Acute and Critical Care

Acute and Critical Care 2025 August 40(3):482-490
https://doi.org/10.4266/acc.000975

| pISSN 2586-6052 | eISSN 2586-6060

Low vitamin C concentrations and prognosis in critically ill children

Min Jung Kim[1], Yoon Hee Kim[2], Soo Yeon Kim[3], Jong Deok Kim[3], Mireu Park[3], Hamin Kim[3], Myung Hyun Sohn[3], Kyung Won Kim[3]

[1]Department of Pediatrics, Yongin Severance Hospital, Yonsei University College of Medicine, Yongin, Korea
[2]Department of Pediatrics, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
[3]Department of Pediatrics, Severance Hospital, Institute of Allergy, Yonsei University College of Medicine, Seoul, Korea

Background: The administration of high-dose vitamins has been focused on in critically ill patients as adjunctive therapy for life-threatening conditions. We evaluated the association between serum vitamin C concentrations and patient prognosis.

Methods: We retrospectively reviewed and collected clinical and biochemical data, including thiamine and vitamin C levels, of patients admitted to the pediatric intensive care unit (PICU).

Results: In total, 177 patients were admitted to the PICU during the study period, and 63 children were enrolled in this study. The most common reason for PICU admission was sepsis (33.3%). The median thiamine and vitamin C levels were 3.6 μg/dl (interquartile range [IQR], 2.9–4.5 μg/dl) and 2.84 μg/ml (IQR, 1.61–4.55 μg/ml), respectively. Thiamine deficiency was observed in 10 patients (15.9%), and 17 (27.0%) had vitamin C deficiency. There were no differences in the vitamin levels according to the reason for PICU admission. Vitamin C levels were affected by nutritional status. The length of stay in the PICU and duration of mechanical ventilation were longer in patients with vitamin C deficiency than in those without (P=0.035 and P=0.010, respectively). The serum delta neutrophil index and C-reactive protein and lactate levels increased in the vitamin C-deficient group (P=0.028 and P=0.039, respectively). There was a significant difference in Pediatric Index of Mortality 3 scores according to vitamin C levels but not in mortality directly.

Conclusions: Vitamin C deficiency was associated with elevated inflammatory marker levels, increased mechanical ventilation durations, and PICU admission. Our results support the potential benefits of vitamin C administration in critically ill children.

Key Words: child; critical care; nutrients; prognosis; vitamins

Original Article

Received: March 14, 2025
Revised: June 29, 2025
Accepted: August 8, 2025

Corresponding author
Kyung Won Kim
Department of Pediatrics, Severance Hospital, Institute of Allergy, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea
Tel: +82-2-2228-2050
Fax: +82-2-393-9118
Email: kwkim@yuhs.ac

INTRODUCTION

Most critically ill patients, such as those with septic shock or those undergoing cardiac surgery, experience pathophysiological conditions that lead to a systemic inflammatory response, which can increase oxidative stress. The hypermetabolic state in critical illnesses can

drastically reduce the plasma levels of various micronutrients and trace elements with antioxidant properties. In contrast, the levels of circulating oxidative molecules increase significantly, leading to energy wastage, organ failure, and even death. Micronutrient therapy is considered a potential supportive treatment to improve high-energy expenditure statuses and mortality in critical illness [1,2].

As a high dose of vitamins along with hydrocortisone administration has been suggested as an effective adjunctive therapy for sepsis and septic shock [3], several studies have shown the influence of vitamins on critical illness and the effects of their supplementation on clinical outcomes in critically ill patients [4-6]. As thiamine (vitamin B1) acts as a cofactor for pyruvate dehydrogenase, thiamine deficiency results in activated anaerobic metabolism and elevated lactate levels [3]. Vitamin C, also known as ascorbic acid or ascorbate, is an antioxidant that reduces oxidative stress and exerts immune-modulating effects [4]. For these reasons, vitamin therapy for critical illnesses is considered an adjunct method for metabolic resuscitation [5,6].

However, the role of vitamins in critical illnesses remains disputed, even in sepsis [7-9]. Few studies have investigated vitamin concentrations and the use of vitamin therapy in pediatric patients [10,11]. Pediatric patients should be approached differently from adults owing to variations in underlying diseases, reasons for intensive care unit (ICU) admission, and host characteristics, including immunological and nutritional disparities and vulnerability to new drugs.

In this study, we investigated the initial serum thiamine and vitamin C levels upon pediatric intensive care unit (PICU) admission and the clinical factors affecting patients' vitamin levels. We also aimed to determine the correlation between the initial serum vitamin levels and prognosis in PICU patients.

KEY MESSAGES

- Vitamin deficiency is common in critically ill children.
- The nutritional status of patients could affect vitamin C levels but not thiamine levels.
- Vitamin C deficiency is associated with elevated inflammatory marker levels and increased mechanical ventilation and pediatric intensive care unit stay durations, suggesting a potential benefit of vitamin C administration in critically ill children.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board of Severance Hospital, Seoul, Korea (No. 4-2020-0790), and the requirement for informed consent was waived.

Study Design and Data Collection

We reviewed critically ill pediatric patients and collected their initial biochemical data, including thiamine and vitamin C levels, at PICU admission in a tertiary university hospital between June 2019 and December 2019. Critically ill pediatric patients eligible for PICU admission include (1) life-threatening cardiovascular instability, imminent cardiac arrest, or post-cardiopulmonary resuscitation requiring intensive monitoring; (2) acute or chronic respiratory failure, airway obstruction requiring ventilatory support; (3) severe neurologic conditions with altered consciousness or complications needing close observation; (4) decreased urine output (<1 ml/kg/hr over 4 hours) or renal failure requiring renal replacement therapy; and (5) other life-threatening conditions such as critical metabolic imbalances or massive bleeding.

A total of 177 patients aged 1 month to 19 years were admitted to the PICU during the study period; 75 were screened in this study, and 63 were included in the final analysis. Patients who died within 24 hours of PICU admission, those with mineral supplementation, and those with chronic renal failure were excluded. There were no patients receiving renal replacement therapy or vitamin supplement therapy during the study period (Figure 1). Thiamine and vitamin C levels were measured at the time of PICU admission. Low serum thiamine and vitamin C levels were defined as <2.36 μg/dl (70 nmol/L) [11] and <1.94 μg/ml (11 μmol/L), respectively [12].

Demographic and clinical data, including in-hospital mortality, length of stay (LOS) in the PICU, underlying etiology, reasons for admission, requirements for mechanical ventilation, Glasgow Coma Scale scores, Pediatric Index of Mortality 3 (PIM-3) scores, and Pediatric Risk of Mortality III (PRISM III) scores, were recorded. According to the World Health Organization child growth standards, nutritional status was assessed using z-scores of weight for age, height for age, and body mass index. Malnutrition was identified when the z-score was less than –2 standard deviations [13,14].

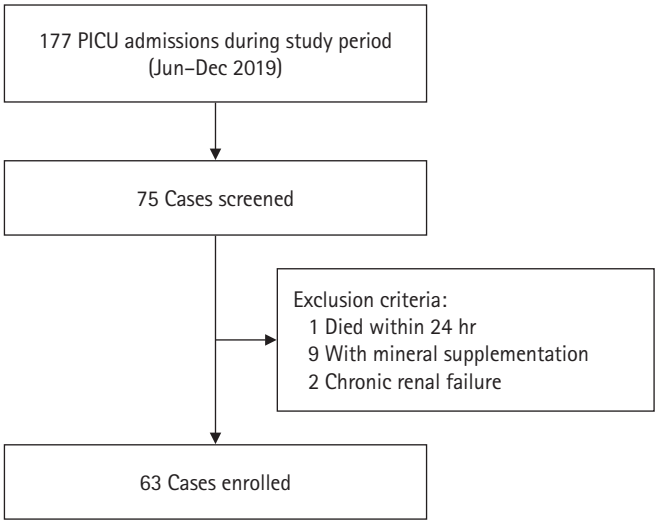

Figure 1. Study flow diagram for critically ill children. PICU: pediatric intensive care unit.

Statistical Analyses

We compared the baseline characteristics of the patients using the Mann-Whitney U-test or Fisher's exact test, as appropriate. Normal distribution was determined using the Kolmogorov-Smirnov test. Numerical variables are presented as means and standard deviations. We used the median and interquartile range (IQR) for numerical parameters with non-normal distributions. Spearman's method was used to evaluate the correlation between serum vitamin levels and other parameters. Statistical significance was set at $P<0.05$. All analyses were performed using statistical software (SPSS version 27.0, IBM Corp.), and graphs were created using GraphPad Prism (version 10.1, GraphPad Software).

RESULTS

Characteristics of Study Population

Among the 63 pediatric patients, the most common underlying medical diseases were neurological conditions (40 patients, 63.5%), such as intractable epilepsy or status epilepticus. The baseline patient characteristics are presented in Table 1. The median patient age was 6 years, and 52.4% (33/63) were male. The overall in-hospital mortality rate was 4.8% (3/63), with a median LOS in the PICU of 11 days. Sepsis was the most common reason for PICU admission (33.3%). Forty-five patients (71.4%) required mechanical ventilation within 24 hours of PICU admission. The percentage of patients with a malnourished nutritional state was 42.9% (n=27).

Table 1. Clinical characteristics of patients

Variable	Value (n=63)
Age (yr)	6 (2–11)
Male	33 (52.4)
LOS in PICU (day)	11 (4–20)
In-hospital mortality	3 (4.8)
Reason for PICU admission	
Sepsis	21 (33.3)
Respiratory failure	20 (31.7)
Intensive monitoring	8 (12.7)
Neurologic problem	4 (6.3)
Post-resuscitation	4 (6.3)
Acute renal insufficiency	3 (4.8)
Requirement for MV[a]	45 (71.4)
Malnourished nutritional state[b]	27 (42.9)
GCS	10 (8–15)
PIM-3 (mortality rate, %)	3.7 (1.2–6.3)
PRISM III	3 (0–9)

Values are presented as median (interquartile range) or number (%).
LOS: length of stay; PICU: pediatric intensive care unit; MV: mechanical ventilation; GCS: Glasgow Coma Scale; PIM-3: Pediatric Index of Mortality 3; PRISM III: Pediatric Risk of Mortality III.
a) Requirement for mechanical ventilation within 24 hours of PICU admission; b) z score of anthropometric index less than –2 of the World Health Organization growth standards.

Vitamin Levels in PICU Patients

Regarding serum vitamin levels in PICU patients, the median thiamine level was 3.6 μg/dl (IQR, 2.9–4.5 μg/dl), and the median vitamin C level was 2.84 μg/ml (IQR, 1.61–4.55 μg/ml). Among all 63 patients, 10 (15.9%) exhibited thiamine deficiency, and 17 (27.0%) had vitamin C deficiency. There were no differences in serum vitamin levels when comparing patients with underlying problems, regardless of whether they had sepsis or not (Figure 2). Vitamin C showed different serum levels according to nutritional status, especially between well-nourished and severely malnourished patients (median level, 3.56 vs 1.73 μg/ml); however, thiamine did not (Figure 3).

Vitamin Levels and Prognostic Parameters in PICU

We examined the characteristics of the patients with vitamin deficiencies. For thiamine deficiency, the only parameter that showed a statistically significant difference was C-reactive pro-

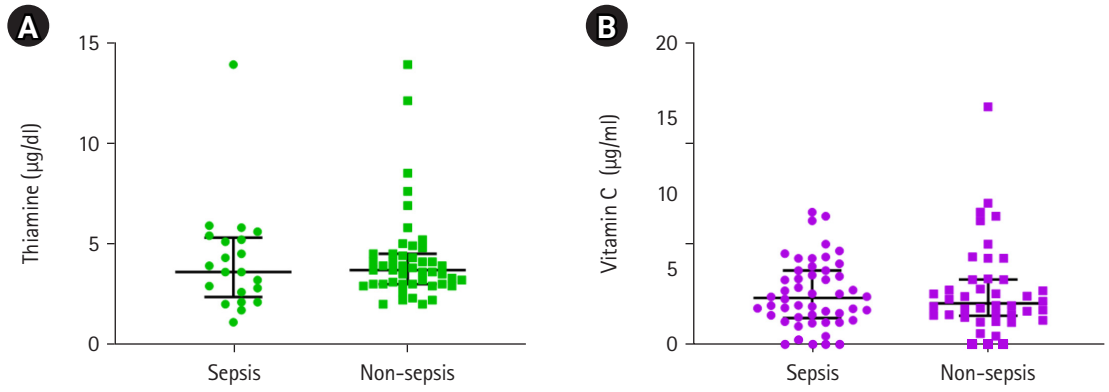

Figure 2. Median vitamin levels in critically ill pediatric patients. (A) Thiamine levels. (B) Vitamin C levels. There were no significant differences in vitamin levels between patients with and without sepsis.

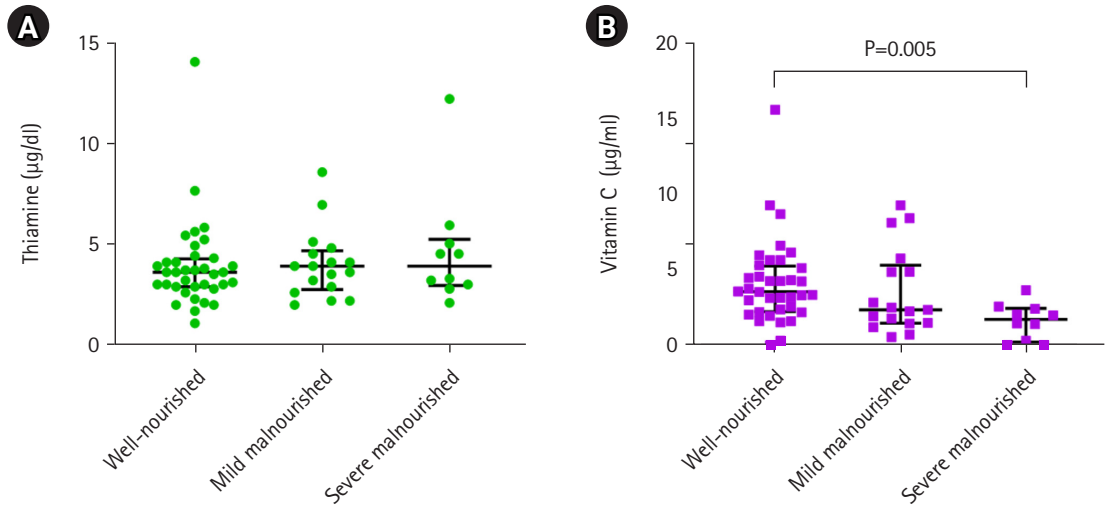

Figure 3. Vitamin levels according to nutritional status. (A) Thiamine levels. (B) Vitamin C levels. According to the nutritional status of the patients at pediatric intensive care unit admission, thiamine levels did not differ based on nutritional status, whereas vitamin C levels were affected. Severely malnourished children tended to have low vitamin C levels.

tein (CRP) levels. The median CRP level was lower in patients with thiamine deficiency (median, 8.0 mg/L [IQR, 1.1–35.9] vs. 41.4 mg/L [IQR, 12.9–202.7]).

When the patients were grouped based on their vitamin C levels, significant differences were found between those with and without vitamin C deficiencies (Table 2). Patients with vitamin C deficiency had longer PICU stays and required mechanical ventilation for longer durations (P=0.035 and P=0.010, respectively). There were no differences in the reasons for PICU admission; however, the differences in delta neutrophil index (DNI), CRP, and lactate levels were statistically significant (P=0.042, P=0.039, and P=0.028, respectively). Mortality increased in the vitamin C-deficient group; however, the difference was not statistically significant (P=0.113). Prognostic scoring systems, such as the PIM-3 and PRISM III scores, were also higher in vitamin C-deficient patients, with a statistically significant difference in PIM-3 scores (P=0.012).

The correlations between serum vitamin levels and other parameters are summarized in the correlation matrix (Figure 4). As shown in Table 3, the variables that differed between the vitamin C-deficient and non-deficient groups were negatively correlated with vitamin C levels. However, these variables did not predict vitamin C deficiency, as estimated by logistic regression analysis (data not shown). Among these variables,

Table 2. Vitamin C status at PICU admission

Variable	Deficiency (–) (n=46)	Deficiency (+) (n=17)	P-value
Age (yr)	7±5	7±5	0.808
Male	25 (54.3)	8 (47.1)	0.607
LOS in PICU (day)	11.7±9.6	18.7±15.8	0.035
In-hospital mortality	1 (2.2)	2 (11.8)	0.113
Requirement for MV[a]	30 (65.2)	15 (88.2)	0.073
Length of MV (day)	7 (0–13)	15 (7.5–24)	0.010
Reason for PICU admission			
Respiratory failure	15 (32.6)	5 (29.4)	0.809
Sepsis	14 (30.4)	7 (41.2)	0.422
Intensive monitoring	7 (15.2)	1 (5.9)	0.323
Neurologic problem	2 (4.3)	2 (11.8)	0.284
Post-resuscitation	2 (4.3)	2 (11.8)	0.284
Acute renal insufficiency	3 (6.5)	0	0.281
Biochemical value			
Thiamine (μg/dl)	4.0±2.1	4.1±2.4	0.944
WBC ($\times10^3$/μl)	12,465 (7,905–15,525)	8,170 (3,455–19,795)	0.448
DNI (%)	1.0 (0.0–3.8)	5.8 (0–9.5)	0.042
Hb (g/dl)	10.8±1.9	11.3±2.7	0.436
Platelets ($\times10^3$/μl)	298±202	250±197	0.398
D-dimer (ng/ml)	383 (267–1002)	677 (301–1482)	0.269
Creatinine (mg/dl)	0.3 (0.2–0.6)	0.3 (0.2–0.7)	0.751
CRP (mg/L)	7.5 (1.1–35.9)	30.3 (7.1–144.1)	0.039
Acid-base variable			
pH	7.35±0.09	7.30±0.11	0.089
BE (mEq/L)	–2.7±5.3	–5.1±4.3	0.095
cAG (mEq/L)	13.5 (11.6–16.5)	15.5 (11.1–18.3)	0.394
Lactate (mmol/L)	1.4 (0.9–1.8)	1.8 (1.1–4.3)	0.028
PICU mortality scoring system			
GCS	10.7±3.5	9.5±3.3	0.231
PIM-3 (mortality rate, %)	3.3 (0.9–5.1)	6.4 (2.9–16.9)	0.012
PRISM III	3.0 (0–8)	6.0 (1–16.5)	0.145

Values are presented as mean±standard deviation, number (%), or median (interquartile range).
PICU: pediatric intensive care unit; LOS: length of stay; MV: mechanical ventilation; WBC: white blood cell count; DNI: delta neutrophil index; Hb: hemoglobin; CRP: C-reactive protein; BE: base excess; cAG: corrected anion gap; GCS: Glasgow Coma Scale; PIM-3: Pediatric Index of Mortality 3; PRISM III: Pediatric Risk of Mortality III.
a) Requirement for mechanical ventilation within 24 hours of PICU admission.

CRP levels exhibited the strongest correlation with vitamin C levels (r=–0.389; 95% CI, –0.598 to –0.114; P=0.002) and showed a significant correlation with thiamine levels (r=–0.306; 95% CI, –0.520 to –0.056; P=0.01).

DISCUSSION

Critically ill patients often experience significant inflammation and oxidative stress, leading to malnutrition and a hypermetabolic state. They may undergo complex systemic inflammatory responses, which involve the release of pro-inflammatory cytokines and activation of inflammatory cells rather than anti-inflammatory responses. This can lead to weakened immune functions and dysfunction of multiple organs [15,16].

Given that critically ill patients often exhibit low micronutrient levels, there is increasing interest in the potential benefits of micronutrient supplementation in critical care settings [7,17-19]. Micronutrients are essential for meeting metabolic

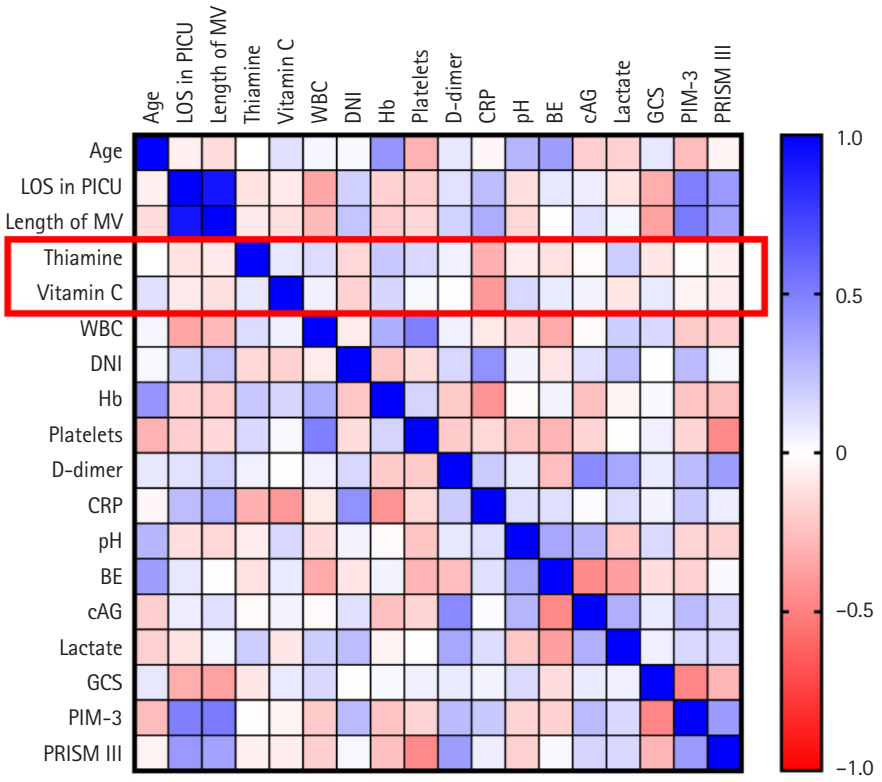

Figure 4. Correlation matrix. Correlations between serum vitamin levels and other parameters are shown in the red boxes. LOS: length of stay; PICU: pediatric intensive care unit; MV: mechanical ventilation; WBC: white blood cell count; DNI: delta neutrophil index; Hb: hemoglobin; CRP: C-reactive protein; BE: base excess; cAG: corrected anion gap; GCS: Glasgow Coma Scale; PIM-3: Pediatric Index of Mortality 3; PRISM III: Pediatric Risk of Mortality III.

Table 3. Correlations between vitamin C levels and other parameters

Variable	Correlation coefficient	95% CI	P-value
LOS in PICU (day)	−0.253	−0.478 to −0.010	0.047
Length of MV (day)	−0.295	−0.506 to −0.052	0.020
DNI (%)	−0.316	−0.521 to −0.049	0.012
CRP (mg/L)	−0.389	−0.598 to −0.114	0.002[a]
Lactate (mmol/L)	−0.090	−0.331 to 0.171	0.488
PIM-3 (mortality rate, %)	−0.200	−0.449 to 0.066	0.120

LOS: length of stay; PICU: pediatric intensive care unit; MV: mechanical ventilation; DNI: delta neutrophil index; CRP: C-reactive protein; PIM-3: Pediatric Index of Mortality 3.
a) Correlation is significant at P=0.01.

demands, combating oxidative stress, and supplying energy. Thiamine and vitamin C are gaining recognition as essential micronutrients because of their clinical implications, particularly in combination with hydrocortisone, for the treatment of sepsis [1,9,20]. However, the study designs and methods varied significantly, leading to mixed results even among patients with sepsis [2,15,16,21]. Additionally, in critically ill children, the evaluation of micronutrient status has been limited, and there are no established protocols for supplementing these micronutrients [10,11].

We reviewed critically ill children in the PICU for their initial serum thiamine and vitamin C levels. Low thiamine and vitamin C levels were observed in PICU patients, even in those without sepsis. Vitamin C deficiency was more common than thiamine deficiency. Almost half of the patients were malnourished, and their nutritional status affected vitamin C levels more than thiamine levels. The LOS in PICU and mechanical ventilation duration increased in the vitamin C deficiency group. Although vitamin C deficiency was not directly related to hospital mortality, prognosis-related markers in critically ill patients, such as the DNI [22], CRP [23], and lactate levels [24] and PIM-3 scores [25], were increased in the vitamin C deficiency group. Based on these results, we hypothesized that low

serum vitamin C levels could be associated with a poor prognosis in PICU patients.

During critical illness, oxidant levels increase due to the activation of pro-oxidant enzymes such as nicotinamide adenine dinucleotide phosphate oxidase (NOX) and inducible nitric oxide synthase (iNOS). Additionally, leukocytes and anaerobic cells produce high levels of reactive oxygen species (ROS) and reactive nitrogen species. Patients may also experience decreased antioxidant levels during treatments such as renal replacement therapy, extracorporeal membrane oxygenation, and the use of certain medications. Consequently, elevated oxidative stress during critical illness can lead to mitochondrial dysfunction and subsequent organ failure [16].

Vitamin C is an essential, water-soluble vitamin. The role of vitamin C in critically ill patients has been established. Vitamin C influences the pathophysiological processes of sepsis, trauma, burns, and other inflammatory illnesses [16,19,26]. As a cofactor in various biosynthetic pathways, Vitamin C contributes to the synthesis of catecholamines, immune cell neurotransmitters, cortisol, and peptide hormones. Vitamin C may limit further formation of ROS by inhibiting NOX and iNOS. Additionally, Vitamin C can act directly as a scavenger of radicals [16,19,26].

Although concerns remain regarding the timing and method of measuring serum vitamin C levels, vitamin C deficiencies are common in ICU patients. Even if vitamin C administration was not directly linked to mortality in some studies, outcomes such as LOS in ICU could be reduced [19,27]. In earlier clinical trials, the administration of more than 2 g/day of vitamin C in adults resulted in better outcomes than lower doses of administration. The adverse effects of vitamin C administration are limited to renal stones or oxalate nephropathy [19,28]. Therefore, high-dose vitamin C is recommended as a potential adjunctive therapy for critically ill patients [14,25].

This retrospective and cross-sectional study provides little insight into the cause-and-effect relationship between vitamin levels and patients' prognosis. However, we can investigate their association in the PICU. Although the data collected in this retrospective study were from 2019, insights into vitamins and vitamin replacement therapy in critically ill children have not changed significantly. Other studies conducted after 2019 have also reported the association between initial vitamin C levels and patients' prognosis, even in adults [2,10]. Therefore, we believe that our results remain relevant today. The small number of participants in a single center, with only 63 enrolled patients, was also a limitation of this study. Some subgroups of underlying diseases included only one to seven patients, so no statistical significance could be found. The routes of nutrient supplementation could also affect the patients' vitamin levels, which we did not consider. More patients requiring detailed nutritional considerations need to be monitored.

Given the clinical characteristics and limited accessibility of PICU patients, clinical trials involving the administration of vitamin C should be conducted with caution, particularly regarding dosage or duration. However, our data demonstrated that vitamin C deficiency was more common in patients in the PICU with mixed conditions. Lower serum vitamin C levels were related to the nutritional status of patients and are associated with poor prognostic factors in the PICU. Therefore, the administration of vitamin C is a potential intervention for PICU patients to improve their prognosis.

CONFLICT OF INTEREST

Kyung Won Kim is an editorial board member of the journal but was not involved in the peer reviewer selection, evaluation, or decision process of this article.

No other potential conflict of interest relevant to this article was reported.

FUNDING

This study was supported by the Technology Innovation Program of the Ministry of Trade, Industry, and Energy (MOTIE, Korea) (Project no. 20018111), and a new faculty research seed money grant from Yonsei University College of Medicine for 2025.

ACKNOWLEDGMENTS

None.

ORCID

Min Jung Kim https://orcid.org/0000-0002-5634-9709
Yoon Hee Kim https://orcid.org/0000-0002-6045-9927

Soo Yeon Kim https://orcid.org/0000-0003-4965-6193
Jong Deok Kim https://orcid.org/0000-0002-4266-5655
Mireu Park https://orcid.org/0000-0003-4342-6143
Hamin Kim https://orcid.org/0000-0002-0601-7300
Myung Hyun Sohn https://orcid.org/0000-0002-2478-487X
Kyung Won Kim https://orcid.org/0000-0003-4529-6135

AUTHOR CONTRIBUTIONS

Conceptualization: MJK, SYK, KWK. Methodology: MJK, HK, YHK. Formal analysis: MJK. Data curation: MJK, SYK, MP. Visualization: MJK, JDK, HK. Project administration: MJK, MP. Funding acquisition: MJK. Writing-original draft: MJK. Writing-review & editing: MHS, KWK. All authors read and agreed to the published version of the manuscript.

REFERENCES

1. Belsky JB, Wira CR, Jacob V, Sather JE, Lee PJ. A review of micronutrients in sepsis: the role of thiamine, l-carnitine, vitamin C, selenium and vitamin d. Nutr Res Rev 2018;31:281-90.
2. Tariq MA, Amin H, Ali U. Meta-analysis assessing the effectiveness of intravenous vitamin C in patients with sepsis and septic shock. Acute Crit Care 2022;37:674-7.
3. Leite HP, de Lima LF, Taddei JA, Paes ÂT. Effect of blood thiamine concentrations on mortality: influence of nutritional status. Nutrition 2018;48:105-10.
4. Putzu A, Daems AM, Lopez-Delgado JC, Giordano VF, Landoni G. The effect of vitamin C on clinical outcome in critically ill patients: a systematic review with meta-analysis of randomized controlled trials. Crit Care Med 2019;47:774-83.
5. Amrein K, Oudemans-van Straaten HM, Berger MM. Vitamin therapy in critically ill patients: focus on thiamine, vitamin C, and vitamin D. Intensive Care Med 2018;44:1940-4.
6. Shin TG, Kim YJ, Ryoo SM, Hwang SY, Jo IJ, Chung SP, et al. Early vitamin C and thiamine administration to patients with septic shock in emergency departments: propensity score-based analysis of a before-and-after cohort study. J Clin Med 2019;8:102.
7. Park JE, Shin TG, Jo IJ, Jeon K, Suh GY, Park M, et al. Impact of vitamin C and thiamine administration on delirium-free days in patients with septic shock. J Clin Med 2020;9:193.
8. Wei XB, Wang ZH, Liao XL, Guo WX, Wen JY, Qin TH, et al. Efficacy of vitamin C in patients with sepsis: an updated meta-analysis. Eur J Pharmacol 2020;868:172889.
9. Wald EL, Badke CM, Hintz LK, Spewak M, Sanchez-Pinto LN. Vitamin therapy in sepsis. Pediatr Res 2022;91:328-36.
10. McWhinney B, Ungerer J, LeMarsey R, Phillips N, Raman S, Gibbons K, et al. Serum levels of vitamin C and thiamin in children with suspected sepsis: a prospective observational cohort study. Pediatr Crit Care Med 2024;25:171-6.
11. Weiss SL, Blowey B, Keele L, Ganetzky R, Murali CN, Fitzgerald JC, et al. Matched retrospective cohort study of thiamine to treat persistent hyperlactatemia in pediatric septic shock. Pediatr Crit Care Med 2019;20:e452-6.
12. Rowe S, Carr AC. Global vitamin C status and prevalence of deficiency: a cause for concern? Nutrients 2020;12:2008.
13. Black RE, Allen LH, Bhutta ZA, Caulfield LE, de Onis M, Ezzati M, et al. Maternal and child undernutrition: global and regional exposures and health consequences. Lancet 2008;371:243-60.
14. de Onis M, Blössner M, Borghi E. Global prevalence and trends of overweight and obesity among preschool children. Am J Clin Nutr 2010;92:1257-64.
15. Halim Z, Huang Y, Lee ZY, Lew CC. New randomized controlled trials on micronutrients in critical care nutrition: a narrative review. Nutr Clin Pract 2024;39:1119-49.
16. Dresen E, Pimiento JM, Patel JJ, Heyland DK, Rice TW, Stoppe C. Overview of oxidative stress and the role of micronutrients in critical illness. JPEN J Parenter Enteral Nutr 2023;47 Suppl 1:S38-49.
17. Mahmoodpoor A, Shadvar K, Sanaie S, Hadipoor MR, Pourmoghaddam MA, Saghaleini SH. Effect of vitamin C on mortality of critically ill patients with severe pneumonia in intensive care unit: a preliminary study. BMC Infect Dis 2021;21:616.
18. Voelkle M, Gregoriano C, Neyer P, Koch D, Kutz A, Bernasconi L, et al. Prevalence of micronutrient deficiencies in patients hospitalized with COVID-19: an observational cohort study. Nutrients 2022;14:1862.
19. Langlois PL, Lamontagne F. Vitamin C for the critically ill: is the evidence strong enough? Nutrition 2019;60:185-90.
20. Marik PE, Khangoora V, Rivera R, Hooper MH, Catravas J. Hydrocortisone, vitamin C, and thiamine for the treatment of severe sepsis and septic shock: a retrospective before-after study. Chest 2017;151:1229-38.
21. Koekkoek KW, Berger MM. An update on essential micronutrients in critical illness. Curr Opin Crit Care 2023;29:315-29.
22. Kong T, Park YS, Lee HS, Kim S, Lee JW, You JS, et al. The delta

neutrophil index predicts development of multiple organ dysfunction syndrome and 30-day mortality in trauma patients admitted to an intensive care unit: a retrospective analysis. Sci Rep 2018;8:17515.
23. Ho KM, Lee KY, Dobb GJ, Webb SA. C-reactive protein concentration as a predictor of in-hospital mortality after ICU discharge: a prospective cohort study. Intensive Care Med 2008;34:481-7.
24. Chebl RB, Tamim H, Dagher GA, Sadat M, Enezi FA, Arabi YM. Serum lactate as an independent predictor of in-hospital mortality in intensive care patients. J Intensive Care Med 2020;35:1257-64.
25. Jung JH, Sol IS, Kim MJ, Kim YH, Kim KW, Sohn MH. Validation of pediatric index of mortality 3 for predicting mortality among patients admitted to a pediatric intensive care unit. Acute Crit Care 2018;33:170-7.
26. Teng J, Pourmand A, Mazer-Amirshahi M. Vitamin C: the next step in sepsis management? J Crit Care 2018;43:230-4.
27. Hemilä H, Chalker E. Vitamin C can shorten the length of stay in the ICU: a meta-analysis. Nutrients 2019;11:708.
28. Khoshnam-Rad N, Khalili H. Safety of vitamin C in sepsis: a neglected topic. Curr Opin Crit Care 2019;25:329-33.