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Original Research Article

Assessment of Alterations in Red Blood Cell Indices, Platelet Indices, and White Blood Cell Counts in Patients with Long-Standing Type 2 Diabetes Mellitus: A Case-Control Study

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Abstract

Background: Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder associated with persistent hyperglycemia and systemic complications. This study evaluated alterations in red blood cell (RBC) indices, platelet indices, and white blood cell (WBC) counts in patients with T2DM of more than 10 years' duration compared to healthy controls.

Methods: This case-control study was conducted over an 18-month period at a tertiary healthcare center in Northern India. A total of 272 patients with long-standing T2DM (>10 years post-diagnosis) and 272 age- and sex-matched healthy controls were enrolled. Complete blood counts and glycemic profiles (HbA1c and fasting plasma glucose) were analyzed. Statistical analysis was executed using SPSS version 24.0.

Results: The study included 272 diabetic patients and 272 controls, mostly aged 40–60 years. Gender distribution differed significantly between groups ($p = 0.002$). Obesity was more common among diabetics with higher BMI ($p < 0.001$), along with poor glycaemic control. Significant haematological changes in diabetics included altered RBC count ($p = 0.03$), RDW ($p = 0.04$), platelet indices, PDW ($p = 0.002$) and MPV ($p = 0.004$) and abnormal WBC counts ($p = 0.036$). Overall, long-standing diabetes was associated with obesity, hyperglycaemia, and significant blood cell alterations.

Conclusion: Long-standing T2DM is strongly associated with distinct modifications in hematological profiles. The statistical elevations in RDW, MPV, PDW, and leukocyte abnormalities highlight ongoing subtle red cell structural fragility, enhanced thrombotic platelet activation, and sustained low-grade systemic inflammation. Routine monitoring of these simple hematological markers can serve as reliable indicators to gauge cellular risk and prevent vascular complications.

Keywords: Type 2 diabetes mellitus, Red blood cell indices, Red cell distribution width (RDW), Mean platelet volume (MPV), Low-grade inflammation, and Hematological markers.

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Introduction

Diabetes mellitus (DM) is an escalating global metabolic pandemic characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. [1,2] The International Diabetes Federation (IDF) estimated that India alone harbored 77 million diabetic individuals in 2019, a number projected to expand to 134 million by 2045.

Type 2 diabetes mellitus (T2DM) represents approximately 90% of these cases and drives extensive macrovascular and microvascular pathology. [4,5] While traditional research extensively captures diabetic nephropathy, retinopathy, and neuropathy, modern hematology has turned its focus toward the subtle structural, biochemical, and morphologic changes occurring within circulating blood cell lines. [6,7] Red blood cells (RBCs) undergo chronic morphological and functional remodeling when exposed to a persistent hyperglycemic milieu.

High blood glucose levels cause irreversible, non-enzymatic glycation of hemoglobin and membrane proteins, which fundamentally alters erythrocyte deformability, reduces lifespan, and accelerates

mechanical fragility via reactive oxygen species (ROS). These red cell shifts are clinically measured using indices such as Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), and Red Cell Distribution Width (RDW). [8,9]

Simultaneously, insulin resistance and metabolic distress alter bone marrow erythropoiesis and drive a state of chronic, low-grade systemic inflammation marked by elevated pro-inflammatory cytokines (e.g., IL-6, TNF-alpha). This inflammatory state not only suppresses standard erythropoiesis but also activates white blood cells (WBCs) and changes homeostatic platelet dynamics, shifting parameters like Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW).[10, 11]

Although studies have separately touched upon individual hematological markers, consolidated literature looking comprehensively at patients with prolonged disease duration (exceeding 10 years) remains minimal. Therefore, this case-control study designed a comprehensive evaluation of red cell indices, leukocyte counts, and platelet parameters in patients surviving with type 2 diabetes mellitus for over a decade.

Materials and Methods

Study Design and Setting: This case-control clinical study was conducted over a continuous period of 18 months at F.H. Medical College and Hospital, Agra, India. Institutional Ethics Committee approval was formally obtained, and written informed consent was acquired from all participants prior to study initialization.

Sample Size Estimation: The sample size was calculated based on baseline outcome differences reported in antecedent comparative medical literature. To detect a statistically validated difference at an 80% statistical power and a 95% confidence interval, the minimum enrollment criteria was 247 individuals per arm. Adjusting for a potential 10% dropout rate, the final cohort was set at 272 diabetic patients and 272 age- and sex-matched healthy controls (Total N = 544).

Inclusion and Exclusion Criteria:

Inclusion Criteria (Study Group): Patients confirmed with a documented clinical diagnosis of T2DM for a duration exceeding 10 years.

Inclusion Criteria (Control Group): Age- and sex-matched healthy individuals presenting with normal glycemic levels and no history of diabetes.

Exclusion Criteria (Both Groups): Individuals diagnosed with nutritional anemias, inherited hemoglobinopathies, bleeding disorders, chronic renal disease, chronic liver failure, malignancies, or active infectious states (such as HIV, HBV, HCV). Chronic smokers, alcohol consumers, pregnant women, and women of childbearing age were also excluded to eliminate external confounding factors impacting baseline hematopoietic parameters.

Methodology

Structured clinical and sociodemographic questionnaires were documented for each subject. Following an overnight fast, 5 mL of venous blood was drawn via aseptic venipuncture by expert personnel. Samples were distributed into evacuated tubes containing ethylenediaminetetraacetic acid (EDTA) for hematological profiling and sodium fluoride tubes for fasting plasma glucose analysis. Glycemic indexing included automated Fasting Plasma Glucose (FPG) quantification and Glycated Hemoglobin (HbA1c) profiling. Complete automated blood counts—comprising Red Blood Cell Count, Hemoglobin (Hb), Hematocrit/Packed Cell Volume (PCV), MCV, MCH, MCHC, RDW, Total White Blood Cell Count, Platelet Count, MPV, and PDW—were processed within 2 hours of collection via verified automated hematology analyzers.

Statistical Analysis: Data analysis was performed using SPSS software (Version 24.0). Continuous metrics are presented as Mean pm Standard Deviation (SD), and categorical clinical variables are depicted as frequencies and percentages. Two-tailed independent student t-tests evaluated differences between continuous variables, while Chi-square tests were utilized for categorical datasets. A p-value of <0.05 was designated as the threshold for statistical significance.

Results

Demographic and Baseline Clinical Anthropometrics: The final study analysis encompassed 272 diabetic patients and 272 matched healthy controls. The average age distribution was well-matched across both cohorts ($p = 0.29$). However, distinct variations were noted in gender distributions ($p = 0.002$) due to a higher prevalence of female participants in the diabetic study group. The body mass index (BMI) showed a stark statistical difference between the groups ($\chi^2 = 42.8$, $p < 0.001$). Overweight and obesity classes were heavily prominent within the diabetic group, with aThe mean BMI was also significantly higher in the study group (31.2 ± 6.4 kg/m²) compared to controls (27.4 ± 5.8 kg/m², $p < 0.001$), indicating a greater burden of obesity among the study population.

The mean HbA1c level in the study group was 7.44%, which was clearly higher than that of the control group (5.84%), indicating poor long-term glycaemic control among diabetic patients. Similarly, fasting plasma glucose levels were elevated in the study group (6.69mmol/L) compared

to controls (5.78mmol/L). The narrow confidence intervals suggest consistent findings within each group.

Red Blood Cell Indices Profile: Diabetic patients showed slightly lower mean haemoglobin levels (12.9 g/dL) and haematocrit values (38.7%) compared to controls (13.4 g/dL and 39.8%, respectively).

The red blood cell count was also marginally reduced in the study group. Mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC) were largely comparable between the two groups, indicating preserved red cell size and haemoglobin content. However, red cell distribution width (RDW) was marginally higher in diabetic patients (14.8% vs 14.6%), suggesting increased variability in red cell size.

However, critical shifts emerged when evaluating the frequencies of abnormal variances. Structurally abnormal RBC counts were significantly more frequent within the diabetic cohort (26.9% vs.10.2%, p = 0.03). Furthermore, Red Cell Distribution Width (RDW), reflecting size variation (anisocytosis), was significantly higher and more frequently abnormal in the diabetic group (28.7% abnormal vs. 17.0% in controls, p = 0.04$).

Table 1: Distribution of Red Blood Cell Indices, Categorized by Clinical Status

Parameter	Classification	Study Group (n = 272) (%)	Control Group (n = 272) (%)	p-value
Hemoglobin (Hb)	Normal Abnormal	220 (81.1%) 52 (18.9%)	216 (79.4%) 56 (20.6%)	0.58
Hematocrit (HCT)	Normal Abnormal	197 (72.5%) 79 (27.5%)	199 (73.1%) 73 (26.9%)	0.77
RBC Count	Normal Abnormal	199 (73.1%) 73 (26.9%)	244 (89.8%) 28 (10.2%)	0.03*
MCV	Normal Abnormal	197 (72.3%) 75 (27.7%)	193 (71.0%) 79 (29.0%)	0.11
MCH	Normal Abnormal	204 (75.0%) 68 (25.0%)	208 (76.5%) 64 (23.5%)	0.81
RDW	Normal Abnormal	194 (71.3%) 78 (28.7%)	226 (83.0%) 46 (17.0%)	0.04*

***Denotes statistical significance at p < 0.05$.**

Platelet Profile and Volumetric Indices: Total numerical platelet distribution counts remained within standard physiological limits for the vast majority of both populations, showing no broad statistical variance in terms of numerical absolute count (p = 0.13). However, platelet structural characteristics differed significantly. Platelet Distribution Width (PDW), a direct reflection of structural size variation, was significantly abnormal in 41.9% of the long-standing diabetic population compared to only 25.0% of controls (p = 0.002). Similarly, Mean Platelet Volume (MPV), a strong marker of young, reactive metabolic platelet turnover, was significantly abnormal in $39.3% of diabetic subjects compared to 25.4% in controls (p = 0.004).

Table 2: Comparative Distribution of Volumetric Platelet Indices

Parameter	Status	Study Group (n = 272) (%)	Control Group (n = 272) (%)	p-value
Platelet Count	Normal Abnormal	264 (97.1%) 8 (2.9%)	255 (93.8%) 17 (6.2%)	0.13
Platelet Distribution Width (PDW)	Normal Abnormal	158 (58.1%) 114 (41.9%)	204 (75.0%) 68 (25.0%)	0.002*
Mean Platelet Volume (MPV)	Normal Abnormal	165 (60.7%) 107 (39.3%)	203 (74.6%) 69 (25.4%)	0.004*

White Blood Cell Counts: Total White Blood Cell (WBC) testing indicated a strong upward trend in structural alterations. Abnormal WBC elevations were verified in 44.9% of the long-standing diabetic cohort, whereas only 22.8% of healthy controls exhibited values outside the normal reference boundaries. This difference was statistically significant ($p = 0.036$).

Discussion

The results of this case-control analysis show that while absolute hemoglobin and baseline erythrocytic volume properties (MCV, MCH) remain within standard physiological limits, patients with a history of T2DM for over 10 years' experience subtle but significant cellular deviations. The significant increase in abnormal RBC counts

and RDW confirms that chronic hyperglycemia drives morphological instability. Persistent blood glucose tracking leads to structural modifications via non-enzymatic glycation of erythrocyte membrane scaffolding. This leads to mechanical cell fragility, an increase in anisocytosis (size variation), and a reduction in red cell survival, which explains the high frequency of RDW abnormalities (28.7%) in our study group. [12,13]

Our findings align with observations by Arkew et al. (2022),[14] who reported lower average RBC indices paired with an elevated RDW in long-standing diabetic cohorts, confirming that size variation acts as a valid cellular proxy for glucose stress. In contrast, studies such as Basak et al. (2025)[15] observed severe decreases in absolute hemoglobin levels. This variation is likely due to our strict exclusion of active nutritional anemias and advanced chronic kidney disease, allowing us to accurately isolate pure diabetic metabolic stress on red cell structures.

Crucially, our study highlights that structural modifications extend to platelet and white blood cell lines. While total absolute platelet numbers remained stable, volumetric indices like MPV and PDW showed significant increases in abnormalities ($p = 0.004$ and $p = 0.002$, respectively). This aligns with findings by Biadgo et al. (2016),[16] who noted similar variations in volumetric profiles. An increased MPV indicates a high proportion of large, newly synthesized platelets released into circulation. These structurally larger platelets are metabolically reactive, exhibit increased enzymatic activity, produce more thromboxane A2, and show heightened hyper-aggregability. [17]

In patients with a disease duration exceeding 10 years, this structural change acts as a reliable marker for enhanced pro-thrombotic activation and vascular risk. The significant increase in total white blood cell abnormalities (44.9%, p = 0.036) further supports this mechanism. This alteration reflects the low-grade systemic inflammatory response driven by advanced glycation end-products (AGEs) and pro-inflammatory cytokines like IL-6 and TNF-alpha. This persistent low-grade immune activation affects the vascular endothelium and accelerates microvascular risks.

Ultimately, this study demonstrates that analyzing simple, low-cost parameters like RDW, MPV, and PDW within standard complete blood counts provides valuable clinical utility. For patients managing diabetes for over a decade, these volumetric markers offer insight into ongoing low-grade inflammation and vascular risks, allowing for earlier clinical intervention.

Conclusion

This study confirms that type 2 diabetes mellitus lasting longer than 10 years is associated with distinct changes in complete blood cell lines, even when absolute hemoglobin values are preserved. The significant variations in Red Cell Distribution Width (RDW), Mean Platelet Volume (MPV), and Platelet Distribution Width (PDW), alongside elevated leukocyte counts, highlight a state of persistent red cell fragility, increased platelet reactivity, and low-grade systemic inflammation.

Because these indices are automatically calculated during routine complete blood counts (CBC), they offer a cost-effective, accessible tool for clinical tracking. Regularly monitoring these volumetric trends alongside standard glycemic markers can help clinicians identify subtle cellular changes early, optimizing risk management and improving long-term outcomes for patients with advanced T2DM.

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