ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 10, Issue – 4, July – 2025, Page No. : 137 – 143

Prospective Observational Study: Correlation between Type 2 Diabetes Mellitus and Hematological Indices

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Citation this Article: Dr. Pravinkumar F. Dungarwal, Dr. Vaishali M. Katkar, "Prospective Observational Study: Correlation between Type 2 Diabetes Mellitus and Hematological Indices", IJMSIR - July – 2025, Vol – 10, Issue - 4, P. No. 137 – 143.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background Information: Hematological changes and systemic inflammation are linked to Type 2 Diabetes Mellitus (T2DM), which may exacerbate its consequences. The purpose of this study was to look at the relationship between T2DM and several hematological parameters.

Techniques: 120 T2DM patients participated in an 18-month prospective observational research at a tertiary care institution. Fasting blood glucose (FBS), glycated hemoglobin (HbA1c), and an extensive panel of hematological markers were among the demographic, clinical, and hematological data gathered. Statistical analyses determined independent factors and evaluated relationships.

Results: Glycemic control parameters 36 (FBS and HbA1c) and total white blood cell count, neutrophil count, lymphocyte count, 7 neutrophil-to-lymphocyte ratio (NLR), red cell distribution width (RDW-CV), mean platelet volume (MPV), platelet distribution width (PDW), and platelet-to-lymphocyte ratio (PLR) were found to be significantly positively correlated. Hemoglobin, red blood cell count, and HbA1c were found to be negatively correlated. HbA1c was found to be an independent predictor of hemoglobin, MPV, NLR, and total white blood cell count using multivariate analysis.

Conclusion: elevated inflammatory 18 markers, platelet activation, and reduced hemoglobin levels are linked to poor glycemic control in type 2 diabetes. In T2DM 14 patients, tracking these hematological markers may help determine risk stratification and disease state.

Keywords: Platelet distribution width (PDW), red cell distribution width (RDW-CV), neutrophil-to-lymphocyte ratio (NLR), type 2 diabetes mellitus (T2DM)

Introduction

Type 2 Diabetes Mellitus (T2DM) poses a major global public health concern, contributing significantly to both microvascular and macrovascular complications that increase morbidity and mortality. Systemic low-grade chronic inflammation plays a critical role in the

development and progression of diabetes and its associated complications.

Atherosclerosis, a primary pathology underlying macrovascular complications, is now recognized as a chronic inflammatory condition. Inflammatory cells participate in plaque formation, progression, and rupture, ultimately precipitating cardiovascular events. Similarly, inflammation contributes to the pathogenesis of microvascular complications in diabetes. Blood leukocytes, in particular, are central to vascular damage, atherogenesis, and plaque destabilization, culminating in atherothrombotic events.

India currently ranks second globally in terms of diabetes prevalence, with approximately 77 million people affected—a number expected to reach 134 million by 2045. Alarmingly, a significant proportion of the population, including youth, is either prediabetic or at high risk of developing diabetes.

Despite the known impact of inflammation in T2DM, routine monitoring of hematological parameters is not currently recommended in standard guidelines. Diabetes, characterized by persistent hyperglycemia, triggers various biochemical and cellular alterations, including oxidative stress and the formation of advanced glycation end products (AGEs), leading to endothelial dysfunction. These changes result in hematological disturbances such as red blood cell (RBC) abnormalities, platelet hyperactivity, and compromised immune cell function.

Insulin resistance and chronic hyperglycemia are linked with elevated white blood cell counts, increasing the likelihood of vascular complications. Alterations in hematological indices—including red cell parameters, white cell counts, and platelet metrics—may manifest as anemia, immune dysregulation, and pro-thrombotic states. Notably, reductions in RBC count, hemoglobin (Hb), and hematocrit (Hct) have been documented in T2DM patients compared to healthy individuals. Anemia, although common, is frequently underdiagnosed in this population.

This study aims to examine the correlation between glycemic control and hematological indices in T2DM patients, offering insights into potential biomarkers for disease monitoring and complication risk assessment.

Materials & Methods

Study Design and Participants

This prospective observational study was conducted over a period of 18 months at a tertiary care hospital. A total of 120 adult patients (≥18 years) with a confirmed diagnosis of T2DM were recruited consecutively.

Exclusion criteria included patients with pre-existing hematological disorders, acute infections, chronic inflammatory conditions unrelated to T2DM, malignancies, or those receiving medications such as chemotherapy or immunosuppressants that could influence hematological parameters.

Ethical approval was obtained from the Institutional Ethics Committee, and informed written consent was secured from all participants.

Data Collection

Participants were interviewed to collect demographic data (age, sex, body mass index), clinical history (duration of diabetes, existing complications, and current medications), and laboratory investigations. Fasting venous blood samples were collected after an overnight fast of at least 8 hours for analysis of glycemic markers (FBS, HbA1c) and hematological parameters.

Hematological Indices Measurement

Blood samples were collected using EDTA vacutainers and processed within 2 hours using a fully automated hematology analyzer (e.g., Sysmex XN-1000 or Mindray BC-6800). The following hematological indices were evaluated:

- Red Blood Cell (RBC) Parameters: Hemoglobin (Hb), RBC count, Hematocrit (Hct), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Red Cell Distribution Width (RDW-CV, RDW-SD)
- White Blood Cell (WBC) Parameters: Total WBC count, Neutrophils, Lymphocytes, Monocytes, Eosinophils, Basophils
- Platelet Parameters: Platelet count, Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), Plateletcrit (PCT), Platelet-Large Cell Ratio (P-LCR)

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS v26.0. Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), while categorical variables were presented as frequencies and percentages. Normality of distribution was assessed using the Shapiro-Wilk test. Correlation between glycemic markers and hematological indices was determined using Pearson's or Spearman's correlation coefficients, depending on data distribution. Independent t-tests or Mann-Whitney U tests were used for group comparisons. Multivariate linear regression was performed to identify independent predictors of hematological indices, adjusting for age, sex, and BMI. A p-value < 0.05 was considered statistically significant.

Results & Discussion

Table 1: Demographic and Clinical Characteristics

Characteristic	Mean ± SD / n (%)
Age (years)	58.5 ± 9.2
Male Sex	78 (65%)
Female Sex	42 (35%)
Duration of Diabetes (years)	8.3 ± 4.1
FBS (mg/dL)	158.7 ± 35.6
HbA1c (%)	8.1 ± 1.2

The demographic and clinical characteristics of the sample population, which included 120 individuals with type 2 diabetes mellitus (T2DM), were examined in this investigation. The average age of the twenty-six participants was 58.5 ± 9.2 years, and the majority of them were men (65% males, n = 78) as opposed to women (35%, n = 42). A moderately chronic diabetic population was indicated by the mean duration of diabetes, which was 8.3 ± 4.1 4 years. In terms of glycemic parameters, the majority of the 52 patients had inadequate glycemic control, as indicated by the mean glycated hemoglobin (HbA1c) level of 8.1 ± 1.2% and the mean fasting blood sugar (FBS) of 158.7 ± 35.6 mg/dL.

Table 2: Mean Values of Hematological Indices in T2DM Patients (n=120)

Hematological Index	Mean ± SD
Hemoglobin (g/dL)	12.8 ± 1.5
RBC (x10^12/L)	4.5 ± 0.6
Hct (%)	39.2 ± 4.8
MCV (fL)	87.5 ± 5.2
MCH (pg)	29.8 ± 2.1
MCHC (g/dL)	33.5 ± 1.1
RDW-CV (%)	15.8 ± 1.9
TWBC (x10^9/L)	9.5 ± 2.3
Neutrophils (x10^9/L)	6.2 ± 1.8
Lymphocytes (x10^9/L)	2.5 ± 0.7
Monocytes (x10^9/L)	0.6 ± 0.2
Eosinophils (x10^9/L)	0.1 ± 0.1
Basophils (x10^9/L)	0.05 ± 0.03
Platelet Count (x10^9/L)	280 ± 65
MPV (fL)	10.5 ± 1.2
PDW (%)	13.2 ± 1.5
PCT (%)	0.29 ± 0.07
NLR	2.48 ± 0.75
PLR	112.0 ± 25.0

The mean ± SD values of several hematological parameters among T2DM patients are shown in our study. The average red blood cell (RBC) count was 4.5 ± 0.6 $x10^{12}$/L, and the average hemoglobin content was 12.8 ± 1.5 g/dL. The mean corpuscular volume (MCV) was 87.5 ± 5.2 fL, the mean corpuscular hemoglobin (MCH) was 29.8 ± 2.1 pg, the mean corpuscular hemoglobin concentration (MCHC) was 33.5 ± 1.1 g/dL, and the hematocrit (Hct) was 39.2 ± 4.8%. At 15.8 ± 1.9%, the red cell distribution width-coefficient of variation (RDW-CV) was marginally higher. With neutrophils 7 6.2 ± 1.8 $x10^9$/L, lymphocytes 2.5 ± 0.7 $x10^9$/L, monocytes 0.6 ± 0.2 $x10^9$/L, eosinophils 0.1 ± 0.1 $x10^9$/L, and basophils 0.05 ± 0.03 $x10^9$/L, the total white blood cell count (TWBC) averaged 9.5 ± 2.3 $x10^9$/L.

The mean platelet volume (MPV) was 10.5 ± 1.2 fL, the platelet distribution width (PDW) was 13.2 ± 1.5%, the platelet count was 280 ± 65 $x10^9$/L, and the plateletcrit (PCT) was 0.29 ± 0.07%. Neutrophil-to-lymphocyte ratio (NLR) 28 and platelet-to-lymphocyte ratio (PLR) were inflammatory markers that were 2.48 ± 0.75 and 112.0 ± 25.0, respectively.

Table 3:

Hematological Index	FBS (r, p-value)	HbA1c (r, p-value)
TWBC	0.35, <0.001	0.32, <0.001
Neutrophils	0.30, 0.001	0.27, 0.003
Lymphocytes	0.28, 0.002	0.20, 0.025
NLR	0.40, <0.001	0.38, <0.001
Hemoglobin	-0.15, 0.090	-0.25, 0.006
RBC	-0.12, 0.180	-0.20, 0.028
RDW-CV	0.18, 0.045	0.22, 0.015
MPV	0.20, 0.025	0.18, 0.045
PDW	0.23, 0.012	0.15, 0.095
PLR	0.25, 0.008	0.22, 0.015

Correlation Analysis

The relationship between glycemic parameters (FBS and HbA1c) and hematological indices is shown by the Pearson correlation coefficients (r) and p-values. Both FBS (r=0.35, 13 p<0.001) and HbA1c (r=0.32, p<0.001) exhibited a strong positive connection with total WBC count (TWBC). Additionally, there was a favorable correlation between neutrophil counts and HbA1c (r=0.27, p=0.003) and FBS (r=0.30, p=0.001). There was a weaker but significant connection between lymphocyte counts and HbA1c (r=0.20, p=0.025) and FBS (r=0.28, 21 p=0.002). Strong positive 38 correlations were found between the NLR and FBS (r=0.40, p<0.001) and HbA1c (r=0.38, p<0.001). There were negative relationships between hemoglobin and RBC counts and HbA1c (r=-0.25, p=0.006 and r=-0.20, p=0.028, respectively). Significant positive associations were also found between RDW-CV, MPV, PDW, and PLR and glycemic indices (46; MPV correlated with FBS (r=0.20, p=0.025)HbA1c (r=0.18, p=0.045), and PLR correlated with FBS (r=0.25, p=0.008)HbA1c (r=0.22, p=0.015).

Multivariate Regression Analysis

HbA1c emerged as an independent predictor of:

- TWBC ($\beta = 0.45$, $p < 0.001$)
- MPV ($\beta = 0.28$, $p = 0.002$)
- NLR ($\beta = 0.35$, $p < 0.001$)
- Hemoglobin ($\beta = -0.30$, $p = 0.001$)

Discussion

This study demonstrates a significant relationship between glycemic control and several hematological indices in patients with Type 2 Diabetes Mellitus (T2DM). Our findings align with the growing body of evidence suggesting that T2DM is not only a metabolic disorder but also a chronic inflammatory condition with systemic hematological implications.

We observed positive correlations between FBS and HbA1c with total WBC count, neutrophils, and lymphocytes. Notably, the neutrophil-to-lymphocyte ratio (NLR)—a recognized marker of systemic inflammation—was significantly associated with both glycemic markers. These results are consistent with prior research, such as the study by Al-Dewachi et al., which

reported elevated WBC components in diabetic patients, positively correlated with blood glucose levels. This chronic low-grade inflammation characteristic of T2DM may stimulate increased leukocyte production and activation, thereby exacerbating vascular injury.

Red blood cell parameters also showed notable changes. Hemoglobin and RBC count were negatively correlated with HbA1c, suggesting a higher likelihood of anemia or impaired erythropoiesis in poorly controlled diabetics. These findings are supported by studies such as that of Ebrahim et al., which highlighted reductions in these parameters among diabetics. The pathophysiology may involve reduced RBC lifespan due to glycation, oxidative stress, or renal dysfunction, all of which are common in T2DM.

Additionally, we found RDW-CV to be positively associated with HbA1c, implying increased red cell size variability in patients with poor glycemic control. This may be attributable to oxidative stress and nutritional deficiencies, further emphasizing the inflammatory burden in T2DM. RDW is increasingly being recognized as a potential marker of systemic inflammation and cardiovascular risk.

Platelet indices such as MPV and PDW were elevated and showed significant positive correlations with FBS and HbA1c. PLR was also positively associated with both glycemic parameters. These results suggest that platelets in T2DM patients are larger and more reactive, supporting the notion of a prothrombotic state. Shahmoradi et al. and Zou et al. similarly identified elevated platelet indices in T2DM patients. Larger platelets are metabolically and enzymatically more active, which could increase the risk of thrombotic complications.

Multivariate analysis revealed that HbA1c independently predicted several key hematological indices, including TWBC, MPV, NLR, and hemoglobin, even after adjusting for confounders such as age, sex, and BMI. This highlights the direct role of glycemic status in modulating inflammation, erythropoiesis, and platelet activation in T2DM.

While our findings are consistent with the literature, it is important to recognize the limitations of our study. Being observational in design, causal relationships cannot be definitively established. Additionally, the study was conducted in a single tertiary care center, which may limit the generalizability of the results. Future multi-center studies with larger, more diverse populations and longitudinal follow-up are warranted to validate these findings and explore their prognostic utility.

Conclusion

This study underscores the strong correlation between glycemic control and a range of hematological indices in patients with Type 2 Diabetes Mellitus. Elevated inflammatory markers such as TWBC, NLR, and PLR, along with increased platelet activity (MPV, PDW), were associated with poor glycemic control. Concurrently, reductions in hemoglobin and RBC count point toward an increased risk of anemia.

These hematological parameters, which are routinely available and cost-effective, could serve as valuable tools in monitoring disease progression and stratifying risk in T2DM patients. Incorporating these markers into routine clinical assessments may improve the management of diabetes and help predict complications earlier.

Further research is recommended to evaluate the potential of these indices as prognostic markers and therapeutic targets in the management of Type 2 Diabetes Mellitus.

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