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A Study of Neonatal Vitamin D Levels and its Association with Maternal Factors

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Abstract: ***Background: This study was done to find the relation of vitamin D status in neonates and their mothers and its association with maternal factors. Objective: The aim of the study was to determine the association of vitamin D status of term neonates and maternal factors. Participants: 140 term neonates and their mothers between October 2015 to September 2016. Procedure: Term neonates vitamin D levels compared with their mother's vitamin D levels and its association with maternal factors. Main outcome measure: 1) Comparison of maternal and neonatal vitamin D levels. 2) Association of neonatal vitamin D levels with maternal factors. Results: 1) Maternal vitamin D levels were lower in winter and autumn. Neonatal vitamin D level was lower in all seasons. 2) When sun protective clothes were used by mothers their vitamin D levels were lower. (p-value<0.001). 3) More number of babies also had inadequate and severe vitamin D deficiency where the duration of mother's exposure to sunlight was less.(p value <0.05.). Conclusion: Neonatal vitamin D levels affected by seasonal variation, sun protecting clothing by mothers and duration of mother's exposure to sunlight.***

Keywords: Vitamin D, Term neonates, maternal factors

1. Introduction

Vitamin D is a fat-soluble steroid hormone that contributes to the maintenance of normalcalcium homeostasis and skeletal mineralization.[1] Vitamin D also has immune modulatory effects on immune function. [2] It has been 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. [2,3] Newborns are more susceptible to infections as both innate and adaptive immune systems are not entirely developed.[4]The relationship between vitamin D deficiency and sepsis has been demonstrated in children and newborns.[5-8]Low cord blood (25-OHD) levels in healthynewborns were found to be associated with increased risk of developing respiratory syncytialvirus infections during infancy.[9]Studies have also shown increased incidence of neonatal sepsis in babies with vitamin D deficiency.[4,10]More recent studies [4] suggest the role of appropriate vitamin D supplementation that leads tohigher maternal 25-OHD levels during pregnancy which would subsequently have beneficialeffects in prevention of both maternal and neonatal morbidities.Hence present study was planned in term neonates admitted in Neonatal Intensive CareUnit of tertiary care hospital and their mothers to assess vitamin D levels in them. The objective of this observational study was to determine thepossible role of influence of maternal factors on neonatal plasma vitamin D levels.

2. Literature Survey

Robert J. Schroth et al[11] conclCded that maternal prenatal 25OHD levels may have an influence on the primary dentition and the development of early childhood caries. Ian Marshall et al[12] found evidence that: (1) During pregnancy vitamin D participates in fetal skeletal mineralization and growth, (2) Neonatal vitamin D levels are dependent on the maternal vitamin D status at delivery. Study found that inconsistency in the recognition of sufficient levels of vitamin D in mothers and their infants affects the identification of adequate doses for vitamin D supplementation during pregnancy, lactation and infancy. Hollis BW et al[13] Studies suggested that higher vitamin D supplementation might be required for prevention of hypo vitaminosis D and achievement of normal circulating 25-OHD levels (40 to 60ngml−1) during pregnancy, which would also decrease the incidence of co-morbidities of pregnancy.[13,14]M Cetinkaya et al[4]study that reports significantly lower maternal and neonatal 25-OHDlevels in term infants with EOS compared with those who did not have sepsis. Neonatal 25-OHDlevels were well correlated with maternal levels. The 25-OHD levels were found to be associated with seasonality, regular intake of vitamin D, socioeconomic status and dress preference of themother. Both maternal and neonatal 25- OHD levels were significantly higher in summer.Similarly, both maternal and neonatal 25- OHD levels were significantly higher with regular vitamin D supplementation during pregnancy & there is no association between the presence of vitamin D deficiency and culture proven EOS in this study. These data suggest the importance of adequate vitamin D supplementation during pregnancy may be helpful to prevent EOS in term neonates.

3. Methodology

Setting:
This prospective study was performed in tertiary care hospital referral center in the NICU on term neonates and their mothers who were admitted to Neonatal Care Unit of tertiary care hospital between October 2015 and September 2016.

***Type of study*:** Observational study

Subjects: Both intramural & extramural babies were included.

1) Inclusion criteria:
Term neonates who are admitted in NICU and their mothers (intramural and extramural) in our hospital.

2) Exclusion criteria
- Refusal of parental consent
- Lack of laboratory data
- Those who are preterms

Sample size
Total- 140
Calculate by (1-α) error with 95% confidence level with power 80%

Study period: 1 year

Consent: An informed consent was obtained from the parents/guardians prior to enrolment. All data was recorded in predesigned structured proforma.

Ethics: The study was approved by institutional Ethics Committee.

Sample collection
Vitamin D levels: Blood was drawn at the time of admission of both groups (neonates and their mothers) for measurement of 25-hydroxyvitamin D (25-OHD) levels. Analyses of 25-OHD levels in both groups was performed. Other explanatory variables, which can be the potential cofounders was included in the study and considered for analysis. Plasma of both maternal & neonatal blood samples were separated and stored at -80℃.levels of 25-OHD were determined using ECLIA 411 Model with chemileuminence system attached with ultraviolet detector at biochemistry laboratory of our tertiary care hospital.

Statistical analysis
Data were analyzed using SPSS software. (SPSS, version 20.0) Descriptive statistics were given as mean ± standard deviation (mean ± s.d.) for continuous data with normal distribution.

Frequencies and percentages for quantitative data. The differences between groups were evaluated using X2 tests for qualitative data and t-test for independent sample for continuous data with normal distribution. ANOVA & POST HOC test were used to indicate interaction between season and other season group. Values of P<0.05 were considered statistically significant.

4. Result

This study was done between October 2015 to September 2016 in the NICU of referral tertiary care hospital. During this period the total NICU admissions were 1431, from this 140 patients were included in study.There was no significant difference in maternal demographic profile and comorbidities.

1) Comparison of maternal and neonatal 25-hydroxyvitamin D (25-OHD) levels in terms of season at birth

25-OHDlevel (ng ml^{-1})	*Winter*	*Summer*	*Monsoon*	*Spring*
Maternal 25-OHD level (ng ml^{-1}), mean± s.d.	15.22±6.08	20.9±10.44	20.25±9.47	16.6±5.02
Neonatal 25-OHD level (ng ml^{-1}), mean±s.d.	18.19±6.38	22.53±11.05	25.57±8.50	13±5.32

When the effects of season on maternal and neonatal 25-OHD levels were evaluated, maternal vitamin D levels were low in winter and autumn.

Similar pattern was seen in neonatal vitamin D level. Sun protecting clothing in mothers, affects vitamin D levels. More number of mothers had severe deficiency if sun protective clothes were used. (P-value <0.001)Sun protecting clothing in mothers, affects vitamin D levels in baby also. More no. babies had severe deficiency if mother used sun protective clothes. (P- value <0.05.)

Number of hours of exposure, show direct relation with maternal vitamin D levels. Less number of hours exposure lead to more vitamin D deficiency in mothers. Mean vitamin D levels are lower in 2-4 hours as compared to 4-8 hrs. Number of hours of exposure to sunlight by mother also show direct relation with neonatal vitamin D levels .Less number of hours exposure can lead to more vitamin D deficiency in neonates. Mean vitamin D levels are lower in cases in 2-4 hours as compared to 4-8 hours in neonates.

5. Discussion

This observational study showed that maternal and neonatal 25-OHD levels association. These findings are similar to other studies done in newborns .[4,10] Factors affecting maternal Vitamin D levels in our study, were, duration of exposure to sunlight, season and use of sun protective clothes in the mother. We found lower maternal vitamin D levels in monsoon and winter months. Maternal 25-OHD levels correlated with seasonality, regular intake of vitamin D, socioeconomic status and dress preference of the mother in another study.[4] In our study, we found that severity of vitamin D deficiency in mother affects the baby. Cetikanya et al [4] have shown that 85% cases of sepsis group in comparison to 2% in the control group had very low levels of vitamin D. The severity of vitamin D deficiency increased the risk of EOS in these infants. These data indirectly suggest that adequate vitamin D supplementation during pregnancy may be helpful in preventing EOS in term neonates since, vitamin D status of the newborn at birth is primarily dependent on the vitamin D status of the mother during pregnancy. Therefore, it is important to establish optimal amount of vitamin D intake to maintain adequate levels for prevention of maternal and neonatal vitamin D deficiency and subsequent adverse health effects, by further studies.

6. Conclusion

1) When the effects of season (birth season of baby) on maternal and neonatal 25-OHD levels were evaluated, maternal vitamin D levels were low in winter and

autumn. Similar pattern was seen in neonatal vitamin D levels.

2) Sun protecting clothing in mothers affected vitamin D levels in mothers. More number of mothers had severe deficiency if sun protective clothes were used. **(P -value <0.001)**
3) Sun protecting clothing in mothers affected vitamin D levels in babies also. More number of babies had severe deficiency if mother used sun protective clothes. **(P-value <0.05)**
4) Duration of sunlight exposure, showed a direct relation with maternal vitamin D levels. Lessduration of exposure led to more vitamin D deficiency in mothers. Mean vitamin D levels were lower in 2-4 hours as compared to 4-8 hours ofexposure.
5) Duration of sunlight exposure to mother also showed direct relation with neonatal vitamin D levels. Less duration of exposure led to more vitamin D deficiency in neonates. Mean neonatal vitamin D levels were lower in 2-4 hours exposure as compared to 4-8 hours of exposure. Number of babies having inadequate and severe vitamin D deficient levels were higherwhere the duration of sunlight exposure mother was less.

7. Future Research

1) Whether intervention in mother with vitamin D deficiency (dose, duration , preparation) can affect prevalence of vitamin D deficiency in babies.
2) Studies to evaluate utility of cord blood vitamin D level for knowing vitamin D status of babies to ensure timely supplementation if indicated.

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