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Association between Vitamin D Level at Birth and Respiratory Morbidities Among Preterm Neonates

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Abstract

Background: Prematurity and its related challenges are one of the major problems for neonatal medicine. Many studies showed relation between prematurity and vitamin D (Serum 25OHD).

Aim of Study: This researchwas conducted to assess the prevalence of Serum 25OHD deficiency among preterm infants at birth and to ascertain if lung disease morbidities are connected to serum 25OHD status at birth.

Patients and Methods: This investigation was prospective cross-sectional research which was carried out at the Neonatal Intensive care unit (NICU) in Kasr Al-Ainy University Hospitals, between September 2021 and March 2022, on 80 preterm neonates with a gestation age <34 weeks assessed by the last menstrual cycle or ultrasound who admitted in NICU within 24 hours of life. Serum 25 OHD was assayed by ELISA.

Results: Serum 25OHD wasdeficient (<20ng/mL) in 58 cases (63.8%) with serum 25OHD Level, mean ± SD was 6.54±3.2, it's insufficient (20-30ng/ml) in 7 cases (8.8%) with serum 25OHD Level mean ± SD was 23.03±1.58 and it's sufficient (>30ng/ml) in 15 cases (18.8%) with serum 25OHDLevel, mean ± SD was 35.08±2.05.

Conclusion: Low 25(OH)D levels are much more common in preterm infants from Egypt. Lack of serum 25OHD is a distinct risk factor for the development of RDS in preterm newborns.

Key Words: *Vitamin D (Serum 25OHD) – Bronchopulmonary dysplasia – RDS – Prematurity.*

Introduction

BETWEEN 34 and 37 weeks, the typical human fetus experiences the maturation of various organ systems, and by the conclusion of this time, the fetus is sufficiently developed. The lungs are one of the primary organs that are severely impacted by preterm delivery **[1]**.

In the majority of nations, preterm birth rates are growing. Preterm birth rates have been trending upward, with the worldwide incidence increasing from 9.8% in 2000 to 10.6% in 2014 **[2]**.

On one hand, the idea that vitamin D aids in lung development, cell proliferation, and differentiation has been taken into consideration.On the other hand, animal and laboratory research have shown that vitamin D has an impact on the alveolar type II cell, fibroblast proliferation, surfactant production, and alevorization **[3]**. Moreover, investigations on humans have shown how vitamin D affects the creation of lung surfactant **[4]**. Hence, it is suggested that a lack of vitamin D may serve as a risk factor for lung illnesses in premature newborns **[5]**.

Several investigations have shown that compared to more developed newborns, preterm infants born before 32 weeks (and particularly those born before 28 weeks) are more likely to have vitamin D insufficiency **[6]**. Despite current dietary efforts, 10% to 20% of newborns with exceptionally low birth weight exhibit radiographic signs of rickets with metaphyseal abnormalities **[7]**.

The purpose of this investigation was to assess the frequency of vitamin D insufficiency in premature babies at birth and to ascertain if lung disease morbidities are connected to vitamin D status at birth.

Patients and Methods

The Neonatal Intensive Care Unit (NICU) of Kasr Al-Ainy Hospitals, Cairo University, performed this prospective cross-sectional analytic investigation on 80 preterm neonates with a gestation age <34 weeks who were identified by the last menstrual cycle or ultrasound and both sexes and were hospitalized to the NICU within 24 hours following birth, between September 2021 and March 2022. The study was carried out after ap-

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proval by the Research Ethics Committee of Cairo University Hospital (MS-299-2021) and in accordance with the Declaration of Helsinki. A written informed consent was obtained from all the parents of participants enrolled in the present study.

Neonates who hadmajor congenital anomalies or malformation, chromosomal disorder, metabolic diseases, congenital rickets, renal or hepatic problems, who had suspected of inborn error of metabolism, whose mothers had parathyroid hormones problems, calcium metabolism problems, and renal or hepatic problems were excluded.

All parents of the participants were subjected to complete maternal, perinatal, obstetric history (history of premature rupture of membrane (PROM) signs of fetal distress and method of delivery). If the mother had any associated medical problems during pregnancy such as oligohydramnios, hypertension, diabetes mellitus, anemia, epilepsy, fever, any rash, medicine consumption during pregnancy other than iron and folic acid supplements, and maternal vitamin D consumption during pregnancy had all been ruled out.

Complete neonatal history, demographic and clinical variables were taken includingname, age, sex, consanguinity, gestational age (weeks). Also, resuscitation data were taken includingrequiring for resuscitation, Apgar score at first and fifth minute, cause of admission and diagnosis, full general and systemic examination, respiratory support and Laboratory sheet, length of hospital stay, birth weight (kg), weight at presentation, weight loss if happened, anthropometric measures at birth, vital signs at birth, cause of admission, duration of NICU staying, route of feeding, breast/bottle feeding data and the type of milk, growth assessment of the neonate, current medication, complete clinical examination, onset of jaundice by history if happened, level of bilirubin at presentation, duration of phototherapy in case it had happened, requirement of blood exchange was recorded and symptoms suggestive of UTI or infections including non-specific symptoms, such as fever, vomiting, hypothermia, poor suckling, urine retention, irritability or lethargy, anuria, and irregularities in the urine stream or urine flow.

Complete general physical evaluationwas performed on each neonate included in the study including vital signs,blood pressure, oxygen saturation. General appearance of the neonate was assessed according to exercise, posture, muscular tone, degree of awareness, or if a baby is awake and alert. Measurements were done to assess the length and circumference of the skull, and documenting them together with the weight. Blood culture, chest X-ray, echocardiography and cranial & Abdominal U/S were done. Diagnosis of RDS was graded according to Downes scores.

Laboratory analysis was carried out in the Chemical Pathology Department, Molecular Unit, Cairo University Investigations includingserum total/corrected Calcium, Phosphate, magnesium, complete blood count (CBC) and C-reactive protein (CRP).

Complications related to prematurity were evaluated such as bronchopulmonary dysplasia (BPD) **[8]**, pulmonary bleeding **[9]**, Apnea **[10]**, Necrotizing Enterocolitis (NEC) **[11]**.

Determination of 25(OH)D levels: Within 24 hours following delivery, venous blood samples were taken from a peripheral vein. A non-anticoagulant vacutainer was utilized to collect 2mL of whole blood, and the separated serum was kept at –20º before being utilized to measure the 25(OH)D content utilizing the ELISA method by Bioassay Technology Lab (Code: EA0057Hu), China. Based on advice from the US Endocrine Society, serum 25OHD values are classified into three groups as follows: Group 1 (<20ng/mL): Serum 25OHD deficient, group 2 (20-30ng/mL): Serum 25OHD insufficient and group 3 (>30ng /mL): Serum 25OHD sufficient **[12]**.

Statistical analysis: The data was analyzed utilizing IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA), Microsoft Excel 2016, and other social science statistical applications. Statistical significance was determined to be a p-value of <0.05. Continuous normally distributed factors were displayed as mean ± SD with a 95% confidence interval, while nonnormally distributed factors were summed up as median with 25 and 75 percentiles and utilizing the frequencies and percentage for categorical data. The Mann-Whitney U test was performed for nonnormal variables, while the student's t-test was utilized to compare the means of normally distributed data across groups. Fisher's exact test or the x^2 test was employed to ascertain how categorical variables were distributed across groups.

Results

Table (1) reveals the classification of the studied group according to the serum level of 25OHD. Serum 25OHD is compared to Low birth weight (LBW) which is defined as a birth weight of less than 2500g as per the World Health Organization

(WHO). Low birth weight is further categorized into very low birth weight (VLBW, <1500g) and extremely low birth weight (ELBW, <1000g) (Table 2). There was no statically significant difference between the mean of demographic data of the study population and serum 25OHD level of the 3 groups of our cases with *p*-value (>0.05), except for Gestational age with *p*-value 0.013. The World Health Organization (WHO) defines preterm birth as any birth before 37 completed weeks of gestation. This is further subdivided on the basis of gestational age (GA): Extremely preterm (<28 weeks); very preterm (28-<32 weeks); moderate or late preterm (32-<37 completed weeks of gestation). (Table 2). Also, there was no statically significant difference-between the mean APGAR score of the study group and serum 25OHD Level of the 3 Groups of the study cases (Table 3).

Table (1): Classification of the studied group according to serum 25OHD.

	Deficient <20 (n=58; 90.9%)	Insufficient 20-30 (n=7; 8.8%)	Sufficient >30 (n=15; 18.8%)	All (n=80)
Serum 25OHD Level, mean ± SD (ng/mL)	6.54±3.2	23.03±1.58	35.08±2.05	13.3±11.8

Table (2): Relationship between the research population's demographics and the concentration of serum 25OHD.

Neonatal	Deficient <20ng/ml (n=58; 90.9%)		Insufficient 20-30ng/ml (n=7; 8.8%)		Sufficient >30ng/ml (n=15; 18.8%)		All (n=80)		*p*-value	X^2
	N	%	N	%	N	%	N	%		
Sex:										
- Male	29	50.0	3	42.9	8	53.3	40	50.0	0.901	0.210
- Female	29	50.0	4	57.1	7	46.7	40	50.0		
Birth Weight in Kg:										
- Extremely Low Birth Weight (ELBW)	12	20.7	2	28.6	1	6.7	15	18.8	0.767	3.324
- Very Low Birth Weight (VLBW)	22	37.9	2	28.6	6	40.0	30	37.5		
- Low Birth Weight (LBW)	23	39.7	3	42.9	7	46.7	33	41.3		
- More than 2.5Kg	1	1.7	0	0.0	1	6.7	2	2.5		
Gestational Age in weeks:										
- Extremely preterm	8	13.8	4	47.1	0	0.0	12	15.0	0.013	12.62
- Very preterm	40	69.0	2	28.6	12	80.0	54	67.5		
- Moderate preterm	10	17.2	1	14.3	3	20.0	14	17.5		

Table (3): Relation between the mean APGAR score of the study group and Vitamin D (Serum 25OHD) Level.

	Deficient <20ng/ml (n=58; 90.9%)	Insufficient 20-30ng/ml (n=7; 8.8%)	Sufficient >30ng/ml (n=15; 18.8%)	All (n=80)	*p*-value	X^2
APGAR, mean ± SD:						F-value
1'	3.66±1.9	4±1.91	4.07±1.59	3.76±1.84	0.707	0.348
5'	6.29±1.41	6.57±2.07	6.07±1.63	6.28±1.5	0.769	0.264
10'	8.16±1.35	8±1.15	8.14±0.94	8.14±1.24	0.954	0.047

The cause of admission in preterm infants in link to vitamin D level status is shown in Table (4), which reveals that there was a statically significant difference between 3 Groups of RDS, congenitalpneumonia, transient tachypnea of newborn and LBW with *p*-value of 0.001, While there was no statically significant difference between 3 groups of Bradycardia, and Apnea (*p*-value >0.05).

Table (4): Relation between the cause of admission in preterm infants and vitamin D level status.

Cause of admission	Deficient <20ng/ml (n=60; 90.9%)		Insufficient 20-30ng/ml (n=7; 8.8%)		Sufficient >30ng/ml (n=15; 18.8%)		All (n=80)		*p*-value	X^2
	N	%	N	%	N	%	N	%		
RDS:										
No	5	8.6	5	71.4	15	100.0	25	31.3	<0.001	52.084
Yes	53	91.4	2	28.6	0	0.0	55	68.8		
Cong. Pneumonia:										
No	53	91.4	2	28.6	7	46.7	62	77.5	<0.001	24.196
Yes	5	8.6	5	71.4	8	53.3	18	22.5		
TTN:										
No	58	100.0	7	100.0	11	73.3	76	95.0	<0.001	18.246
Yes	0	0.0	0	0.0	4	26.7	4	5.0		
LBW:										
No	57	98.3	7	100.0	11	73.3	75	93.8	0.001	13.165
Yes	1	1.7	0	0.0	4	26.7	5	6.3		
Bradycardia:										
No	55	94.8	7	100.0	15	100.0	77	96.3	0.554	1.182
Yes	3	5.2	0	0.0	0	0.0	3	3.8		
Apnea:										
No	56	96.6	7	100.0	15	100.0	78	97.5	0.678	0.778
Yes	2	3.4	0	0.0	0	0.0	2	2.5		

Regarding the association between pulmonary diseases morbidity and vitamin D level status, there was a statically significant difference in 3 Groups of RDS (p<0.001), while there was no statically significant difference in any of the following conditions: BPD, pulmonary hemorrhage, and apnea (p=0.446, p=0.146, and p=0.181; respectively).

Table (5): Relation between pulmonary diseases morbidity and vitamin D level status of the study group.

	Deficient <20ng/ml (n=60; 90.9%)		Insufficient 20-30ng/ml (n=7; 8.8%)		Sufficient >30ng/ml (n=15; 18.8%)		All (n=80)		*p*-value	X^2
	N	%	N	%	N	%	N	%		
RDS:										
No	5	8.6	5	71.4	15	100.0	25	31.3	<0.001	52.084
Yes	53	91.4	2	28.6	0	0.0	55	68.8		
BPD:										
No	53	91.4	6	85.7	12	80.0	71	88.8	0.446	1.616
Yes	5	8.6	1	14.3	3	20.0	9	11.3		
Pulmonary Hge.:										
No	49	84.5	7	100.0	15	100.0	71	88.8	0.146	3.847
Yes	9	15.5	0	0.0	0	0.0	9	11.3		
Apnea:										
No	44	75.9	3	42.9	11	73.3	58	72.5	0.181	3.419
Yes	14	24.1	4	57.1	4	26.7	22	27.5		

The connection of vitamin D level status with the clinical outcomes of preterm infants in the cases 3 groups is demonstrated in Table (6), there wasstatically significant difference in the rate of pneumothorax (22 [37.9%] vs. 0 [0.0%] vs. 1 [6.7%] in groups 1-3, p=0.012), surfactant, and death before discharge (p=0.001, and p=0.022; respectively).

Table (6): Relation between vitamin D level status and clinical outcomes of the study group.

	Deficient <20ng/ml (n=60; 90.9%)		Insufficient 20-30ng/ml (n=7; 8.8%)		Sufficient >30ng/ml (n=15; 18.8%)		All (n=80)		*p*-value	X^2
	N	%	N	%	N	%	N	%		
Sepsis:										
No	26	44.8	1	14.3	6	40.0	33	41.3	0.299	2.416
Yes	32	55.2	6	85.7	9	60.0	47	58.8		
Intraventricular hemorrhage (IVH):										
No	18	43.9	4	66.7	7	77.8	29	51.8	0.136	3.988
Yes	23	56.1	2	33.3	2	22.2	27	48.2		
Pneumothorax:										
No	36	62.1	7	100.0	14	93.3	57	71.3	0.012	8.782
Yes	22	37.9	0	0.0	1	6.7	23	28.7		
Persistent Pulmonary Hypertension of the Newborn (PPHN):										
No	9	28.1	1	25.0	1	14.3	11	25.6	0.749	0.579
Yes	23	71.9	3	75.0	6	85.7	32	74.4		
Necrotizing Enterocolitis (NEC):										
No	50	86.2	5	71.4	13	86.7	68	85.0	0.574	1.110
Yes	8	13.8	2	28.6	2	13.3	12	15.0		
Surfactant:										
No	18	31.0	2	28.6	12	80.0	32	40.0	0.001	23.766
Once	32	55.2	4	57.1	2	13.3	38	47.5		
Twice	8	13.8	0	0.0	1	6.7	9	11.3		
3 times	0	0.0	1	14.3	0	0.0	1	1.3		
Outcome:										
Died	33	56.9	2	28.6	3	20.0	38	47.5	0.022	7.608
Discharged	25	43.1	5	71.4	12	80.0	42	52.5		
Total O2 Support Duration, mean ± SD	12.34±9.36		18.14±14.43		11.87±13.69		12.76±10.73		0.382	0.975
Length of hospital stay, mean ± SD	17.74±15.48		30.43±23.34		22.13±18.28		19.68±16.96		0.144	1.990

Multiple regression was run to predict vitamin D deficiency from the enlisted variables in Table (7). Only Gestational Age, premature rupture of membrane (PROM), Total O_2 Support Duration, Apnea, persistent pulmonary hypertension of the newborn (PPHN), Hypothyroidism, Congenital pneumonia, and Apnea statistically significantly predicted vitamin D deficiency, $F(4, 85) = 9.672$, $p<0.005$, $R^2 = 0.986$. All these 3 variables added statistically significant difference to the prediction, $p<.05$.

Table (7): Study variables to predict vitamin D deficiency.

Model	Unstandardized Coefficients		Standardized Coefficients	*p*-value	95.0% Confidence Interval for B	
	B	Std. Error	Beta		Lower Bound	Upper Bound
(Constant)	34.301	20.093		.163	–21.486	90.088
Sex	–5.275	3.760	–.230	.233	–15.713	5.164
Birth Weight in Kg	2.194	2.956	.141	.499	–6.013	10.401
Gestational Age in weeks	19.349	4.640	.917	.014	6.465	32.233
PROM	–16.288	3.615	–.711	.011	–26.325	-6.252
Method of delivery	–2.774	3.127	–.103	.425	–11.457	5.908
Apgar score 1st min	–2.223	1.326	–.303	.169	–5.904	1.458
Apgar score 5th min	–.228	1.617	–.025	.895	–4.716	4.260
Apgar score 10th min	–1.119	1.426	–.107	.477	–5.079	2.841
Total O2 Support Duration	–1.227	.435	–1.296	.048	–2.435	-.020
Length of hospital stay	.817	.315	1.310	.061	–.058	1.692
BPD	–7.648	5.461	–.285	.234	–22.811	7.514
Pulmonary Hge.	–15.981	7.974	–.453	.116	–38.121	6.160
Apnea	11.328	3.477	.476	.031	1.674	20.983
Sepsis	–.190	4.227	–.008	.966	–11.927	11.547
IVH	6.174	2.734	.271	.087	–1.417	13.765
Pneumothorax	–15.482	5.940	–.670	.060	–31.975	1.010
PPHN	12.302	4.097	.493	.040	.926	23.678
NEC	–4.576	4.373	–.171	.354	–16.718	7.566
Total Ca	–13.403	5.449	–.639	.070	–28.533	1.727
Corrected Ca	.788	2.975	.044	.804	–7.470	9.047
PO4	–5.431	2.928	–.223	.137	–13.561	2.700
Mg	5.272	7.685	.157	.530	–16.064	26.608
Surfactant	4.414	2.317	.300	.129	–2.018	10.846
Outcome	–13.611	6.935	–.597	.121	–32.866	5.644
DM	–5.036	5.719	–.126	.428	–20.914	10.841
HTN	14.634	11.815	.303	.283	–18.171	47.438
Hypothyroidism	–21.122	7.295	–.437	.044	–41.376	-.868
Congenital Pneumonia	13.631	4.057	.582	.028	2.367	24.894
Apnea2	–35.372	8.577	–.525	.015	–59.186	-11.558

Discussion

The severity of vitamin D insufficiency has been highlighted by numerous reports from around the world, making it a problem of global public health. Even developed and sunny nations have a high prevalence of the condition **[13]**. Vitamin D plays a crucial "non-classic" role in the body's immune system in addition to its well-known classic role in the maintenance of bone mineral density. It does this via controlling the innate and adaptive immune systems, as well as the inflammatory cascade and the generation of essential endogenous antimicrobial peptides like cathelicidin **[14]**.

The primary cause of death in premature infants is respiratory distress syndrome (RDS), which is brought on by a lack of surfactants and an immature lung anatomical development **[15]**. The most prevalent long-term condition affecting very preterm neonates that survive is bronchopulmonary dysplasia (BPD), which affects 20% of preterm newborns and up to 60% of very preterm infants born before 26 complete weeks of pregnancy [**16**].

The current prospective cross-sectional analytic study, which was conducted at the NICU in Kasr-Alainy University Hospitals, between September 2022 and March 2022, on Preterm neonates with a gestation age <34 weeks assessed by the last menstrual cycle or ultrasound who admitted in NICU within 24 hours of life. The goals of this research are to ascertain the incidence of vitamin D insufficiency in preterm babies at birth and the connection between pulmonary illness morbidities and vitamin D status at birth. The present study included 80 Preterm neonates with a gestation age <34 weeks. The following were administered to each patient who participated in the study: complete history taking, maternal and perinatal history, Resuscitation Data, physical examination, Chest X-ray, total serum 25(OH)D value (Vitamin D was measured by HPLC which can detect both levels of vitamin D2 and D3 separately), Diagnosis of RDS (respiratory discomfort seen in conjunction with a chest X-ray), The National Heart, Lung, and Blood Institute [NHLBI] classified respiratory distress according to Downes scores, and BPD was

diagnosed if there was a prolonged need for supplemental oxygen in premature infants after 28 days of age or after 36 weeks postmenstrual age and no other conditions requiring oxygen, such as pneumonia or congenital heart disease.

The present research revealed that the mean ± SD Vitamin D value of the study cases was 13.3±11.8. We found that Its Deficient (<20nmol/L) in 63.8% with Vitamin D Level, mean ± SD was 6.54±3.2, Its Insufficient (20-30ng/ml) in 8.8% with Vitamin D Level mean ± SD was 23.03±1.58 and Its Sufficient (>30ng/ml) in 18.8% with Vitamin D Level, mean ± SD was 35.08±2.05. Our results revealed that its deficient in most of our cases which is in line with Al_Beltagi et al. **[17]** as theyrevealed that 45% of their children had concentrations of 25(OH)D <30ng/ml, and 18% had values of 25(OH)D under 20ng/ml at delivery. Just 7% of the preterm newborns in their research, whether they had RDS or not, had normal 25(OH)D values.Another study by Onwuneme et al. **[18]** found that 92% of newborns had 25OHD levels below 50nmol/L at delivery, while 64% had levels below 30nmol/L. Also a study by Zhang et al. **[19]** found that in their research, 25.8% of newborns had insufficient vitamin D, while 33.3% of infants had vitamin D inadequacy and 40.9% of infants had severe vitamin D inadequacy.

We found that there was no statically significant differene between the mean of demographic data of the study population and Vitamin D (Serum 25OHD) Level of the 3 Groups of our cases, except for Gestational age in Groups 1-3 of extremely preterm babies, very preterm, and moderate preterm. as lower 25(OH)D value had found in cases with less gestational age. Which agree with finding observed by Boskabadi et al. **[20]**. Revealed that Neonatal vitamin D levels correlated significantly with hospital stay length and gestation ageAlso, a study by Gatera et al. **[21]**. Found that in their investigation, there was no relationship between gestation age and vitamin D values.

Another research carried out in Ireland by Mc Carthy et al. **[22]**. Revealed that not just in pregnancy but also in preterm newborns, where vitamin D insufficiency affected 78% of preterm infants with gestational ages under 32 weeks.

On the other hand, our findings slightly differs from Al_Beltagi et al. **[17]**. As they found there were no statistically substantial variations between the average of demographic factors of their research group and Vitamin D (Serum 25OHD) Levels, including the maternal age, unlike our study, as regard gestation age, sex (male%), method of delivery (CS%), percentage of twin pregnancy, birth weight, birth head circumference, maternal 25(OH)D level, and neonatal 25(OH)D levels before therapy, they had no substantial variations between any of their three investigated subgroups.

Whileour findings are in contrast with research by Boskabadi et al. **[20]**.

Who found that Substantial relationships were found between neonatal vitamin D values and the 1-5 minute APGAR scores. In this study regarding the cause of admission in preterm infants in relation to vitamin D level status we found a statically substantial variations between 3 Groups of RDS, Pneumonia, TTN, and LBW, while there are no statically substantial variations between 3 Groups of Bradycardia, and Apnea. Regarding theconnection between pulmonary diseases morbidity and vitamin D level status, our study found that there is a statically significant difference in 3 Groups of RDS, while there were no statistical substantial variations in any of the following conditions: BPD, pulmonary hemorrhage, and apnea.

Many previous studies found associations between pulmonary diseases morbidity and vitamin D level status as we found. Glasgow et al. **[23]**. The results of an analysis of four participants who got vitamin D treatment with various clinical outcomes revealed that vitamin D helped to reduce problems in preterm infants with RDS Recent research by Al-Beltagi et al. **[17]**. Revealed that the preterm group with RDS had a lower 25(OH)D level than the preterm group without RDS, and their mothers had a lower 25(OH)D level as well. This may suggest that vitamin D deficit or insufficiency has a role in the development of RDS in preterm newborns Our results concur with Ataseven et al. **[24]**. Study who revealed that Preterm infants with severe vitamin D deficit compared to mild-moderate insufficiency had a higher incidence of RDS Furthermore Yu et al. **[25]**.

Revealed that the incidence of RDS in premature newborns may be enhanced by vitamin D insufficiency. They also discovered that human lung development may benefit from an adequate vitamin D content.

Rowisha et al. **[26]** revealed that Vitamin D shortage or inadequacies affected a large proportion of the preterm newborns with RDS studied, with 41.67% of the patients having serum 25-OHD levels at day one below 15ng/ml (indicating vitamin D defect), 25% having serum 25-OHD levels at day one between 15 and 20ng/ml (indicating vita-

min D inadequacy), and 33.3% having serum 25-OHD levels at day one between 20 and 100ng/ml (indicating (normal vitamin D level) The researchers found that newborns with respiratory distress and their mothers had considerably lower blood levels of vitamin D than the control group. Neonates with respiratory distress had median maternal levels of vitamin D that were about 5mg/dl lower than neonates without respiratory distress. These results show that infants with RDS have inadequate maternal vitamin D levels.According to research by Fettah et al. **[27]**.

Among 81 preterm infants who were 32 weeks pregnant, RDS occurred in 94.7% of neonates with vitamin D levels <5ng/ml, 89.5% of those with levels between 10 and 15ng/dl, and 5.4% of those with levels higher than 15ng/ml.

Additionally, research by Nicolaidou et al. **[28]**. showed a substantialconnection between the mother's serum 25-OH vit D level and the fetal umbilical cord. Due to the severe maternal vitamin D insufficiency, the fetus may have vitamin D insufficiency and rickets while still in the womb. Low vitamin D values in the mother cause the placenta to transmit less vitamin D, and low vitamin D values in babies are the result Cord blood 25-OH vit D values were significantly correlated with utilizing vitamin D supplements during pregnancy, according to a prior study by Belderbos et al. **[29]**.

All that previous animal and human investigations provide significant evidence for the presence of associations between pulmonary diseases morbidity and vitamin D level status. Regardingthe connection of vitamin D level and the clinical outcomes, the present study revealed that there were statically significant differences in the rate of pneumothorax, surfactant, and death before discharge. We found that multipleregressions were run to predict vitamin D deficiency and only Gestational Age, PROM, Total O_2 Support Duration, PPHN, Hypothyroidism, Congenital pneumonia, and Apnea statistically significantly predicted vitamin D deficiency.

This is close to Onwuneme et al. **[18]** study, as they found that Infants in the 25OHD <30nmol/L group required a greater oxygen level during resuscitation in the delivery room, with the difference in median O_2 level being substantial. Moreover, during resuscitation in the delivery room, the neonates in the 25OHD <30nmol/L group needed a longer period of intermittent positive pressure ventilation (IPPV) In Boskabadi et al. **[20]** study, the hospital discharge of 56 newborns in the case group and 72 neonates in the control group occurred without any issues, whereas sepsis, pneumothorax, and mortality occurred in the other group of neonates. They discovered that vitamin D's significance in the development of the innate and adaptive immune systems may account for the greater occurrence rate of problems in their case group.

Before coming to a conclusion, it is important to note that this study has some limitations that should not be disregarded when the results are interpreted. The primary one is the absence of a comparison with a group of full-term neonatal infants. The study's small sample size and lack of information on prenatal maternal 25(OH)D levels were additional limitations. Additionally, premature infants are more likely to experience multiple issues at once, which affect the ability to accurately identify patients with respiratory issues. It is necessary to conduct additional research on a larger population of preterm newborns in order to determine the connection between maternal and neonatal vitamin D level and the later onset of pulmonary diseases. Additionally, vitamin D supplementation interventional trials are required. To prevent the onset of pulmonary diseases, particularly RDS, we advise pregnant women to regularly take vitamin D supplements.

Conclusion:

Low 25(OH)D levels are much more common in preterm infants from Egypt. Lack of vitamin D is a distinct risk factor for the development of RDS in preterm newborns.

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الارتباط بين مستوى فيتامين د عند الولادة وأمراض الجهاز التنفسى بين الخدج

الخداج وما يرتبط به من تحديات هى واحدة من المشاكل الرئيسية لطب حديثى الولادة. أظهرت العديد من الدراسات وجود علاقة بين الخداج وفيتامين (د) فى الدم.

تم إجراء هذا البحث لتقييم انتشار نقص OHD٢٥ فى الدم بين الخدج عند الولادة وللتأكد مما إذا كانت أمراض الرئة مرتبطة بمستوى OHD٢٥ عند الولادة.

هذه الدراسة مستقطعة تم إجراؤها فى وحدة العناية المركزة لحديثى الولادة (NICU) فى مستشفيات جامعة قصر العينى، بين سبتمبر ٢٠٢١ ومارس ٢٠٢٢، على الخدج الذين يبلغ عمر حملهم أقل من ٣٤ أسبوعاً تم تقييمه حسب آخر دورة شهرية أو الموجات فوق الصوتية الذين تم قبولهم فى NICU خلال ٢٤ ساعة من الولادة.

كان المصل OHD 25 ناقصاً (<٢٠ نانو مول / لتر) فى ٥٨ حالة (٦٣.٨٪) بمستوى OHD25 بمتوسط ومعيار انحرافى 3.2±6.54، وهو غير كاف (٢٠–٣٠ نانوغرام / مل) فى ٧ حالات (٨.٨٪) مع مصل كان OHD25 بمتوسط ومعيار انحرافى 1.5±23.03 وهو كافٍ (<٣٠ نانو غرام/ مل) فى ١٥ حالة (١٨.٨٪) مع مستوى OHD 25 بمتوسط ومعيار انحرافى 2.05±35.08.

المستويات المنخفضة من D 25 (OH) أكثر شيوعاً عند الخدج من مصر. يعد نقص عامل خطر واضحاً لتطور أمراض الرئة عند الخدج حديثى الولادة.