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Research Paper

Vitamin D status and ventilator-associated pneumonia in critically ill patients: A case-control study in Northern Iran

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ABSTRACT

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Ventilator-associated pneumonia (VAP) is a major contributor to illness and death among patients in intensive care units (ICUs). While vitamin D deficiency is known to compromise immune defenses and elevate the risk of infections, its specific association with VAP has yet to be clearly established. So, we aimed to evaluate vitamin D in patients with VAP admitted to the ICU. In this case-control study, 141 ICU patients from two hospitals in northern Iran were enrolled. Serum 25-hydroxyvitamin D levels were measured within 48 hours of ICU admission. VAP diagnosis was based on clinical and microbiological criteria ≥48 hours after mechanical ventilation. Demographic data, laboratory parameters, and mechanical ventilation duration were recorded. Vitamin D insufficiency was present in 73.7% of patients. The mean serum vitamin D level did not differ significantly between VAP and non-VAP groups; however, sufficiency was nearly twice as common in the non-VAP group. Multivariate analysis identified elevated white blood cell count (OR = 2 per 1000 cells/μL, $p < 0.001$) and reduced platelet count (OR = 0.98, $p = 0.005$) as independent predictors of VAP, while vitamin D status was not statistically significant. Vitamin D deficiency is highly predominant in ICU patients but was not an independent predictor of VAP in this study. Nevertheless, the observed trend toward higher vitamin D sufficiency in non-VAP patients, along with previous evidence, suggests potential benefits of supplementation. Larger randomized controlled trials are warranted to clarify its preventive role in VAP.

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1. Introduction

In intensive care units (ICUs), ventilator-associated pneumonia (VAP) ranks among the most prevalent hospital-acquired infections and is linked to a high mortality rate. Accounting for nearly 80% of all nosocomial pneumonias, VAP develops in patients undergoing intubation and mechanical ventilation. The cumulative risk of ventilation pneumonia is approximately 1% for daily mechanical ventilation, but increases on the first day after intubation. The risk of death for patients with VAP is higher if they require mechanical ventilation for over 10 days, remain in ICU for more than 6 days, or stay in the hospital for more than 11 days [1-4]. The three vital factors in the pathogenesis of VAP are colonization of the oropharyngeal region with pathogenic microorganisms, aspiration of these organisms from the oropharyngeal region to the lower respiratory tract, and disruption of the body's natural defense mechanisms. The most obvious risk factor is the endotracheal tube (ET), which bypasses the natural mechanical factors that prevent aspiration. ET may prevent aspiration of large amounts of material, but in fact micro aspiration increases due to the accumulation of secretions at the top of the cuff. ET and the need for suction can damage the tracheal mucosa and facilitate tracheal colonization. In addition, the pathogen can form a glycocalyx biofilm on the ET surface that protects the bacteria against antibiotics and host defense. Bacteria may also be removed during suction and inoculated into the trachea again, or small portions of the glycocalyx may be embolized into the terminal airways and carry the bacteria to these sites [5, 6]. Usually, the mortality rate due to multi-drug resistant pathogens is significantly higher than that of non-MDR pathogens [7-9].

Due to the high complications of this disease and the special conditions of intubated patients and medical treatment problems, the best thing is to prevent this disease. Because of the importance of ET as a risk factor for VAP, the most important intervention for prevention is to avoid or minimize endotracheal intubation. Successful use of non-invasive ventilation through the nasal mask or the whole face prevents many of the problems caused by ET. Strategies that minimize the length of the ventilation period, such as daily discontinuation of sedatives and serious separation protocols, have also been very effective in preventing VAP. Because VAP is caused by microorganisms, the body's defense mechanisms are important in preventing disease. Studies have shown that vitamin D deficiency is a risk factor for infections and sepsis in critically ill patients [10]. According to the American Endocrine Society vitamin D deficiency is defined as the serum level of the active form of vitamin D below 20 ng / ml. Vitamin D level between 21 to 29 is considered as insufficiency and vitamin level more than 30 ng / ml is considered as sufficient level of vitamin D [11,12]. Numerous studies have shown that vitamin D deficiency is higher in patients admitted to the ICU and there is a significant relationship between the amount of vitamin D and survival in patients and the duration of hospitalization [13-15]. Vitamin D supplements have been shown to boost the immune system. Therefore, a deficiency of this vitamin may have an adverse effect on the strength of the immune system. Studies have shown that 85% of Iranians of both sexes are deficient in vitamin D [16,17]. So far, in our region no study have been directed to explore the link between vitamin D deficiency and the incidence of VAP in adults, so we decided to conduct a study to evaluate vitamin D in patients with pneumonia admitted to the ICU.

2. Materials and Methods

2.1 Study population

In this case-control study, 141 patients admitted to the intensive care units of Razi and Poursina hospitals in Rasht, Northern Iran were selected. Pregnant women, patients using vitamin D supplementation, patients using corticosteroids, patients who have diabetes, malabsorption syndrome, chronic kidney disease and metastatic cancers, and patients with community-acquired pneumonia were excluded from this study. Based on the report by Amri Maleh et al. [18], and a case-to-control ratio of 1:2 the sample size calculation yielded a required sample of 47 cases and 94 controls. A written informed consent was obtained from all patients.

2.2 Definitions and data collection

According to the ICU protocol, beds of all these patients were 30° elevated, the cuff pressure was set to 25 cm of water, and chlorohexidine and gentamycin mouth wash was used for all patients. Intravenous pantoprazole was also used as an anti-acid agent for all patients. Incident VAP was adjudicated ≥48 hours after initiation of mechanical ventilation, using clinical criteria (CPIS) supported by microbiological evidence (quantitative culture of endotracheal aspirate or BAL where available). According to this criteria, patients were divided into 2 groups with and without pneumonia. Serum 25-hydroxyvitamin D [25(OH)D] was measured for all enrolled patients within 24 hours of ICU admission and before 48 hours of mechanical ventilation using a validated enzyme-linked immunosorbent assay (ELISA) (ELISA/Stat Fax 3500, USA). Samples were processed within 2 hours and stored at −80 °C until batch analysis. Choice of the third day was due to the fact that studies have shown that the loss of vitamin D is greater on the third day of hospitalization. Vitamin D levels <20 ng/ml were classified as insufficient [19]. Demographic characteristics of patients including age, sex and laboratory parameters of mechanical ventilation use were collected and recorded by design colleagues or ICU nurses.

2.3 Statistical analysis

The collected data were analyzed using IBM SPSS Statistics, Version 21 (IBM Corp., Armonk, NY, USA). To compare vitamin D levels, mean statistical indices and standard deviation and Independent T-test were used. In case of abnormality of vitamin D distribution, median and interquartile range indices, and Mann Whitney test were used. Chi-square test was used to compare the frequency distribution of vitamin D status in the two groups with and without pneumonia, as well as with and without mortality and with and without sepsis. In order to determine the relationship between vitamin D and pneumonia, researchers used logistic regression. This statistical method was employed after controlling for individual and other variables that could have influenced the outcome. The significance level of the tests was determined with $P < 0.05$.

3. Results

The study included patients with a mean age of 57.74 years (SD=20.02). The ages ranged from 18 to 93 years, with most patients falling into the 61-80 age bracket. In terms of gender, the cohort was almost evenly split between men (54.3%) and women (45.7%). The frequency distribution of patients based on age ($p = 0.907$) and also the distribution of sex ($p = 0.122$) in two groups with and without pneumonia were not statistically significant and there was no statistically significant difference. Table 1 compares blood parameters and days of intubation in the two groups with and without pneumonia. In this study, 62.4% of the patients had insufficient blood vitamin D levels, and 11.3% of patients had severe serum vitamin D deficiency. Overall, 73.7% (n = 104) of the total patients admitted to the ICU were somehow deficient in vitamin D. Table 2 compares the main research variable, serum vitamin D levels in the two groups with and without pneumonia. According to the data in this table, the serum levels of vitamin D in the two groups were not statistically significant and had almost the same mean and median. Multivariate analysis using logistic regression was performed to evaluate the true association between vitamin D levels and the incidence of pneumonia, adjusting for age, sex, WBC, RBC, and platelet counts. According to the final model, only two variables were identified as significant predictors of pneumonia risk: WBC ($p < 0.001$) and platelets ($p < 0.005$). Specifically, with every increase of 1000 units in WBC, the odds of developing pneumonia doubled (odds ratio = 2). Conversely, an increase in platelet count was associated with a slight decrease in pneumonia risk (odds ratio = 0.98).

4. Discussion

A recent study investigated the link among VAP and vitamin D deficiency in critically ill patients requiring mechanical ventilation. Consistent with prior epidemiological data, the study found a high prevalence of vitamin D insufficiency among patients admitted to the ICU, with nearly 75% of participants having deficient levels. However, no statistically significant difference in mean serum vitamin D concentration was observed between patients who developed VAP and those who did not. Additionally, our multivariate analysis identified elevated white blood cell count and reduced platelet count as the only independent predictors of VAP risk, supporting their role as established markers of infection severity in ICU settings. This finding is consistent with the expected leukocytosis that typically accompanies pneumonia, reflecting the host's inflammatory response to infection. Thrombocytopenia has been widely reported as a post-hospitalization complication in ICU patients and is often associated with disease severity [20-22]. Various etiologies for thrombocytopenia in critically ill patients have been identified, including sepsis, disseminated intravascular coagulation (DIC), acute respiratory distress syndrome (ARDS), certain medications, invasive monitoring devices, and blood transfusions [20,23]. In our study, a total of 73.7% of ICU-admitted patients were vitamin D deficient. These findings are consistent with previous studies, such as that by Amri Maleh et al., who reported a prevalence of 72.6% in ICU patients [18]. Similarly, Vosoughi et al. observed vitamin D insufficiency in 93.5% of ICU patients [24], and Venkatram et al., in a study of 437 patients, reported a prevalence of 88.8% [25]. Vitamin D deficiency has been associated with several adverse outcomes, including prolonged hospitalization [26], hypoalbuminemia [27], and increased mortality in critically ill patients [28].

Table 1. Comparison of blood parameters and intubation time in the two groups with and without pneumonia

Parameter	Pneumonia		P value
	Yes	No	
WBC (m/mm^3)	14.76 ± 2.09	8.14 ± 2.61	<0.001
RBC (m/mm3)	5.50 ± 0.99	5.20 ± 1.19	0.027
Hb (gr/dl)	13.26 ± 1.41	12.94 ± 1.25	0.116
Plt (m/mm3)	282.04 ± 68.73	396.56 ± 114.79	<0.001
Intubation time (Day)	8.30 ± 3.57	5.61 ± 3.86	<0.001

Table 2. Comparison between serum vitamin D levels in the two groups with and without pneumonia

Variable	Unit	Pneumonia		P value
		Yes	No	
Vitamin D levels	ng/ml	23.10±11.25	23.34±11.13	0.969

Although the exact mechanisms remain unclear, vitamin D is thought to enhance innate immunity by stimulating the activity of macrophages, lymphocytes, and monocytes. Jeng et al. demonstrated a significant correlation between vitamin D levels and cathelicidin, an antimicrobial peptide effective against Gram-positive, Gram-negative, fungal, and mycobacterial pathogens [27]. In our study, serum vitamin D levels did not differ significantly between patients with and without pneumonia. However, the proportion of patients with sufficient vitamin D was nearly twice as high in the non-pneumonia group compared to the pneumonia group. Notably, most patients with pneumonia had varying degrees of vitamin D deficiency. Miroliaee et al. reported that vitamin D supplementation in VAP patients significantly reduced mortality, independent of the causative microorganism [29]. Similarly, Han et al. found that adequate vitamin D levels were associated with shorter ICU stays in mechanically ventilated patients [30]. Large epidemiological studies also support an inverse association between vitamin D status and respiratory infection risk, as shown by Ginde et al., who demonstrated that lower serum 25-hydroxyvitamin D levels were linked to increased upper respiratory tract infections [31]. Given the quantitative nature of serum vitamin D measurements and the high prevalence of deficiency in ICU patients, using vitamin D status as a clinical indicator may be valuable in patient risk assessment. While our study did not find a statistically significant protective effect of adequate vitamin D levels against pneumonia, the observed trend toward higher sufficiency in the non-pneumonia group, combined with previous evidence, supports the potential role of supplementation. Considering the affordability, accessibility, and safety of vitamin D, alongside the poor nutritional status common among ICU patients, routine supplementation may represent a simple and cost-effective strategy to improve patient outcomes

This study's findings should be interpreted with a few key limitations in mind. First, the small sample size and the fact that all participants were from just two hospitals in a single geographic region may limit the generalizability of the results, making it difficult to apply them to a wider population. Second, because vitamin D levels were measured only once within the first 48 hours of ICU admission the data may not accurately reflect any dynamic changes in a patient's vitamin D status that might occur later on during their hospitalization. Additionally, unmeasured confounders, such as variations in nutritional status, sun exposure history, seasonal effects, and genetic factors influencing vitamin D metabolism, could have influenced the results. In this case-control study of ICU-admitted patients, vitamin D deficiency was highly prevalent, affecting nearly three-quarters of the study population. While serum vitamin D levels did not differ significantly between patients with and without VAP, the proportion of patients with sufficient vitamin D was nearly twice as high in the non-pneumonia group, suggesting a potential protective trend. White blood cell count and platelet count were the only independent predictors of VAP risk in multivariate analysis. Given the high burden of vitamin D deficiency and its potential impact on immune function, routine assessment and correction of vitamin D status in critically ill patients may be a low-cost, low-risk intervention worth considering. Further large-scale, multicenter, randomized controlled trials are warranted to clarify the role of vitamin D supplementation in the prevention and management of VAP.

Authors' contributions

AA, SS: contributed to the study concept, design, methodology, and resource acquisition. NJ, HA: performed data collection, statistical analysis, and manuscript drafting. AA, SS: provided critical revisions to the manuscript. All authors read and approved the final version of the manuscript.

Conflict of interest

No potential conflict of interest was reported by the authors.

Ethical declarations

The study protocol was approved by the Ethics Committee of Guilan University of Medical Sciences (Approval code: IR.GUMS.REC.1397.470). Patient data were analyzed anonymously. Written informed consent was obtained from all patients.

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References

1. Torres A, Niederman MS, Chastre J, Ewig S, Fernandez-Vandellos P, Hanberger H, et al. International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia: Guidelines for the management of hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT). Eur Respir J. 2017;50(3):1700582. DOI: 10.1183/13993003.00582-2017 PMID: 28890434
2. Niederman MS, Lee PC, Barriere SL, Barnes CN, Castaneda-Ruiz B. Telavancin in Hospital-Acquired and Ventilator-Associated Pneumonia (HAP/VAP) Caused by Staphylococcus aureus: Post Hoc Analysis of 2 Randomized, Controlled Trials. Infect Dis Ther. 2019;8(3):445-452. DOI: 10.1007/s40121-019-0255-0 PMID: 31372837
3. Browne E, Hellyer TP, Baudouin SV, Conway Morris A, Linnett V, McAuley DF, et al. A national survey of the diagnosis and management of suspected ventilator-associated pneumonia. BMJ Open Respir Res. 2014;1(1):e000066. DOI: 10.1136/bmjresp-2014-000066 PMID: 25553248

4. Cook DJ, Walter SD, Cook RJ, Griffith LE, Guyatt GH, Leasa D, et al. Incidence of and risk factors for ventilator-associated pneumonia in critically ill patients. Ann Intern Med. 1998;129(6):433-40. DOI: 10.7326/0003-4819-129-6-199809150-00002 PMID: 9735080
5. Drakulovic MB, Torres A, Bauer TT, Nicolas JM, Nogué S, Ferrer M. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. Lancet. 1999;354(9193):1851-8. DOI: 10.1016/S0140-6736(98)12251-1 PMID: 10584721
6. Do SI, Do KA, Akella C. Intubation Performed In The Emergency Department Is Associated With Increased Pulmonary Complications. International Journal of Scientific Research. 2019;8(5):2277-8179. URL: https://www.worldwidejournals.com/international-journal-of-scientific-research-(IJSR)/fileview/May_2019_1556782878_9106519.pdf
7. Ibn Saied W, Mourvillier B, Cohen Y, Ruckly S, Reignier J, Marcotte G, et al. A Comparison of the Mortality Risk Associated With Ventilator-Acquired Bacterial Pneumonia and Nonventilator ICU-Acquired Bacterial Pneumonia. Crit Care Med. 2019;47(3):345-352. DOI: 10.1097/CCM.0000000000003553 PMID: 30407949
8. Eliasson S, Wanecek M, Block T. Hand-och benstyrka vid intensivvårdsavdelning (IVA)-mottagning,-en retrospektiv studie. Nordisk tidsskrift for helseforskning. 2020;16(1):24. DOI: 10.7557/14.4849
9. Tuon FF, Graf ME, Merlini A, Rocha JL, Stallbaum S, Arend LN, et al. Risk factors for mortality in patients with ventilator-associated pneumonia caused by carbapenem-resistant Enterobacteriaceae. Braz J Infect Dis. 2017;21(1):1-6. DOI: 10.1016/j.bjid.2016.09.008 PMID: 27821248
10. de Haan K, Groeneveld AB, de Geus HR, Egal M, Struijs A. Vitamin D deficiency as a risk factor for infection, sepsis and mortality in the critically ill: systematic review and meta-analysis. Crit Care. 2014;18(6):660. DOI: 10.1186/s13054-014-0660-4 PMID: 25475621
11. Hollis BW, Wagner CL. Normal serum vitamin D levels. N Engl J Med. 2005;352(5):515-6. DOI: 10.1056/NEJM200502033520521 PMID: 15689596
12. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2024;109(10):e1991. DOI: 10.1210/clinem/dgae373 PMID: 21646368
13. Higgins DM, Wischmeyer PE, Queensland KM, Sillau SH, Sufit AJ, Heyland DK. Relationship of vitamin D deficiency to clinical outcomes in critically ill patients. JPEN J Parenter Enteral Nutr. 2012;36(6):713-20. DOI: 10.1177/0148607112444449 PMID: 22523178
14. Matthews LR, Ahmed Y, Wilson KL, Griggs DD, Danner OK. Worsening severity of vitamin D deficiency is associated with increased length of stay, surgical intensive care unit cost, and mortality rate in surgical intensive care unit patients. Am J Surg. 2012;204(1):37-43. DOI: 10.1016/j.amjsurg.2011.07.021 PMID: 22325335
15. McNally JD, Nama N, O'Hearn K, Sampson M, Amrein K, Iliriani K, et al. Vitamin D deficiency in critically ill children: a systematic review and meta-analysis. Crit Care. 2017;21(1):287. DOI: 10.1186/s13054-017-1875-y PMID: 29169388
16. Pugin J, Auckenthaler R, Mili N, Janssens JP, Lew PD, Suter PM. Diagnosis of ventilator-associated pneumonia by bacteriologic analysis of bronchoscopic and nonbronchoscopic "blind" bronchoalveolar lavage fluid. Am Rev Respir Dis. 1991;143(5 Pt 1):1121-9. DOI: 10.1164/ajrccm/143.5_Pt_1.1121 PMID: 2024824
17. Rahnavard Z, Eybpoosh S, Homami MR, Meybodi HA, Azemati B, Heshmat R, et al. Vitamin d deficiency in healthy male population: results of the Iranian multi- center osteoporosis study. Iran J Public Health. 2010;39(3):45-52. PMID: 23113022
18. Amri Maleh P, Firouzjahi A, Heidari B, Malaki S, Bijani A, Heidarnia F. The Relationship between Serum Vitamin D Level and the Outcome of Patients Hospitalized in the Medical Intensive Care Unit. J Babol Univ Med Sci. 2017;19(1):7-13. URL: http://jbums.org/article-1-6395-en.html
19. Sanaie S, Mahmoodpoor A, Hamishehkar H, Fattahi S, Soleymani S, Faramarzi E. The Relationship of Serum Vitamin D Level With the Outcome in Surgical Intensive Care Unit Patients. Iran J Pharm Res. 2019;18(2):1052-1059. DOI: 10.22037/ijpr.2019.1100658 PMID: 31531086
20. Vanderschueren S, De Weerdt A, Malbrain M, Vankersschaever D, Frans E, Wilmer A, et al. Thrombocytopenia and prognosis in intensive care. Crit Care Med. 2000;28(6):1871-6. DOI: 10.1097/00003246-200006000-00031 PMID: 10890635
21. Stéphan F, Hollande J, Richard O, Cheffi A, Maier-Redelsperger M, Flahault A. Thrombocytopenia in a surgical ICU. Chest. 1999;115(5):1363-70. DOI: 10.1378/chest.115.5.1363 PMID: 10334154
22. George JN, Raskob GE, Shah SR, Rizvi MA, Hamilton SA, Osborne S, et al. Drug-induced thrombocytopenia: a systematic review of published case reports. Ann Intern Med. 1998;129(11):886-90. DOI: 10.7326/0003-4819-129-11_part_1-199812010-00009 PMID: 9867731
23. Wade EE, Rebuck JA, Healey MA, Rogers FB. H(2) antagonist-induced thrombocytopenia: is this a real phenomenon? Intensive Care Med. 2002;28(4):459-65. DOI: 10.1007/s00134-002-1233-6 PMID: 11967601
24. Vosoughi N, Kashefi P, Abbasi B, Feizi A, Askari G, Azadbakht L. The relationship between Vitamin D, clinical outcomes and mortality rate in ICU patients: A prospective observational study. J Res Med Sci. 2016;21:75. DOI: 10.4103/1735-1995.189692 PMID: 27904620
25. Venkatram S, Chilimuri S, Adrish M, Salako A, Patel M, Diaz-Fuentes G. Vitamin D deficiency is associated with mortality in the medical intensive care unit. Crit Care. 2011;15(6):R292. DOI: 10.1186/cc10585 PMID: 22152332
26. Aung K, Burnett J, Smith SM, Dyer CB. Vitamin D deficiency associated with self-neglect in the elderly. J Elder Abuse Negl. 2006;18(4):63-78. DOI: 10.1300/j084v18n04_07 PMID: 17972660
27. Jeng L, Yamshchikov AV, Judd SE, Blumberg HM, Martin GS, Ziegler TR, et al. Alterations in vitamin D status and anti-microbial peptide levels in patients in the intensive care unit with sepsis. J Transl Med. 2009;7:28. DOI: 10.1186/1479-5876-7-28 PMID: 19389235
28. Lee P, Nair P, Eisman JA, Center JR. Vitamin D deficiency in the intensive care unit: an invisible accomplice to morbidity and mortality? Intensive Care Med. 2009;35(12):2028-32. DOI: 10.1007/s00134-009-1642-x PMID: 19756497
29. Miroliaee AE, Salamzadeh J, Shokouhi S, Fatemi A, Ardehali SH, Hajiesmaeili MR, et al. Effect of Vitamin D Supplementation on Procalcitonin as Prognostic Biomarker in Patients with Ventilator Associated Pneumonia Complicated with Vitamin D Deficiency. Iran J Pharm Res. 2017;16(3):1254-1263. PMID: 29201115
30. Han JE, Jones JL, Tangpricha V, Brown MA, Brown LAS, Hao L, et al. High Dose Vitamin D Administration in Ventilated Intensive Care Unit Patients: A Pilot Double Blind Randomized Controlled Trial. J Clin Transl Endocrinol. 2016;4:59-65. DOI: 10.1016/j.jcte.2016.04.004 PMID: 27419080
31. Ginde AA, Mansbach JM, Camargo CA Jr. Association between serum 25-hydroxyvitamin D level and upper respiratory tract infection in the Third National Health and Nutrition Examination Survey. Arch Intern Med. 2009;169(4):384-90. DOI: 10.1001/archinternmed.2008.560 PMID: 19237723