

# The predictors of prognostic nutritional index and its association with in-hospital mortality among critically ill geriatric patients

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## ABSTRACT

**Purpose:** The study aimed to determine the predictors of prognostic nutritional index (PNI) and its association with in-hospital mortality among critically ill geriatric patients

**Materials and methods:** Prospective cohort study included 113 critically ill older patients at a geriatrics hospital in Egypt. Clinical history, laboratory analyses, Charlson comorbidity index, and simplified acute physiology score II were conducted on admission. Immuno-nutritional biomarkers included PNI, neutrophil/lymphocyte ratio (NLR), systemic immune inflammation index (SII), and platelet/lymphocyte ratio (PLR). The hospital outcome was in-hospital mortality.

**Results:** Median PNI was 33.45. Predictors of PNI were albumin and hematocrit. PNI showed a negative correlation with NLR ( $r = -0.475$ ,  $p < 0.001$ ), PLR ( $r = -0.263$ ,  $p = 0.005$ ), and SII ( $r = -0.287$ ,  $p = 0.002$ ). PNI  $< 35.475$  and NLR  $> 6.5$  defined in-hospital mortality with an area under the curve of 0.633,  $p = 0.011$  and  $p = 0.612$ ,  $p = 0.036$ , respectively.

**Conclusion:** PNI  $< 35.475$  and NLR  $> 6.5$  are associated with in-hospital mortality. PNI had an inverse correlation with NLR, SII, and PLR.

**Keywords:** geriatric patients, prognostic nutritional index, immuno-nutrition, mortality

## INTRODUCTION

Malnutrition is a highly prevalent syndrome in acutely ill geriatric patients, worsening immune function and hospital outcomes [1]. Immuno-nutritional (IN) status is the changes of nutrients in diet that are capable of modifying the immunological system. It depends on the availability of immuno-active nutrients as arginine, omega 3 fatty acids, and antioxidants such as L-ascorbic acid. Deficiency of these nutrients could negatively influence immune functions including both humoral and cell-mediated immunological activity [1].

Several recent studies found that IN status could influence morbidity among patients undergoing surgery. However, its impact on clinical outcomes such as infections, length of hospital confinement, and mortality, remains deficient in acute geriatric care settings [1]. Critically ill patients are at a higher risk of worsening due to rapidly progressive disorders. Therefore, having simple objective IN indicators can aid clinicians to rapidly stratify patients and improve their clinical outcomes [2].

There are several simple laboratory markers of prognostic utility such as serum albumin, transthyretin, and inflammatory markers such as C-reactive protein (CRP) and white blood cells counts. Currently, combinations of these markers could form more efficient prognostic indicators such as the prognostic nutritional index (PNI), neutrophil/lymphocyte ratio (NLR), and the platelet/lymphocyte ratio (PLR) [3]. However, PNI is a simple and objective indicator of IN status and has a high predictive utility among patients [4]. Accordingly, assessing the effectiveness and prognostic value of these IN prognostic scores in critically ill geriatric patients is crucial. In the current study we selected PNI as a representative for IN status. This study aimed to determine the predictors of PNI and its association with in-hospital mortality among critically ill geriatric patients.

## MATERIALS AND METHODS

### Ethical Approvals

The study's protocol underwent two steps of ethical approvals. First, it was checked and accepted by the ethical committee of the geriatrics hospital, Ain Shams University

hospitals where the study was accomplished. Second, the study's protocol was revised and accepted by the research ethics committee at the faculty of Medicine, Ain Shams University. Approval number: FMASU R 197/2024. Informed consents were obtained from participants or their proxies.

### Representative Sample Calculation

Using PASS 15 program and based on data of previous related research [5], setting statistical power at 80% and alpha level of error at 0.05, it was estimated that a minimum 75 patients were needed to detect an expected area under the ROC curve of 0.79 for PNI for prediction of in-hospital mortality of 12%.

### Research Strategy and Place

A prospective cohort study included 113 geriatric patients aged  $\geq 60$  years old. These patients were admitted at high dependency units (HDUs) in a specialized geriatrics hospital, Ain Shams university hospitals, Egypt between August and October 2024. Each participant was initially subjected to clinical history taking. Socio-demographic data included age and sex. Charlson comorbidity index (CCI) was calculated to assess the burden of multi-morbidity. It is one of the most widely utilized scoring tools to assess comorbidity and survival [6]. Comorbidities and geriatric syndromes included cardiovascular disease (CVD), diabetes, chronic live disease, chronic renal disease/end stage renal disease, cognitive impairment, falls/accidents and urinary/fecal incontinence.

### Selection Criteria and Inclusion in the Study

The inclusion criteria were, as follows: critically ill patients admitted in HDUs, aged  $\geq 60$  years; the laboratory analysis within the first 48 hours of admission. Patients with recurrent admissions were excluded, except for the data on the first admission. Patients who had on-demand discharge and those transferred to other hospital before completion of treatment regime were excluded.

### Acute Illness Severity Evaluation

$\text{PaO}_2/\text{FiO}_2$  ratio (PFR) was utilized to assess oxygenation status and calculated based on arterial blood gases and oxygen saturation on admission [7, 8]. Simplified acute physiology score II (SAPS II) was used to determine acute illness severity [9]. SAPS II score depends on patients admission criteria including vitals, conscious level, urine output over 24 hours, chronic diseases, type of admission, base-line laboratory results, and PFR value [9].

### Laboratory Analysis

Blood sampling was conducted by qualified nursing personnel at the hospital. Samples were analyzed at the laboratories of Ain Shams University. Hematological testing included complete blood count (CBC) with differential count analysis. It was measured with CELL-DYN RUBY hematology operator (Abbott, USA), XN 1000 (Sysmex, Germany), and ADVIA 560 (Siemens, Mumbai). CBC reports included hemoglobin, hematocrit, red cell distribution width (RDW), platelets, total leucocytes count, and differential counts of white blood cells. Biochemical analyses included the serum levels of albumin, total proteins, electrolytes, creatinine, blood urea nitrogen, alanine aminotransferase, aspartate aminotransferase, total bilirubin, and CRP. These analyses were processed through these devices: AU680, AU480 analyzers (Beckman Coulter, USA) and COBAS C311 analyzer-Roche.

### Immuno-Nutritional Status Evaluation

Several blood-derived IN biomarkers have prognostic and predictive utility in practical settings due to the interplay between malnutrition and chronic inflammatory reaction [10]. We utilized different combinations of prognostic indices including

- PNI is an objective IN biomarker. It was calculated by using serum albumin level and peripheral lymphocyte count, as follows,  $\text{PNI} = \text{serum albumin (g/l)} + 5 \times \text{lymphocyte count (} 10^3/\text{mm}^3 \text{)}$  [4, 10].
- NLR is a simple inflammatory index and has a prognostic value in clinical polices. It was evaluated by dividing the absolute neutrophils by peripheral absolute lymphocytes count as reported in differential CBC analyses, as follows:  $\text{NLR} = \text{neutrophil count (} 10^3/\text{mm}^3 \text{)}/\text{lymphocyte count (} 10^3/\text{mm}^3 \text{)}$  [10, 11].
- PLR is the proportion of platelets count to peripheral lymphocytes count. It is an integral inflammatory biomarker in different diseases and cancer. PLR can be calculated easily utilizing parameters from CBC reports.  $\text{PLR} = \text{platelet count (} 10^3/\text{uL)}/\text{lymphocyte count (} 10^3/\text{mm}^3 \text{)}$  [10, 12].
- Systemic immune inflammation index (SII) is a novel systemic inflammatory indicator. It can be considered as a predictor of survival and calculated easily from CBC reports, as follows:  $\text{SII} = \text{neutrophil count (} 10^3/\text{mm}^3 \text{)}/\text{lymphocyte count (} 10^3/\text{mm}^3 \text{)} \times \text{platelet count (} 10^3/\text{uL)}$  [10, 13].

### Hospital Outcome

The target observed outcome was in-hospital mortality. The follow up process started when the patient was initially admitted to the HDUs and ended on either discharge alive or death at the hospital.

### Statistical Testing

The statistical package for the social sciences version 28 (IBM Corp., Armonk, NY, USA) was utilized for data analysis. Data was organized and presented as mean and standard deviation for normally distributed quantitative parameters or median and interquartile range for non-normally distributed quantitative parameters and frequencies (numbers) and relative frequencies (percentages) for categorical elements. Comparisons between groups were done using unpaired t- test in normally distributed quantitative parameters while non-parametric Mann-Whitney test was used for non-normally distributed quantitative parameters. For categorical elements, Chi square ( $\chi^2$ ) test was performed for comparisons. Exact (Fisher-Irwin) test was used instead when the expected frequency is less than 5. Correlations between quantitative parameters were done using Spearman correlation coefficient ( $r$ ). The ROC curve was used with an area under curve (AUC) analysis to detect optimal cutoffs of the studied biomarkers for detection of in-hospital mortality. Logistic regression testing was performed to detect the independent predictors of low PNI with the odds ratio (OR). p-values  $< 0.05$  were considered as statistically significant.

**Table 1.** Comparison between patients based on PNI

Variable	PNI				p-value
	≤ 33.45		> 33.45		
	C	P (%)	C	P (%)	
Sex (male/female)	21/36	36.8/63.2	20/36	35.7/64.3	0.901
CVD	46	80.7	49	87.5	0.323
Diabetes mellitus	25	43.9	28	50.0	0.513
Old CVA/TIA	23	40.4	16	28.6	0.188
CKD/ESRD	17	29.8	17	30.4	0.951
Chronic liver disease	10	17.5	9	16.1	0.834
Incontinence	5	8.8	9	16.1	0.239
Malignancy	11	19.3	6	10.7	0.202
Cognitive impairment	19	33.3	17	30.4	0.734
Falls/accidents	12	21.1	18	32.1	0.182
Chronic pulmonary disease	5	8.8	10	17.9	0.155
Thyroid dysfunction	3	5.3	1	1.8	0.618
In-hospital mortality	36	63.2	26	46.4	0.074

Note. C: Count; P: Percentage; CVA/TIA: Cerebro-vascular accidents/transient ischemic attacks; & CKD/ESRD: Chronic kidney disease/end stage renal disease

**Table 2.** Association between PNI and quantitative variables

Quantitative variables	PNI				p-value
	≤ 33.45		> 33.45		
	M	SD	M	SD	
Age	73.49	8.62	73.98	9.64	0.776
GCS	12.11	3.07	12.42	3.35	0.611
Respiratory rate	23.70	5.86	25.59	6.61	0.114
Heart rate	91.30	22.48	88.83	18.83	0.534
MBP	82.79	16.56	89.20	14.39	0.032
Temperature	37.37	0.36	37.30	0.32	0.334
Sodium	134.46	9.27	136.47	8.20	0.230
Potassium	3.78	0.84	4.19	0.85	0.013
Calcium	9.07	0.95	9.12	1.47	0.827
Magnesium	1.82	0.45	2.09	0.50	0.006
Total proteins	5.44	0.93	6.70	0.69	<0.001
Hemoglobin	9.87	2.15	11.74	2.16	<0.001
Hematocrit	29.97	6.69	35.82	7.60	<0.001
RDW	16.48	3.30	14.76	2.14	0.003
Albumin	2.26	0.38	3.18	0.48	<0.001
CCI	8.02	2.66	7.59	2.41	0.383
SAPS II Score	41.42	10.66	34.73	10.86	0.004

Note. M: Mean; SD: Standard deviation; GCS: Glasgow coma scale; MBP: Mean blood pressure; & Normal range of sodium (136-145 mmol/l), potassium (3.5-5.1 mmol/l), calcium (8.6-10.3 mg/dl), magnesium (1.8-2.6 mg/dl), total proteins (6-8.3 g/dl), hemoglobin (12-15g/dl), hematocrit (40.0-50.0%), RDW (11.5-14.0%), & albumin (3.5-5.4 g/dl)

## RESULTS

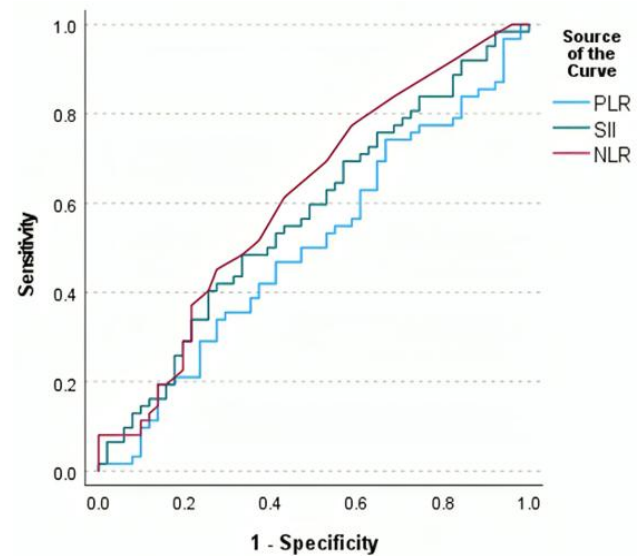
The mean age of participants was 73.73 ± 9.10 years. Median values of PNI was 33.45, accordingly, patients were classified into 2 groups: low PNI (≤ 33.45) and high PNI (> 33.45). Those with low PNI had a significantly higher SAPS II score 41.42 ± 10.66 vs. 34.73 ± 10.86, p = 0.004. Among the laboratory variables studied, RDW was significantly higher 16.48 ± 3.30 vs 14.76 ± 2.14, p = 0.003. They had significantly lower serum albumin and total proteins.

Mean serum total proteins and albumin measured 5.44 ± 0.93 vs. 6.70 ± 0.69 and 2.26 ± 0.38 vs. 3.18 ± 0.48, respectively with p-value < 0.001 for both. Similarly, they had significantly lower hematocrit 29.97 ± 6.69 vs. 35.82 ± 7.60 and hemoglobin 9.87 ± 2.15 vs. 11.74 ± 2.16, p-value < 0.001 (Table 1 and Table 2).

**Table 3.** Association between PNI and quantitative variables

QV	PNI						p-value
	≤ 33.45			> 33.45			
	MD	1 <sup>st</sup> Q	3 <sup>rd</sup> Q	MD	1 <sup>st</sup> Q	3 <sup>rd</sup> Q	
TLC	12.00	7.50	16.70	10.40	7.75	13.65	0.484
PL	200.00	131.00	305.00	245.50	186.00	301.50	0.137
BUN	43.00	23.00	69.00	28.00	17.50	66.50	0.267
Cr	1.40	1.00	3.10	1.30	0.80	2.70	0.240
PH	3.30	2.60	4.30	3.40	2.70	4.30	0.787
TB	0.80	0.45	1.00	0.60	0.40	0.90	0.268
ALT	16.00	10.00	26.00	14.50	10.00	21.00	0.587
AST	26.00	19.00	44.00	28.00	19.00	36.00	0.545
PFR	347.62	262.00	447.62	300.00	242.86	368.10	0.060
CRP	94.20	41.00	172.00	45.00	18.60	122.70	0.016
PLR	210.68	127.89	347.30	156.88	121.17	249.05	0.053
SII	1,708.6	880.0	4,321.7	1,364.6	673.3	1,987.2	0.058
NLR	11.00	5.00	19.00	6.00	3.00	8.00	<0.001

Note. QV: Quantitative variables; MD: Median; Q: Quartile; TLC: Total leucocyte count; BUN: Blood urea nitrogen; PL: Platelets; Cr: Creatinine; PH: Phosphorus; TB: Total bilirubin; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; & Normal range of total leukocyte count (4-10×10<sup>3</sup>/μL), platelets (150-410×10<sup>3</sup>/μL), BUN (8-20 mg/dl), creatinine (0.6-1.2 mg/dl), phosphorus (2.5-5.0 mg/dl), total bilirubin (0.3-1mg/dl), ALT (7-52 IU/l), AST (13-39 IU/l), & CRP (< 6 mg/l)



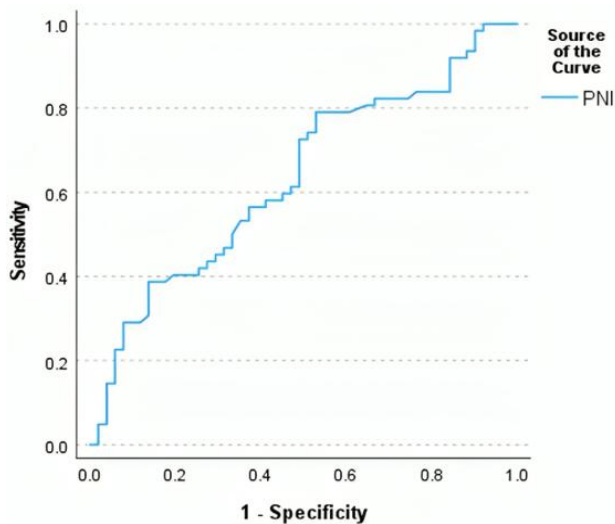
**Figure 1.** ROC for prediction of mortality using PLR, SII, & NLR (Source: Authors' own elaboration)

Compared to patients with higher PNI, patients with low PNI had significantly higher median values of NLR and CRP 11.00 vs. 6.00, p < 0.001, and 94.20 vs. 45.00, p = 0.016, respectively (Table 3).

The ROC curve determined the specified cut-off values of IN biomarkers associated with in-hospital mortality. PNI at a cut-off < 35.475 had the highest predictive utility with an AUC of 0.633, p = 0.011 (Figure 1, Figure 2, and Table 4).

Based on logistic regression testing, we determined the OR of factors significantly associated with low PNI. Both hematocrit and albumin were the independent predictors of low PNI with an OR of 0.795, p = 0.019 and and OR of 0.000013, p = 0.015, respectively (Table 5).

Spearman correlation analysis revealed a significant negative correlation between PNI and other IN biomarkers. PNI-PLR (r = -0.263, p = 0.005), PNI-NLR (r = -0.475, p < 0.001), PNI-SII (r = -0.287, p = 0.002) (Table 6).



**Figure 2.** ROC for prediction of mortality using PNI (Source: Authors' own elaboration)

**Table 4.** ROC of different IN biomarkers for prediction of mortality

IN-B	AUC	P-value	95% CI		Cut-off	Sensitivity (%)	Specificity (%)
			LB	UB			
PLR	0.503	0.959	0.395	0.610	-	-	-
SII	0.571	0.187	0.465	0.678	-	-	-
NLR	0.612	0.036	0.507	0.718	> 6.500	61.3	56.9
PNI	0.633	0.011	0.530	0.735	< 35.475	72.6	51.0

Note. IN-B: IN biomarkers; LB: Lower bound; & UB: Upper bound

**Table 5.** Logistic regression analysis to identify predictors of PNI

Predictive factors	Univariate logistic regression		Multivariate logistic regression	
	p-value	OR (95% CI)	p-value	OR (95% CI)
MBP	0.035	0.973 (0.949-0.998)	-	-
Potassium	0.015	0.564 (0.355-0.896)	-	-
Magnesium	0.009	0.287 (0.113-0.732)	-	-
Total protein	< 0.001	0.119 (0.045-0.310)	-	-
Hemoglobin	< 0.001	0.668 (0.547-0.815)	-	-
Hematocrit	< 0.001	0.892 (0.841-0.947)	0.019	0.795 (0.656-0.963)
RDW	0.006	1.310 (1.081-1.587)	-	-
Albumin	< 0.001	0.002 (0.000-0.024)	0.015	0.000013 (0.000-0.112)
SAPS II	0.007	1.062 (1.017-1.109)	-	-
CRP	0.100	1.004 (0.999-1.008)	-	-

**Table 6.** Correlation between PNI with PLR, NLR, and SII

	PLR	SII	PNI	
SII	Correlation coefficient	0.789		
	p-value	< 0.001		
	N	113		
PNI	Correlation coefficient	-0.263	-0.287	
	p-value	0.005	0.002	
	N	113	113	
NLR	Correlation coefficient	0.504	0.798	-0.475
	p-value	< 0.001	< 0.001	< 0.001
	N	113	113	113

Note. \*Yellow color indicates significance

## DISCUSSION

The study explored the impact of IN status on hospital outcomes among critically ill geriatric patients. The study provided these main findings: first, provision of specified cut-off of PNI and NLR for predicting in-hospital mortality. Second, it showed inverse correlations between PNI and other IN biomarkers. Third, the study revealed independent predictors of PNI values among critically ill older patients. It is the first study examining these issues among geriatric patients with critical illnesses.

In the current study low PNI represented poor IN status; it had the highest predictive utility in comparison to other IN biomarkers. PNI is an easily obtainable biomarker at hospital sittings. It demonstrated a good predictive utility in postoperative, cancer, and CVD patients while its role in critically ill geriatric patients is still deficient [14].

Both PNI and NLR were significantly associated with in-hospital mortality at specified cut-offs. PNI at cut-off < 35.475 was associated with in-hospital mortality (AUC = 0.633, 95% confidence interval [CI] = 0.530-0.735,  $p = 0.011$ ) with a sensitivity of 72.6% and specificity of 51%. These results confirm the burden of malnutrition combined with inflammation among hospitalized older adults. This is consistent with a previous retrospective observational study including critically ill older adults aged 85 years and above. It revealed a significant association between low PNI and 28 days mortality where PNI at a cut-off 33.8 predicted mortality with a sensitivity of 56.1% and specificity of 56.9% (AUC = 0.600, 95% CI = 0.514-0.685) [14].

Similarly, NLR at cut-off at > 6.5 was associated with in-hospital mortality (AUC = 0.612, 95% CI = 0.507-0.718,  $p = 0.036$ ) with a sensitivity of 61.3% and specificity of 56.9%. These results are similar to another prospective cohort study included older patients at emergency department where the NLR at cut-off > 8 had a good predictive value for mortality (AUC = 0.70, 95% CI 0.670-0.730,  $p < 0.001$ ) [15]. These data supported the superiority of PNI as a prognostic biomarker over other IN biomarkers as evidenced in another retrospective observational study among breast cancer patients [16]. Both PLR and SII did not show a significant association with mortality in comparison to other studies demonstrating their potential predictive utility in cancer patients [10]. These discrepancies could be attributed to differences in populations and sittings of various studies.

The superiority of PNI could be attributed to its ability to provide comprehensive IN representation. Because of the inclusion of serum albumin and lymphocytes count in the same equation [4, 10]. Serum albumin reflects both immune and nutritional status. Lower albumin levels signify poor nutrition and/or active inflammatory condition. Also, peripheral lymphocytes count reflects immunological activity. Reduced lymphocytes count has been linked to worse clinical outcomes including mortality. Similarly, NLR reflects the balance between neutrophils driven innate immune response and lymphocytes mediated adaptive immunity. Higher NLR reflects immune dysregulation and pro-inflammatory status [10, 11]. Compared to PLR and SII, NLR shows a more rapid response to various stressors, further supporting its prognostic significance. Conversely, SII and PLR, through useful inflammatory indicators, may not comprehensively represent the complex interplay between immunity, nutrition and

inflammation. PLR mainly reflects platelet driven inflammatory reaction, which are important in vascular pathology and thrombus formation. Likewise, SII lacks direct nutritional parameters, limiting its prognostic role in cases where malnutrition is a major contributor to death [10, 13].

The study explored significant relationships between PNI and other IN biomarkers as demonstrated by the significant inverse relationship between PNI and NLR ( $r = -0.475$ ,  $p < 0.001$ ). That is consistent with another retrospective study among 83 hepatocellular carcinoma patients where inverse correlation was demonstrated between PNI and NLR ( $r = -0.2600$ ,  $p = 0.0176$ ) [17]. Similarly, PNI values showed significantly inverse correlation with the NLR values ( $r = 0.4974$ ,  $p < 0.0001$ ) in previous reports [16]. Accordingly, the study confirmed that high PNI and low NLR are associated with worse hospital outcomes including mortality as demonstrated in other studies [16, 17].

The study did not showed a significant relationship between PNI and specific diseases or geriatric syndromes. Also, CCI was not significantly related to PNI. It is against data from a previous study where higher CCI and malignancy were significantly associated with lower PNI [18].

The study assessed the association between PNI and vital signs at admission including respiratory rate, heart rate, mean blood pressure (MBP), body temperature and PFR. Our analysis showed that MBP was the only significant variable as demonstrated in another study [18]. Moreover higher SAPS II scores were associated with lower PNI as supported by another study where higher PNI quartiles had lower acute disease severity scores at admission [18].

Also, the study showed that both age and sex were not related to PNI. It contradicted another study included 1,673 heart failure patients showed patients in the higher PNI group were younger in age. However the same mentioned study showed that sex was not related to PNI similar to our results [19].

Regarding hematological parameters influencing PNI values Hemoglobin and hematocrit were significantly associated with PNI with an OR of 0.668 ( $p < 0.001$ ) and 0.892 ( $p < 0.001$ ), respectively. Also, RDW had an OR of 1.310 ( $p = 0.006$ ) with PNI. These data is consistent with a previous study, which included 1,608 patients with pneumonia where patients with higher PNI had lower levels of hemoglobin, hematocrit and RDW at admission [18].

Regarding biochemical parameters; low PNI was associated with lower serum total proteins and albumin with an OR of 0.119 ( $p < 0.001$ ) and 0.002 ( $p < 0.001$ ), respectively

Also, lower serum potassium and magnesium levels were significantly related to low PNI. These data are supported by previous studies; however analyzing association between PNI and serum electrolytes is unique to our study [20].

Upon multivariate regression analysis, serum albumin and hematocrit were independent predictors of PNI among participants. These data are consistent with findings from a previous prospective study including ovarian cancer patients where PNI values post chemotherapy were independently related to body mass index, prealbumin, albumin, absolute lymphocyte count, and hemoglobin levels at admission [20].

Limitations in the study include its relatively small number of participants from a single geriatric acute care facility in Egypt. It impairs the general applicability of results. However,

the study is the first to document specified cut-off values of both PNI and NLR for predicting in-hospital mortality among critically ill older population. Also, the study highlights the potential benefits of PNI as an easily obtainable IN biomarker and tries to fulfill its related gap of knowledge in acute geriatric care sittings.

## CONCLUSION

Poor IN status is highly prevalent among hospitalized geriatric populations. PNI is a pertinent biomarker of IN status. Predictors of PNI include serum albumin and hematocrit values. Both PNI and NLR are associated with in-hospital mortality at cut-offs  $< 35.475$  and  $> 6.5$ , respectively. PNI has a significant inverse correlation with other IN biomarkers including NLR, SII, and PLR.

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**Ethical statement:** The authors stated that the study was approved by the Research Ethics Committee at Ain Shams University on 17 August 2024 with approval number FMASU R 197/2024. Written informed consents were obtained from the participants.

**Declaration of interest:** No conflict of interest is declared by the authors.

**Data sharing statement:** Data supporting the findings and conclusions are available upon request from the corresponding author.

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