



Original Article

Sex Differences and Glycemic-Control Effects on Routine Hematological Inflammatory Markers in Adolescents with Type 2 Diabetes: A Secondary Analysis

AbdulHakem AI-Tawil¹, Abdurrahman.M. Bakkar², Mabroukah Abdullah Al-Rateeb¹

¹. Department of Biotechnology, College of Health Sciences, University of Al-Jafara

². Faculty of Medicine, University of Zawia

Corresponding author: AbdulHakem AI- Tawil: hakeemtawil1990@gmail.com

Received:11-09-2026-Accepted: 20-10-2026 -Published: 27-10-2026

Abstract

Background: Type 2 diabetes mellitus (T2DM) is associated with low-grade inflammation, and routine complete blood count (CBC) measures may provide accessible indicators of this process. Whether the association between glycemic control and selected hematological markers differs by sex is a clinically relevant question. **Objective:** To describe sex-related differences in CBC-derived inflammatory markers and assess whether sex modifies the association between glycemic-control status and these markers in adolescents with T2DM. **Methods:** This secondary analysis uses the summary results reported for 161 adolescents with T2DM attending Al-Zahra General Hospital. Patients were categorized as having controlled HbA1c ($<7\%$; $n=69$) or uncontrolled HbA1c ($\geq 7\%$; $n=92$). The source report included two-way analyses of variance for sex, glycemic-control status, and their interaction. No patient-level dataset was available for re-analysis. **Results:** The source report found higher mean WBC count, absolute neutrophil count, and NLR in males than females (sex-effect $p=0.019$, $p=0.034$, and $p=0.016$, respectively). The sex effect was not statistically significant for HbA1c ($p=0.633$) or MLR ($p=0.086$). Glycemic-control status was associated with all listed hematological markers (reported $p<0.001$). No sex-by-glycemic-status interaction was statistically significant for the listed outcomes (interaction p -values 0.192–0.673 for the hematological variables shown, and 0.402 for HbA1c). **Conclusion:** In the reported cohort, some CBC measures differed by sex, while the association between glycemic-control category and hematological markers appeared broadly similar in males and females. These findings are exploratory and do not establish causality or clinical diagnostic utility. Confirmation requires access to patient-level data, full model diagnostics, and external validation.

Keywords Type 2 diabetes mellitus; sex differences; glycemic control; complete blood count; neutrophils; neutrophil-to-lymphocyte ratio; monocyte-to-lymphocyte ratio; secondary analysis

Introduction

Type 2 diabetes mellitus is a metabolic disorder in which chronic hyperglycemia and low-grade inflammation may coexist and reinforce one another. Inflammatory signaling, oxidative stress, and altered immune-cell activity have been implicated in the pathophysiology of diabetes and its complications [1,2]. Although cytokines and high-sensitivity inflammatory assays can provide additional information, they may not be routinely available in every clinical setting.

Complete blood count (CBC) parameters are widely measured in routine care. Total white blood cell (WBC) and absolute neutrophil counts, together with ratios such as the neutrophil-to-lymphocyte ratio (NLR) and monocyte-to-lymphocyte ratio (MLR), have therefore been investigated as accessible correlates of inflammatory status. Previous work has examined associations between NLR and glycemic control, including a systematic review and meta-analysis [3], and studies comparing controlled and uncontrolled T2DM have reported differences in inflammatory ratios [4].

Sex may be relevant when interpreting hematological measures because leukocyte dis

tributions can differ between males and females. However, a difference between sexes is not the same as evidence that the relationship between glycemic control and a marker differs by sex. The latter question is tested by an interaction term between sex and glycemic-control status. The present secondary analysis focuses on this distinction using the sex-stratified and two-way analysis results already reported in the source document.

Aim and research questions

The aim was to examine (1) whether selected CBC-derived markers differ between males and females in the reported T2DM cohort, and (2) whether sex modifies the association between glycemic-control status and these markers. The analysis is descriptive and secondary; it does not introduce new patient-level calculations.

Materials and Methods

Study design and population

The source study was described as a retrospective study conducted at the diabetes clinic of Al-Zahra General Hospital. The reported cohort included 161 adolescents with T2DM: 82 males and 79 females. According to the source document, 69 patients were in the controlled group (HbA1c $<7\%$; 36 males and 33 females) and 92 were in the





uncontrolled group (HbA1c $\geq 7\%$; 46 males and 46 females).

Measures

The source document reported HbA1c, total WBC count, absolute neutrophil, lymphocyte and monocyte counts, NLR, and MLR. CBC measurements were reported to have been performed using a Sysmex automated hematology analyzer and HbA1c using a Cobas Integra analyzer. NLR and MLR were calculated as neutrophil-to-lymphocyte and monocyte-to-lymphocyte ratios, respectively.

Statistical approach available for this secondary analysis

The manuscript uses the summary statistics and p-values reported in the source document, particularly the two-way analysis of variance results for sex, glycemic-control status, and the sex-by-status interaction. Because the underlying patient-level dataset was not supplied, we could not independently reproduce the analyses, check assumptions, or recalculate confidence intervals or additional effect sizes. The original report states that $p < 0.05$ was considered statistically significant.

Ethics and data governance

The source document supplied for this draft did not provide a clearly identifiable ethics committee name, approval

number, or consent waiver. These details must be obtained from the investigators and added before journal submission; they must not be inferred or invented.

Results

The reported sample comprised 161 patients, including 82 males (50.9%) and 79 females (49.1%). The controlled group comprised 69 patients (42.9%), and the uncontrolled group comprised 92 patients (57.1%). These percentages are calculated directly from the sample counts reported in the source document.

Sex-related differences

The source report described higher mean WBC and absolute neutrophil counts among males than females. The reported WBC means were $7.50 \pm 1.27 \times 10^3/L$ in males and $7.16 \pm 1.22 \times 10^3/L$ in females (sex-effect $p=0.019$). Absolute neutrophil counts were $4.50 \pm 1.10 \times 10^3/L$ in males and $4.25 \pm 0.99 \times 10^3/L$ in females ($p=0.034$). NLR was also higher in males (2.06 ± 0.48) than in females (1.92 ± 0.43 ; $p=0.016$). The sex effect was not statistically significant for HbA1c ($7.96 \pm 1.74\%$ in males versus $8.13 \pm 2.34\%$ in females; $p=0.633$) or MLR (0.20 ± 0.05 versus 0.19 ± 0.04 ; $p=0.086$).

Table 1. Sex-stratified summary values and sex-effect p-values as reported in the source document. Values are mean $\pm$ SD. These are reproduced from the source, not recalculated from raw data.

Variable	Male (n=82)	Female (n=79)	Sex-effect p-value
HbA1c (%)	7.96 ± 1.74	8.13 ± 2.34	0.633
WBC ($\times 10^3/L$)	7.50 ± 1.27	7.16 ± 1.22	0.019
Absolute neutrophils ($\times 10^3/L$)	4.50 ± 1.10	4.25 ± 0.99	0.034
MLR	0.20 ± 0.05	0.19 ± 0.04	0.086
NLR	2.06 ± 0.48	1.92 ± 0.43	0.016

Glycemic-control status and interaction with sex

The source document reported statistically significant main effects of glycemic-control status for HbA1c and the hematological variables listed in its two-way analysis (reported $p < 0.001$ for WBC, absolute neutrophils, MLR, NLR, and the glycemic-status effect). However, the sex-by-glycemic-status interaction was not statistically significant for the reported outcomes: HbA1c, $p=0.402$; WBC, $p=0.673$; absolute neutrophils, $p=0.502$; MLR, $p=0.192$; and NLR, $p=0.643$. Thus, the available results do not show statistical evidence that the association between glycemic-control category and these measures differs by sex.

Discussion

This secondary analysis highlights an important interpretive distinction: sex-related differences in the average level of a hematological marker do not necessarily mean that sex modifies the marker's relationship with

glycemic control. In the reported cohort, male participants had higher mean WBC, absolute neutrophil, and NLR values, while no statistically significant sex effect was reported for HbA1c or MLR. At the same time, the reported interaction tests were not statistically significant, suggesting that the observed association between glycemic-control status and these markers was broadly parallel across sexes in this sample.

The findings are compatible with the wider literature investigating CBC-derived indices as correlates of inflammatory activity in T2DM. Adane et al. [3] synthesized evidence on NLR and glycemic control, while Dayama et al. [4] examined HbA1c and inflammatory markers in controlled and uncontrolled T2DM. The present report should not be interpreted as independently confirming those studies; rather, it offers a focused interpretation of the sex-stratified results already present in the source dataset. Several cautions are necessary. First,



non-significant interaction tests do not prove equivalence between sexes; the sample may lack power to detect modest interaction effects. Second, the source provides summary results rather than individual observations, preventing verification of model assumptions, assessment of outliers, and calculation of adjusted estimates beyond those already reported. Third, the supplied tables do not consistently provide confidence intervals for the sex effects. Fourth, this is a retrospective, single-hospital cohort and the results may not generalize to other settings. Finally, CBC-derived markers are nonspecific and can be influenced by factors beyond glycemic control. They should not be described as diagnostic replacements for HbA1c or as validated predictors of complications based on these data alone.

Strengths and limitations

Strengths include use of routinely collected laboratory measures, inclusion of both sexes, and explicit reporting of sex-by-glycemic-status interaction tests. Limitations include the retrospective design, single-centre sample, modest cohort size, lack of patient-level data for independent reanalysis, limited information about potential confounders, and incomplete reporting of ethics approval and confidence intervals in the supplied source. The present draft also reuses a cohort and analyses described in the source manuscript; its suitability as a separate publication depends on whether this constitutes a genuinely distinct, prespecified research question and whether the original work has been published or submitted elsewhere.

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Conclusion

In the reported cohort of adolescents with T2DM, males had higher mean WBC, absolute neutrophil, and NLR values than females, whereas sex differences in HbA1c and MLR were not statistically significant. No statistically significant sex-by-glycemic-control interaction was reported for the selected outcomes. These findings suggest that sex should be considered when describing baseline haematological variation, but the available data do not demonstrate that sex changes the relationship between glycemic-control status and these markers. Independent verification using patient-level data and external validation are required before drawing clinical conclusions.

Declarations requiring completion before submission

Ethics approval and consent/waiver: obtain the exact committee name, approval number, and consent status from the investigators.

Data availability: state whether de-identified patient-level data can be shared and under what conditions.

Funding and conflicts of interest: insert investigator-confirmed statements; do assume none.

Author contributions: confirm roles with all authors.

Prior dissemination: disclose any related thesis, manuscript, conference abstract, or publication using this cohort.

Statistical verification: ideally obtain the anonymised dataset and rerun the analyses before submission.

Funding

This research received no external funding.

Conflict Of Interest: The authors declare no competing interests.

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