

Platelet Profile Findings Might Associate with Comorbidities on Erectile Dysfunction: A Cross-sectional Study in Indonesia

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ABSTRACT

Introduction: Erectile dysfunction (ED) is a prevalent condition with a multifactorial etiology, including vascular, endocrine, neurological, and psychological factors. Platelet indices such as platelet count (PC), mean platelet volume (MPV), and platelet distribution width (PDW) have been studied as potential biomarkers for ED, but findings remain inconsistent. This study aims to investigate the relationship between platelet indices and ED severity and their association with comorbidities. **Methods:** A cross-sectional observational study was conducted using medical records of ED patients in a single center in Surabaya, Indonesia. Platelet indices, metabolic parameters, and hormone levels were analyzed. ED severity was assessed using the International Index of Erectile Function-5 questionnaire. Statistical analysis included one-way ANOVA or Kruskal–Wallis tests for severity comparisons and *t*-tests or Mann–Whitney tests for comorbidities. **Results:** A total of 226 patients were analyzed, with a mean age of 55.37 ± 11.33 years. Severe ED was the most common category (49.11%). No significant differences were found between platelet indices and ED severity (PC: $P = 0.579$, PDW: $P = 0.758$, MPV: $P = 0.994$). However, patients with comorbidities, particularly dyslipidemia and metabolic syndrome, showed significantly higher PC values ($P = 0.021$ and $P = 0.03$, respectively). **Conclusions:** While platelet indices did not correlate with ED severity, PC was significantly associated with ED in patients with metabolic comorbidities. These findings highlight the role of systemic metabolic disturbances in ED pathophysiology, suggesting that comorbidity management may be crucial in ED treatment.

KEYWORDS: Blood biomarkers, comorbidities, erectile dysfunction, hypertension, metabolic syndrome

INTRODUCTION

Erectile dysfunction (ED) is a common male sexual disorder defined as the persistent inability to achieve or maintain an erection sufficient for satisfactory sexual activity for at least 3 months.¹ It is a significant global health issue, affecting approximately 10% of men under 50, 20%–40% of men aged 60, and 50%–100% of men over 70, with projections estimating 322 million cases worldwide by 2025.^{2–4}

The pathophysiology of ED is multifactorial, involving endocrine, neurological, vascular, and psychological factors.⁵ Vascular dysfunction plays a key role, with

conditions such as diabetes mellitus, hypertension, dyslipidemia, obesity, metabolic syndrome (MetS), smoking, and physical inactivity contributing to ED development.⁶ ED is associated with increased central arterial stiffness. Therefore, early detection of ED may contribute to the prevention or early intervention of cardiovascular disease.⁷

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Recent studies have explored the role of hematological parameters, particularly platelet indices – platelet count (PC), platelet distribution width (PDW), and mean platelet volume (MPV) – as potential biomarkers for ED.⁶ Platelets play a crucial role in hemostasis and vascular integrity, with increased platelet activation being linked to atherothrombotic events.⁸ However, the relationship between platelet indices and ED remains inconsistent. Wang, Xue-Sheng *et al.* (2019).⁸ reported significantly higher MPV and PC in arteriogenic ED patients compared to venogenic ED and controls,⁹ whereas a meta-analysis by Ren *et al.* (2017) found no significant differences in PDW and PC between ED patients and healthy individuals. Despite these discrepancies, higher MPV levels have been associated with ED incidence and severity, suggesting a possible role of platelet dysfunction in its pathogenesis.¹⁰

Given the inconsistent findings on the role of platelet indices in ED, further research is needed to clarify their potential as diagnostic and prognostic biomarkers. ED, particularly of vascular origin, is closely linked to endothelial dysfunction and atherosclerosis, conditions that alter platelet activity. While platelet indices such as PC, MPV, and PDW have been suggested as markers of ED severity, conflicting results necessitate further investigation. In addition, since ED often coexists with MetS, hypertension, diabetes mellitus, and dyslipidemia – conditions that influence platelet function – understanding their impact on platelet indices is crucial. This study aims to examine the relationship between platelet indices and ED severity, assess the influence of comorbidities, and evaluate their potential as predictive biomarkers. These findings could enhance early diagnosis, risk stratification, and treatment strategies for ED, particularly in patients with vascular comorbidities.

METHODS

Study population and design

This study was designed as an analytic observational study with a cross-sectional approach. The study population consisted of patients diagnosed with ED and patients of any age were included if they had comorbidities such as MetS, hypertension, diabetes mellitus, or dyslipidemia. Who sought treatment at the Andrology Clinic of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, between January 2017 and July 2022. The study utilized medical record data to extract relevant clinical and laboratory parameters. Ethical approval for this research was granted by the institutional ethics committee under protocol number 1070/LOE/301.4.2/X/2022.

Subject determination

The inclusion criteria for this study required male patients diagnosed with ED, defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance for at least 6 months. Patients included in this study were those who had complete medical history records, including clinical symptoms, comorbidities, and laboratory results. In addition, only patients who had not received any prior ED treatment, such as phosphodiesterase-5 inhibitors or other therapeutic modalities, were eligible.

Exclusion criteria included patients with incomplete clinical or laboratory records, those with a prior history of ED treatment before their initial visit to the clinic, and patients with severe systemic diseases or malignancies that could interfere with study parameters.

Erectile dysfunction profile

All patients who meet the criteria must have an International Index of Erectile Function-5 (IIEF-5) record for the first time at the visit to the andrology clinic without being given any treatment. The IIEF-5 information assessed will be grouped according to mild (22–25), mild-moderate (17–21), moderate (11–16), and severe (6–10) categories.

Questionnaire

The IIEF-5 questionnaire a validated tool for assessing erectile function, was used. This self-reported questionnaire comprises five questions evaluating erectile frequency, firmness, penetration ability, maintenance, and overall satisfaction.

Anthropometric measurements

Body mass index was calculated and categorized based on Asian-specific criteria. Waist circumference was measured to assess abdominal obesity, with cut-offs defined by the International Diabetes Federation (IDF) criteria for MetS.

Patient with metabolic syndrome

Diabetes mellitus was defined as a chronic metabolic condition characterized by persistent hyperglycemia. Dyslipidemia was identified by increased serum levels of triglycerides (TG), low-density lipoprotein (LDL) cholesterol, and total cholesterol (TC), as well as decreased serum concentrations of high-density lipoprotein (HDL) cholesterol. Hypertension was defined according to the JNC8 guidelines, with a blood pressure cut-off of >140/90 mmHg. MetS was diagnosed based on the IDF 2005 criteria, requiring the presence of abdominal obesity, defined as a waist circumference above the standard Asian reference, in addition to any combination of comorbidities such as diabetes mellitus, hypertension, and dyslipidemia.

Patients were grouped based on the number and type of comorbidities. For instance, if a patient had only one comorbidity, such as hypertension, they were categorized accordingly. Patients with more than one comorbidity were grouped by combination types, such as hypertension and diabetes mellitus, or hypertension and dyslipidemia.

Laboratory examination

Venous blood samples (15 mL) were collected from each participant between 07:00 and 09:00 in the morning following an overnight fast of 8–10 h. Laboratory analyses included complete blood count (PC, PDW, and MPV), lipid profile (HDL, LDL, TG, and TC), fasting blood glucose, and total testosterone. All parameters were assessed using whole blood in accordance with standardized laboratory procedures.

Statistical analysis

Statistical analysis was conducted using GraphPad Prism version 9.0 (GraphPad Software, LLC, San Diego, CA, USA). Numerical data were tested for normality using the Kolmogorov–Smirnov test. Data that followed a normal distribution were presented as mean \pm standard deviation (SD), whereas nonnormally distributed data were expressed as median (interquartile range). The relationship between platelet profile parameters and ED severity was assessed using one-way ANOVA for parametric data and the Kruskal–Wallis test for nonparametric data. To further examine differences between groups, *post hoc* analysis was performed when necessary.

In addition, to assess the relationship between platelet indices and comorbidities in ED patients, the independent *t*-test was used for parametric data, whereas the Mann–Whitney *U*-test was applied for nonparametric data. A $P < 0.05$ was considered statistically significant, indicating meaningful differences between groups.

RESULTS

Comorbid metabolic disorders such as diabetes mellitus, hypertension, and dyslipidemia have been reported to predominate in patients presenting with ED. In this study, a total of 226 patient records were analyzed. The mean age of the patients was 55.37 ± 11.33 years, indicating that ED predominantly affects older adults.

Based on the IIEF-5 assessment, 111 patients (49.11%) reported severe symptoms, with an average duration of complaints of 2.5 ± 2.7 years. An evaluation of comorbidities revealed that 217 patients (96%) had at least one comorbidity, and 169 patients (74.8%) presented with two or more comorbidities.

Table 1: Baseline characteristic data of the patients

Parameters	Results (n=226), n (%)
Age (years)	55.37 \pm 11.33
Duration of ED (years)	2.5 \pm 2.7
IIEF-5	8.00 (5–13)
Mild ED	32 (14.15)
Mild-moderate ED	35 (15.48)
Moderate ED	48 (21.23)
Severe ED	111 (49.11)
BMI (kg/m ²)	25.27 (23.14–27.30)
Waist circumference (cm)	93 (86.99)
TC (mg/dL)	194.5 \pm 37.66
HDL (mg/dL)	44.0 \pm 39.52
LDL (mg/dL)	126.5 (101–143)
TG (mg/dL)	121.5 (87.75–166.3)
2 h postprandial glucose (mg/dL)	147 (119–220)
Fasting glucose (mg/dL)	107 (94–136.5)
PC (10 ³ /uL)	278 (236.8–328.3)
MPV (fL)	9.7 (9.2–10.3)
PDW (fL)	10.65 (9.6–11.8)
Total testosterone (ng/dL)	476.3 (373.4–574.2)
Comorbidities	
Without comorbid	9 (3.98)
One comorbid	
DM	2 (0.88)
Dyslipidemia	33 (14.6)
Hypertension	13 (5.75)
Two comorbid	
Hypertension + dyslipidemia	92 (40.7)
DM + dyslipidemia	22 (9.73)
DM + hypertension	4 (1.76)
>2 comorbid	
DM + hypertension + dyslipidemia	12 (5.3)
MetS	39 (17.25)

DM: Diabetes mellitus, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, BMI: Body mass index, ED: Erectile dysfunction, IIEF-5: International index of erectile function-5, PC: Platelet count, PDW: Platelet distribution width, MPV: Mean platelet volume, MetS: Metabolic syndrome, TG: Triglycerides, TC: Total cholesterol

Laboratory results, which included assessments of inflammatory markers, metabolic profiles, and hormone levels, are summarized in Table 1.

Platelet profiles, erectile dysfunction severity, and comorbidity

Platelet profile analysis was conducted according to the severity of ED [Table 2]. An overall analysis was performed to evaluate the relationship between platelet profile parameters and ED severity, followed by a *post hoc* analysis to compare differences between groups.

The study results indicated that PC ($P = 0.579$), PDW ($P = 0.758$), and MPV ($P = 0.994$) did not show significant differences across the severity levels of ED. Similarly, the *post hoc* analysis did not reveal

Table 2: Statistical analysis between platelet parameters and the International Index of Erectile Function-5 degree

Variable	IIEF-5 grade				P
	Mild	Mild-moderate	Moderate	Severe	
PC (overall analysis) [#]	278.2±45.61	284.5±71.22	296.3±92.10	279.5±70.08	0.5795
PC (<i>post hoc</i> analysis)					0.6694
					0.3073
					0.9211
					0.5266
					0.7113
					0.2133
PDW (overall analysis)*	10.7 (9.9–11.8)	10.7 (9.55–12.0)	10.5 (9.25–11.35)	10.6 (9.6–11.7)	0.7584
PDW (<i>post hoc</i> analysis)					0.8809
					0.4040
					0.3686
					0.5977
					0.5009
					0.9993
MPV (overall analysis)*	9.65 (9.3–11.8)	9.65 (9.1–9.65)	9.7 (9.1–10.3)	9.7 (9.2–10.3)	0.9941
MPV (<i>post hoc</i> analysis)					0.8758
					0.8948
					0.9875
					0.7944
					0.7972
					0.9448

[#]The data were analyzed using one-way ANOVA, *Analysis performed using the Kruskal–Wallis test. PC: Platelet count, PDW: Platelet distribution width, MPV: Mean platelet volume, IIEF-5: International index of erectile function-5

any statistically significant differences between groups [Table 2].

In the analysis of comorbidities, an initial comparison was conducted between groups without comorbidities and those with comorbidities, including hypertension, diabetes mellitus, dyslipidemia, and MetS. The results revealed a significant difference in PC between patients with and without comorbidities ($P = 0.030$). However, no significant differences were observed for PDW ($P = 0.982$) or MPV ($P = 0.481$).

Further independent analyses of specific comorbid conditions revealed that patients with dyslipidemia had a significantly higher mean PC ($291.7 \pm 63.86 \times 10^3/\mu\text{L}$, $P = 0.021$), as did those with MetS ($289.5 \pm 56.13 \times 10^3/\mu\text{L}$, $P = 0.030$). Overall, PCs in patients with comorbidities were higher compared to those without comorbidities [Figure 1]. However, MPV and PDW were not significantly different between these groups. Due to the small sample size for some individual comorbidities, we did not perform analyses comparing each specific comorbidity to the noncomorbid group.

For the overall comparison of variables across the four groups classified by the IIEF-5 grade (Mild, Mild-Moderate, Moderate, and Severe), a one-way ANOVA

was employed for normally distributed data, as indicated by the presentation of means and SDs.

DISCUSSION

This study investigated the association between platelet indices – PC, MPV, and PDW – and ED severity, as well as their relationship with metabolic comorbidities. Although no statistically significant differences were found between platelet indices and ED severity across IIEF-5 groups, PC was significantly elevated among patients with dyslipidemia and MetS.

ED is frequently recognized as an early manifestation of systemic endothelial dysfunction and subclinical atherosclerosis, particularly in vascular-related cases. Previous studies reported that the penile vasculature, due to its small diameter, is particularly vulnerable to atherosclerotic changes, often preceding overt cardiovascular disease events such as myocardial infarction and stroke.^{11,12} This pathophysiological link is further supported by evidence showing that ED predicts future cardiovascular events.^{7,13}

Platelets are crucial mediators in atherosclerosis and endothelial dysfunction, releasing cytokines and chemokines that promote leukocyte adhesion and vascular inflammation.^{8,14} Nevertheless, in our study, no

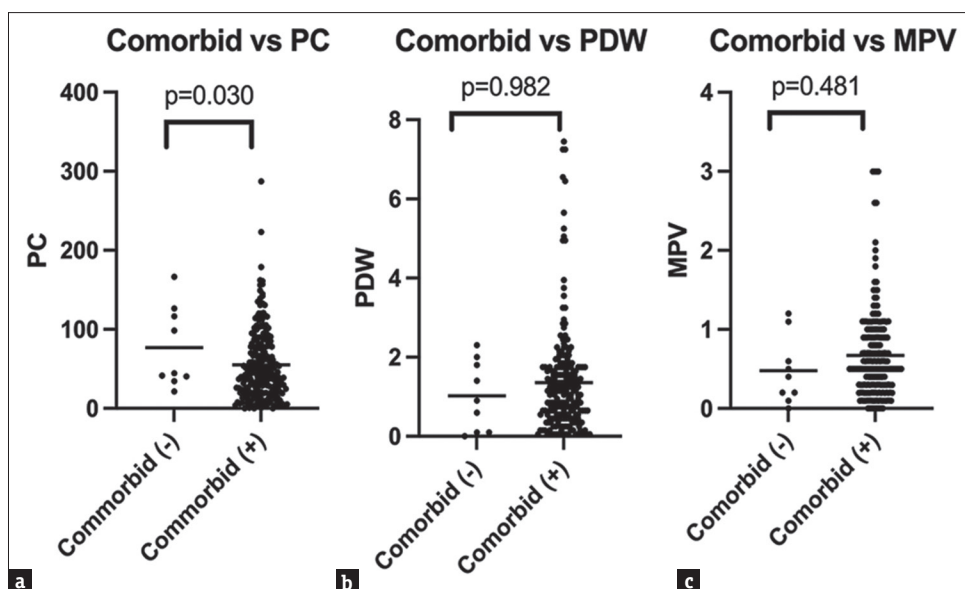


Figure 1: Analysis results between platelet findings and comorbidity status. (a) Comorbid vs Platelet Count (PC), (b) Comorbid vs Platelet Distribution Width (PDW), (c) Comorbid vs Mean Platelet Volume (MPV). PC: Platelet count, PDW: Platelet distribution width, MPV: Mean platelet volume

significant differences were observed in PC, MPV, or PDW between ED severity groups. This may be partially explained by the nature of the IIEF-5 scoring system, which does not differentiate between psychogenic and organic etiologies of ED. As such, patients with severe IIEF-5 scores may include cases with predominant psychogenic factors, thereby reducing the sensitivity to detect vascular associations through platelet markers.^{15,16}

Pozzi *et al.* (2022) demonstrated that psychogenic ED cases often present with higher IIEF-5 scores than organic ED, indicating that the questionnaire may not reflect the true vascular burden.¹⁶ Similarly, Xi *et al.* (2021) found potential bias in IIEF-5 among ED patients with premature ejaculation, further limiting its utility in pathophysiological classification.¹³ This may explain the absence of a correlation between platelet indices and ED severity in our data.

On the other hand, when stratified by comorbidities, we found significantly elevated PC in patients with dyslipidemia and MetS ($P = 0.021$ and $P = 0.030$, respectively). This finding is supported by previous studies linking metabolic disorders with increased PCs, attributed to systemic inflammation and platelet activation.^{17,18} MetS triggers chronic low-grade inflammation via increased adipokines (leptin and adiponectin) and pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor- α , which stimulate megakaryopoiesis and platelet production.^{14,19}

Although MPV is frequently cited as a marker of platelet activity and size heterogeneity, our results showed no significant differences in MPV and PDW across

comorbidity groups. This aligns with the meta-analysis by Yang and Muzepper, which reported inconsistent findings on MPV and PDW in ED patients.⁹ Similarly, Ren *et al.* (2017) found no clear differences in platelet indices between ED patients and controls, suggesting that platelet indices alone may have limited discriminative power in mixed ED populations.¹⁰ The variability in results across studies may also be influenced by unmeasured lifestyle or biosocial confounders, such as smoking, alcohol intake, and physical activity.¹⁸

Several limitations of this study should be noted. The retrospective design and reliance on self-reported IIEF-5 data may have introduced selection and classification biases. Moreover, the lack of vascular imaging (e.g. penile Doppler ultrasound) limits our ability to distinguish organic from nonorganic ED.²⁰ In addition, lifestyle and inflammatory variables that may affect platelet parameters were not included in the analysis.

Future research should incorporate objective vascular assessments and inflammatory biomarkers to better elucidate the role of platelet indices in ED pathophysiology. PC may still serve as a useful marker in patients with vascular comorbidities, although MPV and PDW appear less reliable in this context.

CONCLUSIONS

This study demonstrates that while platelet indices, including PC, MPV, and PDW, is not significantly associated with ED severity as measured by the IIEF-5, PC is significantly elevated in patients with comorbid metabolic conditions, particularly dyslipidemia and

MetS. These findings suggest that systemic inflammation and vascular alterations associated with metabolic disorders may influence platelet activation, contributing to ED pathophysiology. Although platelet indices may not serve as reliable markers of ED severity, PC could be considered a potential indicator of underlying comorbid conditions in ED patients. Further studies incorporating objective vascular assessments are warranted to validate these associations and explore their clinical implications in ED management.

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Conflicts of interest

There are no conflicts of interest.

Author contribution

Concepts and data analyses: W.S., C.P., and A.R.; manuscript writing and creation of figures: S.R., A.R., and C.P.; review and editing: P.I., P.N., and M.I.

Data availability

All data have been provided within the manuscript.

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