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25-Hydroxyvitamin D and the Inflammation–Nutrition Axis in Critically Ill Adults: Associations with Neutrophil-to-Lymphocyte Ratio and Prognostic Nutritional Index

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ABSTRACT: Vitamin D deficiency is common in critical illness, but its relationship with integrated inflammatory and immunonutritional markers remains incompletely characterized. This cross-sectional study evaluated associations of serum 25-hydroxyvitamin D [25(OH)D] with the neutrophil-to-lymphocyte ratio (NLR) and Prognostic Nutritional Index (PNI) in 81 critically ill adults admitted to a tertiary intensive care unit in Indonesia. Total lymphocyte count, serum albumin, and C-reactive protein (CRP) were examined as complementary biomarkers. Associations were assessed using Spearman correlation and multivariable linear regression adjusted for age, sex, APACHE II score, and systemic corticosteroid use; bootstrap analyses with 5,000 resamples assessed robustness. Median 25(OH)D was 20.00 ng/mL, and 90.1% of participants had concentrations ≤ 30 ng/mL. Serum 25(OH)D correlated inversely with NLR ($r_s = -0.266$, $p = 0.016$), although this association did not remain significant after false-discovery-rate correction. In adjusted analysis, each 10-ng/mL increase in 25(OH)D was associated with a 2.74-unit lower NLR (95% CI, -5.55 to 0.06 ; $p = 0.055$) and a 2.07-point higher PNI (95% CI, 0.19 to 3.96 ; $p = 0.032$). The PNI association remained supported by bootstrap analysis (BCa 95% CI, 0.34 – 4.46 ; $p = 0.043$). No significant unadjusted associations were observed with total lymphocyte count, albumin, or CRP. Higher 25(OH)D may therefore be selectively associated with immunonutritional status in critically ill adults, warranting prospective confirmation.

1. INTRODUCTION

Vitamin D deficiency is common in critically ill adults. A multicenter ICU study reported deficiency in 59% of patients using a 25-hydroxyvitamin D [25(OH)D] threshold of <20 ng/mL, while a large database analysis also found abnormal 25(OH)D levels to be frequent and their prognostic significance uncertain [1,2]. Beyond calcium and bone metabolism, vitamin D participates in immune regulation; however, intervention evidence in critical illness remains mixed. A systematic review found possible reductions in pro-inflammatory cytokines but no consistent effect on C-reactive protein (CRP) [3].

Clinical-outcome meta-analyses show similar uncertainty. Shen et al. (2021) found no significant reduction in overall mortality but reported shorter ICU stay and mechanical ventilation [4], whereas Menger et al. (2022) reported reductions in mortality, ICU stay, and ventilation duration while noting substantial heterogeneity [5].

The neutrophil-to-lymphocyte ratio (NLR), derived from routine differential blood counts, is an accessible inflammatory marker associated with adverse outcomes in general ICU cohorts and adults with sepsis [6,7]. Outside critical care, lower vitamin D status has also been associated with higher NLR, providing indirect evidence for a vitamin D–leukocyte relationship [8].

The Prognostic Nutritional Index (PNI), calculated from serum albumin and total lymphocyte count, integrates nutritional, inflammatory, and immune information. Lower PNI has been associated with mortality in ICU populations and with acute kidney injury and delirium in critical illness [9–11]. Direct evidence evaluating 25(OH)D in relation to both NLR and PNI within the same heterogeneous critically ill population remains limited. This study evaluated associations of 25(OH)D with NLR and PNI, while examining total lymphocyte count, albumin, and CRP as complementary biomarkers.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

This analytical cross-sectional study was conducted in the intensive care unit (ICU) of Dr. Wahidin Sudirohusodo General Hospital, Makassar, Indonesia, between April and June 2026. All patients admitted to the ICU during the study period were screened using a total-sampling approach. Each participant was evaluated at a single study time point.

2.2 Study Participants

Eligible participants were adults aged ≥ 18 years who had been treated in the ICU for more than 24 hours, had passed the initial ebb phase of critical illness, and provided written informed consent to participate. When appropriate, study information and consent procedures were completed with the participant's family representative.

Patients were excluded if they had hyperparathyroidism, rickets, liver cirrhosis, chronic kidney disease, hematologic disorders, malabsorption, chronic hepatitis, fatty liver disease, autoimmune disease, tuberculosis, or HIV/AIDS; had received vitamin D supplementation exceeding 3,000 IU/day during the preceding month; had a history of gastrointestinal surgery; or were pregnant or breastfeeding.

During the study period, 331 ICU patients were screened and 81 met the study eligibility criteria and were included in the final analysis.

2.3 Clinical and Laboratory Data Collection

Demographic and clinical information was collected using the study data form. Variables available for the present analysis included age, sex, primary diagnostic category, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, systemic corticosteroid use, and anticonvulsant use.

Venous blood was collected for measurement of serum 25-hydroxyvitamin D [25(OH)D], routine hematologic parameters, serum albumin, and C-reactive protein (CRP). Serum 25(OH)D concentrations were measured using an enzyme-linked immunosorbent assay (ELISA), whereas routine hematologic, albumin, and CRP measurements were obtained using the hospital laboratory procedures used for the original study.

For descriptive purposes, vitamin D status was categorized as deficient (<20 ng/mL), insufficient (20–30 ng/mL), or sufficient (>30 ng/mL). Serum 25(OH)D was retained as a continuous variable in all primary association analyses to avoid loss of information resulting from categorization.

2.4 Calculation of Inflammatory and Nutritional Indices

The neutrophil-to-lymphocyte ratio (NLR) was calculated from the differential leukocyte count as:

$$NLR = \frac{\text{neutrophil percentage}}{\text{lymphocyte percentage}}$$

Total lymphocyte count (TLC) was calculated from the total leukocyte count and lymphocyte percentage:

$$TLC = \text{total leukocyte count} \times \frac{\text{lymphocyte percentage}}{100}$$

and was expressed as cells/ μL .

The Prognostic Nutritional Index (PNI) was calculated using serum albumin and TLC:

$$PNI = (10 \times \text{serum albumin [g/dL]}) + (0.005 \times \text{TLC [cells/}\mu\text{L]})$$

NLR and PNI were recalculated from their component variables before the final analysis to ensure internal consistency.

For the present analysis, NLR and PNI were the principal outcomes evaluated in multivariable models, representing inflammatory and immunonutritional dimensions, respectively. TLC, serum albumin, and CRP were additionally examined as supportive biomarkers.

2.5 Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 30.0 (IBM Corp., Armonk, NY, USA). Data were checked for completeness, coding errors, implausible values, and internally inconsistent derived variables before analysis. Clinically plausible extreme observations were retained, and no observations were excluded solely on the basis of statistical outlier status.

The distributions of continuous variables were evaluated using the Shapiro–Wilk test, supplemented by inspection of histograms, normal probability plots, skewness, and the relationship between the mean and median. Approximately symmetrically distributed continuous variables were summarized as mean $\pm$ standard deviation (SD), whereas skewed variables were summarized as median and first and third quartiles (Q1–Q3). Categorical variables were presented as frequencies and percentages.

Unadjusted associations between serum 25(OH)D and NLR, PNI, TLC, albumin, and CRP were evaluated using Spearman rank correlation coefficients (r_s). Because five biomarker correlations were examined simultaneously, the Benjamini–Hochberg procedure was applied to control the false discovery rate (FDR). Both nominal two-sided P values and FDR-adjusted q values were reported.

Separate multiple linear regression models were constructed for NLR and PNI. Serum 25(OH)D was entered as the exposure variable, with adjustment for age, sex, APACHE II score, and systemic corticosteroid use. These covariates were selected to account for demographic characteristics, severity of critical illness, and potential treatment-related effects on inflammatory indices. Regression coefficients for 25(OH)D were rescaled for presentation as the estimated change in the outcome per 10-ng/mL increase in serum 25(OH)D.

Multicollinearity was assessed using tolerance and variance inflation factor (VIF) statistics. Model diagnostics included inspection of standardized residuals, residual histograms, and normal P–P plots. Observations with standardized residuals exceeding ± 3 were examined for potential data or calculation errors but were retained when the underlying values were clinically plausible and internally consistent.

As a robustness analysis, regression coefficients were additionally estimated using nonparametric bootstrap resampling with 5,000 samples. Bias-corrected and accelerated (BCa) 95% confidence intervals were obtained for both NLR and PNI models.

All statistical tests were two-sided. A nominal $P < 0.05$ was considered statistically significant. For the five exploratory biomarker correlations, an FDR-adjusted $q < 0.05$ was additionally used to identify associations that remained significant after adjustment for multiple comparisons. No imputation was performed.

3. RESULTS AND DISCUSSION

3.1 Participant Characteristics

A total of 81 critically ill adults were included in the analysis. The mean age was 48.31 ± 16.71 years, and 43 participants (53.1%) were female. Malignancy and trauma were the most frequent diagnostic categories, each accounting for 23 patients (28.4%), followed by neurologic conditions in 19 patients (23.5%). The median APACHE II score was 10.0 (Q1–Q3, 7.0–13.5). Systemic corticosteroids were used by 18 patients (22.2%), while 20 (24.7%) received anticonvulsant medications.

The median serum 25-hydroxyvitamin D [25(OH)D] concentration was 20.00 ng/mL (Q1–Q3, 15.55–25.45). Forty patients (49.4%) were classified as vitamin D deficient and 33 (40.7%) as insufficient; only eight patients (9.9%) had concentrations above 30 ng/mL. The median neutrophil-to-lymphocyte ratio (NLR) was 18.71 (11.13–27.19), while the mean Prognostic Nutritional Index (PNI) was 35.46 ± 7.53 . Additional laboratory characteristics are presented in Table 1.

Table 1. Clinical and laboratory characteristics of critically ill adults (n = 81)

Characteristic	Overall (n = 81)
Age, years	48.31 ± 16.71
Sex, n (%)	
Male	38 (46.9)
Female	43 (53.1)
Primary diagnostic category, n (%)	
Malignancy	23 (28.4)
Musculoskeletal	12 (14.8)
Neurologic	19 (23.5)
Pulmonary/respiratory	2 (2.5)
Sepsis	2 (2.5)
Trauma	23 (28.4)
APACHE II score	10.0 (7.0–13.5)
Systemic steroid use, n (%)	18 (22.2)
Anticonvulsant use, n (%)	20 (24.7)
25-hydroxyvitamin D, ng/mL	20.00 (15.55–25.45)
Vitamin D status, n (%)	
Deficient (<20 ng/mL)	40 (49.4)
Insufficient (20–30 ng/mL)	33 (40.7)
Sufficient (>30 ng/mL)	8 (9.9)
Neutrophil-to-lymphocyte ratio	18.71 (11.13–27.19)
Prognostic Nutritional Index	35.46 ± 7.53
Total lymphocyte count, cells/μL	730.70 (538.05–1033.51)
Serum albumin, g/dL	3.13 ± 0.65
C-reactive protein, mg/L	98.70 (33.40–216.50)

Note: Data are presented as mean ± SD, median (Q1–Q3), or n (%), as appropriate. APACHE II, Acute Physiology and Chronic Health Evaluation II.

3.2 Unadjusted Associations of 25(OH)D With Inflammatory and Nutritional Biomarkers

In unadjusted analyses, serum 25(OH)D was weakly and inversely correlated with NLR (Spearman $r_s = -0.266$, $p = 0.016$). Higher 25(OH)D concentrations therefore tended to accompany lower NLR values. Positive correlations were observed with PNI ($r_s = 0.203$, $p = 0.069$) and serum albumin ($r_s = 0.200$, $p = 0.073$), although neither reached conventional statistical significance. No meaningful correlations were identified between 25(OH)D and total lymphocyte count or C-reactive protein (CRP).

Because five biomarker associations were evaluated, the Benjamini–Hochberg procedure was applied to control the false discovery rate. The nominal association between 25(OH)D and NLR did not remain significant after multiplicity adjustment (FDR-adjusted $q = 0.080$), and none of the five associations met an FDR threshold of 0.05.

Table 2. Unadjusted associations of serum 25-hydroxyvitamin D with inflammatory and nutritional biomarkers

Biomarker	n	Spearman r_s	P value	FDR-adjusted q
Neutrophil-to-lymphocyte ratio	81	−0.266	0.016	0.080
Prognostic Nutritional Index	81	0.203	0.069	0.122
Total lymphocyte count	81	0.092	0.413	0.503
Serum albumin	81	0.200	0.073	0.122
C-reactive protein	81	−0.075	0.503	0.503

Note: P values are two-sided. False discovery rate was controlled across the five biomarker correlations using the Benjamini–Hochberg procedure. FDR, false discovery rate.

3.3 Adjusted Associations of 25(OH)D With NLR and PNI

Multivariable linear regression was subsequently performed for NLR and PNI, adjusting for age, sex, APACHE II score, and systemic steroid use. In the NLR model, each 10-ng/mL higher 25(OH)D concentration was associated with a 2.74-unit lower NLR (adjusted B = −2.74; 95% CI, −5.55 to 0.06; $p = 0.055$). Thus, the inverse direction observed in the unadjusted analysis persisted after covariate adjustment, although the confidence interval included zero. The overall NLR model explained 12.5% of the observed variance ($R^2 = 0.125$; adjusted $R^2 = 0.066$) and did not reach conventional statistical significance overall ($F[5,75] = 2.134$; $p = 0.071$).

In contrast, higher 25(OH)D was positively associated with PNI after covariate adjustment. Each 10-ng/mL higher 25(OH)D concentration corresponded to a 2.07-point higher PNI (adjusted B = 2.07; 95% CI, 0.19 to 3.96; $p = 0.032$). Female sex was also associated with higher PNI compared with male sex (B = 4.28; 95% CI, 0.81 to 7.75; $p = 0.016$). The PNI model had an R^2 of 0.104 and an adjusted R^2 of 0.045, with an overall F test of $F(5,75) = 1.748$ ($p = 0.134$). No substantial multicollinearity was detected, with variance inflation factors ranging from approximately 1.01 to 1.55.

Bootstrap sensitivity analyses using 5,000 resamples supported the direction and magnitude of the principal findings. For 25(OH)D, the bias-corrected and accelerated 95% confidence interval was −5.94 to 0.35 for NLR (bootstrap $p = 0.054$) and 0.34 to 4.46 for PNI (bootstrap $p = 0.043$), when expressed per 10-ng/mL increase.

Table 3. Adjusted associations of serum 25-hydroxyvitamin D with NLR and PNI

Outcome and predictor	Adjusted B	95% CI	P value
NLR			
25(OH)D, per 10 ng/mL	−2.74	−5.55 to 0.06	0.055
Age, per year	−0.051	−0.233 to 0.130	0.576
Female vs male	−0.224	−5.386 to 4.938	0.931
APACHE II score, per point	−0.030	−0.587 to 0.526	0.913
Systemic steroid use, yes vs no	5.770	−0.083 to 11.623	0.053
PNI			
25(OH)D, per 10 ng/mL	2.07	0.19 to 3.96	0.032
Age, per year	−0.053	−0.175 to 0.069	0.392
Female vs male	4.277	0.807 to 7.747	0.016
APACHE II score, per point	0.025	−0.349 to 0.399	0.894
Systemic steroid use, yes vs no	0.743	−3.192 to 4.678	0.708

Note: Values are unstandardized linear regression coefficients. Models were adjusted for age, sex, APACHE II score, and systemic steroid use. The 25(OH)D coefficient is expressed per 10-ng/mL increase for clinical interpretability. Model fit: NLR, $R^2 = 0.125$, adjusted $R^2 = 0.066$, $F(5,75) = 2.134$, $p = 0.071$; PNI, $R^2 = 0.104$, adjusted $R^2 = 0.045$, $F(5,75) = 1.748$, $p = 0.134$. Bootstrap sensitivity analysis with 5,000 resamples yielded BCa 95% CIs of −5.94 to 0.35 for NLR and 0.34 to 4.46 for PNI. APACHE II, Acute Physiology and Chronic Health Evaluation II; BCa, bias-corrected and accelerated; NLR, neutrophil-to-lymphocyte ratio; PNI, Prognostic Nutritional Index; 25(OH)D, 25-hydroxyvitamin D.

3.4 Graphical Patterns of the Associations

The scatterplots were directionally consistent with the statistical analyses. Serum 25(OH)D showed a downward fitted trend with NLR, whereas an upward fitted trend was observed with PNI. Considerable between-patient variability remained across the range of 25(OH)D concentrations, particularly for NLR, consistent with the modest effect sizes observed in the correlation and multivariable analyses.

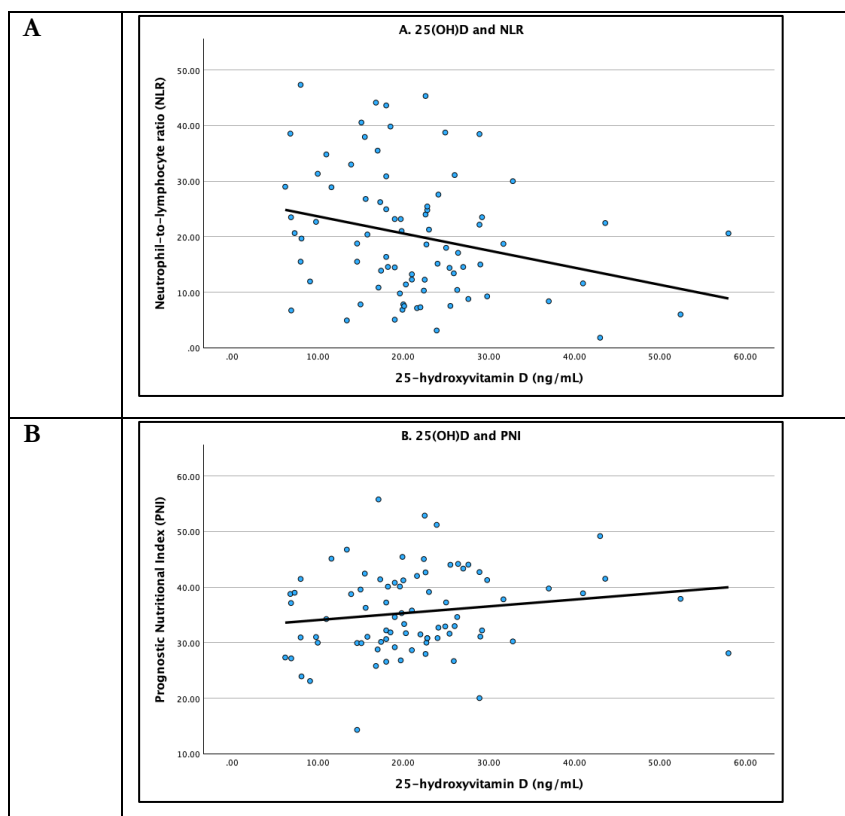


Figure 1. Associations of serum 25-hydroxyvitamin D with inflammatory and nutritional indices. (A) Association between serum 25-hydroxyvitamin D and neutrophil-to-lymphocyte ratio (NLR). **(B)** Association between serum 25-hydroxyvitamin D and Prognostic Nutritional Index (PNI). Each point represents an individual participant. Solid lines represent linear fitted trends for visualization; inferential associations are reported in Tables 2 and 3.

3.5 Discussion

The present study examined the relationship between serum 25-hydroxyvitamin D [25(OH)D] and inflammatory-immunonutritional markers in 81 critically ill adults. Low vitamin D status was common, with 90.1% of participants having concentrations ≤ 30 ng/mL. Serum 25(OH)D was inversely correlated with NLR in the unadjusted analysis, although this association did not remain significant after false-discovery-rate correction. After adjustment for age, sex, APACHE II score, and systemic corticosteroid use, the inverse estimate persisted but narrowly included the null, as did the bootstrap confidence interval. In contrast, PNI showed a positive adjusted association with 25(OH)D that remained supported by bootstrap resampling, whereas TLC, albumin, and CRP showed no significant unadjusted associations. These findings suggest that the relationship between vitamin D and inflammatory-immunonutritional status in critical illness is present but not uniform across biomarkers.

The high frequency of low 25(OH)D is consistent with previous ICU studies. Xie et al. (2022) reported deficient 25(OH)D in approximately 70% of critically ill patients, although deficiency itself was not independently associated with hospital mortality in their adjusted analysis [2]. Mayr et al. (2020) likewise observed severe deficiency in 55% and moderate deficiency in another 23% of ICU patients [12]. Vitamin D concentrations during critical illness should therefore not necessarily be regarded as a simple reflection of pre-illness vitamin D stores; systemic illness and treatment-related factors may influence measured concentrations during the ICU course [4,5]. In patients with sepsis specifically, Li and Ding (2020) found that lower admission 25(OH)D was associated with mortality, particularly when concentrations were <10 ng/mL [13]. This observational evidence supports clinical relevance but does not establish a causal role for vitamin D deficiency.

The inverse 25(OH)D–NLR pattern observed in the present study is biologically plausible. NLR represents the balance between neutrophil predominance and lymphocyte abundance and has been associated with mortality in general ICU populations and adverse prognosis in adult sepsis [6,7]. The latter meta-analysis included 12 studies and more than 10,000 adults with sepsis.

Outside critical care, vitamin D deficiency has also been associated with higher NLR in type 2 diabetes [8]. Mechanistically, vitamin D signaling participates in innate immune responses through VDR- and CYP27B1-dependent pathways, regulation of antimicrobial peptides, macrophage responses, and modulation of adaptive immunity [14,15]. Nevertheless, our NLR result should remain cautiously interpreted: the nominal Spearman association did not survive FDR correction, and both adjusted and bootstrap estimates crossed zero.

The PNI result provides a different perspective. Although the crude correlation between 25(OH)D and PNI was not statistically significant, the association became positive after adjustment and remained supported by bootstrap analysis. PNI has established prognostic relevance in critically ill populations. Lu et al. (2021) reported higher short- and long-term mortality among ICU patients with lower PNI [9], while Wu et al. (2022) demonstrated an association between PNI and 30-day, 90-day, and 1-year mortality in sepsis [16]. In a heterogeneous ICU cohort, Shao et al. (2022) similarly found PNI to be independently associated with in-hospital and 1-year mortality [17]. Its relevance has subsequently been reported for acute kidney injury and delirium in critically ill populations [10,11]. The present finding therefore supports an association between 25(OH)D and a composite immunonutritional index, but not evidence that vitamin D is a strong determinant of PNI. The modest model R^2 and non-significant overall F test warrant particular caution, and the observed association between sex and PNI should be regarded as exploratory.

Interpretation of PNI also requires attention to its components. Serum albumin should not be considered a direct marker of nutritional status in critical illness. The ASPEN position paper emphasizes that inflammation alters albumin through hepatic reprioritization, increased capillary permeability, redistribution, and other illness-related mechanisms; low albumin therefore reflects inflammatory burden and nutrition risk rather than protein-energy malnutrition itself [18]. Because PNI combines albumin with lymphocyte count, it is more appropriately described as an immunonutritional or inflammation–nutrition index than as a pure measure of nutritional status. Its mathematical dependence on albumin and lymphocytes should also prevent interpretation of PNI as independent of those components. Critical illness is metabolically dynamic, and nutritional requirements and substrate tolerance vary substantially according to disease phase, comorbidity, and recovery trajectory [19].

The lack of a significant association between 25(OH)D and CRP is also compatible with available evidence. Arabi et al. (2020) found that vitamin D supplementation in critically ill adults may influence selected pro-inflammatory cytokines but showed no consistent effect on CRP [3]. CRP itself is a positive acute-phase protein whose concentration changes substantially during systemic inflammation [18]. More broadly, clinical trials have not produced uniform evidence that correcting vitamin D deficiency improves major ICU outcomes. Peng et al. (2020) found no reduction in mortality, ICU stay, hospital stay, or mechanical ventilation across nine randomized trials [20], while subsequent meta-analyses have reported some differing estimates according to outcome and administration strategy [4,5]. Thus, the biomarker associations observed here should not be translated directly into recommendations for vitamin D supplementation.

Strengths of this analysis include verification and recalculation of derived indices from their source components, adjustment for illness severity and corticosteroid exposure, control for multiple biomarker testing, and bootstrap assessment of regression estimates. Several limitations remain. The cross-sectional, single-center design prevents establishment of temporal or causal relationships; the sample size was modest and included heterogeneous diagnostic groups; and biomarkers were measured at a single time point. Unmeasured confounding and acute physiological changes may also influence circulating 25(OH)D and the component variables of NLR and PNI. Prospective multicenter studies incorporating serial measurements and clinically relevant outcomes would help determine whether these associations are reproducible and whether they change across phases of critical illness.

4. CONCLUSION

Low vitamin D status was highly prevalent among critically ill adults in this study. Higher serum 25-hydroxyvitamin D [25(OH)D] was associated with lower neutrophil-to-lymphocyte ratio (NLR) in the unadjusted analysis, although this association was attenuated after adjustment for multiple testing and clinical covariates. In contrast, higher 25(OH)D was positively associated with the Prognostic Nutritional Index (PNI) after adjustment for age, sex, APACHE II score, and systemic corticosteroid use, and this association remained supported by bootstrap analysis. No significant associations were observed with total lymphocyte count, serum albumin, or C-reactive protein. These findings suggest that vitamin D status may relate selectively to inflammatory–immunonutritional characteristics in critical illness, particularly PNI, rather than uniformly across

inflammatory biomarkers. Given the cross-sectional design, causal interpretation is not warranted. Larger prospective studies with serial biomarker measurements are needed to clarify temporal relationships and clinical relevance.

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AUTHOR CONTRIBUTIONS

ATA: Conceptualization, Investigation, Data Curation, Formal Analysis, Visualization, and Writing – Original Draft.

NAD: Conceptualization, Methodology, Supervision, Validation, Interpretation of Findings, and Writing – Review & Editing.

AYS: Conceptualization, Methodology, Supervision, Validation, Interpretation of Findings, and Writing – Review & Editing.

C: Methodology, Supervision, Validation, Interpretation of Findings, and Writing – Review & Editing.

FM: Methodology, Clinical Validation, Interpretation of Findings, and Writing – Review & Editing.

M: Methodology, Supervision, Validation, Interpretation of Findings, and Writing – Review & Editing.

All authors critically reviewed the manuscript, approved the final version, and agreed to be accountable for the accuracy and integrity of the work.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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ETHICS STATEMENT

The study protocol was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Hasanuddin/Dr. Wahidin Sudirohusodo General Hospital, Makassar, Indonesia (Approval No. 101/UN4.6.4.5.31/PP36/2026; Protocol No. UH26010057; January 19, 2026). Written informed consent was obtained from all participants or their legally authorized representatives before enrollment. Participation was voluntary, and participant confidentiality was maintained throughout the study. Personally identifying information was excluded from the analytical dataset.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to applicable ethical and institutional restrictions.

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