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Assessment of 25 (oh) Vitamin D3 in Asthmatic Children in S.P.M.C.H.I, Jaipur

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Abstract
Objective: *To determine the difference in mean of 25-OH-D_3in different groups of asthmatic children (i.e. mild, moderate and severe).*
Study design:*A hospital based observational, descriptive and comparative analysis.*
Setting: *This study was conducted in the Department of Pediatrics, S.P.M.C.H.I, attached to S.M.S Medical college, Jaipur,from May 2014 to April 2015.*
Methods*: This cross-sectional study included 75 (25 severe, 25 moderate and 25 mild asthmatic children) children aged between 6 and 15 years. Serum 25-hydroxy vitamin-D levels were determined and compared between the three groups. The association between vitamin-D levels and lung function was studied in the asthmatic children.*
Results*: Serum vitamin-D level was significantly lower in severe asthmatic children than in mild asthmatic children and vitamin-D levels had a significant positive correlation with FEV1%.*
Conclusion*: Vitamin-D deficiency is highly prevalent in asthmatic children and there was a significant inverse relationship between vitamin D levels and severity of asthma symptoms. Vitamin D is also associated with airway limitation.*
Keywords: *bronchial asthma , vitamin-D, FEV1*

I. Introduction

Asthma is one of the most common chronic respiratory disease of childhood; in up to half of people with asthma , symptom begin during childhood , often early in life. School absence, emergency department visit and hospitalisation make asthma the leading cause of childhood morbidity from chronic disease.[1]
Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of recurrence respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.Asthma is classified as intermittent, mild persistent, moderate persistent and severe persistent, according to Global Initiative for asthma[1]. Although the role of vitamin D in bone health is well known, recent studies have described new non skeletal roles for vitamin D in human health, including a role in preventing chronic diseases such as cardiovascular disease, diabetes and cancer[3].In addition to these chronic diseases, vitamin D which is a potent modulator of immune system and is involve in regulating cell proliferation and differentiation, may also be linked to bronchial asthma[29].

Asthma is a common, chronic respiratory disease affecting 1–18% of the population in different countries. Its prevalence is increasing in many countries, especially among children. Although some countries have seen a decline in hospitalizations and deaths from asthma, asthma still imposes an unacceptable burden on health care systems, and on society through loss of productivity in the workplace and, especially for pediatric asthma, disruption to the family[15].

Many previous studies showed the hypovitaminosis D was more prevalent with patient of bronchial asthma, this study try to establish the correlation between the severity of asthma and vitamin D levels.

II. Material and method

This cross-sectional study was carried out on 75 children aged 6 to 15 years, visited Pulmunology Clinic or admitted in Department of Pediatrics, Sir Padampat Maternal and Child Instituted, S.M.S Medical colleges, Jaipur, India, from May 2014 to April 2015. All the families filled out a written consent form. The Ethics committee of the institute approved of the study.

The subjects included 75 asthmatic patients, diagnosed according to the Global Initiative for Asthma (GINA) criteria: 1) a physician's diagnosis of asthma, 2) symptoms of recurrent (i.e. more than two) episodes of wheezing, cough, shortness of breath, or a combination of these, 3) documented reversibility with bronchodilators and 4) symptoms of and/or use of medication for asthma in the previous six months[1]. Children with disease known to effect bone metabolism (e.g. renal disease and parathyroid dysfunction) and other severe disease (e.g. cancer, gastrointestinal disorder etc), those with malnutrition, those on vitamin D supplementation and on oral steroid were excluded from the study.

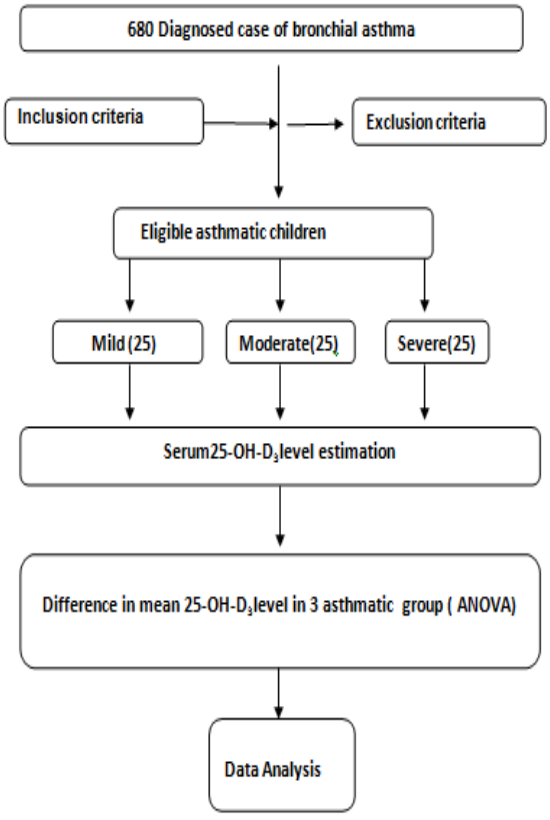
680 patients of asthma were screen, out of which 25 eligible severe asthmatic children was included on first cum first serve basis and 25 moderate, 25 mild age matched asthmatic children reporting just next to each severe asthmatic children were included in the study. Patients' detailed personal medical histories were recorded and complete physical examination and analysis of information was done. Socio-demographic characteristics such as age, sex and place of residence and morphometric measurements such as height and weight were recorded during meetings with the children's family.

Appropriate laboratory tests were conducted to establish white blood cell count, eosinophil count,plasma vitamin D level, plasma calcium (Ca), phosphorus(P) and alkaline phosphatase (ALP). Chest X-rays were also carried out to eliminate cases of disease other than asthma

A single measurement of 25-OH-D_3 was made in all subjects using a chemiluminescent method in Central Laboratory of S.M.S Hospital, Jaipur. All aseptic measure was taken and blood was collected in a serum vial and allow it to stand for 30 minutes at room temperature to ensure full clotting. All samples are subsequently centrifuged at 3000rpm for 5 minutes, and the supernatant is aliquoted and analyzed by ADVIA Centaur XP immunoassay system. 25-OH-D_3 level are classified as Sufficient (30-60ng/ml), insufficiency (20-<30ng/ml) and deficiency (<20 ng/ml.) [4,5]. Peripheral leukocyte analyses included total leukocyte counts and percentages of eosinophil, using an automated cell counter(Name of the machine). The absolute count of eosinophil was calculated as the product of its percentage and the total leukocyte count. Serum total calcium, inorganic phosphorus and

alkaline phosphatase were measured using an automated analyser (Cobas C 311, Roche Diagnostics). Serum calcium was adjusted for albumin; corrected serum calcium= (serum calcium [measured] + 0.8 * [4-serum albumin]).

Flow chart:



III. Statistical analysis

Continuous datas were summarized in form of mean ± SD. The difference in mean was analyzed using ANOVA test. Continuous data was express in form of proportion. The level of significance would be kept at 95% for all statistical analysis.

IV. Result

Atotal of 75 asthmatic children aged between 6 and 15 years were studied; the mean age of children was 8.56 ± 2.1 years. 46 [61.3%] of the children were male and only 29 [38.7%] were females. The male, female ratio was 1.58:1(Table 1). The mean serum Alkaline phosphatase level was calculated for all three group of patients. It was highest in severe asthmatics 248.38±97.138mg /dl and was lowest in mild asthmatics 180.72±74.982mg /dl. This difference was statistically significant [p=0.006] (Table 2).

As shown in Table 3, 97.3% of cases have serum vitamin D level of less than 30ng/ml; 81.3% of the patients had vitamin D deficiency (<20ng/ml) and16% had insufficiency(20-<30ng/ml)

There was statistically significant negative correlation between vitamin D level and severity of asthma. The mean levels of serum 25(OH) D3 (vitamin D) in asthmatic patients are; mild persistent: 21.54±11.05ng/dl, moderate persistent: 15.43 ±4.60ng/dl and severe persistent: 10.60±5.57ng/dl; p value of < 0.001 which is highly significant.(Table 4)

As shown in Table 5, the mean value of vitamin D3 level is 11.50 ±4.74ng/ml, 15.07 ± 5.9ng/ml, and 19.79 ± 9.70ng/ml for % predicted FEV1 of <60%, 60-79% and >80% of respectively.p value is <0.001 which is statistically significant.

Table-1: Distribution of subjects according to sex

Sex	**No of patients**	**Percent**
Female	29	38.7
Male	46	61.3
Total	75	100.0

Table- 2-Serum Alkaline phosphatase with severity of Asthma

SEVERITY OF ASTHMA	**Mean S.ALK PHOSPHATASE(IU/L)**	**SD**
Mild Persistent [25]	180.72	74.982
Moderate persistent [25]	203.43	48.273
Severe persistent [25]	248.38	97.138

Table 3. Serum 25 (OH) D3 level with severity of asthma

SEVERITY OF ASTHMA	Vitamin D levels		
	<20	20--30	>30
Mild Persistent	17(68%)	6(24%)	2(8%)
Moderate persistent	20(80%)	5(20%)	0(0%)
Severe persistent	24(96%)	1(4%)	0(0%)
Total	61(81.3%)	12(16%)	2(2.7%)

Table 4. Mean serum vitamin D3 with severity of asthma

SEVERITY OF ASTHMA	No of patients	Mean S. VITAMIN D3(ng/ml)	± SD	Minimum	Maximum	p value
Mild	25	21.54	11.05	9.50	48.00	<0.001 [significant] ANOVA F=10.64
Moderate	25	15.43	4.60	9.50	25.50	
Severe	25	10.60	5.57	4.10	21.40	
Total	75	15.57	8.52	4.10	48.00	

Table 5: Serum Vitamin D level with % of predicted FEV1

% Predicted FEV1	**Mean S. VITAMIN D3(ng/ml)**	**± SD**	**No of cases**
<60	11.50	4.748	22
60-79	15.07	5.994	29
>80	19.79	9.704	24
Total	15.53	7.750	75

V. Discussion

Bronchial asthma is a major health problem especially among children. It has dramatically increased worldwide over the last few decades, in both developed and developing countries. Vitamin D deficiency may predispose to allergic phenotype of asthma and epidemiological evidences suggest that lack of vitamin D has been linked to increased incidence of asthma and increased severity of asthma in children.Vitamin D is a potent modulator of the immune system[11].

Being a tropical country, Vitamin D deficiency is supposed to be uncommon in India (31). However from the data available in published literature vitamin D deficiency is very common in India in all the age groups and both the sexes across the country. This had been shown by Harinarayan and Marwaha (20,23,24). Prolonged breastfeeding without vitamin D supplementation, maternal vitamin D deficiency, poor diet and limited exposure to sunshine have been suggested as major contributors to vitamin D deficiency (32,33).

This study sought to detect the incidence of vitamin D deficiency(<20ng/ml), insufficiency(20-<30ng/ml) and normal level(30-60ng/ml) among 75 asthmatic children and to correlate the relation between vitamin D levels and severity of asthma.

A total of 75 asthmatic children aged between 6 and 15 years were studied; equal number of age matched asthmatic patients with mild persistent(25), moderate persistent (25) and severe persistent asthma(25) was taken according to GINA guidelines[1].There were 46 (61.3%) boys and 29 (38.7%) girls in the study. This also reflect the OPD attendance of Pulmonary clinic, Department of Pediatrics in S.P.M.C.H.I , S.M.S medical college,Jaipur where the ratio is 1.7:1. It also show that the incidence of asthma is predominant in boy than in girls. The same finding was also seen in the previous study conducted by Mahmoud T on Egyptian children [3]. It is also in accordance with the study conducted on 3283 Qatari children by Jenahi[14]; a study conducted in Lucknow, India by Awasthi [25] and also in Thailand by Wijittra Krobtrakulchai[29]. In childhood, twice as many males as females are asthmatic, but by adulthood the sex ratio has equalized [5]. Male gender is a risk factors for having childhood asthma in the U.S [4].

The mean value of serum alkaline phosphatase was significantly higher in all patients with asthma. This is shown in a study byMahmoud T. Abd in Eygyptian children where 100%(n=60 out of 60) of asthmatic children show raised serum alkaline phosphatase (ALP) as compared to 37.5% (n=14 0ut of 40) of control have normal ALP; p value is <0.001 which is highly significant[3]. In the our study we observe the elevated serum levels of alkaline phosphatase. It was highest in severe asthmatics group 248.38±97.138mg /dl and was lowest in mild asthmatics group180.72±74.982mg /dl. This difference is statistically significant [p=0.006]. This could be explained by vitamin D deficiency which causes secondary hyperparathyroidism leading to increase turnover of osteoid tissue and elevated serum levels of alkaline phosphatase.

Several studies in the past have concluded that vitamin D deficiency is associated with an increased incidence of asthma and other allergy symptoms. In a cross sectional study carried out in 170 children of age range from 2-14 years by Uysalol et al , it show that 90.6% (n=77 out of 85) of asthmatic patient have vitamin D deficiency as compared to 67.7% (n=55 out of 85) in control group with p value of <0.001.The finding is also in accordance with a cross sectional study conducted by Somashekar on 44 asthmatic and 44 healthy children in Bangalore,India which show that the mean serum 25 hydroxy cholecalciferol (Vitamin-D) levels in asthmatic children was 12.88±1.79ng/mL, which was significantly lower than the mean serum vitamin D levels in the healthy controls (16.49±1.13ng/mL). 68.18% of the asthmatic children had deficient serum vitamin D levels (≤15ng/mL) and 31.28% of them had insufficient serum vitamin D levels (>15ng/mL to <20ng/mL) that is 100% of asthma children have deficient serum vitamin D level[42]. This is also seen in several epidemiological studies conducted in African American(13), Costa rica(12) , Iran(17) and Turkey(28). In our study, we found that serum vitamin D was significantly lower among 97.3% of cases; 81.3% of the patients had vitamin D deficiency and16% had insufficiency. Hence our study finding is in accordance with the previous studies and vitamin D deficiency is common in asthmatic patient.

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and16% had insufficiency. Hence our study finding is in accordance with the previous studies and vitamin D deficiency is common in asthmatic patient.

Several studies have examined the relationship between vitamin D deficiency and asthma exacerbations and markers of more severe disease. Many studies have shown that low vitamin D levels were associated with increase in severity of bronchial asthma [3,7,8,11,12,16,28,30,42].El-naggar et al observe that serum vitamin D level in intermittent asthma is 41.1±11.8ng/ml,mild persistent asthma is 35.1±6.4ng/ml, moderate persistent asthma is 24.7±3.8ng/ml and severe persistent asthma is 20.7±3.8ng/ml with p value of < 0.001 which is statistically significant. It conclude that there is a inverse correlation between vitamin D level and severity of asthma[39]. In another study conducted by Elnady et al in Egyptian children show that there is highly significant negative correlation between the vitamin D level and the grade of severity ($r = -0.903$, $P < 0.000$) and the degree of control of bronchial asthma ($r = -0.923$, $P < 0.000$) The accuracy of vitamin D as a predictor of asthma was found to be 88% by automatic linear modeling[41]. Avinash Kumar et al observed serum vitamin D level of <10ng/ml in 7.69% of intermittent asthma, 3.5% of mild persistent asthma, 35% of moderate persistent asthma and 100% of severe persistent asthma; p value is < 0.001 which is highly significant and conclude that vitamin D deficiency is associated with severity of childhood asthma[48]. In our study, the mean levels of serum vitamin D in asthmatic patients are; mild persistent: 21.54±11.05ng/dl, moderate persistent: 15.43 ±4.60ng/dl and severe persistent: 10.60±5.57ng/dl; p value of < 0.001 which is highly significant. 64% (n=16 out of 25) of severe asthmatic patients have serum vitamin D level of < 10ng/ml while none of the mild asthmatic patient have levels < 10ng/ml; p value is 0.021 which is also statistically significant. This means that the higher the level of serum vitamin D, the lesser the degree of bronchial asthma severity. This finding is consistent with the above mention studies. Our finding is also in accordance with the work conducted by Litonjua *et al.* [16], who proved that low vitamin D levels were associated with worse bronchial asthma symptoms and poorer lung function measures. Thus our study demonstrated a highly significant negative correlation between serum vitamin D levels and the severity of asthma.

Few studies have shown that children with insufficient vitamin D levels were found to have a slightly lower mean FEV1 with lower vitamin D3 levels [19,26].A.R Somashekar et al observe that predicted FEV1for serum vitamin D level of <15ng/ml is 68±4.1% and 81.5±3.7% for level of >15ng/ml - <20ng/ml; p value of <0.001 which is statistically significant and show a direct correlation between vitamin D levels and predicted FEV1 [42]. Significant positive correlations were found between the serum vitamin D level and % of predicted FEV1 ($r = 0.871$, $P < 0.001$) in a study conducted by Elnady in Egypt [41]. In our study, we observe that the predicted FEV1 for the mean value of vitamin D level of 11.50 ±4.74ng/ml, 15.07 ± 5.9ng/ml, and 19.79 ± 9.70ng/ml is <60, 60-79 and >80% respectively; p <0.001, which is significant. This is also supported by study conducted by Brehm which conclude that insufficient vitamin D status predicts a lower FEV1 [19]. The same is observe by Alyasin and suggest that lower predicted FEV1 were significant predictors of lower 25(OH) D levels [17].

Irreversible loss of lung function can be caused by airway adaptation occurring early on in asthma. Airway adaptation or remodelling involves structural changes in the walls of the airways caused by continual injury and repair processes.Vitamin-D may modulate airway remodelling and lung function by affecting the growth and contractility of airway smooth muscle. Vitamin-D inhibits transforming growth factor- β (TGF-β), matrix metalloproteinases and fibroblast proliferation[9].

Our study has some limitations: The sample size was relatively small (n =75). A larger sample size would have increased our statistical power to detect associations. As with most other studies investigating the role of vitamin-D in asthma, our design was cross-sectional, thus limiting our ability to establish a causal link between vitamin-D and asthma morbidity. A healthy control was not taken but at the same time age match patients were compared in each group of patient like control group. In our study we tried but could not match the sex of the patients beause boys were out numbered as compared to girls and secondly total numbers of patient studied were limited i.e 25 in each group of severity of asthma. Even though there is a strong relation of lung function and 25(OH) D level, we could not establish a direct mechanistic link between vitamin D deficiency and asthma in children Furthermore, many confounding factors can affect vitamin-D levels or asthma severity. Long-term follow-up studies focusing on changes in vitamin-D status and asthma parameters will be needed to elucidate the effect of vitamin-D status on asthma.

VI. Conclusion

The present study suggests that vitamin D deficiency is relatively frequent in asthmatic patients (97.3%) who were attending to pediatric department of S.P.M.C.H.I, S.M.S Medical college, Jaipur.

There was a significant inverse relationship between vitamin D levels and severity of asthma symptoms. Measuring serum levels of vitamin D may be considered in patients with bronchial asthma especially

un-controlled or severe asthmatic patients. Further studies are needed to determine the role of vitamin D in the treatment of asthma in term of improvement of lung function test and severity of asthma.

References

[1]. Global Initiative for Asthma [GINA] (2015): Global Strategy for Asthma Management and Prevention (2015 update)
[2]. The Global Asthma Report 2014
[3]. Mahmoud T. Abd El-Menem, Manal M. Abd Al-Aziz, Waleed M. El-Guindy,Nihal A. El Banna et al. The frequency of vitamin D deficiency among asthmatic Egyptian children. Egypt J Pediatr Allergy Immunol 2013;11(2):69-73.
[4]. Kleigman, Stanton, ST Geme, Schor, Behrman. Nelson Textbook of Pediatrics 20th Edition; Part XV.
[5]. Longo, Fauci, Kasper, hauser,Jameson, Loscalzo. Harrison's Principles of Internal Medicine; 18th Edition.
[6]. Piyush gupta, PSN Menon, Siddarth Ramji, Rakesh Lodha- PG Textbook of Pediatrics, part viii.
[7]. Bener A, Ehlayel MS, Tulic MK, Hamid Q. Vitamin D Deficiency as a Strong Predictor of Asthma in in Qatari children. Int Arch Allerg Immunol 2012; 157(2):168-175.
[8]. Chinellato I, Piazza M, Sandri M, Peroni D, Piacentini G, Boner al. Vitamin D serum levels and markers of asthma control in Italian children. J Pediatr.2011; 158: 437-41.
[9]. Hollick MF: Vitamin D deficiency. N Engl J Med 2007; 357: 266-281.
[10]. Holick MF. High prevalence of vitamin D inadequacy and implications for health. Mayo Clin Proc 2006; 81:353–373.
[11]. Barday L: Vitamin D insufficiency linked to asthma severity. Am J Respir Crit Care Med 2009; 179: 739–742.
[12]. Brehm JM, Celedón JC, Soto-Quiros ME, Avila L, Hunninghake GM, Forno E, Laskey D, Sylvia JS, Hollis BW, Weiss ST, Litonjua AA: Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica. Am J Respir Crit Care Med 2009; 179: 765–771.
[13]. Freishtat RJ, Iqbal SF, Pillai DK, Klein CJ, Ryan LM, Benton AS, Teach SJ: High prevalence of vitamin D deficiency among inner city-African-American youth with asthma in Washington, D.C. J Pediatr 2010; 156: 948-952.
[14]. Bener A, Janahi I, Sabbah A: Genetics and environmental risk factors associated with asthma in school children. Eur Ann Allergy Clin Immunol 2005; 37: 163–168.
[15]. ISAAC Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood.Lancet 1998; 351: 1225–1232.
[16]. Litonjua AA, Weiss ST: Is vitamin D deficiency to blame for the asthma epidemic? J Allergy Clin Immunol 2007; 120: 1031–1035.
[17]. Alyasin S, Momen T, Kashef S, Alipour A, Amin R. The relationship between serum 25 hydroxy vitamin D levels and asthma in children. Allergy Asthma Immunol Res 2011; 3:251–255.
[18]. Janahi IA, Bener A, Bush A. Prevalence of asthma among Qatari school children. International Study of Asthma and Allergies in Childhood, Qatar. Pediatr Pulmonol 2006; 41: 80–86.
[19]. Brehm JM, Schuemann B, Fuhlbrigge AL, Hollis BW, Strunk RC, Zeiger RS et al. Serum vitamin D levels and severe asthma exacerbations in the Childhood Asthma Management Program study. J Allergy Clin Immunol 2010; 126: 52–58
[20]. Prevalence of Vitamin D Deficiency among Healthy School Children in Jaipur District, Rajasthan, India. Int J Pediatr, Vol.3, N.4-2, Serial No.20, Aug 2015.
[21]. American Thoracic Society. Standardization of spirometry: 1994 update. Am J Respir Crit Care Med1995;152:1107–1136.
[22]. Papadopoulos et al.International consensus on (ICON) pediatric asthma. Allergy 67 (2012) 976–997 © 2012 John Wiley & Sons A/S
[23]. Khadilkar AV. Vitamin D deficiency in Indian Adolescents. Indian Paediatr 2010; 47:756-757.
[24]. Harinarayan CV, Joshi SR. Vitamin-D status in India: Its implications and remedial measures. J Assoc Physicians India 2009; 57:40-48.
[25]. Awasthi S, Kalra E, Roy S, Awasthi S. Prevalence and risk factors of asthma and wheeze in school-going children in Lucknow, North India. Indian Pediatr 2004; 41: 1205-1210.
[26]. Searing DA, Zhang Y, Murphy JR, Hauk PJ, Goleva E, Leung DY. Decreased serum vitamin D levels in children with asthma are associated with increased corticosteroid use. J Allergy Clin Immunol 2010; 125:995-1000.
[27]. Manbir S, Thomas B. The role of vitamin D in asthma. Ann Allergy Asthma Immunol 2010; 105:191–199.
[28]. Childhood asthma and vitamin deficiency in Turkey: is there cause and effect relationship between them? Metin Uysalol, Levent cem mutlu,Gemze Varol Saracoglu, Erkut Karasu, Savas Guzel, Semra Kayaoglu and Nadret Uzel. Italian Journal of Pediatrics 2013,39:78.http://www.ijponline.net/content/39/1/78.
[29]. The effect of vitamin D status on Pediatrics Asthma at University Hospital, Thailand. Wijittra Krobtrakulchai, Jittima Praikanahok and Orathai Jirapongsananuruk.Allergy Asthma immune res. September 2013; 5(5) : 289-29
[30]. Severe and uncontrolled adult asthma is associated with vitamin D insufficiency and deficiency.Stephanie Korn, Marisa Hübner, Matthias Jung, Maria Blettner, and Roland Buhl.Korn et al. Respiratory Research 2013, 14:25.
[31]. Hodgkin P, Hine PM, Kay GH, Lumb GA, Stanbury SW. Vitamin-D deficiency in Asians at home and in Britain. Lancet 1973; 92: 167-171.
[32]. Bener A, Alsaied A, Al-Ali M, Al-Kubaisi A, Basha B, Abraham A, Guiter G, Mian M. High prevalence of vitamin D deficiency in type 1 diabetes mellitus and healthy children. ActaDiabetol 2009; 46: 183–189.
[33]. Bener A, Alsaied A, Al-Ali M, Hassan AS, Basha B, Al-Kubaisi A, Abraham A, Mian M, Guiter G, Tewfik I. Impact of lifestyle and dietary habits on hypovitaminosis D in T1DM and healthy children from Qatar: a sun rich country. Ann Nutrition Metab 2008; 53: 215–222.
[34]. Bener A, Ehlayel MS, Tulic MK, Hamid Q. The Childhood Asthma Management Program Research Group.Long-term effects of budesonide or nedocromil in children with asthma. N Engl J Med 2000;343(15):1054–63.
[35]. Camargo CA Jr, Ingham T, Wickens K, Thadhani R, Silvers KM, Epton MJ, et al. Cord-Blood 25-Hydroxyvitamin D Levels and Risk of Respiratory Infection, Wheezing, and Asthma. Pediatrics.2011; 127: e180- 187
[36]. Keet CA, McCormack MC, Peng RD, Matsui EC. Age- and atopy-dependent effects of vitamin D on wheeze and asthma.J Allergy Clin Immunol. 2011;128):414-416.e5
[37]. Kumar, Abbas, Aster. Robbins Basic Pathology (9th Edition) chapter 12.
[38]. The Relationship between Vitamin D Statuses and. Young Adult Women Asthma. ShiyingBian
[39]. Eman M. El-naggar, Nesrin M. Handoka, Soha E. Younes, Adel A. Abd El-Rahman. Detection of Vitamin (D) deficiency in children and adolescents suffering from bronchial asthma in Suez Canal University Hospital, Ismailia.Egypt J Pediatr Allergy Immunol 2015;13(2):73-77.

[40]. Atul Gupta, AliesSjoukes, David Richards,WinstonBanya, Catherine Hawrylowicz, Andrew Bush, and Sejal Saglani1.Relationship between Serum Vitamin D, Disease Severity, and Airway Remodeling in Children with Asthma.Am J Respir Crit Care Med. 2011 December 15; 184(12): 1342–1349. doi:10.1164/rccm.201107-1239OC.
[41]. Hala G. Elnady, Eman M. Fouda, Ola M. Elsheikh, Inas R. ElAlameey, Amal I. Elshafie, Lobna S. Sherif, Eman R. Youness, Nadia A. Mohamed. Serum vitamin D level as a predictor of bronchial asthma in Egyptian children, 1687-4293 © 2013 Journal of the Arab Society for Medical Research.
[42]. A. R. Somashekar,[1] Ashwini B Prithvi,[2] and M. N. VanithaGowda. Vitamin D Levels In Children with Bronchial Asthma. ClinDiagn Res. 2014 Oct; 8(10): PC04–PC07.
[43]. CantornaMT,Zhu Y, Froicu M, Wittke A. VitaminDstatus, 1,25-dihydroxyvitamin D3, and the immune system.Am J ClinNutr 2004;80:1717S-20S.
[44]. Van Etten E, Mathieu C. Immunoregulation by 1,25-dihydroxyvitamin D3: basic concepts. J Steroid BiochemMolBiol 2005;97:93-101.
[45]. May E, Asadullah K, Zugel U. Immunoregulation through 1,25-dihydroxyvitamin D3 and its analogs. Curr Drug Targets Inflamm Allergy 2004;3:377-93.
[46]. Cantorna MT. Vitamin D and its role in immunology: multiple sclerosis,and inflammatory bowel disease. ProgBiophysMolBiol 2006;92:60-4.
[47]. Taback SP, Simons FE. Anaphylaxis and vitamin D: a role for the sunshine Hormone. J Allergy Clin Immunol 2007;120:128-30
[48]. Avinash Kumar, Ratan Gupta, P K Debata, Dinesh K Taneja, K C Aggarwal. Levels of Vitamin D in Patients of Childhood Asthma.