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Original Article

Glycemic control modifies the association between systemic inflammatory indices and diabetic neuropathy: Evidence from NHANES

Yian Lu[1], Xiaoyan Wu[2], Haijun Xiao[3]

ABSTRACT

Background and Objective: Chronic low-grade inflammation is increasingly recognised as a key contributor to diabetic peripheral neuropathy (DPN). However, there is limited evidence on inflammatory markers. We therefore examined the association between hematologic inflammatory indices, namely, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and systemic immune-inflammation index (SII), with lower limb neuropathy.

Methodology: We conducted a cross-sectional analysis of adults with diabetes aged ≥40 years from the National Health and Nutrition Examination Survey (NHANES) 1999–2004. Lower limb neuropathy was defined using standardized 10-g monofilament testing. Inflammatory indices (NLR, PLR, MLR, and SII) were calculated from complete blood counts and analyzed as continuous variables and tertiles. Survey-weighted logistic regression models were used to evaluate associations after adjustment for demographic factors, glycemic control, cardiovascular comorbidities, and lifestyle variables. Subgroup analyses were performed among individuals with poor glycemic control (HbA1c >8%).

Results: In the overall cohort, inflammatory indices were not independently associated with lower limb neuropathy in fully adjusted models. However, among individuals with HbA1c >8%, higher NLR was significantly associated with increased odds of neuropathy, whereas SII showed a statistically significant inverse association. Neither association was confirmed in the tertile-based analyses.

Conclusions: Although systemic inflammatory indices were not significantly associated with neuropathy in the overall diabetic population, elevated NLR was associated with neuropathy among individuals with poor glycemic control. Given the cross-sectional nature of data and limited adjustment of confounders, results must be interpreted with caution.

KEYWORDS: Diabetic Neuropathies; Inflammation; Hemoglobin A, Glycosylated; Neutrophils; Biomarkers.

doi: https://doi.org/10.12669/pjms.42.10.19711

How to cite this: *Lu Y, Wu X, Xiao H. Glycemic control modifies the association between systemic inflammatory indices and diabetic neuropathy: Evidence from NHANES. Pak J Med Sci. 2026;42(10):2650-2656. doi: https://doi.org/10.12669/pjms.42.10.19711*

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1. Yian Lu
2. Xiaoyan Wu
3. Haijun Xiao

1-3: Department of Orthopedics, Fengxian Central Hospital, Shanghai 201400, P.R. China.

Correspondence:

Haijun Xiao
Department of Orthopedics,
Fengxian Central Hospital,
6600 Nanfeng Hwy,
Shanghai 201400, P.R. China.
Email: 18018820150@163.com

* Pre-submission Review: April 28, 2026
* Received for Publication: May 18, 2026
* Revision Received: August 24, 2026
* Revision Accepted: August 29, 2026

INTRODUCTION

Diabetes mellitus (DM) has emerged as a significant global health concern in the twenty-first century, affecting hundreds of millions of individuals worldwide and contributing to a rapidly increasing burden of chronic complications.[1] Among these, diabetic neuropathy is recognised as the most common and disabling microvascular complication. The most prevalent form, diabetic peripheral neuropathy (DPN), affects up to 50% of individuals with DM over their lifetime.[2] It is characterised by a length-dependent loss of sensory function, typically initiating in the feet and advancing proximally. In addition to sensory deficits, neuropathy markedly increases the risk of falls, foot ulceration, amputation, diminished quality of life, and mortality.[3,4] Painful DPN represents a particularly debilitating phenotype, characterised by burning, tingling, or electric shock–like sensations that are often worse at night.[5,6] A recent systematic review and meta-analysis shows

that about 47% of patients with DPN have painful DPN, highlighting the magnitude of the problem in contemporary clinical practice.[7]

DPN involves multiple complex pathogenic mechanisms. Persistent hyperglycemia, dyslipidemia, insulin resistance, and components of metabolic syndrome collectively lead to oxidative stress, mitochondrial dysfunction, microvascular damage, and low-grade inflammation in peripheral nerves.[3] Increasing evidence suggests that chronic, low-level inflammation significantly contributes to both the onset and progression of DPN.[8,9] Studies from experimental models and clinical research have shown elevated circulating pro-inflammatory cytokines like interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and other inflammatory mediators in affected individuals.[10,11] Additionally, studies indicate that systemic inflammatory markers can predict the development and progression of neuropathy, regardless of other risk factors.[9,11] These findings suggest that inflammation may be a mechanistic link between metabolic disturbances and nerve damage.

While inflammatory cytokines and adhesion molecules are involved in DPN pathophysiology, measuring them routinely in clinical practice is expensive and often impractical in large-scale epidemiological studies. Conversely, simple hematologic indices such as the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and systemic immune inflammation index (SII), derived from complete blood counts, are inexpensive indicators of systemic inflammation and have been linked to adverse cardiovascular and metabolic outcomes.[12-14] Nonetheless, their association with objectively diagnosed DPN in large, representative populations has not been fully examined. Therefore, this study aimed to examine the relationship between systemic inflammatory markers and lower-limb neuropathy in adults with DM, using data from a nationally representative cohort.

METHODOLOGY

We conducted a cross-sectional study utilizing data from the NHANES cycles of 1999–2004. NHANES, conducted by the National Center for Health Statistics, is a nationally representative survey of the non-institutionalized U.S. population. It features a complex, multistage, stratified probability sampling design, including standardized interviews, physical examinations, and laboratory assessments. Data from the 1999–2000, 2001–2002 and 2003–2004 cycles were combined for this analysis. Following NHANES guidelines for analysing multiple cycles, six-year sample weights were generated by dividing the two-year MEC weights (WTMEC2YR) by three. All analyses incorporated sampling weights, strata, and primary sampling units to account for the survey's complex design. As all the data were publicly available and de-identified, the current study did not require institutional review board approval.

Inclusion Criteria: Participants aged 40 or older with diabetes mellitus were eligible for inclusion. Diabetes was identified through either a self-reported diagnosis by a physician or an HbA1c level of ≥6.5%. Participants needed complete data for monofilament testing, blood count parameters, and HbA1c measurements; those with missing monofilament data were excluded. After applying these criteria, a total of 1,371 participants formed the final analytic cohort.

The primary outcome was sensory impairment in the lower limb, assessed using standardized 5.07 (10 g) Semmes-Weinstein monofilament testing during the NHANES examination. Participants were considered to have neuropathy if at least one tested site was insensate. Those with complete testing results and no insensate sites were categorized as not having neuropathy.

Exposure Variables: Inflammatory indices were obtained from the absolute counts of leukocytes and platelets in the complete blood count. The NLR was determined by dividing the absolute neutrophil count by the absolute lymphocyte count. The MLR was calculated as the ratio of the absolute monocyte count to the absolute lymphocyte count. The PLR was derived by dividing the platelet count by the absolute lymphocyte count. The SII was calculated by multiplying the platelet count by the neutrophil count and then dividing by the lymphocyte count. These inflammatory markers were analyzed both as continuous variables and by dividing them into tertiles, with the lowest tertile used as the reference category in the categorical analysis.

Covariates: Covariates were chosen beforehand based on their clinical importance and availability of data. Demographic variables encompassed age and sex. Lifestyle factors involved physical activity status, obtained from questionnaire data. Glycemic control was measured using HbA1c levels. Cardiovascular comorbidities were identified through self-reported physician diagnoses and included hypertension, congestive heart failure, coronary artery disease, myocardial infarction, and stroke. These variables were incorporated into multivariable models to adjust for potential confounders.

Statistical Analysis: We summarized baseline data as means and standard deviations for continuous variables, and percentages were used for categorical variables. Comparisons between participants with and without neuropathy were conducted using appropriate survey-weighted statistical tests. Univariate logistic regression models evaluated the relationship between individual variables and neuropathy, with odds ratios (OR) and 95% confidence intervals (CI) reported. Multivariable logistic regression models then assessed the independent association between inflammatory indices and neuropathy, adjusting for demographic, lifestyle, glycemic, and cardiovascular covariates. Inflammatory markers were included as continuous variables and, in separate analyses, as tertiles.

A predefined subgroup analysis was performed on individuals exhibiting poor glycemic control, defined as those with an HbA1c level >8%. In this subgroup, we used multivariable logistic regression models to assess the relationships between inflammatory markers and neuropathy, using both continuous and tertile-based data.

Table-I: Details of participants.

	No Neuropathy	*Neuropathy*	*P-value*
Age (years)	64.13 ± 11.78	65.10 ± 11.08	0.221
HbA1c (%)	7.50 ± 1.75	7.77 ± 2.02	0.048
NLR	2.33 ± 1.37	2.24 ± 1.28	0.350
MLR	0.30 ± 0.14	0.30 ± 0.12	0.623
PLR	131.53 ± 58.37	127.98 ± 59.62	0.395
SII	598.08 ± 503.35	557.86 ± 413.87	0.185
Male (%)	52.7%	56.5%	0.319
Physically Active (%)	46.6%	43.5%	0.427
Hypertension (%)	44.9%	45.6%	0.900
Congestive Heart Failure (%)	9.0%	12.1%	0.166
Coronary Heart Disease (%)	11.6%	10.5%	0.704
Myocardial Infarction (%)	11.5%	12.5%	0.734
Stroke (%)	7.7%	8.9%	0.644

NLR, neutrophil lymphocyte ratio; MLR, monocyte lymphocyte ratio;
PLR, platelet lymphocyte ratio; SII, systemic immune inflammation index.

These models were adjusted for all covariates, excluding HbA1c. P<0.05 indicated statistical significance.

RESULTS

The current study included 1,371 participants with DM and aged ≥40 years of which 248 individuals (18.1%) experienced lower limb sensory impairment. The patient characteristics grouped by neuropathy status are shown in Table-I. Those with neuropathy had notably higher HbA1c levels compared to those without (7.77 ± 2.02% vs. 7.50 ± 1.75%, p = 0.048). The analysis demonstrated no significant differences between the two groups for age,

Table-II: Univariate and multivariate analysis of the full cohort.

Variable	*Unadjusted OR (95% CI)*	*P value*	*Adjusted OR (95% CI)*	*P value*
Age	1.007 (0.995–1.019)	0.238	1.008 (0.995–1.022)	0.229
Male	1.163 (0.881–1.534)	0.286	1.195 (0.888–1.608)	0.239
Physically Active	0.885 (0.671–1.168)	0.387	0.921 (0.691–1.227)	0.573
HbA1c	1.082 (1.007–1.163)	0.030	1.100 (1.021–1.186)	0.012
Hypertension	1.028 (0.780–1.355)	0.844	1.042 (0.776–1.399)	0.785
CHF	1.392 (0.903–2.147)	0.134	1.580 (0.960–2.598)	0.072
CHD	0.895 (0.573–1.397)	0.624	0.711 (0.421–1.200)	0.201
MI	1.101 (0.724–1.673)	0.653	1.035 (0.630–1.701)	0.892
Stroke	1.159 (0.711–1.891)	0.554	1.084 (0.656–1.794)	0.752
NLR	0.950 (0.850–1.062)	0.370	0.905 (0.704–1.164)	0.438
MLR	1.262 (0.465–3.422)	0.648	2.578 (0.548–12.132)	0.231
PLR	0.999 (0.996–1.001)	0.387	1.000 (0.996–1.004)	0.894
SII	1.000 (0.999–1.000)	0.232	1.000 (0.999–1.001)	0.791

NLR, neutrophil lymphocyte ratio; MLR, monocyte lymphocyte ratio; PLR, platelet lymphocyte ratio;
SII, systemic immune inflammation index; OR, odds ratio; CI, confidence intervals;
CHF, congestive heart failure; CHD, coronary heart disease; MI, myocardial infarction.

gender, physical activity, hypertension, congestive heart failure, coronary artery disease, heart attack, or stroke. Likewise, inflammatory markers namely, NLR, MLR, PLR, and SII also showed no significant differences at baseline (all p > 0.05).

Full cohort Analysis: Univariate logistic regression results are shown in Table-II. Among all baseline variables, only HbA1c was significantly associated with neuropathy (OR 1.082, 95% CI 1.007–1.163, p = 0.030). None of the inflammatory markers (NLR, MLR, PLR, SII), demographic variables, lifestyle factors, or cardiovascular comorbidities demonstrated significant associations in unadjusted analyses. Fully adjusted multivariate logistic regression results are also presented in Table-II. The model included age, sex, physical activity, HbA1c, hypertension, congestive heart failure, coronary heart disease, myocardial infarction, stroke, and inflammatory indices (NLR, MLR, PLR, SII). HbA1c remained independently associated with neuropathy (adjusted OR 1.10, 95% CI 1.021–1.186, p = 0.012). None of the inflammatory ratios were independently associated with neuropathy in the overall cohort (NLR: OR 0.905, p = 0.438; MLR: OR 2.578, p = 0.231; PLR: OR 1.000, p = 0.894; SII: OR 1.000, p = 0.791). Congestive heart failure demonstrated a borderline association (OR 1.58, p = 0.072). Tertile-based analyses are shown in Table-III. Compared with the lowest tertile (T1), neither intermediate (T2) nor highest tertile (T3) of NLR, MLR, PLR, or SII was significantly associated with neuropathy after adjustment for confounders. A borderline inverse trend was observed for PLR in the highest tertile (T3 vs T1: OR 0.741, 95% CI 0.527–1.040, p = 0.083), but this did not reach statistical significance.

Subgroup Analysis for patients with poor glycemic control (HbA1c > 8%): A predefined subgroup analysis was conducted among individuals with poor glycemic control (HbA1c > 8%; n = 381). Multivariate results are presented in Table-IV. In this subgroup, NLR was independently associated with neuropathy (adjusted OR 1.846, 95% CI 1.050–3.247, p = 0.033). SII was also significantly associated (OR 0.997, 95% CI 0.995–0.999, p = 0.008). No significant associations were observed for MLR or PLR. Congestive heart failure showed a strong but borderline association (OR 2.911, p = 0.079). When inflammatory markers were modeled as tertiles within the HbA1c > 8% subgroup (Table-III), no significant associations were observed for any tertile comparisons.

DISCUSSION

In this nationally representative cohort of adults aged 40 and above with diabetes mellitus, systemic inflammatory markers derived from standard complete blood counts showed no independent association with lower limb sensory impairment in the overall population after adjusting for demographic factors, glycemic control, cardiovascular comorbidities, and lifestyle variables. Hemoglobin A1c (HbA1c) remained the only consistent independent predictor of neuropathy in fully adjusted models. However, within a preselected subgroup exhibiting poor glycemic control (HbA1c >8%), higher NLR was positively associated with neuropathy, whereas SII showed an inverse association when these markers were modelled as continuous variables.

Numerous recent studies have indicated strong links between prediabetes, DM, inflammation, and DPN. It is now understood that persistent low-grade inflammation is a key mechanism in the onset and progression of DPN, and that the inflammatory state associated with type-2 DM significantly contributes to the development of various complications, including neuropathy.[8,10] Nevertheless, the key inflammatory marker that accurately predicts DPN remains uncertain. A wide range of inflammatory biomarkers has been investigated in this context, including classical inflammatory proteins such as C-reactive protein and erythrocyte sedimentation rate, circulating cytokines such as interleukin-1, interleukin-6,

Table-III: Tertile-based analysis of full cohort and poor glycemic control subgroup.

Marker	*Comparison*	*Full cohort OR (95% CI)*	*P value*	*Poor glycemic control subgroup OR (95% CI)*	*P value*
NLR	T2 vs T1	0.968 (0.693–1.351)	0.848	0.999 (0.539–1.848)	0.996
	T3 vs T1	0.756 (0.529–1.079)	0.123	1.053 (0.565–1.961)	0.871
MLR	T2 vs T1	0.871 (0.616–1.233)	0.437	1.095 (0.597–2.009)	0.770
	T3 vs T1	1.016 (0.709–1.456)	0.930	0.900 (0.462–1.751)	0.755
PLR	T2 vs T1	0.775 (0.555–1.084)	0.136	1.145 (0.631–2.077)	0.657
	T3 vs T1	0.741 (0.527–1.040)	0.083	0.921 (0.493–1.720)	0.795
SII	T2 vs T1	0.816 (0.584–1.140)	0.232	0.926 (0.512–1.676)	0.799
	T3 vs T1	0.760 (0.541–1.069)	0.115	0.774 (0.418–1.431)	0.413

OR, odds ratio; CI, confidence intervals; NLR, neutrophil lymphocyte ratio; MLR, monocyte lymphocyte ratio; PLR, platelet lymphocyte ratio; SII, systemic immune inflammation index; T3, tertile 3; T2, tertile 2; T1, tertile 1.

Table-IV: Multivariate analysis of patients with poor glycemic control (HbA1c > 8%).

Variable	*Adjusted OR*	*CI lower*	*CI upper*	*P value*
Age	1.005	0.981	1.029	0.694
Male	0.653	0.386	1.107	0.113
Physically Active	0.858	0.511	1.439	0.562
Hypertension	0.957	0.548	1.67	0.877
CHF	2.911	0.882	9.604	0.079
CHD	0.442	0.138	1.418	0.17
MI	0.972	0.348	2.713	0.957
Stroke	1.185	0.471	2.98	0.719
NLR	1.846	1.05	3.247	0.033
MLR	1.463	0.071	30.192	0.805
PLR	1.004	0.996	1.012	0.297
SII	0.997	0.995	0.999	0.008

OR, odds ratio; CI, confidence intervals; NLR, neutrophil lymphocyte ratio;
MLR, monocyte lymphocyte ratio; PLR, platelet lymphocyte ratio;
SII, systemic immune inflammation index; CHD, coronary heart disease;
CHF, congestive heart failure; MI, myocardial infarction

interleukin-10, and tumour necrosis factor-α, as well as chemokines, adipokines, and other immune mediators identified through genetic and molecular studies.[9] In addition, several studies have explored hematologic indices derived from routine blood counts, as potential surrogate markers of systemic inflammatory activity. While many studies have reported elevated levels of these markers in individuals with DPN, findings have been inconsistent, with some reporting positive associations and others showing no significant relationship.

Enumerating the positive results, a cross-sectional study of patients with type-2 DM found that the NLR was markedly elevated in those with DPN compared with those without. Moreover, both NLR and HbA1c independently predicted neuropathy severity, as measured by the Michigan Neuropathy Screening Instrument.[15] Similarly, Zhu et al.,[16] in a study of 1154 DM patients, used machine learning models and found that NLR was significantly elevated in subjects with DPN and that multivariate models supported an independent role for NLR in predicting DPN, with moderate AUC performance (0.62). Another study by Li et al.[17] has shown that patients with DPN have higher MLR and HbA1c levels than those without DPN, but MLR has limited discriminative ability for identifying DPN (AUC: 0.625).

A cross-sectional Chinese study on 1460 DM patients has demonstrated that SII is significantly associated with DPN prevalence, and the results remained significant on adjusted analysis.[18] However, stratified analysis showed that results were significant only in men aged <65 years, non-obese, with DM >5 years, hypertension, dyslipidaemia, poor glycaemic control and estimated glomerular filtration rate <90 mL/min/1.73 m^2.[2,18] Nevertheless, the literature also contains contrasting evidence, and a small number of studies have reported no significant association between blood-based inflammatory markers and DPN. Agrawal et al.,[19] in a case-control study, showed no statistically significant difference in the values of NLR and PLR between those with DPN and those without DPN. Alshareef et al.,[20] in a large study from the Middle East, also noted no significant difference in NLR values according to DPN status.

The present study builds on this limited and conflicting evidence to suggest that NLR, PLR, MLR, and SII may not be reliable markers for predicting lower-limb sensory impairment in adults with DM. In the overall cohort, these inflammatory indices were not independently associated with neuropathy after adjustment for demographic characteristics, glycemic status, lifestyle factors, and cardiovascular comorbidities. This indicates that although systemic inflammation is implicated in the pathogenesis of DPN, simple hematologic ratios derived from routine blood counts may not adequately capture the complex inflammatory processes involved in nerve injury.

Indeed, DPN arises from multiple interrelated mechanisms, including chronic hyperglycemia, oxidative stress, mitochondrial dysfunction, and microvascular damage, which may dilute the independent contribution of systemic inflammatory signals detectable through circulating leukocyte-based indices.[3,11,21] Moreover, these markers reflect generalised systemic inflammation rather

than the localised inflammatory and neurovascular changes occurring within peripheral nerves.[12] Consequently, their ability to predict DPN across a heterogeneous diabetic population may be limited.

Nevertheless, an interesting finding in our study was that higher NLR was positively associated with neuropathy in patients with poor glycemic control, whereas SII, modelled as a continuous variable, showed an inverse association. Higher NLR was associated with an approximately 85% increase in the odds of neuropathy. Because the inverse association with SII was not confirmed in the tertile-based analysis, it should be interpreted cautiously and may have been influenced by extreme values, non-linearity, residual confounding, or model instability. It is also important to note that both NLR and SII were significantly associated with neuropathy only when used as continuous variables. Neither marker remained significant on tertile-based analysis, which may be due to the reduced statistical power from splitting a relatively small subgroup, or a non-linear, threshold effect. Considering these limitations, the present findings should not be taken to imply a clear dose–response relationship between these markers and neuropathy risk.

The stronger correlations seen in individuals with poor glycemic control support the hypothesis that systemic inflammation may have a more significant role in neuropathy development when metabolic dysregulation persists. Chronic hyperglycemia triggers several harmful pathways, including the formation of advanced glycation end products, increased polyol pathway activity, mitochondrial dysfunction, and activation of nuclear factor-κB–driven inflammatory signaling.[23] These pathways lead to oxidative stress and endothelial cell damage in the peripheral nerve microvasculature, resulting in nerve ischemia and axonal injury. In such conditions, inflammatory cells and cytokines can exacerbate tissue damage through heightened immune response and vascular inflammation.[22,23] Consequently, inflammatory markers such as NLR and SII might more accurately represent the underlying disease processes when glycemic control is poor, suggesting that the impact of systemic inflammation on neuropathy risk may depend on glycemic status.

Congestive heart failure showed a strong but statistically borderline association with neuropathy in the poor glycemic control subgroup. Similar borderline results were also noted in the fully adjusted overall-cohort model. Although this association did not reach statistical significance, the trend deserves mention. It is possible that neurohumoral activation and microcirculatory disturbance associated with congestive heart failure could contribute to peripheral nerve ischemia and thereby to neuropathy risk. Reduced cardiac output may also increase the endothelial and microvascular injury already caused in diabetic neuropathy. On the other hand, congestive heart failure could be a marker of overall cardiometabolic burden. Hence, it may be an unmeasured confounder linking systemic inflammation, vascular disease, and neuropathy rather than an independent contributor.

Limitations: The cross-sectional nature of the NHANES data prevents conclusions regarding causality, specifically, whether systemic inflammation occurs before or after neuropathy develops due to metabolic or vascular issues. Neuropathy was identified using monofilament testing, which mainly detects loss of protective sensation but may miss early or subclinical cases. More advanced tests, such as nerve conduction studies or sensory testing, could have provided a more detailed assessment of nerve health, but these were not available. The inflammatory indices were based on a single blood test, which can be influenced by transient physiological states and may not reflect long-term inflammation. Despite using adjusted analysis in our study, residual confounding remains a possibility. Additional factors not available in the dataset, including diabetes duration, use of glucose-lowering medications (particularly insulin), renal function (estimated glomerular filtration rate), nutritional status (e.g., vitamin B12 levels), and history of alcohol consumption, were not captured. It is plausible to suggest that unmeasured insulin use and impaired renal clearance could have impacted the associations between inflammatory indices and neuropathy, while undiagnosed vitamin B12 deficiency, a recognised cause of peripheral neuropathy, may have confounded outcome ascertainment itself. Such unmeasured factors may therefore have contributed to residual confounding in either direction. Data on comorbidities were partly self-reported, which could introduce reporting bias. Finally, the study focused on adults aged 40 and older with available monofilament and laboratory data, limiting the applicability of the findings to younger individuals with diabetes or to other populations outside NHANES.

Strengths: It combined data from three NHANES cycles to assess in detail the relationship between inflammatory markers and DPN. Four commonly used markers were assessed to allow comparisons and detection of the best marker. A subgroup analysis of patients with poor glycemic control was conducted to allow better interpretation of the results. From a clinical perspective, our findings suggest that hematologic markers such as NLR, PLR, MLR, and SII may have limited utility as universal screening markers for DPN. However, the observed associations in individuals with poor glycemic control indicate that inflammatory activity may play a greater role in neuropathy risk under conditions of sustained metabolic dysregulation. Further large-sample studies using more recent data and more comprehensive adjustment for confounders are needed.

CONCLUSIONS

Analysis of cross-sectional data indicates that NLR, PLR, MLR, and SII did not independently correlate with sensory impairment in the lower limbs of older adults

diagnosed with DM. Nevertheless, elevated NLR was significantly associated with sensory impairment within the subgroup of individuals with poor glycemic control. Considering the study's inherent constraints, these findings necessitate careful interpretation.

Recommendations: Future multicenter prospective cohort studies are required to understand the temporal link between systemic inflammation and DPN. Using more advanced diagnostic tools, such as nerve conduction studies, quantitative sensory testing, and assessments for small fiber neuropathy, can improve the accuracy of identifying early signs of neuropathy. Furthermore, integrating established inflammatory markers with novel molecular and cytokine-based biomarkers could improve the ability to predict neuropathy risk. Additional investigation should also assess the potential of inflammatory indices as prognostic tools within high-risk populations, particularly those exhibiting poor glycemic control, and whether interventions aimed at modulating inflammatory pathways might provide therapeutic advantages in the prevention or delay of neuropathy progression.

Acknowledgement: The authors used Grammarly to refine the tone and language of the manuscript.

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Authors' contributions:

YL: Literature search, study design and manuscript writing, manuscript revision and validation and is responsible for the integrity of the study.
XW and **HX:** Data collection, data analysis and interpretation, critical review.
All authors have read and approved the final manuscript.