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Original Article

Asthma is associated with levels of vitamin D3 and blood group in the southwest of Iran

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Abstract

Introduction

The prevalence of vitamin D3 deficiency (VDD) is high even though it exert several consequences. According to the literature, there is a likely relationship between vitamin D3 levels and the development of asthma. IgE is one of the critical factors in developing the symptoms of allergic diseases. The present study aimed to investigate the association between vitamin D3,IgE, and blood group with asthma in patients in the Southwest of Iran.

Methods

Following a cross-sectional design, individuals with asthma and healthy volunteers aged 16 years old, who visited hospitals and clinics in Abadan (a city in the Southwest of Iran), were studied. The ELISA kit measured the serum levels of vitamin D3 and IgE, and the participants' blood groups were also determined.

Results

The serum levels of vitamin D3 were significantly lower in the asthma patients than in the control group, and there was a negative relationship between these variables. There was also a relationship between asthma and blood group. Furthermore, the serum level of IgE in asthma patients increased significantly compared to the control group. A negative correlation was also noticed between the serum levels of IgE and vitamin D3 in the asthma patients.

Conclusion

Given the relationship between asthma and VDD, it is necessary to evaluate the serum level of vitamin D3 in a population, even in low latitude regions, and provide vitamin D3 supplements to adjust lifestyle.

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1. Introduction

Asthma is a widespread chronic disorder with a global prevalence of 334 million [1], the main symptoms of which are volatile respiratory signs and airflow obstruction. The symptoms are triggered by various factors, such as airway inflammation and remodeling. However, it is worth noting that such symptoms are non-specific and may include wheezing, dyspnea, chest pain, and cough. The main characteristic features of asthma are caused by the pattern of symptoms, such as nature, timing, triggers, and treatment responses [2]. In humans, the primary source of vitamin D3 is exposure to sunlight (wavelength band of 290–315 nm).

Special attention has been paid to vitamin D3 deficiency (VDD) in recent years. In a similar vein, lifestyle changes, particularly nutritional and behavioral, are mentioned as the leading causes of VDD [3]. Several studies have introduced the musculoskeletal effects of VDD; nevertheless, the development of several pulmonary diseases, such as asthma, is attributed to VDD [4-6]. The IgE

antibody, stimulated by inflammation, is similar to allergic disorders affecting one-fifth of the world's population. It is a significant part of immediate hypersensitivity reactions [7].

IgE and mast cells are available in the mucosal tissues; hence, the IgE antibodies are the primary defensive molecules against invading pathogens. The main part of allergic reactions mediated by the IgE–FcεRI complex on mast cells is highly sensitive and is characterized by the presentations of various allergy target organs, including the skin, nose, respiratory system, and gut (food-allergic responses) [7, 8].

As a complicated carbohydrate-based molecule, the activities of the antigen of the ABO blood group system affect the membrane of red blood cells [9]. However, the biological activity of blood groups is not well-recognized. Furthermore, most blood group antigens contribute remarkably to cell-cell recognition and self-declaration mechanisms by acting as receptors or surface markers [10]. Accordingly, such antigens can act as a receptor for micro-organisms or substances, including toxins or allergens, affecting sensitivity against different infections [11]. According to the evidence, ABO blood type is not associated with the increased likelihood of allergy development.

Nevertheless, several studies have reported relationships between ABO blood groups with enhanced sensitivity to health issues, such as cardiovascular problems, cancer, and parasite-related diseases [12, 13]. In the 1960s, some observational research reported that the ABO agglutinins, found in several pollens such as grasses, flowers, and trees, might affect cells containing blood group antigens in the respiratory epithelium [14]. This would, in turn, increase the likelihood of the relationship between ABO blood groups and allergic disorders. Limited evidence is available on the relationship between vitamin D3 levels and asthma in Iran. Accordingly, the present study aimed to evaluate the relationship between the serum levels of vitamin D3 and IgE and ABO blood groups in cases suffering from asthma in the Southwest of Iran.

2. Methods

2.1. Study population

This case-control study was conducted on 15-to-65-year-old patients referring to the hospitals and clinics in Abadan from 2019-2020. We categorized patients with and without asthma into two case (n=60) and control (n= 60) groups. The Ethics Committee of the Abadan University approved the study. Oral and written informed consent was received from the participants.

Inclusion criteria were confirmed asthma, and no treatment received yet. Exclusion criteria were suffering from chronic disorders such as rheumatoid arthritis, multiple sclerosis, Crohn's disease, cystic fibrosis, hepatic and renal disorders, pregnant ones, and those using vitamin D3 supplements. The participants' demographic information, including age and gender, was collected. Moreover, Spirometry was performed to investigate the lung function of all subjects.

2.2. Chemicals and materials

The human vitamin D ELISA kit was obtained from Sigma (Germany). The human IgE ELISA kit was purchased from Multisciences (China). Monoclonal antibodies for the blood group typing kit were obtained from the Cinnaclon Company (Iran).

2.3. Measurement of 25-hydroxyvitamin D [25(OH)D3]

We evaluated the serum levels of 25-hydroxyvitamin D [25(OH)D3] in all participants according to the manufacturer's instructions using ELISA. VDD was considered serum 25(OH)D3 < 10 ng/ml. Furthermore, the serum vitamin D levels of 10-30 ng/mL were defined as insufficient, while the serum levels of

30-100 ng/mL were defined as sufficient. The levels >100 ng/ml were described as vitamin D toxicity.

2.4. IgE Measurement

Immunoglobulin E (IgE) serum levels were measured in all subjects according to the manufacturer's instruction and using ELISA.

2.5. Detection of ABO blood group

The ABO blood groups of all participants were determined using the blood sample.

2.6. Lung function

Spirometry was performed in accordance with the American Thoracic Society guidelines. FEV1, FVC, and FEV1 /FVC were assessed in all participants.

2.7. Statistical analysis

Data were analyzed with the SPSS software version 26. The results are expressed as mean ± SD. An unpaired t-test was used to compare the two groups. In this study, $p < 0.05$ was set as the significance level. Linear regression was used to find the relationships between variables.

3. Results

3.1. Participants

The participants' demographic characteristics are presented in Table 1. The mean age of the asthma patients and the healthy volunteers was 38.1 and 35 years, respectively. In this study, 60% of the asthmatic subjects were female, while the frequencies of gender were the same.

According to the predicted FEV1 ratio, lung function characteristics were 94% in the control group and 81% in the asthma subjects. The expected FEV1 ratios in the healthy and asthmatic subjects were 96% and 93%, respectively. Furthermore, the FEV1 /FVC ratio was 92 in the control group and 78 in the asthma group.

Table 1. Participants' demographic characteristics

	Control group	Asthma group
Sex	50% Female 50% Male	60% Female 40% Male
Average Age(Year)	35.6	38.1
FEV1	94%	81%
FEC	96%	93%
FEV1/FVC ratio	92	78

3.2. Serum 25(OH) D3 and IgE levels in subjects with asthma and the controls

Figure 1 shows that serum 25(OH) D3 levels were considerably lower in the patients with asthma than in the controls ($p< 0.001$). Serum IgE levels in subjects with asthma and the controls are presented in Fig. 2, according to which serum IgE levels significantly increased in the asthmatic cases than in the controls ($p< 0.001$).

3.3. Frequency of blood groups

Figure 3.a shows the frequency of the blood groups in the patients with asthma and the controls. According to the results, blood groups A and B had the same frequency and were more frequent phenotypes (n=19), and the AB phenotype was

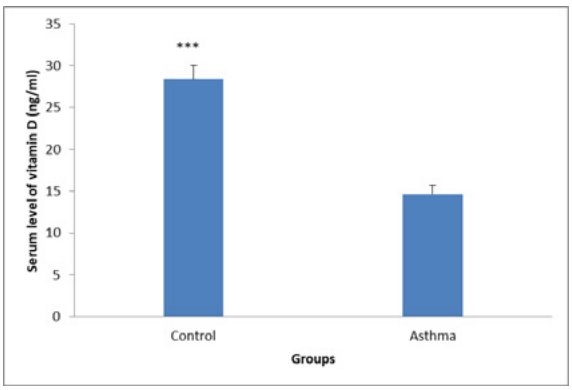

Figure 1. Serum levels of vitamin D3 in control and asthma subjects. The level of vitamin D3 was significantly lower in compare to control group. (t-test, *** $p<0.001$)

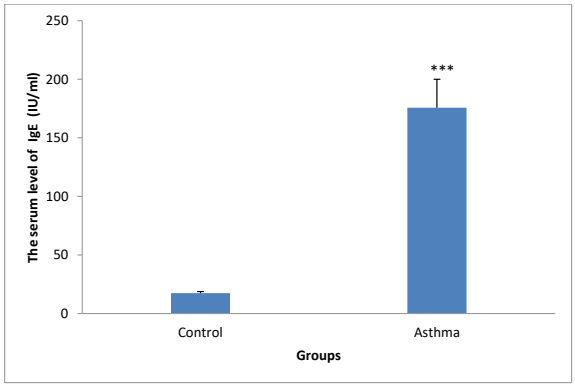

Figure 2. Serum levels of IgE in control and asthma subjects. The level of IgE was significantly increased in compare to control group. (t-test, *** p<0.001)

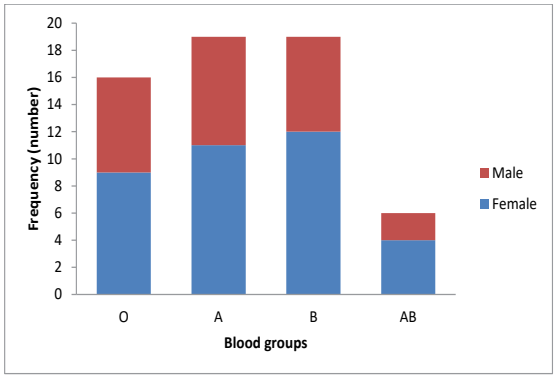

Figure 3 a. Frequency of blood groups based on sex in asthmatic patients. Patients with A and B blood groups had more frequency and less frequency was belonging to AB blood group.

the least regular in asthmatic patients (n=6). As depicted in Fig 3. b, AB phenotype was the most frequent blood group (n=22) in healthy volunteers, and blood group O was the least frequent (n=12) in the control group.

3.4. Frequency of asthma patients and healthy volunteers by vitamin D3 levels

Regarding serum vitamin D3 levels in asthma subjects, four levels were considered: deficient (<10ng/ml), insufficient (10-30ng/ml), sufficient (30-100ng/ml), and toxicity (>100ng/ml). The results showed that 30% of asthma patients had VDD (14 females and six males), and 58.3% (19 females and 16 males), and 5% (three females and two males) had insufficient and sufficient vitamin D3 levels (Fig. 4.a).

As presented in Fig.4.b, vitamin D3 levels in the control group were as follows: 6.6% had VDD (one female and three males), 61.6 % (18 female

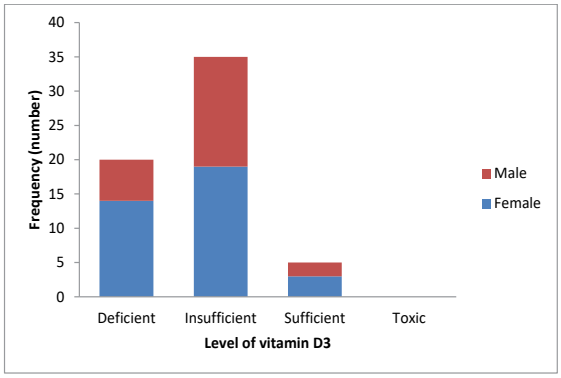

Figure 4a. Frequency of different levels of vitamin D3 in asthmatic patients. 30% of asthma patients had VDD (14 females and six males).58.3% of them had insufficient vitamin D3 (19 females and 16 males), and 5% had sufficient (three females and two males) levels of vitamin D3.

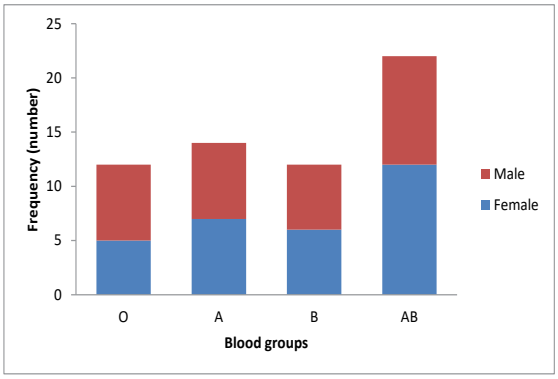

Figure 3b. Frequency of blood groups based on sex in healthy subjects. Volunteers with AB and B blood groups had more and less frequency respectively.

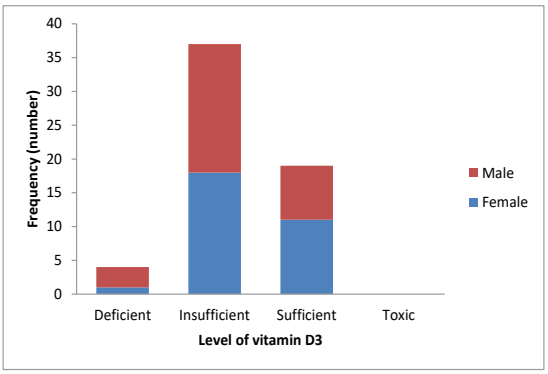

Figure 4b: Frequency of different levels of vitamin D3 in healthy volunteer. 6.6% had VDD (one female and three males), 61.6 % (18 females and 19 male) had insufficient, and 31.6 % of had sufficient (11 females and eight males) levels of vitamin D3.

and 19 male) had insufficient vitamin D3 levels, and 31.6 % of had sufficient (11 females and eight males) vitamin D3 levels. Nobody had vitamin D3 toxicity in both groups.

3.5. Relationship between asthma with serum levels of vitamin D, gender, and blood group

The linear regression model was used to find the relationship between asthma with vitamin D3 levels, gender, and blood group. In this model, asthma was considered a dependent variable.

Gender, vitamin D3, and blood group were independent variables. According to the analysis, there was a significant negative correlation between vitamin D3 and asthma (p=0.001) (Table 2). Furthermore, the blood group significantly correlated with asthma (p=0.038); however, there was no correlation between asthma and gender (p=0.7).

Table 2. Relationship between asthma with serum vitamin D 3 level, gender, and blood group

Parameters		B	Std. Error	95% Wald Confidence Interval		Hypothesis Test			95% Wald Confidence Interval for Exp(B)		
				lower	Upper	Wald Chi-Square	df	sig	Exp(B)	Lower	Upper
Thereshould	[asthma=1,00]	-1.115	1.1520	-3.373	1.143	.936	1	.333	.328	.034	3.137
	[asthma=2,00]	.722	1.1516	-1.535	2.979	.393	1	.531	2.059	.216	19.675
D-level		-.139	.0427	-.223	-.056	10.637	1	.001	.870	.800	.946
Sex		-.154	.5273	-1.188	.880	.085	1	.770	.857	.305	2.410
Blood groups		.591	.2844	.033	1.148	4.313	1	.038	1.805	1.034	3.152
(Scale)		1[a]									

Table 3. Correlation between IgE and vitamin D3 levels in asthma patients

		IgE	D- level
IgE	Pearson correlation	1	-.298*
	Sig. (2-tailed)		.021
	N	60	60
D-level	Pearson correlation	-.298*	1
	Sig. (2-tailed)	.021	
	N	60	60

*. Correlation is significant at p= 0.05 (two-tailed).

3.6. Correlation between serum level of vitamin D3 and IgE levels

As presented in Table 3, Pearson Correlation was used to evaluate the correlation between the serum level of vitamin D3 and IgE levels. There is a significant negative correlation between the serum level of vitamin D3 and IgE levels in asthma patients (p=0.021)

4. Discussion

The findings revealed that the serum levels of vitamin D3 were associated with asthma in the southwest of Iran. VDD can be considered an effective factor in the incidence of asthma. Although the area is located at a low latitude and the sunlight is intense, the VDD is observed in the population. Naturally, vitamin D3 is not available in a majority of foods.

The primary sources of vitamin D3 are exposure to sunlight, fortified foods, and supplements [15], among which the first one has the highest contribution. Despite reports of high solar exposure in some regions, VDD has been observed in healthy individuals[16]. It can be attributed to several behavioral parameters such as sunscreen use, time spent outside, clothes, and intrinsic variables, including melanin content of the skin or declined/enhanced cutaneous production of vitamin D3 [17]. These factors arouse VDD in the southwest of Iran.

Vitamin D3 blocks smooth muscle escalation in a dose-dependent way in human smooth muscle cells sensitized with asthmatic serum [18], which inhibits cell growth by preventing the advancement of the cell cycle, not through cell death. Moreover, vitamin D3 can intervene in cell proliferation in the cell cultures of the muscle [19]. The exact relationship between VDD and asthma development is unclear yet, and several mechanisms have been hypothesized. First, it affects the T helper cell types 1 and 2 and regulatory T cells [20-22]. Second, consuming foods rich in vitamin D3 affects the respiratory system of those with asthma (the same may happen for healthy individuals) [23]. Third, vitamin D3 affects the microarray gene expression signatures in bronchial smooth muscle cells. According to the literature, cell movement, growth, and survival have the highest susceptibility to such effects, reflecting the contribution of vitamin D3 in remodeling airways [24]. Fourth, there is an association between polymorphisms in the gene encoding the vitamin D3 receptor and asthma pathogenesis [25, 26].

Such studies have documented the relationship between asthma and vitamin D3. Brehm et al. (2009) showed that youngsters with asthma have considerably declined 25(OH)D3 levels compared to their healthy counterparts (4). Montero-Arias et al. (2013) showed that vitamin D3 levels in 91% of the asthmatic patients were < 20 ng/dl in Costarica [27]. Gupta et al. (2011) demonstrated that lower vitamin D3 levels in youngsters with asthma were correlated with poor asthma management and

respiratory system [28]; therefore, our findings confirm these findings.

The remarkable role of IgE under allergic conditions stimulates mast cells to secrete biologically-active mediators in an antigen-specific way. Mast cells are available in all vascularized tissues of vertebrates [29]. In response to stimulation by IgE through FcεRI and specific antigens or several other endogenous or exogenous materials, the mast cells can release various mediators either enhancing or down-regulating the inflammation. Moreover, it can affect the remodeling and activity of tissues [30]. Further, IgE can be secreted locally by B cells in the gut- or respiratory system-associated lymphoid tissues and in the lymph nodes of those suffering from allergic reactions to foods [31], allergic rhinitis (either seasonal or perennial) [32], or atopic and non-atopic asthma [32].

In this survey, the levels of IgE significantly increased in the asthma patients compared to the control group. On the other hand, a negative correlation was observed between the levels of vitamin D3 and IgE in asthma patients. Since the IgE level increases in asthma, and the levels of vitamin D3 play a critical role in the development of asthma; thus, the correlation between vitamin D3 and IgE levels was examined. Our findings revealed a negative correlation between these variables. Brehm et al. demonstrated a relationship between the severity of asthma with vitamin D3 and IgE levels [4]. Hatami et al. (2014) reported that asthma in children was associated with vitamin D3 and IgE levels [33], which is consistent with our findings.

The antigens of the ABO histo-blood group contain carbohydrate-based molecules secreted on the surface of erythrocytes, platelets, epithelium, sensory neurons, and vascular endothelium (34). Regardless of their major contribution to transfusion, growing evidence has documented the relationship between such antigens and the development of many health problems, including infectious and neoplastic disorders [35]. According to some studies, those with the O blood group are at the increased risk of asthma development [36-39]. Furthermore, Yaro et al. (2015) reported that most asthmatic patients had blood group A compared to the controls [40].

The present study revealed a relationship between asthma and blood groups in the southwest of Iran. These findings also indicated that some ABO blood groups were associated with an increased risk of developing allergic health problems. Moreover, there was a correlation between allergic health problems and ABO blood groups, which can be affected by genetic variations in different populations. Nevertheless, the precise relationship between blood type and asthma is not clear yet.

Since individuals with asthma have lower levels of vitamin D3, continuous monitoring of vitamin D3 is recommended for the better management of those suffering from VDD. Moreover, lifestyle and nutrition patterns must be directed toward removing nutritional deficiencies in societies. However, more evaluations are suggested to clarify the close relationship between asthma and blood groups.

5. Conclusion

In this study, a close relationship was noticed between vitamin D3, IgE levels, and blood group with asthma. Accordingly, further attention to the diet or taking supplements containing vitamin D3 are suggested for this population.

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Conflicts of interests

The authors declare that there is no conflict of interest in this study.

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This project was approved by the Abadan University of Medical Sciences, Abadan, Iran.

References

1. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. lancet. 2012 ;380(9859):2163-96.
2. Papi A, Brightling C, Pedersen SE, Reddel HK. Asthma. Lancet. 2018 feb. 24;391(10122):783-800.
3. Holick MF. Vitamin D deficiency. N Engl J Med. 2007;357(3):266-81.
4. Brehm JM, Celedón JC, Soto-Quiros ME, Avila L, Hunninghake GM, Forno E, et al. Serum vitamin D levels and markers of severity of childhood asthma in Costa Rica. Am J Respir Crit Care Med. 2009;179(9):765-71.
5. 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(1):52-8. e5.
6. 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(3):437-41.
7. Gould H, Sutton B, Beavil A, Beavil R, McCloskey N. Th e biology of IGE and the basis of allergic disease. Annu Rev Immunol. 2003;21:579-628.
8. Kraft S, Kinet J-P. New developments in FcεRI regulation, function and inhibition. Nat Rev Immunol. 2007;7(5):365-78.
9. Hosoi E. Biological and clinical aspects of ABO blood group system. J Med Invest. 2008;55(3, 4):174-82.
10. Chigira M. Origin of blood-group antigens: a self-declaration mechanism in somatic cell Society. Med hypotheses. 1996;46(3):290-4.
11. Cooling L. Blood groups in infection and host susceptibility. Clin Microbiol Rev. 2015;28(3):801-70.
12. Iodice S, Maisonneuve P, Botteri E, Sandri MT, Lowenfels AB. ABO blood group and cancer. Eur J Cancer. 2010;46(18):3345-50.
13. Risch HA, Yu H, Lu L, Kidd MS. ABO blood group, Helicobacter pylori seropositivity, and risk of pancreatic cancer: a case–control study. J Natl Cancer Inst. 2010;102(7):502-5.
14. Carpeggiani C. Allergic rhinitis and association with the O blood group. Rev Bras Hematol Hemoter. 2011;33(6):406-7.
15. Lamberg-Allardt C. Vitamin D in foods and as supplements. Prog Biophys Mol Biol. 2006;92(1):33-8.
16. Binkley N, Novotny R, Krueger D, Kawahara T, Daida YG, Lensmeyer G, et al. Low vitamin D status despite abundant sun exposure. J Clin Endocrinol Metab. 2007;92(6):2130-5.
17. Heaney RP, Davies KM, Chen TC, Holick MF, Barger-Lux MJ. Human serum 25-hydroxycholecalciferol response to extended oral dosing with cholecalciferol. Am J Clin Nutr. 2003;77(1):204-10.
18. Song Y, Qi H, Wu C. Effect of 1, 25-(OH) 2D3 (a vitamin D analogue) on passively sensitized human airway smooth muscle cells. Respirol. 2007;12(4):486-94.
19. Banerjee A, Damera G, Bhandare R, Gu S, Lopez-Boado Y, Panettieri Jr R, et al. Vitamin D and glucocorticoids differentially modulate chemokine expression in human airway smooth muscle cells. Br J Pharmacol. 2008;155(1):84-92.
20. Cantorna MT, Zhu Y, Froicu M, Wittke A. Vitamin D status, 1, 25-dihydroxyvitamin D3, and the immune system. Am J Clin Nutr. 2004;80(6):1717S-20S.
21. May E, Asadullah K, Zugel U. Immunoregulation through 1, 25-dihydroxyvitamin D 3 and its analogs. Curr Drug Targets Inflamm Allergy. 2004;3(4):377-93.
22. van Etten E, Mathieu C. Immunoregulation by 1, 25-dihydroxyvitamin D3: basic concepts. J Steroid Biochem Mol Biol. 2005;97(1-2):93-101.

23. Black PN, Scragg R. Relationship between serum 25-hydroxyvitamin d and pulmonary function in the third national health and nutrition examination survey. Chest. 2005;128(6):3792-8.
24. Bossé Y, Maghni K, Hudson TJ. 1α, 25-Dihydroxy-vitamin D3 stimulation of bronchial smooth muscle cells induces autocrine, contractility, and remodeling processes. Physiol Genomics. 2007;29(2):161-8.
25. Poon AH, Laprise C, Lemire M, Montpetit A, Sinnett D, Schurr E, et al. Association of vitamin D receptor genetic variants with susceptibility to asthma and atopy. Am J Respir Crit Care Med. 2004;170(9):967-73.
26. Raby BA, Lazarus R, Silverman EK, Lake S, Lange C, Wjst M, et al. Association of vitamin D receptor gene polymorphisms with childhood and adult asthma. Am J Respir Crit Care Med. 2004;170(10):1057-65.
27. Montero-Arias F, Sedó-Mejía G, Ramos-Esquivel A. Vitamin D insufficiency and asthma severity in adults from Costa Rica.Allergy Asthma Immunol Res. 2013;5(5):283.
28. Gupta A, Sjoukes A, Richards D, Banya W, Hawrylowicz C, Bush A, et al. Relationship between serum vitamin D, disease severity, and airway remodeling in children with asthma. Am J Respir Crit Care Med. 2011;184(12):1342-9.
29. Carroll N, Mutavdzic S, James A. Distribution and degranulation of airway mast cells in normal and asthmatic subjects. Med Respir J. 2002;19(5):879-85.
30. Galli SJ, Tsai M. IgE and mast cells in allergic disease. Naure med. 2012;18(5):693-704.
31. Coeffier M, Lorentz A, Manns M, Bischoff S. Epsilon germ-line and IL-4 transcripts are expressed in human intestinal mucosa and enhanced in patients with food allergy. Allergy. 2005;60(6):822-7.
32. Kleinjan A, Vinke J, Severijnen L, Fokkens W. Local production and detection of (specific) IgE in nasal B-cells and plasma cells of allergic rhinitis patients. Med Respir J. 2000;15(3):491-7.
33. Hatami G, Ghasemi K, Motamed N, Firoozbakht S, Movahed A, Farrokhi S. Relationship between Vitamin D and Childhood Asthma: a case–control study. Iran J Pediatr. 2014;24(6):710.
34. Franchini M, Liumbruno GM. ABO blood group: old dogma, new perspectives. Clin Chem Lab Med. 2013;51(8):1545-53.
35. Franchini M, Bonfanti C. Evolutionary aspects of ABO blood group in humans. Clin Chim Acta. 2015;444:66-71.
36. Kauffmann F, Frette C, Pham Q-T, Nafissi S, Bertrand J-P, Oriol R. Associations of blood group-related antigens to FEV1, wheezing, and asthma. Am J Respir Crit Care Med. 1996;153(1):76-82.
37. Ronchetti F, Villa M, Ronchetti R, Bonci E, Latini L, Pascone R, et al. ABO/Secretor genetic complex and susceptibility to asthma in childhood. Med Respir J. 2001;17(6):1236-8.
38. Chen YL, Chen JC, Lin TM, Huang TJ, Wang ST, Lee MF, et al. ABO/secretor genetic complex is associated with the susceptibility of childhood asthma in Taiwan. Clin Exp Allergy. 2005;35(7):926-32.
39. Saini M, Yadav A. Distribution of ABO & Rh (D) allele frequency among asthmatic patients. IMPACT Int J Res Appl Nat Soc Sci. 2014;2:217-22.
40. Alo MN, Eze UA, Yaro SA, Jubril B, Nwanoke NN. Relationship between ABO and rhesus blood groups and susceptibility to asthma within Sokoto Metropolis, Nigeria. Int J mmunol. 2015;3(3):37-41.