Study of the Role of 25-dihyroxy Vitamin D Concentration in Critically Ill Neonates

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Abstract:

Vitamin D has a role in innate immunity, including the prevention of respiratory tract infections. Adequate concentrations of vitamin D stimulate genetic expression of antimicrobial peptides in human monocytes, neutrophils and other human cell lines.

Objective:

To assess serum level of vitamin D and to evaluate the role of vitamin D deficiency in critically ill neonates with respiratory distress syndrome (RDS), neonatal sepsis, pneumonia and bronchopulmonary dysplasia.

Methods:

The study included one hundred neonates (full term and preterm) of both sex admitted with Respiratory Distress Syndrome (RDS), neonatal sepsis, pneumonia and bronchopulmonary dysplasia. Additionally, one hundred healthy neonates aged from 0 to 28 days were recruited. A commercial radioimmunoassay was used to measure the serum (25 -OH vitamin D) in both patients and control for assessing vitamin D status.

Sample:

Patients group had highly significant lower gestational age, birth weight, length and head circumference than control group. Patients group were divided into 4 subgroups:

1. Subgroup 1: RDS was 39% of cases.
2. Subgroup 2: neonatal sepsis was 24% of cases.
3. Subgroup 3: pneumonia was 31%
4. Subgroup 4: BPD was 6%.

Results:

The mean of serum (25 -OH vitamin D) of patients group was significantly lower than that of control group which was 10.84± 2.08ng/ ml and 31.87± 3.19 ng/ ml, respectively (P value < 0.01). There was no significant difference between the mean value of serum (25 -OH vitamin D) in the four different subgroups of patients (P value > 0.05). As regard vitamin D status in patients group, 90% had moderate vitamin D deficiency serum (25 -OH vitamin D) was 8- 14 ng/ ml, mild deficiency serum (25

-OH vitamin D) 14- 20 ng/ ml was 7% while 2% had severe vitamin D deficiency serum (25 -OH vitamin D)< 8 ng/ ml) and 1% had no deficiency serum (25 -OH vitamin D)> 20 ng/ ml). There was a significant positive correlation between serum (25 -OH vitamin D) and gestational age and anthropometric measurements in patient group (P < 0.01). In control group, serum 25 OH- vitamin D positively correlated only with birth weight (P value< 0.01). As regard the correlation between serum25 -OH vitamin D and different subgroups of patients, there was only significant negative correlation between serum 25 -OH vitamin D and pneumonic subgroup (P value< 0.05). As regard the outcome of patients, 83% was improved while 17% was died, from the improved cases 84% had moderate vitamin D deficiency (S.25OH- vitamin D 8- 14 ng/ ml). There was no significant difference between improved and died cases as regard grades of vitamin D.

Conclusion:

The mean serum (25 -OH vitamin D) of patients group was significantly lower than that of control group. There was no significant difference between the mean of serum (25 -OH vitamin D) in patients with respiratory distress syndrome (RDS), neonatal sepsis, pneumonia and bronchopulmonary dysplasia. There was highly significant positive correlation between serum (25 -OH vitamin D) and gestational age and anthropometric measurements in patients group, while in control group, serum (25 -OH vitamin D) positively correlated only with birth weight (p value< 0.01). There was significant negative correlation between serum (25 -OH vitamin D) and pneumonia. There was no significant difference between improved and died cases as regard grades of vitamin D.

Keywords:

(25 -OH vitamin D), vitamin D deficiency, respiratory distress syndrome, neonatal sepsis, pneumonia, bronchpulmonary dysplasia.

Introduction:

Vitamin D is a steroid hormone essential for calcium homeostasis and maintenance of bone health (De Luca, 2004). There are also other benefits of vitamin D that have been reported (Grant and Holick, 2005). Autocrine and paracrine effects of vitamin D are becoming increasingly recognized, and may also play a role in critical illness (Pilz et al., 2010).

Vitamin D is produced in the skin through a photolytic reaction of 7- dehydrocholesterol induced by ultraviolet B radiation (290- 315) nm. It also occurs naturally in foods. The metabolite formed in the skin and the vitamin D absorbed in the gut must be hydroxylated in the liver to form 25- hydroxy Vitamin D (25(OH)D) and then hydroxylated in the kidney to form 1, 25- dihydroxyvitamin D (1, 25(OH)2D) (Holick, et al.,1980). After these transformations, vitamin D is a biologically active substance, a hormone that is chemically akin to steroid hormones. The main function of vitamin D in the body is to regulate calcium and phosphorous homeostasis, a process essential for bone mineralization (Holick, 2003). Vitamin D deficiency is known to lead to secondary hyperparathyroidism, which causes rickets in children and osteomalacia and osteoporosis in adults (Compston, 1998).

A study suggests a role for vitamin D in innate immunity, including the prevention of respiratory tract infections (Ginde et al., 2009). Liu et al., 2006 showed that the action of vitamin D was a key link between Toll- like receptor (TLR) activation and antibacterial responses in innate immunity. They showed a dose- dependent up- regulation of one known antimicrobial peptide (cathelicidin) in human monocytes. Clarification of the role of vitamin D in relation to infections, such as acute respiratory tract infections, deserves a high priority (Raiten and Picciano, 2004). Furthermore, vitamin D is known to play a role in the human antimicrobial response (Cannell et al., 2006; Liu et al., 2006) and

pulmonary function (Black and Scragg, 2005).

Jeng et al. (2009) demonstrated that critical illness was associated with lower 25(OH)D levels. Also vitamin D deficiency may increase mortality in ICU patients (Lee et al., 2009).

Vitamin D deficiency has been linked to adverse and more costly outcomes in veterans with Clostridium difficile and methicillin- sensitive Staphylococcus aureus infections (Youssef et al., 2010).

Aim Of The Study:

Assessment of the serum level of vitamin D in critically neonates with RDS, with sepsis, pneumonia and bronchopulmonary dysplasia and determine the impact of vitamin D deficiency on disease severity, prognosis and outcome

Subjects And Methods

This study is a prospective case control study done on one hundred neonates aged from 0 to 28 days of life admitted to the Neonatal Intensive Care Unit (NICU) of Children Hospital Mansoura University, with RDS, neonatal sepsis, pneumonia, broncho pulmonary dysplasia during the period from July 2009 to October 2010. One hundred healthy neonates served as a control group. Signed approval consents were taken from parents. The sample was simple random sample. The study included 2 groups:

1. Patients group: it comprised 100 critically ill (full terms, preterms), The patients group was subclassified later according to clinical diagnosis on admission into 4 subgroups:
    a. Subgroup 1: patients suffering from respiratory distress syndrome.
    b. Subgroup 2: patients suffering from neonatal sepsis.
    c. Subgroup 3: patients suffering from pneumonia.
    d. Subgroup 4: patients suffering from bronchopulmonary dysplasia.
2. Control group: it comprised 100 healthy neonates as reference group.

All cases were subjected to the following:

1. Careful history taking: personal, antenatal, natal and postnatal.
2. Assessment of gestational age using New Ballard Score (Ballard et al., 1991).
3. Determination of birth weight, length and skull circumference.
4. Thorough Clinical Examination.
5. Laboratory Investigations:
    a. Complete blood count (CBC) using coulter counter (T660 Coultronics, France) with total and differential leucocytic count, neutrophil count, hemoglobin, hematocrit, platelets count.
    b. CRP by latex agglutination test (Avitex-CRP test, Omega Diagnostic, Ltd, Scotland, UK).
    c. Blood culture and sensitivity on both aerobic and anaerobic media (from Egyptian Diagnostic Media).
    d. Serum electrolytes (Na, K) using automated synchchron (CX9- ALX).
    e. Blood gas analysis using (blood gas analyzer, Mod995, HB- Trust Medical Company).
    f. Blood glucose level (by glucostrips).
    g. Serum calcium by photometric method using kits purchased from Human Gmb H-65205 Wiesbaden- Germany according to the manufacture's instruction.
    h. Serum phosphorus by photometric method using kits purchased from Human Gmb H-65205 Wiesbaden- Germany according to the manufacture's instruction.
    i. Imaging studies: Chest and abdominal x-ray when needed.
    j. Serum 25 OH- vitamin D level was

measured on admission by using ELISA by 25 -OH vitamin D EIA Kit (EPBE). EU# EP1097132 Austrialisches patent/ Australien.

Sample Collection: From each neonate of the present study, three milliliters of blood were collected on the day of admission. The sample was centrifuged, the serum taken was put in ependrof then stored in -20°c till the time of analysis. The serum collected was used to determine the level of serum 25 OH- vitamin D and serum level of phosphorus. Other investigations were done in the intensive care unit.

6. Determination of severity of vitamin D: Defining vitamin D deficiency by measurement of 25(OH) vitamin D. (Gartner& Greer, 2003)

	ng/ Ml	Nmol/ L
Severe	< 5- 8	< 12.5- 20
Moderate	< 14	< 35
Mild Insufficiency	< 20	< 50

7. Determination of severity of neonatal sepsis: Clinical signs of sepsis were determined and classified according to the clinical sepsis score of Toliner et al. (1982) into mild, moderate and severe using seven clinical groups of signs of sepsis which are:
   a. Apnea, tachypnea, cyanosis, respiratory distress.
   b. Bradycardia, Tachycardia.
   c. Hypotonia, Seizures.
   d. Poor skin colour, sluggish peripheral circulation.
   e. Irritability, lethargy, poor feeding.
   f. Hepatosplenomagly, Abdominal Distension.
   g. Hypothermia, Hyperthermia.

   A score of one is given to for each group of signs so that if the patient has more than one than one sign in the same group, he will be scored one for this group. Clinically, sepsis was classified into mild (score of 3), moderate score of (4- 5) and severe (6- 7).
8. Determination of severity of respiratory distress in cases of pneumonia by Silverman retraction score.

Silverman Retraction Score

Feature	Score 0	Score 1	Score 2
Chest Movement	Equal	Respiratory Lag	Seesaw Respiration
Intercostal Retraction	None	Minimal	Marked
Xiphoid Retraction	None	Minimal	Marked
Nasal Flaring	None	Minimal	Marked
Expiratory Grunting	None	Audible With Stethoscope	Audible

(Awhonn, 2004)

9. Determination of severity of RDS by chest radiographic changes and staging according to (Halliday, 1998).
10. Determination of severity of BPD by Diagnostic criteria and classification of (BPD) severity (Anita and Vineet, 2009).
11. Follow up of patients for one year by:
    a. Chest X- Rays
    b. Anthropometric Measurements

Statistical Methods:

All studied statistical methods were performed using SPSS 12 soft ware package (Statistical Package of Social Science). All numeric variables were expressed as Mean± SD. Comparison of different variables in various groups was done using student (t) test. Analysis of variance (ANOVA) test was applied for comparison of paired observation. Statistical significant was set at $P< 0.05$. The relation between the various numerical parameters was studied by Person correlation coefficient (r) test. Moreover, Chi square test was used to analyze

qualitative variables (SPSS ver 12).

Results:

Table (1): Comparison between patients and control groups as regard gestational age, postnatal age, birth weight, length, head circumference and sex distribution:

		Patient N=100 (Mean±S.D)	Control N=100 (Mean±S.D)	t	P
Gestational Age(Weeks)		33.29 ± 4.28	36.96± 1.95	7.8	0.001**
Postnatal Age (Days)		9.44±10.16	4.19±1.71	12.46	0.001**
Birth Weight (Kg)		1.97 ±0.92	2.83 ±0.41	8.58	0.001**
Length Cm)		42.24 ±5.58	47.60 ±3.48	8.14	0.001**
Head Circumference (Cm)		30.26 ±3.74	33.87 ±2.34	8.17	0.001**
Sex	Male	69 (69%)	38 (38%)	19.3	0.001**
	Female	31 (31%)	62 (62%)		

P value> o.o5= non significant P< 0.05= significant P< 0.01= highly significant

Table (1) shows that patients had highly significant lower gestational age, birth weight, length and head circumference as compared to control group (P< 0.01). while they had significantly higher postnatal age as compared to control group (P< 0.01).

Table (2): Frequency distribution of different diagnoses

Diagnosis	No. Of Patients	%
RDS	39	39%
Neonatal Spesis	24	24%
Pneumonia	31	31%
Bronchopulmonary Dysplasia	6	6%
Total	100	100%

Table (2) shows that 39% of the patient was suffering from RDS, 24% was suffering from neonatal sepsis, 31% had pneumonia while 6% had Broncho pulmonary dysplasia.

Table (3): Comparison between patient and control groups as regard lab. investigations:

		Patients (Mean ± S.D)	Control (Mean ± S.D)	t	p
CBC	HB (gm/ dl)	15.08 ±2.71	15.03± 2.85	0.13	0.89
	WBC(X103/ ul)	15.44± 7.56	10.86±3.11	5.61	0.001*
	Neutrophil (X103/ ul)	8.64 ± 5.9	5.11±2.65	5.52	0.001*
	Platelets (X103/ ul)	216.72 ±120.61	286.89±111.24	0.43	0.001*
Bl. Gas Parameters	Ph	7.38± 0.11	7.38 ± 0.03	0.55	0.58
	Pco^2(mm Hg)	38.18 ±12.69	38.46 ±2.00	0.22	0.83
	Po2 (mm Hg)	63.12 ±31.2	91.30 ±4.2	8.95	0.001*
	Hco3- (mEq/ L)	21.97 ±5.16	23.59 ±1.79	3.00	0.001*
	Base excess (mmol/ L)	- 2.3 ±5.62	0.02 ± 1.5	4.7	0.001*
Serum Electrolytes	Na (mmol/ L)	139.66 ±9.13	142.21 ±5.17	2.43	0.001*
	K (mmol/ L)	4.24 ±0.93	3.95 ± 0.33	2.9	0.001*
	Bl.glucose (mg/ dl)	98.18 ±26.76	76.83 ± 21.17	6.14	0.07
	Ca (mg/ dl)	8.24 ± 1.24	8.29 ±0.48	0.36	0.72
	Phosphorus (mg/ dl)	4.09 ±0.72	4.91 ± 0.68	8.25	0.001*
25 -OH.Vit.D (ng/ ml)		10.84 ± 2.08	31.87 ± 3.19	55.4	0.001*

P value> 0.05= non significant P< 0.05= significant P< 0.01= highly significant

Table (3) shows that patients group had significantly higher WBC and Neutrophils count, serum K and base excess. On the other hand platelets, PO_2, HCO_3, serum Na, serum phosphorus and serum 25 -OH. Vitamin D were significantly lower in patient than control groups. This table also shows that there was no significant difference between patients and control as regard HB, PH, PCO_2 and Bl. glucose

Table (4): Frequency of various vitamin D status among patients

	Cases	%
Severe deficiency< 8 ng/ ml	2	2%
Moderate deficiency 8- 14 ng/ ml	90	90%
Mild deficiency 14- 20 ng/ ml	7	7%
No deficiency> 20 ng/ ml	1	1%
Total	100	100%

Tab.(4) show that nearly most of the studied cases (90%) have moderate vitamin D deficiency while only 2% with severe deficiency.

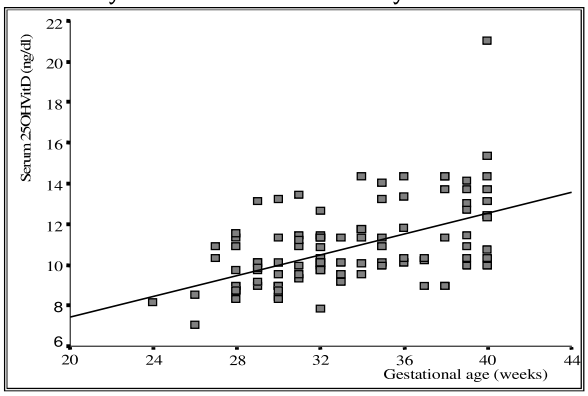

Fig.(1): Correlation between serum 25 OH vitamin D and gestational age in patient group (P< 0.01) , r=0.526

Figure (1) shows that there was highly significant positive correlation between serum 25 OH- vitamin D and gestational age in patient group.

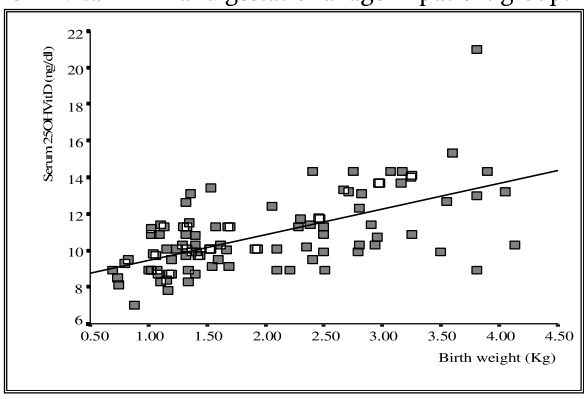

Fig. (2): Correlation between serum 25 OH vitamin D and birth weight in patient group (P< 0.01), r= 0.615

Figure (2) shows that there was highly significant positive correlation between serum 25 OH- vitamin D and birth weight in patient group.

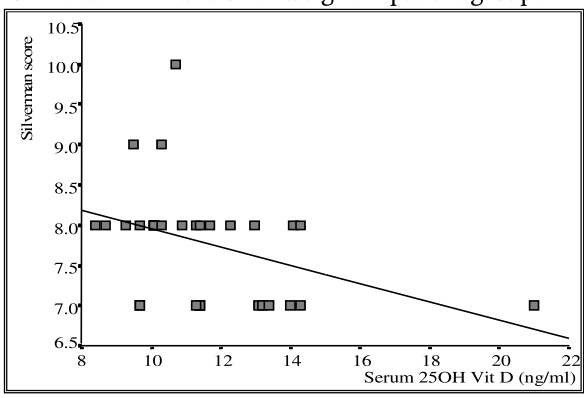

Fig.(3) Correlation between serum 25 OH vitamin D and Silverman score in pneumonic group. (P< 0.05), r=0.386

Figure (3) shows that there was significant negative correlation between serum 25 OH vitamin D and severity of respiratory distress in pneumonic patients.

Table (5): Relation between vitamin D status and the outcome of patients:

Outcome		Grades Of Vit.D				Total	χ^2	P
		normal	Mild Def.	Mod. Def.	Severe Def.			
Improved	N	1	4	76	2	83	4.06	0.25
	% within grades of Vit.D	100%	57%	84%	100%	83%		
Died	N		3	14		17		
	% within grades of Vit.D		42.9%	15.6%		17%		
Total	N	1	7	90	2	100		
	% within grades of Vit.D	100%	100%	100%	100%	100%		

Table (5) shows that 83% of cases improved while 17% died, 84% from the improved cases had moderate vitamin D deficiency. Also, the table shows that there was no significant difference

between improved and died cases as regard vitamin D status (P> 0.05).

Table (6): Comparison between died and improved cases as regard mean serum 25 OH Vit.D, s.calcium and s. phosphorus

Outcome		no	Mean ± S.D	t	p
S. Calcium (Mg/ Dl)	Improved	83	8.36 ±0.94	2.25	0.02*
	Died	17	7.69 ± 2.14		
S. Phosphorus(Mg/ Dl)	Improved	83	4.15 ±0.68	1.76	0.08
	Died	17	3.82 ±0.87		
S. 25 Oh Vit.D (ng/ Ml)	Improved	83	10.79 ± 2.15	0.55	0.58
	Died	17	11.10 ± 1.79		

P value> 0.05= non significant P< 0.05= significant p< 0.01= highly significant.

Table (6) shows that improved cases had significantly higher mean of serum calcium as compared to died cases (P< 0.05) while there was no significant difference as regard mean serum phosphorus and vitamin D.

Discussion:

Vitamin D is a steroid hormone essential for calcium homeostasis and maintenance of bone health (De Luca, 2004). There are also other benefits of vit. D that have been reported (Grant and Holick, 2005). Autocrine and paracrine effects of vit. D are becoming increasingly recognized, and may also play a role in critical illness (Pilz et al., 2010).

From the data of the present study, 39% of the patient suffered from RDS, 24% suffered from neonatal sepsis, 31% had pneumonia while 6% had broncho pulmonary dysplasia. The main finding of the present study was that serum 25 OH- Vit. D concentration in the newborn of the studied groups were significantly lower than those of healthy newborn (10.84± 2.08 ng/ ml and 31.87 ± 3.14 ng/ ml respectively (p< 0.01).

In support to the current study, (Karatekin, et al. 2007) in Turkey reported the same results but the mean serum 25 OH- vit. D of his studied group was 9.12± 8.88 ng/ ml and for the control group was 16.33± 13.4 ng/ ml (P< 0.01). On comparing the result of the study of (Karatekin, et al. 2007) and the current study, it was found that our healthy control group had higher mean of serum 25OH- vit. D compared to Turkian healthy newborn (31.87±3.14) ng/ ml vs (16.33± 13.4) ng/ ml respectively, this may be due to the abundance of sun rays allover the day in Egypt which leads to higher serum 25 OH-vit. D concentration in the Egyptian mothers.

As regard Vit. D status among studied groups and by the cutoff point for serum 25OH- vit. D which was 21.1 ng/ ml, 99% of studied cases had vit. D deficiency, this percentage is high as compared to the study of Karatekin et al. (2007), who had 82% vit. D deficiency, this difference may be due to Karatekin et al. (2007) studied small group (25 cases) with pneumonia only. As regard control group, 80% of them in the study of Karatekin et al. (2007) had vit. D deficiency serum (25 -OH vit. D)< 20 ng/ ml while no cases of vit. D deficiency in the present study.

From the data of the present study, 2% (2/ 100) had severe vit. D deficiency (serum 25OH vit. D< 8 ng/ ml), 90% (90/ 100) had moderate vit. D deficiency (serum 25OH vit. D< 8- 14 ng/ ml), 7% (7/ 100) had mild vit. D deficiency (serum25OH vit. D< 14- 20 ng/ ml).

On the basis of the present study, there was positive correlation between serum 25 -OH vit. D and gestational age, birth weight, length and head circumference in patient group, while in control group serum 25 -OH vit. D positively correlated only with birth weight (P value< 0.01), this coincide with (Wayse et al. 2004), who stated that serum 25 -OH

vit. D increased significantly with age. The correlation between serum 25 -OH vit. D and age in months appeared stronger for control (P< 0.001) than for case children (P=0.05). (Karatekin et al. 2007) found positive correlation between serum 25 -OH vit. D of newborn with serum 25 -OH vit. D of their mother in both study and control group.

The finding from the present study shows that there was negative correlation between serum 25OH vit. D and Silverman retraction score in pneumonia i.e. when pneumonia was severe (as detected by Silverman retraction score= 10), there was low serum 25OH vit. D concentration. In pneumonic group, 100% of cases had Silverman score= 10 with impending respiratory failure and 87.1% had moderate vit. D deficiency.

As regard the outcome of the patients in the present study, 83% of all patient subgroups improved and 17% died. According to vit. D status, improved cases had 1 case (1.2% from the improved cases) with normal vit. D level, 4 cases (4.8%from the improved cases) with mild vit. D deficiency, 76 cases (91.5% from the improved cases) with moderate vit. D deficiency and 2 cases (2.4% from the improved cases) with severe vit. D deficiency. In died cases, 3 cases (17.7%) had mild vit. D deficiency,14 cases (82.3%) had moderate vit. D, no cases had severe vit. D deficiency.

here was no significant difference between improved and died cases as regard grades of vit. D (P> 0.05), this because most of the improved and died cases had moderate vit. D deficiency (84% vs. 82.3% respectively) while other vit. D status was minimal.

As regard mean serum 25 -OH vit. D in improved and died cases, our study found that there was no significant difference between improved and died cases as regard mean serum 25 -OH vit. which was (10.79± 2.15) vs. (11.1± 1.79) ng/ ml respectively (P> 0.05). Our study disagree with the study of (McKinny et al. 2011) who found that 59% survived and 41% died and they found that patients who survived, compared with those who did not, had significantly higher 25 (OH) vit. D levels (26.4± 11.1) vs. (21.6±11.8) ng/ ml respectively, and were significantly less likely to be classified as vit. D deficient. This difference between our study and study of (McKinny et al. 2011) may be due to most of our studied cases (99%) had serum 25 -OH vit. D< 20 ng/ ml and more likely to be classified as vit. D deficient.

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الملخص

دراسة دور ٢٥- داى هيدروكسى فيتامين (د) فى الحالات الحرجة فى الأطفال حديثى الولادة

إن فيتامين (د) ضرورى وهام جدا للمحافظة على نسبة الكالسيوم فى الدم وكذلك دوره فى المهم فى تكوين العظام هذا بالإضافة إلى فوائد أخري. يتكون فيتامين (د) تحت الجلد عن طريق التعرض لأشعة الشمس كما أنه يوجد فى بعض الأطعمة.

إن نقص فيتامين (د) وكذلك عدم التعرض لأشعة الشمس قد يؤدى إلى زيادة الإصابة ببعض الأمراض مثل مرض البول السكرى والروماتيد وغيرها. كما أن فيتامين (د) له دور مهم فى زيادة مقاومة الجسم الميكروبات وكذلك تحسن وظائف الرئة.

حديثا تم إكتشاف دور مهم لفيتامين (د) فى زيادة المناعة الطبيعية للجسم والتى يقوى بها على مقاومة بعض الأمراض وخاصة الإلتهاب الرئوي، متلازمة الكرب التنفسي، التسمم الدموي.

لقد وجد أن نقص فيتامين (د) فى الدم والذى يسبب مرض الكساح عند الأطفال يضاعف احتمالات الإصابة بالإلتهاب الرئوى وكما أن نقص فيتامين (د) له علاقة بزيادة إحتمالات الإصابة بالدرن لدى الكبار فقد وجد أن وظائف الرئة عند الكبار الذين يعانون نقص فيتامين (د) أكثر سوءا من الذين لا يعانون هذا النقص.

الهدف من الدارسة:

١. تحديد مستوى فيتامين (د) فى الحالات الحرجة لدى الأطفال حديثى الولادة.
٢. تقيم دور فيتامين (د) فى الحالات الحرجة لدى الأطفال حديثى الولادة ودوره فى زيادة شدة الإصابة بالإلتهاب الرئوي، متلازمة الكرب التنفسي، التسمم الدموى وأمراض الرئة المزمنة كذلك دوره فى تحسين هذه الحالات.

منهجية البحث:

تمت الدراسة علي مائة طفل حديثي الولادة مكتملى ناقصي الوزن من عمر يوم وحتى عمر ٢٨ يوم الذين تم إدخالهم وحدة الرعاية المركزة للأطفال حديثى الولادة بمستشفى الأطفال الجامعى بالمنصورة وكانوا يعانون من متلازمة الكرب التنفسى أو تسمم دموى أو إلتهاب رئوى أو مرض التنسج الرئوى وكذلك تم دراسة مائة طفل حديثي الولادة من الأصحاء كمجموعة ضابطة. هؤلاء الأطفال هم من الموجدين بوحدة الرعاية المركزة للأطفال حديثى الولادة فى مستشفى الأطفال الجامعى بالمنصورة فى الفترة بين يوليو ٢٠٠٩ حتى أكتوبر ٢٠١٠. وقد تم تقسيم المرضى إلى أربع مجموعات: المجموعة الأولي: الرضع الذين يعانون من متلازمة الكرب التنفسي، المجموعة الثانية: الرضع الذين يعانون من تسمم دموي، المجموعة الثالثة: الرضع الذين يعانون من إلتهاب رئوي، المجموعة الرابعة: الرضع الذين يعانون من مرض التنسج القصبى الرئوي.

ولقد خضعت جميع الحالات لما يلي:

١. تاريخ مرضى كامل مع تحديد العمر الرحمى للطفل
٢. فحص أكلينيكى شامل
٣. التحاليل الآتية عند دخول وحدة الرعاية المركزة:
   - قياس تركيز ٢٥ هيدروكسى فيتامين (د) فى الدم.
   - صورة دم كاملة وتفصيلية.
   - قياس نسبة البروتين التفاعلى"سى فى الدم.
   - عمل مزرعة دم فى حالات التسمم الدموي
   - تحليل غازات فى الدم.
   - نسبة الكالسيوم، الفسفور، والصوديم، البوتاسيوم والجلوكوز فى الدم.
   - أشعة عادية على الصدر والبطن.

نتائج الدراسة:

من خلال الدراسة وجد أن هناك:

١. إنخفاض مستوى فيتامين (د) فى الدم فى الأطفال حديثى الولادة المصابين بمتلازمة الكرب التنفسى أو تسمم دموى أو إلتهاب رئوى أو مرض التنسج القصبى الرئوي.
٢. يوجد علاقة إيجابية بين مستوى فيتامين (د) فى الدم فى وبين العمر الرحمى والوزن والطول وكذلك محيط الرأس فى الأطفال حديثى الولادة المصابين بمتلازمة الكرب التنفسى أو تسمم دموى أو إلتهاب رئوى أو مرض التنسج القصبى الرئوي.
٣. يوجد علاقة سالبة بين مستوى فيتامين (د) فى الدم وبين درجات الإصابة بالإلتهاب الرئوى عند الأطفال حديثى الولادة حيث تم تحديد درجات الإصابة بالإلتهاب الرئوى عن طريق مقياس سيلفرمان.
٤. لا يوجد فرق واضح فى مستوى فيتامين (د) بين الحالات التى تم شفائها والحالات التى توفت.