

Influence of Vitamin D and IgE Levels on Recurrent wheezy Chest in Children under Two Years of Age; A Hospital-Based Case-Control Study

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Abstract

Background and objectives: Wheezing is a common presenting symptom of respiratory disease in children. Thirty percent of children experience at least one acute wheezing illness before the age of three years, and it is one of the most common causes of morbidity and mortality, the most frequent causes of wheezing are bronchiolitis and asthma. Recurrent wheezing has significant morbidity. It is estimated that about one third of children manifest symptoms during the first years of life. Vitamin D is fat soluble and its role is helping growth of bone and function of immunity is crucial. IgE has essential role in type I hypersensitivity reaction like allergic asthma, allergic rhinitis and others. Our study aimed to estimate serum vitamin D and IgE level in infants and children less than 2 years of age with recurrent wheeze.

Methods: This case control study was carried in Raparin teaching hospital in Erbil city where we estimated serum levels of vitamin D and IgE of 50 children documented to have recurrent wheeze of more than 2 attacks in comparison to 50 normal children. **Results:** Vitamin D level was deficient in both groups with no significant difference in vitamin D and IgE levels between both groups. **Conclusions:** The study revealed that vitamin D was low in both studied groups and there was no clear relation between vitamin D deficiency and IgE level with recurrent wheezy chest.

Keywords: Vitamin D; IgE; Infants; Wheezing chest.

Introduction

Wheezing is a common presenting symptom of respiratory disease in children¹. Thirty percent of children experience at least one acute wheezing illness before the age of three years, and it is one of the most common causes of morbidity and mortality². There is detailed research determining the risk factors of recurrent wheezing³. Vitamin D is vital nutrient and fat soluble vitamin and is the only vitamin that is synthesis by humans through endogenous production in the skin with exposure to ultra violet B⁴.

There are two major forms of vitamin D: Vitamin D2 (Ergocalciferol) available from plant sources like mushroom and vitamin D3 (Cholecalciferol) available from animal sources such as oily fish and produced in human skin upon exposure to ultraviolet (UV – B) radiation. Vitamin D3 is the potent type^{5,6}.

Systemic vitamin D status is reliably indicated by the serum level of 25-hydroxy vitamin D (25 Oh) D which reflect cutaneous photosynthesis and oral intake from both diet and supplements, currently there is no consensus on optimal level of 25 (OH) D⁷. The 2010 institute of medicine (IOM) recommended that vitamin D deficiency be defined as 25 (OH) D levels less than 50 nmol/L with levels more

than 50 nmol/L represent vitamin D sufficiency⁸. However these guidelines have been criticized as being overly conservative by being based almost solely on studies of bone health^{9, 10}. New studies suggest that vitamin D plays an important role in the lung development and vitamin D deficiency may be a risk factor for asthma, recurrent wheezing and respiratory infections⁷⁻¹⁰. Higher 25 (OH) D level of more than 100 nmol/L has been suggested to be necessary for optimal immune function and good respiratory outcome¹¹⁻¹⁵. IgE is a type of antibody found in the immune system; IgE has function in the immunity and atypical hypersensitivity which manifests as allergy or asthma and other, IgE also play a role in response to allergy¹⁶. IgE is synthesized by plasma cells its main function is immunity also has an essential role in type I hypersensitivity, which manifests in various allergic diseases¹⁷.

Patients and Method

A case control study carried out on fifty infants less than two years with recurrent wheezy chest in Raparin pediatric teaching hospital in Erbil city over nine months from November 1st 2016 to August 1st 2017. Children

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less than two years of age with documented two or more attacks of wheezy chest out of any known chronic medical disease included in this study (group one, cases), fifty healthy children less than two years out of any medical problems were involved as control in Raparin teaching hospital in Erbil city (group two, control).

A well-organized history taken for each single participant including name, age, gender, residence, gestational age, family history and history of allergic problems.

Serum vitamin D3 level and IgE levels were sent for both groups, vitamin D3 level between (20-50 ng/dl) regarded to be normal for age (15- 20 ng/dl) insufficient and (less than 15 ng/dl) deficient¹⁸.

While IgE level (less than 36 ng/ml in first year and less than 144 ng/ml from one to five years) was regarded to be normal¹⁹. Statistical analysis was performed with software

package SPSS version 21, Chi square and fishers test were used when indicated, p-value ≤ 0.5 was considered to be significant.

Results

The mean age of the studied sample was 9.80 + 5.64 months, ranging from 3 to 23 months. Twenty-two cases (44%) showed history of upper respiratory tract infection in previous 3 months in cases with vitamin D deficient and complaining from recurrent wheezing chest, while only (10%) of cases had same history in control group this finding was statistically significant (p-value < 0.001, OR=7.07).

Family history of asthma observed in 13 (26%) cases while seen in 4 (8%) in control group with significant p-value= 0.017, as shown in Table 1.

Table (1): Factors associated with wheezy chest

Factors	Wheezy chest (Group One)		Normal (Group Two)		Total		p-value	OR (95%CI)
	No.	%	No.	%	No.	%		
URTI before 3 months								
Yes	22	(44.0)	5	(10.0)	27	(27.0)	< 0.001	7.07(2.40-20.81)
No	28	(56.0)	45	(90.0)	73	(73.0)		
Hospital Admission								
None	0	(0.0)	24	(48.0)	24	(24.0)	< 0.001	NA
First	12	(24.0)	15	(30.0)	27	(27.0)		
Second	10	(20.0)	11	(22.0)	21	(21.0)		
third	6	(12.0)	0	(0.0)	6	(6.0)		
Fourth	22	(44.0)	0	(0.0)	22	(22.0)		
Family history of asthma								
Yes	13	(26.0)	4	(8.0)	17	(17.0)	0.017	4.04(1.21-13.43)
No	37	(74.0)	46	(92.0)	83	(83.0)		
Food allergy								
Yes	2	4.0	0	0.0	2	2.0	0.495*	∞
No	48	96.0	50	100.0	98	98.0		
Atopy , eczema								
Yes	4	(8.0)	0	(0.0)	4	(4.0)	0.117*	∞
No	46	(92.0)	50	(100.0)	96	(96.0)		
Total	50	(100.0)	50	(100.0)	100	(100.0)		

*By Fisher’s exact test. NA: Not applicable. ∞: Infinity.

The study showed that 16 (32%) cases in group one had history of vitamin D intake compared with 9(18%) in group two (p-value = 0.106). The study showed that less than one third (28%) of children in group one had normal vitamin D3 level, compared with 26% of children of group two (p-value = 0.631). Four (8%) children in group one has deficient vitamin D level compared with 7(14%) in group two. While 32(64%) children in group one has insufficient vitamin D level compared with 31(62%) of children in group two. Study showed that 9 (18%) of children had high levels of IgE in group one compared to 8(16%) of children in group two, the difference between the two groups was not statistically significant (p-value = 0.790) as shown in Table 2.

Table (2): Vitamin D3 and IgE levels in the two study groups.

Vitamin D3 & IgE levels	Wheezy chest (Group One)		Normal (Group Two)		Total		p-value	OR (95%CI)
	No.	(%)	No.	(%)	No.	(%)		
Vitamin D3 intake (In drops 400 U/day in tow divided doses)								
Yes	16	(32.0)	9	(18.0)	25	(25.0)	0.106	2.14(0.842-5.45)
No	34	(68.0)	41	(82.0)	75	(75.0)		
Vitamin D3 blood level								
Deficient	4	(8.0)	7	(14.0)	11	(11.0)	0.631	NA
Insufficient	32	(64.0)	30	(60.0)	62	(62.0)		
Normal	14	(28.0)	13	(26.0)	27	(27.0)		
Ig E level								
High	9	(18.0)	8	(16.0)	17	(17.0)	0.790	1.15(0.405-3.27)
Normal	41	(82.0)	42	(84.0)	83	(83.0)		
Total	50	(100.0)	50	(100.0)	50	(100.0)		

*By Fisher’s exact test.

Discussion

Vitamin D deficiency and insufficiency is now a global public health problem affecting an estimated one billion people worldwide²⁰.

In our study we found the relation between upper respiratory tract infection and recurrent wheezy with low vitamin D deficiency it appeared that twenty two cases 44% in group one had history of upper respiratory tract infection in previous 3 months comparing to only 10 % in case control group two, This result goes with the Observational studies that reported consistent independent associations between low serum concentrations of 25-hydroxyvitamin D and susceptibility to acute respiratory tract infection^{21,22}. The 25-hydroxyvitamin D supports induction of antimicrobial peptides in response to both viral and bacterial stimuli^{23,24,25}. Suggesting a potential mechanism by which vitamin D inducible protection against respiratory pathogens might be mediated. Vitamin D metabolites have also been reported to induce other innate antimicrobial effector mechanisms, including induction of autophagy and synthesis of reactive nitrogen intermediates and reactive oxygen intermediates²⁶.

Also this consistent why recurrent hospital admission more common among cases in group one comparing with control cases group two as 12 % third admission in group one, while 0% in group two, also 4th admission 44%

among group one, while 0% in group two.

A Prospective population study has showed that children with early sensitization and persistent wheezing had high IgE levels throughout childhood²⁷.

A meta-analysis of randomized controlled trials showed that prophylactic vitamin D supplementation in pediatric subjects significantly reduced the odds of contracting respiratory tract infections and recurrent wheezy chest; while currently total IgE level is regarded as a weak indicator of allergic respiratory disease²⁸. Even many patients with allergic disease have elevated levels of total IgE, there is no specific cutoff value that discriminates patients with allergic disease from those without allergic disease and there is considerable overlap^{29,30}. Thus total IgE by itself is rarely adequate to diagnose allergic disease. Our research consistent with the result of Ozaydin, et al¹¹ who could not find any relationship between serum vitamin D and recurrent wheezy chest, this may be due to the fact that there is controversy about the impact of vitamin D on the immune system, some authors have claimed that the beneficial effect of stimulating the vitamin D pathway include decrease inflammation and enhanced defense against pathogens^{7,9,15,16}. Furthermore exposure of immature immune system (as in infants) to vitamin D may skew T- Cell towards a more allergic TH-2 cytokine expression profile³¹⁻³⁶.

Current study was consistent with similar observation reported in the United States, by Litonjua³⁷ where no association was found between vitamin D level and exacerbations in asthmatic children, although asthma was more severe in those with vitamin D insufficiency. Moreover, Hibbs, et al³⁸ mentioned that there are some potential mechanisms by which vitamin D supplementation may increase wheezing.

Our study results were against many researches like Soner et al³⁹ who found linear positive relationship in their patients group between vitamin D and IgE level with exacerbation of wheezy and asthma.

Metin et al⁴⁰ found also significant relationship between recurrent wheezy chest and the level of vitamin D and IgE. Katarina et al⁴¹ evaluated the risk factors for acute wheezy in preschool children, they found that preschool children with acute wheezy had significantly lower vitamin D levels than healthy controls.

Growing evidence suggests a role for Vitamin D in the regulation of IgE and development of allergic sensitization; Brehm et al⁴² also reported a similar relationship and found that each ten (10) ng/ml increase in vitamin D level resulted in (25 IU/ml) decrease in the IgE level for asthmatic patient.

Abdul-Bari et al⁴³ found 23.4% of wheezy chest children and 10.5% of healthy children have severe vitamin D deficiency.

Conclusions

The study revealed that vitamin D was low in both studied groups and there is no clear relation between vitamin D deficiency and IgE level with recurrent wheezy chest.

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