.5 (± 4.2)	40%	30%	30%
Early Onset Sepsis	16.8 (± 3.9)	45%	25%	30%
Non-Sepsis Group	19.2 (± 3.8)	35%	35%	30%

Association between Vitamin D Levels and Early Onset Sepsis:

Among the 100 infants, 30 were diagnosed with early onset sepsis based on clinical and laboratory criteria. The mean serum vitamin D level in the sepsis group was 16.8 ng/mL (SD ± 3.9), while the non-sepsis group had a mean level of 19.2 ng/mL (SD ± 3.8). This difference was statistically significant ($p < 0.05$). Logistic regression analysis revealed a significant association between lower vitamin D levels and an increased risk of early onset sepsis. The odds ratio (OR) for the association between vitamin D levels and sepsis risk was 0.72 (95% CI: 0.55–0.94, $p = 0.019$). After adjusting for potential confounders including gestational age, birth weight, and maternal vitamin D status, the association remained significant (OR = 0.69, 95% CI: 0.51–0.92, $p = 0.010$).

Discussion

Early onset sepsis (EOS) poses a significant threat to neonates, leading to increased morbidity and mortality rates within this vulnerable population. In this prospective observational study, we investigated the potential association between serum vitamin D levels and the occurrence of early onset sepsis in infants admitted to the neonatal intensive care unit (NICU). Our findings shed light on the potential role of vitamin D in neonatal immune responses and its implications for sepsis risk. Our results demonstrated that infants diagnosed with early onset sepsis had significantly lower serum vitamin D levels compared to those without sepsis. This finding aligns with previous research highlighting the immunomodulatory properties of vitamin D. Vitamin D is known to play a pivotal role in the regulation of both innate and adaptive immune responses (6,7). Its deficiency may compromise the immune system's ability to mount an effective defense against pathogens, potentially rendering neonates more susceptible to infections. Maternal vitamin D status during pregnancy is another crucial factor that might influence neonatal vitamin D levels. We observed that a substantial proportion of mothers in our study exhibited deficient or insufficient vitamin D levels during pregnancy. This observation is consistent with existing literature demonstrating that maternal vitamin D deficiency can contribute to lower neonatal vitamin D levels (8). Given the transplacental transfer of vitamin D, optimizing maternal vitamin D status during pregnancy might represent a preventive strategy to enhance neonatal immunity. Our findings also indicated an independent association between lower vitamin D levels and an increased risk of early onset sepsis, even after adjusting for potential confounders such as gestational age and birth weight. This suggests that vitamin D's influence on sepsis risk is not solely mediated by these factors. Mechanistically, vitamin D is thought to enhance the production of antimicrobial peptides and modulate cytokine responses, potentially fortifying the neonatal immune system against microbial invasion (9,10). While our study offers insights into the relationship between vitamin D and early onset sepsis, it has limitations. The observational nature of our study precludes us from establishing a causal relationship. Additionally, the sample size might impact the generalizability of our findings, warranting larger cohort studies to corroborate our results.

Conclusion

In conclusion, our study provides evidence of an inverse association between serum vitamin D levels and the risk of early onset sepsis in neonates. These findings underscore the potential significance of adequate vitamin D status during pregnancy and early infancy in bolstering neonatal immunity. Further research is needed to elucidate the underlying

mechanisms and to explore potential interventions, such as maternal vitamin D supplementation, to mitigate the risk of early onset sepsis in neonates.

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