

Status of 25-OH Vitamin D Serum Level among Wheezy Chronic Respiratory Diseases with Airway Obstructive Patterns; Office- Base Study

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ABSTRACT

Background: Vitamin D is a homeostasis hormone of the calcium and bone metabolism. It has additional effects in the infections, cardiovascular, immunity, anti-inflammatory, chronic respiratory diseases and small airway disease (SAD). Wheezing is the common clinical feature of small airway obstructive diseases. Prevalent of asthma and chronic obstructive pulmonary disease (COPD) are noticeable among SAD. Propose of the study assessed status of vitamin D level among wheezy chronic respiratory diseases with airway obstructive pattern.

Methods: Sample population sequentially enrolled among office base- wheezy patients with chronic obstructive pattern. Vitamin D level was measured by ELISA.

Results: We studied on 67 patients. Mean age was 42.9±1.5 SD years, ranged between 17-76 years. Their sex distribution was male 51% and female 49%. Vitamin D deficiency and insufficiency recorded 13% and 40%, respectively. Frequency of lower than set point value of vitamin D among subtypes of SAD was asthma, COPD and other subtypes of SAD, respectively.

Conclusion: Outcome of the study disclosed relevant 25-OH vitamin D deficiency and insufficiency among wheezy respiratory diseases with airway obstructive pattern. COPD and asthma small airways were noticeable within population. Deficiency and insufficiency of vitamin D were considerable in female and male, respectively.

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► *Implication for health policy/practice/research/medical education:* Chronic Respiratory Diseases with Airway Obstructive Patterns

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1. Introduction:

Wheeze is a common symptom of lower respiratory system diseases. It is originated within small airway tracts and clinically developed obstructive features. Wheezing phenotype may be guided in epidemiologic risk factors (1) and distinct asthma phenotype (2). Wheezing appears in different clinical conditions as small airway disease, respiratory allergic base-diseases, infectious and extra pulmonary diseases. Moreover, wheezes as adventitious sound has correlation with PFT parameter quality (3), presentation of airway flow limitation (4) and useful clinical sign in obstructive airway diseases (5).

Vitamin D (VD) is a known old steroid hormone. It has a classic role in the homeostasis of calcium and bone metabolism. The sources are vitamin D₂ and D₃. They are supported by the food and skin exposed–sunshine with ultraviolet radiation 290-312 nm. Then, they are converted within the body through liver and kidney or extra-renal tissues to calcidiol and finally to calcitriol, respectively. Biological active form is 1-25 dehydroxyvitamin D₃ (calcitriol). It bounds with vitamin D nuclear receptor complex (VDR) and induced biologic functions. 25(OH) vitamin D is the liver metabolism of skin and dietary VD. Total 25-OH VD is contributed with 25-OH D₂ reflects general VD status in human (6).

In current years, the multi potential roles were detected for VD. They included cardiovascular events (7), cancer (8), infectious diseases (9), chronic diseases, being an anti-inflammatory effect and extraskeletal effects (10). Moreover, it has roles in the asthma, COPD (11), respiratory diseases (12). Lower set point of VD level is

the universal health problem. Its prevalence was (61-92%) in American population 10 and 78% in Iran (13).

Propose of the study was to assess status of vitamin D level among wheezy chronic respiratory diseases with airway obstructive pattern.

2. Materials and Methods:

The study was cross-sectional and descriptive. It conducted in the office setting in Loghman Hahim Hospital, Shahid Beheshti University of Medical Sciences (SBUMS). Study designed at winter in 2014. Sample population was enrolled among patients with wheezes. They were patients with chronic respiratory diseases who were coming to the office for diagnosis, treatment and management. All the subjects were previously diagnosed as small airway disease with obstructive pattern or as new patients (first time visit). Prevalence of asthma and COPD are noticeable in the Iranian population.

In the first step, the entire subjects with wheezes were detected. Then, baseline spiromerty in office and chest X-Ray was carried out. Global Initiative for Asthma (14) (GINA) criteria and Global Initiative for Chronic Obstructive Lung diseases (GOLD) (15) instruction applied on the new patients with obstructive pattern FEV₁<80%. Chronic respiratory diseases defined as patient with duration of diseases up to 3 years.

FEV₁/FVC <70% predicted and FEV₁<80% defined as COPD with clinical manifestations. In addition, improvement of FEV₁ to standard bronchodilator was less than 12%. Asthma diagnosed based on the medical history, physical examination, and pulmonary function test. Aside, Pre/post bronchodilator FEV₁ responses was changed over >12% or 200 ml. Methacholine bronchial challenge test was performed if needed as additional diagnostic test; PC₂₀<8 mg/ml.

Inclusion criteria established respiratory diseases with obstructive pattern and being wheezed with duration of a symptom over 12 months. The consent of patients was influential in following the study. Taking

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calcium and vitamin D, active cancer, diabetes mellitus, chronic kidney diseases, pregnant, breastfeeding, sarcoidosis and hypercalcemic disorders leads to deleted from the study. Moreover, medication as orlistat, cholestyramine, Phenobarbital, ionized, gastric bypass surgery and malabsorption syndrome also prevented the subjects from the following study 25.

Serum samples were obtained in unique laboratory. Vitamin D end point divided into three level of serum concentration. Deficiency, insufficiency and optimal range defined as less than 10, among 10-29 and up to 30 until 100ng/ml, respectively.

Vein blood samples were obtained in the laboratory, and was sequentially performed total VD in serum. The principle of test was established on competitive binding. The kit was Calbiotech (catalog No: VD220B, made in; CA, USA), and solid phase enzyme-linked immunoassay. The measurement was carried out according to the manufacture recommendation. Microplate reader detected the VD level (Hiperion, MPR4+).

Analyzing data performed with SPSS program, Version 18. Normality test of kolmogrov-Smirnov was $P=0.2$. Frequency was presented with percent. Crosstab and chi-square tests were performed on the data. P value was set through the study at <0.05 (Two tailed).

3. Results:

A total 67 patients with wheezes SAD was completed entrance criteria of the study. Mean age was $(42.9 \pm 15.4 \pm SD)$ years. It ranged between 17-76 years; Media=41 years and mode=27 years. Gender frequency was 51% male and 49% female.

The mean of VD levels recorded 28.8 ± 17.2 SD ng/ml, ranged between 1.3-67 ng/ml, Median=27.5 ng/ml. Total VD deficiency was recorded in 56.7% target population. Of those were deficiency 13.4%, insufficiency 40.3% and sufficiency 46%.

Frequencies of SAD subtypes were 61% asthma, 29% COPD and 10% others. Figure 1 shows sex distribution within wheezes SAD subtypes. Asthma and COPD were more frequently distributed in male and female, respectively. Figure 2 displays VD

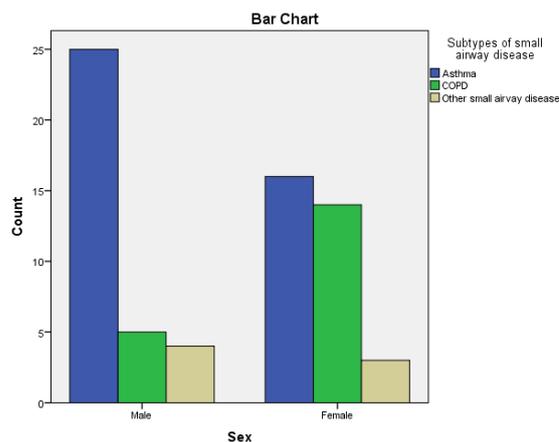


Fig. 1. Sex distribution within wheezes small airway disease subtypes.

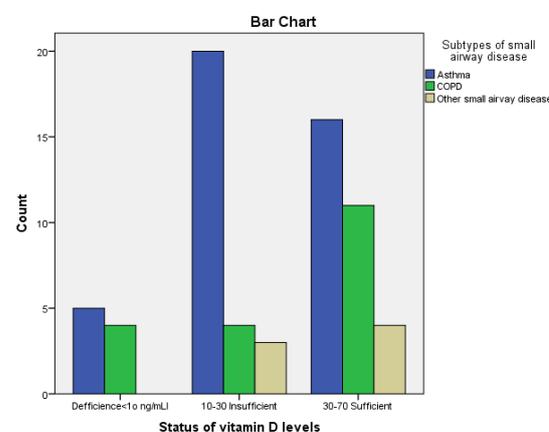


Fig. 2. It displays vitamin D status among small airway disease subtypes.

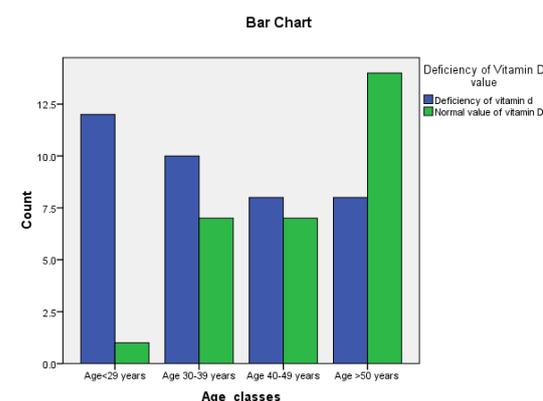


Fig. 3. It discloses status of vitamin D deficiency among age-classes.

status among wheezes SAD subtypes. There were not significant differences between VD status levels and SAD subtypes. In addition there were relevant differences between sexes and SAD subtype ($\chi=0.04$).

Figure 3 discloses status of VD deficiency

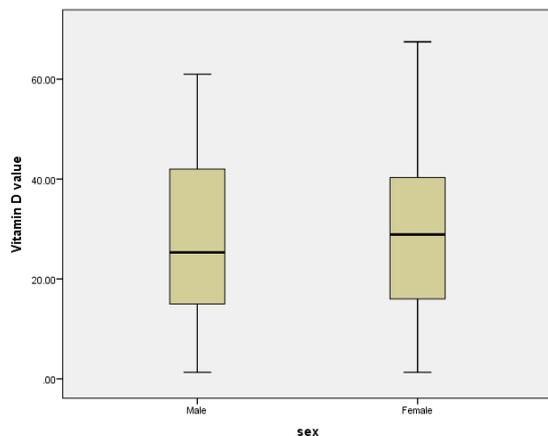


Fig. 4. It reveals sex distribution within vitamin D levels in serum.

among age- classes. Global VD deficiency was noticeable in the young age group than older age. There were relevant differences between age classes and VD deficiency ($\chi < 0.015$).

Figure 4 reveals sex distribution within VD levels in serum. Frequencies of sex's distribution within VD status were 44% deficiency in female and 56% insufficiency in the male samples. However, global deficiency of VD level was equal in both sexes. Figure 5 presents the frequency of VD status between sexes. There were no statistically differences between sexes in VD status ($\chi > 0.05$).

4. Discussion:

Small airway disease (SAD) is the inflammatory of airway less than two millimeter diameter. They are broad spectrum of diseases of pulmonary or extra-pulmonary origins. Wheeze, dyspnea and airway obstructive patterns are the most common clinical features. Small airway area of lung calls a silent area, and clinical aspect of disease only appears if the obstruction occurs in at least 75% of all small airways (16). Symptoms of bronchial airway obstruction led to refer the patient to the physician. Asthma and chronic obstructive pulmonary disease are the important subtype of SAD. They are induced and developed within rural areas with environmental air pollution (17).

VD insufficiency is common and estimated

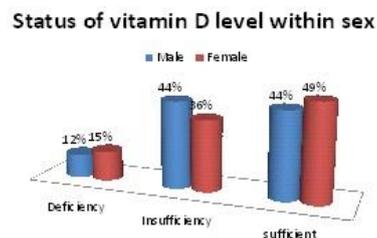


Fig. 5. It presents frequency of status Vitamin D within sexes.

that approximately 50% of people in the world have this insufficiency (18). Global VD deficiency was assessed based on the different measurement 57-93% in patient population (19). Numerous factors may be influenced on the obtained VD level recording. Vitamin D value has seasonal variation in measurement. It is the higher value in winter and spring months than other months (20). It is due to oblique angle of sunlight exposure that leads to more photon absorbed by the stratospheric zone. Our study set in the winter season. Latitude influences on the rate of UV exposure. Tehran capital of Iran places in the 35° 44' 44he 35° 44' N a. The recent report indicated production of VD₃ was little in the coetaneous during the winter above latitude of 35° N and below 35° S (21). In addition, skin pigmentation is effective on the VD value. It is higher in darken skin than the lighter color. 70% of focus population was light skin color. VD intake is the essential source in the providing body VD. The report of intake milk was insufficient in the Iranian population. We cannot follow the current issue. Moreover, photochemical reaction occurs in the epidermis with solar radiation wavelengths of 291-315 nm (Ultra violet; UV). It can convert pre-Vitamin D₃ to VD₃ in the body temperature at least in 12 hours (22). Rate of penetration of UV is considerable. It may be decreased with sun protection factor and dress style (23, 24).

The recent concept is controversial and is not as an alone factor.

Atmospheric air pollutant is relevant depended role in the VD status in human serum level. It has inverse relation to the rate of absorption UV in the ground level (25). Limited studies supported the recent concept (26, 27). Tehran is pollutant rural area, and UV absorption was less than Gazvin city in the ground (25).

VD deficiency and insufficiency were reported among respiratory disease, particularly in chronic obstructive diseases (28). Chronic and inflammatory disease can be changed VD level. The mechanisms are poor understood and complex. One of the suggested mechanisms in chronic inflammation may be directly reduced circulating VD level throughout depletion of pooled 25-(OH) D (29).

Bronchial asthma is a chronic inflammatory airway tract disorder, and marked with airway hyperresponsiveness. Asthma disease appears in clinical with wheeze, dyspnea and cough. The global prevalence of adult asthma and wheezing were 4.3% and 8.6%, respectively (30). Its prevalence among Iranian is 2.8% (31)-6.1% (32). Prevalence of VD insufficiency rose among asthma population in the last several decades. Recent report indicated that there was inverse relation between asthma and VD level (33). Moreover, VD level in the insufficient status increased severity of asthma (34). Recent concept suggested the hypothesis that VD had a contributor in the outbreak of asthma. It has a direct effect on the T regulator and secretion of IL-10 (35).

Aging may be effective in the VD level. 7-dehydrocholesterol is decreased in the skin in the aging process (36). Old age has one-fourth (25%) of young adult 7-dehydrocholesterol. However, another suggested mechanism is corticosteroid effect that can reduce calcium absorption from gastrointestinal tract and decreased VD metabolism (18, 37).

VD deficiency detected more frequency in males but insufficiency was in females in our study. It is compatible with the outcome of the recent study from Iran (38). However, total prevalence of VD deficiency reported

in Tehran 81.3% (39). Tehran had high hypovitaminosis D than other cities in Iran. Moreover, VD deficiency was more prevalent in the 4th and 5th decades in Iranian population (40). Our study resulting indicated younger age classes hypovitaminosis D. It was agreement with study in Isfahan (38).

COPD is a chronic inflammatory disease with irreversible airway obstruction. There is the link between COPD and VD deficiency. It has been anti-inflammatory, efficient in native and adaptive immune system and anti-bacterial effects. They can be the effects on the COPD pathogenesis. In addition, it influences on the pulmonary function test (41). Global prevalence of VD deficiency was reported in COPD 45.9% (42).

5. Conclusion:

Relevant vitamin D deficiency observed among wheezy chronic small airway disease with the obstructive patterns. Asthma and COPD had more frequently within SAD subtypes. Insufficiency and deficiency of vitamin D were noticeable in female and male, respectively. In addition, insufficiency of vitamin D was considerable in focus population. Younger age groups presented more vitamin D deficiencies in recording.

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