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Review Article

Maternal vitamin D status and its implications on the newborn – A narrative review

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ABSTRACT

The pandemic of vitamin D deficiency affects all ages, including pregnant women and newborns. The functional significance of maternal and neonatal vitamin D deficiency is incompletely understood. Neonatal vitamin D insufficiency has been linked with preterm birth, seizures, neonatal respiratory distress syndrome, sepsis, acute gastroenterocolitis, and a higher risk of hospital admissions. The potential underlying mechanisms include the effect of vitamin D receptor polymorphism, defective immune effector cells, placental inflammation and gut dysbiosis. About 50% of all neonatal hypocalcemic seizures are attributable to vitamin D deficiency. Serum total calcium levels below 8.0 mg/dL should lead to a high index of suspicion for vitamin D deficiency-related seizure. With appropriate supplementation, hypocalcemic seizures recover without any long-term neurodevelopmental sequelae. Several studies also indicate the benefit of vitamin D supplementation during pregnancy on neonatal anthropometric measures, that is, birth weight (BW), birth length, femur length, head circumference, and ponderal index. The BW has an inverted U shape relationship with vitamin D levels, with benefit observed up to 20 ng/mL. Thus, current evidence underscores the possible detrimental effects of maternal vitamin D deficiency on adverse neonatal outcomes. Hence, maternal vitamin D supplementation may be beneficial for optimal health of the newborns.

Keywords: Birth weight, Bone-mineral homeostasis, Hypocalcemic seizures, Maternal status, Perinatal and neonatal periods, Vitamin D

INRODUCTION

Vitamin D is a fat-soluble vitamin which is necessary for bone mineral homeostasis. Vitamin D status is assessed by serum 25-hydroxyvitamin D [25(OH)D] levels due to its longer half-life of 21 days. About 95% of circulating 25(OH)D is endogenously produced in the skin by the action of ultraviolet rays from sunlight. The pandemic of hypovitaminosis D affects all ages, including pregnant women and their newborns with varied prevalence depending on the cutoffs used.[1-5] Two different cutoffs are currently in use.[4,5] The Endocrine Society, USA recommends circulating 25(OH)D levels >30 ng/mL as sufficient and <20 ng/mL as deficient, whereas Institute of Medicine, USA recommends >20 ng/mL as sufficient and <12 ng/mL as deficient, respectively.[4,5]

CASE SCENARIOS

Vitamin D is often overlooked as a potentially treatable parameter in various neonatal conditions and resultant outcomes. The relationship between vitamin D status and small for gestational age (SGA) is postulated to be mediated by placental vascularization. The impact of vitamin D status on fetal growth

is often confounded by perinatal risk factors. Furthermore, the pleiotropic role of vitamin D in immune regulation is often linked to the risk of development of neonatal sepsis. Herein, we describe two babies where hypovitaminosis D was observed in the setting of neonatal sepsis and SGA.

Case 1

A female baby was born at term by lower segment cesarean section to a mother with no apparent risk factors for sepsis. Birth weight (BW) was 3 kg and she was shifted to neonatal intensive care unit for respiratory distress. She was diagnosed with early onset neonatal sepsis as suggested by positive sepsis screen of raised total leukocyte counts and positive C-reactive protein (CRP). She was managed with intravenous antibiotics and discharged on 7th day. Maternal and cord blood 25(OH)D, available in retrospect showed a value of 4.51 and 6.91 ng/mL, respectively.

Case 2

A male baby was born at 38 weeks and 2 days of gestational age by vaginal delivery. Mother had no apparent comorbidities affecting fetal growth during pregnancy. Baby had a BW of 2.51 kg which was <10th centile for gestational age. Serum 25(OH)D levels of mother and cord blood were 3.9 and 4.18 ng/mL, respectively, available in retrospect.

These cases highlight the possible link between vitamin D deficiency in neonatal sepsis and anthropometric parameters including SGA. However, hypovitaminosis D in both these cases was missed in the absence of routine assessment of maternal and newborn 25(OH)D levels. Herein, we summarize a brief review of the relevant studies on the functional significance of vitamin D in neonates.

VITAMIN D STATUS IN INDIAN PREGNANT WOMEN AND NEWBORN DYAD

The exposure of sunlight in India ranges from approximately 3–4 h in winters to 7 h in summer.[6] However, rapid urbanization with prolonged indoor work hours and traditional cultural attire where people cover most body surface have possibly led to further diminutive exposure of sunlight resulting in significant prevalence of hypovitaminosis D in native Indians.[6,7] Vitamin D deficiency is a concern, especially in pregnancy as it potentially affects both mother and fetus. Several studies have shown widespread prevalence of vitamin D deficiency during pregnancy in India.[3-6,8-10] Some of the salient studies are summarized in Table 1. Briefly, Goswami *et al*., assessed vitamin D status in 29 pregnant women in a public hospital of New Delhi. The mean maternal and cord blood 25(OH)D was 8.8 ± 4.3 and 6.7 ± 2.0 ng/mL, respectively.[6] Subsequently, Sachan *et al*., reported similar findings for 117 mother and newborn dyads from Lucknow.[8] With increased awareness about hypovitaminosis D, calcium and vitamin D supplementation is being commonly prescribed in India. Recently, Gowtham *et al*., reported hypovitaminosis D in 65% of mothers and 68.6% newborns in 121 cases from Puducherry, India.[9] A 5-fold higher risk of hypovitaminosis D was observed in newborns of vitamin D deficient mothers. Similar findings were reported from the Middle East, African, and Western countries.[11,12] Goswami *et al*., in 2016, showed that mother with twin pregnancy had higher vitamin D deficiency with 25(OH)D <12 ng/mL in 89% cases.[13]

FUNCTIONAL SIGNIFICANCE OF MATERNAL VITAMIN D DEFICIENCY

Global and Indian data on maternal and newborn vitamin D deficiency and its functional significance are limited.[6-9,13,14] The fetus, deprived of sunlight, depends entirely on maternal supply of calcium and vitamin D. Neonatal hypovitaminosis D has been linked with preterm birth, alteration in bone mineral content, neonatal respiratory distress syndrome (RDS), seizures, sepsis, acute gastroenterocolitis and increased risk of hospitalization.[15,16] Various anthropometric parameters including BW, birth length, head circumference, femur length, and fontanelle size are also being assessed for their relationship with vitamin D.[17,18] Maternal vitamin D status may have long-term implications on the health of offsprings.[14] Vitamin D deficiency during pregnancy causes various manifestations such as childhood obesity and increased risk of recurrent wheeze in early childhood. In a longitudinal follow-up study involving 198 children born in UK, children of vitamin D deficient mothers had reduced whole body and lumbar spine bone mineral density at 9 year of age.[14] Recently, El-Heis *et al*., showed that vitamin D supplementation reduced the risk of infantile atopic eczema.[19] However, the effect of maternal vitamin D supplementation on neonatal and childhood bone health is variable. In a large randomized placebo-control trial on vitamin D supplementation, there was no difference in neonatal whole body bone mineral content assessed by dual-energy X-ray-absorptiometry.[15] Figure 1 provides the brief depiction of role of vitamin D in various neonatal outcomes.

VITAMIN D DEFICIENCY AND NEONATAL SEIZURES

Maternal vitamin D deficiency leads to poor placental transfer of calcium resulting in reduced stores and decreased intestinal calcium absorption in newborns. Decreased serum ionized calcium, in turn, increases the risk of neonatal hypocalcemic seizure.[20-24] The serum total calcium cutoff to define neonatal hypocalcemia ranges from

Table 1: Summary of studies that describe the prevalence of vitamin D deficiency in mothers and newborns in Asian Indian women during pregnancy.

Authors (Reference)	Subjects	(*n*)	Serum 25(OH)D (ng/mL)		Comments
			Maternal	Newborn	
Goswami *et al*., 2000[6]	Pregnant women belonging to poor socioeconomic status and their newborns	29	8.8±4.3	6.7±2.0	High prevalence of vitamin D deficiency in Asian Indian pregnant women with good correlation between maternal and cord blood 25(OH)D.
Sachan *et al*., 2005[8]	Urban and rural pregnant women at term and their newborns	117	14±9.3	8.4±5.7	84% prevalence of maternal hypovitaminosis D with good correlation between maternal and cord blood 25(OH)D
Sahu *et al*., 2009[3]	Pregnant women in the second trimester	139	15.12±7.92	Not done	74% of pregnant women had vitamin D deficiency.
Seth *et al*., 2009[4]	Healthy lactating mothers and exclusively breastfed infants, 2–24-weeks-old	180	10.9±5.8	11.6±8.3	Vitamin D <10 ng/mL were found in 48% of the mothers and 43% of the infants
Jani *et al*., 2014[5]	68 affluent and 82 non-affluent healthy pregnant women between 32 and 36 weeks of pregnancy	150	Mean (95% confidence interval) Affluent: 11.8 (10.8, 12.9) Non-affluent: 9.8 (9.1, 10.6)	Not done	25(OH)D <20 ng/mL in 91%
Gowtham *et al*., 2022[9]	Pregnant women with singleton pregnancy	121			Hypovitaminosis D in 65% of mothers and 69% of newborns
Ravinder *et al*., 2022[10]	Pregnant women in their last trimester	100	18.61±6.8	Not done	Serum 25(OH)D level <20 ng/mL in 62% cases

25(OH)D: 25-hydroxyvitamin D

<7.0 to <8.0 mg/dL.[21] Serum ionized calcium cutoff of <4 mg/dL has also been used in disorders affecting albumin levels.[20,21] Immature parathyroid hormone (PTH) response and hyperphosphatemia have been reported in neonatal hypocalcemia.[22] Neonatal hypocalcemia manifests as increased neuromuscular excitability, irritability, tetany, laryngospasm, cardiac arrhythmias, seizures, apnea, cyanosis, and feeding problems.[24]

The prevalence and characteristics of neonatal hypocalcemic seizures have been reported by various investigators. These seizures, occur more commonly in males, and in South Asian or African ethnicity, can be generalized or focal and can occur early at birth, or later, at 4–8 days.[20,23,25] Huang *et al*., assessed 1029 Taiwanese newborns admitted in intensive care unit and observed neonatal hypocalcemic seizures in 16 cases.[26] Nearly 50% of these seizures were attributed to vitamin D deficiency and remaining to various etiologies including DiGeorge syndrome and hypoparathyroidism. Unlike syndromic cases, those neonates with vitamin D deficiency-related seizures recovered completely with no long-term neurodevelopmental sequelae.[26] Seymen-Karabulut *et al*. assessed 96 Turkish newborns with late-onset neonatal hypocalcemia, occurring at a median age of 5 days with a male preponderance of 60%.[25] The median cord blood 25(OH)D was 6.3 ng/mL with vitamin D deficiency (<12 ng/mL) in 86% and neonatal seizures in 18%. Interestingly, 54.2% of these neonates had low or normal intact PTH (iPTH).[25] Soliman *et al*. reported cases of neonatal seizures occurring within 10 days of birth.[27] Mothers of affected neonates had 25(OH)D values <10 ng/mL. The seizures were generalized, eight newborns had craniotabes and serum iPTH was normal in 40% of the cases. Treatment with alphacalcidiol and calcium lead to resolution of symptoms within 2 days.[27] Thomas *et al*. described 78 cases of neonatal hypocalcemia at a children's medical center in USA.[28] Median age at admission was 8 days, 72% were male, and median duration of hospital stay was 3 days. Majority had hypomagnesemia and low iPTH. The seizures responded to supplementation with calcium, calcitriol, low phosphorus formula, and magnesium.[28]

Although hypovitaminosis D is common in India, the prevalence of neonatal hypocalcemia and seizures is not clear. Mehrotra *et al.,* evaluated vitamin D deficiency in 60 neonates with seizures and their mothers and compared them with

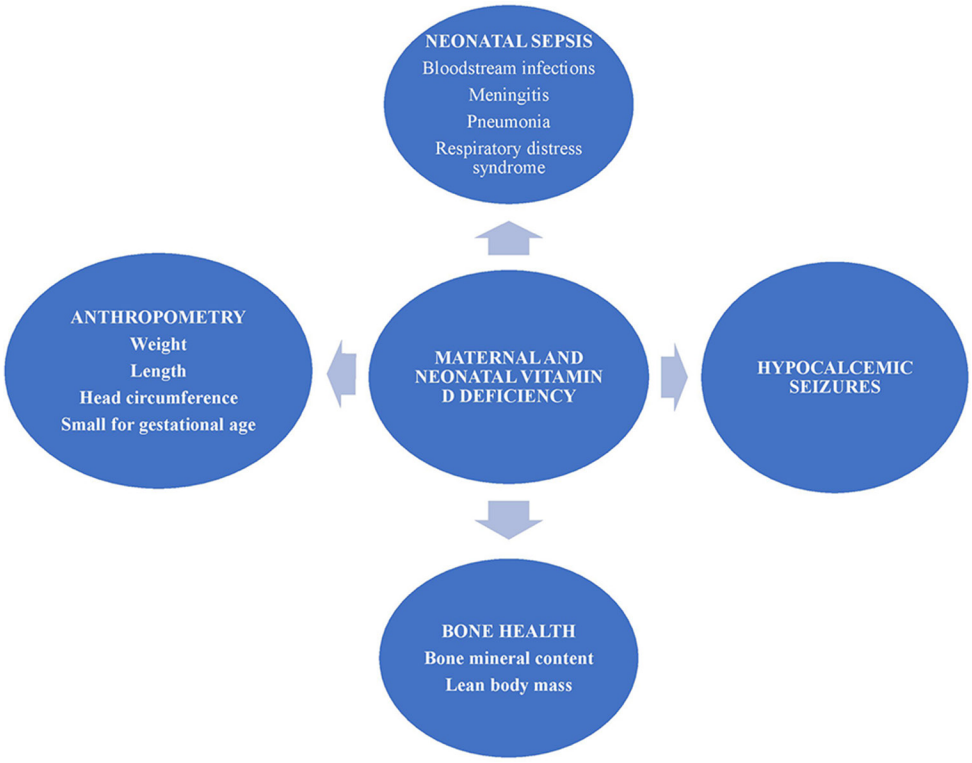

Figure 1: Salient manifestations of maternal and newborn vitamin D deficiency.

healthy neonate-mother pairs in New Delhi, India.[21] Serum 25(OH)D levels were below 10 ng/mL in 90% of newborns with seizures versus 42% in healthy neonates. Around 85% mothers with affected neonates had vitamin D deficiency when compared to 50% in mothers of healthy neonates.

Thus, up to 50% of all neonatal hypocalcemic seizures could possibly be attributed to vitamin D deficiency with a greater risk in males than females. Serum total calcium level <8.0 mg/dL should alert about possibility of a vitamin D deficiency-related seizure. PTH response is often blunted despite severe hypocalcemia due to inadequate maturation. Appropriate treatment leads to complete recovery without long-term neurodevelopmental sequelae.

VITAMIN D DEFICIENCY AND NEONATAL INFECTIONS

Neonatal sepsis manifests within the first 4 weeks of birth. It can occur early within 72 h, or late beyond 72 h of life.[29] Bloodstream infections, meningitis, and pneumonia are common causes of neonatal septicemia. Sepsis results in about 20% of neonatal mortality.[29] Neonatal respiratory diseases also have long-term sequalae, predisposing to respiratory dysfunction, asthma, chronic obstructive disease, and increased mortality at adult age. The burden of neonatal sepsis is high in low-income Asian and African countries.

Several studies have demonstrated possible association between vitamin D and RDS, wheezing, and infections of respiratory tract in infancy.[30] Novel mechanisms are being proposed to explain increased susceptibility to neonatal infections in hypovitaminosis D.[16,31-34]

Recently, Treiber *et al.*, assessed 402 Slovenian mother and newborn dyads.[16] Cord blood 25(OH)D was <10 ng/mL in 18% of newborns. Risk of neonatal RDS, hospitalization, and acute gastroenterocolitis was high in vitamin D deficient state, with odd ratio ranging from 3.9 to 5.9.[16] Similar findings have been reported across India [Table 2]. Dhandai *et al.,* observed significantly low serum 25(OH)D in 60 neonates with late-onset sepsis from a tertiary care center in New Delhi.[35] Singh and Chaudhari examined 70 cases with and without sepsis each, from Surat.[36] Cord blood 25(OH)D was low in 80% of newborns with sepsis unlike in 52% of cases without sepsis, with increased mortality in those with 25(OH)D level <11 ng/mL. Similar observations have also been reported by Behera *et al.*, in culture-positive neonatal sepsis from Odisha[37] and by Agrawal *et al.*, in 225 term neonates from Bhopal.[38] Cases of neonatal sepsis associated with vitamin D deficiency have associated high CRP and longer hospital stay, especially in those with raised serum iPTH.[39,40]

Workneh Bitew *et al.*, reported meta-analysis of 14 observational studies (four from India), which included

Table 2: Summary of recent salient studies in Indian population highlighting the association vitamin D deficiency and neonatal infection.

Authors (Reference)	Subjects	(*n*)	Comments
Dhandai *et al*., 2018[35]	Neonates with late onset sepsis (New Delhi, India)	60	Infants with neonatal sepsis have significantly low vitamin D.
Singh and Chaudhari, 2020[36]	Newborns with and without sepsis (Surat, Gujarat, India)	70	Cord blood 25(OH)D lower in 80% of newborns with sepsis and 52% in cases without sepsis. Mortality high when serum 25(OH)D <20 ng/mL.
Behra *et al*., 2020[37]	Newborns with culture positive sepsis. Control newborns without sepsis (Bhubaneswar, Odisha, India)	40	25(OH)D in sepsis group (12.7±2.8 ng/mL). Controls (25.5±7.0 ng/mL). Odds ratio 273 (95% CI 30.39–2451.6) for culture positive sepsis.
Agrawal *et al*., 2019[38]	Term neonates with sepsis and controls without sepsis (Bhopal, Madhya Pradesh, India)	225 Sepsis=175 Controls=50	25(OH)D in cases (12.3±6.1 ng/mL) Controls (14.9±7.2 ng/mL). 86.3% of neonates with sepsis and 74.0% of controls had vitamin D deficiency.
Workneh Bitew *et al*., 2020[29]	Meta-analysis of 40 observational studies including 4 studies from India	748 with sepsis	80% of newborn with sepsis were vitamin D deficient and 44% without sepsis. Mean cord 25(OH)D was lower by 8.78 ng/mL in neonatal sepsis

CI: Confidence interval, 25(OH)D: 25-hydroxyvitamin D

748 neonates with sepsis and 573 neonates without sepsis and their respective mothers. About 80% of neonates with sepsis had vitamin D deficiency compared to 44% without sepsis. The mean cord 25(OH)D levels were lower by 8.78 ng/mL in neonatal sepsis. The forest plot showed association of neonatal sepsis with hypovitaminosis D in 13 of the 14 studies.[29]

Information on the maternal vitamin D supplementation and newborn infections is scarce. Loddo *et al.,* in 2023, assessed the effect of antenatal administration of a single dose of 100,000 IU of cholecalciferol.[30] The supplemented cohort of 54,596 subjects with supplementation had 3.0% lower odds of term infants with perinatal asphyxia, respiratory distress, and meconium aspiration syndrome.

While these studies highlight the role of vitamin D deficiency in neonatal sepsis, underlying pathogenetic mechanisms are not completely understood. Tayel *et al*., observed a high prevalence of FokI TT polymorphism of vitamin D receptor in vitamin D deficient infants with neonatal sepsis, indicating a possible defect in vitamin D action.[31] The effect of vitamin D deficiency on the immune system is being elucidated in both experimental and clinical studies.[32-34] In a mouse model of lung injury, prenatal vitamin D supplementation reduced monocytes/macrophage migration and transforming growth factor–beta-mediated inflammatory pathway activation at the injured site.[32] Wang *et al*., observed that winter-born neonates had higher risk of vitamin D deficiency, pneumonia, sepsis, cytomegalovirus infection, and low circulating serum CD3+, CD4+, and IgA.[33] Youssef *et al.* observed similar alterations in effector T-cells in 52 Egyptian neonates with hypovitaminosis D.[34] Zhang *et al.* observed an association between maternal vitamin D deficiency, placental inflammation, and neonatal sepsis in Chinese women.[41] Intrauterine infection (15.6 vs. 5.7%) and neonatal sepsis (2.4% vs. 0.5%) were higher in mothers with placental inflammation than in those without inflammation. Marsubrin *et al*., in 2024, assessed the association of vitamin D deficiency with intestinal dysbiosis in 43 preterm infants below 32 weeks.[42] The ratio of fecal commensal *Lactobacillaceae* to pathogenic *Enterobacteriaceae* was lower in those with vitamin D deficiency.

Thus, neonates with vitamin D deficiency, especially those with high iPTH, are possibly at higher risk of neonatal sepsis, RDS, wheezing, and prolonged hospital stay. Potential postulated mechanisms include effect of vitamin D receptor polymorphism, defect in immune effector cells, placental inflammation, and gut dysbiosis. Randomized-control trials would help to substantiate the role of prenatal vitamin D supplementation in the prevention of neonatal infections. The ongoing double-blind "D-Kids" trial involving weekly supplementation with 14,000 IU of cholecalciferol in 300 Australian pregnant women will probably help understand the effect of antenatal vitamin D supplementation in neonatal infections.[43]

VITAMIN D AND ANTHROPOMETRY

Anthropometric parameters such as BW, length, head circumference, and anterior fontanelle size reflect the general health and nutritional status of the newborn. The concept of fetal origin of adult onset illnesses suggests that BW is significantly linked to several adult-onset diseases including diabetes mellitus, hypertension, insulin resistance, polycystic ovarian disease, and cardiovascular diseases.[44,45] However, evidence on possible association between maternal

and cord blood vitamin D status with anthropometry is conflicting [Table 3].

Positive association between maternal 25(OH)D and newborn anthropometry

Chen *et al*., in 2024, assessed vitamin D status of Chinese mothers during pregnancy. Serum 25(OH)D ≤14.7 ng/mL was an independent risk factor for deliveries at ≤38 weeks and BW <3.4 kg.[17] Similarly, Luo *et al*., reported lower neonatal BW by 65 g in Chinese mothers with a serum 25(OH)D of 15.1 ng/mL.[46] Lee *et al*., assessed maternal and neonatal vitamin D status and gene polymorphism of vitamin D receptor in Malaysian women.[47] Maternal 25(OH)D <12 ng/mL was associated with lower BW, head circumference, and crown–heel length. Fok 1 polymorphism showed an additive effect on reduced head circumference. This interaction between vitamin D receptor gene and vitamin D nutrition may affect anthropometric parameters at birth.[47] Meng *et al*., observed that mothers with high iPTH levels had 3-fold higher risk of SGA newborns, and BW lower by 125 g.[48]

Maternal body mass index (BMI) before pregnancy can confound the effect of hypovitaminosis D on fetal anthropometry. Francis *et al*., assessed 321 maternal-newborn pairs in the USA and observed that obese women with 25(OH)D <20 ng/mL had lower and shorter lengths of their newborns as compared to newborns of women with normal BMI.[49] Casey *et al*. observed that higher maternal serum 25(OH)D by two-fold in second trimester in Irish women was associated with higher BW and length standard-deviation score, by 0.05 and 0.07, respectively.[50]

Sarma *et al*., assessed 250 primigravida and their newborns who had mean 25(OH)D of 17.5 ± 2.2 ng/mL and 14.5 ± 1.8 ng/mL, respectively.[51] Fetal length at birth including

Table 3: Summary of salient studies depicting the relationship between vitamin D status and newborn anthropometry.

Authors (Reference)	Subjects	(*n*)	Comments
Positive association between maternal 25(OH) D and neonatal anthropometry			
Chen *et al*., 2024[17]	Chinese women between 16 and 20 weeks of gestation	510	Serum 25(OH)D ≤14.7 ng/mL a risk factor for deliveries <38 weeks and BW<3.4 Kg
Luo *et al*., 2022[46]	Chinese women-newborn dyad	103	BW lower than 65 g in mothers with 25(OH)D of 15 ng/mL
Lee *et al*., 2022[47]	Mother-newborn dyad, Malaysia	217	Maternal 25(OH)D <12 ng/mL led to lower BW, HC and crown heel length
Meng *et al*., 2020[48]	Chinese women in 2nd trimester and their newborns	3407	Vitamin D deficient mothers with high PTH had 3 fold risk of SGA newborn with BW lower by 125 g
Francis *et al*., 2018[49]	Mother-newborn dyad, USA	321	Obese women with 25(OH)D <20 ng/mL had lower BW and shorter length than non-obese women with similarly low vitamin D
Casey *et al*., 2018[50]	Irish women between 24 and 32 weeks gestation	1585	Increased maternal 25(OH)D by two-fold associated with higher BW and length
Sarma *et al*., 2018[51]	Mother-newborn dyad from north-east India	250	Vitamin D deficient mother had significantly lower length of their newborn
Boghossian *et al*., 2019[52]	African-American, Caucasian women and their newborns	343	Vitamin D deficient male newborns had lower BW and lean body mass by 308 and 217 g, respectively
Inverted U shaped relationship between 25(OH) D and neonatal anthropometry			
Keller *et al*., 2018[53]	Neonates, Germany	2686	Inverted U-shaped relation between 225(OH)D with BW and ponderal index. Positive relationship till serum 25(OH)D 20 ng/mL and decline beyond this level
Zhu *et al*., 2015[54]	Neonates, China	1491	Every 4 ng/mL increase in cord blood 25(OH)D, increased BW by 61 g, up to a 16 ng/mL. Further increase in 25(OH)D led to a decrease in BW by 68.5 g
Lack of relationship between maternal 25(OH) D and neonatal anthropometry			
Yang *et al*., 2023[55]	Chinese women and their newborns	199	No association between cord blood 25(OH)D and BW.
Bhowmik *et al*., 2019[56]	Pregnant women from Bangladesh	498	46% women had 25(OH)D <12 ng/mL. No correlation between cord blood level and BW
Yuniati *et al*. 2020[57]	Indonesian mother-newborn pair	203	No correlation between maternal vitamin D status and BW adjusted for maternal age, body weight, and parity
Van der Pligt 2023[58]	Vitamin D sufficient Australian mother and their newborns	221	No correlation between maternal 25(OH)D and BW and size of newborn.

BW: Birth weight, HC: Head circumference, SGA: Small for gestational age, g: Grams, PTH: Parathyroid hormone, 25(OH)D: 25-hydroxyvitamin D

femur length was significantly shorter in newborns of vitamin D deficient mothers. Boghossian *et al*. reported that vitamin D deficient male newborns of African-American and Caucasian women had lower BW and lean body mass by 308 and 217 g, respectively.[52] The newborns of women with serum total calcium in the lowest tertile had a lower ponderal index and bone mineral density. These studies indicate a probable non-linear relationship between vitamin D levels and BW of the newborns.

U-shaped association between 25(OH)D and newborn anthropometry

Keller *et al*. reported an "inverted U-shaped" association of neonatal 25(OH)D with BW and ponderal index. A positive relation of the parameters with 25(OH)D is observed with up to <20 ng/mL, with a decline beyond this level.[53] Similarly, Zhu *et al*., reported that every 4 ng/mL increase in cord blood 25(OH)D levels led to increase in BW by 61 g up to a level of 16 ng/mL.[54] Further increase in 25(OH)D led to a decrease in BW by 68.5 g.

Lack of association between maternal 25(OH)D and newborn anthropometry

Several studies indicate lack of beneficial effect of maternal vitamin D supplementation on anthropometry of newborns.[55-59] Yang *et al*., in 2023, reported lack of relationship between cord blood 25(OH)D and small (SGA), appropriate, and large for gestational age newborns among Chinese women.[55] Bhowmik *et al*., in 2019, observed serum 25(OH)D <12 ng/mL in 46% of 498 pregnant women in Bangladesh, with no correlation observed between BW and cord blood 25(OH)D.[56] Similarly, Yuniati *et al*. observed lack of relationship between maternal vitamin D levels and BW of newborn adjusted for maternal age, body weight, and parity in Indonesian mother-newborn pairs.[57] Van der Pligt *et al*., also, did not observe significant correlation between serum 25(OH)D and BW and size of newborns in vitamin D-sufficient Australian women, with serum 25(OH) D >33 ng/mL.[58]

Given the importance of 25(OH)D in bone-mineral homeostasis, maternal and neonatal vitamin D status may determine fontanelle size in neonates. Cho *et al*., 2023 observed that among 18 infants with large anterior fontanelle, 16 had decreased serum vitamin D levels.[18] A randomized-control trial Brooke *et al*., reported that newborns of vitamin D supplemented mothers had smaller anterior fontanelle size.[60] Similarly, Kalra *et al*., observed that maternal vitamin D supplementation in doses varying from 60,000 IU to 120,000 IU, was associated with anterior fontanelle size of 2.5 cm as compared to 3.3 cm in the non-supplemented group.[61] It seems that hypovitaminosis D is associated with larger anterior fontanelle size that can be corrected by its supplementation.

In summary, various studies indicate a possible beneficial effect of vitamin D on neonatal BW, length, femur length, head circumference, ponderal index, lean body mass, and bone density. The BW seems to follow an inverted U shape with vitamin D, with maximum benefit observed at approximately 20 ng/mL. Role of vitamin D on fetal anthropometry is not completely understood. vitamin D increases the lean mass and bone mineral density, indicating its direct effect through parameters of bone mineral homeostasis.

There is a lack of prospective studies on the role of vitamin D supplementation in determining neonatal anthropometric parameters. Some studies have indicated a beneficial effect of vitamin D on BW and size.[62,63] Tao *et al*. assessed the effect of antenatal cord blood supplementation with 600 IU/day of cholecalciferol for at least 2 months.[62] Mean 25(OH)D was higher by 1.4 ng/mL in the supplemented group. However, even with this modest improvement, the risk of SGA newborns decreased by nearly two-fold from 11.8% to 6.9%. Similarly, Kılıcaslan *et al*., observed improved head and chest circumference and height of newborns of 100 Turkish women who had received vitamin D supplementation.[63] Kalra *et al*., reported that antenatal vitamin D supplementation with either one oral dose of 60,000 IU or two doses of 120,000 IU led to increased head circumference, length, and weight of newborns.[61] However, intermitted doses of vitamin D are not recommended in neonates.[64,65]

CONCLUSION

Thus, current evidence indicates that Vitamin D deficiency may be associated with adverse neonatal outcome in the perspective of hypocalcemic seizures, sepsis, and anthropometry. The guidelines from the Indian Academy of Pediatrics (IAP) which recommend physiological maintenance dose of 400 IU of 25-hydroxycholecalciferol in all asymptomatic neonates till 1 year of age should be followed. Neonates with hypovitaminosis D should be managed with daily doses of 2000 IU of vitamin D for a period of 3 months along with calcium supplementation. However, further prospective studies with vitamin D supplementation are required to assess its role in neonatal seizures, infection, and anthropometry.

Author's contributions

Both the authors contributed in the concept, design, intellectual content, literature search, manuscript preparation, editing, and review. Both the authors are guarantors of the work.

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