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Prevalence of Neonatal Hypocalcemia and its relation to Supplementation

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Abstract

Objectives:

To assess the prevalence of hypocalcemia in outpatient clinic neonates and its relation to vitamin D and calcium supplementation.

Methods:

This cross-sectional analytical study was conducted in the department of Pediatrics at Sri Guru Ram Das Institute Of Medical Sciences and Research, Amritsar from March 2018 to October 2018. Data was collected from 100 neonates by interviewing mothers using a structured questionnaire; which included a socio-demographic information, maternal and neonatal history; in addition to investigations of serum calcium (total & ionized) and also serum vitamin D levels.

Results:

The prevalence of hypocalcemia was found to be 76% out of which 55% neonates presented with early hypocalcemia and 45% of neonates presented with late hypocalcemia. The prevalence of hypovitaminosis D was found to be 88%. Hypocalcemia was found to be more prevalent among neonates with no history of vitamin D supplementation (98.7%), no history of maternal calcium supplementation (57.9%), while the prevalence of hypocalcemia was significantly higher in neonates who had a history of neonatal jaundice and were put on phototherapy.

Conclusion:

Neonatal hypocalcemia is widely prevalent in Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar with significant association with a history of neonatal jaundice on phototherapy, not receiving maternal calcium or neonatal vitamin D supplementation.

Keywords: Hypocalcemia, neonates, vitamin D and calcium supplementation.

Introduction

The Neonatal Mortality Rate in India has gone down from 84.80/1000 live births in 1969 to 25.4.00/1000 live births in 2018. The prime reason in this drastic improvement has been the improvement in health care facilities provided by the government and brilliant doctors of the country. However, India is still the 12th country among the 52 lower-middle income countries (as reported by UNICEF 2018) when it comes to Neonatal Mortality Rate. Therefore, if India has to achieve the goal of Sustainable Development 2030 then the death rate of newborns needs to be significantly improved towards the betterment. One major reason for this death rate is the nutritional deficiencies that newborns suffer due to lack of proper nutrition. Of all the deficiencies, one of the most common deficiency is the calcium deficiency (hypocalcemia) and Vitamin D deficiency (Hypovitaminosis D). Hypocalcemia is a common metabolic manifestation in neonates. It is a potentially life-threatening condition, with reported prevalence varying by gestational age, maternal and infant comorbidities, and perinatal factors. Neonatal hypocalcemia is classified according to its onset to early onset which manifests within the first 72 hours of birth and delayed onset after 3 days of birth. Calcium is the most abundant mineral in the human body. Ionized calcium is essential for many biochemical functions. Hypocalcemia is usually asymptomatic disease but may present with lethargy, vomiting, abdominal distension, poor muscle tone, or poor feeding, and irritability. Another common manifestation of hypocalcemia is tetany characterised by irritability, seizures and muscle spasms. Vitamin D and its metabolites are fat soluble pro-hormones. In addition to their well-known classic functions of hemostasis of calcium, magnesium, and phosphorus level and keeping skeletal integrity, there are non-classic functions which are related to promoting insulin secretion and action, lung development, antibacterial effects, immune regulation and controlling blood pressure. Some common signs of Hypovitaminosis D are delayed closure of anterior fontanelle, pepperpot skull, rickety rosary, craniotabes etc. Nutritional status of mothers has a strong effect on fetal development; maternal supplementation of vitamin D and calcium during pregnancy reflects neonatal vitamin D and calcium level. Maternal calcium supplementation reduces the risk of preterm birth which is the leading cause of neonatal mortality. The current study aims to assess the prevalence of hypocalcemia in outpatient clinic neonates and assess its relation to vitamin D and calcium supplementation.

Materials and Methods

This cross-sectional analytical study was conducted in the department of Pediatrics at Sri Guru Ram Das Institute Of Medical Sciences and Research, Amritsar from March 2018 to October 2018. Data was collected from 100 neonates by interviewing mothers using a structured questionnaire; which included socio-demographic information, maternal and neonatal history; in addition to investigations of serum calcium (total and ionized) and serum vitamin D levels.

100 neonates (under 28 days old) from total 150 neonates (66.7%) were recruited in the study by systemic random sampling of every 2nd eligible child.

Inclusion criteria:

Neonates under 28 days of life seeking neonatology outpatient clinic medical care.

Exclusion criteria:

No congenital anomalies, no medications, no metabolic syndromes.

Data collection:

Data was collected by interviewing mothers using a pre-prepared and pretested structured questionnaire which included the following 3 sections: the first section introduces sociodemographic information including age, gender, and residence. The second section discusses maternal history including mode of delivery, maternal chronic disease, perinatal maternal complications, and calcium supplementation during pregnancy. The third section discusses neonatal history including gestational age, birth weight, neonatal complications, type of feeding, symptoms of hypocalcemia or other associated symptoms and vitamin D supplementation.

A full general examination was done with special emphasis on CNS examination. Serum ionized, total calcium level and Serum 25 Hydroxy vitamin D level were investigated in all neonates. In the current study, neonatal hypocalcemia is defined by total serum calcium below 8.8 mg/dl (2.2 mmol/L), and serum ionized calcium below 4.41 mg/dl (1.1 mmol/L). As far as vitamin D is concerned hypovitaminosis is defined when serum vitamin D is below 75 ng/ml; Vitamin D levels less than 50 ng/ml is defined as Vitamin D deficient while vitamin D insufficiency is defined when Vitamin D levels are between 50-75 ng/mL. Enzyme Linked Florescent Assay (ELFA)

technique mini-VIDAS instrument (Bio Mérieux Company) was used to measure serum 25 Hydroxy vitamin D3 levels.

Data Analysis:

The collected data was statistically analyzed using the Statistical Package for the Social Science (SPSS) software version 18.

Ethical consideration:

From the ethical point of view, the mothers of all children gave written consent for inclusion in the study. The process of the treatment was simplified and explained to the childrens' mothers and only after they completely understood the study protocol and became aware of their rights during the study, the written consent form was signed by them. The institutional review board of Sri Guru Ram Das Institute of Medical Sciences and Research approved the protocol of this study.

Results

Neonates included in the current study had a mean age of (9.5±8.1) days, and mean birth weight of (2.8±0.50) kg. In the study group, 56% were males and 44% were females. As for the gestational age, 88% of them were full term and 12% were preterm. With regards to the feeding types, 69% of the neonates were being breastfed, while 22% were being formula fed, only 9% depended on combined feeding.

More than half of the study group (56%) were delivered by caesarian section, and 44% by normal vaginal delivery. Only 12% underwent perinatal complications, with 9% premature rupture of membranes (PROM), 1% pre-eclampsia, and 2% with a history of asphyxia.

With regards to the mother illness, only 7% had an illness in the form of the following: 4% hypertension, 2% diabetes mellitus, and 1% nutritional hypocalcemia.

Half of the infants included in the study suffered from associated symptoms which were as follows: 38% had jaundice and received phototherapy, 1% showed hypoglycemia, 1% had a convulsion, 7% had respiratory distress and 3% presented with mixed symptoms (case of jaundice with hypoglycemia, case

of jaundice with respiratory distress (RD), and finally case of RD with hypoglycemia).

The prevalence of neonatal hypocalcemia among a sample of 100 neonates included in the current study was 76%. Among them, 42 (55 %) had early hypocalcemia, and 34 (45%) had late hypocalcemia. The mean ionized calcium among the study group was (0.95±0.19) mmol/L, and mean serum total calcium was (7.8±1.31) mg/dl. The mean Serum vitamin D level was (73.7±22.6) ng/mL. Hypovitaminosis of vitamin D (<75 ng/mL) represented 88% of the study group out of which 36% were deficient (<50 ng/mL), and 52% were insufficient (50-75 ng/mL). Almost half of the mothers (51%) took calcium supplementation during the antenatal period and 8% of the neonates had a history of vitamin D supplementation.

There was a statistically significant high prevalence of neonatal hypocalcemia among neonates who had a positive history of neonatal jaundice on phototherapy, who had not received vitamin D supplementation and whose mothers had not received calcium supplementation. There was a statistically significant correlation between hypocalcemia and maternal factors such as maternal illness (For example, Diabetes) and neonatal factors such as perinatal complications and mode of feeding. On the other hand, there was no statistically significant association with other neonatal factors (sex) and maternal factors (residence and mode of delivery).

There was a statistically significant positive correlation between total and ionized serum calcium levels and the age of the neonates, which indicated an improvement in total and ionized serum calcium levels with age. Similarly, there was a statistically significant positive correlation between serum vitamin D levels and birth weight, which indicated that an increase in neonatal serum vitamin D level will be associated with an increase in birth weight.

Discussion

Data on the incidence and prevalence rates of hypocalcemia in the neonatal period are limited. This study is of value because we included symptomatic and asymptomatic hypocalcemic neonates and provided some new predictors as supplementations to clinicians, which may explain the mechanisms of neonatal hypocalcemia and hypovitaminosis D. Early hypocalcemia was more frequent (55%) than late hypocalcemia (45 %) in the current study. The

prevalence of hypovitaminosis D (<75 ng/mL) in the current study was 88%. The current study found a statistically significant high prevalence of neonatal hypocalcemia among neonates who did not receive vitamin D supplementation. Additionally, our study revealed a high prevalence of neonatal hypocalcemia among neonates whose mothers had not received calcium supplementation during pregnancy. Moreover, exclusive breastfeeding without vitamin D supplementation is another risk factor for vitamin D and calcium deficiency in neonates. Reserves of vitamin D in neonates are related to maternal vitamin D supply. So vitamin D deficiency in mothers will reduce placental vitamin D transmission and cause neonate deficiency. This study illustrated the association between late neonatal hypocalcemia and neonatal jaundice on phototherapy. Also, there is a statistically significant association between preterm and low level of serum vitamin D. There was a statistical significant positive correlation between total and ionized serum calcium level and the age of neonates. It indicated that hypocalcemia improves with age. There was also a statistically significant positive correlation between serum vitamin D level and birth weight. There was a remarkable correlation between hypocalcemia and maternal factors such as maternal illness (For example, Diabetes) and neonatal factors such as perinatal complications and mode of feeding. On the other hand, there was no statistical association between serum calcium levels and sex, residence, mode of delivery.

Limitations of the study:

Authors could not afford the cost of vitamin D calcium axis investigations (parathyroid hormone, vitamin D, phosphorus, and magnesium) as it affects neonatal serum calcium levels. Maternal serum calcium and vitamin D levels were not assessed in this study also, due to financial constraints. All the factors associated with hypocalcemia could not be presented. Further studies are needed to assess these factors.

Conclusion

The current study concluded that Neonatal hypocalcemia is widely prevalent in Sri Guru Ram Das Institute Of Medical Sciences and Research, Amritsar especially early-onset with significant association with neonatal jaundice on phototherapy, no maternal calcium or neonatal vitamin D supplementation. Also there was a high prevalence of hypovitaminosis D among urban inhabitant, and

preterm neonates. It recommended the implementation of preventative strategies as an effective public health measure for maternal and neonatal health care programs through: 1) calcium and vitamin D supplementation to mothers during pregnancy and lactation; 2) oral vitamin D supplementation to neonates since birth; 3) Routine investigations of serum calcium as a part of maternal and child health care program for early detection and management of neonatal hypocalcemia; 4) Health education program to raise awareness about healthy and dietary lifestyles.

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