Research Article

Elevated Plasma Neutrophil Gelatinase-Associated Lipocalin Level as a Risk Factor for Anemia in Patients with Systemic Inflammation

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Studies on neutrophil gelatinase-associated lipocalin (NGAL) as an iron-regulatory protein are limited. This study investigated the relationships between plasma NGAL levels and indices of anemia in 187 patients with systemic inflammation. Plasma NGAL levels were significantly higher in patients with anemia versus in patients without anemia (185 ng/mL versus 98 ng/mL; $P < 0.001$). Serum iron levels were lower in patients with NGAL > 156 ng/mL than in those with NGAL ≤ 156 ng/mL (27.4 ± 25.3 μg/dL versus 58.1 ± 43.5 μg/dL; $P < 0.001$). In a receiver operating characteristic curve, the diagnostic ability of NGAL to identify anemia was superior to that of high-sensitivity C-reactive protein [0.712 (95% CI, 0.618–0.787) versus 0.649 (95% CI, 0.573–0.744); $P < 0.01$]. In a multivariate logistic regression analysis, the elevated NGAL level was significantly associated with the presence of anemia after adjusting for potential confounders [odds ratio, 1.30 (95% CI, 1.07–2.58); $P = 0.010$]. In conclusion, enhanced NGAL production may contribute to the development of anemia in patients with systemic inflammation.

1. Introduction

Neutrophil gelatinase-associated lipocalin (NGAL) is a glycoprotein belonging to a lipocalin superfamily, which is normally expressed in various human tissues, such as in kidneys, the liver, bone marrow, lungs, and adipose tissues [1, 2]. Lipocalins generally act as transporters with several different functions, including functions within immune response, cell growth, iron transportation, and synthesis of prostaglandins [3].

Serum creatinine concentration is influenced by the subject's age, sex, and muscle mass. Furthermore, serum creatinine levels may not increase until nearly 50% loss of kidney function [4, 5]. In contrast to serum creatinine, NGAL is specifically induced in damaged nephrons and is then released into blood and urine where it can be readily measured [6]. Because NGAL is upregulated shortly after damage in renal tubular cells, recent interests in NGAL have centered on its role as an early biomarker of acute kidney injury and as a predictor of the progression of chronic kidney disease [7].

Although NGAL has been known as a prominent marker of renal injury, NGAL was initially identified as a bacteriostatic agent secreted from activated human neutrophils [8]. NGAL is capable of binding with bacterial ferric siderophores that are small iron-carrying molecules [9]. The potency of NGAL as a bacteriostatic agent is due to the sequestration of iron, thereby depriving iron from bacteria and leading to a failure of growth [10, 11]. In systemic inflammation states, disturbed iron utilization has been described as a common cause of anemia [12, 13].

Previous studies for NGAL have largely focused on its competence to predict worsening kidney function. There have been few studies which have closely examined the role of

NGAL as an iron-regulatory glycoprotein in systemic inflammation. In the present study, we investigated whether elevated plasma NGAL levels may serve as a potential risk factor for the presence of anemia in patients with inflammation, particularly in conjunction with body iron status and severity of inflammation.

2. Materials and Methods

2.1. Study Population. A total of 187 patients under clinical investigation for systemic inflammation were studied by measuring NGAL, hematologic parameters, and high-sensitivity C-reactive protein (hsCRP). Subjects' ages ranged from 23 to 81 years (median age, 59 years) and 91 patients were males (48.7%). Their medical records were reviewed for clinical and demographic data. As a control group, age-matched healthy individuals ($n = 35$), who had no history of recent infection or impaired renal function, were enrolled.

The patients were admitted to the hospital via emergency room or outpatient departments and suffered from the following diseases: upper respiratory tract infection ($n = 45$), pneumonia ($n = 38$), urinary tract infection ($n = 27$), acute hepatitis ($n = 20$), acute pyelonephritis ($n = 17$), acute cholecystitis ($n = 15$), acute pancreatitis ($n = 10$), cellulitis ($n = 9$), sinusitis ($n = 4$), and acute otitis media ($n = 2$). Blood sample was obtained from patients at admission before antibiotics treatment.

Patients with renal dysfunction ($n = 19$), cardiovascular diseases ($n = 5$), and stroke ($n = 3$) were excluded in this study because these conditions may have influenced plasma NGAL levels. Subjects who had incomplete data for physical examinations, laboratory tests, and anthropometric measures were also excluded from the analysis ($n = 7$). This study was approved by the Institutional Review Board of Inha University Hospital.

2.2. Measurement of Parameters. Samples for NGAL analysis were collected in EDTA-anticoagulated tubes, processed, and immediately frozen in aliquots at −80°C until analyzed. Plasma NGAL concentrations were measured by a fluorescence immunoassay using the Triage NGAL assay (Alere, Inc., San Diego, CA, USA), which could analyze plasma NGAL with a measurable range from 15 ng/mL to 1300 ng/mL. The intra-assay CVs ($n = 20$) for three samples (mean NGAL, 72–530 ng/mL) were 4.1–6.3%; the interassay CVs calculated from duplicate results in 10 subsequent assays were 4.3–6.8%. A provisional cutoff point was determined (156 ng/mL) using a receiver operating characteristic (ROC) curve analysis, which was based on the optimal cutoff value showing the maximal sensitivity and specificity to identify anemia in patients with systemic inflammation.

Serum hsCRP levels were measured by the particle-enhanced immunonephelometry assay (Dade Behring, Inc., Deerfield, IL, USA). Serum concentrations of serum creatinine and iron parameters were analyzed using a chemical analyzer (Hitachi 7600; Hitachi, Tokyo, Japan). Assays for cardiac biomarkers, including creatine kinase-MB (CK-MB) and troponin-I, were performed on a Cobas 411 immunoassay analyzer (Roche Diagnostics GmbH, Mannheim, Germany).

Erythrocyte sedimentation rate (ESR) was determined by the Westergren sedimentation technique using StaRRsed Auto-Compact (Mechatronics Manufacturing BV, Zwaag, Netherlands). The corrected ESR (cESR) was calculated, based on a normal hematocrit of 45%, from the following formula: cESR (mm/h) = (subject's hematocrit/45) × ESR (mm/h).

Complete blood cell counts and red cell indices were measured with an automated analyzer (ADVIA 120; Siemens, Forchheim, Germany) using EDTA-anticoagulated blood. Anemia was defined as hemoglobin <13.0 g/dL for men and <12.0 g/dL for women [14]. The eGFR was calculated using the Modification of Diet in Renal Disease (MDRD) formula: eGFR = $186 \times$ [serum creatinine (mg/dL)]$^{-1.154} \times$ [age (years)]$^{-0.203}$ [15]. An impaired renal function was defined as an eGFR level < 60 ml/min/1.73 m^2 [16].

The subject populations were classified into two groups: elevated NGAL group (>156 ng/mL; $n = 62$) and nonelevated NGAL group (≤156 ng/mL; $n = 125$). Patients were further stratified into two groups according to intensity of inflammation: active inflammation (inflammation index > 1.0; $n = 145$) and nonactive inflammation (inflammation index ≤ 1.0; $n = 42$). This categorization was based on the scoring system of an inflammation index using hsCRP and cESR levels, as described previously [17].

2.3. Statistical Analysis. Continuous variables were presented as mean ± standard deviation if normally distributed and as median (interquartile range) if not normally distributed. Categorical variables were described using frequencies and proportions. The normality of the data was confirmed by the Shapiro-Wilk test. A Mann–Whitney U test and a Student's t-test were used to analyze the data between the two groups. The association between the presence of anemia and plasma NGAL concentrations was assessed by a multivariate logistic regression analysis after adjusting for age, gender, body mass index (BMI), eGFR, troponin-I, and hsCRP. The odds ratio for the risk of anemia was determined, comparing patients with elevated NGAL levels (>156 ng/mL) to those with nonelevated NGAL levels (≤156 ng/mL). A multivariate linear regression analysis was performed to test the association between NGAL and the values of hemoglobin and serum iron levels following adjustment for potential confounders. The data were analyzed using SPSS software (version 19.0 for Windows, SPSS, Inc., Chicago, Illinois, USA). For all analyses, P values < 0.05 were considered statistically significant.

3. Results

3.1. Baseline Characteristics of the Study Population. Of the 187 patient population, 76 (40.6%) had anemia. An increased NGAL level > 156 ng/mL was observed in 33.1% of the patient population, which was significantly above the value of healthy individuals (0.0%; $P < 0.001$). Serum iron concentrations were significantly lower in the patient group than in the control subjects; however, there were no significant differences in anthropometric parameters, eGFR, and serum creatinine levels between the two groups (Table 1).

TABLE 1: Baseline characteristics of study population included in the study.

	Patients ($n = 187$)	Healthy controls ($n = 35$)	P value
Anthropometric parameters			
Age (years)	59 (28–74)	57 (29–72)	0.687
Gender (male, %)	91 (48.7)	17 (48.5)	0.953
BMI (kg/m^2)	22.1 ± 3.6	23.0 ± 2.7	0.175
NGAL			
Plasma NGAL level (ng/mL)	165 (76–320)	68 (53–89)	<0.001
NGAL > 156 ng/mL (n, %)	62 (33.1)	0 (0.0)	<0.001
Hematologic parameters			
Hemoglobin (g/dL)	12.1 ± 2.5	14.9 ± 2.0	<0.001
Anemia (n, %)	76 (40.6)	0 (0.0)	<0.001
Erythrocytes (×10^{12}/L)	3.99 ± 0.79	4.74 ± 0.62	0.002
Red cell distribution width (%)	14.0 ± 2.4	13.1 ± 1.2	0.003
Iron parameters			
Serum iron (μg/dL)	43.7 ± 39.1	72.6 ± 35.3	<0.001
Transferrin saturation (%)	25.1 ± 24.3	32.7 ± 19.5	0.065
Serum ferritin (ng/mL)	282.7 (102.5–560.2)	41.0 (25.1–374.2)	<0.001
Renal parameters			
eGRF (mL/min/1.73 m^2)	85.7 ± 16.3	89.4 ± 9.5	0.512
Serum creatinine (mg/dL)	0.88 ± 0.15	0.83 ± 0.12	0.583
Inflammation indices			
hsCRP (mg/dL)	3.60 (0.98–7.55)	0.09 (0.05–0.18)	<0.001
cESR (mm/h)	34.9 ± 29.8	4.2 ± 5.7	<0.001
Cardiac markers			
Troponin-I (ng/mL)	0.1 (0.1–0.3)	0.1 (0.1–0.3)	0.652
CK-MB (ng/mL)	2.6 (1.3–5.8)	2.4 (1.1–4.1)	0.407

Data are expressed as median (interquartile range), mean ± SD, or frequency (%).
BMI, body mass index; NGAL, neutrophil gelatinase associated lipocalin; eGFR, estimated glomerular filtration rate; hsCRP, high-sensitivity C-reactive protein; cESR, corrected erythrocyte sedimentation rate; CK-MB, creatine kinase-MB.

3.2. Plasma NGAL Levels and Hematologic Parameters. Anemic patients had a higher NGAL level than did the nonanemic subjects [185 ng/mL (interquartile range, 85–269 ng/mL) versus 98 ng/mL (interquartile range, 65–162 ng/mL); $P < 0.001$] (Figure 1). As shown in Table 2, mean values of hemoglobin and erythrocyte counts in the elevated NGAL group were 10.9 ± 2.3 g/dL and 3.71 ± 0.69 (×10^{12})/L, which were significantly lower than those in the nonelevated NGAL group [12.9 ± 2.5 g/dL and 4.16 ± 0.83 (×10^{12})/L, respectively; $P < 0.001$]. The prevalence of anemia was 2.4 times higher in patients with NGAL > 156 ng/mL than in those with NGAL ≤ 156 ng/mL. The elevated NGAL group exhibited a low serum iron level compared to the nonelevated NGAL group (27.4 ± 25.3 μg/dL versus 58.1 ± 43.5 μg/dL; $P < 0.001$) (Table 2).

3.3. Anemia in Active and Nonactive Inflammation. Mean hemoglobin level was significantly lower in active inflammation than nonactive inflammation (12.3 ± 2.2 g/dL versus 13.2 ± 2.4 g/dL, $P < 0.001$). Of the 145 patients with active inflammation, 65 (44.8%) had an anemia, which was higher than that of nonactive inflammation (26.2%, $P < 0.001$). Patients with active inflammation exhibited a significantly decreased
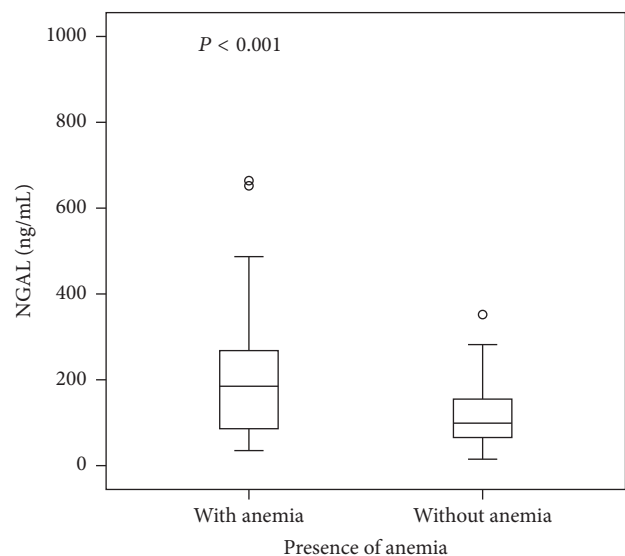

FIGURE 1: Plasma NGAL concentrations according to presence of anemia in patients with inflammation ($n = 187$). Plasma NGAL levels are significantly higher in patients with anemia than in those without anemia [185 ng/mL (interquartile range, 85–269 ng/mL) versus 98 ng/mL (interquartile range, 65–162 ng/mL); $P < 0.001$].

TABLE 2: Plasma NGAL levels and hematologic parameters in patients with inflammation.

	Patients with inflammation		
	NGAL > 156 ng/mL ($n = 62$)	NGAL ≤ 156 ng/mL ($n = 125$)	P value
NGAL			
Plasma NGAL level (ng/mL)	269 (197–472)	84 (65–131)	<0.001
Hematologic parameters			
Hemoglobin (g/dL)	10.9 ± 2.3	12.9 ± 2.5	<0.001
Anemia (*n*, %)	42 (67.7)	34 (27.2)	<0.001
Erythrocytes ($\times 10^{12}$/L)	3.71 ± 0.69	4.16 ± 0.83	<0.001
Red cell distribution width (%)	14.5 ± 2.5	13.6 ± 2.1	0.017
Iron parameters			
Serum iron (μg/dL)	27.4 ± 25.3	58.1 ± 43.5	<0.001
Transferrin saturation (%)	22.1 ± 18.6	29.0 ± 27.8	0.482
Serum ferritin (ng/mL)	342.9 (163.7–631.8)	196.4 (125.8–512.3)	0.376
Inflammation indices			
hsCRP (mg/dL)	6.85 (3.74–12.06)	2.18 (0.86–4.15)	<0.001
cESR (mm/h)	47.5 ± 20.7	16.8 ± 13.2	<0.001

Data are expressed as median (interquartile range), mean ± SD, or frequency (%).
NGAL, neutrophil gelatinase associated lipocalin; hsCRP, high-sensitivity C-reactive protein; cESR, corrected erythrocyte sedimentation rate.

TABLE 3: Indices of anemia in patients with active and nonactive inflammation.

	Patients with inflammation		
	Active inflammation (inflammation index > 1.0; $n = 145$)	Nonactive inflammation (inflammation index ≤ 1.0; $n = 42$)	P value
NGAL (ng/mL)	102 (68–197)	68 (55–83)	<0.001
Inflammation indices			
hsCRP (mg/dL)	1.65 (0.15–5.90)	0.11 (0.05–0.19)	<0.001
cESR (mm/h)	22.7 ± 16.7	5.3 ± 4.7	<0.001
Renal parameters			
eGFR (mL/min/1.73 m^2)	85.3 ± 23.5	92.5 ± 14.3	<0.001
Serum creatinine (mg/dL)	0.90 ± 0.16	0.86 ± 0.15	0.001
Hematologic parameters			
Hemoglobin (g/dL)	12.3 ± 2.2	13.2 ± 2.4	<0.001
Anemia (*n*, %)	65 (44.8)	11 (26.2)	<0.001
Erythrocytes ($\times 10^{12}$/L)	4.04 ± 0.69	4.31 ± 0.71	<0.001
Red cell distribution width (%)	13.7 ± 2.0	13.2 ± 1.9	0.018

Data are expressed as median (interquartile range), mean ± SD, or frequency (%).
NGAL, neutrophil gelatinase associated lipocalin; hsCRP, high-sensitivity C-reactive protein; cESR, corrected erythrocyte sedimentation rate; eGFR, estimated glomerular filtration rate.

eGFR compared to those with nonactive inflammation (85.3 ± 23.5 versus 92.5 ± 14.3 mL/min/1.73 m^2, $P < 0.001$) (Table 3).

3.4. Univariate and Multivariate Regression Analysis. Plasma NGAL concentrations were inversely correlated to hemoglobin levels and erythrocyte counts (standard $\beta = -0.253$ and -0.241, respectively; $P < 0.05$), after adjusting for age, gender, BMI, eGFR, troponin-I, and hsCRP (Table 4). An example of scatter plots showing the correlations between plasma, the NGAL levels, and the values of hemoglobin is illustrated in Figure 2.

3.5. NGAL as a Risk Factor for Anemia. In a multivariate logistic regression analysis, elevated plasma NGAL concentrations (>156 ng/mL) were significantly associated with

a presence of anemia following adjustment for potential confounders, such as age, gender, BMI, eGFR, troponin-I, and hsCRP [odds ratio, 1.30 (95% CI, 1.07–2.58); $P = 0.010$] (Table 5).

3.6. ROC Curve Analysis. The diagnostic values of NGAL, hsCRP, and cESR to identify anemia in patients with systemic inflammation were investigated using an ROC curve analysis (Figure 3). The diagnostic accuracies of NGAL (area under the curve [AUC], 0.712; 95% confidence interval [CI], 0.618–0.787) and cESR (AUC, 0.751; 95% CI, 0.674–0.836) for identifying anemia were significantly higher ($P < 0.01$) than those for hsCRP (AUC, 0.649; 95% CI, 0.573–0.744). The AUC for NGAL did not significantly differ from that for cESR ($P = 0.072$).

TABLE 4: Univariate and multivariate linear regression analysis between plasma NGAL levels and indices of anemia in 187 patients with inflammation.

	Univariate		Multivariate*	
	Standard β	P value	Standard β	P value
Hematologic parameters				
Hemoglobin (g/dL)	−0.381	<0.001	−0.253	0.021
Erythrocytes (×10^{12}/L)	−0.359	<0.001	−0.241	0.036
Red cell distribution width (%)	0.247	0.031	0.186	0.195
Iron parameters				
Serum iron (μg/dL)	−0.302	<0.001	−0.146	0.378
Transferrin saturation (%)	−0.262	0.014	−0.174	0.230
Serum ferritin (ng/mL)	−0.152	0.269	−0.073	0.671

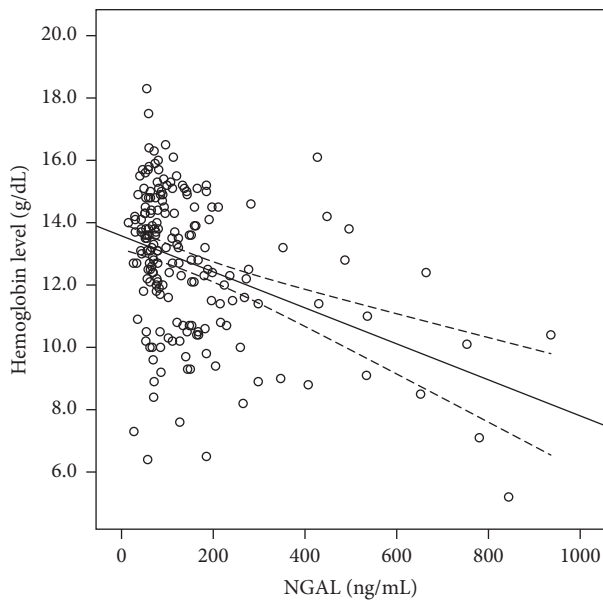*Adjusted for age, gender, BMI, eGFR, troponin-I, and hsCRP.

FIGURE 2: An example of scatter plots showing the correlation between plasma NGAL levels and the values of hemoglobin in 187 patients with inflammation. Plasma NGAL levels are inversely correlated to hemoglobin levels ($y = -0.005x + 13.57$, $r^2 = 0.145$; $P < 0.001$).

TABLE 5: A multivariate logistic regression analysis for the presence of anemia in 187 patients with inflammation.

NGAL > 156 ng/mL as a categorical variable	Presence of anemia	
	Odds ratio (95% confidence interval)	P value
Unadjusted	3.14 (1.29–6.05)	<0.001
Adjusted for age, gender, and BMI	2.37 (1.24–5.12)	<0.001
Adjusted for age, gender, BMI, and eGFR	2.15 (1.13–7.08)	<0.001
Adjusted for age, gender, BMI, and troponin-I	2.28 (1.20–7.94)	<0.001
Adjusted for age, gender, BMI, eGFR, and troponin-I	1.99 (1.05–6.26)	<0.001
Adjusted for age, gender, BMI, eGFR, troponin-I, and cESR	1.27 (1.12–3.24)	0.025
Adjusted for age, gender, BMI, eGFR, troponin-I, and hsCRP	1.30 (1.07–2.58)	0.010

NGAL, neutrophil gelatinase associated lipocalin; BMI, body mass index; eGFR, estimated glomerular filtration rate.

The optimal cutoff value for NGAL was 156 ng/mL, at which the sensitivity and specificity were 58.3% and 81.4%, respectively. The optimal diagnostic cutoff values of cESR and hsCRP were 25 mm/h and 2.05 mg/dL. The sensitivity and specificity of cESR were 79.5% and 73.2%, and those of hsCRP were 63.2% and 57.6% at the corresponding cutoffs.

4. Discussion

In this study, the relationship between plasma NGAL levels and the indices of anemia was investigated. The plasma NGAL level was significantly elevated in patients with anemia versus in those without anemia, demonstrating inverse correlations with hemoglobin levels. Anemia was observed 2.4 times as often in the elevated NGAL group as in the nonelevated NGAL group. The results suggest that augmented NGAL levels may contribute to the development of anemia in patients with systemic inflammation.

NGAL is known to be a key factor in the regulation of erythrocyte growth due to its ability to inhibit the maturation of bone marrow erythroid precursors [18]. In an experimental model, NGAL was found to induce inhibition of erythropoiesis through induction of apoptosis [19, 20]. However, a wide heterogeneity of the results was reported concerning the association between plasma NGAL levels and indices of anemia in various clinical conditions.

Shrestha et al. [21] demonstrated that plasma NGAL concentrations were closely linked to erythrocytes, hemoglobin,
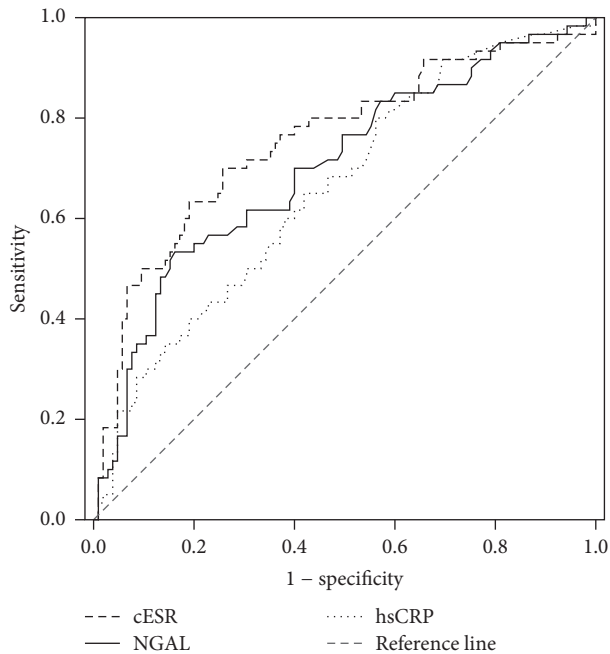
FIGURE 3: ROC curves showing the diagnostic abilities of NGAL, hsCRP, and cESR to identify anemia in patients with systemic inflammation ($n = 187$). Area under the curve was calculated for cESR (AUC, 0.751; 95% CI, 0.674–0.836; sensitivity 79.5% and specificity 73.2% at the optimal cutoff of 25 mm/h), NGAL (AUC, 0.712; 95% CI, 0.618–0.787; sensitivity 58.3% and specificity 81.4% at the optimal cutoff of 156 ng/mL), and hsCRP (AUC, 0.649; 95% CI, 0.573–0.744; sensitivity 63.2% and specificity 57.6% at the optimal cutoff of 2.05 mg/dL).

and red cell distribution width in relation to inflammation in patients with chronic systolic heart failure. In contrast, Bolignano et al. [22] reported that there were no significant correlations between NGAL and the levels of hemoglobin, hematocrit, and erythrocytes in patients on hemodialysis. In our study, a multivariate regression analysis revealed that plasma NGAL concentrations were inversely associated with hemoglobin levels after adjusting for age, gender, BMI, eGFR, troponin-I, and hsCRP. These inconsistencies may reflect the differences of subject populations, severity of diseases, and the presence of renal dysfunction in the patient populations among the studies. Our observations suggest that elevated NGAL concentrations may account for decreased hemoglobin levels in patients with systemic inflammation.

Systemic inflammation is frequently accompanied by kidney damage owing to its pathogenesis of hypoperfusion, microvascular thrombosis, and infiltration of immune cells [23]. Hence, it is hard to interpret the significance of raised NGAL levels in patients with both inflammation and renal dysfunction. In our study, to minimize the influence of kidney function on plasma NGAL concentration, patients with preserved renal function were enrolled. As a result, patients exhibited no statistically significant differences with respect to kidney function indices compared to healthy individuals. In the current study, 33.1% of patients exhibited

an elevated NGAL level (>156 ng/mL), which is in contrast with the results (42.1%) of previous studies [17]. The strict restriction for the study population is a likely explanation as to why our patients had a low positive rate for plasma NGAL levels.

To test a potential role of plasma NGAL level as a risk factor for anemia, a multivariate logistic regression analysis was conducted. Based on the odds ratio, a high plasma NGAL level (>156 ng/mL) resulted in a 1.3 times' increase in the risk of anemia compared to a low plasma NGAL level (≤156 ng/mL). The association between NGAL levels and anemia was still significant following the adjustment for potential confounders. It appears that plasma NGAL levels serve as a risk factor for the development of anemia. Our data are in general agreement with the previous results of Shrestha et al. [21], which disclosed that plasma NGAL levels were associated with the presence of anemia in patients with chronic heart failure.

NGAL has been considered to play a physiological role during increased iron utilization and mobilization from stores [24]. A recent investigation showed that NGAL levels were markedly increased in anemic conditions induced by iron deprivation or a phlebotomy [25]. However, conflicting data have been reported regarding the relationship of iron parameters and plasma NGAL levels in a variety of pathologic conditions.

Yazdani et al. [26] reported that serum NGAL levels were negatively correlated with serum iron, transferrin saturation, and serum ferritin levels in children on chronic hemodialysis. Conversely, Bolignano et al. [22] demonstrated that serum NGAL levels had a positive correlation to transferrin saturation and a negative correlation to serum transferrin levels in hemodialysis patients. Interestingly, the same investigator asserted that the lowered NGAL levels were significantly increased after the correction of iron deficiency with iron supplements [22].

In our study, the elevated NGAL group exhibited significantly low levels in erythrocyte counts and serum iron compared to the nonelevated NGAL group. Based on these findings, it can be speculated that anemia, which was observed in the elevated NGAL group, is presumably due to inhibition of erythrocyte production in conjunction with disturbed iron utilization.

To assess the diagnostic values of NGAL, hsCRP, and cESR to identify anemia in systemic inflammation, an ROC curve analysis was performed. The AUC of NGAL was similar to that of cESR but was significantly larger than that of hsCRP. These results suggest that the diagnostic efficacy of NGAL is superior to that of hsCRP and is comparable to that of cESR for identifying anemia in systemic inflammation.

There are several limitations in the current study. We did not measure plasma NGAL levels in serial samples to assess the changes in NGAL in association with the progression of anemia. In this study, we did not investigate the duration of infection and the type of inflammation according to the kinds of bacteria. The cross-sectional study of our investigation limited the demonstration of a cause-and-effect relationship between NGAL and anemia. Additionally, we stress that plasma NGAL level might be influenced by possibly missing

information on renal or other organ injuries. Despite these limitations, our data may provide additional benefits for monitoring patients with anemia in myriad inflammation states.

5. Conclusions

This study demonstrates that an increased plasma NGAL level has a significant implication in regard to blood hemoglobin levels. Anemia was more frequently observed in the elevated NGAL group than in the nonelevated NGAL group, suggesting that enhanced NGAL production plays a role as a weak but significant risk factor for anemia in patients with systemic inflammation.

Competing Interests

The authors declare that they have no conflict of interests regarding the publication of this paper.

Acknowledgments

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