e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(4); 306-309

Original Research Article

Impact of Vitamin D Deficiency on Morbidity & Mortality in Early Onset Sepsis among Term Neonates

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Received: 01-01-2026 /Revised: 15-02-2026 / Accepted: 21-03-2026
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Conflict of interest: Nil

Abstract

Introduction: Early-onset neonatal sepsis (EONS) is a significant cause of neonatal morbidity and mortality, particularly in developing countries. Vitamin D has important immunomodulatory functions, and neonates are entirely dependent on maternal vitamin D stores. Deficiency may increase susceptibility to infections; however, Indian data on its association with early-onset sepsis are limited.

Aim and Objective: To study the impact of serum vitamin D levels on early-onset neonatal sepsis in term neonates, and to assess its impact on clinical outcomes.

Materials and Methods: This hospital-based prospective case-control study was conducted at Santosh Medical College and Hospital, Ghaziabad. A total of 138 term neonates were enrolled, including 69 neonates with early-onset sepsis (≤72 hours of life) and 69 healthy term neonates as controls. Diagnosis of sepsis was based on clinical features supported by laboratory parameters including C-reactive protein, complete blood count, immature-to-total neutrophil ratio, platelet count, and blood culture. Serum 25-hydroxyvitamin D levels were measured in all neonates. Maternal risk factors and intrapartum antibiotic prophylaxis were recorded. Statistical analysis was performed using STATA MP-17, with $p < 0.05$ considered statistically significant.

Results: Mean serum vitamin D levels were significantly lower in neonates with early-onset sepsis than in controls (10.30 ± 3.23 vs 24.71 ± 5.43 ng/mL; $p < 0.001$). Vitamin D deficiency was more common among septic neonates. Maternal fever, infections, and inadequate intrapartum antibiotic prophylaxis were significantly associated with early-onset sepsis. Blood culture was positive in 73.9% of cases. Septic neonates required longer NICU stay, prolonged antibiotic therapy, and greater respiratory support, with worse outcomes seen in those with severe vitamin D deficiency.

Conclusion: Vitamin D deficiency has significant impact on early-onset neonatal sepsis in term neonates and correlates with increased disease severity. Affected neonates required longer NICU stay, prolonged antibiotic therapy, and greater respiratory support. Since vitamin D deficiency is preventable, maternal screening and supplementation may help reduce early-onset neonatal sepsis and improve outcomes.

Keywords: Early-onset neonatal sepsis; Vitamin D deficiency; Term neonates; Neonatal outcomes; maternal risk factors.

DOI: 10.25258/ijcpr.18.4.50

Introduction

One of the most dangerous causes of illness and death in newborns is neonatal sepsis. It is thought that vitamin D (calciferol) supports the body's ability to fight infections by helping cells including epithelial cells, neutrophils, and macrophages produce chemicals that fight infections. [1] Low levels of vitamin D in cord blood have also been linked to an increased risk of infection. We evaluated the vitamin D levels of newborns in this prospective case-control study and looked into any possible connections between vitamin D status and the development of neonatal sepsis. Vitamin D, a fat-soluble vitamin, is also essential for immune system performance. Whether or not blood bacteria are present, infection-related signs and symptoms that manifest within the first three days of birth are referred to as early onset sepsis (EOS). This study aimed to identify whether low neonatal vitamin D

levels in term neonates were associated with early-onset sepsis. [2] Compared to patients with normal vitamin D levels, individuals with low levels were more likely to have severe sickness, stay in the hospital longer, and die. Low vitamin D levels have also been connected to longer ventilator support periods in pediatric intensive care units. [3] Some neonatal studies suggest that normal vitamin D levels, or correction of deficiency in newborns and infants, may help reduce illness and death related to neonatal sepsis. Clinical trials also indicate that adequate vitamin D supplementation during pregnancy may help prevent early onset sepsis in term newborns. Vitamin D deficiency has been found to be more common in babies with sepsis. Vitamin D has also been considered as a possible supportive treatment in neonatal sepsis. Vitamin D administration has been shown in therapeutic studies to enhance sepsis scores and lower high-sensitivity C-reactive protein (hsCRP) levels. According to new recommendations, pregnant women may need more than 400 IU of vitamin D per day because some research indicate that vitamin D levels in mothers and cord blood remain low even after regular supplementation programs. This shows the need for better supplementation strategies during pregnancy. [4,5]

Materials and Methods

A hospital-based prospective case-control study was conducted in the Neonatal Intensive Care Unit (NICU) and postnatal wards of Santosh Medical College and Hospital, Ghaziabad. The study included 138 term neonates, comprising 69 cases with early-onset neonatal sepsis (onset within 72 hours of life) and 69 healthy term neonates as controls. Early-onset sepsis was diagnosed based on clinical features supported by laboratory parameters including C-reactive protein (CRP), complete blood count, immature-to-total neutrophil ratio, platelet count, and blood culture results. Serum 25-hydroxyvitamin D levels were measured in all neonates. Maternal risk factors such as fever during labour, urinary tract infection, gestational diabetes mellitus, pregnancy-induced hypertension, and intrapartum antibiotic prophylaxis were documented. Statistical analysis was performed using STATA MP-17, and a p-value <0.05 was considered statistically significant.

Results

The age distribution of participants revealed that the majority of neonates in both the early-onset sepsis and control groups were either early term or full term, with nearly equal proportions in each category. Only a single neonate belonged to the late-term group. The overall gestational age distribution was comparable between the two groups, and the difference was not statistically significant (p = 0.552), indicating that gestational maturity did not have a significant association with early-onset neonatal sepsis in this study population.

Table 1: Mode of Delivery

Delivery Route	EONS Cases	Controls	Total	p-value
Em. LSCS	0 (0%)	3 (4.3%)	3 (2.2%)	0.189
LSCS	27 (39.1%)	23 (33.3%)	50 (36.2%)	
NVD	42 (60.9%)	43 (62.3%)	85 (61.6%)	
Total	69 (100%)	69 (100%)	138 (100%)	

The majority of the neonates in both the AEONS (60.9%) and control (62.3%) groups were delivered vaginally, with caesarean sections accounting for about one-third of deliveries and emergency procedures being rare. There was no statistically significant association between mode of delivery and neonatal sepsis (p = 0.189), suggesting that maternal or intrapartum infections rather than delivery method influenced the occurrence of AEONS.

Table 2: Maternal Risk Factors

Maternal Risk Factor	EONS Cases	Controls	Total	p-value
None	21 (30.4%)	47 (68.1%)	68 (49.3%)	<0.001
GDM	5 (7.2%)	9 (13.0%)	14 (10.1%)	
GDM + UTI	5 (7.2%)	0 (0%)	5 (3.6%)	
PIH	8 (11.6%)	5 (7.2%)	13 (9.4%)	
Type 2 DM	6 (8.7%)	1 (1.4%)	7 (5.1%)	
UTI	21 (30.4%)	0 (0%)	21 (15.2%)	
Others (mixed)	3 (4.3%)	7 (10.1%)	10 (7.2%)	
Total	69 (100%)	69 (100%)	138 (100%)	

The maternal risk factors associated with neonatal sepsis- Urinary tract infections were the most frequent risk followed by pregnancy-induced hypertension, gestational diabetes, and type 2 diabetes. In contrast, 68.1% of control mothers had no detectable risk factors. The difference between the groups was highly significant (p <

0.001).

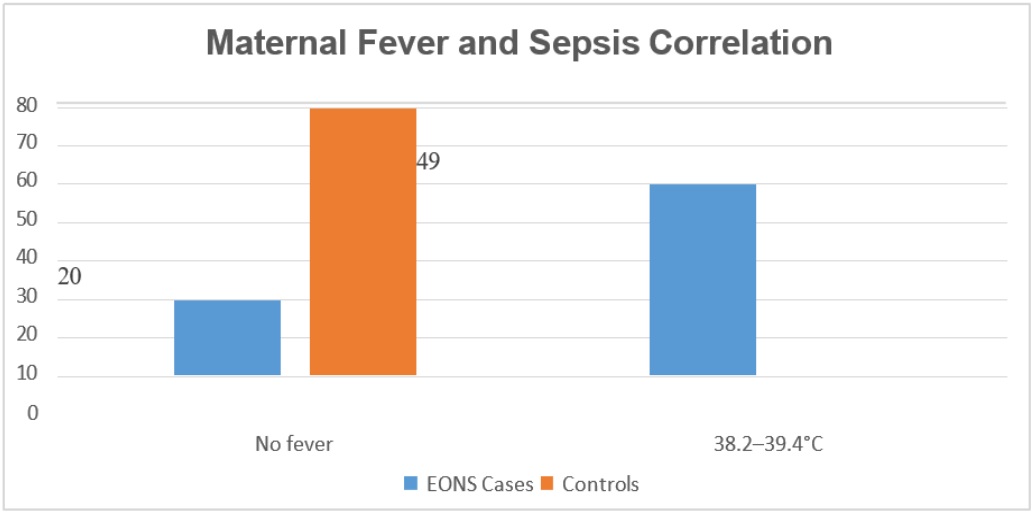

Figure 1: Maternal Fever and Sepsis Correlation

The figure illustrates the relationship between maternal fever during labour and early-onset neonatal sepsis. A significantly higher proportion of mothers of AEONS cases had documented fever (38.2–39.4°C), whereas none of the mothers in the control group had fever. This finding indicates a strong association between maternal intrapartum fever and the occurrence of early- onset neonatal sepsis.

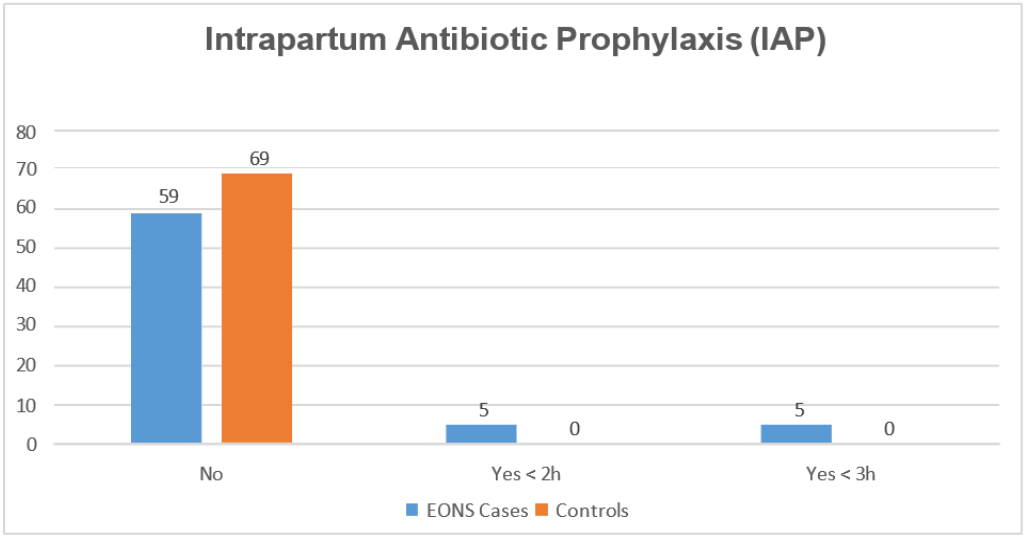

Figure 2: Intrapartum Antibiotic Prophylaxis (IAP)

The figure illustrates the distribution of intrapartum antibiotic prophylaxis among mothers of neonates with early-onset neonatal sepsis and controls. A significantly higher proportion of mothers in the EONS group did not receive intrapartum antibiotic prophylaxis, whereas all mothers in the control group received antibiotics. Only a small number of mothers in the EONS group received antibiotics within 2–3 hours prior to delivery. These findings suggest that absence or inadequate timing of intrapartum antibiotic prophylaxis is strongly associated with the occurrence of early-onset neonatal sepsis.

Discussion

In the present study, most neonates with early-onset sepsis were either early term (47.8%) or full term (50.7%), with no significant difference compared to controls ($p = 0.552$), indicating that gestational age did not influence infection risk. Similar observations were reported by Cetinkaya et al. [6], who found comparable gestational ages among septic and non-septic neonates. Singh and Chaudhari [7] also demonstrated that neonatal maturity did not significantly affect the occurrence of early-onset sepsis, emphasizing that maternal and intrapartum factors play a more critical role than gestational age alone. In the present study, the mode of delivery showed no significant association

with early-onset neonatal sepsis, as the majority of both cases (60.9%) and controls (62.3%) were delivered vaginally ($p = 0.189$). Caesarean and emergency caesarean deliveries were also not significantly related to sepsis occurrence. Similar findings have been reported by Cetinkaya et al [6] and Mohamed et al. [8], suggesting that the mode of delivery does not independently influence the risk of early- onset sepsis. In contrast, maternal risk factors were significantly more common among mothers of septic neonates ($p < 0.001$), highlighting the predominant role of maternal and intrapartum factors in the development of early-onset neonatal sepsis. Prolonged antibiotic requirement among septic neonates suggests impaired immune function associated with vitamin D deficiency. In the present study, 82.6% of affected neonates recovered, 7.2% developed complications, and 10.1% died, with mortality significantly associated with severe vitamin D deficiency ($p = 0.004$).

Similar findings were reported by Singh and Chaudhari [7], Mohamed et al. [8], and Yu et al. [9], who demonstrated higher mortality among neonates with low vitamin D levels.

Septic neonates also exhibited significantly lower haemoglobin, leukocyte counts, ANC, and platelet counts, along with elevated inflammatory markers, and markedly lower mean vitamin D levels compared to controls (10.3 vs 24.7 ng/mL; $p < 0.001$). These findings, consistent with earlier studies [6,10,8,11], highlight the role of vitamin D in immune regulation and support its potential value in risk stratification and outcome prediction in neonatal sepsis.

Conclusion

Neonates with vitamin D levels below 20 ng/mL had a higher risk of developing early-onset sepsis, with increased need for respiratory support, prolonged antibiotic therapy, and higher mortality. Maternal factors such as urinary tract infection, diabetes, fever during labour, and inadequate intrapartum antibiotic prophylaxis significantly increased the risk of neonatal sepsis.

Neonatal vitamin D status was closely related to maternal vitamin D levels, highlighting the importance of maternal sufficiency during pregnancy.

As vitamin D deficiency is preventable, routine screening and appropriate supplementation in pregnant women and neonates, along with the timely infection control measures, may help reduce the incidence and severity of early-onset neonatal sepsis.

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