

## The Relationship of Serum Vitamin D Level With the Outcome in Surgical Intensive Care Unit Patients

Sarvin Sanaie<sup>a</sup>, Ata Mahmoodpoor<sup>b</sup>, Hadi Hamishehkar<sup>c</sup>, Shirin Fattahi<sup>d</sup>, Saideh Soleymani<sup>e</sup> and Elnaz Faramarzi<sup>f\*</sup>

<sup>a</sup>Tuberculosis and lung disease research center, Tabriz University of Medical Sciences, Tabriz, Iran. <sup>b</sup>Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran. <sup>c</sup>Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran. <sup>d</sup>Faculty of dentistry, Tabriz University of Medical Sciences, Tabriz, Iran. <sup>e</sup>Students research committee, Tabriz University of Medical Sciences, Tabriz, Iran. <sup>f</sup>Liver and gastrointestinal diseases research center, Tabriz University of Medical Sciences, Tabriz, Iran.

---

### Abstract

The aim of this study was to assess the correlation of serum vitamin D with ICU length of stay, mortality rate, length of mechanical ventilation, and incidence of sepsis. We conducted a descriptive analytic study on 793 patients admitted to surgical ICU wards in northwest of Iran from March 2015 to March 2016. Patients were assessed during the ICU stay and the following data were collected: Glasgow Coma Score (GCS), APACHE II score, incidence of sepsis, duration of mechanical ventilation, LoS, mortality rate, and laboratory data (such as serum vitamin D, calcium, phosphorus, etc). The effect of vitamin D deficiency and the confounding factors on length of stay was assessed using the multinomial regression. Of 793 patients, 161 patients (20.3%) were in vitamin D deficiency group, 306 (38.6%) in vitamin D insufficiency group, 326 (41.1%) in vitamin D sufficiency group. Vitamin D deficiency increased risk of sepsis (OR = 22.93; 95%CI: 10.631-49.78) and mortality rate (OR = 42.93; 95%CI: 15.2-121.22). Vitamin D deficiency/insufficiency is a result of chronic and severe comorbidities of patients and can be considered as a helper but not a real risk factor for mortality and its level should be assessed in surgical critically ill patients. The way that various levels of vitamin D impact outcome in critically ill patients remains to be elucidated and further multi-center trials are needed to validate our results.

**Keywords:** Vitamin D; ICU, Sepsis; Mortality rate; Length of stay.

---

### Introduction

Despite the increased advances in critical care medicine, critically ill patients are still at high risk for mortality (1, 2). Some of the risk factors associated with mortality are modifiable ones and their identification and management

can be an important way to improve outcome (3).

Vitamin D deficiency has a high prevalence in critically ill patients (4, 5) and some studies have shown an association between vitamin D deficiency and ICU outcomes (5-7). The vital role of vitamin D in calcium and phosphorous homeostasis is well recognized. Nowadays, other important roles have been determined for vitamin D such as modulating the innate

---

\* Corresponding author:

E-mail: elnazfaramarzi849@gmail.com

and adaptive immune response to infectious pathogens, anti-inflammatory properties, and affecting cellular growth, proliferation and apoptosis (8-15). Therefore, vitamin D deficiency is associated with many diseases including certain cancers, immune system dysfunction, diabetes, cardiovascular disease, hypertension, lower respiratory infections, and metabolic syndrome (9, 16, 17). The prevalence of vitamin D deficiency has been reported to be between 40 to 80% among ICU patients (18-21). Taking into account the high prevalence of vitamin D insufficiency and deficiency and its important role in health status of humans, some studies have evaluated the association between serum vitamin D and outcome of critically ill patients. The findings of these studies indicated that vitamin D deficiency is correlated with disease severity and mortality, hospital costs, ICU length of stay, amount of time requiring mechanical ventilation, infection rates, bacteremia, multisystem organ failure, discharge location, and both short- and long-term mortality (22-29). However, this association has not been found in other studies (30-33) and the results of studies are conflicting. This observed discrepancy of the results may be due to the differences in sample size, method of measurements of vitamin D, and type of underlying disease. On the other hand, most of these observational studies have suggested to conduct further studies with large sample size to answer this question: "does vitamin D deficiency worsen the outcome of ICU patients?" Therefore, we decided to assess the correlation of serum vitamin D with the outcome in surgical ICU patients.

### Experimental

We conducted a descriptive analytic study on 793 patients admitted to surgical ICU of two university affiliated hospitals in northwest of Iran from March 2015 to March 2016, to assess the serum level of vitamin D and its relation with outcomes in this patient population. After obtaining approval from ethics committee of Tabriz University of Medical Sciences, the patients aging >18 years with completed informed consent were enrolled in this study. The patients with the history of intake of vitamin

D, recent ICU admission (during the last month), and end stage cancer were excluded.

The patients were assessed during the ICU stay and the following data were collected: age, sex, medical history, Glasgow Coma Score (GCS), APACHE II score, incidence of sepsis, duration of mechanical ventilation, ICU length of stay (LoS), mortality rate, and laboratory data including levels of serum vitamin D, calcium, phosphorus, urea, creatinine, albumin, hemoglobin and CRP. Vitamin D levels were measured in all patients during the first 24 hours of admission to the ICU with the chemiluminescence method. Based on the guidelines of the endocrine Society, vitamin D deficiency was defined as serum levels of 25(OH)D < 20 ng/mL, insufficiency as levels of 25(OH)D = 20–30 ng/mL, and sufficiency as 25(OH)D >30 ng/mL (21).

The primary outcome assessed in our study was ICU LoS. The secondary outcomes were mortality rate, length of mechanical ventilation, and incidence of sepsis.

### Statistical Analysis

The data were analyzed using Statistical Package for the Social Sciences (SPSS, version 11.5, Chicago, IL). We classified patients on the basis of vitamin D status into 3 groups (vitamin D deficiency, vitamin D insufficiency and vitamin D sufficiency). Descriptive statistics were obtained for all study variables and reported as mean  $\pm$  SD and also number (percent) where applicable. One Way ANOVA test on quantitative parameters and the  $\chi^2$  test on qualitative variables (gender, sepsis rate, GCS, mortality rate, duration of mechanical ventilation, APACHI Score) were used to determine whether these parameters differed between study groups. Multinomial regression was used to estimate Crude and adjusted odds ratios (OR) and their corresponding 95% confidence intervals (95% CI). ICU outcome (Sepsis rate, mortality rate, GCS, duration of mechanical ventilation) was considered as variable. Each variable was entered in the model one by one. The effect of confounding factors (age, serum calcium, phosphor, CRP, BUN, Cr, Hb, and Alb) were adjusted, and vitamin D sufficiency group was considered as a reference group. A P-value

**Table 1.** Demographic and clinical characteristics of patients stratified by vitamin D status.

		Vitamin D deficiency (n=161)	Vitamin D insufficiency (n=306)	Vitamin D sufficiency (n=326)	P-value
Age(year)		66.28±14.6	65.33±14.27	53.76±17.25	<0.001**
Gender	Male	67(41.6)	180(58.8)	255(78.2)	<0.01***
	Female	94(58.4)	126(41.2)	71(21.8)	
GCS		8.22±3.21	11.18±3.23	12.78±2.89	<0.001***
APACHE		26.30±4.72	22.45±4.11	20.38±3.14	<0.001***
Calcium(mg/dl)		7.80±0.47	8.01±0.39	8.18±0.47	<0.001***
Phosphorous(mg/dl)		3.44±0.44	3.58±0.41	3.67±0.37	<0.001***
Hb(g/dl)		11.14±1.09	11.55±1	12.02±1.28	0.01***
BUN		25.61±5.81	24.64±5.47	20.38±3.14	<0.001***
Cr		1.58±0.52	1.46±0.42	1.40±0.32	<0.001***
Alb(g/dl)		3.16±0.36	3.32±0.29	3.67±0.37	<0.001***
Dialysis		24 (14.9)	14(4.6)	8(2.5)	<0.001**
Hospital (LoS)*		24.13±11.18	12.26±7.91	6.21±4.52	<0.001***
Duration of mechanical ventilation(day)		16.58±9.04	9.02±5.98	7.10±11.27	<0001***

\* LoS: length of stay; #Number (percent), \* P value: Comparison within group by  $\chi^2$  test; \*\*\*P value: Comparison within group by One Way ANOVA; Vitamin D deficiency (<20 ng/mL); Vitamin D insufficiency (20-30 ng/mL); Vitamin D sufficiency (>30 ng/mL).

of less than 0.05 was considered statistically significant.

### Results

Demographic and clinical characteristics of patients stratified by vitamin D status are presented in Table 1. Of 793 patients, 161 patients (20.3%) were in vitamin D deficiency group, 306 (38.6%) in vitamin D insufficiency group, 326 (41.1%) in vitamin D sufficiency group. The results of one way ANOVA analysis indicated that clinical parameters of patients in vitamin D deficiency group significantly differ from the other two study groups (vitamin D insufficiency and sufficiency) ( $P < 0.05$ ). The mean length of stay in hospital and duration of mechanical ventilation for vitamin D deficiency group were  $24.13 \pm 11.18$  and  $16.58 \pm 9.04$  days which were significantly higher than the other groups.

As shown in Table 2, the incidence of sepsis, low GCS (sever brain injury), mortality rate, and duration of mechanical ventilation in vitamin

D deficiency group were more frequent than other groups. Most of the patients in vitamin D deficiency group had hospital LOS and mechanical ventilation more than 20 days while in other groups were less than 20 days. Moreover, according to APACHE score, the risk of death >40% were similar in the study groups.

Predictor factors of ICU outcome are presented in table3. Vitamin D deficiency increased the risk of sepsis (OR = 22.93; 95%CI: 10.631-49.78 ) and mortality rate (OR = 42.93; 95%CI: 15.2-121.22) versus ( OR = 8.9; 95% CI:4.16-19.02) and (OR: 3; 95% CI: 0.94-9.53) in vitamin D insufficiency respectively. In addition, vitamin D deficiency were significantly correlated (OR = 29.07; 95% CI: 15.99-53.03) with low GCS <8-9. However, the correlation of vitamin D deficiency with ICU outcomes decreased after adjusting for age, serum calcium and phosphor, BUN, Cr, CRP, Hb, and Alb.

### Discussion

Our results showed that almost 57% of

**Table 2.** The prevalence of Sepsis, GCS, duration of mechanical ventilation according to vitamin D status.

	Vitamin D deficiency		Vitamin D insufficiency		Vitamin D sufficiency	
	N	%	N	%	N	%
Sepsis	59	36.66	56	18.3	8	2.5
<b>GCS</b>						
Sever (<8-9 )	95	59	72	23.5	38	11.7
Moderate (9-12)	47	29.2	113	36.9	66	20.2
Minor ≥13	19	11.8	119	38.9	221	67.8
In hospital mortality rate	56	34.8	11	3.6	4	1.2
Mechanical ventilation	156	96.2	191	62.4	83	25.5
<b>Duration of mechanical ventilation (day)</b>						
0-5	10	6.2	74	24.2	51	15.6
6-10	30	18.6	46	15	13	4
10-15	32	19.9	40	13.1	14	4.3
16-20	33	20.5	21	6.9	4	1.2
21-25	31	19.3	8	2.6		
26-30	5	3.1	2	0.7	-	-
31-35	9	5.6	-	-	-	-
36-40	4	2.5	-	-	-	-
41-45	2	1.2	-	-	-	-
<b>Hospital (LoS)*</b>						
1-10	14	8.7	150	49	278	85.3
11-20	48	29.8	97	31.7	44	13.5
21-30	55	34.2	52	17	-	
31-40	29	18	7	2.3	2	0.6
41-50	10	6.2	-	-	-	-
51-65	4	2.5	-	-	-	-
<b>APACHE Death risk</b>						
4	-	-	-	-	-	-
8	-	-	-	-	-	-
15	2	1.2	-	-	2	0.6
25	2	1.2	67	21.9	149	45.7
40	71	44.1	171	55.9	139	42.6
55	42	26.1	45	14.7	30	9.2
75	33	20.5	12	3.9	4	1.2
85	9	5.6	8	2.6	-	-

\*LoS: length of stay; Vitamin D deficiency (<20 ng/mL); Vitamin D insufficiency (20-30 ng/mL); Vitamin D sufficiency (>30 ng/mL).

patients admitted to our surgical ICUs had vitamin D insufficiency/deficiency which was much higher rate compared to previous large trials showing prevalence between 20-40% (6, 20, 34). These results may be attributed to low economic status of our study population since they were selected from governmental hospitals.

In addition, our samples have totally low

exposure to sun light due to religious covering (hijab) and the geographical position of our region which is in north of Iran with high altitude. We showed a relation between 25 (OH) vitamin D deficiency and mortality. Similar to our findings, lee *et al.* showed a threefold mortality rate in vitamin D insufficient patients compared to patients with normal levels (5). Aygençel *et al.*

Table 3. Predictor factors of ICU outcome.

	Vitamin D deficiency			Vitamin D insufficiency			Vitamin D sufficiency					
	Unadjusted			Adjusted			Unadjusted			Adjusted		
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Sepsis	22.93 (10.631-49.78)	<0.001	10.83(4.33-23.44)	<0.001	8.9(4.16-19.02)	<0.001	6.94(3.17-15.22)	<0.001	Ref	-	Ref	-
<b>GCS</b>												
Sever (<8-9)	29.07(15.99-53.03)	<0.001	26.92(13.53-53.57)	<0.001	3.51(2.24-5.52)	<0.001	3.4(2.1-5.49)	<0.001	Ref	-	Ref	-
Moderate (9-12)	8.28(4.54-15.08)	<0.001	6.92(3.43-13.97)	<0.001	3.18(2.18-4.63)	<0.001	3.25(2.14-4.93)	<0.001	Ref	-	Ref	-
Mortality	42.93(15.2-121.22)	<0.001	14.3(4.57-44.74)	<0.001	3(0.94-9.53)	0.06	1.5(0.41-5.01)	<0.001	Ref	-	Ref	-

Adjusted for serum Ca, P, Hb, BUN, Cr, CRP  
 Vitamin D deficiency (<20 ng/mL); Vitamin D insufficiency (20-30 ng/mL); Vitamin D sufficiency (>30 ng/mL).

showed that vitamin D deficiency is significantly associated with higher mortality rate but vitamin D deficiency is not an independent risk factor for mortality (32). Vitamin D levels were more significant in survivors compared to non-survivors. The explanation for the association of higher mortality rate with low levels of vitamin D may be due to the endothelial or immune cell dysfunction and impaired glucose and calcium metabolism accompanied with low levels of vitamin D. Contrary to previous trials, we didn't find any significant correlation between serum levels of albumin and vitamin D deficiency (35) which may be due to the economic status and low levels of medical care of our patients. Risk factors for vitamin D deficiency are older age, diminished sunlight exposure, obesity, pigmentation and dark skin, low intake and malabsorption syndromes (19). Level of Vitamin D declined more during ICU stay because of insufficient replacement and absent sunlight exposure. We showed that vitamin D deficiency/insufficiency were more in older patients and females which is similar to previous trials (36). Higher prevalence of lower levels of vitamin D in females is related to religious and covering in our country and also could be a reflection of general vitamin D deficiency in our country. Our univariate analysis showed that vitamin D deficiency is associated with occurrence of sepsis which is similar to previous studies (37, 38). But after adjustment of different cofactors (Calcium, phosphorus, hemoglobin, blood urea nitrogen, creatinine and CPR) there was not a significant relation between sepsis and vitamin D levels which shows the possibility of being a cofactor, not a biomarker, for mortality in critical ill patients. A recently performed observational study showed that vitamin D deficiency is not associated with 90 day mortality in septic patients, but is associated with more hospital acquired infections and more acute kidney injury (39). We didn't show any correlation between vitamin D levels and total calcium levels which could explain that the association of mortality and vitamin D levels is not modified by calcium levels. However, the best method for calcium assay in critically ill patients is measurement of ionized calcium not total calcium. Recently, Brook *et al* in a retrospective analysis showed

that vitamin D level may be a modifiable risk factor for non-home discharge destination in surgical critically ill patients. Arnson in another study showed that vitamin D level in critically ill patients may be a marker of survival or a cofactor and they recommended assessment of vitamin D supplementation in critically ill patients (40). Ebenezer *et al* showed that Vitamin D deficiency is also common in critically ill pediatric patients admitted to ICU. Low serum 25 (OH) D level was associated with higher severity of illness, more days on mechanical ventilation, more vasopressor use and lower serum calcium levels. They couldn't show any relation between vitamin D levels and mortality rate which may be due to the small sample size of their population (41). Anwar *et al.*, in their recently performed study in 250 critically ill patients, showed a high prevalence of vitamin D deficiency in these patients and showed its relation with severity of disease, but they could not confirm vitamin D as an independent risk factor for mortality in critically ill patients(42).

#### Limitation

First, we only analyzed surgical patients; so we cannot generalize these results to whole (surgical/medical) critically ill population. Second, we didn't assay ionized calcium and PTH levels in our study and we could not exclude the confounding effects of these variables. Third, we did not determine vitamin D level sequentially; so its level on admission could be a reflection of preadmission deficiency as resuscitation and hemodilution can decrease the vitamin D levels. Thus, interpreting vitamin D levels in critically ill patients during resuscitation on ICU admission should be performed with caution (43).

#### Conclusion

Vitamin D deficiency is common in critically ill patients and causes different systemic effects in surgical ICU patients. Our study showed a strong association between hospital mortality and 25 (OH) vitamin D levels in critically ill patients. Vitamin D deficiency is associated with increase in length of ICU stay and sepsis. Vitamin D deficiency/insufficiency is a result

of chronic and severe comorbidities of patients and can be considered as a helper but not a real risk factor for mortality and its level should be assessed in surgical critically ill patients. The way that various levels of vitamin D impact outcome in critically ill patients remains to be elucidated and further multi-center trials are needed to validate our results.

#### Acknowledgment

The authors are grateful for the financial support of Research vice-chancellor, Tabriz University of Medical Sciences.

#### References

- (1) Groeger JS, Strosberg MA, Halpern NA, Raphaely RC, Kaye WE, Guntupalli KK, Bertram DL, Greenbaum DM, Clemmer TP and Gallagher TJ. Descriptive analysis of critical care units in the United States. *Crit. Care Med.* (1992) 20: 846-63.
- (2) Groeger JS, Guntupalli KK, Strosberg M, Halpern N, Raphaely RC, Cerra F and Kaye W. Descriptive analysis of critical care units in the United States: patient characteristics and intensive care unit utilization. *Crit Care Med* 279-91 :21 (1993) ..
- (3) Chen Y-C, Lin S-F, Liu C-J, Jiang DD-S, Yang P-C and Chang S-C. Risk factors for ICU mortality in critically ill patients. *J. Formos Med. Assoc.* (2001) 100: 656-61.
- (4) McKinney T, Patel JJ, Bennis MV, Nash NA and Miller KR. Vitamin D status and supplementation in the critically ill. *Curr. Gastroenterol. Rep.*(2016) 18: 18.
- (5) Lee P, Eisman JA and Center JR. Vitamin D deficiency in critically ill patients. *N Engl. J. Med.* (2009) 360: 1912-4.
- (6) Braun A, Chang D, Mahadevappa K, Gibbons FK, Liu Y, Giovannucci E and Christopher KB. Association of low serum 25-hydroxyvitamin D levels and mortality in the critically ill. *Crit. Care Med.* (2011) 39: 671.
- (7) Lee P, Nair P, Eisman JA and Center JR. Vitamin D deficiency in the intensive care unit: an invisible accomplice to morbidity and mortality? *Intens Care Med.*(2009) 35: 2028.
- (8) Arnson Y, Amital H and Shoenfeld Y. Vitamin D and autoimmunity: new aetiological and therapeutic considerations. *Ann. Rheum. Dis.* (2007) 66: 1137-42.
- (9) Holick MF. Vitamin D deficiency. *N. Engl. J. Med.* (2007) 357: 266-81.
- (10) Peelen E, Knippenberg S, Muris A-H, Thewissen M, Smolders J, Tervaert JWC, Hupperts R and Damoiseaux J. Effects of vitamin D on the peripheral adaptive immune system: a review. *Autoimmun. Rev.* (2011) 10: 733-43.
- (11) Pelajo CF, Lopez-Benitez JM and Miller LC. Vitamin D and autoimmune rheumatologic disorders. *Autoimmun.*

- Rev. (2010) 9: 507-10.
- (12) Shapira Y, Agmon-Levin N and Shoenfeld Y. Mycobacterium tuberculosis, autoimmunity, and vitamin D. *Clin. Rev. Allergy Immunol.* (2010) 38: 169-77.
  - (13) Souberbielle J-C, Body J-J, Lappe JM, Plebani M, Shoenfeld Y, Wang TJ, Bischoff-Ferrari HA, Cavalier E, Ebeling PR and Fardellone P. Vitamin D and musculoskeletal health, cardiovascular disease, autoimmunity and cancer: Recommendations for clinical practice. *Autoimmun. Rev.* (2010) 9: 709-15.
  - (14) Toubi E and Shoenfeld Y. The role of vitamin D in regulating immune responses. *Isr. Med. Assoc. J.* (2010) 12: 174.
  - (15) Zold E, Szodoray P, Nakken B, Barath S, Kappelmayer J, Csathy L, Hajas A, Sipka S, Gyimesi E and Gaal J. Alfacalcidol treatment restores derailed immune-regulation in patients with undifferentiated connective tissue disease. *Autoimmun. Rev.* (2011) 10: 155-62.
  - (16) Pludowski P, Holick MF, Pilz S, Wagner CL, Hollis BW, Grant WB, Shoenfeld Y, Lerchbaum E, Llewellyn DJ and Kienreich K. Vitamin D effects on musculoskeletal health, immunity, autoimmunity, cardiovascular disease, cancer, fertility, pregnancy, dementia and mortality—a review of recent evidence. *Autoimmun. Rev.* (2013) 12: 976-89.
  - (17) Awad AB, Alappat L and Valerio M. Vitamin d and metabolic syndrome risk factors: evidence and mechanisms. *Crit. Rev. Food Scien. Nutr.* (2012) 52: 103-12.
  - (18) Nair P, Lee P, Reynolds C, Nguyen ND, Myburgh J, Eisman JA and Center JR. Significant perturbation of vitamin D–parathyroid–calcium axis and adverse clinical outcomes in critically ill patients. *Intens. Care Med.* (2013) 39: 267-4.
  - (19) Venkatram S, Chilimuri S, Adrish M, Salako A, Patel M and Diaz-Fuentes G. Vitamin D deficiency is associated with mortality in the medical intensive care unit. *Crit. Care* (2011) 15 :R292.
  - (20) Lucidarme O, Messai E, Mazzoni T, Arcade M and du Cheyron D. Incidence and risk factors of vitamin D deficiency in critically ill patients: results from a prospective observational study. *Intens. Care Med.* (2010) 36: 1609-11.
  - (21) Flynn L, Zimmerman LH, McNorton K, Dolman M, Tyburski J, Baylor A, Wilson R and Dolman H. Effects of vitamin D deficiency in critically ill surgical patients. *Am. J. Surgery* (2012) 203: 379-82.
  - (22) Braun AB, Litonjua AA, Moromizato T, Gibbons FK, Giovannucci E and Christopher KB. Association of low serum 25-hydroxyvitamin D levels and acute kidney injury in the critically ill. *Crit. Care Med.* (2012) 40: 3170-9.
  - (23) Braun AB, Gibbons FK, Litonjua AA, Giovannucci E and Christopher KB. Low serum 25-hydroxyvitamin D at critical care initiation is associated with increased mortality. *Crit. Care Med.* (2012) 40: 63.
  - (24) Youssef D, Bailey B, El Abbassi A, Copeland R, Adebonojo L, Manning T and Peiris A. Healthcare costs of *Staphylococcus aureus* and *Clostridium difficile* infections in veterans: role of vitamin D deficiency. *Epidemiol. Infect.* (2010) 138: 1322-7.
  - (25) Thickett DR, Moromizato T, Litonjua AA, Amrein K, Quraishi SA, Lee-Sarwar KA, Mogensen KM, Purtle SW, Gibbons FK and Camargo CA. Association between prehospital vitamin D status and incident acute respiratory failure in critically ill patients: a retrospective cohort study. *BMJ. Respir Res.* (2015) 2:e000074.
  - (26) Brook K, Camargo CA, Christopher KB and Quraishi SA. Admission vitamin D status is associated with discharge destination in critically ill surgical patients. *Ann. Intens. Care.* (2015) 5: 23.
  - (27) Sriram K, Perumal K, Alemzadeh G, Osei A and Voronov G. The relationship between immediate preoperative serum 25-hydroxy-vitamin D 3 levels and cardiac function, dysglycemia, length of stay, and 30-d readmissions in cardiac surgery patients. *Nutrirnts* (2015) 31: 820-6.
  - (28) Higgins DM, Wischmeyer PE, Queensland KM, Sillau SH, Sufit AJ and Heyl DK. Relationship of vitamin D deficiency to clinical outcomes in critically ill patients. *J. Parenter. Enteral Nutr.* (2012) 36: 713-20.
  - (29) Quraishi SA, Bittner EA, Blum L, McCarthy CM, Bhan I and Camargo Jr CA. 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.
  - (30) Kempker JA, West KG, Kempker RR, Siwamogsatham O, Alvarez JA, Tangpricha V, Ziegler TR and Martin GS. Vitamin D status and the risk for hospital-acquired infections in critically ill adults: a prospective cohort study. *PLoS One.* (2015) 10: e0122136.
  - (31) Alizadeh N, Khalili H, Mohammadi M and Abdollahi A. Serum Vitamin D levels at admission predict the length of intensive care unit stay but not in-hospital mortality of critically ill surgical patients. *J. Res. Pharm. Pract.* (2015) 4: 193.
  - (32) Aygencel G, Turkoglu M, Tuncel AF, Candir BA, Bildacı YD and Pasaoglu H. Is vitamin D insufficiency associated with mortality of critically ill patients? *Crit. Care Res. Practi.* (2013) 2013.
  - (33) Azim A, Ahmed A, Yadav S, Baronia AK, Gurjar M, Godbole MM and Poddar Band Singh RK. Prevalence of vitamin D deficiency in critically ill patients and its influence on outcome: experience from a tertiary care centre in North India (an observational study). *J. Intens. Care* (2013) 1: 14.
  - (34) McKinney JD, Bailey BA, Garrett LH, Peiris P, Manning T and Peiris AN. Relationship between vitamin D status and ICU outcomes in veterans. *J. Am. Med. Directors Assoc.* (2011) 12: 208-11.
  - (35) Melamed ML, Michos ED, Post W and Astor B. 25-hydroxyvitamin D levels and the risk of mortality in the general population. *Arch. Inter. Med.* (2008) 168: 1629-37.
  - (36) Adams JS and Hewison M. Update in vitamin D. *J. Clin. Endocrinol. Metab.* (2010) 95:471-8.

- (37) de Haan K, Groeneveld AJ, de Geus HR, Egal M and 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) 18:660.
- (38) Rech MA, Hunsaker T and Rodriguez J. Deficiency in 25-hydroxyvitamin D and 30-day mortality in patients with severe sepsis and septic shock. *Am. J. Criti. Care.* (2014) 23: e72-e79.
- (39) Ala-Kokko TI, Mutt SJ, Nisula S, Koskenkari J, Liisanantti J, Ohtonen P, Poukkanen M, Laurila JJ, Pettilä V and Herzig K-H. Vitamin D deficiency at admission is not associated with 90-day mortality in patients with severe sepsis or septic shock: Observational FINNAKI cohort study. *Ann. Med.* (2016) 48:67-75.
- (40) Arnon Y, Gringauz I, Itzhaky D and Amital H. Vitamin D deficiency is associated with poor outcomes and increased mortality in severely ill patients. *QJM. Inter. J. Med.* (2012) 105: 633-39.
- (41) Ebenezer K, Job V, Antonisamy B, Dawodu A, Manivachagan M and Steinhoff M. Serum vitamin D status and outcome among critically ill children admitted to the pediatric intensive care unit in South India. *Indian J. Pediatrics* (2016) 83: 120-5.
- (42) Anwar E, Hamdy G, Taher E, Fawzy E, Abdulattif S and Attia MH. Burden and Outcome of Vitamin D Deficiency Among Critically Ill Patients: A Prospective Study. *Nutr. Clin. Pract.* (2017) 32: 378-84.
- (43) Krishnan A, Ochola J, Mundy J, Jones M, Kruger P, Duncan E and Venkatesh B. Acute fluid shifts influence the assessment of serum vitamin D status in critically ill patients. *Crit. Care.* (2010) 14: R216.

---

This article is available online at <http://www.ijpr.ir>