International Journal of Gerontology 17 (2023) 237–242
https://doi.org/10.6890/IJGE.202310_17(4).0005

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Original Article

Effect of Obesity and Vitamin D Levels on Outcome Prediction in Critical Patients

I-Ting Wang [a,b], Hsiu-Wu Yang [b,c], Kuo-Song Chang [b,d], Yu-Jang Su [b,d,e,f,g *], Chung-Wei Chen [h], Kuo-Ching Yuan [i], An-Yi Wang [i,j,k], Yin-Chin Wang [l], Yin-Yi Han [m], Li-Kuo Kuo [a,b], Yu-Chang Yeh [l]

[a] *Department of Pulmonary and Critical Care, MacKay Memorial Hospital, Taipei, Taiwan,* [b] *Department of Medicine, MacKay Medical College, New Taipei City, Taiwan,* [c] *Surgery Division, Department of Emergency Medicine, MacKay Memorial Hospital, Taipei, Taiwan,* [d] *Department of Emergency Medicine, MacKay Memorial Hospital, Taipei, Taiwan,* [e] *Toxicology Division, Department of Emergency Medicine, MacKay Memorial Hospital, Taipei, Taiwan,* [f] *MacKay Junior College of Medicine, Nursing, and Management, Taipei, Taiwan,* [g] *Yuanpei University of Medical Technology, Hsinchu, Taiwan,* [h] *Department of Surgical Intensive Care Unit, Far Eastern Memorial Hospital, New Taipei City, Taiwan,* [i] *Department of Critical Care Medicine, Taipei Medical University Hospital, Taipei, Taiwan,* [j] *Department of Emergency Medicine, School of Medicine, College of Medicine, Taipei Medical University Hospital, Taipei, Taiwan,* [k] *Graduate Institute of Injury Prevention and Control, College of Public Health, Taipei Medical University, Taipei, Taiwan,* [l] *Department of Anesthesiology, National Taiwan University Hospital, Taipei, Taiwan,* [m] *Department of Traumatology, National Taiwan University Hospital, Taipei, Taiwan*

ARTICLE INFO

Accepted 6 April 2023

Keywords:
vitamin D,
obesity,
critical care outcomes,
critically ill

SUMMARY

Background: Vitamin D is an important nutrient for maintaining cardiovascular, endocrine, immune, and nervous system health. Body mass index (BMI) is one of the factors influencing vitamin D levels. We aimed to study the factors that play a role in the outcomes and prognoses of critically ill patients.
Method: This study was conducted at four teaching hospitals in Northern Taiwan between August 2018 and July 2020. A total of 1421 critically ill patients admitted to the intensive care units (ICUs) were eligible for assessment. Patients were classified into two groups based on serum 25(OH)D levels: sufficiency (≥ 20 ng/ml) and insufficiency (< 20 ng/ml); and into four groups according to BMI: underweight (BMI < 18.5), normal weight (BMI 18.5–24.9), overweight (BMI 25–29.9), and obesity (BMI ≥ 30). Statistical analyses were performed, and a p-value < 0.05 indicated a significant difference.
Results: More than half (57.9%) of the critically ill ICU patients had vitamin D deficiency (VDD); and VDD lengthened ICU stay by 2.5 days in vitamin D-deficit patients as compared to that in vitamin D-sufficient patients. Patients with obesity had a 4.2-day longer ICU stay (16.7 days) than that of the BMI < 30 group (12.5 days), which was significant (p = 0.009). They also had the lowest vitamin D levels (17.3 ng/mL) and the highest 90-day mortality rate (17.3%) compared to the other BMI groups.
Conclusion: In caring for critical patients, physicians need to pay more attention to vitamin D levels and BMI factors, which may impact their outcome prediction.

1. Introduction

The clinically significant form of vitamin D (VD) in the blood is 25-hydroxy vitamin D[25(OH)D]. According to the American Geriatrics Society Workgroup, for 25(OH)D levels to be considered normal, they must be at least 30 ng/mL. Levels between 21–29 ng/mL are considered insufficient, whereas levels less than 20 ng/mL are defined as[1] vitamin D deficiency (VDD) leads to malfunction of various biological processes that rely on the presence of VD, such as reduced absorption of calcium and phosphate from the diet, which negatively affects bone health. In children, VDD results in rickets, whereas in adults it results in osteomalacia and osteoporosis, which are characterized by a loss of bone density and an increased risk of fractures.[2] Vitamin D also contributes to various biological processes such as cell development, growth, and immune system regulation. Vitamin D deficiency has been linked to various disorders of the cardiovascular, endocrine, immune, and nervous systems.[3]

Research has demonstrated that hypercalcemia, a condition characterized by high levels of calcium in the blood, occurs when the concentration of 25(OH)D3 in the serum exceeds 150 ng/mL (375 nmol/L).[4] Clinical manifestations of hypercalcemia include nausea, abdominal pain, nephrocalcinosis, polyuria with acute kidney injury, dysrhythmias, and altered mental status.[5]

While the normal range of 25(OH)D is constant in all age groups, the recommended dietary allowance in people over 70 years of age increases from 600 to 800 IU.[6]

Many obese individuals have VDD; their body mass index (BMI) and amount of visceral fat are often used to determine their serum VD status.[7] Research has shown that there is an inverse relationship between VD levels and weight, BMI, and markers of type 2 diabetes, such as a high waist circumference and elevated HbA1c levels.[8,9]

Factors contributing to VDD include reduced VD intake owing to inadequate intake of VD-rich foods. Cutaneous production and storage of VD decline in older adults or those living in countries distant from the equator, where there is a lack of sun exposure.[10] Malabsorption usually relates to a post-gastrectomy state, or steatorrhea, which disturbs fat emulsification and chylomicron-facilitated absorption. In this study, we analyzed various prognostic factors and calculated the relative risk between normal VD and VDD patient

* Corresponding author. Poison Center, MacKay Memorial Hospital, No. 92, Section 2, North Chung Shan Road, Taipei 10449, Taiwan.
E-mail address: yjsu.md@msa.hinet.net (Y.-J. Su)

groups, and patients with and without obesity to understand the clinical significance of how they may affect prognosis.

2. Material and method

2.1. Ethical approval

This multicenter, prospective, observational cohort study was approved and reviewed by the Institutional Review Board of MacKay Memorial Hospital (approval reference no. 18MMHIS117e) and registered with the ClinicalTrials.gov protocol (ID: NCT03639584).

2.2. Patients

This study was conducted at four hospitals in Northern Taiwan between August 2018 and July 2020. Patients admitted to the intensive care units (ICUs) were eligible for enrollment in the study.

Patients were excluded if they met the following criteria: age < 20 years, lower BMI (< 18 kg/m^2), severe anemia (hemoglobin level < 7 g/dl), received additional VD supplementation (> 3,000 IU/day) within 4 weeks of admission, prior admission to the ICU within 3 months, hyperparathyroidism, rickets, or liver cirrhosis (Child-Pugh C).

Written informed consent was obtained from the critically ill patients or their legally authorized representatives prior to enrollment in the study. In the four participating hospitals, the usual VD supplementation was only daily regular nutrition, mostly ranging from 800 to 2,000 IU. No routine high-dose VD therapy was administered in any of the four hospitals. At enrollment, blood samples were obtained at enrollment and serum 25(OH)D, parathyroid hormone (PTH), and cortisol levels were measured. Subsequent time points (e.g., length of ICU stay and 28-day mortality) were defined as the time on or after the day of enrollment. Patient characteristics, comorbidities on admission, hemodynamic status, and laboratory data were recorded, and acute physiology and chronic health evaluation II (APACHE II) scores were calculated. Clinical outcomes were followed up for 90 days after patient enrollment, including the duration of ventilator use, ICU stay, hospital stay, ICU-free days to day 28, and survival status.

2.3. Examination and category of vitamin D level, and body mass index (BMI)

Blood serum samples were stored at –80 °C. Serum 25(OH)D levels were measured using a commercially available TOTAL LIAISON chemiluminescence assay (LIAISON, Diasorin S.p.A., Saluggia, Italy). Accordingly, patients were classified into the following two categories: sufficiency (≥ 20 ng/ml) and insufficiency (< 20 ng/ml).

We divided the patients into four groups based on BMI: underweight (BMI < 18.5), normal weight (BMI 18.5–24.9), overweight (BMI 25–29.9), and obese (BMI ≥ 30).

2.4. Statistical analysis

All statistical analyses were performed using SPSS version 20 (IBM Corp., Armonk, NY, USA). The t-test was used to compare the means between the two groups. Normally distributed numerical data were compared using one-way analysis of variance (ANOVA) and post-hoc Tukey tests and are expressed as means (± standard deviation). Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate, and are presented as percentages. Logistic regression models were used to estimate the relationship between the associated factors and VDD, and the relationship between VD level and ICU stay. Statistical significance was set at $p < 0.05$.

3. Results

A total of 1421 patients admitted to the ICU during the study period were assessed for eligibility. Of these, 51 patients were excluded due to having a BMI < 18, 36 patients were excluded due to hemoglobin levels < 7 g/dl, and nine patients were excluded due to receiving high-dose VD supplementation within 4 weeks of admission. A total of 147 patients were excluded due to prior ICU admission within 3 months, 98 were excluded due to excluded diseases, and 2 were excluded due to being non-native speakers. A total of 416 patients were excluded owing to a decline to enter this study. A total of 661 subjects were enrolled and classified into two groups: 338 with VDD and 278 with sufficient VD levels (Figure 1). More males than females were included in this study. Baseline characteristics were comparable in both groups (Table 1). The mean age of the VDD was lower compared to that in the sufficient VD group (63.5 ± 16.9 vs. 69.0 ± 14.8, $p < 0.001$). Albumin levels were higher in the sufficient VD group than in the VDD group (3.2 ± 0.6 g/dl vs. 3.1 ± 0.6 g/dl, $p < 0.009$). More individuals with obesity were prevalent in the VDD group than in the sufficient VD group (8.3% vs. 3.9%, $p = 0.026$). Length of hospital stay was 4.2 days longer in the VDD group than that in the sufficient VD group (36.8 ± 27.5 vs. 32.6 ± 22.4, $p = 0.037$).

The regression analysis of VD levels and ICU stay revealed that the lower the VD level, the longer the ICU stay (Figure 2). The ICU stay is 2.5 days longer in the VDD group than in the sufficient VD group (14.1 ± 14.9 vs. 11.6 ± 11.6, $p = 0.023$) (Figure 3). There was no significant difference between the two groups in APACHE II, white blood cell count (WBC count), C-reactive protein (CRP), lactate, PTH, BMI, the 28-day and 90-day mortality rates.

A comparison of the four BMI groups is outlined in Table 2. Regarding patient age, it was 58 years (SD: 15.5) in the obesity group, 65.3 (SD: 16.6) in the overweight group, 68.0 (SD: 15.2) in the normal weight group, and 63.4 (SD: 23.3) in the underweight group. Creatinine and PTH levels were the highest in the obesity group, whereas the VD level was the lowest in the obesity group.

The obese group had a higher comorbidity of diabetes mellitus, whereas the underweight group had a higher rate of liver cirrhosis,

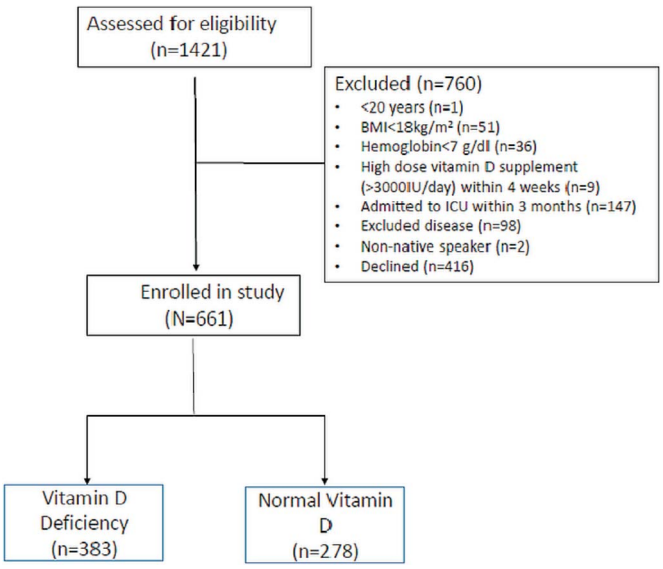

Figure 1. Flowchart of enrolled cases.

Table 1
Comparisons between Vitamin D deficiency and normal Vitamin D in demographic, vital signs, laboratory data, body weight, comorbidities, and outcome.

	Vitamin D deficiency (383, 57.9%)	Sufficiency vitamin D (278, 42.1%)	p-value (2-tailed)
Gender (M:F)	215:168 (1.3:1)	190:88 (2.2:1)	< 0.001*
Age (years old)	63.5 ± 16.9	69.0 ± 14.8	< 0.001*
Height (cm)	161.9 ± 9.1	162.5 ± 8.9	0.343
APACHE II	15.8 ± 6.3	15.3 ± 6.0	0.374
Heart rate per minute	89.3 ± 16.6	87.2 ± 16.4	0.106
MAP (mmHg)	88.8 ± 14.3	87.1 ± 13.4	0.121
WBC (/micro-L)	11722 ± 5613	11528 ± 4914	0.644
CRP (mg/dl)	11.1 ± 8.4	10.0 ± 7.3	0.102
Bilirubin (mg/dl)	1.6 ± 3.0	1.3 ± 2.1	0.071
Creatinine (mg/dl)	1.8 ± 2.7	1.5 ± 1.6	0.061
Lactate (mmol/L)	6.7 ± 11.3	5.6 ± 7.4	0.187
Albumin (g/dl)	3.1 ± 0.6	3.2 ± 0.6	0.009*
PTH (pg/mL)	52.7 ± 62.7	38.6 ± 45.6	0.002
Cortisol (ug/dl)	22.0 ± 16.0	22.8 ± 16.6	0.507
BMI	25.1 ± 5.2	24.5 ± 4.4	0.131
Underweight (29, 4.4%)	(17, 4.4%)	(12, 4.3%)	0.956
Normal weight (360, 54.5%)	(207, 54.0%)	(156, 56.1%)	0.946
Overweight (191, 28.9%)	(104, 27.2%)	(84, 30.2%)	0.202
Obesity (81, 12.2%)	(55, 14.4%)	(26, 9.4%)	0.026*
Diabetes mellitus (202, 30.6%)	(122, 31.9%)	(80, 28.8%)	0.861
Liver cirrhosis (35, 5.3%)	(24, 6.3%)	(11, 4.0%)	0.984
Uremia (37, 5.6%)	(25, 6.5%)	(12, 4.3%)	0.556
Metastasis (48, 7.3%)	(27, 7.0%)	(21, 7.6%)	0.755
LOS	36.8 ± 27.5	32.6 ± 22.4	0.037*
ICU stay	14.1 ± 14.9	11.6 ± 11.6	0.023*
28-day mortality (59, 8.9%)	(19, 5.0%)	(40, 14.4%)	0.290
90-day mortality (105, 15.9%)	(65, 17.0%)	(40, 14.4%)	0.588

* Indicates reaching a statistical significance p-value less than 0.05.
APACHE = Acute Physiology and Chronic Health Evaluation; PTH = parathyroid hormone; BMI = body mass index.

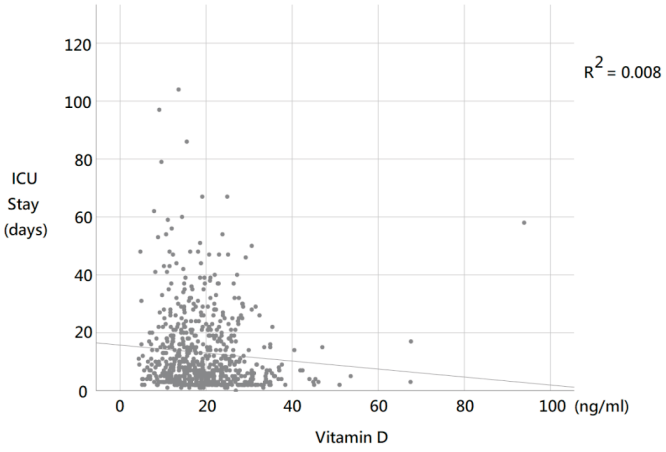

Figure 2. Regression analysis between vitamin D levels and ICU stay. Lesser the vitamin D level, longer is the ICU stay needed.

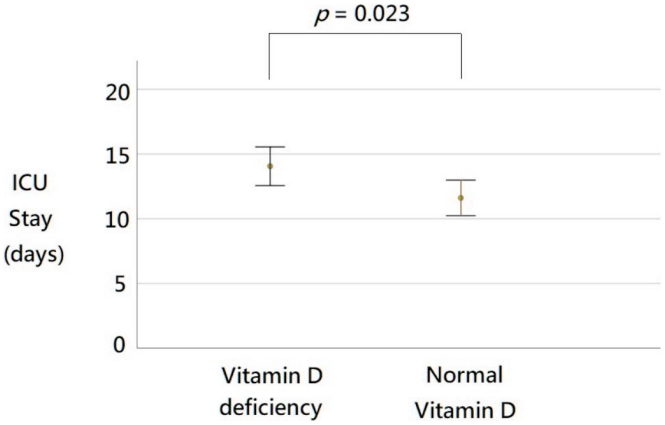

Figure 3. The ICU stay is 2.5-day longer in the vitamin D deficiency group than in the sufficient vitamin D group (14.1 ± 14.9 vs. 11.6 ± 11.6, p = 0.023).

uremia, and cancer metastasis. In the obesity group, ICU stays were the longest (16.7 ± 18.4 days) than in the other groups. The underweight group had a significantly higher 28-day mortality rate, and the obese group had a significantly higher 90-day mortality rate than the other groups.

We also compared the ICU stay between the obese (BMI ≥ 30, n = 81) and non-obese groups (BMI < 30, n = 580), and found that the obese group had a 4.2 day longer ICU stay (16.7 days) than the BMI < 30 group (12.5 days), which was significant (p = 0.009) (Figure 4).

4. Discussion

4.1. VD deficiency increases ICU stay and costs more

Vitamin D deficiency occurred in 57.9% of the critical patients in our study and in 69% of the critical patients in a study from Egypt in 2016.[11] Therefore, it is important to pay attention to patient care in the ICU. Our research revealed that the duration of ICU stay is significantly longer (by 2.5 days) in the VDD group than in the sufficient VD group (14.1 ± 14.9 vs. 11.6 ± 11.6, p = 0.023). This result is similar to the meta-analysis by Zhang et al., which reported that the duration of hospital stay was prolonged in hypovitaminosis D.[12] Vitamin D is important to promote antimicrobial responses in macrophages to pathogens and to regulate the maturation of antigen-presenting cells. It is also an important factor that links the innate and adaptive immunities, and both functions may be compromised during VDD.[13]

VDD leads to prolonged ICU stay, elevated C-reactive protein (CRP) level, increased rate of infections, increased inflammation, and vascular dysfunction.[14–16]

Table 2
Comparisons between underweight, normal weight, overweight and obesity in demographic, vital signs, laboratory data, body weight, comorbidities, and outcome.

	Underweight (BMI < 18.5) (29, 4.4%)	Normal weight (BMI 18.5–24.9) (360, 54.5%)	Overweight (BMI 25–29.9) (191, 28.9%)	Obesity (BMI ≥ 30) (81, 12.2%)	p-value, 2-tailed
Gender (M:F)	17:12 (1.4:1)	223:137 (1.6:1)	114:77 (1.5:1)	51:30 (1.7:1)	< 0.001*
Age (years old)	63.4 ± 23.3	68.0 ± 15.2	65.3 ± 16.6	58 ± 15.5	< 0.001*
Height (cm)	160.7 ± 8.5	162.2 ± 8.9	161.7 ± 8.8	163.6 ± 10	0.169
APACHE II	15.3 ± 6.7	15.7 ± 6.0	15.4 ± 6.1	15.6 ± 7.0	0.484
Heart rate per minute	91.8 ± 17.1	87.8 ± 16.7	88.8 ± 15.7	88.8 ± 17.9	0.983
MAP (mmHg)	87.9 ± 12.4	87.3 ± 14.1	89.3 ± 13.8	89.0 ± 13.8	0.053
WBC (/micro-L)	11406 ± 5048	11484 ± 5292	11849 ± 5545	11979 ± 5112	0.244
CRP (mg/dl)	10.4 ± 5.3	10.6 ± 8.1	10.7 ± 8.3	10.6 ± 7.0	0.807
Bilirubin (mg/dl)	1.2 ± 0.9	1.5 ± 2.7	1.5 ± 2.7	1.6 ± 2.7	0.520
Creatinine (mg/dl)	1.3 ± 1.1	1.6 ± 2.6	1.6 ± 1.8	2.2 ± 2.4	0.006*
Lactate (mmol/L)	6.2 ± 7.9	6.9 ± 11.7	5.5 ± 6.8	6.0 ± 7.1	0.585
Albumin (g/dl)	3.1 ± 0.5	3.1 ± 0.6	3.2 ± 0.6	3.0 ± 0.5	0.876
PTH (pg/mL)	53.7 ± 72.2	42.5 ± 48.1	49.6 ± 65.6	55.6 ± 60.1	0.004*
Cortisol (ug/dl)	21.3 ± 18.9	23.0 ± 16.2	20.8 ± 13.9	22.9 ± 19.7	0.415
Vitamin D (ng/mL)	20.1 ± 9.3	19.7 ± 8.9	20.3 ± 9.5	17.3 ± 6.0	0.015*
Diabetes mellitus (202, 30.6%)	(2, 6.9%)	(110, 30.6%)	(55, 28.8%)	(35, 43.2%)	< 0.001*
Liver cirrhosis (35, 5.3%)	(2, 6.9%)	(20, 5.6%)	(8, 4.2%)	(5, 6.2%)	< 0.001*
Uremia (37, 5.6%)	(2, 6.9%)	(20, 5.6%)	(10, 5.2%)	(5, 6.2%)	< 0.001*
Metastasis (48, 7.3%)	(3, 10.3%)	(31, 8.6%)	(11, 5.8%)	(3, 3.7%)	< 0.001*
LOS	35.0 ± 25.4	34.6 ± 25.4	35.1 ± 24.6	36.0 ± 27.3	0.395
ICU stay	15.3 ± 14.8	12.3 ± 12.9	12.5 ± 12.0	16.7 ± 18.4	0.009*
28-day mortality (59, 8.9%)	(5, 17.2 %)	(18, 5.0%)	(24, 12.6%)	(12, 14.8%)	< 0.001*
90-day mortality (105, 15.9%)	(5, 17.2 %)	(59, 16.4%)	(27, 14.1%)	(14, 17.3%)	< 0.001*

* Indicates reaching a statistical significance p-value less than 0.05.
APACHE = Acute Physiology and Chronic Health Evaluation; PTH = parathyroid hormone; BMI = body mass index.

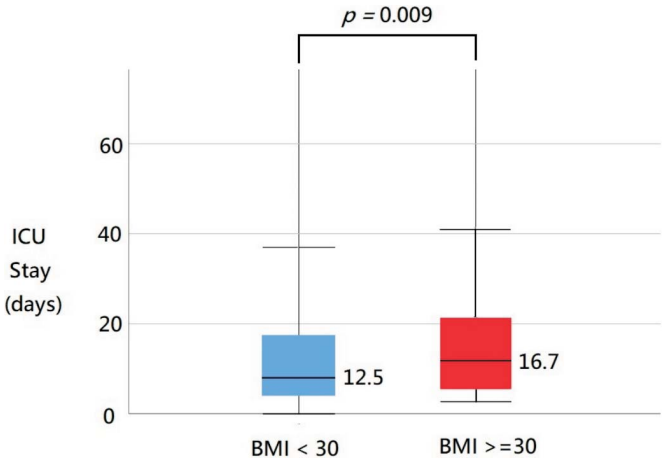

Figure 4. Duration of intensive care unitstay in obesity group (BMI ≥ 30, n = 81) is 4.2 days longer (16.7 days) than that in the BMI < 30 group (12.5 days), p = 0.009.

Another study in India reported an increased duration of pediatric ICU stay in the 25(OH)D-deficient group by approximately 72 hours compared to that in the VD sufficient group.[17] Recent evidence by Matthews et al. suggests that an increased number of days in the surgical ICU in the severe VD-deficiency group versus that in the mild and moderate deficiency groups was not significant; however, the additional 7 to 8 mean days of ICU stay were clinically significant. The additional time spent in the surgical ICU doubles the cost of the hospital stay.[18]

The mean medical expenses of ICU patients in Taiwan are 1173 USD per day. If an ICU patient with VDD needs approximately 59 USD per day to pay for a VD 70000 IU bottle, our research suggests an estimated savings cost of around 16402 USD per day in the sufficient VD group (n = 278). The ICU stay is significantly longer (by 2.5 days) in the VDD group than in the sufficient VD group; thus, they need to pay more for medical expenses, approximately 2933 USD for one patient. Therefore, we conclude that maintaining a normal VD level can save huge amounts of medical expenses for critically ill patients. In our study, VDD obviously influenced the length of hospital and ICU stays, leading to higher medical expenses in caring for these critical patients, without any increment in the 28-day and 90-day mortality rates.

4.2. More obese men than women among critically ill patients

In our study, the male-to-female ratio was 1.7:1 in the obese group, which was the highest among all the BMI groups. Experimental models have shown gender differences in innate immune responses that may influence the clinical progression of ICU admission, such as shock, trauma, and sepsis.[19] Estrogen has been suggested to be immunoprotective after previously described stress; meanwhile, androgens have been demonstrated to suppress immune reactions.[20] A retrospective, observational cohort study in 2020 using clinical epidemiological information provided by the Korea Disease Control and Prevention Agency reported that Coronavirus Disease 2019 (COVID-19) infection in male patients showed higher mortality than that in females (5.4% vs. 3.45%, p < 0.001), and overall mortality is also higher (5.4% vs. 3.45%, p < 0.001).[21] Another observational study in the United States also reported that male patients, as well as those who are older, and the severely obese (BMI > 35) are likely to be at the greatest risk of COVID-19 severity and fatality.[22]

Obesity is also an independent risk factor for mortality in patients with severe respiratory diseases. In a retrospective cohort study conducted in a tertiary academic center located in Montreal between March and August 2020, results revealed that obesity was prevalent in hospitalized patients with critical illness secondary to

COVID-19, and a higher BMI was associated with higher hospital mortality.[23]

4.3. Obese patients have the lowest vitamin D level than non-obese critical patients

Not only obesity but also metabolic syndrome leads to VDD.[24] The obesity group had the lowest level of VD (17.3 ng/mL) compared to other BMI groups ($0.015 < p < 0.05$). Many individuals with obesity have VDD, and their BMI and amount of visceral fat are often used to determine serum VD status.[7] There are several proposed explanations for why obesity is often linked to VDD, such as inadequate dietary intake, limited exposure to sunlight, deficiencies in enzymes that aid in VD metabolism and sequestration into adipose tissue, decreased VD synthesis in the adipose tissue and liver, and dilution of VD in a larger body volume.[3,25] A report from Brazil in 2022 described that abdominal obesity increased the risk of 25(OH)D deficiency (relative risk ratio = 1.64; 95% CI: 1.05–2.58).[26] Vitamin D level in obesity is lower than that in overweight, normal, and underweight conditions ($17.3 < 20.3$, 19.7, and 20.1, respectively, $0.015 < p < .05$). Therefore, we believe that apart from resulting in more comorbidity and metabolic syndrome in patients with obesity, lower levels of VD also result in a worse outcome in these critical patients (longer ICU stays, higher 28-day mortality, and 90-day mortality rates).

4.4. Synergistic effect of obesity and VDD exacerbated renal dysfunction

We found that all VDD and obesity groups had renal dysfunction. The creatinine levels of obese, overweight, normal, and underweight groups are 2.2, 1.6, 1.6, and 1.3 mg/dL, respectively, $0.006 < p < 0.05$). The creatinine level in the VDD group was 1.8 mg/dL. Vitamin D deficiency is considered a risk factor for kidney disease and is associated with tubulointerstitial damage, which exacerbate the hemodynamic and morphological changes resulting in evolution of renal disease, induced by ischemia or reperfusion, contributing to the progression of kidney disease. Obesity is directly related to diabetes mellitus and hypertension, the two main metabolic disorders that result in the progression of kidney disease.[27]

4.5. Patients with obesity have longer ICU stay than non-obese patients

Based on the daily ICU medical expenses of 1137 USD in Taiwan, the 81 enrolled patients with obesity spent 3386807.4 USD more in total compared to patients whose BMI was < 30. The burden on the national health insurance system increases if it is calculated on a national scale. Patients with obesity also had the highest 90-day mortality rate (17.3%, $p < 0.001$). Thus, we find that body weight influenced the outcome more than VD levels.

4.6. Underweight patients had the highest 28-day mortality rate

In our study, the patients in the underweight group had the highest 28-day mortality rate (17.2%) and were susceptible to comorbidities such as liver cirrhosis (6.9%), uremia (6.9%), and metastasis of malignancies (10.3%), all of which were significant, all $p < 0.001$. In 2020, an Asian report on BMI and long-term risk of sepsis-related mortality (n = 1957) found that underweight, lower normal weight, and abdominal obesity were associated with increased future risk of sepsis-related mortality.[28]

4.7. Limitations

Our study had some limitations. First, we assessed 1421 patients admitted to the ICU, including all medical and surgical patients; thus, in some circumstances, the outcome in critically ill patients might be influenced by the injury pattern and extent of trauma. These factors may have affected the outcomes and length of hospital stay. Second, some critical patients, such as those with myocardial infarction who do not receive intubation, may take VD supplements themselves, causing changes in serum levels of VD, which might bias the outcome analysis.

5. Conclusion

Vitamin D is an important nutrient for maintaining cardiovascular, endocrine, immune, and nervous health. Of the critically ill patients, 57.9% of critical patients had VDD of which 56% were male. They faced an increased rate of infection and vascular dysfunction, and VDD results in a 2.5-day longer ICU stay than VD-sufficient patients, and thus they spend more on medical expenses. More obese men than women were noted among critically ill patients, and in our study, there was a male:female ratio of 1.7:1 in the obese group compared to the other BMI groups. Many individuals with obesity had VDD (with a VD level of 17.3 ng/mL) than critical patients with no obesity. However, the synergistic effects of obesity and VDD on renal dysfunction require further investigation. Patients with obesity had a 4.2-day longer ICU stay than patients with no obesity, and obese critical patients had the highest 90-day mortality rate (17.3%) compared to other BMI groups. Thus, in caring for critical patients, physicians need to pay more attention to VD levels and determine the BMI factors impacting outcomes.

Acknowledgements

Not applicable.

Funding

There is no funding in this article.

Conflict of interest

We all declare no conflict-of-interest statement.

References

1. Holick MF, Chen TC. Vitamin D deficiency: A worldwide problem with health consequences. *Am J Clin Nutr.* 2008;87(4):1080S–1086S. doi:10.1093/ajcn/87.4.1080S
2. Holick MF. High prevalence of vitamin D inadequacy and implications for health. *Mayo Clin Proc*. 2006;81(3):353–373. doi:10.4065/81.3.353
3. Vranić L, Mikolašević I, Milić S. Vitamin D deficiency: Consequence or cause of obesity? *Medicina (Kaunas)*. 2019;55(9):541. doi:10.3390/medicina55090541
4. Dudenkov DV, Yawn BP, Oberhelman SS, et al. Changing incidence of serum 25-hydroxyvitamin D values above 50 ng/mL: A 10-year population-based study. *Mayo Clin Proc*. 2015;90(5):577–586. doi:10.1016/j.mayocp.2015.02.012
5. Lee JP, Tansey M, Jetton JG, Krasowski MD. Vitamin D toxicity: A 16-year retrospective study at an Academic Medical Center. *Lab Med.* 2018;49(2):123–129. doi:10.1093/labmed/lmx077
6. National Institutes of Health. Vitamin D: Fact Sheet for Health Profes-

sionals. Office of Dietary Supplements. Updated August 12, 2022. Accessed January 21, 2023. https://ods.od.nih.gov/factsheets/VitaminD-HealthProfessional/
7. Duan L, Han L, Liu Q, Zhao Y, Wang L, Wang Y. Effects of vitamin D supplementation on general and central obesity: Results from 20 randomized controlled trials involving apparently healthy populations. *Ann Nutr Metab*. 2020;76(3):153–164. doi:10.1159/000507418
8. McGill AT, Stewart JM, Lithander FE, Strik CM, Poppitt SD. Relationships of low serum vitamin D3 with anthropometry and markers of the metabolic syndrome and diabetes in overweight and obesity. *Nutr J*. 2008;7:4. doi:10.1186/1475-2891-7-4
9. Alkhatatbeh MJ, Abdul-Razzak KK, Khasawneh LQ, Saadeh NA. High prevalence of vitamin D deficiency and correlation of serum vitamin D with cardiovascular risk in patients with metabolic syndrome. *Metab Syndr Relat Disord*. 2017;15(5):213–219. doi:10.1089/met.2017.0003
10. Tsai KS, Wahner HW, Offord KP, Melton LJ 3rd, Kumar R, Riggs BL. Effect of aging on vitamin D stores and bone density in women. *Calcif Tissue Int*. 1987;40(5):241–243. doi:10.1007/BF02555255
11. Anwar E, Hamdy G, Taher E, Fawzy E, Abdulattif S, Attia MH. Burden and outcome of vitamin D deficiency among critically ill patients: A prospective study. *Nutr Clin Pract*. 2017;32(3):378–384. doi:10.1177/0884533616671741
12. Zhang YP, Wan YD, Sun TW, Kan QC, Wang LX. Association between vitamin D deficiency and mortality in critically ill adult patients: A meta-analysis of cohort studies. *Crit Care*. 2014;18(6):684. doi:10.1186/s13054-014-0684-9
13. Hewison M. Vitamin D and immune function: An overview. *Proc Nutr Soc*. 2012;71(1):50–61. doi:10.1017/S0029665111001650
14. Kostoglou-Athanassiou I, Pantazi E, Kontogiannis S, Kousouris D, Mavropoulos I, Athanassiou P. Vitamin D in acutely ill patients. *J Int Med Res*. 2018;46(10):4246–4257. doi:10.1177/0300060518792783
15. Dickerson RN, Van Cleve JR, Swanson JM, et al. Vitamin D deficiency in critically ill patients with traumatic injuries. *Burns Trauma.* 2016;4:28. doi:10.1186/s41038-016-0054-8
16. Mirza I, Mohamed A, Deen H, et al. Obesity-associated vitamin D deficiency correlates with adipose tissue DNA hypomethylation, inflammation, and vascular dysfunction. *Int J Mol Sci*. 2022;23(22):14377. doi:10.3390/ijms232214377
17. Sankar J, Lotha W, Ismail J, Anubhuti C, Meena RS, Sankar MJ. Vitamin D deficiency and length of pediatric intensive care unit stay: A prospective observational study. *Ann Intensive Care.* 2016;6(1):3. doi:10.1186/s13613-015-0102-8
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(1):37–43. doi:10.1016/j.amjsurg.2011.07.021
19. Lat TI, McGraw MK, White HD. Gender differences in critical illness and critical care research. *Clin Chest Med*. 2021;42(3):543–555. doi:10.1016/j.ccm.2021.04.012
20. Federman DD. The biology of human sex differences. *N Engl J Med*. 2006;354(14):1507–1514. doi:10.1056/NEJMra052529
21. Kim J, Heo N, Kang H. Sex-based differences in outcomes of coronavirus disease 2019 (COVID-19) in Korea. *Asian Nurs Res (Korean Soc Nurs Sci).* 2022;16(4):224–230. doi:10.1016/j.anr.2022.07.003
22. Rapp JL, Lieberman-Cribbin W, Tuminello S, Taioli E. Male sex, severe obesity, older age, and chronic kidney disease are associated with COVID-19 severity and mortality in New York City. *Chest*. 2021;159(1):112–115. doi:10.1016/j.chest.2020.08.2065
23. Plourde G, Fournier-Ross E, Tessier-Grenier H, Mullie LA, Chassé M, Carrier FM. Association between obesity and hospital mortality in critical COVID-19: A retrospective cohort study. *Int J Obes (Lond).* 2021;45(12):2617–2622. doi:10.1038/s41366-021-00938-8
24. Melguizo-Rodríguez L, Costela-Ruiz VJ, García-Recio E, De Luna-Bertos E, Ruiz C, Illescas-Montes R. Role of vitamin D in the metabolic syndrome. *Nutrients.* 2021;13(3):830. doi:10.3390/nu13030830
25. Karampela I, Sakelliou A, Vallianou N, Christodoulatos GS, Magkos F, Dalamaga M. Vitamin D and obesity: Current evidence and controversies. *Curr Obes Rep*. 2021;10(2):162–180. doi:10.1007/s13679-021-00433-1
26. da Silva TBP, Luiz MM, Delinocente MLB, Steptoe A, de Oliveira C, Alexandre TDS. Is abdominal obesity a risk factor for the incidence of vitamin D insufficiency and deficiency in older adults? Evidence from the ELSA study. *Nutrients.* 2022;14(19):4164. doi:10.3390/nu14194164
27. Bernardo DRD, Canale D, Nascimento MM, et al. The association between obesity and vitamin D deficiency modifies the progression of kidney disease after ischemia/reperfusion injury. *Front Nutr.* 2022;9:952028. doi:10.3389/fnut.2022.952028
28. Weng L, Fan J, Yu C, et al. Body-mass index and long-term risk of sepsis-related mortality: A population-based cohort study of 0.5 million Chinese adults. *Crit Care.* 2020;24(1):534. doi:10.1186/s13054-020-03229-2