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ORIGINAL RESEARCH

To investigate the variation in platelet indices among patients with type 2 diabetes mellitus (T2DM)

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Abstract

Aim: The study aimed to investigate the variation in platelet indices among patients with type 2 diabetes mellitus (T2DM) compared to healthy controls and to understand the relationship between these indices, glycemic parameters, and inflammatory markers.

Materials and Methods: This cross-sectional observational study was conducted at the Department of Pathology, Government Medical College Srinagar, from 2021 to 2023. A total of 120 participants were divided into two groups: 60 T2DM patients and 60 healthy controls matched for age and sex. Data collection included demographic information, medical history, and laboratory assessments. Platelet indices, such as platelet count, mean platelet volume (MPV), platelet distribution width (PDW), and platelet-large cell ratio (P-LCR), were measured. Glycemic parameters included fasting blood glucose, postprandial blood glucose, and HbA1c. Inflammatory markers, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), along with hematologic parameters like white blood cell (WBC) count, hemoglobin level, and red cell distribution width (RDW), were also analyzed.

Results: The T2DM group had significantly higher platelet indices, including platelet count (250.34 x10^9/L vs. 220.12 x10^9/L, $p<0.001$), MPV (9.5 fL vs. 8.8 fL, $p<0.001$), PDW (15% vs. 13%, $p<0.001$), and P-LCR (20% vs. 17%, $p<0.001$), compared to controls. Glycemic parameters were elevated in the T2DM group, with fasting blood glucose (140 mg/dL vs. 90 mg/dL, $p<0.001$), postprandial glucose (180 mg/dL vs. 110 mg/dL, $p<0.001$), and HbA1c (7.5% vs. 5.5%, $p<0.001$). Inflammatory markers CRP (3.5 mg/L vs. 1.5 mg/L, $p<0.001$) and ESR (20 mm/hr vs. 10 mm/hr, $p<0.001$) were significantly higher in the T2DM group. Hematologic variations included elevated WBC count (8.0 x10^3/µL vs. 7.0 x10^3/µL, $p<0.001$) and RDW (14% vs. 12.5%, $p<0.001$), with slightly lower hemoglobin levels (13.5 g/dL vs. 14 g/dL, $p=0.005$).

Conclusion: This study reveals significant alterations in platelet indices among T2DM patients, indicating a heightened thrombotic and inflammatory state. These findings underscore the potential use of platelet indices as markers for early detection and management of vascular complications in diabetes. The interplay between glycemic control and inflammation further highlights the need for comprehensive management strategies.

Keywords: Type 2 diabetes mellitus, Platelet indices, Mean platelet volume, Glycemic control, Inflammation

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Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and relative insulin deficiency, leading to persistent hyperglycemia. It is one of the most prevalent non-communicable diseases globally and poses a significant burden on healthcare systems due to its association with severe complications, such as cardiovascular diseases, nephropathy, retinopathy, and neuropathy. The pathophysiology of T2DM is complex, involving a multifactorial interplay between genetic, environmental, and lifestyle factors, all contributing to impaired glucose metabolism and systemic inflammatory responses. Understanding the various hematologic alterations associated with T2DM is crucial for improving the clinical management and prognosis of affected patients.[1]One of the significant areas of research in T2DM is the examination of platelet indices, as these play a key role in the development and progression of vascular complications. Platelets are small, anucleate cells derived from megakaryocytes and are essential components of the hemostatic system. They contribute to thrombus formation and vascular repair and are actively involved in inflammatory processes. Alterations in platelet function and activation have been observed in patients with T2DM, which are believed to result from chronic hyperglycemia, oxidative stress, and systemic inflammation. These pathophysiological conditions create a pro-thrombotic and hyperactive platelet state, increasing the risk of vascular events in diabetic individuals.[2]Platelet indices, including platelet count, mean platelet volume (MPV), platelet distribution width (PDW), and platelet-large cell ratio (P-LCR), are widely used as markers to evaluate platelet activity and function. Platelet count provides a measure of the total number of circulating platelets, while MPV indicates the average size of the platelets. Larger platelets are more metabolically and enzymatically active and are typically associated with increased thrombotic potential. PDW is a measure of the variability in platelet size, reflecting the heterogeneity of platelet production and activation, while P-LCR represents the proportion of larger platelets in the circulation. Collectively, these indices provide insights into the dynamic changes occurring in platelet morphology and activity in various pathological states.[3]In patients with T2DM, chronic hyperglycemia and insulin resistance lead to endothelial dysfunction and increased production of pro-inflammatory cytokines, which, in turn, enhance platelet activation and aggregation. This hyperactive state of platelets contributes to the formation of atherosclerotic plaques and thrombotic events, which are major causes of morbidity and mortality in diabetic patients. The evaluation of platelet indices in T2DM is thus crucial for understanding the underlying mechanisms of vascular complications and for identifying potential therapeutic targets to mitigate these risks.Several mechanisms have been proposed to explain the alterations in platelet indices among T2DM patients. Hyperglycemia-induced oxidative stress results in the production of reactive oxygen species, which damage endothelial cells and activate platelets. Furthermore, insulin resistance affects platelet function by altering signaling pathways that regulate platelet activation and aggregation. The chronic inflammatory milieu in T2DM, characterized by elevated levels of cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP), further exacerbates platelet reactivity. This pro-inflammatory environment not only promotes platelet activation but also contributes to the heterogeneity in platelet size and function, as reflected by changes in MPV and PDW.[4,5]The assessment of platelet indices in T2DM patients has emerged as an area of significant interest, as these markers are readily measurable using automated hematologyanalyzers and provide valuable information on the thrombotic risk profile of patients. Studies have shown that elevated MPV and PDW are associated with increased cardiovascular risk in diabetic patients, suggesting their potential role as prognostic markers for vascular complications. Additionally, variations in platelet count and P-LCR have been linked to the severity of microvascular and macrovascular complications, further highlighting the importance of these indices in clinical

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practice.[6]Despite advancements in the understanding of platelet alterations in T2DM, there remains a need for comprehensive studies that explore the relationship between platelet indices and the various clinical manifestations of diabetes. Factors such as the duration of diabetes, the degree of glycemic control, and the presence of comorbid conditions may influence platelet behavior, adding complexity to the interpretation of these indices. Moreover, the impact of antiplatelet therapies and glycemic management strategies on platelet indices warrants further investigation to optimize the prevention and treatment of thrombotic events in diabetic patients.[7]

Materials and Methods

This cross-sectional observational study was conducted in the department of pathology, Government medical college Srinagar from 2021-2023. The primary objective was to evaluate the variation in platelet indices and additional hematological and metabolic parameters among patients diagnosed with type 2 diabetes mellitus (T2DM), comparing them to a healthy control group.A total of 120 participants were included in the study, divided into two groups: **Study Group:** 60 patients with confirmed T2DM for at least one year. **Control Group:** 60 age- and sex-matched healthy individuals without diabetes.

Inclusion criteria for the T2DM group included adults aged 35-65 years with stable glycemic control. Exclusion criteria covered individuals with hematologic disorders, recent infections, malignancies, or those on medications affecting platelet or metabolic function.The Institutional Review Board granted ethical approval for this study, and written informed consent was obtained from each participant.

Methodology

Data collection involved gathering demographic information, medical history, and a series of laboratory assessments for each participant. The study evaluated various parameters across four main categories to understand platelet indices and related biomarkers in patients with type 2 diabetes mellitus.The platelet indices measured included platelet count (PLT), recorded in x10^9/L, mean platelet volume (MPV) in femtoliters (fL) to represent the average platelet size, platelet distribution width (PDW) as a percentage reflecting variability in platelet size, and platelet-large cell ratio (P-LCR), which indicated the proportion of larger platelets associated with platelet activation.For glycemic and metabolic parameters, fasting blood glucose (FBG) was recorded in mg/dL, with postprandial blood glucose (PPBG) measured two hours post-meal to gauge postprandial glycemic levels. Glycated hemoglobin (HbA1c) was used as a marker for long-term glycemic control, while a comprehensive lipid profile, including total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides, provided insights into each patient's metabolic status.Inflammatory markers included C-reactive protein (CRP), recorded in mg/L as a general indicator of systemic inflammation, and erythrocyte sedimentation rate (ESR), measured in mm/hr as an additional marker of inflammation. Hematologic parameters, assessed to evaluate broader blood cell variations, included white blood cell (WBC) count in x10^3/µL for immune response variations, hemoglobin (Hb) level in g/dL to identify any potential anemic conditions that could impact platelet behavior, and red cell distribution width (RDW) as a percentage to capture variability in red blood cell size, often associated with chronic disease conditions like diabetes.Blood samples were collected in EDTA tubes for hematological indices and serum-separating tubes for metabolic and inflammatory markers. Samples were processed within two hours of collection, adhering to standard laboratory protocols, with the hematologyanalyzer calibrated daily to ensure accuracy. All analyses were conducted using automated analyzers, following precise protocols to maintain data integrity and reliability across parameters.

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Statistical Analysis

Data were analyzed using SPSS version 25.0. Descriptive statistics were used to summarize baseline characteristics. Continuous variables were presented as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. An independent t-test was used to compare platelet indices, metabolic parameters, and inflammatory markers between T2DM and control groups.Additionally, Pearson's correlation analysis was performed to assess the relationship between HbA1c levels, platelet indices, and inflammatory markers. A multivariate linear regression model was used to adjust for potential confounders. A p-value of <0.05 was considered statistically significant.

Results

Demographic Profile

The demographic profile shows that the mean age of participants in the T2DM group was 56.35 years, with a standard deviation of 5.21, indicating slightly older participants compared to the control group, which had a mean age of 53.00 years with a standard deviation of 4.07. Gender distribution revealed a nearly equal split in the T2DM group, with 32 males and 28 females, while the control group had a higher proportion of females (25 males and 35 females). The Body Mass Index (BMI) was significantly higher in the T2DM group, averaging 28.62 kg/m² compared to 24.27 kg/m² in the control group, reflecting a common trend of higher BMI among diabetic patients. The T2DM group also had an average diabetes duration of 9.41 years, emphasizing the chronic nature of the disease.

Platelet Indices

The analysis of platelet indices demonstrated significant differences between the T2DM and control groups. The mean platelet count was notably higher in the T2DM group (250.34 x10^9/L) compared to the control group (220.12 x10^9/L), with a p-value of <0.001, indicating statistical significance. The mean platelet volume (MPV) was also elevated in the T2DM group (9.5 fL) versus the control group (8.8 fL), with a p-value of <0.001, suggesting increased platelet activation in diabetic patients. Similarly, platelet distribution width (PDW) and platelet-large cell ratio (P-LCR) were significantly higher in the T2DM group (15% and 20%, respectively) compared to the control group (13% and 17%, respectively), both with p-values of <0.001.

Glycemic Parameters

The glycemic parameters revealed substantial differences between the T2DM and control groups, as expected. Fasting blood glucose levels were markedly higher in the T2DM group (140 mg/dL) compared to the control group (90 mg/dL), with a p-value of <0.001. Postprandial blood glucose and HbA1c levels were also significantly elevated in the T2DM group, with postprandial values averaging 180 mg/dL versus 110 mg/dL in the control group and HbA1c levels at 7.5% compared to 5.5%. All p-values were <0.001, emphasizing the marked difference in glycemic control between the groups.

Inflammatory Markers

Inflammatory markers were higher in the T2DM group, indicating a state of chronic inflammation associated with diabetes. The mean C-reactive protein (CRP) level was 3.5 mg/L in the T2DM group, compared to 1.5 mg/L in the control group, with a highly significant p-value of <0.001. The erythrocyte sedimentation rate (ESR) was also significantly elevated in the T2DM group (20 mm/hr) compared to the control group (10 mm/hr), with a p-value of <0.001, further supporting the presence of an inflammatory response.

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Hematologic Parameters

The hematologic profile showed significant variations between the groups. The white blood cell (WBC) count was higher in the T2DM group (8.0 x10^3/µL) compared to the control group (7.0 x10^3/µL), with a p-value of <0.001, suggesting an increased immune response in diabetic patients. Hemoglobin levels were slightly lower in the T2DM group (13.5 g/dL) compared to the control group (14 g/dL), with a p-value of 0.005, indicating a potential risk of anemia. Red cell distribution width (RDW) was significantly higher in the T2DM group (14%) compared to the control group (12.5%), with a p-value of <0.001, reflecting greater variability in red blood cell size, which is often associated with chronic disease states.

The ANOVA test results confirmed the statistical significance of the differences observed in the study parameters. High F-values and corresponding p-values <0.001 for most parameters, such as platelet count, MPV, glycemic markers (fasting blood glucose, postprandial blood glucose, and HbA1c), CRP, ESR, WBC count, and RDW, underscored the robustness of the findings. Hemoglobin levels had a lower F-value of 8.32, but the p-value was still statistically significant at 0.005.

Table 1: Demographic Profile

Parameter	T2DM (Mean ± SD / Count)	Control (Mean ± SD / Count)
Age (years)	56.35 ± 5.21	53.00 ± 4.07
Gender (Male/Female)	32/28	25/35
BMI (kg/m²)	28.62 ± 2.65	24.27 ± 2.00
Duration of Diabetes (years)	9.41 ± 2.83	N/A

Table 2: Platelet Indices (Mean ± SD with p-value)

Parameter	T2DM (Mean ± SD)	Control (Mean ± SD)	p-value
Platelet Count (x10^9/L)	250.34 ± 40.12	220.12 ± 30.45	<0.001
Mean Platelet Volume (fL)	9.5 ± 1.0	8.8 ± 0.8	<0.001
Platelet Distribution Width (%)	15 ± 2	13 ± 1.5	<0.001
Platelet-Large Cell Ratio (%)	20 ± 3	17 ± 2	<0.001

Table 3: Glycemic Parameters (Mean ± SD with p-value)

Parameter	T2DM (Mean ± SD)	Control (Mean ± SD)	p-value
Fasting Blood Glucose (mg/dL)	140 ± 20	90 ± 10	<0.001
Postprandial Blood Glucose (mg/dL)	180 ± 30	110 ± 15	<0.001
HbA1c (%)	7.5 ± 0.5	5.5 ± 0.3	<0.001

Table 4: Inflammatory Markers (Mean ± SD with p-value)

Parameter	T2DM (Mean ± SD)	Control (Mean ± SD)	p-value
CRP (mg/L)	3.5 ± 1.0	1.5 ± 0.5	<0.001
ESR (mm/hr)	20 ± 5	10 ± 3	<0.001

Table 5: Hematologic Parameters (Mean ± SD with p-value)

Parameter	T2DM (Mean ± SD)	Control (Mean ± SD)	p-value
WBC Count (x10^3/µL)	8.0 ± 1.0	7.0 ± 0.8	<0.001

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Hemoglobin (g/dL)	13.5 ± 1.0	14 ± 1	0.005
RDW (%)	14 ± 1	12.5 ± 0.7	<0.001

Table 6: ANOVA Test Results

Parameter	F-value	p-value
Platelet Count (x10^9/L)	16.19	0.000
Mean Platelet Volume (fL)	19.90	<0.001
Platelet Distribution Width (%)	38.50	<0.001
Platelet-Large Cell Ratio (%)	49.10	<0.001
Fasting Blood Glucose (mg/dL)	287.53	<0.001
Postprandial Blood Glucose (mg/dL)	245.51	<0.001
HbA1c (%)	706.90	<0.001
CRP (mg/L)	278.78	<0.001
ESR (mm/hr)	186.38	<0.001
WBC Count (x10^3/µL)	59.31	<0.001
Hemoglobin (g/dL)	8.32	0.005
RDW (%)	56.09	<0.001

Discussion

The demographic profile of the study participants revealed that the mean age of the T2DM group was 56.35 years, which was slightly older than the control group (53.00 years). This age difference is consistent with the general risk increase for T2DM with advancing age. Li et al. (2019) similarly reported a mean age of 57.8 years in their T2DM cohort, emphasizing the age-related risk factors associated with diabetes.[8] Additionally, our study found a higher BMI in the T2DM group (28.62 kg/m²) compared to the control group (24.27 kg/m²), which aligns with Khan et al. (2021), who reported an average BMI of 28.3 kg/m² in their T2DM patients.[9] This finding reinforces the role of obesity as a major risk factor for diabetes. In another study, García et al. (2020) observed a higher BMI of 29.1 kg/m² in T2DM patients, further corroborating the association between elevated BMI and increased diabetes risk.[10]

Our analysis showed that the T2DM group had significantly higher platelet count, MPV, PDW, and P-LCR. The mean platelet count in our T2DM group was 250.34 x10^9/L, compared to 220.12 x10^9/L in the control group. Shah et al. (2020) also observed an elevated platelet count of 248.5 x10^9/L in T2DM patients, supporting the pro-thrombotic state associated with diabetes.[11]Elevated MPV (9.5 fL in our study) is a marker of increased platelet activation, consistent with Jindal et al. (2018), who reported MPV levels of 9.6 fL in diabetic patients.[12] Moreover, Chen et al. (2022) found a PDW of 15.3% and a P-LCR of 21% in T2DM patients, similar to our findings, highlighting the enhanced platelet activation and risk of microvascular complications.[13]

Our study showed significantly elevated fasting blood glucose (140 mg/dL) and postprandial glucose (180 mg/dL) in the T2DM group, along with an HbA1c of 7.5%. Zhang et al. (2021) reported comparable fasting glucose levels of 138 mg/dL and HbA1c of 7.4%, emphasizing the challenges in achieving optimal glycemic control.[14] Additionally, Lee et al. (2023) observed an HbA1c of 7.6% in poorly controlled diabetic patients, reinforcing the importance of glycemic monitoring to prevent complications.[15]Abdul-Ghani et al. (2019) highlighted the role of HbA1c as a predictor of long-term complications, a finding that aligns with our study's results.[16]

Inflammatory markers such as CRP and ESR were significantly higher in the T2DM group, indicating chronic low-grade inflammation. Our study found a mean CRP level of 3.5 mg/L, consistent with De Luca et al. (2018), who reported a CRP level of 3.4 mg/L in diabetic

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patients.[17]Huang et al. (2020) found even higher CRP levels, averaging 3.8 mg/L, in patients with poorly controlled diabetes.[18] The elevated ESR (20 mm/hr) in our study aligns with a report by Singh et al. (2021), which found ESR levels of 21 mm/hr in diabetic patients, emphasizing the role of inflammation in the progression of T2DM.[19]

Our study observed a higher WBC count in the T2DM group (8.0 x10^3/µL) compared to the control group (7.0 x10^3/µL), consistent with findings by Xu et al. (2019), who reported WBC counts of 8.1 x10^3/µL in diabetic patients. This suggests a heightened immune response and its association with insulin resistance.[20]The slightly lower hemoglobin levels (13.5 g/dL) in our T2DM group compared to 14 g/dL in controls are similar to Thomas et al. (2021), who found hemoglobin levels of 13.4 g/dL in diabetics, potentially indicating an increased risk of anemia.[21] Furthermore, Lippi et al. (2020) observed elevated RDW levels (14.2%) in diabetic patients, in line with our RDW findings of 14%, linking it to increased cardiovascular risk and poor glycemic control.[22]

The ANOVA test results provided strong statistical evidence for the differences observed in our study parameters. High F-values and corresponding p-values of <0.001 for most parameters underscore the robustness of these findings. Patel et al. (2023) similarly reported high F-values for glycemic and inflammatory markers in their study on diabetic complications, emphasizing the physiological changes associated with T2DM. The significant difference in hemoglobin levels, although with a lower F-value, remained relevant, highlighting the impact of diabetes on hematologic health.[23]

Conclusion

In conclusion, this study highlights significant variations in platelet indices among patients with type 2 diabetes mellitus compared to healthy controls. The elevated platelet count, MPV, PDW, and P-LCR observed in the T2DM group underscore a heightened thrombotic risk, likely driven by chronic hyperglycemia and systemic inflammation. These findings emphasize the critical role of platelet activation in the pathophysiology of diabetic complications. Additionally, the correlations between glycemic parameters and inflammatory markers provide further insight into the interplay between metabolic control and vascular health in diabetes. Monitoring platelet indices in T2DM patients could serve as a valuable tool for early detection and management of cardiovascular complications, potentially guiding targeted therapeutic interventions.

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