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ORIGINAL ARTICLE

Pre-operative Neutrophil-Lymphocyte and Platelet-Lymphocyte Ratios as Predictors of Morbidity and Mortality in Diabetic Foot Infection Amputation Patients

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ABSTRACT

Background. Diabetic foot infection is a complication of uncontrolled diabetes. Some cases require amputation to avoid the spread of infection; however, this can also lead to poor outcomes. Inflammatory markers, such as neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR), have been explored as predictors of outcomes following amputation; however, only a few published studies are available.

Objective. The study aimed to determine the diagnostic value of pre-operative neutrophil-lymphocyte and platelet-lymphocyte ratios in predicting in-hospital morbidity and mortality among diabetic foot infection patients who underwent amputation in a tertiary government hospital.

Methodology. This retrospective cohort study included a total of 535 diabetic foot ulcer patients who underwent amputation at a tertiary government hospital. Data was collected via medical chart review. Complete blood count (CBC) parameters closest to the time of amputation were obtained to calculate the neutrophil-lymphocyte and platelet-lymphocyte ratios.

Results. Only 10.28% of patients experienced in-hospital morbidity and/or mortality. Based on Youden's index, the optimal cutoff points of neutrophil-lymphocyte and platelet-lymphocyte ratios were 7.27 and 32.40, respectively. Both markers showed 98% sensitivity in predicting the outcome. Specificity was 99% for the neutrophil-lymphocyte ratio and 93% for the platelet-lymphocyte ratio. Accuracy parameters remained high when morbidity and mortality were analyzed separately.

Conclusion. Neutrophil-lymphocyte and platelet-lymphocyte ratios accurately predict in-hospital morbidity and mortality among diabetic foot infection patients who underwent amputation. The low cost and wide availability of a CBC make NLR and PLR valuable options in low-resource settings. Future studies should explore these markers' utility in predicting long-term outcomes after amputation.

Keywords. neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, diabetic foot infection, morbidity, mortality, re-operation

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease that remains a major public health concern worldwide. According to the World Health Organization (WHO), about 422 million people worldwide have diabetes.[1] In the Philippines, there were over 3,993,000 cases of diabetes in 2017, with a 6.3% prevalence of diabetes among adults.[2] The estimated prevalence of diabetes in adults aged 18 to 99 years was at approximately 9.3% and is predicted to rise to 10.9% by 2045.[3]

Foot infections are common in patients with diabetes. Lifetime incidence may be as high as 25% in all individuals with the diagnosis. They are more common in elderly patients with

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comorbidities. Males and females are affected equally.[4,5] In a tertiary government hospital, an average of 140 diabetic foot patients are admitted every year, of whom 50% undergo amputation.[6] One common long-term complication of poorly controlled diabetes is the development of diabetic foot ulcers secondary to neuropathy or angiopathy.[7,8] Foot ulcers are the leading cause of lower leg amputation among diabetic patients.[9] Furthermore, lower extremity amputation is one of the most feared outcomes as it is associated with a significantly higher 5-year mortality rate—2.5 times greater than that of a diabetic individual without foot ulcers.[5,10] Financial burden includes both direct and indirect costs, such as loss of earnings and burden on caregivers. Most amputations are progressive, meaning that the smallest possible amount of tissue is removed sequentially. Diabetic foot infection contributes to the global burden of disability and reduces patients' quality of life, making it a considerable public health problem.[10]

Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) are useful novel biomarkers of systemic inflammation easily obtained from routine blood examinations. They are highly sensitive measures of inflammation in the fields of oncology, cardiology, nephrology, and autoimmune rheumatic diseases.[11,12] Recently, several studies have also reported their significance in predicting mortality in diabetic complications.[13] To date, local studies on NLR and PLR among diabetic foot infection patients are limited. Therefore, this study aims to be one of the first local studies to determine the diagnostic value of pre-operative NLR and PLR in predicting morbidity and mortality among diabetic foot infection patients who underwent amputation in a tertiary government hospital.

Many inflammatory markers have been linked to DM complications such as diabetic nephropathy. These include interleukin (IL)1, IL6, IL8, transforming growth factor beta 1 (TGF-β1), and tumor necrosis factor-alpha (TNF α), which are not routinely performed due to their complexity. As a result, NLR and PLR have emerged as novel surrogate markers and predictors of morbidity and/or mortality among diabetic patients with micro and macrovascular complications. Hence, this study aimed to determine whether NLR and PLR can predict the clinical outcomes of patients with diabetic foot ulcers who underwent amputation.

METHODOLOGY

This study employed an analytic retrospective cohort study design. The participants were diabetic foot ulcer patients who underwent amputation at Jose R. Reyes Memorial Medical Center from January 2015 to January 2022. A simple random sampling design was used to select study participants. Open Epi Random Number Generator was used to generate random numbers.

Data were collected via medical chart review from January 2022 to January 2023.

Inclusion criteria

- Age >18 years
- Pay and service patients
- Diagnosed with Type 2 Diabetes Mellitus
- Presented with diabetic foot ulcer on hospital admission and classified as Wagner 3 to 5
- Underwent lower extremity amputation (toe disarticulation, Ray amputation, Lisfranc amputation, Chopart amputation, Syme amputation, below-the-knee amputation, knee disarticulation, above-the-knee amputation, and hip disarticulation)

Exclusion criteria

- Patients discharged against medical advice
- Outpatient department patients
- Patients with end-stage renal disease, severe pulmonary and liver disease, cerebrovascular disease, and cancer

Power Analysis and Sample Size (PASS) 15 software was used to calculate the minimum sample size required. Parameters were derived from a previously published study.[13] The sample size was computed separately for NLR and PLR:

	Parameters	Sample size
NLR	OR = 5.43 Power = 80% Alpha = 0.05	233
PLR	OR = 3.08 Power = 80% Alpha = 0.05	533

The largest computed sample size, equal to 533, was used as the minimum sample size requirement for this study to achieve 80% statistical power.

Before study implementation, the researcher sought clearance from the hospital's Technical Review Committee and Institutional Ethics Review Board and permission from the Medical Records section.

Data from medical charts were recorded in a Data Abstraction Form from January 2022 to January 2023. The following variables were collected: demographic and clinical profiles, disease duration, comorbidities, smoking and alcohol status, laboratory results such as pre-operative complete blood count, FBS, HbA1c, ulcer classification, level of amputation, estimated intraoperative blood loss, and incidence of morbidity and mortality.

Data were encoded in MS Excel. Stata MP version 17 software was used for data processing and analysis. Continuous data were presented as interquartile range/IQR due to non-normal data distribution based on Shapiro Wilk's test and were analyzed using the Mann-Whitney U test. Categorical data were presented as frequency and percentage and were analyzed using the Chi-square test and Fisher's exact test.

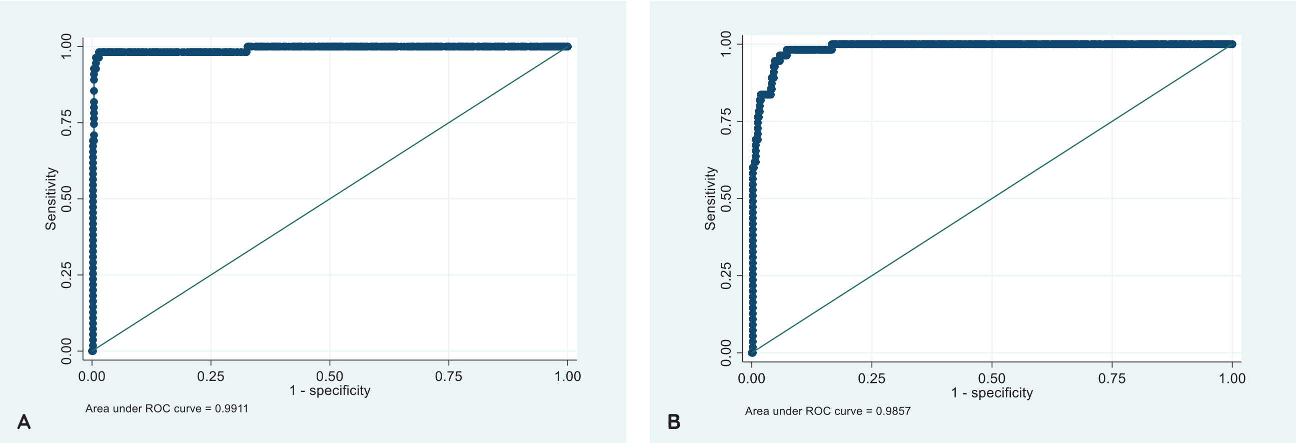

Figure 1. ROC curve in predicting in-hospital morbidity/mortality: **(A)** NLR and **(B)** PLR.

Optimal cutoff points of NLR and PLR were determined based on Youden's index. Discriminative ability was based on the Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC) curve and interpreted as follows: 0.50 (no discrimination), 0.51–0.69 (poor), 0.70–0.80 (acceptable), 0.81–0.90 (excellent), and >0.90 (outstanding).[14] Two by two (2 x 2) tables were constructed, and the following diagnostic value parameters were calculated: accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratios (LR).

The association of NLR and PLR (based on cutoff points) with morbidity and/or mortality was determined using logistic regression analysis. Simple logistic regression was used to identify potential confounding variables, with a cutoff of $p < 0.20$.[14] Potential confounders were entered into the full model and multiple logistic regression was performed. Model building was based on the change-in-estimate (CIE) criterion of 10%. *P* values ≤0.05 were considered statistically significant.

RESULTS

A total of 535 diabetic foot infection patients who underwent amputation were included in the study, of whom 55 patients developed the outcome of interest (i.e., in-hospital morbidity and/or mortality). The incidence was 10.28% (95% CI: 7.97–13.16%). When the outcomes were analyzed separately, in-hospital morbidity was 6.17% (95% CI: 4.28–8.55%). The specific morbidities were post-surgery infection or wound complication (n = 15, 45%), need for re-amputation (n = 12, 36%), and hospital-acquired pneumonia (n = 6, 18%). Meanwhile, the incidence of in-hospital mortality was 4.67% (95% CI: 3.17–6.83%), and the median time to death was 3 days (IQR: 0–10; range: 0–51 days). Sixteen out of 25 deaths (64%) occurred within seven days post-amputation. Among survivors, the median length of stay from the date of amputation was eight days (IQR: 4–15; Range: 0–136 days). Among those who died, the median time to death from the date of amputation was three days (IQR: 0–10; Range: 0–51 days).

The median age was 57 years old (range: 25–89 years old), and most patients were male. About one-third of the patients had a normal BMI, and the median disease duration was 5 years (range: 1–50 years). The most common comorbidity was hypertension affecting about one-third of the patients. Most patients were non-smokers, had never consumed alcohol, and had low hemoglobin, high FBS, and high HbA1c levels. Most patients were classified as Wagner 4, and more than half underwent minor amputation. The most common specific levels of amputation were ray amputation (37%) and below-knee amputation (39%). Only five patients (1%) underwent bilateral amputation. The median NLR was 4.1 (range: 0.3–40.4) and the median PLR was 20 (range: 3.2–163.9).

A higher proportion of patients with morbidity or mortality were female, had hypertension, had kidney disease, and underwent above-knee amputation. The NLR, PLR, and median intraoperative blood loss were also significantly higher in patients with morbidity and mortality. In addition, the median hemoglobin level was significantly lower for overall outcome, but not when morbidity and mortality were analyzed separately.

The receiver operating characteristic (ROC) curves for both NLR and PLR showed outstanding discriminative ability in predicting in-hospital morbidity and/or mortality (Table 1). Based on Youden's index, the optimal cutoff points for NLR and PLR are presented in Table 2.

The discriminative ability of NLR was outstanding (Table 3). NLR also showed very high accuracy, sensitivity, specificity, and NPV when morbidity and mortality were analyzed separately (Table 4).

Likewise, PLR had outstanding discriminative ability (Table 5). PLR also showed high accuracy, sensitivity, specificity, and NPV when morbidity and mortality were analyzed separately (Table 6).

Subgroup analysis was also performed between patients who underwent major and minor amputations (Table 7).

Table 1. Demographic and clinical profile of diabetic foot infection patients who underwent amputation (n = 535)

	All patients (n = 535), n (%)	In-hospital morbidity/ mortality		*P*-value
		YES (n = 55), n (%)	NO (n = 480), n (%)	
Age (in years), median	57 [IQR: 50–64]	59 [IQR: 51–62]	57 [IQR: 50–64]	0.9555[a]
Sex				
Male	338 (63)	27 (49)	311 (65)	0.022*[b]
Female	197 (37)	28 (51)	169 (35)	
Weight (in kg), median	60 [IQR: 55–65]	60 [IQR: 55–65]	60 [IQR: 55–65.5]	0.5714[a]
Height (in cm), median	160 [IQR: 157–165]	160 [IQR: 154–165]	160 [IQR: 157–166]	0.2241[a]
BMI (in kg/m²), median	23.4 [IQR: 22–25]	23.4 [IQR: 21.4–25.4]	23.4 [IQR: 22–25]	0.9101[a]
Normal	181 (34)	18 (33)	163 (34)	0.822[c]
Underweight	19 (4)	3 (5)	16 (3)	
Overweight	202 (38)	19 (35)	183 (38)	
Pre-obese	109 (20)	12 (22)	97 (20)	
Obese	24 (4)	3 (5)	211 (4)	
Disease duration (in years), median	5 [IQR: 2–10]	5 [IQR: 2–10]	5 [IQR: 2–10]	0.7878[a]
Co-morbidities, %yes				
Hypertension	184 (34)	28 (51)	156 (33)	0.006*[b]
Kidney disease	54 (10)	10 (18)	44 (9)	0.036*[b]
Heart disease	26 (5)	2 (4)	24 (5)	1.000[c]
Vascular disease	35 (7)	7 (13)	28 (6)	0.076[c]
Active skin infections	8 (2)	1 (2)	7 (1)	0.583[c]
Anemia	19 (4)	2 (4)	17 (4)	1.000[c]
Pneumonia	15 (3)	1 (2)	14 (3)	1.000[c]
Pulmonary tuberculosis	10 (2)	1 (2)	9 (2)	1.0000[c]
COVID-19	6 (1)	1 (2)	5 (1)	0.480[c]
Others	10 (2)	2 (4)	8 (2)	0.274[c]
Smoking status				
Non-smoker	348 (65)	37 (67)	311 (65)	0.741[b]
Current smoker	121 (23)	13 (24)	108 (22)	
Past smoker	66 (12)	5 (9)	61 (13)	
Alcohol consumption				
Never consumed alcohol	314 (59)	33 (60)	281 (59)	0.195[b]
Frequent drinker	43 (8)	7 (13)	36 (7)	
Occasional drinker	128 (23)	8 (14)	120 (25)	
Past drinker	50 (9)	7 (13)	43 (9)	
Hemoglobin level (g/dL), median	10.7 [IQR: 9.9–11.6]	10.3 [IQR: 9.5–11]	10.7 [IQR: 10–11.6]	0.0137*[a]
Normal	81 (15)	5 (9)	76 (16)	0.306[c]
Low	442 (83)	50 (91)	392 (82)	
High	9 (2)	0	9 (2)	
FBS level (in mmol/L), median	7.5 [IQR: 5.8–9.7]	8 [IQR: 6.3–10.8]	7.4 [IQR: 5.8–9.5]	0.0897[a]
Normal	132 (25)	10 (18)	122 (25)	0.310[c]
Low	11 (2)	0	11 (2)	
High	392 (73)	45 (82)	347 (72)	
HbA1C level (in %), median	8.6 [IQR: 7–10.9]	9.2 [IQR: 7.2–11.8]	8.5 [IQR: 6.9–10.8]	0.1621[a]
Normal	37 (7)	6 (11)	31 (6)	0.255[c]
High	498 (93)	49 (89)	449 (94)	
Wagner classification				
Wagner 3	160 (30)	10 (18)	150 (31)	0.122[b]
Wagner 4	324 (61)	38 (69)	286 (60)	
Wagner 5	51 (10)	7 (13)	44 (9)	
Level of amputation				
Major	297 (56)	28 (51)	269 (56)	0.468[b]
Minor	238 (44)	27 (49)	211 (44)	

Table 1. Demographic and clinical profile of diabetic foot infection patients who underwent amputation (n = 535) *(continued)*

	All patients (n = 535), n (%)	In-hospital morbidity/ mortality		*P*-value
		YES (n = 55), n (%)	NO (n = 480), n (%)	
Specific level of amputation, % yes				
Toe Disarticulation	92 (17)	10 (18)	82 (17)	0.838[b]
Ray Amputation	197 (37)	17 (31)	180 (38)	0.337[b]
Lisfranc Amputation	1 (1)	0	11 (1)	1.000[c]
Chopart Amputation	1 (1)	0	1 (1)	1.000[c]
Syme Amputation	9 (2)	1 (2)	8 (2)	1.000[c]
Below the knee Amputation	211 (39)	21 (38)	190 (40)	0.840[b]
Knee Disarticulation	0	0	0	-
Above the knee amputation	26 (5)	6 (11)	20 (4)	0.041*[c]
Hip Disarticulation	1 (1)	0	1 (1)	1.000[c]
Laterality				
Unilateral	530 (99)	54 (98)	476 (99)	0.420[c]
Bilateral	5 (1)	1 (2)	4 (1)	
Estimated blood loss intra-op (in ml), median	200 [IQR: 100–300]	250 [IQR: 100–500]	160 [IQR: 100–300]	0.0165*
NLR, median	4.1 [IQR: 2.5–5.8]	9.3 [IQR: 8–13.2]	3.8 [IQR: 2.4–5.2]	<0.00001*[a]
PLR, median	20 [IQR: 13.3–29.1]	44.4 [IQR: 38.1–60.1]	18.6 [IQR: 12.7–25.7]	<0.00001*[a]

[a] Mann Whitney U test was used; [b] Chi square test was used; [c] Fisher's Exact test was used.

Table 2. Optimal cutoff point of NLR and PLR based on Youden's index

	Cut-off point
NLR	>7.27
PLR	>32.40

Table 3. Diagnostic value of NLR in predicting in-hospital morbidity/mortality

	In-hospital morbidity/mortality		Total
	Yes	No	
NLR >7.27	54	7	61
NLR ≤7.27	1	473	474
Total	55	480	535
AUC (95% CI)		0.98 (0.97–1.00)	
Accuracy		98.50%	
Sensitivity		98.18%	
Specificity		98.54%	
Positive predictive value		88.52%	
Negative predictive value		99.79%	
Likelihood ratio +		67	
Likelihood ratio -		0.02	

Table 4. Diagnostic value of NLR in predicting in-hospital morbidity and mortality

	In-hospital mortality	In-hospital morbidity
AUC (95% CI)	0.96 (0.95–0.98)	0.96 (0.92–0.99)
Accuracy	93.27%	94.39%
Sensitivity	100%	96.97%
Specificity	92.94%	94.22%
Positive Predictive Value	40.98%	52.46%
Negative Predictive Value	100%	99.79%
Likelihood Ratio +	14.17	16.79
Likelihood Ratio -	0	0.03

Table 5. Diagnostic value of PLR in predicting in-hospital morbidity/mortality

	In-hospital morbidity/mortality		Total
	Yes	No	
PLR >32.40	54	35	89
PLR ≤32.40	1	445	446
Total	55	480	535
AUC (95% CI)		0.95 (0.93–0.98)	
Accuracy		93.27%	
Sensitivity		98.18%	
Specificity		92.71%	
Positive predictive value		88.52%	
Negative predictive value		99.79%	
Likelihood ratio +		13.46	
Likelihood ratio -		0.02	

Table 6. Diagnostic value of PLR in predicting in-hospital morbidity and mortality

	In-hospital mortality	In-hospital morbidity
AUC (95% CI)	0.94 (0.92–0.95)	0.93 (0.90–0.96)
Accuracy	88.04%	89.16%
Sensitivity	100%	96.97%
Specificity	87.45%	88.65%
Positive Predictive Value	28.09%	35.96%
Negative Predictive Value	100%	99.78%
Likelihood Ratio +	7.97	8.54
Likelihood Ratio -	0	0.03

Table 7. Diagnostic value of NLR and PLR in predicting in-hospital morbidity and mortality: major versus minor amputation[a]

	Major amputation (n = 238)		Minor amputation (n = 297)	
	NLR	PLR	NLR	PLR
AUC (95% CI)	1.00 (0.99–1.00)	0.95 (0.92–0.97)	0.97 (0.94–1.00)	0.96 (0.92–1.00)
Accuracy	99.16%	90.34%	97.98%	95.62%
Sensitivity	100%	100%	96.43%	96.43%
Specificity	99.05%	89.10%	98.14%	95.62%
Positive Predictive Value	93.10%	54%	84.38%	69.23%
Negative Predictive Value	100%	100%	99.62%	99.61%
Likelihood Ratio +	105.50	9.17	51.88	21.62
Likelihood Ratio -	0	0	0.04	0.04

Table 8. Association between NLR or PLR, and in-hospital morbidity or mortality (n = 535)

	Crude OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
NLR				
≤7.27	*Ref*	*Ref*	*Ref*	*Ref*
>7.27	2293.85 (388.64–13538.67)	<0.0001*	22797.51 (157.83–3292895)	<0.0001*[a]
PLR				
≤32.40	*Ref*	*Ref*	*Ref*	*Ref*
>32.40	455.96 (86.89–2392.75)	<0.0001*	320.14 (62.69–1634.81)	<0.0001*[b]

[a] Adjusted for the confounding effects of sex, hypertension, kidney disease, vascular disease, alcohol consumption, hemoglobin, FBS, HbA1c, Wagner classification, AKA, blood loss

[b] Adjusted for the confounding effects of hypertension, kidney disease, vascular disease, alcohol consumption, hemoglobin, FBS, blood loss

All parameters remained high in both groups. In addition, a perfect sensitivity in predicting in-hospital morbidity and mortality was obtained for both NLR and PLR among those who underwent major amputation.

Univariable analysis using simple logistic regression was performed to identify potential confounders (Appendices D and E). Using the established cutoffs, both NLR and PLR were significantly associated with in-hospital morbidity or mortality even when controlled for the effect of significant confounders (Table 8).

DISCUSSION

A diabetic foot ulcer is one of the most dreaded complications of uncontrolled diabetes, given its impact on quality of life and the heightened risks of morbidity and mortality.[15–17] In some cases, amputation is necessary to avoid the spread of infection and prevent further tissue damage; however, amputation is also associated with poor patient outcomes. In recent years, few studies have explored the utility of inflammatory markers in predicting patient prognosis among individuals with diabetic foot ulcers, but most have focused on mortality. To the best of the researchers' knowledge, this is the first local study that examined the accuracy of NLR and PLR in predicting both in-hospital morbidity and mortality among diabetic foot infection patients who underwent amputation.

In-hospital mortality in the present study was 4.67%, comparable to published studies.[18–20] Meanwhile, studies reported one-month mortality estimates that ranged from 11 to 18%,[20–22] which rose with longer follow-up periods. Very few studies, however, examined the morbidity rate after amputation. In a study conducted in Tunisia, the morbidity rate after amputation was 9.5%, slightly higher than the present study, where only 6.17% developed complications.[18] Furthermore, out of the 535 patients in this study, 15 (3%) had wound complications, 12 (2%) required re-amputation, and 6 (1%) had hospital-acquired pneumonia. These estimates were lower compared to previous studies. In a Tunisian study, 8% had wound complications, while 5% required re-amputation. Meanwhile, in a local study conducted in PGH, 12% had hospital-acquired pneumonia.[20] Despite its rarity, in-hospital morbidity has been associated with higher mortality rates; thus, identifying patients at risk for these poor outcomes is warranted.[18,20]

Because of the expected low number of events, the authors created a composite measure for poor outcomes, defined as in-hospital morbidity and/or mortality. In this study, only 10.28% of patients had the outcome of interest, and those with the outcome exhibited higher NLR and PLR values than those without the outcome. Furthermore, the association of these markers remained statistically significant even when controlled for the effects of confounders. The study results were consistent with those of other studies, which reported that NLR and PLR are significantly associated with poorer patient outcomes after amputation.[23]

The role of these inflammatory markers in predicting patient prognosis has been recognized in various medical and surgical conditions. As markers of systemic inflammation, high levels may indicate ongoing tissue damage, microangiopathy, and microvascular complications among diabetic patients, which may result in end-organ damage.[24-26] The increased release of neutrophils may lead to endothelial damage, while an increase in platelets heightens the release of inflammatory mediators and may lead to thrombosis and cardiac problems.[27-29] Meanwhile, lymphocytes decrease due to increased apoptosis of these cells during a heightened inflammatory process. These series of events then lead to poorer postoperative outcomes, including death.[13,23]

The present study also examined the validity of pre-operative NLR and PLR in predicting outcomes. Using a cutoff of 7.27, NLR showed high accuracy, sensitivity, and specificity levels in predicting in-hospital morbidity and/or mortality. Most studies focused only on mortality as the outcome. In this study, NLR still showed high accuracy measures—100% sensitivity and 93% specificity in predicting in-hospital mortality.

Previous studies utilized a lower cutoff and exhibited lower sensitivity and specificity. In a study done in Turkey among major amputation patients, a cutoff of 6.37 showed 93% sensitivity but only 52% specificity.[30] Another study from Turkey used a cutoff of 6.80 and yielded a sensitivity of 83% and specificity of 66%.[31] Other studies that used postoperative NLR also exhibited poorer diagnostic performance.[13,23]

Although PLR was found to be an independent predictor of mortality by previous studies, its diagnostic performance was poorer than NLR. A study from Turkey used a cutoff of 247.28 for pre-operative PLR, which showed poor discriminative ability (AUC = 0.55) with 51% sensitivity, and 64% specificity.[23] Postoperative PLR also showed poor performance in published studies with sensitivity ranging from 73–74% and specificity of 44-47%.[13,30] In contrast, the present study proved that pre-operative PLR >32.40 was an excellent measure to predict in-hospital morbidity and/or mortality. Furthermore, PLR showed 100% sensitivity and 87% specificity when focused on mortality alone.

In this study, several patient characteristics were also found to be associated with in-hospital morbidity and/or mortality, which warrants further examination in future studies. For instance, the present study showed that females were more likely to develop the outcome than males, consistent with other studies.[18,21,31,32] Women are more likely to have cardiovascular complications due to diabetes than men, possibly explaining the higher probability of death among females.[33] In addition, one study concluded that females have poorer health status at the time of amputation since they are more likely to delay the procedure than males.[34]

Based on the univariable analysis, hypertension, kidney disease, and vascular disease were all significantly associated with the outcome of interest. In a study done in Tunisia, complications and death were more likely to occur in patients with hypertension than those without hypertension.[18] Previous studies also observed higher mortality among patients with renal impairment, including increased BUN and creatinine, and decreased eGFR.[13,20,32,35,36] Aside from diabetes, comorbidities increase the likelihood of poorer outcomes. Vascular disease, especially peripheral artery disease, is a known risk factor for poor patient outcomes.[37,38] Renal impairment may also enhance cardiovascular risk factors, including hypertension, insulin resistance, oxidative stress, endothelial dysfunction, and inflammation which may result in poorer postoperative outcomes.[39] These comorbidities likely contribute to elevating inflammatory markers.[40]

Patients who developed the outcome also had lower hemoglobin levels and higher intraoperative blood loss. In a previous study from Brazil, the authors concluded that lower hemoglobin level was associated with mortality among those who underwent amputation.[41] Similar to a local study, patients who underwent intraoperative blood transfusion had higher mortality rates.[20]

Across all specific amputation levels, only above-knee amputation was significantly associated with a higher probability of the outcome, similar to previous studies.[20,41] However, Gocer et al. argued that mortality is not really due to the level of amputation. Instead, a higher level of amputation is a marker of the overall progression of the disease; thus, worse outcomes are expected from these patients.

One of the strengths of this study is its large population of diabetic patients who underwent amputation. The present study provides valuable evidence regarding the role of NLR and PLR in predicting patient postoperative outcomes. Most studies have focused only on major amputations and mortality outcomes.

The study has several limitations. First, the main outcomes of this study were in-hospital morbidity and mortality. However, as a government hospital, the length of hospital stay may have been affected by various factors (i.e., financial constraints), which then affected the detection of in-hospital morbidity and mortality. Moreover, mortality is known to increase over time after amputation;[22,36] It will also be worth examining if the inflammatory markers can predict long-term outcomes. Second, the study included patients from a single setting; therefore, the results have limited generalizability. The characteristics and outcomes of patients admitted to a tertiary government hospital may differ from those in other institutions. Third, NLR and PLR were computed based on the CBC result closest before the time of amputation. Although CBC collection is usually done within a week of the surgery, the variation in the timing of blood collection could have affected the study results. Lastly, due to the retrospective nature of this study, only routinely collected data were included in the analysis. An extensive literature review was performed to identify potential confounders, but not all could be controlled if they were not recorded in the charts. Residual confounding is, therefore, possible.

CONCLUSION

The rate of in-hospital morbidity and/or mortality was 10.28% among diabetic foot infection patients who underwent amputation in the chosen institution. Both NLR and PLR performed well in predicting in-hospital morbidity and mortality, demonstrating high discriminative ability, sensitivity, and specificity, even when major and minor amputations were analyzed separately. These markers are inexpensive and easily obtainable; thus, they are particularly helpful and useful, especially in low-resource settings. Future studies should explore the utility of these markers in predicting long-term outcomes after amputation or in predicting standardized assessments of outcomes at specific time points (e.g., 30-day morbidity and mortality), as the length of hospital stay can vary greatly between patients.

STATEMENT OF AUTHORSHIP

Both authors certified fulfillment of ICMJE authorship criteria.

AUTHOR DISCLOSURE

Both authors declared no conflict of interest.

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