



Original Article

Preoperative Platelets to Lymphocyte Ratio in Diabetic Foot A Cost Effective Prognostic Indicator

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Abstract

Objective: To study prognostic value of pre-operative platelets to lymphocyte ratio in diabetic foot patients who underwent amputation.

Methods: This study was conducted in the surgical units of Mayo Hospital Lahore. One hundred and eighty four patients were included in the study. Data was obtained from records of patients admitted between July 2020 to July 2021. Platelet to lymphocyte ratio was noted from investigations done preoperatively. Outcome of patients was noted. Diabetic foot ulcers were classified using Wagner classification. A receiver operator curve was constructed and area under the curve was calculated. A suitable cut-off value of platelet to lymphocyte ratio was decided using the curve. Sensitivity and specificity of the cut off value as a prognostic indicator was compared between discharged and expired groups of patients using independent sample t-test.

Results: All-cause mortality was higher in patients with high platelet to lymphocyte ratio. Area under the receiver operator curve was 0.56. Cut off value of platelet to lymphocyte ratio 244.95 calculated from receiver operator curve was found to have sensitivity of 61.8% and specificity of 53.3%. Out of 184 patients 141 (76.6%) were males and 43 (23.4%) were females with a mean age of 54.9 ± 10.47 years. One hundred and fifty patients (81.5%) were discharged and the remaining expired

Conclusion: Preoperative platelet to lymphocyte ratio can be used as a predictive biomarker of mortality in patients with diabetic foot ulcer undergoing amputation.

Keywords: Diabetic Foot. Lymphocytes, Platelets.

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Introduction

Diabetes mellitus is a highly prevalent metabolic disorder which results from defective insulin secretion, insulin resistance or both leading to hyperglycemia.^{1,2,3,4} Diabetes mellitus causes multisystem complications posing significant mortality and morbidity. Diabetic foot syndrome, one of the most dreaded complications, is a major cause of lower limb amputation, involving a combination of neuropathy, peripheral arterial disease and infection.⁵ Amputation secondary to diabetic foot leads to socioeconomic burden on society. The gravity of the situation can be understood by the fact that one limb is

lost every 30 seconds owing to diabetic foot. A diabetic patient has a 25% lifetime risk of developing diabetic foot ulcer. Adding insult to injury, mortality is twofold higher in patients with diabetic foot ulcers than those not having the condition with a five year mortality rate reaching up to 40%. Prevalence of foot ulcer among diabetics ranges from 3 to 13% around the globe.^{6,7}

Diabetic foot ulcers vary from cellulitis to full foot gangrene requiring amputations.⁸ In a study conducted in India, several factors causing poor outcomes were identified, some of which include barefoot walking, illiteracy, low socioeconomic

status, late presentation by patients, ignorance about diabetic foot care among primary care physicians, and belief in the alternative systems of medicine.⁷ These were the socioeconomic factors of poor outcomes. Jupiter et al found in their systematic review that patients with diabetic foot ulcers have a five-year mortality rate of 40%. Risk factors of death were age, male gender, peripheral vascular disease, and renal disease. It is unknown if this mortality is due to advanced macro- and microvascular complications or it is the result of inflammatory sequelae.⁹

Contribution of inflammation in development of diabetic foot syndrome is a matter of interest in recent times. This aspect of diabetic foot might open new avenues in treatment and might as well work as a prognostic indicator in these patients.¹⁰

Many biochemical parameters of inflammation for predicting prognosis have been studied; some of them include erythrocyte sedimentation rate, C- reactive protein, procalcitonin, and neutrophil to lymphocyte ratio.^{11,12} The platelet-to-lymphocyte ratio (PLR) is a new inflammatory marker and independent predictor of major adverse cardiovascular events in different cardiovascular diseases.¹³ However, PLR has not been studied extensively in settings of diabetic foot ulcers. In a study done by Eren MA et al. on 78 patients, subjects with raised PLR required prolonged hospital stay but aspect of its prognostic implication has not been explored in that study.¹³

In this research we would like to study this novel inflammatory marker as a predictor of mortality in patients with diabetic foot ulcers undergoing amputation as this aspect has not been explored in our population. This might help us in better management of these patients and might as well help us to understand the role of inflammation in diabetic foot ulcers.

Methods

This study was carried out in the Department of Surgery, Mayo Hospital Lahore after taking approval from the Institutional Review Board King Edward Medical University (IRB number :49/RC/KEMU). A total of one hundred and eighty-four patients were recruited. Sample size was calculated using formula:

The sample size was statistically calculated using prevalence rate as 13.9%.¹⁴

Data was obtained from records of diabetic patients who were admitted with diabetic foot ulcer and underwent amputation. Diabetic foot ulcer was

identified based on the Wagner system of classification. Patients were selected by non purposive convenience sampling. It was a retrospective cross-sectional study. Demographic information like name, age and gender, outcome of patients, platelets and lymphocyte counts were noted from preoperative CBC and platelet to lymphocyte ratio was calculated and recorded on predesigned proforma. Both male and female patients aged 18 years or more undergoing amputation due to diabetic foot were included. Patients on immunosuppressive therapy, drugs and hematological disorders which could alter platelet and lymphocyte counts were excluded.

Results

The data was collected from 184 diabetic patients with diabetic foot ulcers requiring amputation and was analyzed using SPSS 26. The mean age of the patients was 54.59 ± 10.47 years. The proportion of male patients was more than three-fourth in the sample. About 141 (76.6%) of the patients were male and 43 (23.4%) of the patients were female. About 150 (81.5%) of the diabetic foot ulcer patients were discharged who underwent foot amputation. Remaining 34 (18.5%) of the patients expired.

Table 1 indicates the mean value of platelets, lymphocytes and PLR across gender and amputation outcome. There was a statistically significant difference between lymphocyte and PLR value across gender. The threshold for PLR was evaluated by area under the curve (AUC) using receiver operating curve (ROC). The area under the curve was found to be 0.56 (Figure I). The sensitivity was observed as 61.8% and specificity was 53.3% for cut-off value 244.95 of PLR. Mortality between the two groups was compared using the independent sample t-test.

Using the cut-off value of PLR as 244.95, a classification table was constructed for the amputation outcome (Table 2). The accuracy was found to be 54.9% from the classification table using the evaluated cut-off point.

Most of the participants i.e., 90 (72.6%) had grade 5 Wagner classification followed by grade 4 forefoot gangrene among 34 (27.4%). No patient was found to have intact skin, superficial ulcer, deep ulcer or ulcer with bone involvement. All the patients with grade 4 classification expired. Nearly 72.2% of the patients with grade 5 classification expired (Table 3).

Table 1: Mean and p-value of Platelets, lymphocyte and PLR

Factors	Categories	Platelets		Lymphocyte		PLR	
		Mean	p-value	Mean	p-value	Mean	p-value
Gender	Male	453.99	0.244	11.45	0.022*	324.96	0.019*
	Female	372.08		17.1		220.26	
Outcome of Amputation	Discharged	448.67	0.657	12.5	0.124	295.78	0.604
	Expired	418.46		8.81		321.27	

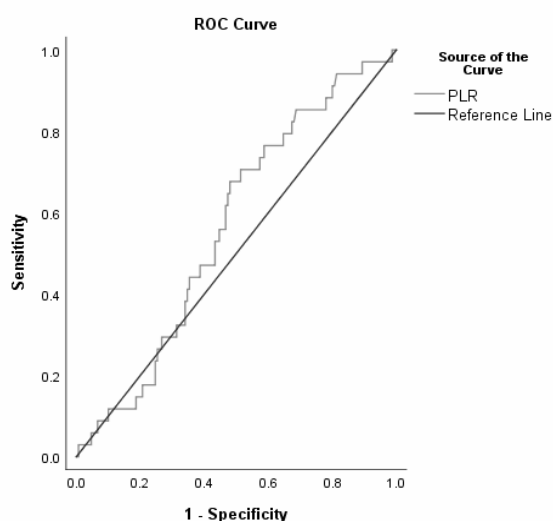
*p-value≤0.05 is statistically significant

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Table 2: Classification Predicted and Actual Amputation outcome

Classification Table		Predicted Outcome		Total
		Discharged	Expired	
Actual Outcome	Discharged	TN = 80	FP = 70	150
	Expired	FN = 13	TP = 21	34
Total		93	91	184

**Figure 1:** Receiver Operating Curve for PLR**Table 3:** Crosstab of Wager classification and outcome of amputation

Grade	Wagner Classification	Total	Outcome of Amputation	
	n	n (%)	Discharged	Expired
Grade 0	Intact Skin	0	0	0
Grade 1	Superficial ulcer	0	0	0
Grade 2	Deep ulcer	0	0	0
Grade 3	Ulcer with bone involvement	0	0	0
Grade 4	Forefoot gangrene	34	0	34
Grade 5	Full-foot gangrene	90	25	65

Discussion

Platelet to lymphocyte ratio is a simple and economical biomarker of predicting mortality and morbidity in various diseases. In this study, the area under the receiver operating curve was 0.56 and preoperative cut off PLR 244.95 calculated from the curve predicted mortality with a sensitivity of 61.8% and specificity of 53.3%. Given the association of preoperative PLR with higher mortality, we suggest using this marker as a prognostic indicator in diabetic foot patients undergoing surgery and planning post operative care accordingly.

Furthermore, our study suggested significant variation in PLR (p value=0.019) and lymphocyte count (p value=0.022) between male and female patients. This prospect has not been evaluated in any other study we went through. This new finding can open prospects in mortality prediction, prognostic factors and even in treatment of disease across the two genders. One of the intriguing findings was mortality was higher in grade 4 ulcers as compared to grade 5.

Study done by Mineoka Y et al, showed that a complicated diabetic foot had a higher platelet to

lymphocyte ratio.¹⁵ A very similar study was conducted by Mehmet AE et al in which they studied correlation of neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) with cost and length of hospital stay in 78 patients with diabetic foot ulcer. Though the length of the stay was not relatable with either of the two markers but cost of hospitalization was positively correlated with PLR only and no relation was found with NLR.¹³ Study done by Chen W et al in China on postoperative value of NLR and PLR in 348 patients undergoing amputation because of diabetic foot ulcer exhibited higher ratios in the high mortality group.¹⁶ Serban D et al conducted a very elaborate study regarding prognostic value of PLR and NLR in diabetic foot ulcer and further implicated use of these results in future therapeutic targets. They found that NLR and PLR were significantly raised in patients with diabetic foot ulcers as compared to type 2 diabetes patients without ulcers. In addition to that, they discovered that PLR and NLR correlated well with severity of ulcers with incidence of osteomyelitis, chance of amputation and septic complications. They implied that calculation of these inexpensive biomarkers at time of presentation will help us to stratify patients at the time of presentation to hospital and hence help us in better care of these patients.¹⁷ Platelet to lymphocyte ratio has importance in not only diabetic foot but also in other conditions. Balta S et al concluded in a study that PLR is a novel inflammatory marker which has importance in inflammation, atherosclerosis and platelets activation.¹⁸

Hence, we conclude that PLR can be established as an economical predictor of mortality. We suggest exploring this ratio to monitor the course of disease during treatment. Maybe in the future, various drugs could be developed that work on this pathway of inflammation in management of various diseases.

In terms of limitations, the current study was conducted at a single center with a small sample size depending upon the study design and prerequisites. The results of our study can only be applied to a very narrow population and have poor generalizability. Further multi-centered trials are warranted to endorse the results of the current study.

Conclusion

In our study, we came across that an increased PLR is a dependable biomarker of mortality predictor in patients undergoing amputation for the diabetic foot ulcers. This marker can be very easily obtained from complete blood count done preoperatively. Given the

high mortality in patients with higher ratios, we suggest managing patients accordingly.

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Ethical Approval: The IRB/EC approved this study via letter no49/RC/KEMU dated January 12, 2021.

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Authors' Contribution

AFB, WA: Conception

KR, NFB: Design of the work

NS, MSA: Data acquisition, analysis, or interpretation

KR, NFB, NS, MSA: Draft the work

AFB, WA: Review critically for important intellectual content

All authors approve the version to be published

All authors agree to be accountable for all aspects of the work

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