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Serum 25-Hydroxyvitamin D Levels as a Predictive Factor for Allergic Rhinitis

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Abstract. Introduction: Allergy and 25-Hydroxyvitamin D deficiency were mentioned to be correlated. Still, there was limited number of studies in determining serum 25-Hydroxyvitamin D levels as a predictive factor, particularly in allergic rhinitis (AR). This study has never been implemented in Indonesia which the main objective was to explore this topic. **Methods:** Consecutive sampling was used in recruiting the fifteen subjects. Serum 25-Hydroxyvitamin D levels were quantified using electrochemiluminescence immunoassay (ECLIA) method while the total nasal symptom scores were acquired by enumerate all nasal symptoms. Data of serum vitamin D levels and TNSS were analysed statistically.**Results:** Based on our previous study, the predictive value was illustrated from linier regresion = 10,230 – 0,281 (vitamin D), with negative moderate correlation (r = -0,613). This result can be comparable for someone with vitamin D level of 5.66 ng/mL that could predicted as 8.64 nasal score. **Conclusion:** 25-Hydroxyvitamin D could be a predictive factor for allergic rhinitis with negative moderate correlation. Hence, in the future research needs to be implemented.

Keyword: Allergic rhinitis, vitamin D, 25-hydroxyvitamin D, allergy, total nasal symptom score, predictive factor.

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1 Introduction

Allergic Rhinitis (AR) was affected 40% in total population and keeps increasing, which is caused by nasal inflammation as the result of allergen exposure [1]. Moderate to severe AR presents in 67.5% worldwide and fazed the quality of life [2].

Family history is one of the commonly used AR as predictive factors, but it is subjective and has 48-67% specificity, 22-72% sensitivity and a predictive value of less than 40%[3]. Total IgE examination has 60-70% specificity, and 26-47% sensitivity, but it cannot predict the severity of AR, while examination of the levels

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of the immunological components in the placenta requires two or three types of tests to increase the predictive value[4].

Recent studies point out to deal with the immunomodulatory role of 25-hydroxyvitamin D that related to AR [5]. Epidemiological data reported a significant relationship between vitamin D and autoimmune, cardiovascular, asthma, cancer, and allergies [6]. Low vitamin D levels are act as predictive factor for atopy at 6 years child and asthma at 14 years patients [7]. Indonesia with a tropical climate exposed to the sun all year round, but the results of the study found that 25-hydroxyvitamin D deficiency rates were 35% in women aged over 65 years, 60% in young adult women, and 78.3% in children [8,9]. This high rate can be caused by many factors that affect blood 25-hydroxyvitamin D levels [8]. However, vitamin D deficiency as the prediction factor in AR in Indonesia has not been found yet [10]. Based on this explanation, the research was intended to discover serum 25-hydroxyvitamin D levels as the predictive factor for AR according to TNSS.

2. Methods

Study design

Consecutive sampling was used in recruiting the fifteen subjects. Beforehand, the study has been approved by the Committee of Hospital Medical Research Ethics with informed consent prior to the study. The exclusion criteria such as the infection and other nasal obstruction diseases like we mentioned before.

Measurement

Serum 25-Hydroxyvitamin D levels were quantified using electrochemiluminescence immunoassay (ECLIA) method. The total nasal symptom scores were acquired by enumerate all nasal symptoms. Data of serum vitamin D levels and TNSS were analysed statistically from our previous study [11].

Statistical Analysis

The correlation among Serum 25-Hydroxyvitamin D levels and AR as well as the cut-off points were already obtained by Pearson correlation test and ROC curve. Linier regression was used to analyze whether vitamin D has a role as predictive factor for AR.

3. Results

The data of patients is tabulated in Table 1.

Table 1. Demographic Characteristic and the Relationship

Variable	Subjects (*n*=15)	
	Mean	**SD**
Age	28.87	9.01
	N	**%**
Characteristics		
Asthma	5	16.67
Dark skin	9	66.67
Body Mass index>30	2	6.67
Allergic dermatitis	6	20
Smoking	4	26.67
AR Classification	**Mean**	**SD**
Mild intermittent	1	6.67
Moderate to severe inter-mittent	1	6.67
Mild persistent	4	26.66
Moderate to severe persistent	9	60.00

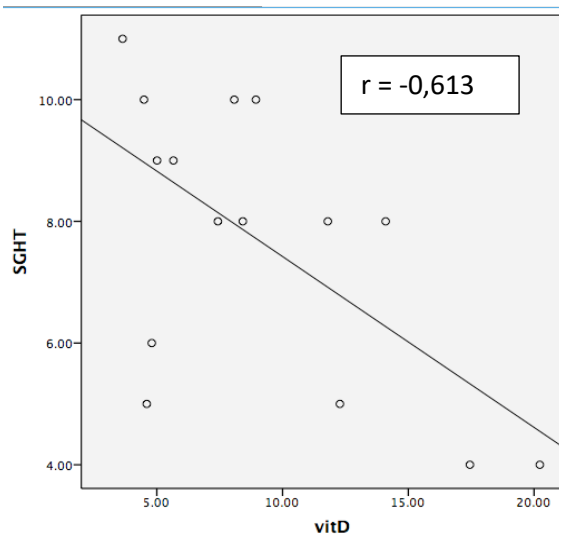

Figure 1. Linier Regression.

Table 2. The Correlation Between Serum 25-Hydroxyvitamin D levels and TNSS.

		25-hydroxyvitamin D level			
TNSS	*n*	Mean	SD	Statistical analysis	*p*
4-6	5	11.87	7.14		
7-9	6	8.74	3.56	r = -0.80*	0.000
10-12	4	6.29	2.61		

*Linier regression test

Our previous study turned up the strong negative relationship with the cut-off points related to AR was 12.83 ng/mL. Linier regression test found the prediction result was illustrated from linier regresion (Figure 1) = 10,230 – 0,281 (25-Hydroxyvitamin D), with negative moderate correlation (r = -0,613). From this result, 25-Hydroxyvitamin D level of 5.66 ng/mL can be analogous with predicted 8.64 nasal score.

4. Discussion

This study obtained a significant divergence of serum 25-Hydroxyvitamin D levels between the AR and non-AR patients, likewise a study by Yalcinkaya et al. The average of serum 25-Hydroxyvitamin D levels in the AR group was 15.39 ng/mL while in the non-AR group was 53.80 ng/mL. Moreover, a study by Modh et al prevailed that 25-Hydroxyvitamin D deficiency turned out in 91% of the total AR samples with a significant recovery after vitamin D augmentation [10,12].

Based on the explanation above, the refinement of TNSS was happened as an immunomodulatory outcome of 25-Hydroxyvitamin D on the immune system. Milovanovic et al. stated that serum 25-Hydroxyvitamin D levels was a significant negative relationship with imunoglobulin E [13]. It was strengthen with the study implemented by Yip et al. that 25-Hydroxyvitamin D could repress the mast cells activity [14]. Furthermore, Vasiliou et al. found related result that serum 25-Hydroxyvitamin D levels were have relationship with asthma [15]. In addition, the escalate mice serum 25-Hydroxyvitamin D levels after UV-B exposure was related with reduction of airway inflammation compared with the non exposed to UV-B mice [16,17].

There are many factors that influence 25-Hydroxyvitamin D level, such as genetic factor , life style that tend to be indoor activities and smoking, climate/atmosphere, age, body mass index, skin pigmentation, and also the time and

duration of sun exposure [18]. Allowing that the previous archetype claimed that 25-Hydroxyvitamin D was completely metabolized from the sun and food intake in kidney, discovery now stated that the production of 25-Hydroxyvitamin D could be generated by some types of immune cells with vitamin D receptor (VDR), such as dendritic cells and T-cells. These cells along with B cells and mast cells could expressed this VDR. The serum 25-Hydroxyvitamin D produced by genetic that regulates two thousand different genes, which one of them is a gene that took parts in allergies [19]. This vitamin encodes the related to allergic rhinitis and asthma chromosome, namely chromosome 12. This vitamin regulates chromosomes influenced by IgE, 13Q14 and 7Q14. This hypothesis explains how genetic factors have the the main role for the serum 25-Hydroxyvitamin D levels in AR patient [16,18].

This study indicated a strong negative correlation between serum 25-Hydroxyvitamin D levels with AR incidence and TNSS, which showed that 25-Hydroxyvitamin D plays an important role in the AR. Moreover, this study were in accordance with Thakkar et al. with negative correlation between serum 25-Hydroxyvitamin D levels with TNSS with a moderate relation strength [20,21].

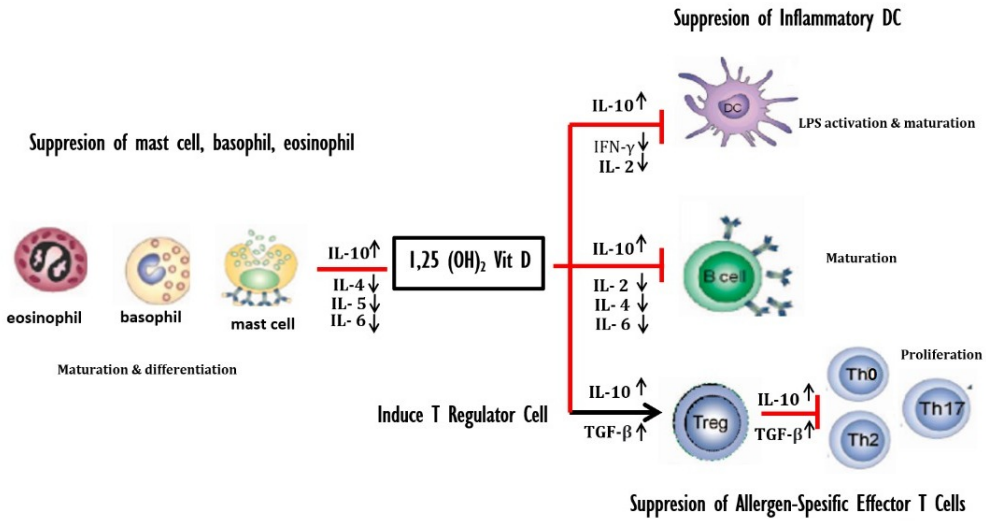

Figure 2. Vitamin D regulation in Allergic rhinitis. Vitamin D regulate the proinflammatory cells by inducing IL-10 and T regulator cell as well supressing pro inflammatory cytokines.

Vitamin D has the capability in controlling regulation of inflammatory Th2-mediated cell, namely the dendritic cell by reducing differentiation and

lipopolysaccharide activity (LPS) [22]. Furthermore, it can reduces differentiation of mast cells and induce its apoptosis in 30-40 days by suppressing Immunoglobulin-E and IL-4 [15]. A research by Yip et al samples found the inhibition of mast cells degranulation in mice after 25-Hydroxyvitamin D supplementation [14]. The study by Hypponen et al. stated that serum 25-Hydroxyvitamin D levels had a significantly have a negative relationship with Immunoglobulin-E [23]. Histamine-receptor binding inhibition in the nasal mucose cause the suppression of Th2 activity in the early stage. Induction of interleukin 10 as anti-inflammatory is influenced by by APC, Th2 cells, and mast cells and can also play role in Th2 suppression (Figure 2) [23].

Still, in restraining the regulation of Th-2 inflammatory cell, 25-Hydroxyvitamin D can impede the differentiation and proliferation of B-cells become plasma cells by increasing the work of IL-10 and suppressing the pro-inflammatory cytokines and chemokines action [22]. The 25-Hydroxyvitamin D can reducing the recruitment of blood eosinophils into mucose in late phase, consequently decreasing the differentiation of B-cells into plasma cells. Inhibition of IL-5 by 25-Hydroxyvitamin D detain the process of eosinophilic maturation, differentiation, migration, and infiltration towards nasal mucosa [14].

Vitamin D also has a role in suppressing the inflammatory responses by increasing the regulation of Th1-mediated cell, for example TGF-β, NK cells and IL-10[14]. It may also respress TLR and MHC class II activation by inhibiting Th1-mediated cells, such as IFN-γ. This action inhibit proinflammatory cytokines regulation [23].

In conclusion, this result found that 25-Hydroxyvitamin D can be a predictive factor for AR. However, future randomized controlled trials are needed.

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