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Relationship between Vitamin D Deficiency and Respiratory Infection in Intensive Care Unit Patients

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Abstract

Objectives: the current study aims to investigate the correlation between vitamin D deficiency and respiratory tract (URT) infection in hospitalized patients. Subjects and methods: a cross sectional observational study was conducted among patients with URT infections admitted to the intensive care unit (ICU). Results: From 30 ICU respiratory infected patients who were included in the study, results showed that all patients' serum vitamin D levels were below normal, where 3.3% of patients showed a relative insufficiency and 96.7% represent deficiency. This study included 16 females and 14 males. The results showed that deficiency in females appears to be more than in males with a mean of 15.42 nmol/L and 16.nmo/L respectively. Variable readings of serum vit. D level appeared with the various microorganisms. The lowest level of the vitamin was found with *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Ataphylococcus aureus* respectively. In addition, the present study showed that the level of WBCS is inversely proportional to the level of vit. D in most patients. Moreover, patients who were on combination therapy of antibiotic and corticosteroid showed lowest mean of serum vit. D level than patients who were on antibiotic or corticosteroid alone. Conclusion: the present study showed that all patients with respiratory tract infection in ICU have either vit D insufficiency or deficiency. Moreover, there was an inverse relationship between vit D and WBCs level. This may be attributed to the role of vit D in immunity, so vit D may be recommended to be prescribed to avoid further deficiency and to boost the immunity in patient with respiratory tract infection.

Keywords: Vitamin D, Respiratory tract infection, Intensive care unit, Immunity, Antibiotic, Cortisone.

Contents

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1. Introduction

Respiratory infection (RTI) involves a vast variety of illness ranging from minor to fatal ones [1]. Bacterial infection of the lower respiratory system is less common than those of the upper system but can be can be sever or fatal [1]. Although viruses, mycoplasma, rickettsia, and fungi can all cause lower respiratory tract infections, bacteria are the dominant pathogens [2]. The incidence of nosocomial infections in ICUs is 5–10 times higher than that observed in general hospital wards [3]. Ventilator-associated pneumonia (VAP) is the most frequent nosocomial infection in ICUs. VAP is associated with high mortality, longer hospital stays and longer mechanical ventilation [4]. It occurs in patients within 48 hours following intubation [5]. The main cause of VAP was *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and Methicillin-resistant *Staphylococcus aureus* (MRSA) [3].

Vitamin D is considered as a prohormone because it is converted to a hormone in the human body [6]. The major function of vitamin D is to promote calcium and phosphorus absorption in the body [6]. In the recent years, much clearer picture of the role of vitamin D has been determined and the immune responsiveness has been discovered. Innate immunity have shown that intracrine induction of antimicrobial activity by vitamin D is a critical component of monocyte/macrophage response to infection [7]. In addition, serum 25.OHD concentrations and circulating levels of human cationic antimicrobial protein were low in patients with sepsis, end-stage kidney disease and upper respiratory tract infection [7]. The aim of the current study is to investigate the possible relationship between vitamin D and respiratory tract infection.

2. Subjects and Methods

A cross sectional observational study was performed at intensive care unit (ICU) in King Abdulaziz University Hospital (KAUH), Jeddah, Saudi Arabia. The study was conducted after approval from KAUH review board. The study period was from November 5, 2014 through July 17, 2015.

All patients in ICU with no respiratory infection and patients with respiratory infection from wards other than ICU were excluded. Patient data were collected from patients' files, these data include age, sex, patient diagnosis, complete blood count profile, causative organism, coadministered medications and the serum vitamin D level after ordering it from nurses. The vitamin levels were obtained on the next day. Vitamin D deficiency is defined by most experience as 25-hydroxyvitamin D level of ≤ 50 nmol/L, 50-72 nmol/L for relative insufficiency and ≥ 72 nmol/L for normal serum level [8].

3. Results

From 30 ICU respiratory infected patients who were included in the study, results showed that all patients included in this study were below normal serum vitamin D level (deficiency ≤ 50 nmol/L, 50-72 nmol/L for relative insufficiency and ≥ 72 nmol/L for normal serum level). 3.3% represent the relative insufficient patients and 96.7% represents the deficient patients (Figure 1).

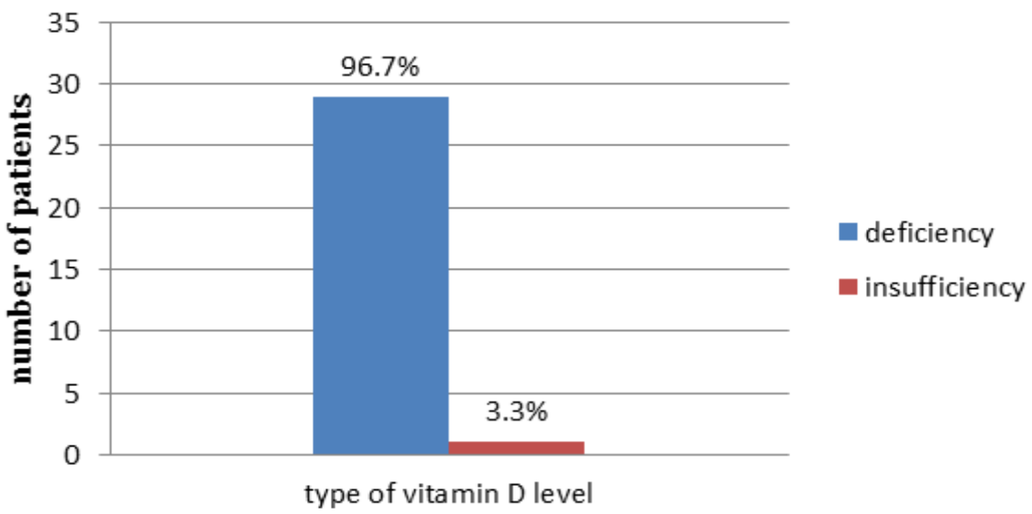

Figure-1. Percentage of deficient (≤ 50 nmol/L) and insufficient (50-72 nmol/L) vitamin D patients

This study included 16 females and 14 males. The results showed that deficiency in females appears more than in males with a mean of 15.42 nmol/L and 16.nmo/L respectively (Figure 2) while the mean of the whole population was 16.09 nmol/L (table 4). Most of the patients (76.7%) of the study population were above 50 years of age. 18 (60%) out of the 30 patients were on antibiotic treatment and 10 (33.3%) patients were on cortisone therapy (Table 1). CBC was done to all patients included in the study and the results showed high serum level of WBCs with a mean of 16.12 k/ul because of the respiratory infection. All of electrolytes levels were within the normal range except for calcium which showed low serum level (Table 1).

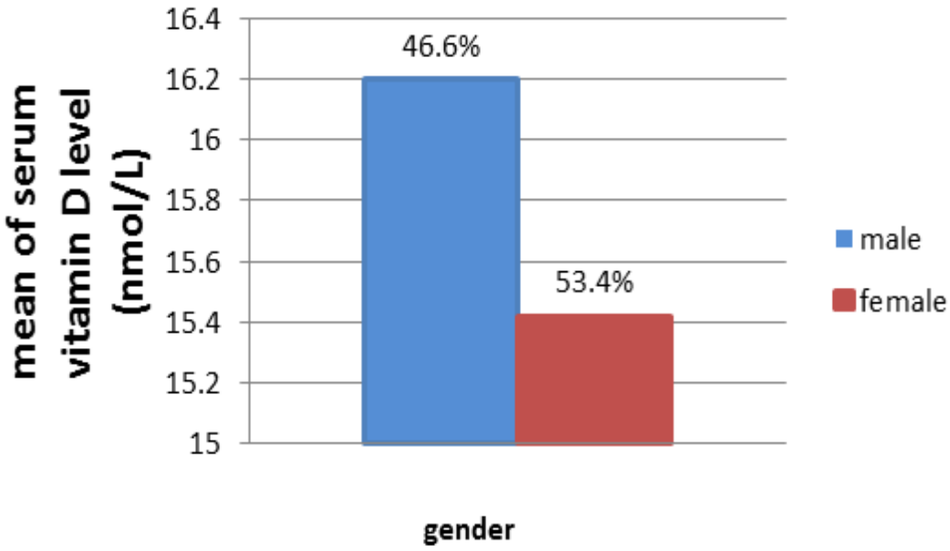

Figure-2. Relation Between Vit.D Levels & Gender

Table-1. Variables affected by vitamin D deficiency (Data are expressed as mean, percentage and normal range)

Variables	**(n=30)**
Age ≥50	23 (76.7%)
Sex	M= 14 f= 16
Antibiotic	18 (60%}
Cortisone	10 (33.33%}
Sodium (mmol/l)	141.43 {136-145}
Potassium (mmol/l)	4.01 {3.5-5.1}
Phosphate (mmol/l)	1.52 {0.81 – 1.58}
Calcium (mmol/l)	1.8 {2.12 – 2.52}
Magnesium (mmol/l)	0.88 {0.7 – 1}
Vitamin d (nmol/l)	16.09 F= 15.42 m=16.2
WBCs (k/ul)	16.12 {4.5 – 11.5}

According to tracheal aspirate culture, the present study revealed that the most frequently causative organisms for URTI were *Acinetobacter baumannii* with a percentage of 40%, followed by *Pseudomonas aeruginosa* with a percentage of 23 % and *Staphyloccoccus aureus* comes third with a percentage of 14%. Then *Klebsiella pneumonia*, *enterobacter cloacae*, *E.coli* and S*erratia marcescens* with percentages of 10%, 7%, 3% 3% respectively (Figure 3).

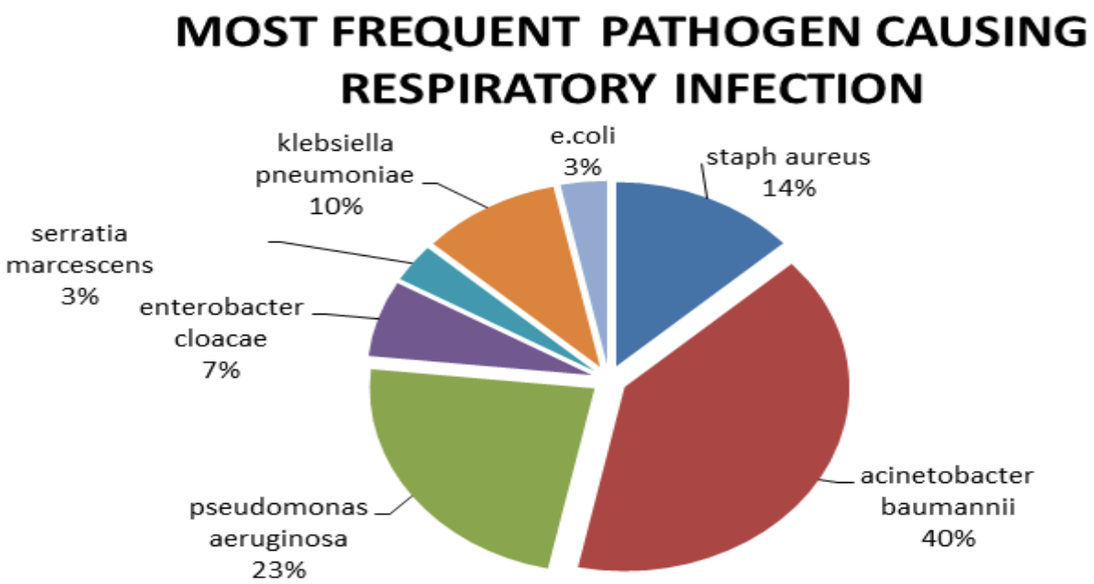

Figure-3. Most Frequent Pathogen Causing Respiratory Infection

Variable readings of serum vitamin D level appeared with the previous mentioned microorganisms. The lowest levels of the vitamin were found with *Acinetobacter baumannii, Pseudomonas aeruginosa and Staphylococcus aureus* respectively (Figure 4).

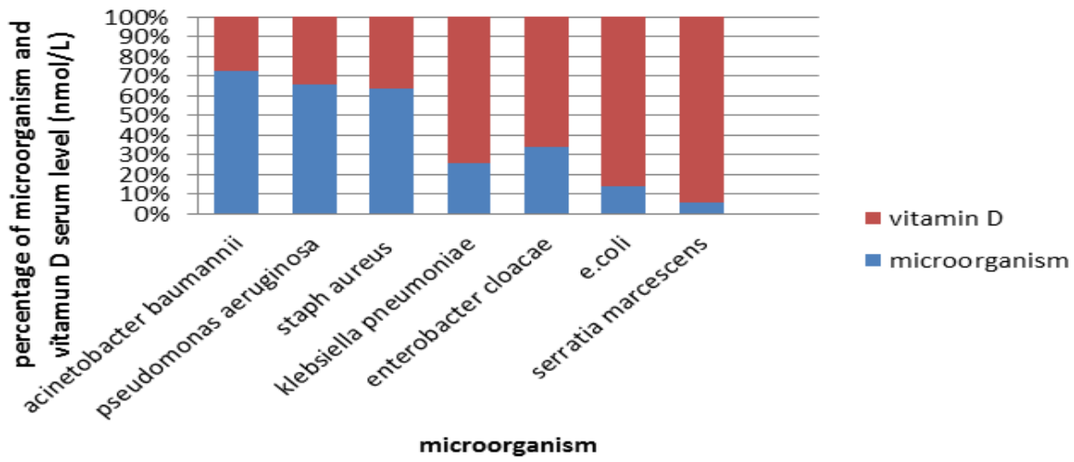

Figure-4. Mean of vitamin D in relation to percentage of microorganism

According to serum readings, there was a relationship between serum level of vit.D and WBCS. This relationship revealed that high level of WBCS is related inversely to low level of vit.D in the most of the patients (Figure 5).

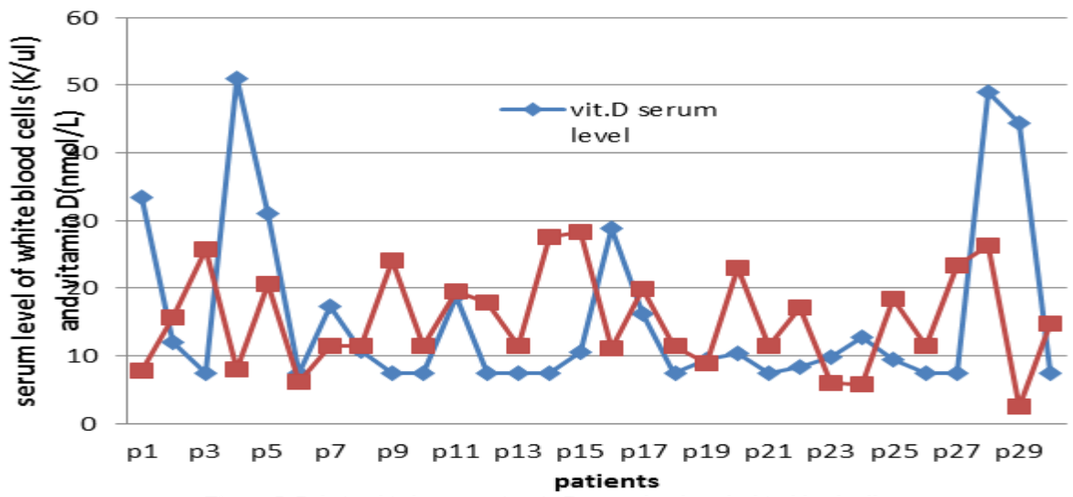

Figure-5. Relationship between vitamin D serum levels and white blood cells

Patients who were on combination therapy of antibiotic and corticosteroid showed lowest mean of serum vit. D level than patients who were on antibiotic or corticosteroid alone (Figure 6).

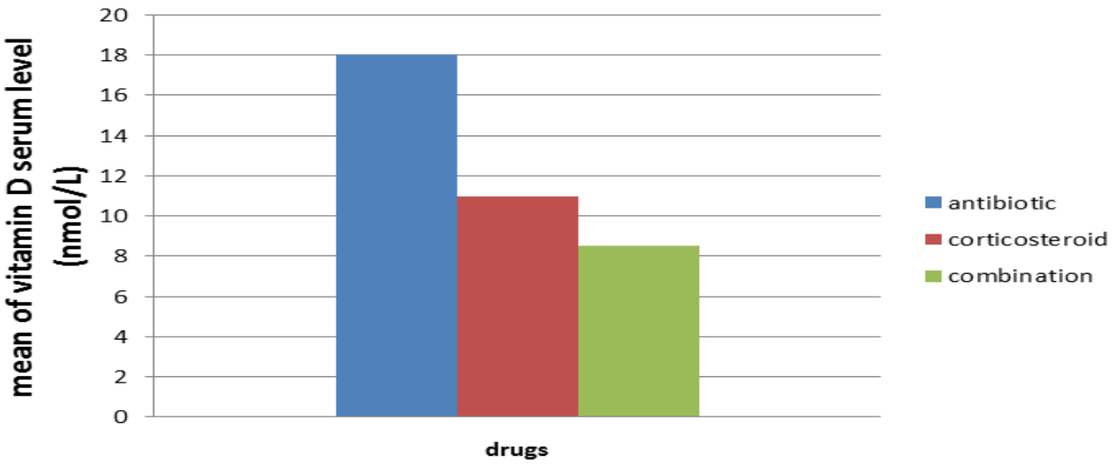

Figure-6. The effect of corticosteroid and antibiotic on serum vitamin D level

4. Discussion

The results of the present study revealed that as all patients with respiratory tract infection included in the study suffered either from vitamin D deficiency (96.7 %) or insufficiency (3.3%). This is in accordance with previous studies which found a positive relationship between vitamin D deficiency and infection. Morris and Zemel [9] showed that vitamin D has anti-infective effect that is related to increase the level of cortisone. They found that 1α,25-dihydroxyvitamin D can stimulate 11β-HSD1 expression and thereby promote the conversion of the glucocorticoid precursor cortisone to cortisol. The current study showed that 76.7 % of patients were above 50 years of age with a notable vitamin D deficiency, which suggests that there is a negative relationship between age and serum vitamin D levels.

Many drugs can interfere with the vitamin D and bone metabolism. The drug-induced activation of the pregnane X receptor (PXR) is likely to enhance CYP24 expression and the catabolism of 25(OH)D, leading to vitamin D

deficiency [10]. PXR is activated by a lot of pharmaceutical compounds including steroid, antibiotic, St. John's wort antidepressant constituents, HIV protease inhibitors as ritonavir and many others [11]. This is in accordance with the results of the present study which revealed that all patients were treated with antibiotic therapy had low serum vitamin level, lower serum vitamin level with corticosteroids and lowest levels with combination therapy. It seems like that corticosteroids lower the vitamin D level more than antibiotics because its fat soluble property and the activation of PXR concomitantly.

The classic function of vitamin D is to maintain optimal calcium and skeletal homeostasis. The majority of chronically ill elderly patients transferred from the ICU had evidence of rapid bone turnover due to vitamin D deficiency [12]. During exposure to sunlight, the ultra violet B photons enter the skin and photolyze 7-dehydrocholesterol to provitamin D3 which in turn is isomerized by the body's temperature to vitamin D3 [13]. According to Morris, et al. [14] calcium absorption was reduced in patients treated with glucocorticoids. That low levels of calcium were found concomitantly with low serum vitamin D levels. Klein, et al. [15] compared fractional calcium absorption in 27 patients receiving prednisone compared to 27 age and sex-matched controls. In patients receiving high doses of prednisone, calcium absorption and serum vitamin D were decreased. This proves that calcium absorption and serum vitamin D level correlated inversely prednisone dose. This is in accordance with the results of the current study as most of the patients included in this study exhibit low serum calcium levels which may be due to the long period of hospitalization in the ICU and less exposure to sunlight with the factor of old age to be taken in consideration in addition to treatment with corticosteroids.

Supplementation of vitamin D to levels > 100 nmol/L resulted in increased expression of Toll-like receptor 2 (TLR2) [16] which is essential for initiating innate immune response of macrophages against *Acinetobacter baumannii* infection [17]. The result of the current study showed that the lowest levels of serum vitamin D are associated with *Acinetobacter baumannii* pathogen. Although previous studies [16, 17] revealed that vitamin D and *Acenitobacter baumannii* affecting different receptors, the results of the present study suggest that there might be a specific receptor in which vitamin D and *Acinetobacter baumannii* are affecting it. Also other microorganisms may affect vitamin D deficiency by the same mechanism.

White blood cells (WBCs) carry a vitamin D receptor that allows the immune system to guard against infection. There are several different types of WBCs, including dendritic cells and macrophages, each requiring vitamin D to perform their jobs. Macrophages may produce an enzyme that is needed to make the active form of vitamin D to enable the macrophages to function properly [18]. In the current study, most of the patients' readings showed that WBCs and vitamin D were correlated inversely. This is may be explained by the use of cortisone in most patients in the study. Glucocorticoid was found to increase renal expression of 24-hydroxylase and decrease expression or renal 1α-hydroxylase deceasing levels of 1,25(OH)2D3 [19, 20].

Limitation of the current study included the lack of patient follow up, the small population among this study and the lack of serum vitamin D measurement in many patients in the ICU.

In conclusion, the deficiency of vitamin D among population of Jeddah, Saudi Arabia may have been initiated due to the lazy life style and the less exposure to sunlight in addition to nature of hot, humid climate of Jeddah which people usually avoid. Lack of routine checkup for the vitamin D serum level may increase the prevalence of deficiency among the society. Because some researches assume that some drugs as antibiotics and corticosteroids my decrease the level of the vitamin, vitamin D supplements should be given to avoid further deficiency. The relationship between patients with respiratory infection and vitamin D deficiency require more new clinical studies aimed at assessing the physiological and disease consequences of vitamin D deficiency.

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