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Original Research Article

Association of Neonatal Anthropometric Parameters with Hyperbilirubinemia and Vitamin D Status

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Abstract

Background: Neonatal hyperbilirubinemia is common during the early neonatal period and may be influenced by nutritional and metabolic factors. Vitamin D status and neonatal growth characteristics have been proposed as potential factors associated with the development of significant jaundice.

Objective: To compare neonatal anthropometric parameters and serum 25-hydroxyvitamin D [25(OH)D] status between term neonates with significant unconjugated hyperbilirubinemia and healthy controls.

Methods: This prospective hospital-based case-control study included 80 healthy term neonates aged 3–10 days, comprising 40 cases with significant unconjugated hyperbilirubinemia requiring phototherapy and 40 controls not requiring phototherapy. Birth weight, length, head circumference, total serum bilirubin, and serum 25(OH)D levels were assessed and compared between the groups.

Results: Mean birth weight was comparable between cases and controls (3.07 ± 0.29 vs. 3.08 ± 0.31 kg; p=0.942). No significant differences were observed in head circumference (34.23 ± 0.70 vs. 34.06 ± 0.60 cm; p=0.311) or length (50.38 ± 0.70 vs. 50.51 ± 0.60 cm; p=0.424). Mean total serum bilirubin was significantly higher among cases (19.8 ± 1.3 vs. 10.6 ± 2.6 mg/dL; p<0.001), while mean serum 25(OH)D was significantly lower (25.23 ± 18.50 vs. 33.85 ± 17.07 ng/mL; p=0.034). Vitamin D sufficiency was observed in 50.0% of cases compared with 80.0% of controls (p=0.004).

Conclusion: Significant unconjugated hyperbilirubinemia in term neonates was associated with lower serum 25(OH)D levels and poorer vitamin D status, whereas birth weight, length, and head circumference showed no significant association. These findings suggest that vitamin D status may have a greater relationship with neonatal hyperbilirubinemia than routine anthropometric parameters.

Keywords: Neonatal hyperbilirubinemia; Vitamin D; 25-hydroxyvitamin D; Birth weight; Neonatal anthropometry; Neonatal jaundice.

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Introduction

Neonatal hyperbilirubinemia is one of the most frequent clinical problems encountered during the early neonatal period. Although jaundice is usually physiological and self-limiting, excessive unconjugated bilirubin may result in bilirubin-induced neurological dysfunction and, in severe cases, kernicterus. Its development is influenced by several maternal and neonatal factors, including gestational maturity, feeding adequacy, birth weight, and other characteristics related to neonatal growth and adaptation after birth [1,2].

Anthropometric parameters such as birth weight, length, and head circumference are readily measurable indicators of fetal growth and nutritional status. Variations in these parameters may reflect intrauterine nutritional and metabolic influences that could potentially modify neonatal bilirubin metabolism. Vitamin D status is another factor of growing interest because maternal vitamin D supply largely determines neonatal vitamin D concentrations, while vitamin D also participates in several metabolic and developmental processes during fetal and neonatal life [3,4].

Recent evidence suggests an association between lower serum 25-hydroxyvitamin D [25(OH)D] concentrations and neonatal hyperbilirubinemia. A meta-analysis by Huang et al. found significantly lower vitamin D concentrations in neonates with hyperbilirubinemia than in healthy neonates [5]. More recently, Ghavi et al. similarly reported lower vitamin D levels among neonates with hyperbilirubinemia in a systematic review and meta-analysis, although heterogeneity among available studies remains substantial [6]. Thus, evaluation of vitamin D together with neonatal growth characteristics may provide a broader understanding of factors associated with neonatal jaundice.

Therefore, the present study was undertaken to compare neonatal anthropometric parameters between neonates with and without significant hyperbilirubinemia and to evaluate their relationship with serum 25(OH) vitamin D status.

Materials and Methods

Study Design and Setting: This prospective hospital-based case-control study was conducted in the Neonatal Intensive Care Unit (NICU) of Cheluvamba Hospital, attached to Mysore Medical College and Research Institute, Mysore. The study was carried out over 18 months, from January 2018 to June 2019.

Study Population: A total of 80 healthy term neonates were enrolled and divided into two groups: 40 cases, comprising neonates with significant unconjugated hyperbilirubinemia requiring phototherapy, and 40 controls, comprising term neonates of comparable age and birth weight who did not require phototherapy. Neonates were aged 3–10 days, had a gestational age of >37 to <42 weeks, and weighed 2.5–4.0 kg at birth.

Inclusion and Exclusion Criteria: Cases included healthy term neonates with hyperbilirubinemia reaching the threshold for phototherapy, while controls were healthy term neonates of similar postnatal age and birth weight who did not require phototherapy. Neonates with identifiable pathological causes of hyperbilirubinemia, including blood-group incompatibility, infection, polycythemia, glucose-6-phosphate dehydrogenase deficiency, cephalhematoma, perinatal asphyxia, or congenital anomalies, were excluded. Neonates with conjugated bilirubin >20% of total bilirubin were also excluded. In addition, infants born to mothers with chronic hepatic or renal disease, gestational diabetes, hypertension, or anticonvulsant use were excluded.

Data Collection and Clinical Assessment: After obtaining informed consent from the mother or caregiver, demographic and relevant perinatal information was recorded using a predesigned proforma. Each neonate underwent detailed clinical examination, including assessment of postnatal age, sex, gestational age, birth weight, length, head circumference, presence and onset of jaundice, and associated risk factors. Examination also included pallor, temperature, icterus, hepatosplenomegaly, cephalhematoma or other extravasated blood, excessive bruising, and neurological manifestations.

Assessment of Hyperbilirubinemia: Serum bilirubin was measured in all eligible neonates. Infants whose bilirubin concentration exceeded the age-specific threshold for phototherapy according to the American Academy of Pediatrics phototherapy chart were classified as cases, whereas those below the treatment threshold constituted the control group. Complete hemogram and peripheral blood smear were performed to exclude underlying pathological causes.

Anthropometric Measurements: Neonatal anthropometric assessment included birth weight, crown–heel length, and head circumference. These parameters were recorded for both groups and subsequently compared to determine whether neonatal growth characteristics were associated with significant hyperbilirubinemia or vitamin D status. The manuscript results confirm that these three anthropometric parameters were analyzed between the 40 cases and 40 controls.

Biochemical investigations: Before initiation of phototherapy, 3 mL of venous blood was collected under aseptic precautions. Serum 25-hydroxyvitamin D [25(OH)D], calcium, phosphorus, and alkaline phosphatase were estimated. Serum calcium was measured using an A25 Biosystems autoanalyzer by the Arsenazo method. Serum 25(OH)D was measured using Vitamin D kit, based on a solid-phase competitive binding immunoenzyme assay.

The principal variables analyzed were neonatal birth weight, length, head circumference, total serum bilirubin, serum 25(OH)D concentration, and vitamin D status.

Serum 25-hydroxyvitamin D [25(OH)D] status was categorized as follows: vitamin D deficiency, <12 ng/ml; vitamin D insufficiency, 12–20 ng/ml and vitamin D sufficiency, >20 ng/ml. These predefined cut-offs were used for classification and subsequent statistical analysis.

Statistical Analysis: Data were analysed using descriptive and inferential statistics. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequency and percentage. Continuous variables between the two independent groups were

compared using the two-tailed independent Student's t-test.

Categorical variables were analyzed using the Chi-square test, with Fisher's exact test or an appropriate correction used when expected cell frequencies were inadequate. A p-value ≤0.05 was considered statistically significant.

Ethics Statement: The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from the parent/guardian of each participant.

Results

The birth-weight distribution was comparable between cases and controls. Mean birth weight was 3.07 ± 0.29 kg among cases and 3.08 ± 0.31 kg among controls, with no statistically significant difference (p=0.942).

Table 1: Birth-weight distribution according to hyperbilirubinemia status

Birth weight (kg)	Cases (n=40)	Controls (n=40)
2.5–2.999	20 (50.0%)	20 (50.0%)
3.0–3.499	17 (42.5%)	16 (40.0%)
3.5–4.0	3 (7.5%)	4 (10.0%)
Mean ± SD (kg)	3.07 ± 0.29	3.08 ± 0.31
p-value	**0.942**	

Neonatal anthropometric parameters were similar between the two groups. No significant differences were observed in birth weight (p=0.942), head circumference (p=0.311), or length (p=0.424), indicating comparable baseline anthropometric characteristics.

Table 2. Comparison of neonatal anthropometric parameters between cases and controls

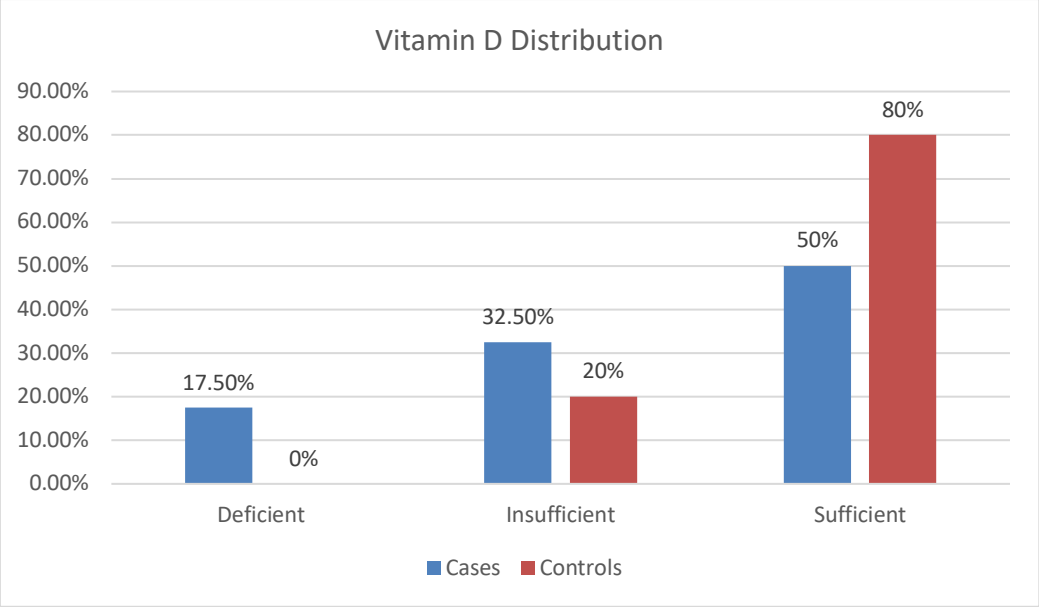
Anthropometric parameter	Cases (n=40), Mean ± SD	Controls (n=40), Mean ± SD	p-value
Birth weight (kg)	3.07 ± 0.29	3.08 ± 0.31	0.942
Head circumference (cm)	34.23 ± 0.70	34.06 ± 0.60	0.311
Length (cm)	50.38 ± 0.70	50.51 ± 0.60	0.424

Cases had significantly higher mean total bilirubin levels than controls (19.8 ± 1.3 vs. 10.6 ± 2.6 mg/dL; p<0.001) and significantly lower mean serum 25(OH) vitamin D levels (25.23 ± 18.50 vs. 33.85 ± 17.07 ng/mL; p=0.034). Vitamin D deficiency/insufficiency was more frequent among cases, while vitamin D sufficiency was significantly more common among controls (80.0% vs. 50.0%; p=0.004).

Table 3: Hyperbilirubinemia and vitamin D profile according to study group

Parameter	Cases (n=40)	Controls (n=40)	p-value
Total bilirubin (mg/dL)	19.8 ± 1.3	10.6 ± 2.6	<0.001
25(OH) vitamin D (ng/mL)	25.23 ± 18.50	33.85 ± 17.07	0.034
Vitamin D deficient	7 (17.5%)	0	
Vitamin D insufficient	13 (32.5%)	8 (20.0%)	
Vitamin D sufficient	20 (50.0%)	32 (80.0%)	0.004

Vitamin D deficiency and insufficiency were more frequent among cases, whereas vitamin D sufficiency predominated among controls (80.0% vs. 50.0%). This distribution demonstrates poorer vitamin D status among neonates with hyperbilirubinemia.



Graph 1: Distribution of serum 25-hydroxyvitamin D categories in the two study groups

Discussion

The present study evaluated neonatal anthropometric characteristics and vitamin D status in term neonates with significant unconjugated hyperbilirubinemia.

The absence of a significant difference in birth weight between the two groups is noteworthy.

Mean birth weight was 3.07 ± 0.29 kg among cases and 3.08 ± 0.31 kg among controls (p=0.942), while head circumference and length were also similar. These findings indicate that, among healthy term neonates within a relatively restricted birth-weight range, significant hyperbilirubinemia may occur independently of gross differences in neonatal size. This observation may partly reflect the study design, as only term neonates weighing 2.5–4.0 kg was included and cases and controls were selected to have comparable baseline characteristics. Consequently, the limited anthropometric variability may have reduced the ability to demonstrate an association between neonatal size and jaundice.

In contrast, a significant difference was observed in vitamin D status. Mean serum 25(OH)D was 25.23 ± 18.50 ng/mL among cases compared with 33.85 ± 17.07 ng/mL among controls (p=0.034). Similar observations have been reported by Aletayeb et al., who demonstrated significantly lower serum vitamin D concentrations among term neonates with indirect hyperbilirubinemia compared with healthy controls [7]. Mutlu et al. also reported lower vitamin D concentrations in jaundiced neonates and suggested an inverse relationship between vitamin D and bilirubin levels [8].

The higher prevalence of deficient or insufficient vitamin D status among cases further supports a possible association. In the present study, only 50% of cases had sufficient vitamin D compared with 80% of controls (p=0.004). Although the biological mechanism underlying this association remains incompletely understood, vitamin D and bilirubin metabolism both involve hepatic pathways, and vitamin D status may also reflect maternal nutritional status and neonatal metabolic adaptation. Nevertheless, the relationship should be interpreted as an association rather than evidence of causation.

Importantly, the published evidence is not entirely consistent. Mehrpisheh et al. found lower mean 25(OH)D concentrations in neonates with indirect hyperbilirubinemia than in controls, but the difference did not reach statistical significance [9]. Such variation between studies may be attributable to differences in sample size, geographic region, maternal vitamin D status, sunlight exposure, feeding practices, laboratory assays, definitions of vitamin D deficiency, and bilirubin thresholds used for case selection. These inconsistencies emphasize the multifactorial nature of neonatal hyperbilirubinemia.

Evidence from maternal studies also supports a possible relationship between vitamin D status and neonatal outcomes. Baker et al. demonstrated associations between maternal vitamin D-related biomarkers and several neonatal outcomes, including birth weight and jaundice, although some associations were attenuated after adjustment for maternal confounders [10].

This highlights the importance of considering maternal vitamin D status when evaluating neonatal vitamin D concentrations because neonatal stores are largely dependent on maternal transfer during pregnancy.

Taken together, the present findings suggest that conventional anthropometric parameters alone may not discriminate term neonates who develop significant hyperbilirubinemia. In contrast, poorer vitamin D status was significantly associated with hyperbilirubinemia despite comparable birth weight, length, and head circumference. Vitamin D deficiency may therefore represent an additional nutritional or metabolic marker associated with neonatal jaundice rather than merely reflecting differences in fetal growth.

Limitations

The findings should be interpreted in view of certain limitations. The relatively small sample size and single-center design restrict generalizability. Maternal serum 25(OH)D concentrations were not incorporated into the present analysis, and potential determinants such as maternal dietary intake, vitamin D supplementation, sunlight exposure, season of birth, and breastfeeding adequacy were not comprehensively evaluated. Moreover, the case-control design establishes association but cannot determine whether low vitamin D contributes directly to hyperbilirubinemia. Larger prospective multicenter studies incorporating paired maternal-neonatal vitamin D measurements and adjustment for relevant confounders are required to clarify the independent role of vitamin D in neonatal hyperbilirubinemia.

Conclusion

Term neonates with significant unconjugated hyperbilirubinemia had significantly lower serum 25(OH) vitamin D levels and a higher frequency of vitamin D deficiency or insufficiency compared with controls. In contrast, birth weight, length, and head circumference were comparable between the groups, suggesting that routine neonatal anthropometric parameters were not significantly associated with hyperbilirubinemia in this study. These findings indicate an association between poorer neonatal vitamin D status and significant hyperbilirubinemia despite comparable anthropometric parameters. Larger prospective studies incorporating maternal vitamin D status and relevant perinatal factors are warranted to clarify this relationship and its clinical significance.

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