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Original Research Article

Analyzed the Influence of Maternal Vitamin D Deficiency on Hyperbilirubinemia risk in Term Newborns: Observational Study

Sanjay Kumar[1], Sujatha Guttala[2]

[1]Chief Specialist, Department of Paediatrics, Visakha Steel General Hospital, Visakhapatnam, Andhra Pradesh, India
[2]Chief Specialist, Department of Obstetrics and Gynecology, Visakha Steel General Hospital, Visakhapatnam, Andhra Pradesh, India

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Corresponding author: Dr. Sanjay Kumar
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Abstract

Aim: To study the effect of Maternal Vitamin D Deficiency on Increased Risk for Hyperbilirubinemia in Term Newborns.

Methods: This prospective observational study was carried out in the Department of Paediatrics, Visakha Steel General Hospital Visakhapatnam, Andhra Pradesh, India for 1 year. Serum 25-hydroxyvitamin D was measured from 100 included pregnant women during birth time. The level of bilirubin was measured in their newborns at 3rd to 5th days of life.

Results: Vitamin D deficiency with range <10 ng/mL was detected in 16(16%), insufficient level of 10-30 ng/mL in 78(78%), and sufficient level in 6(6%) pregnant women. Serum calcium was sufficient in 58(58%); while 42(42%) of them had hypocalcaemia below 8.5 mg/dL. There was a correlation between the level of maternal vitamin D with calcium, phosphorus and alkaline phosphatase of mothers (P< 0.001 each). They reported the use of vitamin D during pregnancy in 84 (84%) mothers. hundred (50 girls and 50 boys) newborns who were delivered by the pregnant women were included in this study. The level of bilirubin more than 15 was detected in 15(15%) newborns at the 3rd to 5th days of life as hyperbilirubinemia.

Conclusion: The presence of maternal vitamin D deficiency could effectively predict the increased risk for neonatal Hyperbilirubinemia.

Keywords: Hyperbilirubinemia, Jaundice, Mothers, Newborns, Vitamin D deficiency.

Introduction

Vitamin D is a precursor for several biochemical reactions in the body and mainly involved in calcium-phosphorus metabolism and mineralisation of the bones. Vitamin D unlike other vitamins does not require daily supplementation; sunlight exposure replenishes the body stores. It is commonly observed when people are subjected to inadequate sunlight exposure, poor dietary habits, bedridden individuals and extremes of age. Vitamin D is also involved in the development of the placenta and feto-maternal wellbeing, thereby helping in prevention of obstetric complication like hypertension in pregnancy.[1] Although the serum bilirubin level in most cases of neonatal

hyperbilirubinemia is in the physiological range, which needs no treatment, some cases develop a peak serum bilirubin level, which, if not treated properly, may have devastating consequences on neonatal life. Kernicterus is one such complication in which a distinct yellowish pattern staining the brainstem, hippocampus, cerebellum, and certain brainstem nuclei (particularly the globus pallidus and sub thalamic nucleus) is seen at autopsy in infants who die due to acute bilirubin toxicity. Most of sequelae of this disease arises from damage to these brain structures.[2,3] Vitamin D is one of the fat-soluble vitamins technically considered a hormone. Many functions of vitamin D have been deciphered in medical research, where derangement can lead to cardiovascular, pulmonary, obesity, diabetes, and neoplastic diseases such as breast and colorectal carcinoma[4] Increased incidence of many diseases including wheezing and asthma[5] acute disseminated encephalomyelitis (ADEM) and future multiple scle- rosis[6] schizophrenia[7] irregular neurocognitive result[8] type 1 diabetes mellitus, and insulin resistance[9] has been correlated with decreased vitamin D concentration in pregnant women and their offspring. Advanced research has revealed the occurrence of 25-hydroxy vitamin D receptors on cells that have their actual origin from hepatic, neural, pancreatic, and genitourinary (prostate) systems. Immune system components such as lymphocytes and macrophages also contain vitamin D receptors[10] The major sources of vitamin D are through the skin and diet. Both these sources contain the inactive form of vitamin D. Its activation occurs in the liver and kidney by hydroxylation[11]. Other cells that can synthesize vitamin D are monocytes and placenta during pregnancy[12]. A hypothetical relationship between vitamin D and bilirubin can be explained by the synthesis of both entities in the liver.[13] Although the metabolism of both compounds occurs through different pathways in the liver, they can affect each other's metabolism, which remains to be proven[14]

Plenty of research is available on risk factors for neonatal hyperbilirubinemia, such as excessive hemolysis due to immune (ABO/Rh incompatibility) causes, nonimmune (hereditary spherocytosis, G6PD deficiency) causes, trauma (cephalohematoma), oxytocin, and diabetes in mothers. Limited number of studies is available on the relationship between hyperbilirubinemia and neonatal serum vitamin D[15] Because of the fact that prevalence of maternal vitamin D deficiency is high in india and its probable effect on neonatal hyperbilirubinemia, the present study aimed to determine the effect of maternal vitamin D levels on increased risk of hyperbilirubinemia in their newborns.

Material and methods

This prospective observational study was carried out in the Department of Paediatrics, Visakha Steel General Hospital Visakhapatnam, Andhra Pradesh, India for 1 year, 100 pregnant women were included in this study.

Methodology

Maternal information including age, gestational age, and education, living area, hypothyroidism, and hypertension, type of delivery and history of vitamin D consumption during pregnancy was collected by interview and their medical files and also measured the mothers' heights and weights. Body mass index (BMI) was calculated as weight (kilograms) divided by height (meters) squared of each mother on the day of interview. 5 mL of blood was obtained from each mother for measuring the level of calcium, phosphorus, alkaline phosphatase and 25-hydroxy vitamin D (25-OH vitamin D).

The newborns' weight, height and head circumference were measured by standard methods, and type of delivery; also, the method of feeding was recorded. The newborns were evaluated for

hyperbilirubinemia at the 3rd to 5th days of life. Increase in the bilirubin level more than 12 mg/dl was considered as hyperbilirubinemia in the 3rd to 5th days of life. Exclusive breast-fed babies, In-born hospital-delivered babies and Term healthy newborn babies > 37 weeks of gestation were included in this study. Newborn with major congenital abnormalities. Rh/ABO incompatibility, Newborn with a history of perinatal asphyxia, meconium aspiration syndrome, pneumonia, sepsis, and conjugated hyperbilirubinemia and Pregnant women with a history of renal, hepatic, gestational diabetes, or hypertension and metabolic bone diseases were excluded from this study.

The level of serum 25-OH vitamin D was measured using RIA (Radio-Immuno-Assay) method. For vitamin D, ranges <10 ng/mL were regarded as deficient, 10-30 ng/mL as insufficient, and >30 ng/mL as sufficient based on its brochures and those reported by Mayo Medical Laboratories.[16] The measurement of calcium, phosphorus and alkaline phosphatase was carried out using Pars Azmoon kits. Likewise, for calcium, the range of 8.5-10.5 mg/dL was regarded as normal and <8.5 mg/dL as deficient.[17] The determination of bilirubin was performed by photometric method, using 2, 4- dichloroaniline in the serum of venous blood samples at 3rd to 5th days of life

Results

100 pregnant mothers in the age range of 18 to 43 years with the mean age of 29.15 ± 3.12 years were included in this study. Table no.1 presents the main demographic characteristics of the pregnant women. Vitamin D deficiency with range <10 ng/mL was detected in 16(16%), insufficient level of 10-30 ng/mL in 78(78%), and sufficient level in 6(6%) pregnant women.

Table 1: demographic profile of pregnant women

Parameter	**Mean (Sd)**
Weight (kg)	71.6 (10.4)
Height (cm)	159 (4.2)
Body mass index (kg/m^2)	30.0(3.2)
Gestational age (week)	37.7(0.8)
Area	
urban area	80(80%)
Rural area	20 (20%)
Education	
12^{th} standard	41(41%)
graduate and postgraduate	59(59%)
Serum calcium level	
sufficient	58(58%);
hypocalcaemia below 8.5 mg/dL	42(42%)
Serum phosphorus sufficient	85 (85%)
Alkaline phosphatase sufficient	86(86%)
Vitamin D used by pregnant women	84 (84%)
Mode of delivery	
vaginal delivery	62(62)
cesarean section	38(38)

Table 2: Vitamin D deficiency with range in pregnant women

Vitamin D deficiency range	Pregnant women
<10 ng/mL	16(16%)
10-30 ng/mL insufficient level	78(78%),
sufficient level	6(6%)

Serum calcium was sufficient in 58(58%); while 42(42%) of them had hypocalcaemia below 8.5 mg/dL. There was no significant relationship between maternal vitamin D and BMI (P=0.1). Based on the living area, 80(80%) mothers were living in the urban area. Among 100 pregnant women, 41(41%) had under 12th standard, 59(59%) had graduate and postgraduate. There was a correlation between maternal vitamin D and the level of their education (P< 0.001). There was a correlation between the level of maternal vitamin D with calcium, phosphorus and alkaline phosphatase of mothers (P< 0.001 each).

They reported the use of vitamin D during pregnancy in 84 (84%) mothers. hundred (50 girls and 50 boys) newborns who were delivered by the pregnant women were included in this study.

Table 3: Baseline characteristics of Term Newborns

Parameter	Mean (SD)	Minimum	Maximum
birth weight grams	3078.5±351.5	2,880	4,590
birth height cm	48.4+ 2.2	40	57
head circumference	33.77 ±1.02	30	38
level of bilirubin newborns at the 3rd to 5th days more than 12 (Hyperbilirubinemia)	30(15%)		

The mean of birth weight in these newborns was 3078.5±351.5 grams, ranging from 2,880 to 4,590 grams; the mean of birth height was 48.4+ 2.2 cm, ranging from 40 to 57 cm; and the mean of head circumference was 33.77 ±1.02 cm, ranging from 30 to 38 cm.

Also, two-thirds (n=62) of the newborns had been born by vaginal delivery and one-third (n=38) by cesarean section. The number of breastfed newborns was 85(85%) and the remaining 16(16%) were formula fed. The level of bilirubin more than 15 was detected in 15(15%) newborns at the 3rd to 5th days of life as hyperbilirubinemia. Maternal vitamin D showed a significant correlation with the levels of bilirubin of the 3rd to 5th days of life in these newborns.

Discussion

The present study revealed that maternal vitamin D had a significant correlation with the levels of bilirubin of 3rd to 5th days of life in the newborns. Few case-controlled studies could show the association between maternal vitamin D deficiency and jaundice in newborns. In a study by Aletayeb et al., it was shown that there was an association between low serum vitamin D levels in mothers with jaundice in their newborns.[18] Multu et al., conducted a study on 51 newborns including 30 newborns with jaundice and 21 as the control; they found a strong relationship between neonatal vitamin D and jaundice (P=0.01)[19] In contrast, Mehrpisheh et al. reported no significant relationship among 30 term-newborns with jaundice, in comparison with 30 control groups for neonatal vitamin D deficiency[20]

In present study, the association between maternal vitamin D deficiency and the increased risk for neonatal jaundice may be explained by focus on a common pathway in the liver for synthesis of vitamin D and for metabolism of bilirubin. This study indicated the prevalence of hyperbilirubinemia was 15% in mature newborns at the 3rd to 5th days of life. The

incidence of referral for neonatal jaundice was 10.5% of live term births in Turkey[21] A multi-center study in six developing countries showed hyperbilirubinemia was a primary diagnosis for hospital admission in 12- 78% of the admissions in the first 6 days of life[22] .Worldwide, it is estimated that 10.5% of live birth newborns require phototherapy for jaundice[23] Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common cause of neonatal jaundice throughout the world; it is noteworthy that the higher rate of G6PD deficiency in this region is one of the reasons for the higher neonates' hyperbilirubinemia[24] The prevalence of vitamin D deficiency has been reported in pregnant women in different countries from 18% in UK to 84% in Netherlands, and the rate of 80% in Iran[25,27] Considering the deficiency and insufficiency levels of vitamin D, we found that (16.5%) and (78.5%),of the mothers had low vitamin D in order. It appears that sunny weather itself is not enough for protection against low vitamin D in pregnant mothers; outdoor activities, dressing habits, and dietary supplements have to be notified. We found a relationship between the mother's education and the level of vitamin D similar to Scholl et al.'s study; it appears that educated mother's pay more attention to food fortification and use regular supplementation[28] It is important to remember that while sunscreen protects the individuals from sunlight, blocking these UV rays can predispose them, especially pregnant women, to vitamin D deficiency. As reported, vitamin D is negatively associated with a BMI of 85 kg/m^2 or higher[29] The effect of vitamin D on BMI was not significant in our study. There was a correlation among the levels of maternal vitamin D with calcium, phosphorus and alkaline phosphatase. Vitamin D stimulates the transport of calcium and phosphorus into the extracellular fluid in the intestine, bone, and kidney; however, the production of the hormone is regulated directly or indirectly by plasma levels of calcium and phosphorus[30] Approximately 84% of our mothers reported using vitamin D supplement; therefore, we suggest that new high strength vitamin D products should be prescribed for pregnant women in future.

Conclusion

The results of this study showed that the presence of maternal vitamin D deficiency could effectively predict the increased risk for neonatal jaundice. Vitamin D deficiency is common in pregnant women; researchers should be encouraged to study new high strength vitamin D supplements for preventing maternal hypovitaminosis D and following neonatal jaundice

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