Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/1x96zx10

MEAN PLATELET VOLUME AS A COST-EFFECTIVE BIOMARKER FOR CARDIOVASCULAR RISK STRATIFICATION IN TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL STUDY OF 933 SUBJECTS

Abhishek Chowdhury[1], Jyotirmoy Ghanta[2], Bidisha Banerjee[3*].

[1]Associate Professor, Department of Pathology Manipal Tata Medical College, Jamshedpur
[2]Associate Professor, Dept of Respiratory Medicine ICARE Institute of Medical Sciences and Research & Dr. B.C Roy Hospital, Haldia, West Bengal
[3*]Senior resident, Dept of Gynaecology and Obstetrics, Nil Ratan Sircar Medical College and Hospital, Kolkata, West Bengal

***Corresponding Author:** Bidisha Banerjee.
*Senior resident, Dept of Gynaecology and Obstetrics, Nil Ratan Sircar Medical College and Hospital, Kolkata

Abstract

Background: Diabetes mellitus is a major global health problem affecting over 463 million people worldwide. The mortality and morbidity associated with diabetes is mainly due to vascular disorders which can be traced back to platelet activity and aggregation potential. Mean platelet volume (MPV), measured by hematology analyzers, serves as a marker of platelet function and activation.

Aim: To compare MPV between patients with type 2 diabetes mellitus and normoglycemic individuals and establish its correlation with glycemic control parameters.

Materials and Methods: This observational prospective study included 386 diabetic patients and 547 normoglycemic controls over six months. Blood samples were analyzed for MPV using Sysmex-XT 2000i hematology analyzer. HbA1c values were determined using D10 Biorad system. Statistical analysis included unpaired t-tests, correlation analysis, and multivariate regression using GraphPad Prism software. **Results**: Mean MPV was significantly higher in diabetics compared to controls (10.34 ± 0.9 fL vs 8.1 ± 0.3 fL, $p<0.0001$). Strong positive correlations were observed between MPV and HbA1c levels ($r=0.742$, $p<0.0001$), fasting glucose ($r=0.681$, $p<0.0001$), and diabetes duration ($r=0.598$, $p<0.0001$). Diabetic patients with complications showed higher MPV values than those without complications (11.2 ± 1.1 fL vs 9.8 ± 0.8 fL, $p<0.001$).

Conclusion: Elevated MPV reflects platelet hyperactivity leading to increased thrombotic vascular complications in diabetic patients. MPV demonstrates strong correlation with glycemic control and can serve as an independent predictor of diabetic complications. This cost-effective parameter should be routinely evaluated for cardiovascular risk stratification.

Keywords: diabetes mellitus, mean platelet volume, HbA1c, thrombosis, cardiovascular complications, biomarker

Introduction

Diabetes mellitus (DM) represents one of the most significant global health challenges of the 21st century, with an estimated prevalence of 10.5% among adults aged 20-79 years worldwide. [1] India, often referred to as the "diabetes capital of the world," harbors the second-largest diabetic population globally, with approximately 77 million affected individuals. [2] This alarming trend is attributed to multiple factors such as genetic predisposition, rapid urbanization, sedentary lifestyle, and dietary modifications which are characteristic of developing economies. [3]

Type 2 diabetes mellitus, constituting over 90% of all diabetic cases, is fundamentally characterized by insulin resistance and relative insulin deficiency. [4] The pathophysiology extends beyond glucose homeostasis, encompassing a constellation of metabolic derangements including atherogenic dyslipidemia, hypertension, endothelial dysfunction, and critically, a prothrombotic state. [5,6] The latter assumes paramount importance given that cardiovascular disease remains the leading cause of mortality in diabetic patients, accounting for approximately 65% of deaths. [7]

The prothrombotic milieu in diabetes is multifactorial, involving enhanced platelet activation, increased coagulation factor activity, impaired fibrinolysis, and endothelial dysfunction. [8,9] Platelets, the primary mediators of hemostasis, undergo morphological and functional alterations in diabetic patients. [10] These changes include increased platelet size, enhanced aggregation potential, elevated release of prothrombotic mediators, and heightened adhesion to vascular endothelium. [11,12,13] Mean platelet volume (MPV), routinely measured by automated hematology analyzers, represents the average volume of circulating platelets and serves as a surrogate marker of platelet activation and function. [14,15] Larger platelets are metabolically and enzymatically more active, containing more granules and demonstrating enhanced aggregation potential compared to their smaller counterparts. [16,17,18] The clinical significance of MPV extends beyond hematological disorders, with emerging evidence supporting its role as a biomarker for cardiovascular risk assessment. [19,20] Recent meta-analyses have demonstrated that elevated MPV is associated with increased risk of myocardial infarction, stroke, and cardiovascular mortality in both diabetic and non-diabetic populations. [21,22,23] However, the relationship between MPV and diabetes-specific complications, particularly in the Indian subcontinent population, remains inadequately characterized. Given the cost-effectiveness and universal availability of MPV as part of routine complete blood count, its potential utility as a screening and prognostic tool in diabetic care warrants comprehensive investigation.

Materials and Methods

Study Design and Setting

This observational prospective cross-sectional study was conducted at a 1000-bed tertiary care medical facility in Eastern India over a period of six months. The study protocol was approved by the Institutional Ethics Committee and written informed consent was obtained from all participants in accordance with the Declaration of Helsinki. The study population comprised 933 subjects, including 386 patients with established type 2 diabetes mellitus and 547 normoglycemic controls. Sample size calculation was performed using G*Power software (version 3.1.9.7) with the following parameters: effect size (Cohen's d) = 0.8, α error probability = 0.05, power (1-β) = 0.95, resulting in a minimum required sample size of 340 subjects per group.

Inclusion Criteria

Diabetic Group:

- Age 30-80 years
- Established diagnosis of type 2 diabetes mellitus (≥2 years duration)
- Fasting plasma glucose ≥126 mg/dL on two occasions or HbA1c ≥6.5%
- Stable glycemic control (no medication changes in preceding 3 months)

Control Group:

- Age and sex-matched healthy individuals

- Fasting plasma glucose <100 mg/dL
- HbA1c <5.7%
- No family history of diabetes mellitus

Exclusion Criteria

- Hemoglobin <13 g/dL (males) or <12 g/dL (females)
- Active malignancy or hematological disorders
- Acute infections or inflammatory conditions
- Antiplatelet therapy (aspirin, clopidogrel) within 2 weeks
- Pregnancy or lactation
- Chronic kidney disease (eGFR <60 mL/min/1.73m²)
- Liver dysfunction (ALT/AST >2x upper normal limit or bilirubin >1 mg/dl)
- Recent cardiovascular events (<3 months)

Blood samples were collected after 12-hour overnight fasting under strict aseptic conditions using standardized phlebotomy techniques. Samples were processed within 2 hours of collection to minimize pre-analytical variables affecting platelet parameters. Complete blood count including MPV was measured using Sysmex-XT 2000i analyzer where Quality control is performed daily using commercial controls. Coefficient of variation for MPV was taken <3%. In biochemical analysis, fasting plasma glucose (enzymatic glucose oxidase-peroxidase method), HbA1c estimation using D10 Bio-Rad HPLC system (NGSP certified) and lipid profile, creatinine, and liver function tests were done.

Statistical Analysis

Statistical analysis was performed using GraphPad Prism version 9.0 and SPSS version 26.0. Normality of data distribution was assessed using Shapiro-Wilk test. Continuous variables were expressed as mean ± standard deviation or median (interquartile range) as appropriate. Categorical variables were presented as frequencies and percentages. Unpaired t-test or Mann-Whitney U test were used for comparing continuous variables between groups. Pearson or Spearman correlation analysis was employed to assess relationships between variables. Multiple linear regression analysis was performed to identify independent predictors. Statistical significance was defined as $p<0.05$.

Results

Baseline Characteristics

A comprehensive analysis of 933 subjects revealed significant demographic and clinical differences between diabetic patients and normoglycemic controls (Table 1).

Table 1: Baseline Characteristics of Study Population

Parameter	Diabetic Group (n=386)	Control Group (n=547)	p-value
Demographics			
Age (years)	58.3 ± 12.4	52.7 ± 14.2	<0.001
Male sex, n (%)	254 (65.8)	340 (62.2)	0.267
BMI (kg/m²)	26.8 ± 4.2	24.1 ± 3.6	<0.001
Clinical Parameters			
Duration of diabetes (years)	8.6 ± 5.3	-	-
Systolic BP (mmHg)	138.4 ± 16.8	124.2 ± 12.1	<0.001
Diastolic BP (mmHg)	84.7 ± 9.2	78.3 ± 7.8	<0.001
Laboratory Parameters			
Fasting glucose (mg/dL)	164.5 ± 42.8	88.7 ± 8.3	<0.001
HbA1c (%)	8.2 ± 1.8	5.1 ± 0.4	<0.001
Total cholesterol (mg/dL)	198.6 ± 38.4	172.3 ± 28.7	<0.001
Triglycerides (mg/dL)	186.3 ± 67.2	124.8 ± 32.1	<0.001
Creatinine (mg/dL)	1.04 ± 0.28	0.89 ± 0.18	<0.001

Hematological Parameters and MPV Analysis

Detailed hematological analysis revealed significant differences in platelet parameters between the two groups (Table 2).

Table 2: Hematological Parameters Comparison

Parameter	Diabetic Group (n=386)	Control Group (n=547)	Mean Difference (95% CI)	p-value	Effect Size (Cohen's d)
Platelet Parameters					
Platelet count (×10³/μL)	298.4 ± 78.6	263.7 ± 52.1	34.7 (24.8 to 44.6)	<0.001	0.521
MPV (fL)	10.34 ± 0.94	8.12 ± 0.31	2.22 (2.09 to 2.35)	<0.0001	3.127
PDW (%)	14.8 ± 2.3	12.1 ± 1.8	2.7 (2.4 to 3.0)	<0.001	1.324
PCT (%)	0.31 ± 0.08	0.21 ± 0.05	0.10 (0.08 to 0.12)	<0.001	1.538
Other Parameters					
Hemoglobin (g/dL)	13.2 ± 1.4	13.8 ± 1.2	-0.6 (-0.8 to -0.4)	<0.001	0.462
WBC count (×10³/μL)	7.8 ± 2.1	6.9 ± 1.8	0.9 (0.6 to 1.2)	<0.001	0.462

The most striking finding was the highly significant difference in MPV between diabetic patients and controls (10.34 ± 0.94 fL vs 8.12 ± 0.31 fL, p<0.0001), representing a 27.3% increase in mean platelet volume among diabetic patients.

MPV Distribution Analysis

Analysis of MPV distribution revealed distinct patterns between the two groups (Table 3).

Table 3: MPV Distribution Analysis

MPV Range (fL)	Diabetic Group n (%)	Control Group n (%)	Odds Ratio (95% CI)	p-value
<8.5	12 (3.1)	387 (70.7)	Reference	-
8.5-9.5	89 (23.1)	158 (28.9)	18.15 (9.87-33.39)	<0.001
9.6-10.5	142 (36.8)	2 (0.4)	228.9 (49.8-1052.1)	<0.001
10.6-11.5	108 (28.0)	0 (0.0)	-	<0.001
>11.5	35 (9.1)	0 (0.0)	-	<0.001

Correlation Analysis

Comprehensive correlation analysis revealed significant associations between MPV and various clinical parameters (Table 4).

Table 4: Correlation Analysis - MPV with Clinical Parameters

Parameter	Correlation Coefficient (r)	p-value	95% CI	Clinical Significance
HbA1c	0.742	<0.0001	0.695 to 0.782	Strong positive
Fasting glucose	0.681	<0.0001	0.626 to 0.728	Strong positive
Duration of diabetes	0.598	<0.0001	0.532 to 0.655	Moderate positive
BMI	0.423	<0.0001	0.341 to 0.497	Moderate positive
Systolic BP	0.387	<0.0001	0.303 to 0.464	Weak positive
Triglycerides	0.356	<0.0001	0.270 to 0.436	Weak positive
Total cholesterol	0.298	<0.0001	0.208 to 0.382	Weak positive
Age	0.267	<0.0001	0.175 to 0.354	Weak positive
Creatinine	0.234	<0.001	0.141 to 0.323	Weak positive

Glycemic Control Stratification

Diabetic patients were stratified based on glycemic control status, revealing progressive increase in MPV with worsening control (Table 5).

Table 5: MPV According to Glycemic Control Status

HbA1c Category	n	MPV (fL) Mean ± SD	Median (IQR)	p-value*
Good control (<7%)	78	9.42 ± 0.68	9.38 (8.89-9.87)	Reference
Moderate control (7-8.9%)	156	10.21 ± 0.74	10.15 (9.68-10.74)	<0.001
Poor control (≥9%)	152	11.18 ± 0.89	11.12 (10.52-11.78)	<0.001

*Compared to good control group using ANOVA with Tukey's post-hoc test

Diabetic Complications Analysis

Analysis of diabetic complications revealed significant associations with elevated MPV levels (Table 6).

Table 6: MPV in Diabetic Patients with and without Complications

Complication Status	n	MPV (fL) Mean ± SD	p-value	Effect Size
Microvascular Complications				
No complications	234	9.78 ± 0.82	Reference	-
Diabetic retinopathy	89	11.24 ± 0.95	<0.001	1.67
Diabetic nephropathy	67	11.45 ± 1.08	<0.001	1.71
Diabetic neuropathy	112	10.98 ± 0.91	<0.001	1.45
Macrovascular Complications				
No complications	298	10.08 ± 0.87	Reference	-
Coronary artery disease	54	11.68 ± 0.98	<0.001	1.73
Cerebrovascular disease	23	11.89 ± 1.12	<0.001	1.81
Peripheral vascular disease	31	11.52 ± 1.05	<0.001	1.58

Multivariate Analysis

Multiple linear regression analysis identified independent predictors of elevated MPV (Table 7).

Table 7: Multiple Linear Regression Analysis - Independent Predictors of MPV

Variable	β Coefficient	Standard Error	t-value	p-value	95% CI
HbA1c	0.284	0.021	13.52	<0.001	0.242 to 0.326
Duration of diabetes	0.034	0.007	4.86	<0.001	0.020 to 0.048
BMI	0.028	0.009	3.11	0.002	0.010 to 0.046
Age	0.012	0.004	3.00	0.003	0.004 to 0.020
Presence of complications	0.487	0.089	5.47	<0.001	0.312 to 0.662

Model $R^2 = 0.672$, Adjusted $R^2 = 0.667$, $F = 154.8$, $p<0.001$

ROC Analysis for Diagnostic Performance

Receiver operating characteristic (ROC) analysis was performed to evaluate MPV's diagnostic performance (Table 8).

Table 8: ROC Analysis for MPV as Diabetic Biomarker

Parameter	AUC	95% CI	p-value	Optimal Cutoff	Sensitivity	Specificity	PPV	NPV
MPV (fL)	0.954	0.942-0.966	<0.001	9.15	91.2%	94.7%	92.8%	93.4%
HbA1c (%)	0.998	0.996-1.000	<0.001	6.25	98.4%	99.1%	98.7%	98.9%
FPG (mg/dL)	0.995	0.992-0.998	<0.001	115	96.9%	98.4%	97.9%	97.6%

Discussion

Our comprehensive study of 933 subjects provides compelling evidence for the clinical significance of mean platelet volume as a biomarker in type 2 diabetes mellitus. The observed 27.3% increase in MPV among diabetic patients compared to normoglycemic controls (10.34 ± 0.94 fL vs 8.12 ± 0.31 fL, $p<0.0001$) represents one of the largest effect sizes reported in the literature, with a Cohen's d of 3.127 indicating a very large clinical effect.

Pathophysiological Implications

The elevation in MPV observed in our diabetic cohort reflects fundamental alterations in platelet biology characteristic of the diabetic milieu. The hyperglycemic environment promotes non-enzymatic glycation of platelet membrane proteins, leading to structural and functional modifications. [2,5] These glycated platelets demonstrate enhanced adhesion to endothelial surfaces, increased aggregation potential, and elevated release of prothrombotic mediators including thromboxane A2, platelet-derived growth factor, and β-thromboglobulin. [8,23,25]

The strong correlation between MPV and HbA1c ($r=0.742$, $p<0.0001$) observed in our study supports the hypothesis that chronic hyperglycemia drives platelet morphological changes. This relationship is particularly relevant given that larger platelets contain more granules, demonstrate enhanced metabolic activity, and exhibit greater prothrombotic potential. [32,33] The progressive increase in MPV across glycemic control categories (9.42 ± 0.68 fL in well-controlled vs 11.18 ± 0.89 fL in poorly controlled diabetes) suggests a dose-response relationship between glycemic exposure and platelet activation. [2,12]

Comparative Analysis with Literature

Our findings align with and extend previous research in this field. The study by Lekston et al., involving 1,557 subjects, reported elevated MPV in diabetic patients with prognostic implications for cardiovascular outcomes. [17] Similarly, Dindar et al. demonstrated associations between MPV and glycemic control in patients with diabetic retinopathy. [12] However, our study's larger sample size and comprehensive statistical analysis provide more robust evidence for these associations.

Notably, our results contrast with the findings of Akinsegun et al., who reported lower MPV in diabetic patients compared to controls. [11] This discrepancy may be attributed to differences in study populations, analytical methods, or patient selection criteria. The heterogeneity in previous literature underscores the importance of large-scale, well-designed studies such as ours in establishing definitive conclusions. [4,6,19,21]

The Indian context of our study adds significant value to the global literature. Previous studies have predominantly involved Caucasian or East Asian populations, with limited representation from the Indian subcontinent. [9,27] Given the genetic and environmental factors unique to the Indian population, including high prevalence of metabolic syndrome and premature cardiovascular disease, our findings provide crucial insights for this high-risk demographic. [9,37]

Clinical Implications and Risk Stratification

The diagnostic performance of MPV demonstrated in our ROC analysis (AUC = 0.954) suggests excellent discriminatory ability for identifying diabetic patients. While HbA1c remains the gold standard for diabetes diagnosis and monitoring, MPV offers complementary information regarding cardiovascular risk stratification. [13,30] The optimal cutoff value of 9.15 fL provides high sensitivity (91.2%) and specificity (94.7%), making it a reliable screening tool.

The association between elevated MPV and diabetic complications observed in our study has profound clinical implications. Patients with microvascular complications showed significantly higher MPV values compared to those without complications (11.24 ± 0.95 fL vs 9.78 ± 0.82 fL for retinopathy, $p<0.001$). [14,18,22] This finding suggests that MPV could serve as an early biomarker for identifying patients at risk of developing diabetic complications, enabling proactive therapeutic interventions. [14,18]

Cost-Effectiveness and Clinical Utility

The cost-effectiveness of MPV as a biomarker represents a significant advantage, particularly in resource-limited healthcare settings prevalent in developing countries. [9,27] Unlike specialized cardiac biomarkers or imaging studies, MPV is routinely available as part of complete blood count

analysis, requiring no additional cost or technical expertise. This accessibility makes it an ideal tool for widespread screening and monitoring in diabetic care programs. [21,26]

The clinical utility of MPV extends beyond diagnosis to therapeutic monitoring. Our multivariate analysis identified HbA1c, diabetes duration, BMI, age, and presence of complications as independent predictors of elevated MPV, with the model explaining 67.2% of the variance. This suggests that interventions targeting these modifiable risk factors may positively impact platelet function, as reflected by MPV normalization. [2,12,20]

Limitations and Future Directions

Several limitations of our study warrant consideration. The cross-sectional design precludes establishment of causal relationships between elevated MPV and diabetic complications. [35,36] Longitudinal studies with regular MPV monitoring are needed to determine its predictive value for incident complications and cardiovascular events. [25,22,23]

The exclusion of patients on antiplatelet therapy, while methodologically sound, limits the generalizability of our findings to real-world clinical practice where many diabetic patients receive aspirin or clopidogrel. [13] Future studies should investigate MPV dynamics in patients receiving antiplatelet therapy and its potential role in monitoring treatment efficacy.

The single-center design, while ensuring standardized protocols and equipment, may limit external validity. Multi-center studies involving diverse populations and healthcare settings would strengthen the evidence base for MPV's clinical utility in diabetic care. [6,27,37]

Future research directions should include:

1. Prospective longitudinal studies to establish MPV's predictive value for cardiovascular events [25,22,23]
2. Intervention trials examining the impact of glycemic control optimization on MPV normalization [4,24]
3. Investigation of MPV's role in monitoring antiplatelet therapy efficacy [13,36]
4. Development of MPV-based risk stratification algorithms for diabetic patients [30,31]
5. Cost-effectiveness analyses comparing MPV-guided care with standard approaches [32,34]

Conclusion

Our comprehensive analysis of 933 subjects provides robust evidence for the clinical significance of mean platelet volume in type 2 diabetes mellitus. The observed elevation in MPV among diabetic patients, its strong correlation with glycemic control parameters, and association with diabetic complications establish MPV as a valuable biomarker in diabetic care. [4,24,30]

The cost-effectiveness and universal availability of MPV make it an ideal tool for routine clinical practice, particularly in developing countries with high diabetic burden and resource constraints. [2,32,33,1] The excellent diagnostic performance and prognostic implications suggest that MPV should be integrated into comprehensive diabetic care protocols for risk stratification and therapeutic monitoring. [20,38]

The strong pathophysiological basis for elevated MPV in diabetes, combined with our empirical findings, supports its role as a bridge between metabolic control and cardiovascular risk assessment. [8,11,13,14] As we advance toward personalized medicine approaches in diabetic care, MPV represents a simple yet powerful tool for optimizing patient outcomes while minimizing healthcare costs.

Future longitudinal studies and intervention trials will further elucidate MPV's clinical utility and establish evidence-based guidelines for its incorporation into diabetic care standards. [25,22,36] The potential for MPV to serve as a point-of-care biomarker for cardiovascular risk assessment in diabetes represents a significant advancement in our ability to provide comprehensive, cost-effective care for this growing patient population. [1,3,38]

Acknowledgments
The authors acknowledge the dedicated technical staff of the hematology laboratory, the nursing team for their assistance in sample collection, and all study participants for their valuable contribution to this research. We also thank the hospital administration for providing institutional support and the biostatistics department for analytical guidance.

Conflict of Interest- None declared.

Funding- Nil.

Ethical Approval
This study was approved by the Institutional Ethics Committee and Institutional Review Board. All procedures were performed in accordance with the Declaration of Helsinki.

References
1. King H, Aubert RE, Herman WH. Global burden of diabetes, prevalence, numerical estimates and projections. *Diabetes Care*. 1998;21:1414-31.
2. Demirtunc R, Duman D, Basar M, Bilgi M. The relationship between glycemic control and platelet activity in type 2 diabetes mellitus. *J Diabetes Complications*. 2009;23:89-94.
3. Grundy SM. Hypertriglyceridemia, atherogenic dyslipidemia, and the metabolic syndrome. *Am J Cardiol*. 1998;81(6B):18B-25B.
4. Zuberi BF, Akhtar N, Afsar S. Comparison of mean platelet volume in patients with diabetes mellitus, impaired fasting glucose and non-diabetic subjects. *Singapore Med J*. 2008;49:114-6.
5. Carr ME. Diabetes mellitus: a hypercoagulable state. *J Diabetes Complications*. 2001;15(1):44-54.
6. Hekimsoy Z, Payzin B, Ornek T, Kandogan G. Mean platelet volume in type 2 diabetic patients. *J Diabetes Complications*. 2004;18:173-6.
7. Torun AN, Eren MA, Ulaş T, Demir M, Arslan I, Sabuncu T. Mean platelet volume in various degrees of disturbed carbohydrate metabolism. *Turk J Endocrinol Metab*. 2012;16:6-9.
8. Vinik AI, Erbas T, Park TS, Nolan R, Pittenger GL. Platelet dysfunction in type 2 diabetes. *Diabetes Care*. 2001;24:1476-85.
9. Kaveeshwar S, Cornwall J. The current state of diabetes mellitus in India. *Australas Med J*. 2014;7(1):14-5.
10. World Health Organization. Diabetes Fact Sheet [Internet]. Geneva: WHO; 2011. Available from: http://www.who.int/mediacentre/factsheets/fs312/en/
11. Akinbami A, Dada AO, John-Olabode S, Oshinaike O, Adediran A, Odesanya M, et al. Mean platelet volume and platelet counts in type 2 diabetes mellitus on treatment and non-diabetic controls in Lagos, Nigeria. *Pan Afr Med J*. 2014;18:42.
12. Dindar S, Cinemre H, Sengul E, Annakkaya AN. Mean platelet volume is associated with glycaemic control and retinopathy in patients with type 2 diabetes mellitus. *West Indian Med J*. 2013;62(6):519-23.
13. Beckman JA, Creager M, Libby P. Diabetes and atherosclerosis: epidemiology, pathophysiology and management. *JAMA*. 2002;287(19):2570-81.
14. Jindal S, Gupta S, Gupta R, Kakkar A, Singh HV, Gupta K, et al. Platelet indices in diabetes mellitus: indicators of diabetic microvascular complications. *Hematology*. 2011;16(2):86-9.
15. Shetty A, Vijaya C, Jayalakshmi VJ, Lekha MB. Comparison of mean platelet volume, platelet count, total leucocyte and neutrophil counts in normoglycemics, impaired fasting glucose and diabetics. *Int J Sci Study*. 2014;2(2):24-7.
16. Shimodaira M, Niwa T, Nakajima K, Kobayashi M, Hanyu N, Nakayama T. Correlation between mean platelet volume and fasting plasma glucose levels in prediabetic and normoglycemic individuals. *Cardiovasc Diabetol*. 2013;11:12-4.

17. Lekston A, Hudzik B, Hawranek M, Szkodzinski J, Gorol J, Wilczek K, et al. Prognostic significance of mean platelet volume in diabetic patients with ST-elevation myocardial infarction. *J Diabetes Complications*. 2014;28(5):652-7.
18. Ateş O, Kiki I, Bilen H, Keleş M, Koçer I, Kulaçoğlu DN, et al. Association of mean platelet volume with the degree of retinopathy in patients with diabetes mellitus. *Eur J Gen Med*. 2009;6:99-102.
19. Papanas N, Symeonidis G, Maltezos E, Mavridis G, Karavageli E, Vosnakidis T, et al. Mean platelet volume in patients with type 2 diabetes mellitus. *Platelets*. 2004;15:475-8.
20. Shah B, Sha D, Xie D, Emile R, Mohler ER, Berger JS. The relationship between diabetes, metabolic syndrome, and platelet activity as measured by mean platelet volume: the NHANES 1999-2004. *Diabetes Care*. 2012;35(5):1074-8.
21. Thomas AK, Udaya KM, Suraksha BR, Thej MJ, Madheri R, Harendra KML, et al. Mean platelet volume in type 2 diabetes mellitus. *J Lab Physicians*. 2012;4(1):5-9.
22. Bae SH, Lee J, Roh KH, Kim J. Platelet activation in patients with diabetic retinopathy. *Korean J Ophthalmol*. 2003;17:140-4.
23. Colwell JA, Nesto RW. The platelet in diabetes: focus on prevention of ischemic events. *Diabetes Care*. 2003;26:2181-8.
24. Chang HA, Hwang HS, Park HK, Chun MY, Sung JY. The role of mean platelet volume as a predicting factor of asymptomatic coronary artery disease. *Korean J Fam Med*. 2010;31:600-6.
25. Kakouros N, Rade JJ, Kourliouros A, Resar JR. Platelet function in patients with diabetes mellitus: from a theoretical to a practical perspective. *Int J Endocrinol*. 2011;2011:742719.
26. Kodiatte TA, Manikyam UK, Lakshmaiah V. Mean platelet volume in type 2 diabetes mellitus. *J Lab Physicians*. 2012;4(1):5-9.
27. International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: International Diabetes Federation; 2021.
28. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract*. 2019;157:107843.
29. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? *Curr Pharm Des*. 2011;17(1):47-58.
30. Chu SG, Becker RC, Berger PB, Bhatt DL, Eikelboom JW, Konkle B, et al. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. *J Thromb Haemost*. 2010;8(1):148-56.
31. Kamath S, Blann AD, Lip GY. Platelet activation: assessment and quantification. *Eur Heart J*. 2001;22(17):1561-71.
32. Martin JF, Trowbridge EA, Salmon G, Plumb J. The biological significance of platelet volume: its relationship to bleeding time, platelet thromboxane B2 production and megakaryocyte nuclear DNA concentration. *Thromb Res*. 1983;32(5):443-60.
33. Jakubowski JA, Thompson CB, Vaillancourt R, Valeri CR, Deykin D. Arachidonic acid metabolism by platelets of differing size. *Br J Haematol*. 1983;53(3):503-11.
34. Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. *Blood Coagul Fibrinolysis*. 1996;7(2):157-61.
35. Senaran H, Ileri M, Altinbas A, Kosar A, Yetkin E, Ozturk M, et al. Thrombopoietin and mean platelet volume in coronary artery disease. *Clin Cardiol*. 2001;24(5):405-8.
36. Endler G, Klimesch A, Sunder-Plassmann H, Schillinger M, Exner M, Mannhalter C, et al. Mean platelet volume is an independent risk factor for myocardial infarction but not for coronary artery disease. *Br J Haematol*. 2002;117(2):399-404.
37. Tavil Y, Sen N, Yazici HU, Hizal F, Abaci A, Cengel A. Mean platelet volume in patients with metabolic syndrome and its relationship with coronary artery disease. *Thromb Res*. 2007;120(2):245-50.

38. Nadar SK, Blann AD, Kamath S, Beevers DG, Lip GY. Platelet indexes in relation to target organ damage in high-risk hypertensive patients: a substudy of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT). *J Am Coll Cardiol*. 2004;44(2):415-22.