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RESEARCH ARTICLE

Neonatal Hypocalcemia and its Association with Neonatal and Maternal Vitamin D Deficiency

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ABSTRACT

Background: In neonates, hypocalcaemia is a common metabolic manifestation. It is a potentially fatal condition, with reported prevalence varying according to gestational age, maternal and infant comorbidities, and perinatal factors.

Methods: All 100 new-borns admitted in the NICU, and having hypocalcaemia, defined as total serum Calcium <8mg/dl and ionic calcium <3mg/dl, during the study period, and whose parents have given informed consent

Results: The male predominance was seen in 58% and females were 42%. The male : female ratio was 1.38:1. Early onset of hypocalcaemia was seen in 83% of the cases of which Males were 59% and females were 41%. The mean gestational age was 36.27) + 1.99 and the mean birth weight was 2.46 + 0.65. The preterm neonates were 27 (32.53%) and term neonates were 56(67.46%)

Conclusion: Vitamin D deficiency was found to be very prevalent in healthy term born infants. Vitamin D deficiency was observed in new-borns, and it was observed that this deficiency was attributed to early neonatal hypocalcaemia. However, the long-term effects of a vitamin D deficiency in childhood are unknown. The use of 25-OH cholecalciferol as a sensitive marker in both term and preterm new-borns is recommended. To prevent neonatal Vitamin D deficiency, mothers were given 1200 IU/day vitamin D supplements from the 12th gestational week to the 6th month of pregnancy.

Keywords: Neonatal Hypocalcaemia, Vit D Deficiency, 25-OH cholecalciferol, hypocalcaemic seizures, jitteriness, sunlight.

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Introduction

Vitamin D is a fat-soluble vitamin that is found naturally in a small number of foods, is added to others, and can be purchased as a dietary supplement.[1] When ultraviolet rays from the sun strike the skin and trigger vitamin D synthesis, it is also produced endogenously. Vitamin D obtained from the sun, food, and supplements is biologically inert and must be activated by two hydroxylations in the body (one in the liver and then in the kidney).[2]Vitamin D is a secosteroid that plays an important role in the human body as a pro-hormone

Vitamin D deficiency is the most common type of nutritional deficiency. Vitamin D has evolved into a hormone that acts throughout the body, not only to regulate calcium and bone metabolism but also to lower the risk of chronic diseases such as autoimmunity, cancer, cardiovascular disease, and infectious disease. Vitamin D deficiency or insufficiency affects an estimated 1 billion people worldwide.[7] Vitamin D deficiency is very common in all age groups and both sexes across India, despite the fact that the majority of the population lives in areas that receive ample sunlight throughout the year[8] Breast-feeding is recommended exclusively until the child reaches the age of six months, with all of the benefits it brings to the child's survival. Several studies have concluded that human milk cannot provide an adequate amount of vitamin D.[9,10] The incidence of vitamin D deficiency rickets is expected to rise as breastfeeding rates rise.

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Neonatal hypocalcemia is widely prevalent in India with significant association with a history of neonatal jaundice on phototherapy, not receiving maternal calcium or neonatal vitamin D supplementation. The prevalence of hypocalcemia was 55%, late hypocalcemia represent 45% of hypocalcemic neonates. Hence the present study was undertaken to assess the prevalence of hypocalcemia in neonates and it's relation with neonatal and maternal vitamin D deficiency

Objectives

To know the prevalence of hypocalcemia in neonates. The primary objective is to assess the hypocalcemia association with neonatal and maternal vitamin D deficiency , and secondary objective is to study the effectiveness of vitamin D supplementation to prevent neonatal hypocalcemia.

Methods

Study Design and Setting

This prospective analytical study was conducted over an 8-month period (February to October 2024) at the Neonatal Intensive Care Unit (NICU) of Princess Esra Hospital, a tertiary care center in Hyderabad, Telangana, India. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from the parents of all participating neonates.

Participants and Sample Size

The study enrolled neonates admitted to the NICU with biochemically confirmed hypocalcemia, defined as total serum calcium (TSC) <8 mg/dL and/or ionized calcium (iCa) <3 mg/dL. Based on a national prevalence of 55% for neonatal hypocalcemia and an allowable absolute error of 15%, a sample size of 50 was determined (including a 10% attrition buffer). Exclusion criteria included parental refusal of consent or refusal to undergo maternal and neonatal Vitamin D assays.

Table 1: Association of Hypocalcaemia with Vitamin– D deficiency

Hypocalcaemia	*Vitamin– D Deficiency*	
	Moderate	*Severe*
<8	53	20
>8	25	2
Chi-Square	4.589	
p-Value	0.01	

The S. Calcium levels of <8was seen in 53%of the cases with moderate Vitamin-D deficiency. While 20% of the hypocalcaemia cases had Severe Vitamin-D deficiency. The S. Calcium levels of >8was seen in 25% of the cases with moderate Vitamin-D deficiency. While only 2% of the cases had Severe Vitamin-D deficiency

Table 2: Association of Neonatal and maternal Vitamin-D deficiency

Neonatal Vitamin-D deficiency	*Maternal Vitamin–D Deficiency*	
	<10 (%)	*<20 (%)*
Moderate	6	64
Severe	2	28
Mean S. Neonatal Vitamin-D	11.43 +3.13	
Mean S. Maternal Vitamin-D	14.70 +2.86	
Chi-Square	0.471	
p-Value	0.492	

Neonatal vitamin-D deficiency was moderate in 6% of the mothers with <10 S. Vitamin- D levels and severe in 1% of the cases. Neonatal vitamin-D deficiency was moderate in 65% of the mothers with <20 S. Vitamin- D levels and severe in 28% of the cases.

Table 3: Correlation of Neonatal vitamin D deficiency with maternal risk factors

Maternal risk factors	*Neonatal Vitamin–D deficiency*		*Chi square* X^2	*p-value*
	Moderate	*Severe*		
LSCS	24	8	2.227	0.135
SVD	11	7		
Obesity	4	1	2.777	0.095
Irregular Antenatal care	11	4	5.827	0.015
Maternal Diabetes	6	4	1.315	0.251
Maternal PIH	10	6	2.612	0.105
Anaemia	15	6	8.804	0.003
Seizures	1	0	1	0.317
Medications	2	1	0.2	0.654
Iron and Calcium supplements	31	11	20.253	0.000006
Vitamin D supplements	7	4	1.636	0.200
Chronic disease	0	1	2	0.157

The maternal risk factors, iron and calcium supplements and anemia was statistically significant with neonatal vitamin-d deficiency. Rest all risk factors were not statistically significant. All the risk factors were not statistically significant.

Table 4: Correlation of Maternal vitamin-D deficiency with maternal risk factors

Maternal risk factors	*Maternal Vitamin – D deficiency*		*Chi square*	*p-value*
	≤10	*≤20*	X^2	
LSCS	3	29	1.132	0.287
SVD	1	17		
Obesity	0	5	9	0.002
Irregular Antenatal care	2	13	25.137	<0.001
Maternal Diabetes	1	9	11.842	0.0005
Maternal PIH	1	14	23.516	<0.001
Anaemia	2	18	29.878	<0.001
Seizures	0	1	1	0.317
Medications	0	3	5	0.025
Iron and Calcium supplements	3	31	64.204	<0.001
Vitamin D supplements	1	10	18.181	0.00002
Chronic disease	0	1	2	0.157

Maternal Vitamin-D and Iron and calcium supplements during pregnancy, Anaemia, PIH, Diabetes, Obesity and Irregular antenatal care were statistically significant. The mode of delivery, Chronic diseases, medications, Seizures were not statistically significant

Table 5: Distribution based on IV Calcium therapy

Duration of IV calciumtherapy	*Frequency*	*Percentage*	*Chi-Square*	*p-value*
1 day	23	46%	14.6	0.0006
2 days	17	34%		
3 days	10	20%		

Duration of IV calcium was 1 day in 46% of the cases, 2 days in 34% of the cases and 3 days in 20% of the cases. The chi-square was 14.6.The p-value was 0.006 which was statistically insignificant.

Data Collection and Clinical Assessment

Maternal and neonatal data were collected using a structured, pre-tested questionnaire. Maternal variables included age, residence, mode of delivery, comorbidities (e.g., PIH, diabetes), perinatal complications, and antenatal calcium/vitamin D supplementation. Neonatal variables included gestational age, birth weight, feeding type,

Table 6: ANOVA of Serum Calcium and Vitamin-D–Initial and discharge

Summary of Data					
	Treatments				
	S. Cal -Initial	*S. cal-Discharge*	*S. Vit-D-Initial*	*S. Vit-D– 2 months*	*Total*
N	50	50	50	50	50
∑X	713.3	870.1	1143	2269	4995.4
Mean	7.133	8.701	11.43	22.69	12.489
∑X2	5194.73	7598.47	14035	51679	78507.2
Std. Dev.	1.0385	0.5292	3.131	1.4049	6.3566

Result Details				
Source	SS	df	MS	
Between-treatments	14821.7561	3	4940.5854	F=1504.5258
Within-treatments	1300.391	396	3.2838	
Total	16122.1471	399		

The mean neonatal Vitamin-D levels improved from from 11.43±3.13 initial to 22.69±1.40 After 2 months of treatment.The mean maternal Vitamin-D levels improved from 14.70±2.86 initial to 23.06 ±1.63 after 2months of treatment. The f-ratio value is 1504.5258. The p-value is<0.00001. The result is significant at p <0.05.

and clinical symptoms of hypocalcemia (e.g., seizures, jitteriness). A comprehensive physical examination, with emphasis on the central nervous system, was performed on all subjects.

Laboratory Measurements

Venous blood was collected from neonates and their mothers to measure TSC, iCa, and 25-hydroxyvitamin D [25(OH)D]. Serum 25(OH)D3 levels were quantified using the Enzyme-Linked Fluorescent Assay (ELFA) technique on a mini-VIDAS automated instrument (BioMérieux). This competitive immunoassay utilizes a solid-phase receptacle (SPR) and alkaline phosphatase conjugate, with fluorescence measured at 450 nm. Vitamin D hypovitaminosis was defined as serum 25(OH)D <30 ng/mL (75 nmol/L), further categorized into deficiency (<50 nmol/L) and insufficiency (50–75 nmol/L).

Statistical Analysis

Data were analyzed using SPSS software, version 23 (IBM Corp). Quantitative variables were expressed as mean (SD) and compared using independent t-tests or ANOVA. Qualitative data were expressed as frequencies and percentages and compared using the Chi-square ($\chi 2$) test. Bivariate Pearson correlation was used to assess the association between maternal and neonatal biochemical parameters. Statistical significance was set at a 2-tailed P <0.05.

Results

All results are depicted in Tables 1-6.

Conclusion

Despite the fact that vitamin D deficiency is preventable and curable, it is a significant health problem for new-borns, according to the finding soft his study. Vitamin D deficiency was found to be very prevalent in healthy term born infants. Vitamin D deficiency was observed in new-borns , and it was observed that this deficiency was attributed to early neonatal hypocalcaemia. However, the long-term effects of a vitamin D deficiency in childhood are unknown. The use of 25-OH cholecalciferol as a sensitive marker in both term and preterm new-borns is recommended. To prevent neonatal Vitamin D deficiency, mothers were given 1200 IU/day vitamin D supplements from the 12th gestational week to the 6th month of pregnancy.

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