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Neonatal Vitamin D Status and Risk of Neonatal Sepsis.

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Abstract:
Objective: *To evaluate the maternal and neonatal 25 hydroxyvitamin D (25(OH)D) level and effect of 25 hydroxyvitamin D level on development of neonatal sepsis.*
Method: *This prospective study was performed in NICU, RIMS RANCHI, between January 2017 – December 2017. 51 term neonates with sepsis group and 56 term neonates with control group were included in this study. Blood samples for whole blood count, CRP, Calcium, Phosphorus, Alkaline phosphatase, cultures, 25 hydroxyvitamin D were obtained from all neonates.*
Results: *Mean vitamin D level for neonates and their mother were found to be 12.5 ± 8.4 ng/ml and 13 ± 8.7 ng/ml respectively. There was a significant correlation between maternal and neonatal 25 hydroxyvitamin D level (r = 0.72, p,0.01). The number of neonates with vitamin D deficiency was significantly higher in sepsis group (n = 31, 60.8%) than in control group (n = 30, 53.6%), corresponding to significant lower level of vitamin D in sepsis group (11± 5.5 ng/ml vs. 13.8 ± 10.6 ng/ml; p = 0.012) as in control group. Similarly maternal vitamin D level was significantly lower in sepsis group than in control group (10.8± 5.6 ng/ml vs. 14.9 ± 10 ng/ml, p =0.001)*
Conclusion: *This study suggests that there may be association between vitamin D deficiency and neonatal sepsis.*
Keywords: *Vitamin D, Sepsis, Neonate.*

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I. Introduction

Vitamin D is lipid soluble prohormone produced in human skin exposed to ultraviolet radiation. It plays an important role in calcium and phosphorus homeostasis. Vitamin D is linked to disorders of bone mineralisation, there is some evidence suggesting that vitamin D plays important role in immune function. Vitamin D receptors are widely expressed in epithelial tissues and cells of immune system. 1, 25 dihydroxyvitamin D is active form of vitamin D, acts as immune modulator to stimulate innate immune system. In some studies significant association between vitamin D deficiency and sepsis is seen.

Neonatal sepsis refers to bacteraemia and associated clinical signs and symptoms occurring in first month of life. It is among leading cause of morbidity and mortality in neonates.

In this study, we aim to evaluate the maternal and neonatal vitamin D status and effect of vitamin D level on development of neonatal sepsis.

II. Methods:

This prospective study was performed in NICU, RIMS RANCHI, between January 2017 – December 2017.
Exclusion criteria for neonates:

1. Presence of congenital malformation or disease.
2. Metabolic disease.
3. Small for gestation age.
4. Prematurity.
5. Twin neonates.
6. Use of antibiotic at admission.
7. Age above 28 days.

Exclusion criteria for mothers:

1. Malnutrition.
2. Metabolic or chronic disease.
3. Twin pregnancy.
4. Use of medications.
5. Chorioamnionitis.
6. Premature rupture of membrane.

7. Age less than 20 years and more than 40 years.

Study group comprised term neonates with laboratory and clinical findings of sepsis which was further categorised as early onset sepsis EOS (within≤ 3 days of birth) or late onset sepsis LOS (after 3 days of birth). Blood samples for whole blood count, CRP, cultures were obtained from all neonates with suspected sepsis at admission and the neonates were divided into 4 groups.
GROUP 1 – Highly probable sepsis.
GROUP 2 – Probable sepsis.
GROUP 3 – Possible sepsis.
GROUP 4 – No sepsis.

The neonates in group 1, 2, 3 were called as sepsis group and group 4 as control group. Demographic features of mother like age, socioeconomic status, education, factor associated with their vitamin D status like sun exposure, vitamin D intake, style of clothing, season were recorded. Limited exposure to sunlight was considered o spend less than 30 minutes outside. Blood samples for calcium (Ca), phosphorus (P), alkaline phosphatase (ALP), 25 hydroxyvitamin D (25 OH D) were obtained from all participants.

III. Results:

This study included 107 term neonates (41 females and 66 males) of which 51 (47.7%) were in sepsis group and 56 (52.3%) were in control group. The number of male neonates was significantly higher in sepsis group ($p = 0.01$). The neonates in sepsis group had significantly higher CRP level ($p =0.001$) and significantly lower platelet count ($p = 0.04$).

The mother of the neonates in 2 groups did not differ significantly with regard to age, socioeconomic status, daily sun exposure and style of clothing. The number of mother who took vitamin D during pregnancy was higher in control group than in sepsis group ($p = 0.02$). Based on seasonal distribution of deliveries, the number of winter deliveries was significantly higher in sepsis group ($p =0.016$).

The mean 25 hydroxyvitamin D level was 12.5 ± 8.4 ng/ml in neonates and 13 ± 8.7 ng/ml in mother with significant correlation between maternal and neonatal 25 hydroxyvitamin D level ($r = 0.72$, $p< 0.01$). Vitamin D deficiency was detected in 61 neonates (57%) and 55 mothers (51.4%). The number of neonates with vitamin D deficiency was significantly higher in sepsis group (n= 31, 60.8%) than in control group (n = 30, 53.6%) corresponding to significant lower level of vitamin D in sepsis group (11±5.5 ng/ml vs 13.8 ±10.6 ng/ml in control group with p value = 0.012. Similarly maternal vitamin D was significantly lower in sepsis group than in control group (10.8 ± 5.6 ng/ml vs 14.9 ± 10 ng/ ml, $p =0.001$)

Other laboratory parameters of maternal and neonatal calcium, phosphorus, alkaline phosphatase were similar in both groups.

Of 51 neonates with sepsis, 39 (76.5%) neonates were having early onset sepsis EOS and 12 (23.5%) were having late onset sepsis LOS. The neonates with EOS had lower vitamin D level (10.4±5.7 ng/ml) than those with LOS (12.8±4.3 ng/ml) but difference was not statically significant.

Mean vitamin D level of neonates with early onset sepsis significantly differed from that of control group ($p = 0.02$) which was not the case for neonates with late onset sepsis ($p = 0.7$).

IV. Discussion

Demonstration of vitamin D receptors in immune system cells other than extraskeletal system draws attention to effect of vitamin D on immune system, especially with sepsis. Vitamin D receptors are found in CD4, CD8 Tcells, B cells, macrophages, neutrophils and dendritic cells that play a role in innate and adaptive immune responses.

There are studies which shows that vitamin D has suppressive effect on proliferation and antibody production of T and B cells as well as immune response of monocytes and dendritic cells.

Vitamin D has been found to activate Toll like receptors (TLR) which in turn induce production of peptides like cathelicidin and beta – defensin which have antimicrobial effect on bacteria, viruses, fungi. Vitamin D has inhibitory effect on staphylococcus aureus, Streptococcus pyognes, Klebsiella pneumonia, E. coli, but its effect on fungus and parasites is unclear.

Madden et al assessed admission vitamin D level in critically ill children and found vitamin D deficiency in 40% of children. However Ponnarmeni et al reported no association between low vitamin D level and severity of illness.

Cetinhaya et al reported mean vitamin D level of 8.6 ng/ml in term neonates with early onset sepsis (EOS) as compared to 19 ng/ml in control group.

Gamal et al found low vitamin D level in neonates with EOS as compared with control group.

Among demographic features male gender was predominant with sepsis. It is well male sex is risk factor for sepsis due to suppressive effect of androgen on immune system. The neonates in sepsis group has high CRP and low platelet count. Mother are the main source of vitamin D in neonates, and it's deficiency not only effects the mother but also their babies.

In this study vitamin D deficiency was seen in 51.4% cases and in control group there are higher rates of vitamin D intake and spring summer deliveries which corresponded well to significant lower maternal and vitamin D level in sepsis group.

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