

Admission Vitamin D Status And Outcome of Critically ILL Patients on Mechanical Ventilation In Our ICU Set

UP: A 60 Days Observational Study.

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Abstract

Background and Aims: ICU patients are mostly deficient in Vitamin D because of poor nutrition as well as no exposure to sunlight. Inadequate Vitamin D is associated with increased risk of infection and organ dysfunction. Hence, our study aimed to find the correlation between admission time serum Vit. D status and clinical outcome in critically ill patients on mechanical ventilator in our ICU set up.

Methods: out of total 41 patient admitted to ICU in 60 days, 30 patients on mechanical ventilator were chosen. Serum vit. D status was assessed with 24hours of ICU admission. Primary outcome studied was mortality status(APACHE II, SOFA score, GCS). Secondary outcome were number of days on mechanical ventilation, biochemical profiles, biophysical profile, advanced care modalities and others.

Results: Low level of Vit. D were present in 60% of patients (50% deficient and 10% insufficient) . 40% were Vit. D sufficient patients. There was a negative correlation between vitamin D level and mortality status (APACHE II p-value , SOFA p-value , GCS p-value)

Conclusion: Vit. D deficiency is prevalent in as high as 60% of critically ill patients on mechanical ventilation. However, its deficiency doesnot affect the outcome of patients. It is not an independent decisive factor for mortality, although it might be related with poor clinical status.

Keywords: Vitamin D, APACHE II, SOFA Score, GCS, Mortality

Introduction

Vitamin D is a fat soluble vitamin. The main source of vitamin D in man is skin. When exposed to sunlight, 7-

Dehydrocholesterol converts into cholecalciferol--vitamin D3--as a result of UV radiation. Cholecalciferol hydroxylates in liver into 25-hydroxyvitamin D3 [25(OH)D, calcidiol]. 25(OH)D hydroxylates in kidneys into 1,25-dihydroxyvitamin D3 [1,25(OH)2D, calcitriol]¹, which is considered an active metabolite of vitamin D.

Vit. D plays an important role in calcium homeostasis. Calcitriol activates the vitamin D receptors in the cells, and this triggers the endocrine and autocrine effects of vitamin D. Vitamin D plays a major role in calcium homeostasis and bone metabolism, as well as in the immunoregulatory system¹. Vitamin D deficiency is defined as serum calcidiol levels below 25 ng/ mL, and the incidence in intensive care patients varies between 17% and 82%^{2,3}. Reduced formation of calcitriol in the tissues might lead to impaired immune responses, mucosal barriers and endothelial functions^{4,5,6}. Its deficiency is associated with organ dysfunction and increased susceptibility to hospital-acquired infections in critically ill patients⁷.

Patients receiving mechanical ventilation are at increased risk of Vitamin D deficiency due to prolonged confinement to bed with decreased exposure to sunlight, poor dietary intake, abnormal gastrointestinal functions and drug interactions⁸. However, the effect of therapeutic administration of Vitamin-D in critically ill patients did not consistently result in a better outcome, rather generated conflicting inferences^{9,10}.

Our primary objective is to investigate the relationship between vitamin D level at ICU admission and mortality.

Methodology

Following approval from Institutional Ethical Committee, 30 adult patients on mechanical ventilation

admitted in the ICU of our setup were included. It is a cross sectional, observational study. Written informed consent was obtained.

Inclusion Criteria: 30 adult patients on mechanical ventilator (both non surgical and post surgical patients, Age >18years.

Exclusion Criteria: patient with chronic renal disease, pregnancy, hypo or hyperthyroidism, thyroidectomy, parathyroidectomy, neck surgery, and readmission in ICU and getting vit D or calcium supplements were excluded.

Demographic profile of patients were recorded using pre designed proforma. All previous laboratory investigations at admission to hospital were collected. Blood samples for serum 25(OH)D estimation were collected within 24hour of admission to the ICU. Based on previous study by Yadav S et al, we have assumed, serum 25(OH)D: >30ng/ml= sufficient, 20-30ng/ml= insufficient, <20ng/ ml= deficient. Patient with normal Vit. D level included sufficient group. Patient with low Vit. D level included (insufficient + deficient) group.

Outcome predictability of patients was measured using Acute Physiology and Chronic Health Evaluation (APACHE II), Sequential Organ Failure Assessment (SOFA) scores and GCS within first 24hour of admission to ICU. Primary outcome studied was mortality (APACHE II, SOFA score, GCS). Secondary outcome were days on mechanical ventilation, biochemical profiles, biophysical profiles, advanced care modalities and others

The data was entered into excel sheet and analysed using SPSS version 16. Mean, Standard deviation and p-value were calculated. Level of significance was considered as p value<0.05

Results

Out of total 30 patients, 6(20%) were post surgery and 24(80%) were non surgical patients on mechanical ventilator in ICU (figure 1)

Male and female percentage in ICU was 4:1. 80% of them were male patients (figure 2)

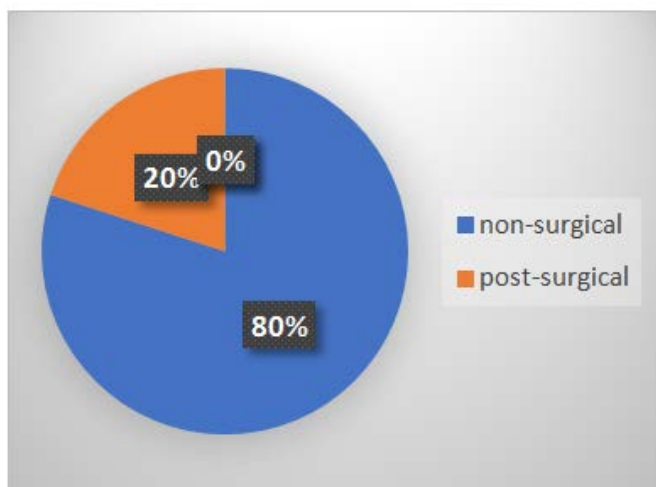


Figure 1: distribution of ICU patients(post-surgical and non-surgical)

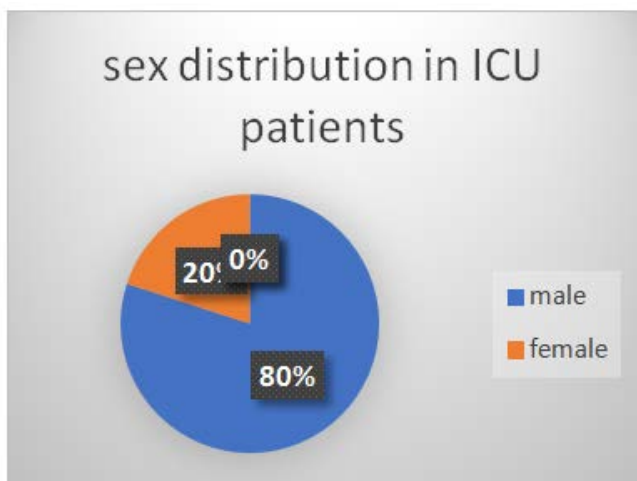


Figure 2: sex distribution in ICU patients

Low level of Vit. D were present in 60% of patients [50% deficient (<20ng/ml) and 10% insufficient(20-30ng/ml)] . 40% were Vit. D sufficient patients with serum vit. D >30ng/ml (figure 3).

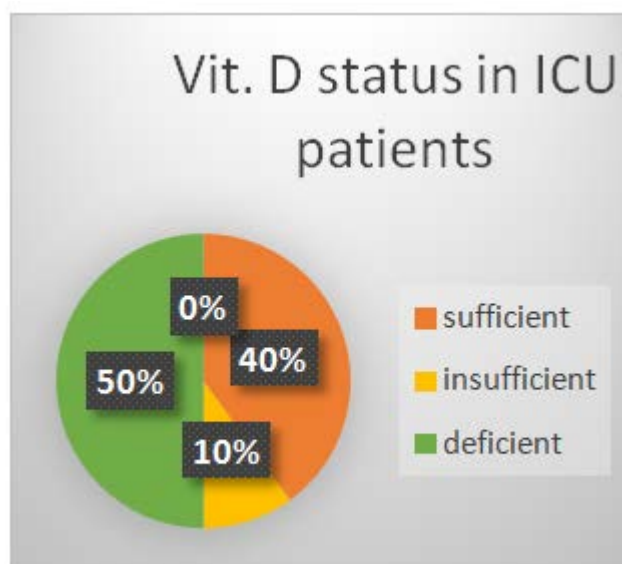


Figure 3: Admission serum Vit. D status in ICU patients

The demographic and biochemical parameters were comparable between sufficient and low vit. D level groups (table 1). P-value>0.05

	Patient with low Vit. D (mean±SD)	Patient with normal Vit. D (mean±SD)	p-value
Age(years)	40.05 ± 9.1	40.41 ± 9.61	0.9180
Hematocrit	33 ± 6.37	34.6 ± 7.9	0.5515
TLC(/mm ³)	8355	8263	
Serum calcium(meq/ml)	6.17 ± 0.89	6.29 ± 1.64	0.7970
Serum phosphate(meq/ml)	4.73 ± 0.88	4.5 ± 0.98	0.5081
Serum albumin(gm/dl)	4.4 ± 0.61	4.57 ± 0.65	0.4723
Serum creatinine(mg/dl)	0.86 ± 0.42	0.71 ± 0.28	0.2877
Serum sodium(meq/l)	142.5 ± 7.31	137.58 ± 7.8	0.0893
Serum potassium(meq/l)	3.75 ± 0.47	4.07 ± 0.62	0.1190

Table 1: demographic and biochemical profile of patients

There is no significant difference between biophysical profiles in both groups (table 2). P-value>0.05

	Patient with low Vit. D (mean±SD)	Patient with normal Vit. D (mean±SD)	p-value
Temperature(*C)	39.4 ± 2.79	38.21 ± 2.02	0.2148
Mean Arterial Pressure(mm Hg)	72.96 ± 5.5	71.54 ± 4.6	0.4857
Respiratory Rate(breaths/min)	22.11 ± 5.21	23.08 ± 3.8	0.5847
Arterial PH	7.18 ± 0.9	7.23 ± 0.18	0.8515
Heart Rate(beat/min)	75.11 ± 13.0	78.12 ± 9.9	0.5021

Table 2: biophysical profile of patients

A statistically insignificant trend was seen towards APACHE II, SOFA score and GCS score. The outcomes were comparable between the two groups (table 3)

	Patient with low Vit. D (mean±SD)	Patient with normal Vit. D (mean±SD)	p-value
GCS	8.6 ± 1.23	8.8 ± 1.5	0.6924
APACHE II	18.7 ± 1.39	19.25 ± 1.42	0.3015
SOFA	4.27 ± 1.01	4.46 ± 1.5	0.6807

Table 3: mortality indicators

Length of days in ICU and number of days on mechanical ventilation are comparable between the groups. However, patients with normal vit. D level reached earlier spontaneous breathing trial than patients with low vit. D level (table 4).

	Patient with low Vit. D (mean±SD)	Patient with normal Vit. D (mean±SD)	p-value
Length of stay in ICU(days)	12.08 ± 2.90	10.94 ± 1.92	0.2422
Days in mechanical ventilation	11.08 ± 2.90	10.16 ± 1.6	0.3266
Days to reach spontaneous breathing trial	21	11.5	

Table 4: outcomes of patients

Respiratory failure was the most common complication of patients on mechanical ventilation, followed by renal failure, hepatic failure and others(cardiac failure, sepsis) (figure 4)

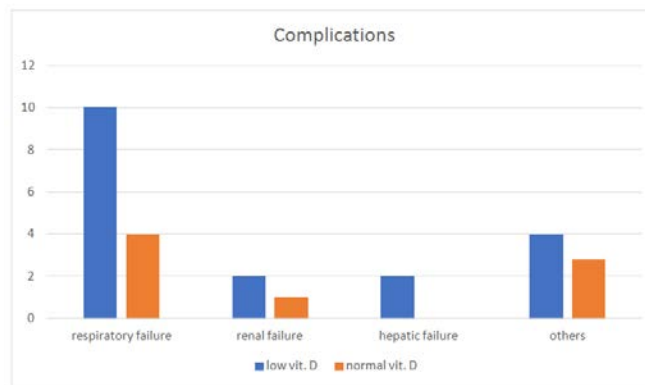


Figure 4: complications in ICU patients

Number of patients requiring advanced care modalities like tracheostomy, dialysis, CVP monitoring was higher in patients with low vit. D level (figure 5)

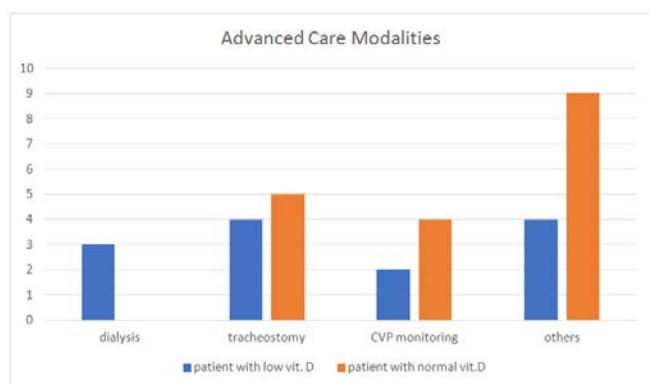


Figure 5: patients requiring advanced care modalities

Discussion

The present study showed that vitamin D deficiency was commonly observed in critically ill patients at ICU admission. This observation is similar to that reported earlier in critically ill patients by other investigators^{11,12}

Patients receiving mechanical ventilation with normal and low serum 25(OH)D had comparable demographic, biochemical and biophysical profile. The outcome of patients in terms of days on mechanical ventilation, Length of stay ICU, days to reach Spontaneous Breathing Trial, complications and requirement for advanced care modalities in both the groups were also similar. However, other studies^{13,14} suggested significant differences among the patients with normal and low serum 25(OH)D levels in terms of serum calcium level, APACHE II score.

Moromizato et al.¹⁵ found that serum vitamin D level below 16 ng/ml is associated with sepsis. Van de Berghe et al.¹⁶ showed significantly lower serum vitamin D levels in non-survivor critically ill patients. Cecchi et al.¹⁷ concluded that serum vitamin D levels do not have any significant effects on the outcome in septic patients. In the present study, we did not find any relationship between vitamin D level at ICU admission and outcomes.

Vitamin D helps to boost immunity; hence, its deficiency predisposes critically ill patients to acquire

nosocomial infections. Matthews LR et al¹⁸ suggested prolonged ICU stay of the critically ill patients with low serum 25(OH)D levels is due to nosocomial infections, complications such as metabolic derangement and immune dysfunctions. We observed no significant difference in ICU stay length and development of complications.

Dancer RC et al concluded that Vitamin D helps to prevent alveolar inflammation and maintains respiratory epithelial and mucosal integrity. Optimal serum Vitamin D levels might reduce duration of mechanical ventilation. However, in the present study, day to reach Spontaneous breathing trial and duration of mechanical ventilation were similar among the patients with normal and low serum Vitamin D levels.

Major limitation of the study was observational design and small sample size. Vitamin D level was measured only once. The primary diagnosis of patient was not specified along with other comorbidities. As it is an observational study, the confounding factors like mode of mechanical ventilation, type of sedative used were not controlled.

Conclusion

This study demonstrated that low vitamin D levels are common among patients admitted to ICU. Our results indicated that vitamin D concentration may be either a biomarker of survival or a co-factor, but not an independent decisive factor for mortality. We recommend assessing the effects of vitamin D supplementation in critically ill patients. Further studies with greater sample size may be required to get better co relationship between serum vit. D level and outcome of critically ill patients on mechanical ventilation

References

1. Bikle D. *J Clin Endocrinol Metab.* 2009 Jan; 94(1):26-34.

2. Arnson Y, Gringauz I, Itzhaky D, Amital H. Vitamin D deficiency is associated with poor outcomes and increased mortality in severely ill patients. *QJM*. 2012;105:633–9. <https://doi.org/10.1093/qjmed/hcs014>.
3. 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:R292. <https://doi.org/10.1186/cc10585>.
4. Adams JS, Hewison M. Update in vitamin D. *J Clin Endocrinol Metab*. 2010;95:471–8. <https://doi.org/10.1210/jc.2009-1773>.
5. Verstuyf A, Carmeliet G, Bouillon R, Mathieu C. Vitamin D: a pleiotropic hormone. *Kidney Int*. 2010;78:140–5. <https://doi.org/10.1038/ki.2010.17>.
6. Zhao H, Zhang H, Wu H, Li H, Liu L, Guo J, et al. Protective role of 1,25(OH)₂ vitamin D₃ in the mucosal injury and epithelial barrier disruption in DSS-induced acute colitis in mice. *BMC Gastroenterol*. 2012;12:57. <https://doi.org/10.1186/1471-230X-12-57>.
7. 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*. 2011;96:1911–30.
8. Yadav S, Joshi P, Dahiya U, et al. Admission Vitamin D status does not predict outcome of critically ill patients on mechanical ventilation: An observational pilot study. *Indian J Anaesth*. 2018;62(1):47–52. doi:10.4103/ija.IJA_531_17
9. Amrein K, Schnedl C, Holl A, Riedl R, Christopher KB, Pachler C, et al. Effect of high-dose Vitamin D₃ on hospital length of stay in critically ill patients with Vitamin D deficiency: The VITdAL-ICU randomized clinical trial. *JAMA*. 2014;312:1520–30.
10. 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.
11. Aygencel G, Turkoglu M, Tuncel AF, Candir BA, Bildacı YD, Pasaoglu H, et al. Is Vitamin D insufficiency associated with mortality of critically ill patients? *Crit Care Res Pract*. 2013;2013:856747.
12. Higgins DM, Wischmeyer PE, Queensland KM, Sillau SH, Sufit AJ, Heyland DK, et al. Relationship of Vitamin D deficiency to clinical outcomes in critically ill patients. *JPEN J Parenter Enteral Nutr*. 2012;36:713–20.
13. Quraishi SA, Bittner EA, Blum L, McCarthy CM, Bhan I, Camargo CA, Jr, et al. Prospective study of Vitamin D status at initiation of care in critically ill surgical patients and risk of 90-day mortality. *Crit Care Med*. 2014;42:1365–71.
14. Lucidarme O, Messai E, Mazzoni T, Arcade M, du Cheyron D. Incidence and risk factors of Vitamin D deficiency in critically ill patients: Results from a prospective observational study. *Intensive Care Med*. 2010;36:1609–11.
15. Moromizato T, Litonjua AA, Braun AB, Gibbons FK, Giovannucci E, Christopher KB. Association of low serum 25-hydroxyvitamin D levels and sepsis in the critically ill. *Crit Care Med*. 2014;42:97–107. <https://doi.org/10.1097/CCM.0b013e31829eb7af>.

16. Van den Berghe G, Van Roosbroeck D, Vanhove P, Wouters PJ, De Pourcq L, Bouillon R. Bone turnover in prolonged critical illness: effect of vitamin D. *J Clin Endocrinol Metab.* 2003;88:4623–32. <https://doi.org/10.1210/jc.2003-030358>.
17. Cecchi A, Bonizzoli M, Douar S, Mangini M, Paladini S, Gazzini B, et al. Vitamin D deficiency in septic patients at ICU admission is not a mortality predictor. *Minerva Anesthesiol.* 2011;77:1184–9.
18. 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;204:37–43.