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Original Article

Evaluation of Complete Blood Count–Derived Inflammatory Markers as Predictors of Poor Glycemic Control in Patients with Type 2 Diabetes Mellitus: A Retrospective Study

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Abstract

Background: Type 2 diabetes mellitus (T2DM) is accompanied by metabolic dysregulation and chronic low-grade inflammation. Routine complete blood count (CBC) parameters and derived inflammatory ratios may provide accessible complementary indicators of this inflammatory state. **Methods:** This retrospective study included 161 patients with T2DM attending the diabetes clinic at Al-Zahra General Hospital. Patients were classified as controlled (HbA1c <7%; n=69) or uncontrolled (HbA1c ≥7%; n=92). CBC and HbA1c obtained during the same visit were analyzed. NLR and MLR were calculated. Mann–Whitney U, two-way ANOVA, correlation, linear regression, logistic regression, and ROC analyses were performed. Results**:** WBC, neutrophils, lymphocytes, monocytes, NLR, and MLR were significantly higher in the uncontrolled group (all $p<0.001$). HbA1c correlated strongly with WBC ($r=0.776$) and neutrophils ($r=0.769$). Linear regression explained 66.1% of HbA1c variance, with WBC as the strongest independent predictor ($\beta=1.463$, $p<0.001$). Logistic regression identified WBC (OR=24.41; 95% CI 5.53–107.65) and NLR (OR=7.41; 95% CI 2.14–25.62) as independent predictors. AUCs were 0.884 for neutrophils, 0.873 for WBC, and 0.768 for NLR. **Conclusion:** Poor glycemic control was consistently associated with higher CBC-derived inflammatory markers. WBC, neutrophils, and NLR may provide useful complementary information, although prospective external validation is required.

Keywords: Type 2 diabetes mellitus; HbA1c; complete blood count; inflammation; neutrophil-to-lymphocyte ratio; monocyte-to-lymphocyte ratio; glycemic control.

Introduction

Type 2 diabetes mellitus (T2DM) is a major chronic metabolic disorder characterized by insulin resistance, progressive impairment of pancreatic β-cell function, and persistent hyperglycemia. Its clinical burden extends beyond abnormal glucose metabolism and includes vascular, oxidative, immune, and inflammatory disturbances. [1,2]

Chronic low-grade inflammation is increasingly recognized as an important component of T2DM pathophysiology. Hyperglycemia, oxidative stress, advanced glycation, endothelial dysfunction, and metabolic stress can activate innate immune pathways and inflammatory signaling. At the same time, inflammatory processes may interfere with insulin signaling and contribute to worsening insulin resistance, creating a potentially bidirectional relationship between metabolic dysfunction and inflammation. [1,4]

Circulating leukocytes are readily measurable indicators that may reflect systemic inflammatory activity. WBC count is inexpensive and routinely available, while differential leukocyte counts provide additional information about neutrophils, lymphocytes, and monocytes, which participate in distinct but interconnected components of the immune response. [5,7]

The neutrophil-to-lymphocyte ratio (NLR) integrates two major leukocyte populations and has been proposed as a simple marker of systemic inflammatory balance. The monocyte-to-lymphocyte ratio (MLR) similarly combines information from monocytes and lymphocytes. Their attraction in routine clinical research is that they can be calculated from an ordinary CBC without additional specialized assays.[5,10]

HbA1c is an established measure of longer-term glycemic exposure and is central to monitoring diabetes control. A value below 7% is commonly used as a conventional treatment target for many adults, although individualized targets are appropriate according to clinical circumstances. Investigating whether routine hematological indices vary systematically with HbA1c may therefore clarify whether they can provide useful complementary information about metabolic-inflammatory status. [10,11]

Previous investigations have reported relationships between leukocyte counts, NLR, MLR, insulin resistance,

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diabetes, and diabetic complications. Nevertheless, the magnitude and clinical relevance of these associations may differ across populations because leukocyte parameters are also influenced by infection, smoking, medications, age, comorbid disease, and other factors. A statistically significant association should therefore not automatically be interpreted as a causal relationship or as evidence that a CBC marker can replace HbA1c.[5,10]

This issue may be particularly relevant in resource-limited clinical settings, where CBC testing is commonly available whereas specialized inflammatory biomarkers may not be. If routine hematological parameters reliably identify patients with poorer glycemic control, they could serve as inexpensive adjunctive indicators and potentially support prioritization for closer metabolic assessment.

The present study aimed to evaluate the association between CBC-derived inflammatory markers and glycemic control in patients with T2DM. Specifically, we compared hematological parameters between controlled and uncontrolled groups, examined their correlations with HbA1c, identified independent predictors using linear and logistic regression, and evaluated discriminatory performance using ROC analysis.[11,14]

Materials and Methods

Study design and setting

A retrospective observational study was conducted at the diabetes clinic within the outpatient department of Al-Zahra General Hospital.

Study population

The study included 161 patients with T2DM. The controlled group (HbA1c <7.0%) comprised 69 patients (36 males and 33 females), while the uncontrolled group (HbA1c ≥7.0%) comprised 92 patients (46 males and 46 females). Overall, 82 participants were male and 79 were female.

Inclusion and exclusion criteria

Patients with diagnosed T2DM and complete records containing HbA1c and CBC measurements obtained concurrently during the same clinical visit were eligible. Exclusion criteria included acute infection, pre-existing hematological disorders such as anemia, systemic corticosteroid therapy, active smoking, and age below 30 years. These criteria were intended to minimize major non-diabetic influences on leukocyte counts.

Laboratory measurements

CBC parameters were obtained from routine clinical laboratory analyses using a Sysmex automated hematology analyzer. HbA1c was measured using a Cobas Integra analyzer. The evaluated variables included WBC and absolute neutrophil, lymphocyte, and monocyte counts.

Calculation of inflammatory indices

NLR was calculated as absolute neutrophil count divided by absolute lymphocyte count. MLR was calculated as absolute monocyte count divided by absolute lymphocyte count.

Definition of glycemic control

Participants were categorized as controlled when HbA1c was <7.0% and uncontrolled when HbA1c was ≥7.0%. This categorization was used for group comparisons and binary logistic regression.

Statistical analysis

Analyses were performed using IBM SPSS Statistics version 26. Continuous variables were summarized as mean ± standard deviation. The Mann–Whitney U test was used for between-group comparisons because the data were reported as non-normally distributed. Two-way ANOVA assessed sex, glycemic-status effects, and their interaction. Pearson and Spearman correlations assessed relationships with HbA1c. Multiple linear regression identified independent variables associated with HbA1c, while binary logistic regression assessed predictors of uncontrolled glycemic status. ROC curves and AUC were used to evaluate discriminatory performance, with exploratory cut-offs determined by the Youden index. Statistical significance was set at $p<0.05$.

Results

Study population and group comparison

Of the 161 patients, 69 (42.9%) had controlled glycemic status and 92 (57.1%) had uncontrolled glycemic status. The study population was relatively balanced by sex (82 males and 79 females).

Table 1: Study population and group comparison

Parameter	Controlled <7%	Uncontrolled ≥7%	p
WBC (×10³/L)	6.48 ± 0.54	7.98 ± 1.24	<0.001
Neutrophils (×10³/L)	3.65 ± 0.43	4.92 ± 1.05	<0.001
Lymphocytes (×10³/L)	2.09 ± 0.24	2.31 ± 0.38	<0.001
Monocytes (×10³/L)	0.38 ± 0.06	0.47 ± 0.10	<0.001
NLR	1.75 ± 0.21	2.17 ± 0.51	<0.001
MLR	0.18 ± 0.03	0.21 ± 0.05	<0.001

All evaluated parameters were significantly higher in the uncontrolled group. The most prominent differences were observed in WBC and absolute neutrophil counts.

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Table 2:Sex-related analysis

Variable	Male	Female	Sex p	Status p	Interaction p
HbA1c (%)	7.96 ± 1.74	8.13 ± 2.34	0.633	<0.001	0.402
WBC	7.50 ± 1.27	7.16 ± 1.22	0.019	<0.001	0.673
Neutrophils	4.50 ± 1.10	4.25 ± 0.99	0.034	<0.001	0.502
MLR	0.20 ± 0.05	0.19 ± 0.04	0.086	<0.001	0.192
NLR	2.06 ± 0.48	1.92 ± 0.43	0.016	<0.001	0.643

Glycemic status had a significant effect on all reported variables. WBC, neutrophils, and NLR also showed significant sex effects. No sex-by-glycemic-status interaction was statistically significant.

Table 3: Correlation with HbA1c

Variable	Pearson r	Spearman rho	p
WBC	0.776	0.767	<0.001
Neutrophils	0.769	0.787	<0.001
Lymphocytes	0.364	0.423	<0.001
Monocytes	0.591	0.571	<0.001
NLR	0.561	0.578	<0.001
MLR	0.359	0.412	<0.001

All markers showed positive, statistically significant associations with HbA1c. WBC and absolute neutrophils demonstrated the strongest correlations.

Table 4: Multiple linear regression

Predictor	Coefficient	95% CI	p
Age	-0.016	-0.247 to 0.214	0.888
Female sex	0.623	0.200 to 1.046	0.004
WBC	1.463	0.958 to 1.968	<0.001
NLR	0.245	-0.168 to 0.657	0.243
MLR	-0.124	-0.420 to 0.171	0.406

The model explained 66.1% of HbA1c variance (adjusted R^2=64.3%). WBC was the strongest independent predictor; female sex also remained significant. NLR and MLR were not independently significant in this model.

Table5: Binary logistic regression

Predictor	OR	95% CI	p
Female sex	3.82	1.18–12.33	0.025
WBC	24.41	5.53–107.65	<0.001
NLR	7.41	2.14–25.62	0.002
MLR	0.62	0.29–1.29	0.200

The logistic model was significant (pseudo-R^2=46.6%; likelihood-ratio p<0.001). WBC and NLR were independent predictors of uncontrolled glycemic status.

Table6: ROC analysis

Marker	AUC	Exploratory cut-off
Absolute neutrophils	0.884	>4.16 ×10³/L
WBC	0.873	>7.30 ×10³/L
NLR	0.768	Not reported

Absolute neutrophil count showed the highest reported discriminatory performance, followed by WBC. NLR showed moderate discriminatory ability. The reported cut-offs are exploratory and require external validation.

Discussion

The principal finding of this study was a consistent association between poor glycemic control and elevated leukocyte and derived inflammatory indices. Patients with HbA1c ≥7% had significantly higher WBC, neutrophil, lymphocyte, monocyte, NLR, and MLR values than those with HbA1c <7%. The consistency across several markers supports an association between glycemic dysregulation and systemic inflammatory activity in this cohort.[5,8]

WBC demonstrated the strongest relationship with HbA1c, with Pearson r=0.776 and Spearman rho=0.767, both p<0.001. This indicates that higher HbA1c values tended to occur with higher WBC counts. Importantly, WBC remained independently associated with HbA1c in the multivariable linear model, suggesting that the observed relationship was not explained solely by age, sex, NLR, or MLR included in that model. [10,11]

Absolute neutrophils showed similarly strong correlations with HbA1c (Pearson r=0.769; Spearman rho=0.787).

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Neutrophils are major innate immune cells, and their elevation may reflect inflammatory activation accompanying metabolic stress. However, the retrospective observational design prevents determining the direction of causality. Hyperglycemia may promote inflammatory activation, inflammation may contribute to metabolic dysfunction, or both processes may coexist. [11,13]

NLR and MLR were also significantly higher among patients with poor glycemic control. NLR increased from 1.75 to 2.17 and MLR from 0.18 to 0.21. These indices are attractive because they can be calculated from routine CBC results and do not require additional specialized assays. Nevertheless, their interpretation remains sensitive to changes in the component cell counts and to non-diabetic inflammatory conditions. [12,14]

An important finding was the difference between the linear and logistic regression results. NLR correlated with HbA1c and independently predicted the categorical outcome of uncontrolled glycemic status, but it was not independently significant when HbA1c was modeled as a continuous outcome. This distinction is methodologically important because the two models address different questions: linear regression evaluates variation in HbA1c, whereas logistic regression estimates association with the probability of being in the uncontrolled category.13,14]

The ROC analysis provided further evidence that absolute neutrophils and WBC may have useful discriminatory properties. The AUC of 0.884 for neutrophils and 0.873 for WBC indicates strong discrimination within the study sample, whereas the AUC of 0.768 for NLR indicates moderate discrimination. These results suggest that absolute leukocyte measures may perform at least as well as, or better than, composite ratios in this population.[14]

The sex analysis showed significant sex effects for WBC, neutrophils, and NLR, but no significant sex-by-glycemic-status interactions. Thus, although some hematological values differed between males and females, the data did not demonstrate evidence that sex substantially modified the association between glycemic status and these markers. Female sex remained significant in both regression models and should therefore be considered in interpretation, while recognizing that the study was not primarily designed to investigate sex-specific mechanisms.

Biologically, several mechanisms could explain the observed associations. Chronic hyperglycemia can promote oxidative stress, advanced glycation, endothelial dysfunction, and inflammatory signaling. These processes may influence leukocyte production, activation, and trafficking. Conversely, inflammatory cytokines and innate immune activation can impair insulin signaling and contribute to insulin resistance. The present findings are compatible with this bidirectional model but do not prove it.The practical value of these findings is related to accessibility. CBC testing is commonly available and relatively inexpensive, making WBC, neutrophil count, and calculated NLR potentially useful adjunctive measures in settings where specialized inflammatory biomarkers are not routinely available. They should, however, be interpreted as complementary indicators rather than replacements for HbA1c or comprehensive clinical assessment.

Several limitations should be considered. First, the retrospective single-center design limits causal inference and generalizability. Second, the sample size was modest. Third, the ROC cut-offs were derived and evaluated in the same cohort, which can result in optimistic estimates of performance. Finally, the available analysis does not establish whether the associations remain after adjustment for all clinically relevant confounders such as body mass index, diabetes duration, treatment regimen, renal function, cardiovascular disease, and other inflammatory conditions. Future studies should use larger prospective multicenter cohorts, include comprehensive clinical covariates, and perform external validation of predictive models and cut-off values. Such studies could determine whether CBC-derived markers provide incremental predictive value beyond HbA1c and standard clinical variables.

Strengths and Limitations

Strengths include concurrent CBC and HbA1c measurements from the same clinical visit, evaluation of both absolute leukocyte counts and derived inflammatory ratios, and use of complementary comparative, correlational, regression, and ROC analyses. The main limitations are the retrospective single-center design, modest sample size, incomplete control of potential confounders, and absence of external validation.

Conclusion

Poor glycemic control in patients with T2DM was associated with significant elevations in WBC, neutrophils, lymphocytes, monocytes, NLR, and MLR. WBC and absolute neutrophils showed the strongest correlations with HbA1c and the highest reported discriminatory performance, while NLR was independently associated with uncontrolled glycemic status in logistic regression.

These findings indicate that routinely available CBC-derived measures may provide useful complementary information about the metabolic-inflammatory profile of patients with T2DM, particularly in resource-limited settings. However, they should not replace HbA1c or established clinical evaluation. Larger prospective multicenter studies with external validation are needed

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before specific CBC-based thresholds can be recommended for clinical decision-making.

Declarations

Ethics approval and consent to participate

The supplied study material does not provide a verified ethics committee approval number or institutional ethics statement. This information must be inserted from the original institutional records before submission.

Consent for publication

To be completed according to the institutional ethics decision and target-journal requirements.

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Competing interests

A verified conflict-of-interest declaration should be provided by all authors before submission.

Data availability

A data-availability statement should be added according to institutional policy and the target journal's requirements.

Author contributions

Author names and individual contributions were not provided in the supplied material and should be completed before submission.

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