RESEARCH PAPER

A Cross-Sectional Comparative Study of Serum Vitamin E in Preterm and Term Neonates and Its Correlation with Umbilical Wound Healing After Cord Fall

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ABSTRACT

Background: Vitamin E is an essential lipid-soluble antioxidant that plays a crucial role in neonatal immunity, cellular protection, and wound healing. Preterm neonates are particularly vulnerable to vitamin E deficiency because placental transfer of alpha-tocopherol occurs predominantly during the third trimester. Deficiency of vitamin E may adversely affect physiological umbilical cord healing and increase susceptibility to omphalitis.

Objective: To compare serum vitamin E concentrations between preterm and term neonates and evaluate the relationship between vitamin E status and umbilical wound healing outcomes.

Methods: A prospective cross-sectional comparative study was conducted among 124 neonates, including 62 preterm and 62 term neonates, at a tertiary care hospital in Tamil Nadu, India. Umbilical cord blood samples were collected immediately after delivery and analyzed for alpha-tocopherol levels using enzyme-linked immunosorbent assay (ELISA). Umbilical wound healing parameters including cord separation time, epithelialization duration, and incidence of omphalitis were prospectively documented. Statistical analysis included independent t-test, chi-square test, Pearson correlation, linear regression, and logistic regression.

Results: Mean serum vitamin E concentration was significantly lower among preterm neonates (0.82 ± 0.28 mg/dL) compared to term neonates (1.45 ± 0.35 mg/dL) ($p<0.001$). Vitamin E deficiency (<0.5 mg/dL) was observed in 27.4% of preterm neonates compared to 3.2% of term neonates. Preterm neonates demonstrated significantly prolonged cord separation time (12.8 ± 2.3 days versus 9.4 ± 1.9 days; $p<0.001$) and higher omphalitis incidence (24.2% versus 4.8%; $p<0.001$). Strong negative correlations were observed between vitamin E concentration and cord separation timing in both preterm ($r=-0.682$) and term neonates ($r=-0.541$). Multiple regression analysis identified vitamin E concentration as the strongest independent predictor of cord separation timing ($\beta=-0.518$, $p<0.001$).

Conclusion: Vitamin E deficiency is significantly associated with delayed umbilical cord separation and increased omphalitis risk among preterm neonates. Serum vitamin E may serve as a clinically relevant biomarker for predicting neonatal wound healing outcomes and identifying neonates at risk for complications.

Keywords: Vitamin E, alpha-tocopherol, preterm neonates, umbilical cord separation, omphalitis, wound healing.

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INTRODUCTION

Preterm birth remains a major public health challenge worldwide and contributes significantly to neonatal morbidity and mortality. According to global estimates, nearly 15 million preterm births occur annually, with India accounting for approximately one-fourth of the global burden [1]. Preterm neonates experience multiple physiological disadvantages due to immature organ development, impaired immune responses, and inadequate micronutrient stores [2]. Among these micronutrients, vitamin E plays a particularly important role in maintaining neonatal cellular integrity and antioxidant defense.

Vitamin E consists of a group of lipid-soluble compounds, of which alpha-tocopherol is the most biologically active form [3]. It functions primarily as an antioxidant by protecting cellular membranes against oxidative stress and lipid peroxidation [4]. In addition to antioxidant properties, vitamin E contributes to immune regulation,

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inflammatory modulation, endothelial function, and tissue repair [5]. During fetal development, vitamin E transfer from mother to fetus occurs mainly during the third trimester through placental transport mechanisms [6]. Consequently, preterm neonates are born with significantly lower hepatic stores and circulating levels of vitamin E.

Umbilical cord healing represents an important physiological wound healing process during the neonatal period. Normally, cord separation occurs within 7–14 days after birth through coordinated stages of inflammation, tissue necrosis, epithelialization, and remodeling [7]. Delayed cord separation and omphalitis are clinically important complications associated with neonatal morbidity and mortality, especially in low-resource settings [8]. The wound healing process requires adequate inflammatory response, fibroblast proliferation, collagen synthesis, angiogenesis, and epithelial repair, all of which may be influenced by antioxidant status and micronutrient availability [9].

Oxidative stress is particularly significant in preterm neonates because of immature antioxidant enzyme systems and sudden exposure to extrauterine oxygen-rich environments [10]. Vitamin E deficiency may impair wound healing by increasing oxidative tissue injury, altering inflammatory signaling, reducing fibroblast activity, and compromising immune defenses [11]. Previous studies have evaluated the role of vitamin E in neonatal complications such as retinopathy of prematurity and intraventricular hemorrhage; however, limited evidence exists regarding its relationship with umbilical wound healing [12].

Understanding the relationship between vitamin E status and umbilical healing may help identify neonates at risk for delayed cord separation and infection. Therefore, the present study aimed to compare serum vitamin E concentrations between preterm and term neonates and evaluate correlations between vitamin E levels and umbilical wound healing outcomes.

MATERIALS AND METHODS

Study Design and Setting

This prospective cross-sectional comparative study was conducted in the Department of Pediatrics at Shri Sathya Sai Medical College and Hospital, Tamil Nadu, India, between January 2023 and June 2024.

Study Population

A total of 124 neonates were enrolled in the study, including 62 preterm neonates (32–36 weeks gestation) and 62 term neonates (37–42 weeks gestation).

Inclusion Criteria

1. Singleton live births.
2. Gestational age confirmed by ultrasound.
3. Institutional deliveries.
4. Parental informed consent.

Exclusion Criteria

1. Gestational age below 32 weeks.
2. Major congenital anomalies.
3. Neonatal sepsis at birth.
4. Birth asphyxia.
5. Umbilical abnormalities.
6. Maternal diabetes mellitus.

Sample Collection and Laboratory Analysis

Umbilical cord blood (3 mL) was collected immediately after delivery using aseptic precautions. Serum was separated by centrifugation and stored at -80°C until analysis. Alpha-tocopherol levels were quantified using a commercially available ELISA kit.

Umbilical Wound Assessment

Umbilical wound healing was assessed daily during the first week and subsequently on alternate days until complete cord separation. Parameters assessed included:

- Cord separation timing.
- Epithelialization duration.
- Presence of erythema.
- Umbilical discharge.
- Omphalitis.

Omphalitis was defined by the presence of purulent discharge, erythema extending beyond 1 cm, edema, or systemic symptoms.

Statistical Analysis

Data were analyzed using IBM SPSS version 26. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as percentages. Independent t-test and chi-square test were used for group comparisons. Pearson correlation assessed relationships between vitamin E and wound healing variables. Multiple linear regression identified predictors of cord separation timing. Statistical significance was set at $p<0.05$.

RESULTS

Baseline Characteristics

The baseline demographic and clinical characteristics of study participants are shown in Table 1.

Table 1: Baseline Demographic and Clinical Characteristics

Characteristic	Preterm (n=62)	Term (n=62)	P-value
Gestational age (weeks)	34.5 ± 1.2	39.2 ± 1.1	<0.001
Birth weight (g)	2098 ± 347	3156 ± 418	<0.001
Male sex n (%)	33 (53.2)	31 (50.0)	0.714

Caesarean delivery n (%)	28 (45.2)	24 (38.7)	0.468
Maternal age (years)	26.3 ± 4.1	26.7 ± 4.3	0.577
Apgar score at 5 min	9 (8–9)	9 (9–10)	0.002

Preterm neonates had significantly lower gestational age and birth weight compared to term neonates.

Vitamin E Concentrations

Mean serum vitamin E concentration was significantly lower among preterm neonates.

Table 2: Serum Vitamin E Concentrations

Parameter	Preterm	Term	P-value
Vitamin E (mg/dL)	0.82 ± 0.28	1.45 ± 0.35	<0.001
Vitamin E deficiency n (%)	17 (27.4)	2 (3.2)	<0.001

Subgroup analysis demonstrated progressive increases in vitamin E concentration with advancing gestational age.

Table 3: Vitamin E Levels Across Gestational Age Groups

Gestational Age Group	Vitamin E (mg/dL)
32–<34 weeks	0.68 ± 0.24
34–<36 weeks	0.83 ± 0.26
36–<37 weeks	0.93 ± 0.28
Term	1.45 ± 0.35

Umbilical Cord Separation and Healing

Preterm neonates exhibited significantly delayed cord separation and prolonged epithelialization.

Table 4: Umbilical Healing Outcomes

Parameter	Preterm	Term	P-value
Cord separation time (days)	12.8 ± 2.3	9.4 ± 1.9	<0.001
Delayed separation n (%)	18 (29.0)	4 (6.5)	<0.001
Epithelialization time (days)	3.2 ± 0.9	2.4 ± 0.7	<0.001
Omphalitis incidence n (%)	15 (24.2)	3 (4.8)	<0.001

Correlation Analysis

Strong negative correlations were observed between serum vitamin E concentration and cord separation timing.

Table 5: Correlation Between Vitamin E and Cord Separation Timing

Group	Pearson r	P-value
Preterm	-0.682	<0.001
Term	-0.541	<0.001
Overall	-0.758	<0.001

Multiple regression analysis revealed vitamin E concentration as the strongest independent predictor of cord separation timing (β=-0.518, p<0.001).

DISCUSSION

The present study demonstrated that preterm neonates possess significantly lower serum vitamin E concentrations compared to term neonates. These findings are consistent with previous studies reporting reduced placental transfer of alpha-tocopherol during shortened gestation [13]. Since fetal vitamin E accumulation occurs predominantly during the third trimester, premature birth interrupts this transfer process and results in inadequate neonatal antioxidant reserves.

The prevalence of vitamin E deficiency among preterm neonates in the present study was 27.4%, significantly higher than among term neonates. Similar observations have been reported in developing countries where maternal malnutrition and prematurity contribute to reduced neonatal micronutrient stores [14]. Progressive increases in vitamin E concentrations across gestational age categories further support the concept of gestational age-dependent vitamin E accumulation.

One of the major findings of this study was the strong inverse relationship between vitamin E concentration and umbilical cord separation timing. Preterm neonates exhibited delayed cord separation and prolonged epithelialization compared to term neonates. Delayed cord separation in preterm neonates may reflect impaired inflammatory and reparative responses due to immature immune function and oxidative stress [15].

Vitamin E contributes to wound healing through multiple biological mechanisms. Its antioxidant function protects fibroblasts, endothelial cells, and keratinocytes from oxidative injury [16]. Oxidative stress impairs angiogenesis, collagen synthesis, and extracellular matrix remodeling, thereby delaying tissue repair [17]. Vitamin E also modulates inflammatory cytokine activity and supports balanced immune responses necessary for normal healing [18].

The present study demonstrated that vitamin E was the strongest independent predictor of cord separation timing even after controlling for gestational age and birth weight. This finding suggests that vitamin E status exerts a clinically significant influence on neonatal wound healing independent of prematurity alone.

Preterm neonates in the study also demonstrated significantly higher omphalitis incidence compared to term neonates. Logistic regression analysis showed that each 1 mg/dL increase in vitamin E concentration reduced omphalitis odds by nearly 89%. These findings highlight the importance of adequate antioxidant and immune defenses in preventing umbilical infection.

Vitamin E deficiency may increase susceptibility to omphalitis by impairing neutrophil function, reducing epithelial barrier integrity, and increasing oxidative tissue injury [19]. Previous studies have similarly demonstrated associations between antioxidant deficiency and impaired infection resistance in neonates [20].

The findings of this study have important clinical implications. Measurement of cord blood vitamin E may help identify neonates at risk for delayed wound healing and infection. Early nutritional interventions and improved monitoring strategies may reduce preventable neonatal morbidity in vulnerable preterm populations.

However, the study has certain limitations. The cross-sectional design limits causal inference. The study was conducted at a single tertiary care center, which may affect generalizability. Extremely preterm neonates were excluded, and maternal vitamin E status was not evaluated.

Despite these limitations, the study provides important evidence regarding the relationship between vitamin E and neonatal wound healing and highlights the need for further longitudinal and interventional studies.

CONCLUSION

Preterm neonates demonstrate significantly lower serum vitamin E concentrations compared to term neonates. Reduced vitamin E levels are strongly associated with delayed umbilical cord separation, prolonged epithelialization, and increased omphalitis risk. Vitamin E concentration independently predicts umbilical wound healing outcomes and may serve as a useful biomarker for identifying neonates at risk for complications. Further randomized controlled trials are required to evaluate the role of vitamin E supplementation in improving neonatal wound healing outcomes.

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