

Prospective observational Study: Role of Vitamin D in Sick Newborn

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Objective: To study whether the newborn are having vitamin D deficiency or not, whether their vitamin d level is related to morbidity of newborn or not and their correlation with mother.

Methods: This study included 350 sick infants admitted in level III NICU of medical college during the period from February 2015 to January 2016.

Blood for neonatal (within 72hrs of admission) and maternal vitamin D levels were obtained from all infants and their mothers at the post partum period at the time of hospital admission. Vitamin D assessment was done by Chemo-immunoassay method.

History taking, clinical examination and other investigations needed for diagnosis of Respiratory distress, Birth asphyxia, neonatal seizure, neonatal encephalopathy, hypoglycemia, prematurity, neonatal sepsis, hyper bilirubinemia, coagulation disorder, renal failure were done.

Results: For study total of 335 infants were taken from NICU, out of which 155 were found to be vitamin D deficient and remaining 180 had normal levels of vitamin D. Vitamin D level of mother of all infants were taken and compared as per deficient and normal infants.

Analysis of studied groups revealed that there was insignificant difference between two groups regarding maternal age ($P=0.65$), gender of baby ($P=0.92$), mode of delivery ($P=0.50$) and rural urban status ($P=0.97$). It was observed that mothers of deficient neonates also had lower levels of vitamin D.

Significant difference in association was found between both two groups regarding all the parameters. Thus it has been concluded that deficient infants has more complains as compare to normal infants.

It was observed that duration of NICU stay of deficient babies given therapeutic vitamin D supplementation was significantly less as compared to babies given routine supplementation of vitamin D.

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I. Introduction

Vitamin D is a fat-soluble steroid hormone that contributes to the maintenance of normal calcium homeostasis and skeletal mineralization. Vitamin D also has immune modulatory effects on immune function. It was suggested that it might have a role in the optimal functioning of the innate immune system by inducing antimicrobial peptides in epithelial cells, neutrophils and macrophages. Newborns are more susceptible to infections as both innate and adaptive immune systems are not entirely developed. Low birth weight is also common in india and these infants are at higher risk of respiratory tract infections and other morbidity. It also plays important for optimal function of striated and smooth muscle strength including heart muscle, and is related to postnatal muscle strength. low cost intervention such as improving vitamin D status are needed to improve the health and survival of these infants. In 2008, the American Academy of Pediatrics (AAP) recommended 400 IU of vitamin D supplementation of all infants. Vitamin D deficiency is frequently defined as serum concentrations less than 20 ng/mL with concentrations between 21–29 ng/mL treated as insufficiency and greater than 30 ng/mL as sufficient. There are various studies which shows the relationship between maternal and newborn vitamin D level. Neonatal sepsis, faulty feeding, dehydration, Respiratory distress, Renal failure, neurological manifestation, lethargy, convulsion are the usual cause of neonatal intensive care unit admission in newborn. In this study we studied that whether the newborn are having vitamin D deficiency or not, whether their vitamin d level is related to morbidity of newborn or not and their correlation with mother.

II. Methods

This study included 350sick infants admitted in level III NICU of medical college during the period from February 2015 to January 2016. Blood for neonatal (within 72hrs of admission) vitamin D levels were obtained from all sick infants. The vitamin D level of mothers of deficient baby were also taken. Vitamin D assessment was done by Chemo-immunoassay method. History taking, clinical examination and other investigations needed for diagnosis of Respiratory distress, Birth asphyxia, neonatal seizure, neonatal

encephalopathy, hypoglycemia, prematurity, neonatal sepsis, hyperbilirubenemia, coagulation disorder, renal failure were done.

Inclusion criteria: All infants admitted in NICU during the study time.

Exclusion criteria: Congenital malformation.

III. Methodology

All sick infants admitted in neonatal ICU with different complain were included in study after obtaining written consent from parents. Thorough clinical examination (vital sign, urine output, anthropometric measures, skin rash, edema, skin infections, Respiratory examination (tachypnea, retraction, air entry, abnormal additional sounds), Cardiovascular system (cyanosis, Heart rate, peripheral pulses, CRT, murmur), neurological examination (lethargy, obtundation, coma, convulsion, jitteriness, muscle tone), abdominal examination (organomegaly, peristalsis, abdomen distension, ascites) was done for all enrolled infants examination. Blood investigation, X-ray chest, abdominal ultrasonography and chest, abdomen or brain CT and MRI if needed according to the case based diagnosis.

2 ml of infant blood were withdrawn for 25-hydroxyvitamin D assessment using Chemoimmunoassay method within 72hrs after admission. Blood sample of mothers of deficient babies were also taken. Vitamin D level values were used as a continuous variable and were categorized in descriptive Vitamin D deficiency is frequently defined as serum concentrations less than 20 ng/mL, with concentrations between 21–29 ng/mL treated as insufficiency and greater than 30 ng/mL as sufficient as previously reported. The study protocol was approved by the Ethical committee.

Results

For study total of 335 sick infants were taken from NICU, out of which 155 were found to be vitamin D deficient and remaining 180 had normal levels of vitamin D. Vitamin D level of mothers of all deficient baby also taken.

TABLE 1: Analysis of studied groups revealed that there was insignificant difference between two groups regarding maternal age (P =0.65), gender of baby (P=0.92), mode of delivery (P=0.50) and rural urban status (P=0.97).

It was observed that mothers of deficient neonates also had lower levels of vitamin D.

TABLE 2: Significant difference in association was found between both two groups regarding all the parameters. Thus it has been concluded that number of patient were higher in deficient group as compare to normal infants.

TABLE 3: It was observed that duration of NICU stay of deficient babies given therapeutic vitamin D supplementation (1000IU/day) was significantly less as compared to babies given routine supplementation of vitamin D(400IU/day).

Table 1:

Parameter		Group 1 Deficiency N = 155	Group 2 Normal N = 180	T value	P value	
Maternal age (years)	Range	18 – 38	18 - 38	0.445	0.65	
	Mean ± SD	26.9 ± 6.1	26.6 ± 6.2			
Maternal Vitamin D (nmol/l)	Range	4 – 16	-	-	-	
	Mean ± SD	10.9 ± 3.34	-			
Gestational age (weeks)	Term	N	90 (58.06%)	112 (62.22%)	2.138	0.034*
		Range	36-42	37-42		
		Mean ± SD	38.3 ± 2.01	38.9 ± 1.96		
	Pre term	N	65(41.94%)	68(37.78%)	2.883	0.005*
		Range	34-36	34-36		
		Mean ± SD	35.1 ± 1.01	35.6 ± 0.99		
				χ² – value	P value	
Gender of baby	Male	80 (51.61%)	95 (52.78%)	0.011	0.92	
	Female	75 (48.39%)	85 (47.22%)			
Mode of delivery	Normal	70 (45.16%)	89 (49.44%)	0.453	0.50	
	CS	85 (54.84%)	91 (50.56%)			
Area of living of mother	Rural	79 (50.97%)	91(50.56%)	0.001	0.97	
	Urban	76 (49.03%)	89 (49.44%)			

Table 2

Parameter	Group 1 Deficiency N = 155	Group 2 Normal N = 180	Total N = 335	χ^2 - value	P value
Cong. Pneumonia	89 (57.42%)	12 (6.67%)	101 (30.15%)	99.47	<0.001*
Neonatal sepsis	102 (65.81%)	32 (17.78%)	134 (40.0%)	78.06	<0.001*
Hyper bilirubinemia	20(12.23%)	25(16.0%)	45 (13.43%)	22.25	<0.5
Birth Asphyxia	45(29.03%)	15 (8.33%)	60 (17.91%)	22.88	<0.001*
Coagulation Disorder	12 (12.90%)	11(1.67%)	23 (6.87%)	53.58	<0.65
Hypernatremic dehydration	35 (22.58%)	13 (7.22%)	48 (14.23%)	14.78	<0.001*
Faulty feeding	37 (23.87%)	20 (11.11%)	57 (17.01%)	8.72	0.003*
Hyperinsulinemic hypoglycemia	13 (8.39%)	10 (1.11%)	24 (4.48%)	8.61	0.24
Renal failure	26 (16.78%)	16 (8.89%)	42 (12.54%)	4.031	0.045*
Neonatal seizure	24 (15.48%)	14 (7.78%)	38 (11.34%)	4.181	0.041*

Fig. 1

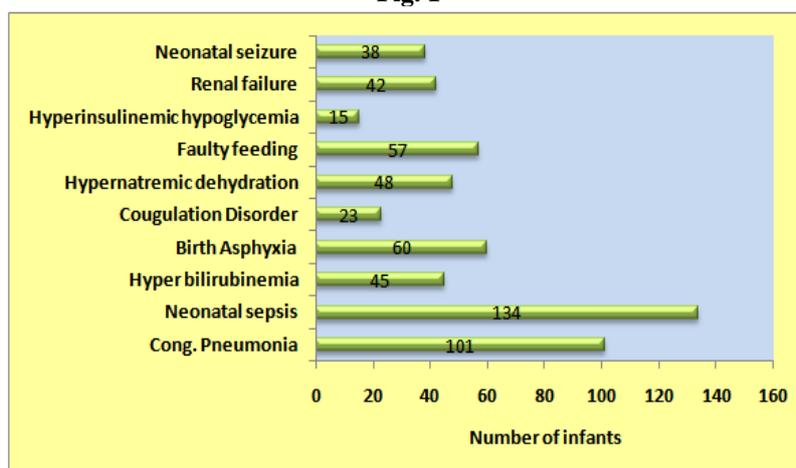
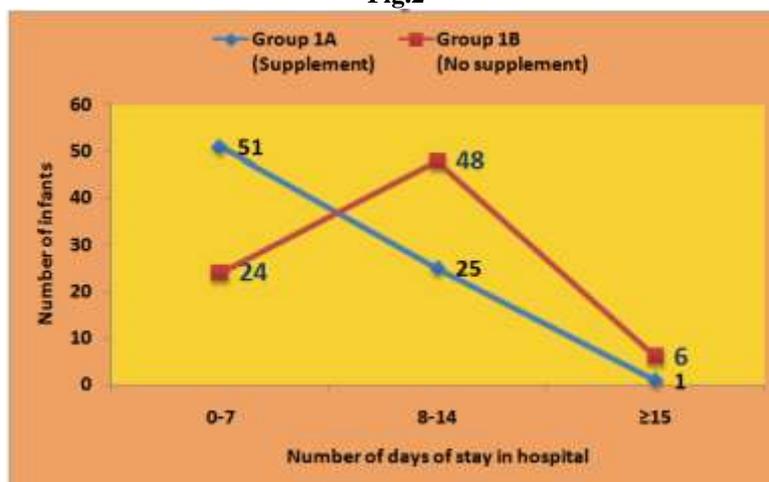


Table 3

Duration of stay	Group 1A (Supplement)	Group 1B (No Supplement)	Total	χ^2 - value	P value
0-7	51 (66.23%)	24 (30.77%)	75 (48.39%)	20.53	<0.001*
8-14	25 (32.47%)	48 (61.53%)	73 (47.1%)		
≥15	1(1.3%)	6 (7.70%)	7 (4.52%)		
Total	77 (100%)	78 (100%)	155 (100%)		

Fig.2



IV. Discussion

Our study was an randomized control prospective study done in tertiary level neonatal Intensive care unit. In our study total 335 sick infants were taken from NICU, out of which 155 were found to be vitamin D deficient and remaining 180 had normal levels of vitamin D. Vitamin D level of mothers of all Vitamin d deficient infants were also taken. In our study we found the association of vitamin d deficiency with various diseases such as congenital pneumonia, neonatal sepsis, neonatal seizure, renal failure, birth asphyxia. Secondary outcomes like severity of disease, morbidity, length of hospital stay were also significantly high in deficient infants. In our study effect of secondary outcomes were reduced after supplementing babies with therapeutic dose of vitamin D(1000 IU/day) as compared to the deficient babies given routine supplementation(400IU/day).These results reflect the role of vitamin D in all organs adaptation in neonatal period.

Our study has similar findings as per previous study which shows relation of vitamin d deficiency and neonatal sepsis.

M Cetinkaya1, F Cekmez et al. evaluated the effect of vitamin D levels on early-onset sepsis (EOS) in term infants. In this study fifty term infants with clinical and laboratory findings of EOS (study group) and 50 healthy infants with no signs of clinical/laboratory infection (control group) were enrolled. Blood was drawn at the time of admission during the first 3 postnatal days of life in both groups for measurement of 25-hydroxyvitamin D (25-OHD) levels. Maternal and neonatal 25-OHD levels (22.2/8.6 ng ml⁻¹, respectively) in the study group were significantly lower than those of the control group (36.2/19 ng ml⁻¹, respectively, Po0.001). A positive correlation was detected between maternal and neonatal 25-OHD levels. Severe vitamin D deficiency was significantly more common in the sepsis group.

Researchers out of Qatar, led by Dr Ashraf Soliman, took a look at 10 full-term newborns who presented to their hospital with symptomatic low blood calcium. The low blood calcium (hypocalcemia) was due to severe vitamin D deficiency. All of the newborns were symptomatic hypocalcemic because they were suffering from seizures.

Dr.Shalini Tripathi et al. had reported a case report in april 2012 on hypovitaminosis d in an infant with hypocalcemic seizures secondary to maternal vitamin d deficiency. Vitamin D deficiency in the neonate secondary to maternal deficiency is an important cause of seizures in the newborn period. Maternal diet low in vitamin D with no extra supplementation is an important risk factor for neonatal vitamin D deficiency. Exclusive breast-feeding is recommended up to 6 months of age with all its beneficial effects on child survival. Several studies have concluded that adequate intake of vitamin D cannot be met with human milk as the sole source of vitamin D. Most of the vitamin D in a neonate is acquired from maternal transfer, so vitamin D deficiency in mothers is likely to have adverse consequences for their infants. The supply of vitamin D in utero, rather than from milk, is the major determinant of vitamin D status in early neonatal life in mammals. These findings were consistent with our study also.

Serkan Bilge Koca et al. reported a case in which patient was admitted with hypocalcaemia seizure at 10 days of age. Both the baby and her mother had low 25(OH) vitamin D3 levels. Osteoporosis was found in the bone mineral densitometer analysis (T score ≤2.6). So they concluded that congenital rickets also should be kept in mind in differential diagnosis for newborns referring with convulsion.

In contrast to other studies which shows Neonatal hypercalcemia due to phosphate depletion usually occurs in low birth weight babies who are fed unsupplemented human milk that lead to hypo phosphatemia, increased renal vitamin D3 and increased calcium absorption and suppressed PTH². But in our case PTH was elevated due to severe vitamin D deficiency. Nephrocalcinosis implies deposition of calcium in the substance of kidney. In infants it may cause renal failure without stone formation⁴. In our case ARF partly caused by nephrocalcinosis(due to hypercalcemia) and partly due to dehydration by hypercalcemia/hypercalciuria(prerenal component).Hypophosphatemic mother milk, increased PTH ,Vitamin D deficient status were the correct explanation of hypercalcemia in our term baby.

During our study time we also found that chances of birth asphyxia was higher in deficient group of babies.Pelle G Lindqvist et al. reported a case control study showing relation of maternal vitamin D deficiency and fetal distress/birth asphyxia.in their study vitamin D levels were significantly lower in mothers delivered by emergency caesarean section due to suspected fetal distress. Birth asphyxia was more common in women with vitamin D deficiency in early pregnancy. If these findings are supported by further studies preferably on severe birth asphyxia, vitamin D supplementation in pregnancy may lower the risk of subsequent birth asphyxia. Like our study there are also various studies which show the immunomodulatory properties of vitamin D associated

with risk of respiratory tract infections like pneumonia. CenKAypak et al reported a relationship between vitamin D deficiency and lower respiratory tract infections.

Nalankarabayir et al. stated that dilated cardiomyopathy can occur secondary to hypocalcaemia that originate from a nutritional vitamin D deficiency induced rickets both were exclusively breastfed by mothers who had vitamin D deficiency. In our study no correlations were found between the maternal age, infant gender, mode of delivery or area of living of mother with vitamin D level.

V. Conclusion

These data suggest that vitamin D deficiency is common in neonate born to vitamin D deficient mother. We found correlation of vitamin D deficiency with illness like congenital pneumonia, neonatal sepsis, renal failure and neonatal seizure, birth asphyxia. After supplementing with therapeutic dose of vitamin D(1000IU/day) in these neonate NICU stay were significantly decreased as compare to deficient neonate supplemented with routine dose(400IU/day).

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