

Association of 25 Hydroxy Vitamin D Levels with Age in Community Acquired Pneumonia.

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Abstract

Background : To determine association of 25 hydroxy vitamin D deficiency with age in patients with community acquired pneumonia (CAP).

Methods: In this descriptive study 150 diagnosed patients of community-acquired pneumonia based on the CURB-65 scoring criteria were enrolled. The 25 hydroxy vitamin D levels were recorded in all patients. Patients were divided into three groups according to their age. Effect modifiers like gender were controlled by stratification. Post stratification chi square test was applied. A p value of 0.05 was considered significant.

Results: Mean age of the patients was 40.05 ± 14.33 years (mean \pm SD). Out of 150 patients 54.7% (n=82) were males while the 45.3% (n=68) were females. The mean level of vitamin D was 18.43 ± 5.005 (mean \pm SD) ng/ml. When the cut off value for deficiency was applied i.e. 20 ng/ml, the 60% (n=90) patients were found deficient while 40% (n=60) patients had normal values. The p value was significant only for the age group to 35 to 50 years. Independent sample t test showed that the difference is statistically significant (p=0.003) in age groups between 35 to 50 years.

Conclusions: Lower concentrations of vitamin D might be associated with CAP particularly in age group between 35 to 50 years.

Key Words: Pneumonia, Vitamin D Deficiency, Chronic, Prognosis

Introduction

In recent years there are number of growing evidences that vitamin D not only helps in metabolism of calcium and bone but also has several immune modulatory effects. It has been described recently that apart from the kidneys, leukocytes also contain 1α -hydroxylase. This 1α -hydroxylase converts 25 hydroxy vitamin D to biologically active 1,25 dihydroxy vitamin D i.e

1,25(OH) D. There are number of factors ranging from dietary deficiency, inadequate exposure to sunlight and malabsorption syndromes such as celiac disease resulting in Vitamin D deficiency. Lower serum levels of Vitamin D are an important risk factor of upper respiratory tract infections. 1-25 dihydroxy vitamin D modulates antimicrobial effects of the innate immune system. By modulating the crosstalk between T cells and cells of the innate immune system, vitamin D attenuates an over-whelming inflammatory response. There are number of growing evidences that apart from having effects on calcium and bone metabolism, vitamin D also hosts several immune modulatory effects¹. To become biological active, vitamin D is initially hydroxylated to 25-OH vitamin D by the 25-hydroxylase (CYP27A1) present in the liver. 1α -hydroxylase (CYP27B1) present in the kidney catalyzes the second hydroxylation and converts 25-OH vitamin D to biologically active form 1-25 dihydroxy vitamin D (1,25-OH₂). As the half live of 1, 25-OH₂ is short i.e 4-6 hours, 25-OH which is much less active precursor having a plasma half life of 3 weeks is considered as a reservoir of vitamin D. It has been suggested recently that apart from the kidneys, leukocytes also contain 1α -hydroxylase and therefore can play a role in activation of 25-OH.^{1,2}

Vitamin D deficiency can result from various factors including decreased exposure to sunlight or malabsorption syndromes; such as short gut syndrome, celiac disease and cystic fibrosis. Some medications such as rifampicin, phenobarbital, and phenytoin can induce hepatic P 450 enzymes and increases the catabolism of vitamin D.³ There is no definitive definition for the measurement of vitamin D level which is measured as serum 25-OH. A recent guideline suggested that vitamin D deficiency is defined as 25-OH below 20 ng/ml, insufficiency as 21-29 ng/ml, and sufficiency as 30-100 ng/ml.^{1,4}

Community-acquired pneumonia (CAP) carries significant mortality and morbidity and is one of the

most common infectious disease worldwide. Important Bacteria that leads to the condition include Streptococcus pneumoniae, causing community acquired pneumonia and Mycoplasma, Legionella and Chlamydia psittaci causing atypical pneumonias.⁵

Patients with typical community acquired pneumonia presents with cough productive of purulent sputum, high-grade fever and pleuritic chest pain. On physical examination coarse crackles and bronchial breathing is heard over involved lobe or segment. Atypical community acquired pneumonias present with a variety of pulmonary or extrapulmonary features including diarrhea, rash, confusion, lethargy, endocarditis, myocarditis, heart blocks, relative bradycardia, etc.^{6,7}

CURB-65 criteria is used to assess severity of community acquired pneumonia, developed by the British Thoracic Society. It comprises of five components confusion, serum urea levels, respiratory rate, blood pressure, and age of the patient. It scores 0-5 more than 2 points is considered for in patient care and categorized as severe pneumonia.^{6,8}

There is an increased risk of upper respiratory tract infection in patients with low serum 25(OH) D levels. This is because of facilitation of antimicrobial effects of the innate immune system mediated by 1-25 dihydroxy vitamin D.² By modulating the crosstalk between T cells and cells of the innate immune system, vitamin D attenuates an over-whelming inflammatory response.¹ Deficiency of vitamin D can impair immune function which may result in immune suppression with poorer resistance to infection as well as over activity and an increase in risk of various autoimmune diseases. Through this route, vitamin D levels influence the bacterial flora and affect immune function^{2, 3}. According to one study conducted by Rimmelts HH et al, deficiency of vitamin D was present in 44% patients with CAP. There is no sufficient data regarding vitamin D deficiency in severe and mild community-acquired pneumonia. This study showed Vitamin D deficiency was present in 44% patients with mild and 56% of patients with severe community acquired pneumonia.⁹

Patients and Methods

A total of 150 patients with recent diagnosis of community-acquired pneumonia based on the CURB-65 scoring criteria of more than two points were enrolled into the six months study from 7 August 2015 to 06 February 2016 at Benazir Bhutto Hospital after getting ethical review board approval. Data was

recorded in self-structured questionnaire. The 25 hydroxy vitamin D levels were recorded in all patients. Data was analyzed by SPSS version 12. Numerical data like age, Vitamin D levels was presented as mean ± standard deviation. Categorical data was presented as frequencies. Effect modifiers like age and gender were controlled by stratification. Post stratification chi square test was applied. A p value of 0.05 was considered significant.

Results

Mean age of the patients was 40.05 ± 14.33 years (mean ± SD). Majority (46.3%) were less than 35 years of age (Table 1). Males constituted 54.7%(n=82) and females constituted 45.3%(n=68) of study population. Mean level of vitamin D was 18.43 ± 5.005 (mean ± SD) ng /ml. When the cut off value for deficiency was applied i.e. 20 ng/ml, the 60% (n=90) patients were found deficient while 40% (n=60) patients had normal values (Figure 1).The p value was significant only for the age group 35 to 50 years. Independent sample t test showed that the difference is statistically significant (p=0.003) in age groups between 35 to 50 years. (Table 1)

Table 1:Age Distribution

Age (years)	No(%)
< 35	68(46.3)
35-50	39 (26.0)
>50	43(28.7)

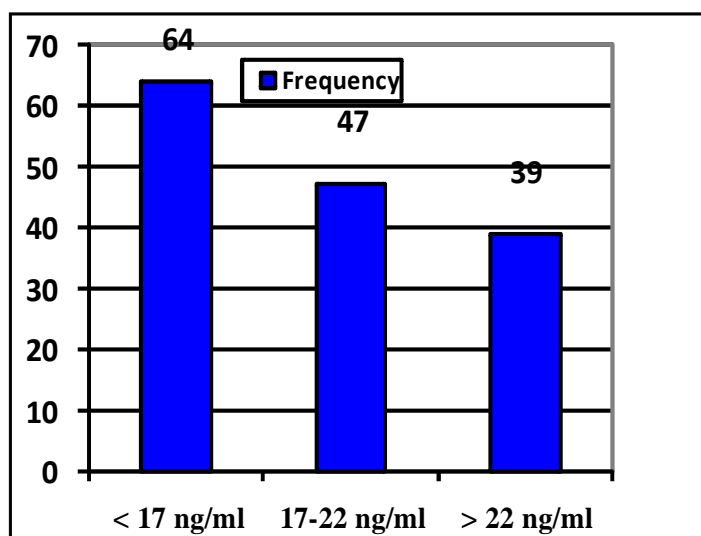


Figure 1: Levels of Vitamin D

Table 1: Vitamin D levels in various age groups

Age	Vitamin D deficiency		Total	P value
	Yes	No		
<35 years	39	29	68	0.073
35 to 50 years	19	20	39	0.015
>50 years	32	11	43	0.922

Discussion

The community-acquired pneumonia (CAP) is one of the most deadly infectious disease worldwide. It is one of the major killers with mortality up to 51 % in complicated cases¹⁰. The CAP can lead to a variety of complications but the patients with more defective immunity are more at risk. This rule also applies to the patients with diabetes, chronic renal and liver failures.¹¹The list of complications of CAP is much diverse and there are various predictors of mortality and morbidity. These include pneumonia severity index (PSI), CURB-65, PIRO scale and various modifications of these scales.^{12, 13} Shah, B. A., et al. in 2010 compared the CURB-65 and PSI for mortality and morbidity of pneumonia. They found that both scoring systems have advantages and disadvantages. They concluded that both PSI and CURB-65 were equally sensitive in predicting death from CAP. Specificity of CURB-65 was higher than that of PSI. However, sensitivity of PSI in predicting ICU admission was higher than CURB-65.⁸ In our study, CURB-65 was used as it was more easily applied on adult populations and parameters are easy to evaluate and elaborate. Based on the score system, the patients having score of more than two and requiring hospital admissions were selected.

Community-acquired pneumonia is more commonly seen in very young and the elderly but is largely under recognized in individuals in middle aged working people.¹⁴ Streptococcus pneumonia is the most common causative organism in adults.¹⁰The association of vitamin D with immunity has been validated in all major literature. Mahmud, MR., et al. in 2016 evaluated the role of vitamin D in immunity and Dengue fever. The study was conducted in 50 patients and showed that mean vitamin D levels in dengue fever patients were higher (21.5 ± 13.6 ng/ml) as compared to Dengue hemorrhagic fever (12.4 ± 5.6 ng/ml) providing evidence that vitamin D deficiency decreases immunity leading to dengue hemorrhagic

fever¹⁵. Another study conducted at Benazir Bhutto Hospital, Rawalpindi on 124 patients showed significant therapeutic role of Vitamin D in progression of infectious diseases.¹⁶

Leow, L., et al. showed relationship between vitamin D and risk of CAP. They found that the titres of cathelicidin or beta-defensin-2, which depict the immunity levels remain unaffected by vitamin D but the pneumonia related mortality was more significant if patients were vitamin D deficient. In more details, 15% of population had severe 25-hydroxyvitamin D deficiency (<30nmol/L) and had a higher 30-day mortality as compared with the patients with sufficient 25-hydroxyvitamin D (>50nmol/L) (P=0.004).¹⁷ In 2012, Remmelts, H. H., et al. found that the vitamin D levels are correlated closely with the ICU admissions and mortality. This study was done on 272 patients and both PSI and CURB-65 scores were used⁹. The effect of vitamin D in reducing CAP risk scores were validated on healthy population in another study on more than 16 thousand individuals.¹⁸

Jovanovich, AJ., et al. evaluated the role of vitamin D level and risk of community-acquired pneumonia and sepsis. All results showed that vitamin D levels and supplementation could reduce risk of infections including CAP and sepsis.¹⁹ A recent study by Kim, H. J., et al. in 2015 showed that the vitamin D deficiency is good predictor of 28 days mortality in CAP (p value 0.01). They found that up to 80% of hospitalized patients were vitamin D deficient.²⁰

The role of vitamin D on CAP related mortality and morbidity is still obscured but some recent genetic research data shows that one of the potential genetic risk factors for CAP might be TT genotype of rs2239185 in VDR gene, and there may be association of T allele of rs2239185 with the susceptibility to CAP and the severity of CAP.²¹

In our study, the vitamin D deficiency was significantly more in high-risk population of CAP (p value 0.009). The age stratification showed that this correlation is only significant for the age group of 35 to 50 years (p value 0.015). All other age groups showed no significant impact. This is in accordance to study conducted by Broulette, J et al which concludes that middle-aged group is under recognized in community acquired pneumonia.¹⁴

Conclusion

Vitamin D may have a role in management of community-acquired pneumonia. The present study suggests that low concentrations of vitamin D might be associated with increased risk of community-

acquired pneumonia; however a multi-centric trial with larger sample size is needed to further investigate the relationship between Vitamin D and community-acquired pneumonia.

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Key for Contribution of Authors : A= Conception/ Study/ Designing /Planning; B= Experimentation/Study conduction;C=Analysis/Interpretation/ Discussion; D= Manuscript writing;E= Critical review;F= Facilitated for reagents/Material/Analysis