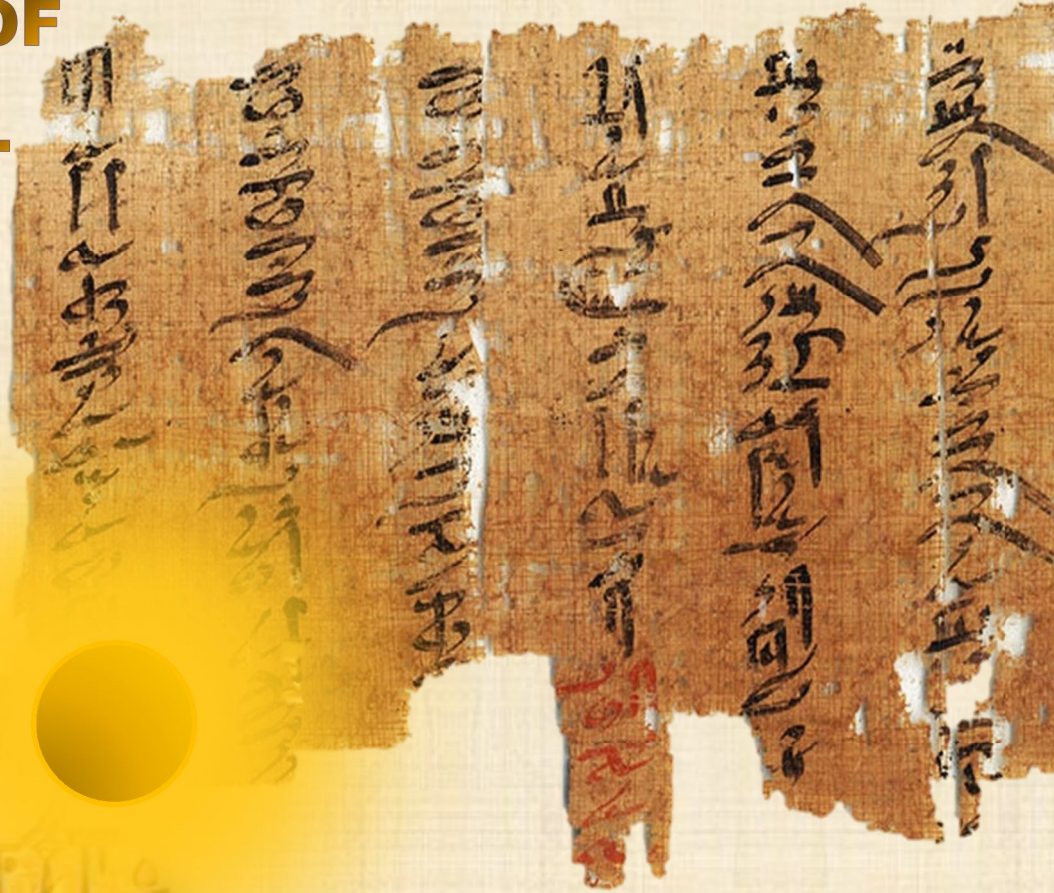


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Original article

Serum 25-hydroxyvitamin D concentration in Children with Lower Respiratory Tract Infection

Asmaa Salah Barania^[a]; Elbakry Mohammed Tharwat Elbakry^[b]; Hany Abdel-Hady Elkhalegy^[b]; Sabah Ibrahim Abdel-Raheem^[c]

Department of Pediatrics, Damanshour Teaching Hospital, Ministry of Health, Egypt^[a].

Department of Pediatrics, Damietta Faculty of Medicine Al-Azhar University, Egypt^[b].

Department of Clinical Pathology, Damietta Faculty of Medicine Al-Azhar University, Egypt^[b].

Corresponding author

Asmaa Salah Barania.

Email: asmaabarania2@gmail.com

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ABSTRACT

Background: Vitamin D plays a critical role in the human body. Its deficiency had been proposed to play a role in lower respiratory tract infections [LRTIs], which responsible for 18% of deaths in young children.

Aim of the work: The purpose of this study was to assess vitamin D concentrations in children with lower respiratory tract infections.

Patients and Methods: After obtaining approval of the ethics committee, a prospective case control study was conducted in pediatric department, Damietta Faculty of Medicine, Al-Azhar University Hospital on children with lower respiratory tract infections and comparing 25-hydroxyvitamin D level between them and normal matched control from December 2018 to September 2019 include 140 children, Group A: 70 cases children had lower respiratory tract infections [LRTIs] either isolated pneumonia or associated with sepsis. Group B: matched with 70 healthy subjects.

Results: There was significant reduction of vitamin D among study group children when compared to control group [13.68±5.50 s 40.64±4.76 ng/dl respectively]. There was no significant association between type of infection and vitamin D levels. However, all children with bronchitis had sufficient vitamin D levels. There were vitamin D-deficiency in 64.3% while No one was deficient vitamin D among control group.

Conclusion: Children with acute lower respiratory tract infection had significant reduction in vitamin D levels. The reduction had no significant association with the type of infection.

Keywords: 25-hydroxyvitamin D; Lower respiratory tract infection; Pneumonia; Bronchiolitis; Bronchitis.

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* Main subject and any subcategories have been classified according to research topic.

INTRODUCTION

Vitamin D, also known as calciferol, is fat-soluble vitamin that plays a critical role in the human body, particularly in bone health. The two major forms of vitamin D are vitamin D₂ [ergocalciferol] and D₃ [cholecalciferol]. Both vitamins D₂ and D₃ are synthesized in response to ultraviolet [UV] radiation of sterols^[1]. Vitamin D has a key role in the development, regeneration and maintenance of good bone health, through regulation of calcium and phosphorus homeostasis^[2].

Serum calcium levels are tightly controlled by the action of calciotropic hormones, including calcitriol, calcitonin, and parathormone hormone [PTH]. If serum calcium levels are low, calcitriol and PTH work in harmony to increase blood levels of both calcium and phosphorus by increasing bowel absorption, facilitating bone resorption and improving kidney reabsorption^[3].

Deficiencies of vitamin D in children result possibly in permanent problems such as rickets, poor bone mass formation and decreased bone mineralization^[6]. In addition to rickets, vitamin D deficiency-related childhood-specific conditions include respiratory infections, atopic dermatitis and allergies to food^[6].

Infection is a major cause of morbidity and mortality in children. Numerous studies have shown a correlation between insufficient levels of vitamin D and respiratory tract infections in infants. Initially, a correlation between vitamin D deficiency and lower respiratory tract infections [LRTIs] in children had been identified after increased incidence of respiratory infections among infants and children with rickets^[8].

The increased incidence of LRTIs in these kids was likely caused by both compromised lung compliance due to the rib deformities associated with severe rickets and poor

nutritional condition. Later, tuberculosis [TB] had been shown to be a prototypical example of a correlation between insufficiency of vitamin D and vulnerability to infectious disease^[9].

We propose that, vitamin D deficiency could play a significant role in pathogenesis of different lower respiratory tract infection. Thus, children with deficient values could be at greater risk for development of LRTIs.

AIM OF THE WORK

The aim of this study is to assess v serum 25-hydroxyvitamin D concentration in children lower respiratory tract infection in comparison to children without such infection.

PATIENTS AND METHODS

After obtaining approval of the institutional local ethics committee, a prospective case control study had been conducted in pediatric department of Al-Azhar University Hospital [Damietta] on hospitalized children [or selected from outpatient clinic] with lower respiratory tract infection and comparing 25-hydroxyvitamin D level between them and normal matched controls over a period of 9 months from December 2018 to September 2019. The study included 70 children with lower respiratory tract infection [study group] and matched with 70 healthy children [control group].

Inclusion criteria: Age up to 3 years.

Exclusion criteria: Congenital diseases, severe protein energy malnutrition, and chronic systemic diseases.

All children were subjected to full history taking [e.g., age, gender, residency, recurrent chest infections, vaccination history, vitamin D intake], and clinical examination, with special attention to local chest examination and manifestations of vitamin D deficiency.

In addition, laboratory investigations included complete blood count [CBC], C-reactive protein [CRP], serum level of 25[OH] vitamin D. Finally, a chest X-ray had been carried out.

A blood sample [5 ml] of venous blood had been drawn from each child and had been monitored using a wide-pore syringe to prevent hemolysis of the red blood corpuscles and had been shielded from light and permitted to coagulate fully at room temperature [within 30-60 minutes]. Then, centrifugation had been conducted for 5-10 minutes at 5000 rpm to isolate the serum.

When tested, the isolated serum had been kept at 20 °C. Vitamin D [25[OH]D] serum level had been assayed by AccuBind ELISA Kits 9425-300A, [Monobid Inc. USA] according to manufacture recommendations.

Statistical analysis:

Using IBM SPSS software package version 20.0, the data had been fed to the computer. Using number and percent, qualitative data were represented. Chi-square test was used to evaluate similarities between different groups on categorical variables. Quantitative data were represented using mean and standard deviation. Comparison had been made using t-tests between two different populations. The significance of the results obtained had been assessed at 5 percent

RESULTS

In the current work, laboratory investigations revealed that, there was no statistically significant difference between study and control groups regarding hemoglobin concentration or platelet count. However, children in the study group had statistically higher levels of both WBCs and CRP [Table 1]. Vitamin D levels in the current study ranged between 6.8 to 54.5ng/dl and there was statistically significant reduction of vitamin D in study when compared to control groups [13.68±5.50 vs 40.64±4.76 ng/dl respectively]. In addition, there was statistically significant decrease of children with sufficient vitamin D in study when compared to control group [4.3% vs 80.0% respectively] [table 2]. Regarding relation between vitamin D and type of lower respiratory tract infection, children with sufficient vitamin D [3 children] all had bronchitis, while children with insufficient vitamin D [22 children], the majority of them had bronchopneumonia followed by pneumonia, and children with deficient vitamin D [45 children], the majority of them had bronchopneumonia [46.7%] followed by bronchiolitis [31.2%] then pneumonia [22.2%] with no significant difference between groups [Table 3]

Table [1]: Comparison between the two studied groups regarding CBC data and CRP level.

	Group A "Cases" "n=70"	Group B "Control" "n=70"	t-test	P value
Hb [mg/dl] Range [Mean±SD]	6.3-13.7[10.75±1.28]	8.3-13.5[11.35±1.29]	1.69	0.082
Platelet count x10 ³ Range [Mean±SD]	143.0-569.0[306.86±94.56]	159-449 [277.37±75.88]	1.98	0.064
WBCs count Range [Mean±SD]	3.3-17.8[9.38±3.53]	3.4-12.4[6.53±2.29]	4.25	0.001*
CRP Range[Mean±SD].	4.0-48.0[15.41±12.63]	3.0-23.0 [8.27±5.39]	3.968	0.003*

Hb: hemoglobin, WBCs: white blood cells, CRP: C-reactive protein; * indicate significant difference

Table [2]: Comparison between the two studied groups regarding [25 [OH]. vitamin D level.

	Group A "Cases" "n=70"		Group B "Control" "n=70"		test P value
	n.	%	n.	%	
Deficiency [<20 ng/ml]	45	64.3	0	0.0	X ² = 94.38 <0.001*
Insufficiency [21-29 ng/ml]	22	31.4	14	20.0	
Sufficient [>30-60 ng/ml]	3	4.3	56	80.0	
Vitamin D Range [Mean±SD]	6.8-33.0[13.68±5.50]		22.8-54.5[40.64±4.76]		t=6.98; <0.001*

*= significant; X² = Chi square test

Table [3]: Different types of pathology in patient group [A] and correlation between them & vitamin D level.

	Deficiency [<20 ng/ml] "n=45"		Insufficiency [21-29 ng/ml] "n=22"		sufficiency [>30-60 ng/ml] "n=3"	
	No	%	No	%	No	%
Bronchopneumonia	21	46.7	9	40.9	0	0.0
Pneumonia	10	22.2	6	27.3	0	0.0
Bronchiolitis	14	31.1	4	18.2	0	0.0
bronchitis	0	0.0	3	13.6	3	100.0
X²: p			6.58; 0.082			

DISCUSSION

The current study assessed vitamin D levels among children with LRTIs and compared values to normal healthy children. The significant results are: significant increase of inflammatory markers [white blood cells and C-reactive protein] among study group. In addition, there was significant reduction of vitamin D among children with LRTIs, which not associated with the type of infection.

In their study, **El-Kassas et al.** [14] reported that, hemoglobin had been significantly reduced, while total leucocyte count [TLC] and CRP were significantly increased among children with pneumonia when compared to controls. In addition, there was significant lower levels of Vitamin D in pneumonia group [9 ± 2.1] when compared to controls [14.1±2.8], P value < 0.01. These results are supported by the current work. The current results are comparable to those reported by **Ruiz-Gonzalez et al.**[15] who reported significant increase of CRP in children with pneumonia and appreciate its role in diagnosis and differentiation between pneumonia and other respiratory infections.

Pampana's study investigated the impact of vitamin D status on the susceptibility and severity of LRTs in children. Vitamin D indices had been compared between subgroups in

LRTs cases. The median [interquartile range [IQR]] serum 25[OH]D level was 23.7 [IQR 17.5-30.6] ng/mL; 26.4% children were vitamin- D sufficient], whereas 73.6% were insufficient[16].

In another study conducted by **Guo et al.**[17] to investigate the relationship between vitamin-D status and LRTIs in children, they found that the median [IQR] serum 25[OH]D level in the LRTIs group was significantly lower than that in the control group [19.6 ng/mL versus 26.6 ng/mL, respectively] [P<0.001]. The proportions of vitamin D deficiency [32.2% versus 19.5%] and severe deficiency [19.1% versus 0.4%] in the cases and control groups respectively [17].

Another prospective study by **Mohamed et al.** [18], tested cord blood for 25 [OH] D. Medical records covering the first 2 years of life were reviewed, and the diagnosis of LRTIs had been recorded. Concentrations of 25 [OH] D were significantly lower in infants who developed LRTIs compared with those did not [p <0.0001]. Vitamin D deficiency was associated with increased risk of LRTIs.

In agreement with the current work, **Mahyar et al.**[20] evaluated serum 25-Hydroxy vitamin-D levels in children with lower respiratory tract infections and reported no significant difference between different diagnoses [types of infection] of lower respiratory tract infections and level of

vitamin D^[20].

Results of the current study could be explained by the hypothesis stated that, vitamin-D deficiency is a risk factor for respiratory infection especially pneumonia. This theory supported by a meta-analysis revealed that, vitamin-D supplementation is associated with decreased episodes of respiratory tract infection^[21].

Besides **Christensen et al.**^[22] reported that vitamin-D supplementation for pregnant females could reduce or prevent respiratory tract infection of offspring.

Another systematic review revealed a significant correlation between vitamin-D levels and both LRTI incidence and severity^[23].

On the other side, McNally et al.^[24] did not observe any significant difference in vitamin D concentrations between children with LRTI and healthy controls. However, their results revealed that, children admitted to intensive care unit [ICU] had significantly lower concentrations of vitamin D. They concluded that, the immunomodulatory functions of vitamin D may predispose to LRTIs and its severity.

Conclusion: In children with acute LRTIs, there was significant reduction of vitamin D levels. Thus, vitamin D supplementation may share in reduction or prevention of such infections.

Financial and Non-financial Relationships and Activities of Interest

Authors announce that no conflicts of interest existed.

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