

Correlation between Serum vitamin D and Asthma Control in Asthmatic Children

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Abstract

Asthma is a chronic ,inflammatory ,respiratory tract disease accompanied by hypersensitivity of airways, recurring wheezing episodes, respiratory distress and coughing. The aim of this study was to estimate vitamin D level and specific IgE level in asthmatic children who were on controller medication and correlated their serum level with asthma control . Our results clarified that The serum vitamin[D] levels were closely related to asthma attacks. As,There were statistically significant positive correlations between serum vitamin D level and asthma control in asthmatic children. There were no significant difference in mean serum vitamin [D] between male and female and according to parent consanguinity while shows significant difference regarding order of sibling. there were no significant difference in mean serum vitamin [D] according to family history of atopy and passive smoking, while shows significant difference regarding family history of asthma, associated allergic condition, day time symptoms, night time awakness, degree of asthma control, recurrent hospital admission , interference with activity and frequency of exacerbation and influenza &pneumococcal vaccination. significant difference in mean serum vitamin [D] according to food born allergen: apple ,banana ,casein ,cow milk ,egg white, peanut while regarding airborne allergen shows nonsignificant difference with ,Der.pteronysinus, Der.farinae ,Cockroach and Honey bee venom and Aspergillus fumigatus . Common wasp venom , Alteaaria alternate, Honey bee venum,Birch ,Candida albican ,Dog epith. and cat epithelium demonstrated significant difference. From our results, it would be concluded that there was a significant correlation between vitamin [D] level and asthma control in asthmatic children .

Keywords: Childhood asthma, Vitamin [D] , Specific IgE.

1. Introduction

Asthma in children has become a public health problem , various epidemiological studies have shown that the global prevalence of asthma in children ranges from 3 to29% [1].

The occurrence of asthma in children can be caused by many factors, environmental, gender, genetic, ethnic factors and socioeconomic status [2]. In recent years, studies have shown that vitamin D levels and the incidence of asthma were closely related. Several clinical trials have tested whether taking Vitamin D as a supplement has an effect on asthma attacks, symptoms and lung function in children and adults with asthma. Vitamin D supplementation can regulate the body's immune function, reduce inflammation and initiate repair functions in the body [3].

VitD may play a role in reducing the risk for respiratory infections,[4] a major trigger factor for asthma[5],viral infections are a known primary risk factor in the onset of asthma attack. During a viral infection, vitamin D is responsible for the production of cathelicidin, an antimicrobial polypeptide. Research exhibits vitamin D supplements reduce upper respiratory tract infection significantly [6].Low levels of vitamin D may reduce the efficacy of steroid action in asthmatics resulting in poor symptoms control [7].The aim of this study was to estimate vitamin D level and Specific IgE in asthmatic

children and correlated their serum with asthma control.

2. Materials and methods

This was a cross-sectional study which included 60 children aged from 4 years up to 15 year diagnosed as bronchial asthma attending pediatric chest and asthma clinic, Benha university Hospitals .

2.1 Inclusion criteria

- The patients presenting with clinical manifestations of cough, chest tightness, lung wheezing, night and/or early morning onset or exacerbate.
- Patients who meet the asthma diagnostic criteria according to GINA guidelines 2017 .
- Children aged 4 years up to 15 year.
- Asthmatic children on asthma controller drugs e.g [inhaled steroid , leuktriens].
- Informed consent will be obtained from parents.

2.2 Exclusion criteria

- Any chest problem other than asthma e.g pneumonia and cystic fibrosis.
- Age < 4years or >15 year
- Any chronic systemic illness e.g Heart,liver, kidney and CNS diseases.

- Children who are on hormonal drugs during the previous 30 days.
- Children who were on Vitamin D therapy during the previous 30 days.

3. Methods

3.1 Every child was subjected to the following:

1- Full History taking

Personal history [name, age, sex, residence and school attendance], History of the present illness: Symptoms related to asthma, [wheezing, dyspnea, cough, fatigue and cyanosis, Onset and duration of asthma, frequency of attacks, and seasonal variation. Other atopic complaints as rhinitis, eczema, urticaria and Conjunctivitis. History of treatment: number of times of hospitalization due to asthma, treatment during acute attack, prophylactic treatment. Family history of similar condition, atopy, asthma, allergic rhinitis, urticaria and Conjunctivitis. Smoking history. Controller medication like inhaled corticosteroids [ICS] and leukotrienes.

2- full clinical examination

General examination and local examination: Chest examination :Inspection, Palpation, Percussion, Auscultation .

CNS examination, Abdominal examination and Cardiovascular system examination.

3- Pulmonary function tests

peak expiratory flow rate [PEFR].

4- Lab. Investigation

Serum level of vitamin D [25-Hydroxyl D₃] was estimated using Vidas [Vitek ImmunoDiagnostic Assay System], Serum level of specific IGE was estimated by The AllergyScreen and the AlleisaScreen .

3.2 Sample collection

serum or plasma [lithium heparin] from 10cm blood sample under complete aseptic technique, using plastic tube with lithium heparin and separation gel.

Serum and plasma samples was stored in primary tube at 18-25c for up to 8 hours or aliquoted at 2-8c for up to 5 days.

For these serum sample ensured that complete clot formation has taken place prior to centrifugation as insufficient clot result information of fibrin with micro-clots lead to erroneous results.

3.3 Statistical data management

3.4 Data management

The clinical data were recorded on a report form. These data were tabulated and analysed using the computer program SPSS [Statistical package for social science] version 20 to obtain.

3.5 Descriptive data

Descriptive statistics were calculated for the data in the form of

1-Mean and standard deviation ($\pm SD$).

Median and inter-quartile range [IQR] for quantitative data.

2-Frequency and distribution for qualitative data.

3.6 Analytical statistics

In the statistical comparison between the different groups, the significance of difference was tested using one of the following tests:-

1- Student's *t*-test:- Used to compare mean of two groups of quantitative data.

2- ANOVA test [F value]:-Used to compare mean of more than two groups of quantitative data.

A P value <0.05 was considered statistically significant [*] while >0.05 statistically insignificant P value <0.01 was considered highly significant [**] in all analyses.

4. Results

There were non-significant difference in mean serum vit. [D] between male and female and according to parent consanguinity while shows significant difference regarding order of sibling [$p < 0,05$] Table (1).

There were non significant difference in mean serum vit. [D] according to family history of atopy and passive smoking, while shows significant difference regarding family history of asthma, associated allergic condition, day time symptoms, night time awakens, degree of asthma control, recurrent hospital admission and interference with activity Table (2) .

There were significant difference in mean serum vit. [D] according to frequency of exacerbation and influenza & pneumococcal vaccination Table (3).

There were significant difference in mean serum vitamin [D] according to food born allergen: apple ,banana ,casein ,cow milk ,egg white, peanut while regarding airborne shows nonsignificant difference with ,Der. pteronyssinus, Cockroach and Der. farinae Honey bee venom and Aspergillus fumigatus . Common wasp venom ,Alternaria alternate, Honey bee venom, Birch ,Candida albican ,Dog epith. and cat epithelium demonstrated significant difference Table (4).

Table (1) Serum vit D differences according to sex,order of sibling and parent consanguinity.

	No	mean	±SD	Statistical test	P value
Serum vit D					
Sex					
Male	30	12.91	7.02	St t= 0.35	0.73
	30	13.44	4.52		
Female					
Order in his sibling					
1 st	24	15.4	7.03	F= 11.35	<0.001**
2 nd	24	14.42	2.33		
3 rd	6	7.93ab	0.0		
4 th	6	4.56ab	0.0		
Parent consanguinity					
Yes	24	13.34	5.85	St t= 0.18	0.86
No	36	13.07	5.95		

Table (2) Serum vit D differences

Serum vit D	No	mean	±SD	Statistical test	P value
Family history of atopy					
Yes	42	13.12	6.46	St t= 0.12	0.91
No	18	13.31	4.3		
Family history of asthma					
Yes	24	16.89	6.8	St t= 4.66	<0.001**
No	36	10.7	3.43		
Associated allergic condition					
Yes	18	15.71	4.25	St t= 2.27	0.027*
No	42	12.09	6.16		
Passive smoking					
Yes	54	13.11	6.18	St t= 0.27	0.79
No	6	13.8	0.0		
Day time symptoms					
<2/w	18	12.61	0.87	F= 8.49	0.001**
>2/w	18	17.23a	6.77		
Daily	24	10.56b	5.78		
Night time awakness					
<2/m	18	12.61	0.87	F= 8.49	0.001**
>2/m	18	17.23a	6.77		
>1/w	24	10.56b	5.78		
Degree of control					
Good	18	12.61	0.87	F= 8.49	0.001**
Fair	18	17.23a	6.77		
Poor	24	10.56b	5.78		
Recurrent hosp admission					
Once	6	22.3	0.0	F= 7.22	<0.001**
Twice	6	11.88a	0.0		
Yes	36	11.94a	6.44		
No	12	12.98a	0.86		
Interference with activity					
Yes	24	10.56	5.78	F= 4.46	0.016*
Minor	12	15.12	7.5		
No	24	14.82	3.98		

Table(3) Serum vit D differences according to frequency of exacerbation and influenza.

Serum vit D	No	mean	±SD	Statistical test	P value
Frequency of exacerbation					
0-1/year	18	12.61	0.87	F= 9.15	<0.001**
<2/year	12	15.12	7.5		
>1/year	6	21.45ab	0.0		
>2/year	12	11.91c	6.5		
>1/month	6	4.56abcd	0.0		
Frequent	6	13.88ce	0.0		
Influenza & pneumococcal					
Yes	48	12.27	5.78	St t= 2.5	0.015*
No	12	16.81	4.85		

Table (4) Serum vit D differences according to food borne and air borne

Serum vit D	No	mean	±SD	Statistical test	P value
Food borne					
Apple, banana, casein and cow milk	6	18.13	0.0	F= 13.53	<0.001**
Banana	18	8.22a	3.2		
Egg white	6	21.45b	0.0		
Pea nut	6	13.88bc	0.0		
No	24	13.42abc	6.07		
Air borne					
Aspergillus fumigatus	18	13.29	4.3	St t=	0.09
Cat epithelium	6	7.93	0.0	2.4	0.019*
Der farinae	24	13.3	6.79	0.13	0.90
Der pteronyssinus	30	13.07	6.06	0.14	0.89
Common wasp venum	36	11.04	4.73	3.85	<0.001**
Alternaria alternata	18	9.46	6.33	3.52	0.001**
Cockroach	12	15.15	3.12	1.31	0.20
Honey bee venum	6	11.88	0.0	0.57	0.57
Birch	6	4.56	0.0	4.33	<0.001**
Candida albican	6	4.56	0.0	4.33	<0.001**
Dog epith	6	18.13	0.0	2.26	0.028*

4. Discussion

Asthma is a chronic airway inflammation with a very high incidence in children. The aggravating factors like activation of allergen, hyperventilation, excessive exercise, cold air and strong emotional changes can increase symptoms of airway inflammation thus, inducing asthma attacks. So, the key to reduce the asthmatic attacks is to control the airway inflammation [8]

vitamin D [1,25 dihydroxycholecalciferol] known to modulate fetal lung maturation and airway smooth muscle cell proliferation and differentiation [9] also, VitD levels and early transient wheezing are closely related to each other [10], Studies suggest that low vitamin D levels in children with asthma is associated with more symptoms, exacerbations, decreased lung function, increased medication use. [11]

The strong association between asthma and food allergy is well recognized, 48% of asthmatic patients have food allergy [12]. Indoor inhalant allergens mostly involved in

the development of asthma include house dust mites [HDM], animal proteins [particularly cat and dog allergens] and fungi, outdoor inhalant allergens has less significant role in the development of asthma, but associated with the precipitation of asthma attacks [13].

Our study aimed to estimate serum vitamin D and specific IgE levels [foodborne allergen, airborne allergen] and correlate their levels with asthma control in asthmatic children. Our results revealed a significant correlation between vitamin D level and asthma control.

The study showed the correlation between vitamin [D] level and asthma control in asthmatic children. our study was cross-sectional study conducted on 60 asthmatic child aged 4-15 years old 80% of them were vitamin D deficient [levels <20 ng/ml] and 20% were in insufficient range with levels [20-30 ng/ml]

our results showed no significant difference between mean serum vit. [D] regarding age and sex. This in agreement with [14] study

conducted on 96 asthmatic children aged 5-12 years showed no significant correlation between age, sex and Vitamin D. Also [15] study showed no statistically significant differences in age, sex and BMI of the asthmatic children between the high and low 25-[OH]D groups [$P > 0.05$].

In our study there was significant correlation between child Order in his sibling and vitamin [D] level < 0.001 .

This in agreement with [16] study which showed statistically significance between Birth order [1st or 2nd[173] 3rd or 4th [196] $\geq 5^{\text{th}}$ [114].] and vitamin D level with P value < 0.003 .

Family history of asthma was found in 60% of asthmatic children and showed statistically significance with vitamin D level $P < 0.001$.

This in agreement with [16] in his study family history of asthma in asthmatic children represent 63.6 % and show significance with Vitamin D level $P < 0.009$.

In our study Vitamin D showed a significant correlation regarding Annual vaccination [influenza, pneumococcal vaccine] evidenced by [$P = 0.015$].

This in agreement with [17] study that showed significant correlation between children who received influenza vaccine coupled to Vitamin D compared to children who received the isolated vaccine [$p = 0.001$].

In our study recurrent exacerbations and hospitalizations increased in those with deficient vitamin D levels, number of hospitalizations/ and frequency of asthma exacerbation per year significantly correlate vitamin D level [$p < 0.001^{**}$, highly significant].

In agreement with our results [15] his results showed that the level of 25-[OH]D was decreased in children with recurrent asthma attack, which is associated with the inflammatory mediators, IL-6 and TNF- α , as well as pulmonary functions [$P < 0.05$].

Our study revealed statistically significant difference between serum vitamin D level and associated atopic conditions.

This in agreement with [18] prospective study determined that vitamin D insufficiency increased the risk of atopy and asthma development.

Our study revealed no significant difference in mean serum vit. [D] according to passive smoking.

In agreement with our results [19] found that Children with both non-smoking parents presented significantly higher serum levels of 25[OH]D than children with both smoking parents.

Our results showed statistically significant difference between vitamin D level and degree of interference of activity [$p < 0.016$].

This in agreement with [16] case control study found that asthmatic children with vitamin D deficiency [$p < 0.001$] showed less physical activity.

A significant inverse association was observed between vitamin D levels and severity of asthma [$p < 0.001^{**}$]. 20% of cases with MILD asthma had insufficient vitamin D levels as compared to 80% cases with moderate/severe asthma with vitamin D deficiency.

In agreement with our results [20], [21],[14] found a significant correlation between vitamin D levels in asthmatic children and asthma severity [$p < .001$] study,

Levels of asthma control in our study were classified as good control, fair control and poor control as GINA guidelines [22] Significant [$p = 0.001$] inverse correlation was found between vitamin D levels and level of asthma control, 40% of children with deficient levels of vitamin D were associated with poor asthma control.

This in agreement with [14],[23],[24] and 15 study which showed statistically significant correlation between asthma control and vitamin D status [$p \text{ value} < 0.001$].

Our study showed 60% of asthmatic children had food allergy 30% of them were allergic to banana, 10% to egg white, 10% to peanut and 10% were multiple food allergy to [banana, apple, casein and cow milk].

This in hand with [25] showed significant results in food-specific serum IgE measured to peanut, cow's milk, egg white, and shrimp higher in asthmatic children associated with vitamin D deficiency.

our study showed that asthma in children associated with increase specific IgE of airborne allergen [Aspergillus fumigatus and Alternaria alternata constituted 30% of the studied group, Der. farinae 40%, Der. pteronyssinus 50%, 60% common wasp venom and cockroach 20%. Honey bee venom, Birch, Candida albican, Dog epith and Cat epithelium represented 10% for each].

In agreement with our results [7] found Sensitivity to outdoor pollens not associated with Vitamin [D] levels, Mold allergens cat aeroallergen and Alternaria species in particular showed a trend toward lower VitD levels that did not achieve significance. However, sensitivity to the indoor aeroallergens dog [$P = .045$] and house dust mite [$P = .05$] were significantly associated with lower Vitamin [D] levels.

[26] reported that Vitamin D levels in asthmatic children were also significantly associated with reductions in levels of IgE to dust mite. There was no significant association between vitamin D levels and serum IgE to cockroach.

5. Conclusion

This study concluded that, Deficient vitamin [D] associated with poor asthma control in asthmatic children. Targeting that vitamin [D] was positively and significantly associated with asthma control.

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