



Research Article

CORRELATIONAL STUDY OF VITAMIN-D DEFICIENCY LEVELS AND ITS SEVERITY OF COMMUNITY-ACQUIRED PNEUMONIA IN PATIENTS ADMITTED INTO A TERTIARY CARE HOSPITAL

M. Sai Varun¹, Mudipalli Deepthi^{2*}

Article Information

Received: 19th January 2024
 Revised: 21st March 2024
 Accepted: 9th April 2024
 Published: 30th April 2024

Keywords

Community-acquired infections, CURB-65, Vitamin-D deficiency, pneumonia

ABSTRACT

Background: Recent studies have emphasized that people who have low levels of Vitamin D are more prone to the development of infectious diseases, particularly of a community-acquired nature, which has differential morbidity and mortality. **Aims & objectives:** The present study aimed to determine the correlation between different levels of vitamin D deficiency and severity and outcomes in patients diagnosed with community-acquired pneumonia. **Methods:** In this study, the serum level of Vitamin D of 100 consecutively admitted community-acquired pneumonia patients was measured. Depending on the level of Vitamin D deficiency, patients diagnosed with community-acquired pneumonia (CAP) were assessed for severity of illness by CURB-65 score. **Results & Discussion:** In the study population, out of 100 patients, 82% of the study sample had deficient serum vitamin D levels. In the study sample, 41 patients with higher deficiency levels of serum Vitamin D have severe illness and scored high on CURB-65, which is in the range of three to four on the scale. 59 patients with low deficiency levels of serum Vitamin D had low scores of one or two on the CURB-65. On severity assessment in patients with severe deficiency of Vitamin D, the mean length of hospital admission was 12.30±8.47 days compared to patients with mild deficiency of Vitamin D, where the average hospital stay was 8.58±4.04 days. **Conclusion:** As the severity of deficiency of Vitamin D increases, the frequency of CAP increases, and it is also observed that a severe degree of deficiency is associated with severe illness and prolonged hospital stay.

INTRODUCTION

Community-acquired pneumonia (CAP) is a type of lung infection occurring in the community setting [1]. Despite having the widespread healthcare infrastructure in developed countries like the United States, pneumonia is still one of the leading

causes of mortality, and it is worse when it comes to developing and underdeveloped countries [2]. Pneumonia usually affects extremes of age populations, that is, the elderly or those under 5 years of age [3]. Usually, pneumonias are common in people over the age of 50 years and in the winter months or early spring

¹Department of Medicine, Narayana Medical College, Nellore, Andhra Pradesh, India

²Department of Gynecology, ACSR Government Medical College, Nellore, Andhra Pradesh, India

*For Correspondence: deepthimudipalli@gmail.com

©2024 The authors

This is an Open Access article distributed under the terms of the Creative Commons Attribution (CC BY NC), which permits unrestricted use, distribution, and reproduction in any medium, as long as the original authors and source are cited. No permission is required from the authors or the publishers. (<https://creativecommons.org/licenses/by-nc/4.0/>)

season [4]. Pneumonia develops in people who have defective host defense mechanisms caused either by the defective immunological system or by patients adapting to risk-taking behaviors such as smoking, alcohol consumption, etc [5].

The clinical presentation of pneumonia also varies depending on age; some may have an entire spectrum of symptoms, while others have only tachypnea, which is mainly seen in people over the age of 80 [6]. In either case, if a ray of suspicion emerges, imaging is a diagnostic modality for diagnosing pneumonia [7].

Pneumonia, apart from causing severe morbidity and mortality in patients, also contributes to financial and emotional burdens at various levels of society [8]. It significantly contributes to disability-adjusted life years (DALY) that hamper the country's economy. Different risk factors were identified to decrease the prevalence of pneumonia or severity of infection, including deprivation of micronutrients like vitamins and minerals such as zinc, which are essential for the effective functioning of various vital immunological systems of the body [9, 10].

Current research findings suggest the probable role of Vitamin D in the methodical function of both humoral immunity by producing antibodies and cytokines and cell-mediated immunity by recruiting different cell lineages for regulating host defense by differentiation of lymphocytes [11,12]. Different immune cells working in the body, like lymphocytes and monocytes, have specific Vitamin D binding receptors on the cell membrane [13]. Adequate levels of Vitamin D are required for prompt functioning of lineages of immune cells to protect the human body against microorganisms like bacteria and viruses [14].

Western studies identified that deficiency of Vitamin D has a role in the causation of various infections like urinary tract infections, different types of autoimmune diseases like psoriasis, pneumonia of various etiologies, bacterial infections like tuberculosis, viral infections, and many more, including cancers [15,16].

In India, the role of Vitamin D deficiency in the causation of community-acquired pneumonia is established in a few studies. However, the relationship between the severity of Vitamin D deficiency severity and the outcome of pneumonia is less studied. Hence, an attempt is made to study their relationship in the current study.

MATERIALS & METHODS:

The present study was a case-control, observational study conducted on patients who came for admission with symptoms of pneumonia. 100 consecutively admitted patients with a diagnosis of pneumonia attending internal medicine OPD, Narayana Medical College, Nellore, were recruited into the study. The study period was between May 2023 to December 2023

The inclusion criteria:

1. Study subjects were 18 years of age or older
2. Both sexes
3. Patients with a confirmed diagnosis of Community-acquired pneumonia.
4. Patients with an established diagnosis of pneumonia within 48 hours after admission
5. Willing to give informed consent.

The exclusion criteria:

1. The patient has been hospitalized for the past 3 months.
2. Patients suffering from chronic diseases like chronic kidney disease, heart disease, etc.
3. Patients who reside in hospitals for any other illness,
4. Patients who are Pregnant or lactating mothers.
5. Patients who have consumed supplemental calcium and Vitamin D during the last 3 months,
6. Patients with a history or diagnosis suggestive of previous malabsorption diseases
7. Not willing to give informed consent.

According to the results of a case-control study conducted by Talebi F et al. in 2016, the prevalence of vitamin D deficiency among cases of severe acute lower respiratory infection was reported to be 50%. Based on these results, we arrived at a sample size 94 at 98% significance level and 94% statistical power [4]. All subjects satisfied with the inclusion and exclusion criteria were recruited into the study. Prior to enrollment, all patients signed an informed consent form, and the study protocol was approved by the Institution's ethics committee (NMC/ADM/ETHICS/approval/013/04/2023).

The patient's sociodemographic data was collected on a template prepared according to the modified Kuppaswamy classification; diagnosis of pneumonia is done by physical examination and chest x-ray. A physical examination is done to evaluate findings of pneumonia, and the severity of pneumonic illness is assessed

by using the CURB-65 score (confusion, uremia, respiratory rate, low blood pressure, age \geq 65 years) [16], which is corroborated with radiological (x-ray) findings. After the patient's admission, the blood sample is collected the following day. Serum Vitamin D levels were estimated using the chemiluminescence method using a liaison auto-analyzer (Stillwater, MN, USA). The basic principle of Chemiluminescence is an immune assay analyzer used to detect the ultra-trace level of substances in the blood or other body fluids. Vitamin D levels were classified based on WHO guidelines into mild insufficiency if the value of Vitamin D is between 21-29 ng/ml, moderate if the value is between 11-20 ng/ml, and severe if the value is \leq 10 ng/ml.

Statistical analyses

To study the association between Vitamin D deficiency and severity and the outcome of community-acquired pneumonia, Logistic regression analyses were done using the SPSS statistical software program package (SPSS version 25.0 for Windows, Armonk, NY: IBM Corp.) Continuous variables were summarized using mean and standard deviation (mean \pm SD). For the bivariate analysis, when the variables were parametric, the difference of averages test (Student's *t*-test) was used; in the case of variables with more than two categories, the one-way ANOVA test was carried out. Also, chi-square tests were used for categorical variables. Simple and multiple logistic regression analysis was performed to assess the association between vitamin D deficiency and pneumonia. Two-tailed tests determined significance levels, and 95% CIs for relative risks were calculated. A *P*-value of less than 0.05 was considered statistically significant in all tests.

RESULTS

Socio-demographic details of the study population are described in Table 1. Out of 100 study participants, 72% were male, and 28 % of the sample were females. The mean age and standard deviation of the study sample is 65.45 \pm 11.36.

The study sample was not statistically significant among all socio-demographic variables, except in age group distribution. In the study sample, mean and standard deviation values of serum Vitamin D levels measured among different sociodemographic variables are enlisted in Table 2 of all the study variables. Statistically significant correlational values were obtained in the differentiation of study participants' age group and education status variables.

Table 1: Socio-demographic details, smoking status, and past medical history of the study sample

Variables	Case (n=100)	P-value
Gender		
Male	72 (72%)	0.813
Female	28 (28%)	
Age, years (mean \pm SD)	65.45 \pm 11.36	0.04
Age group		
<70 years	34 (34%)	0.007
>70 years	66 (66%)	
Education		
Illiterate	71(71%)	0.789
Educated	29 (29%)	
Resident in		
Urban area	32(32%)	0.261
Rural area	68 (68%)	
Occupation		
Not working	63 (63%)	0.798
Self-employed	35 (35%)	
Employee	2 (2%)	
Smoking status		
Current smoker	20(20%)	0.693
Former smoker	30 (30%)	
Never smoker	50 (50%)	
Underlying disease		
IHD	20 (20%)	0.089
HTN	37 (37%)	
COPD	15 (15%)	
None	28(28%)	

The correlation between community-acquired pneumonia and serum levels of Vitamin D is depicted in Table 3. Vitamin D levels are classified based on serum levels of 21-30, classified as mild deficiency, 11-20 as moderate, and <10 as severe deficiencies, respectively. As per the results, the risk of developing community-acquired pneumonia among Vitamin-D deficiency individuals increases as the severity of deficiency increases. The risk of pneumonia among the subjects with deficient Vitamin D levels was 3.72 (1.39, 8.98) times compared to normal serum levels of Vitamin D. Also, the odds ratio of the severe level of vitamin D deficiency in the study sample was 2.56 (1.28, 5.87). Results of the correlation between the severity of pneumonia and the degree of deficiency of Vitamin D are enumerated in Table 4.

Community-acquired pneumonia severity was assessed using the CURB-65 scoring pattern. The duration of hospital stays and ICU admission established the outcome of pneumonia. As per the results, no statistically significant difference existed between low or high levels of pneumonia (CURB-65 scoring) about serum levels of Vitamin D ($p=0.923$).

Table 2: Serum Vitamin D levels on different study variables (Mean \pm Standard deviation)

Variables	Case (n=100)	P-value
Gender		
Male	31.38 \pm 29.73	0.627
Female	16.93 \pm 17.38	0.081
Age group		
<70 years	28.13 \pm 26.39	0.009
>70 years	13.18 \pm 10.23	0.180

Education		
Illiterate	28.29 \pm 25.47	0.819
Educated	10.16 \pm 9.34	0.008
Resident in		
Urban area	23.97 \pm 23.79	0.356
Rural area	24.12 \pm 21.34	0.398
Smoking status		
Never smoker	25.39 \pm 28.45	0.317
Current smoker	17.31 \pm 18.32	0.832
Former smoker	18.19 \pm 19.36	0.787
Past Underlying disease		
None	17.13 \pm 18.79	0.368
COPD	32.29 \pm 19.84	0.218
HTN	26.83 \pm 25.90	0.332
IHD	31.94 \pm 34.69	0.698

Table 3: Association between serum vitamin D levels and CAP

Variables	Cases	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	P-value
Mild deficiency (21-30 ng/mL)	44	0.54	0.021	0.59	0.020
Moderate deficiency (11–20 ng/mL)	36	0.36 (0.21, 0.89)	0.051	0.49 (0.28, 1.31)	0.132
Severe Deficiency (\leq 10 ng/mL)	20	2.56 (1.28, 5.87)	0.019	3.72(1.39, 8.98)	0.008

Table 4: Correlation between serum Vitamin D deficiency levels and CURB-65 score of CAP patients

Variables	CURB-65 score		ICU admission	
	0–2	3–4	Yes	No
Mean levels of 25(OH)D \pm SD	24.12 \pm 18.97	19.82 \pm 31.37	23.92 \pm 35.36	21.11 \pm 19.05
P-value	0.923		0.660	
Category of Vitamin D-Deficiency				
Mild deficiency (21-30 ng/mL)	32 (72.7%)	12 (27.3%)	13 (59.09%)	19 (37.25%)
Moderate deficiency (11–20 ng/mL)	22 (61.2%)	14 (38.8%)	3 (13.64%)	13 (25.49%)
Severe deficiency (\leq 10 ng/mL)	5(25%)	15 (75%)	1 (4.55%)	7 (13.73%)
P-value	0.143		0.279	

DISCUSSION

This observational study was conducted to evaluate the relationship between deficiency of Vitamin D levels and the severity of pneumonia in a tertiary care hospital. A total of 100 patients were recruited for the study. In this case-control study, it was observed that patients with pneumonia had a high prevalence of Vitamin D deficiency in the study population. It was also found that even though not statistically significant, people with severe pneumonia who had higher CURB-65 scores had a severe deficiency of Vitamin D (<10 ng/ml) and also required prolonged hospital admission and even some cases

required ICU admission. Our study revealed a strong association between community-acquired pneumonia and Vitamin D deficiency. Out of the total study sample of 100 patients, 15 patients had severe illness on CURB-65 scoring have severe deficiency of Vitamin D which amounts to 75% of the study population who suffered with severe deficiency of Vitamin D. Our study results are comparable with a study done by Li Wet al in south Korea who found out 80% of patients who were suffered with severe community-acquired pneumonia were having Vitamin D levels <20 ng/ml which is of significantly high

number of patients are suffering with the deficiency of Vitamin D [17].

Another study was conducted by Shojaeefar, E. Wayse et al. in India among children who were of age less than five years old and suffered from infections involving the respiratory tract of both the upper and lower, A total of 150 children who were suffering from respiratory tract infections were analyzed for their serum Vitamin D levels. The study's findings revealed a very high odds ratio (OR) of 11 in children who had a deficiency of serum vitamin <10 ng/ml, which is very significant, and they concluded that Vitamin D deficiency was a definitive risk factor for the development of community-acquired pneumonia. These findings are corroborative with our study findings [18].

In a study conducted by Amrein, K among the elderly population of Finland who is attending hospitals for treatment of community-acquired pneumonia, it was found that patients who had a severe deficiency of serum Vitamin D had developed severe pneumonia when compared to those with no or mild deficiency of Vitamin D. They concluded that people who had severe deficiency were having a 3-fold risk of developing severe illness when compared to other people (95% CI: 2.1, 4.9). The above mentioned findings are consistent with our study results (95% CI: 1.39, 8.98) [19].

Our study findings have revealed a positive correlation between the severity of community-acquired pneumonia and Vitamin D deficiency serum levels. The severity of pneumonia is assessed with a CURB-65 score. The odds ratio (OR) of study participants suffering from severe pneumonia with severe Vitamin D deficiency was estimated at 3.72 on the CURB-65 scoring pattern. Our findings of the study are consistent with a Similar study done among the general population in Germany by Tang et al., which revealed the existence of a positive correlation between serum Vitamin D levels and prevalence as well as the severity of community-acquired pneumonia on the CURB 65 score [20].

LIMITATIONS

The current study should be read with the following limitations kept in mind. The current study is done in a relatively small sample population of only 100 participants and with fewer patients with established pneumonia; hence, the study findings cannot be applicable to the general population. In the current

study, details of the etiology of pneumonias are not considered, so no comparison is possible between different etiological agents and serum Vitamin D levels.

CONCLUSIONS

The current study revealed that patients with Vitamin D deficiency develop more severe community-acquired pneumonia, require longer hospital stays, and have higher rates of ICU admission compared to patients with Vitamin D sufficiency.

FUTURE IMPLICATIONS

Studies done with larger study sample sizes, involving diverse population groups, are needed to establish the existence of a correlation between more prevalent and severe community-acquired pneumonias in vitamin-D deficient individuals. Studies considering the etiological agents, levels of serum vitamin-D in patients, and severity of illness caused by different etiological agents in vitamin-D deficiency patients will be more appropriate.

FINANCIAL ASSISTANCE

Nil

CONFLICT OF INTEREST

The authors declare no conflict of interest

AUTHOR CONTRIBUTION

M. Sai Varun collected data and interpreted the statistical values. He and Mudipalli Deepthi designed the study and contributed to drafting and editing the manuscript. Both authors wrote the final draft of the manuscript, which was read and approved by both authors.

REFERENCES

- [1] Das RR, Singh M, Naik SS. Vitamin D as an adjunct to antibiotics for the treatment of acute childhood pneumonia. *Cochrane Database Syst Rev*, **1**, CD011597 (2023).
- [2] Angelidi AM, Belanger MJ, Lorinsky MK, Karamanis D, Chamorro-Pareja N, Ognibene J, Palaiodimos L, Mantzoros CS. Vitamin D Status Is Associated With In-Hospital Mortality and Mechanical Ventilation: A Cohort of COVID-19 Hospitalized Patients. *Mayo Clin Proc*, **96**, 875-86 (2021).

- [3] Talebi F, Rasooli Nejad M, Yaseri M, Hadadi A. Association of Vitamin D Status with the Severity and Mortality of Community-Acquired Pneumonia in Iran during 2016-2017: A Prospective Cohort Study. *Rep Biochem Mol Biol*, **8**, 85-90 (2019).
- [4] Luchnikova T, Prikhodko O. Vitamin D as a marker of worsening of the course of pneumonia. *European Respiratory Journal*, **56**, 2343 (2020)
- [5] Singh N, Kamble D, Mahantshetti NS. Effect of Vitamin D Supplementation in the Prevention of Recurrent Pneumonia in Under-Five Children. *Indian J Pediatr*, **86**, 1105-11 (2019).
- [6] Miroliaee AE, Salamzadeh J, Shokouhi S, Sahraei Z. The study of vitamin D administration effect on CRP and Interleukin-6 as prognostic biomarkers of ventilator associated pneumonia. *J Crit Care*, **44**, 300-5 (2018).
- [7] Yang C, Lu Y, Wan M, Xu D, Yang X, Yang L, Wang S, Sun G. Efficacy of High-Dose Vitamin D Supplementation as an Adjuvant Treatment on Pneumonia: Systematic Review and a Meta-Analysis of Randomized Controlled Studies. *Nutr Clin Pract*, **36**, 368-84 (2021).
- [8] Sarhan TS, Elrifai A. Serum level of vitamin D as a predictor for severity and outcome of pneumonia. *Clin Nutr*, **40**, 2389-93 (2021).
- [9] Anwar MA, Anis HH, Mehwish, Ahsan M. Vitamin D supplementation protect children from lower respiratory tract infection: a controlled trial. *Indo Am J Pharm Sci.*, **6(3)**, 6097-6103 (2019)
- [10] Alsharkawy AAA, Rezk AR. Role of vitamin D, serum zinc, and serum iron deficiency in community-acquired pneumonia in children. *Egypt Pediatric Association Gaz*, **69**, 19 (2021).
- [11] Fadl N, Ashour A, Yousry Muhammad Y. Pneumonia among under-five children in Alexandria, Egypt: a case-control study. *J Egypt Public Health Assoc*, **95**, 14 (2020).
- [12] Ismail H, Menazie E, Ibrahim S, Elbaky N. Study of Vitamin D Status in Pneumonia among Children between 6 Months to 3 Years of Age. *Open Journal of Pediatrics*, **11**, 254-267 (2021)
- [13] Yadav RK, Kumar D, Singh A, Ziauddin M, Singh DK. Clinical and microbial spectrum of community-acquired pneumonia in children of north India. *Trop Doct*, **51**, 71-7 (2021).
- [14] Ensinck G, Lazarte G, Ernst A, Romagnoli A, López Papucci S, Aletti A, Chiossone A, Pigozzi F, Sguassero Y. Community-acquired methicillin-resistant *Staphylococcus aureus* pneumonia in a children's hospital. Our ten-year experience. *Arch Argent Pediatr*, **119**, 11-7 (2021).
- [15] Panfili FM, Roversi M, D'Argenio P, Rossi P, Cappa M, Fintini D. Possible role of vitamin D in Covid-19 infection in pediatric population. *J Endocrinol Invest*, **44**, 27-35 (2021).
- [16] Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, Lewis SA, Macfarlane JT. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax*, **58**, 377-82 (2003).
- [17] Guo LY, Li W, Cheng XF, et al. Relationship between vitamin D status and viral pneumonia in children. *Pediatr Allerg Immunol Pulmonol.*, **44**, 86–91 (2017)
- [18] Shojaeefar E, Malih N, Rezaei N. The possible double-edged sword effects of vitamin D on COVID-19: A hypothesis. *Cell Biol Int*, **45**, 54-7 (2021).
- [19] Amrein K, Scherkl M, Hoffmann M, Neuwersch-Sommeregger S, Köstenberger M, Tmava Berisha A, Martucci G, Pilz S, Malle O. Vitamin D deficiency 2.0: an update on the current status worldwide. *Eur J Clin Nutr*, **74**, 1498-513 (2020).
- [20] Tang J, Lu Q, Li Y, Huang L. Serum Vitamin D Levels and the Risk of Pneumonia in Children: A Systematic Review and Meta-analysis. *Topics in Clinical Nutrition*, **36(3)**, 252-260 (2021).