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Soluble P-Selectin and Platelet Indices in Metabolic Syndrome: A Cross-Sectional Study of Associations with Atherogenic and Metabolic Parameters

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Abstract

Introduction: Metabolic syndrome (MetS) comprises central obesity, dyslipidaemia, hypertension, and insulin resistance, and carries increased atherothrombotic risk. Soluble P-selectin (sP-selectin), a platelet activation marker, may contribute to vascular complications. This study compared sP-selectin and platelet indices in MetS patients versus controls and examined associations with lipid, atherogenic, and clinical parameters

Methods: A cross-sectional study of 100 participants (50 MetS, 50 controls). Fasting venous blood was analysed for sP-selectin, lipid profile, and platelet indices. Analyses included correlation with false discovery rate correction, hierarchical multiple linear regression, trend analysis, and receiver operating characteristic analysis.

Results: sP-selectin was higher in MetS than controls (100.0 ± 16.1 vs 58.0 ± 12.1 ng/mL; $P < 0.001$). MetS participants also had elevated triglycerides, total cholesterol, LDL-C, non-HDL-C, mean platelet volume (MPV), and platelet distribution width, and lower HDL-C. In MetS, sP-selectin correlated positively with atherogenic index of plasma (AIP) and TyG index; both remained significant after FDR correction ($q = 0.046$). In hierarchical regression, AIP (standardised $\beta = 0.48$; $P < 0.001$), BMI ($\beta = 0.38$; $P = 0.004$), and MPV ($\beta = 0.36$; $P = 0.004$) were independently associated with sP-selectin. sP-selectin increased with MetS component burden and across AIP tertiles.

Conclusion: Patients with MetS showed elevated sP-selectin and adverse lipid and platelet profiles. AIP was most consistently associated with sP-selectin; BMI and MPV were independently associated in the final model. These findings suggest sP-selectin may link atherogenic dyslipidaemia to platelet activation in MetS, but longitudinal studies are needed to establish temporal relationships.

Keywords: soluble P-selectin; platelet indices; metabolic syndrome; atherogenic index of plasma; dyslipidaemia

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Introduction

Metabolic syndrome (MetS) represents a cluster of interrelated metabolic disturbances encompassing central obesity, dyslipidaemia, hypertension, and insulin resistance (IR). The condition was first characterised as "syndrome X" by American endocrinologist Gerald Reaven in 1988, who recognised the interconnected nature of these components in relation to cardiovascular disease (CVD) (1). The core pathophysiology of MetS is shaped by the combined influence of genetic and environmental factors that promote IR and chronic, low-grade inflammation (2).

MetS has been strongly associated with an increased likelihood of developing serious non-communicable diseases, particularly CVD, stroke, and type 2 diabetes mellitus (T2DM) (3). Nevertheless, the precise pathophysiological mechanisms driving MetS remain incompletely understood. While some investigators identify IR as the primary causal factor, others argue that inflammation, oxidative stress, mitochondrial dysfunction, and nutritional imbalances also play contributory roles (2, 4, 5). Additionally, the centrality of obesity as the principal determinant of MetS continues to be debated, with some

researchers suggesting that ectopic fat deposition, adipose tissue dysfunction, or lipotoxicity, each influenced by dietary patterns, may function as key underlying drivers (6, 7).

Platelet hyperreactivity plays a pivotal role in the pathogenesis of atherothrombosis in patients with central obesity, T2DM, or MetS. A variety of platelet function abnormalities have been characterised in obese individuals, including increased adhesiveness and activation both in vitro and in vivo, as well as reduced sensitivity to physiological agonists (8, 9). Mean platelet volume (MPV), a parameter reflecting in vivo platelet activation (10) and an independent predictor of vascular events (11), is elevated in obese patients independently of other cardiovascular risk factors (12), with a positive correlation between BMI and MPV and concurrent reversal following weight loss (13). MPV is also significantly higher in patients with MetS than in control subjects, independently of the presence and severity of angiographically diagnosed coronary artery disease (14). Obese adolescents also exhibit significantly increased MPV compared with their healthy peers, with higher values observed in the presence of non-alcoholic fatty liver disease (NAFLD) (15). Furthermore, NAFLD is an independent predictor of MPV in adult patients (16).

The mechanisms underlying increased platelet volume in this context remain poorly understood. This may reflect an increase in circulating reticulated platelets, representing young, mRNA-rich platelets with enhanced proaggregating and haemostatic potential. Although the mechanisms influencing megakaryocytopoiesis are not fully elucidated, involvement of cytokines (interleukin-1, -3, -6, -8, -11, and -18) (17) and nitric oxide (18) has been proposed. In addition to increased MPV, the proportion of reticulated platelets has been proposed as a marker of enhanced platelet turnover. In healthy volunteers, higher levels of reticulated platelets have been associated with reduced response to aspirin, increased markers of platelet reactivity, and elevated thromboxane B2 production (19). Subjects with MetS exhibit a higher percentage of reticulated platelets in association with increased adenosine diphosphate-induced P-selectin expression (20).

Soluble P-selectin (sP-selectin) plays a pivotal role in the development of vascular complications of atherothrombosis through cellular adhesion pathways. Platelets are the major source of P-selectin, a cellular adhesion molecule with procoagulant activity (21) that can activate leukocyte integrins (22). Circulating levels of the soluble form of P-selectin mirror platelet activation. Stored in the alpha-granules of platelets, P-selectin translocates to the plasma membrane in inflammatory settings, where it can interact with ligands (23), leading to leukocyte-platelet aggregates that promote adhesion and infiltration of inflammatory cells (24, 25). sP-selectin has been associated with adiposity and both clinical and subclinical atherosclerosis (26) and has been shown to predict atherosclerosis independently of BMI and other CVD risk factors. The elevated plasma concentrations of P-selectin observed in overweight and obese insulin-resistant subjects (27, 28) are reduced following weight loss (27).

Although previous studies have examined platelet activation and haematological variation in MetS, the relationships among circulating sP-selectin, individual lipid parameters, and routinely estimated platelet indices warrant further investigation. Examining these parameters together may provide additional information regarding haematological variation corresponding to MetS and the potential relationships between dyslipidaemia and platelet activation. Therefore, this study aimed to compare circulating sP-selectin concentrations and platelet indices between patients with MetS and individuals without the syndrome, and to investigate the associations of sP-selectin with lipid profile parameters, platelet count, MPV, and platelet distribution width (PDW).

Methods

Study Design and Setting

This single-centre, comparative cross-sectional study was conducted in the clinical laboratories of Samarra General Hospital, Samarra, Salah al-Din Governorate, Iraq, in collaboration with the Department of Pathological Analysis, College of Applied Sciences, University of Samarra. Participants were recruited and sampled over eight months of active data collection between September and December 2025. Recruitment continued throughout the study period, with sampling sessions arranged based on participant availability and laboratory scheduling.

Study Population and Eligibility Criteria

A total of 100 adult male and female participants were recruited by convenience sampling from Samarra General Hospital and divided into two groups of equal size based on a structured interview. The MetS group comprised 50 patients meeting the harmonised criteria for MetS, while the control group comprised 50 individuals without MetS.

Eligible participants were aged 18–65 years. MetS was identified according to the harmonised criteria based on the presence of at least three of the following: elevated triglycerides, reduced HDL-C, elevated blood pressure, and increased fasting blood sugar. Exclusion criteria were known haematological diseases affecting platelet indices, severe renal diseases, hepatic diseases, pregnancy, blood transfusion within at least three months, use of anticoagulant medication, and unwillingness to provide informed consent. The interview recorded age, marital status, education, occupation, residence, smoking status, and medication use.

Waist circumference was not recorded in this study; therefore, BMI ≥30 kg/m² was used as a surrogate for central obesity, which represents a methodological limitation acknowledged in the Discussion.

Anthropometric and Haemodynamic Measurements

Anthropometric measurements including height and weight were recorded, and BMI was calculated as weight in

kilograms divided by height in metres squared (kg/m²). Systolic and diastolic blood pressure were measured using standard procedures.

Blood Sampling

Venous blood was withdrawn from an antecubital vein under aseptic conditions (approximately 5 mL) between 08:00 and 12:00. Blood was collected into plain gel-separator tubes, allowed to clot at room temperature for 20–30 minutes, and centrifuged at 3,000 rpm for 10 minutes. Serum was separated, inspected for haemolysis and lipaemia, and analysed on the day of collection or stored at −20°C in aliquots until batch analysis. Repeated freeze-thaw cycles were avoided.

Biochemical Analyses

Routine clinical chemistry was performed on an automated chemistry analyser (Mindray BS-200, Shenzhen Mindray Bio-Medical Electronics, Shenzhen, China) using commercial reagent kits according to the manufacturer's instructions. Fasting blood sugar (FBS) was measured by the enzymatic colourimetric (GOD-PAP) method (kit/BIOLABO, France; Catalogue No. REF 87409/80009). Total cholesterol (TC) was measured by the enzymatic colourimetric (GOD-PAP) method (kit/BIOLABO, France; Catalogue No. REF 80106/87356), and triglycerides (TG) by the enzymatic colourimetric (GPO-PAP) method (kit/BIOLABO, France; Catalogue No. REF 80019/87109). High-density lipoprotein cholesterol (HDL-C) was measured by a direct homogeneous enzymatic assay (kit/BIOLABO, France; Catalogue No. REF 90206/90406), and low-density lipoprotein cholesterol (LDL-C) was determined by a direct homogeneous enzymatic assay (kit/BIOLABO, France; Catalogue No. REF 90416/90816).

Soluble P-selectin was measured by sandwich ELISA (serum, diluted 1:10) (Kit/Elabscience, USA; Catalogue No. E-EL-H6180) on a Rayto RT-2100C reader. Immunoassays were calibrated with the manufacturer's calibrators, and two levels of internal quality-control material were analysed in every run; results were released only when controls fell within the manufacturer's acceptance limits.

Platelet indices were performed on an automated haematology analyser (Mindray BC-5000/BC-5300) using commercial reagent kits according to the manufacturer's instructions. Platelet count (PLT) was measured by electrical impedance (kit/Mindray, China; Catalogue No. M-52 reagent pack). Mean platelet volume (MPV) was measured by automated volume analysis (kit/Mindray, China; Catalogue No. Integrated CBC reagents), and platelet distribution width (PDW) was measured by automated distribution histogram (kit/Mindray, China; Catalogue No. Integrated CBC reagents).

Adult reference intervals applied for interpretation were: FBS 70–99 mg/dL (normal), ≥100 mg/dL (elevated); TC <150 mg/dL (normal), 200–499 mg/dL (high); HDL-C >40 mg/dL (male), >50 mg/dL (female); LDL-C <100 mg/dL (optimal), 160–189 mg/dL (high); TG <150 mg/dL (normal), 200–499 mg/dL (high); sP-selectin standard curve 31.25–2000 pg/mL, human serum approximately 20–120 ng/mL (reported after dilution factor); PLT 150–450 × 10⁹/L; MPV 7.4–10.4 fL; and PDW 9.0–17.0%.

In addition to the biochemical analysis, the atherogenic index of plasma (AIP) was calculated as $\log_{10}$(TG/HDL-C) with both in mmol/L, and the TyG index was calculated as ln(TG (mg/dL) × FBS (mg/dL)/2) (29).

Statistical Analysis

Analyses were performed in Python 3 using the SciPy and statsmodels libraries. The distribution of each continuous variable was assessed with the Shapiro-Wilk test. Normally distributed variables are presented as mean ± standard deviation, and non-normally distributed variables are presented as median (interquartile range) and were compared with the Mann-Whitney U test. Homogeneity of variance was assessed using Levene's test. Categorical variables are presented as counts and percentages and were compared with Pearson's chi-square test. Effect sizes are reported as Hedges' g with 95% confidence intervals.

Because 22 continuous outcomes were compared, P values were adjusted for multiplicity using the Benjamini-Hochberg false-discovery-rate procedure, and adjusted values are reported as q (30). Multivariable regression was used to estimate group differences in selected outcomes after adjustment for age, sex, BMI, MPV, and AIP. To compare across three groups, ANOVA and/or the Kruskal-Wallis test were used, with trend assessed using the Jonckheere-Terpstra test. Hierarchical multiple linear regression was used to examine correlations of soluble P-selectin with lipid, atherogenic, clinical, and platelet parameters. Two-sided P values below 0.05 were considered statistically significant.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki (31). Ethical approval was granted by the Research Ethics Committee of the College of Applied Sciences, University of Samarra, and by the administration of Samarra General Hospital. All participants received a verbal and written explanation of the aims and procedures of the study, and written informed consent was obtained before enrolment. Participation was voluntary, records were anonymised using coded identifiers, and participants with results outside the reference range were advised to seek clinical assessment.

Results

Demographic, Anthropometric, Haemodynamic, and Glycaemic Characteristics

One hundred participants were studied, comprising 50 with MetS and 50 without MetS (controls). The two groups were comparable in age (46.1 ± 8.9 vs 45.9 ± 8.8 years; Hedges' g (95% CI) = 0.02 (−0.37 to 0.42), P = 0.901) and sex distribution was balanced (26/24 males/females in both

groups, P = 1.000). The groups were also comparable in height (164.8 ± 8.6 vs 166.1 ± 8.5 cm; Hedges' g (95% CI) = −0.15 (−0.54 to 0.24), P = 0.456).

In contrast, participants with MetS had significantly higher body weight (84.6 ± 12.3 vs 65.9 ± 9.9 kg; Hedges' g (95% CI) = 1.66 (1.21 to 2.11), P < 0.001), BMI, systolic and diastolic blood pressure, and FBS than the control group (all P < 0.001) (Table 1). Among participants with MetS, elevated FBS was the most prevalent metabolic abnormality (100%), followed by elevated blood pressure (98%), hypertriglyceridaemia (78%), and low HDL-C (76%). BMI ≥30 kg/m² was present in 31 patients (62%). None of these parameters was observed in the control group.

Table 1: Baseline demographic, anthropometric, haemodynamic, and glycaemic characteristics of the study groups

Characteristic	MetS (n = 50)	Control (n = 50)	Hedges' g (95% CI)	P
Age (years)	46.1 ± 8.9	45.9 ± 8.8	0.02 (−0.37 to 0.42)	0.901[a]
Sex, male/female, n	26/24	26/24	—	1.000[c]
Height (cm)	164.8 ± 8.6	166.1 ± 8.5	−0.15 (−0.54 to 0.24)	0.456[a]
Weight (kg)	84.6 ± 12.3	65.9 ± 9.9	1.66 (1.21 to 2.11)	<0.001[b]
BMI (kg/m²)	31.1 ± 3.5	23.8 ± 2.8	2.28 (1.78 to 2.79)	<0.001[a]
SBP (mmHg)	139.0 ± 10.2	115.0 ± 6.6	2.77 (2.22 to 3.32)	<0.001[a]
DBP (mmHg)	87.5 ± 6.7	76.8 ± 4.4	1.88 (1.41 to 2.35)	<0.001[b]
FBS (mg/dL)	120.2 ± 17.9	87.8 ± 6.2	2.41 (1.89 to 2.92)	<0.001[b]
MetS components, n (%)				
TG ≥150 mg/dL	39 (78%)	0 (0%)	—	—
Low HDL-C (M <40; F <50 mg/dL)	38 (76%)	0 (0%)	—	—
BP ≥130/85 mmHg	49 (98%)	0 (0%)	—	—
FBS ≥100 mg/dL	50 (100%)	0 (0%)	—	—
BMI ≥30 kg/m²	31 (62%)	0 (0%)	—	—

Data are mean ± SD or n (%). Hedges' g = bias-corrected standardised mean difference (MetS − Control) with 95% CI. [a] Welch's t-test; [b] Mann-Whitney U test (Shapiro-Wilk P < 0.05 in at least one group); [c] Pearson's chi-square test. MetS components were defined using harmonised NCEP ATP III/IDF thresholds; BMI ≥30 kg/m² was used as a surrogate for central obesity because waist circumference was not recorded. BMI, body mass index; SBP/DBP, systolic/diastolic blood pressure; FBS, fasting blood sugar; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; BP, blood pressure

Lipid Profile, Atherogenic and Metabolic Indices, Platelet Indices, and Soluble P-Selectin

Participants with MetS exhibited a markedly more adverse lipid and platelet profile than the control group. Total cholesterol (225.3 ± 26.8 vs 182.9 ± 24.4 mg/dL; Hedges' g (95% CI) = 1.64 (1.19 to 2.09); P < 0.001), triglycerides (204.3 ± 52.3 vs 104.3 ± 25.7 mg/dL; Hedges' g (95% CI) = 2.41 (1.89 to 2.92); P < 0.001), LDL-C (143.6 ± 25.1 vs 109.7 ± 23.0 mg/dL; Hedges' g (95% CI) = 1.40 (0.96 to 1.84); P < 0.001), and non-HDL-C (186.1 ± 26.5 vs 130.5 ± 24.0 mg/dL; Hedges' g (95% CI) = 2.18 (1.69 to 2.68); P < 0.001) were all significantly higher in the MetS group, whereas HDL-C was significantly lower (39.2 ± 6.4 vs 52.4 ± 6.3 mg/dL; Hedges' g (95% CI) = −2.06 (−2.55 to −1.58); P < 0.001) (Table 2).

Atherogenic and metabolic indices were elevated in the MetS group compared with controls. AIP (0.35 ± 0.14 vs −0.07 ± 0.12; Hedges' g (95% CI) = 3.16 (2.57 to 3.75); P < 0.001), CRI-I (TC/HDL-C) (5.89 ± 1.14 vs 3.54 ± 0.60; Hedges' g (95% CI) = 2.58 (2.05 to 3.11); P < 0.001), CRI-II (LDL-C/HDL-C) (3.77 ± 0.94 vs 2.13 ± 0.55; Hedges' g (95% CI) = 2.11 (1.63 to 2.60); P < 0.001), AC (4.89 ± 1.14 vs 2.54 ± 0.60; Hedges' g (95% CI) = 2.58 (2.05 to 3.11); P < 0.001), and TyG index (9.37 ± 0.30 vs 8.39 ± 0.28; Hedges' g (95% CI) = 3.37 (2.76 to 3.98); P < 0.001) were all significantly higher in the MetS group.

Platelet count showed a modest difference between groups (281.0 ± 55.9 vs 259.7 ± 49.4 × 10⁹/L; Hedges' g (95% CI) = 0.40 (0.00 to 0.80); P = 0.047). MPV and PDW were significantly higher in the MetS group (10.20 ± 0.82 vs 9.15 ± 0.62 fL; Hedges' g (95% CI) = 1.42 (0.98 to 1.86); P < 0.001) and (14.52 ± 1.64 vs 12.27 ± 1.09%; Hedges' g (95% CI) = 1.60 (1.15 to 2.05); P < 0.001), respectively. The study demonstrated a markedly elevated concentration of sP-selectin in the MetS group compared with controls (100.0 ± 16.1 vs 58.0 ± 12.1 ng/mL) with a very large effect size (Hedges' g (95% CI) = 2.93 (2.36 to 3.49); P < 0.001).

Table 2: Lipid profile, atherogenic and metabolic indices, platelet indices, and soluble P-selectin in the study groups

Parameter	MetS (n = 50)	Control (n = 50)	Δ (%)	Hedges' g (95% CI)	P

Conventional lipid profile					
TC (mg/dL)	225.3 ± 26.8	182.9 ± 24.4	+23.2	1.64 (1.19 to 2.09)	<0.001[a]
TG (mg/dL)	204.3 ± 52.3	104.3 ± 25.7	+95.8	2.41 (1.89 to 2.92)	<0.001[a]
HDL-C (mg/dL)	39.2 ± 6.4	52.4 ± 6.3	−25.2	−2.06 (−2.55 to −1.58)	<0.001[a]
LDL-C (mg/dL)	143.6 ± 25.1	109.7 ± 23.0	+30.9	1.40 (0.96 to 1.84)	<0.001[a]
Non-HDL-C (mg/dL)	186.1 ± 26.5	130.5 ± 24.0	+42.6	2.18 (1.69 to 2.68)	<0.001[a]
Atherogenic and metabolic indices					
AIP	0.35 ± 0.14	−0.07 ± 0.12	—	3.16 (2.57 to 3.75)	<0.001[a]
CRI-I (TC/HDL-C)	5.89 ± 1.14	3.54 ± 0.60	+66.7	2.58 (2.05 to 3.11)	<0.001[a]
CRI-II (LDL-C/HDL-C)	3.77 ± 0.94	2.13 ± 0.55	+76.9	2.11 (1.63 to 2.60)	<0.001[a]
AC	4.89 ± 1.14	2.54 ± 0.60	+93.0	2.58 (2.05 to 3.11)	<0.001[a]
TyG index	9.37 ± 0.30	8.39 ± 0.28	+11.6	3.37 (2.76 to 3.98)	<0.001[b]
Platelet indices and activation markers					
PLT (×10⁹/L)	281.0 ± 55.9	259.7 ± 49.4	+8.2	0.40 (0.00 to 0.80)	0.047[a]
MPV (fL)	10.20 ± 0.82	9.15 ± 0.62	+11.4	1.42 (0.98 to 1.86)	<0.001[a]
PDW (%)	14.52 ± 1.64	12.27 ± 1.09	+18.3	1.60 (1.15 to 2.05)	<0.001[a]
sP-Selectin (ng/mL)	100.0 ± 16.1	58.0 ± 12.1	+72.4	2.93 (2.36 to 3.49)	<0.001[a]

Data are mean ± SD. Δ (%) = (mean MetS − mean Control)/mean Control × 100; not calculated for AIP because the control mean is close to zero. [a] Welch's t-test; [b] Mann-Whitney U test. AIP = $\log_{10}$(TG/HDL-C) (both in mmol/L); CRI-I = TC/HDL-C; CRI-II = LDL-C/HDL-C; AC = (TC − HDL-C)/HDL-C; TyG = ln(TG (mg/dL) × FBS (mg/dL)/2). AC is arithmetically equal to CRI-I − 1 and therefore yields identical inferential statistics. TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; PLT, platelet count; MPV, mean platelet volume; PDW, platelet distribution width; sP-Selectin, soluble P-selectin

Correlation of Soluble P-Selectin with Lipid, Atherogenic, Clinical, and Platelet Parameters

a. Correlations with Lipid and Atherogenic Parameters

In the MetS group, sP-selectin showed a significant positive correlation with AIP (Pearson r = 0.37, 95% CI 0.10 to 0.59, P = 0.008; Spearman ρ = 0.40, P = 0.004), and this correlation remained significant after FDR correction (q = 0.046). The TyG index also showed a significant positive correlation with sP-selectin (Pearson r = 0.36, 95% CI 0.09 to 0.58, P = 0.010; Spearman ρ = 0.37, P = 0.008), which also remained significant after FDR correction (q = 0.046). In contrast, HDL-C showed an inverse correlation with sP-selectin (Pearson r = −0.29, 95% CI −0.53 to −0.02, P = 0.038; Spearman ρ = −0.34, P = 0.017); however, this correlation did not remain significant after FDR correction (q = 0.098).

Additional correlations that did not reach statistical significance after FDR correction included TC (Pearson r = 0.05, P = 0.731), TG (Pearson r = 0.25, P = 0.077), LDL-C (Pearson r = 0.01, P = 0.926), non-HDL-C (Pearson r = 0.12, P = 0.400), and CRI-I (Pearson r = 0.29, P = 0.044; q = 0.098) (Table 3).

b. Correlations with Clinical and Platelet Parameters

In the MetS group, neither clinical nor platelet parameters remained significantly correlated with sP-selectin after correction for multiple comparisons. Age showed no significant correlation with sP-selectin (Pearson r = 0.01, 95% CI −0.27 to 0.29, P = 0.955; Spearman ρ = 0.00, P = 0.997; q = 0.955). BMI showed a weak correlation that did not reach statistical significance (Pearson r = 0.26, 95% CI −0.02 to 0.50, P = 0.071; Spearman ρ = 0.21, P = 0.139; q = 0.224). Systolic blood pressure, diastolic blood pressure, and fasting blood sugar also showed weak correlations with sP-selectin. Platelet count was not correlated with sP-selectin (Pearson r = −0.11, 95% CI −0.37 to 0.18, P = 0.466). MPV showed a modest correlation with sP-selectin (Pearson r = 0.29, 95% CI 0.01 to 0.53, P = 0.041), but this correlation was not confirmed by Spearman analysis (ρ = 0.23, P = 0.112) and did not remain significant after FDR correction (q = 0.224). PDW did not show a significant correlation with sP-selectin (Pearson r = 0.19, P = 0.180).

In the control group, most clinical and platelet parameters did not show significant correlations with sP-selectin. Only BMI showed a positive significant unadjusted correlation with sP-selectin (Pearson r = 0.37, P = 0.007); however, this finding should be interpreted cautiously because it was not adjusted for multiple comparisons (Table 3).

Table 3: Correlation of soluble P-selectin with lipid, atherogenic, clinical, and platelet parameters within the MetS group (n = 50), with the control group shown for comparison

Parameter	Pearson r (95% CI)	P	Spearman ρ	P	q (FDR)	Control r (P)

A. Lipid profile and atherogenic indices (primary family)						
TC (mg/dL)	0.05 (−0.23 to 0.32)	0.731	0.09	0.549	0.822	0.03 (0.824)
TG (mg/dL)	0.25 (−0.03 to 0.50)	0.077	0.27	0.060	0.139	0.17 (0.245)
HDL-C (mg/dL)	−0.29 (−0.53 to −0.02)	0.038	−0.34	0.017	0.098	0.03 (0.852)
LDL-C (mg/dL)	0.01 (−0.27 to 0.29)	0.926	−0.02	0.908	0.926	0.01 (0.922)
Non-HDL-C (mg/dL)	0.12 (−0.16 to 0.39)	0.400	0.13	0.372	0.515	0.03 (0.860)
AIP	0.37 (0.10 to 0.59)	0.008	0.40	0.004	0.046	0.13 (0.366)
CRI-I (TC/HDL-C)	0.29 (0.01 to 0.52)	0.044	0.29	0.044	0.098	0.00 (0.993)
CRI-II (LDL-C/HDL-C)	0.19 (−0.09 to 0.45)	0.179	0.21	0.148	0.268	−0.01 (0.961)
TyG index	0.36 (0.09 to 0.58)	0.010	0.37	0.008	0.046	0.12 (0.393)
B. Clinical and platelet parameters (secondary family)						
Age (years)	0.01 (−0.27 to 0.29)	0.955	0.00	0.997	0.955	−0.08 (0.596)
BMI (kg/m²)	0.26 (−0.02 to 0.50)	0.071	0.21	0.139	0.224	0.37 (0.007)
SBP (mmHg)	0.16 (−0.12 to 0.42)	0.266	0.11	0.457	0.426	0.25 (0.081)
DBP (mmHg)	0.11 (−0.17 to 0.38)	0.427	0.06	0.690	0.532	0.13 (0.383)
FBS (mg/dL)	0.25 (−0.03 to 0.49)	0.084	0.19	0.181	0.224	−0.06 (0.676)
PLT (×10⁹/L)	−0.11 (−0.37 to 0.18)	0.466	−0.01	0.927	0.532	0.00 (0.993)
MPV (fL)	0.29 (0.01 to 0.53)	0.041	0.23	0.112	0.224	−0.08 (0.576)
PDW (%)	0.19 (−0.09 to 0.45)	0.180	0.19	0.176	0.361	0.05 (0.741)

FDR, false discovery rate; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; AIP, atherogenic index of plasma; CRI, Castell risk index; TyG, triglyceride-glucose; BMI, body mass index; SBP/DBP, systolic/diastolic blood pressure; FBS, fasting blood sugar; PLT, platelet count; MPV, mean platelet volume; PDW, platelet distribution width

Hierarchical Multiple Linear Regression of Determinants of Soluble P-Selectin in the MetS Group

In hierarchical multiple linear regression analysis, AIP was significantly correlated with sP-selectin when entered alone (B = 41.24, 95% CI of B = 11.04 to 71.45, standardised β = 0.37, P = 0.008), explaining 13.6% of the variance in sP-selectin concentration. AIP remained independently correlated with sP-selectin after adjustment for age, sex, and BMI (standardised β = 0.43, P = 0.003). BMI also emerged as a significant indicator (standardised β = 0.33, P = 0.021). In the full adjustment model including FBS and MPV, the adjusted R^2 was 0.351 (ΔR^2 = 0.187, P(F-change) = 0.002). AIP remained the strongest independent indicator of sP-selectin (B = 53.20, 95% CI of B = 25.14 to 81.26, standardised β = 0.48, P < 0.001), followed by BMI (B = 1.73, 95% CI of B = 0.59 to 2.88, standardised β = 0.38, P = 0.004) and MPV (B = 7.07, 95% CI of B = 2.44 to 11.70, standardised β = 0.36, P = 0.004). FBS, age, and sex showed no independent correlation with sP-selectin, with VIF values of 1.03, 1.07, and 1.24, respectively (Table 4).

Table 4: Hierarchical multiple linear regression of determinants of soluble P-selectin (ng/mL) in the MetS group (n = 50)

Predictor	B	95% CI of B	Standardised β	P	VIF
Model 1: AIP only (R^2 = 0.136; adjusted R^2 = 0.118; ΔR^2 = 0.136, P(F-change) = 0.008)					
AIP	41.24	11.04 to 71.45	0.37	0.008	1.00
Model 2: + age, sex, BMI (R^2 = 0.243; adjusted R^2 = 0.176; ΔR^2 = 0.108, P(F-change) = 0.109)					
AIP	48.32	16.92 to 79.72	0.43	0.003	1.15
Age (years)	0.17	−0.32 to 0.65	0.09	0.496	1.07
Male sex	−1.21	−10.35 to 7.93	−0.04	0.791	1.21
BMI (kg/m²)	1.51	0.24 to 2.78	0.33	0.021	1.13
Model 3: + FBS, MPV (R^2 = 0.431; adjusted R^2 = 0.351; ΔR^2 = 0.187, P(F-change) = 0.002)					
AIP	53.20	25.14 to 81.26	0.48	<0.001	1.17

Age (years)	0.17	−0.27 to 0.60	0.09	0.441	1.07
Male sex	−1.09	−9.31 to 7.12	−0.03	0.790	1.24
BMI (kg/m²)	1.73	0.59 to 2.88	0.38	0.004	1.15
FBS (mg/dL)	0.19	−0.02 to 0.40	0.22	0.071	1.03
MPV (fL)	7.07	2.44 to 11.70	0.36	0.004	1.05

B, unstandardised regression coefficient (change in sP-selectin, ng/mL per unit increase in predictor); β, standardised coefficient; VIF, variance inflation factor (all <1.3 indicating no multicollinearity). Sex was coded male = 1, female = 0. Overall model F-tests: Model 1, F(1,48) = 7.54, P = 0.008; Model 2, F(4,45) = 3.62, P = 0.012; Model 3, F(6,43) = 5.42, P < 0.001. Residual diagnostics: Shapiro-Wilk P = 0.354, 0.348, and 0.048; Breusch-Pagan P ≥ 0.195; maximum Cook's distance 0.17 (no influential observations)

Soluble P-Selectin Across the Number of MetS Components and Across AIP Tertiles

The concentration of sP-selectin increased gradually with the number of MetS components. Mean sP-selectin concentration increased from 89.7 ± 14.8 ng/mL in participants with three MetS components to 96.7 ± 13.3 ng/mL in those with four components and to 110.8 ± 15.3 ng/mL in those with five components. The differences between these groups were significant (ANOVA/Kruskal-Wallis P = 0.003; P for trend by Jonckheere-Terpstra < 0.001). A similar graded pattern was observed across AIP tertiles. Mean sP-selectin concentration increased from 92.8 ± 13.4 ng/mL in the lowest AIP tertile to 100.8 ± 16.0 ng/mL in the middle tertile and to 106.3 ± 16.5 ng/mL in the highest tertile. The differences between these groups were significant (ANOVA/Kruskal-Wallis P = 0.045; P for trend by Jonckheere-Terpstra = 0.009) (Table 5).

Table 5: Soluble P-selectin (ng/mL) across the number of MetS components and across AIP tertiles in the MetS group (n = 50)

Stratum	N	Mean ± SD	Median (IQR)
A. By number of MetS components			
3 components	9	89.7 ± 14.8	85.1 (82.8–94.7)
4 components	25	96.7 ± 13.3	100.8 (87.3–106.5)
5 components	16	110.8 ± 15.3	109.4 (101.2–118.7)
P (ANOVA/Kruskal-Wallis)		0.001	0.003
P for trend (Jonckheere-Terpstra)		<0.001	
Spearman ρ = 0.49, P < 0.001			
B. By AIP tertiles			
T1 (AIP 0.05 to 0.31)	17	92.8 ± 13.4	94.7 (83.8–102.2)
T2 (AIP 0.32 to 0.40)	16	100.8 ± 16.0	103.4 (89.6–109.1)
T3 (AIP 0.42 to 0.71)	17	106.3 ± 16.5	109.0 (96.8–116.4)
P (ANOVA/Kruskal-Wallis)		0.045	0.034
P for trend (Jonckheere-Terpstra)		0.009	

For P rows, the Mean ± SD column reports one-way ANOVA and the Median (IQR) column reports the Kruskal-Wallis test. P for trend from the Jonckheere-Terpstra test for ordered alternatives. IQR, interquartile range. MetS components were counted as defined in Table 1. AIP, atherogenic index of plasma

Receiver Operating Characteristic Analysis of Soluble P-Selectin and MetS Indices

Receiver operating characteristic analysis indicated high discrimination between participants with MetS and controls for sP-selectin, AIP, TyG index, CRI-I (TC/HDL-C), and MPV. sP-selectin showed an AUC of 0.986 (95% CI 0.966–0.998) with an optimal cut-off of ≥73.0 ng/mL, providing 100% sensitivity and 90% specificity. The TyG index showed the highest AUC of 0.993 (95% CI 0.980–1.000) with a cut-off of ≥8.86, sensitivity of 92%, and specificity of 100%. AIP and CRI-I (TC/HDL-C) also showed high discrimination (Table 6). In contrast, MPV showed relatively lower discrimination (AUC = 0.848, 95% CI 0.765–0.918; cut-off ≥9.70, sensitivity = 78%, specificity = 82%). These estimates should be interpreted with caution because control participants had none of the MetS components, creating a comparison between clinically distinct extremes (spectrum bias); therefore, these values should not be interpreted as diagnostic accuracy in unselected populations.

Table 6: Receiver operating characteristic analysis of soluble P-selectin and atherogenic indices for discriminating MetS from controls

Marker	AUC (95% CI)	Cut-off	Sens. (%)	Spec. (%)	PPV (%)	NPV (%)	Youden J

sP-Selectin (ng/mL)	0.986 (0.966–0.998)	≥73.0	100	90	90.9	100.0	0.90
AIP	0.986 (0.968–0.998)	≥0.099	89	90	90.7	97.8	0.88
TyG index	0.993 (0.980–1.000)	≥8.86	92	100	100.0	92.6	0.92
CRI-I (TC/HDL-C)	0.977 (0.949–0.997)	≥4.50	96	94	94.1	95.9	0.90
MPV (fL)	0.848 (0.765–0.918)	≥9.70	78	82	81.2	78.8	0.60

AUC, area under the curve with percentile bootstrap 95% CI (2,000 resamples); optimal cut-off by the maximum Youden index (J = sensitivity + specificity − 1); PPV/NPV, positive/negative predictive values at the study prevalence (50%). Interpretation caution: control participants had none of the MetS components, so these estimates describe discrimination between clinically distinct extremes (spectrum bias) and should not be interpreted as diagnostic accuracy in unselected populations. AIP, atherogenic index of plasma; TyG, triglyceride-glucose; CRI-I, Castell risk index I; MPV, mean platelet volume; sP-Selectin, soluble P-selectin

Discussion

This study aimed to investigate the associations between sP-selectin and lipid profile, atherogenic indices, platelet indices, and metabolic parameters in patients with MetS. The principal findings indicate that participants with MetS exhibited a markedly adverse lipid profile characterised by higher BMI, blood pressure, FBS, TG, TC, LDL-C, and non-HDL-C, alongside lower HDL-C. sP-selectin was significantly elevated in the MetS group compared with controls, with concurrent increases in MPV and PDW. Within the MetS group, sP-selectin showed positive correlations with AIP and TyG index. Hierarchical multiple linear regression identified AIP, MPV, and BMI as independent correlates of sP-selectin concentration. Furthermore, sP-selectin increased gradually with rising MetS component burden and across AIP tertiles.

Lipid Profile in MetS

The lipid profile findings in this study align with the characteristic dyslipidaemia observed in MetS. Triglyceride levels were approximately twice as high in the MetS group compared with controls. When the capacity of adipocytes to store triglycerides as fat is exceeded, fat is deposited in the liver and skeletal muscle (32). Adipocyte expression of monocyte chemoattractant protein-1 and other cytokines promotes infiltration of macrophages and other immune cells into adipose tissue (33). These macrophages release cytokines that may contribute to insulin resistance in muscle, liver, and other tissues by impairing insulin signalling through increased serine phosphorylation of insulin receptor substrate-1 [33]. This process may lead to increased adipocyte lipolysis and elevated levels of free fatty acids, which flux to the liver where increased rates of hepatic triglyceride and apolipoprotein C-III synthesis promote secretion of triglyceride-rich VLDL containing apoC-III, resulting in elevated plasma triglyceride levels (34, 35). Furthermore, reduced HDL-C levels were observed in the MetS group compared with controls. HDL exerts protective and anti-inflammatory effects against atherosclerosis, and low levels may permit free fatty acids to inhibit these effects. Additionally, increased production of apoB, free fatty acids, apoC-III, and VLDL, all of which promote secretion of triglyceride-rich VLDL, is associated with pro-inflammatory mechanisms that may contribute to atherosclerosis and thrombosis (35). Research also indicates that dyslipidaemia may promote platelet activation and aggregation, with increased platelet activation and thrombosis formation associated with impaired HDL cholesterol transport (36, 37). AIP, defined as the logarithmic value of the ratio between serum triglycerides and HDL-C, serves as a valuable indicator of atherogenic dyslipidaemia. This index quantitatively reflects the balance between atherogenic and anti-atherogenic lipoprotein fractions and has emerged as a useful tool in assessing CVD risk associated with MetS. A recent systematic review and meta-analysis of 13 studies reported a significant association between elevated AIP values and MetS, consistent with the findings of the present study (38).

The study also showed elevated TyG index levels in patients with MetS, reflecting the high lipid profile and low HDL-C levels observed. Pathogenic mechanisms proposed to explain this increased risk include endothelial dysfunction, increased oxidative stress, a pro-inflammatory state, and increased thrombosis (39, 40).

Elevation of Soluble P-Selectin in Metabolic Syndrome

The principal finding of this study was the elevation of sP-selectin in patients with MetS. The concentration of sP-selectin was 72.4% higher than in the control group. Additionally, a gradual increase in sP-selectin concentration was observed with increasing metabolic burden. Previous studies have reported that elevated lipid and triglyceride levels are associated with increased concentrations of P-selectin (41). Moreover, in a study of obese women without other cardiovascular risk factors, visceral body fat was found to correlate with endothelial dysfunction and elevated circulating P-selectin levels; in this group, reduction of body weight (of at least 10%) was associated with decreased cytokine levels, reflecting reduced endothelial activation (42). In evaluations of patients with insulin resistance and MetS, platelet expression of P-selectin, platelet-leukocyte aggregates, and plasma P-selectin were all found to be increased (43).

The association between sP-selectin and AIP observed in this study suggests that atherogenic dyslipidaemia may be linked to platelet activation in MetS. The finding that AIP remained the strongest independent correlate of sP-selectin in the regression model supports this relationship, although the cross-sectional design precludes causal inference.

Platelet Indices

The study showed elevated MPV and PDW levels, with a modest increase in platelet count. The biological mechanisms linking MetS with platelet parameters are not yet fully elucidated; however, previous studies provide a biological basis for the present findings. MetS is characterised by a state of chronic low-grade inflammation (44) that may enhance megakaryocyte activity and platelet production, leading to increased platelet count (45). Inflammatory factors and metabolic disturbances, such as hyperglycaemia and dyslipidaemia, may also be associated with platelet activation and increased size heterogeneity, manifested as elevated PDW (46). Although the association between MPV and MetS was statistically significant, the effect size was small, suggesting potentially limited clinical relevance, which may be attributable to the influence of multiple physiological and pathological factors on MPV (47).

Study Limitations

This study has several limitations that warrant consideration. First, the cross-sectional design precludes establishment of temporal or causal relationships between sP-selectin, atherogenic indices, and platelet parameters. Second, the modest sample size (n = 50 per group), particularly for multivariable analyses, limits statistical power and may increase the risk of overfitting in the regression model. Third, waist circumference was not available, and BMI was used as a surrogate for central obesity, which represents a methodological limitation for MetS classification. Fourth, the control group had no MetS components, creating an extreme group comparison that may inflate diagnostic accuracy estimates and effect sizes. Fifth, convenience sampling may introduce selection bias, and the single-centre design limits generalisability. Finally, the study did not measure insulin resistance directly, relying instead on the TyG index as a surrogate marker.

Future Directions

Future studies should aim to replicate these findings in larger, more diverse, and prospective populations. Incorporating waist circumference and direct measurement of insulin resistance would strengthen MetS classification and allow more precise examination of the relationships between atherogenic dyslipidaemia, platelet activation, and cardiovascular risk. Longitudinal designs would enable assessment of temporal relationships and potential causal pathways. Additionally, investigating the predictive value of sP-selectin for cardiovascular events in MetS populations would help clarify its clinical utility.

Conclusion

The present study demonstrated that patients with MetS exhibit elevated concentrations of sP-selectin alongside adverse lipid profiles, metabolic indices, and platelet indices compared with controls. Among the variables studied, AIP showed the most consistent correlation with sP-selectin, while BMI and MPV were independently correlated with sP-selectin concentration in the final regression model. Additionally, sP-selectin concentration increased gradually with metabolic burden and across AIP tertiles. These findings suggest that sP-selectin may serve as a potential marker linking atherogenic dyslipidaemia to platelet activation in MetS. However, given the cross-sectional design and limited sample size, these results should be considered hypothesis-generating, and longitudinal studies are needed to establish temporal relationships and clinical utility.

Abbreviations

AC: Atherogenic coefficient
AIP: Atherogenic index of plasma
ANOVA: Analysis of variance
AUC: Area under the curve
BMI: Body mass index
BP: Blood pressure
CI: Confidence interval
CRI: Castell risk index
CVD: Cardiovascular disease
DBP: Diastolic blood pressure
FBS: Fasting blood sugar
FDR: False discovery rate
HDL-C: High-density lipoprotein cholesterol
IQR: Interquartile range
IR: Insulin resistance
LDL-C: Low-density lipoprotein cholesterol
MetS: Metabolic syndrome
MPV: Mean platelet volume
NAFLD: Non-alcoholic fatty liver disease
NPV: Negative predictive value
PDW: Platelet distribution width
PLT: Platelet count
PPV: Positive predictive value
ROC: Receiver operating characteristic
SBP: Systolic blood pressure
SD: Standard deviation
sP-selectin: Soluble P-selectin
T2DM: Type 2 diabetes mellitus
TC: Total cholesterol
TG: Triglycerides
TyG: Triglyceride-glucose index
VIF: Variance inflation factor

Declarations

Ethics Approval and Consent to Participate: The study was approved by the Research Ethics Committee of the College of Applied Sciences, University of Samarra (1940/7), and by the administration of Samarra General Hospital. It was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from every participant.

Data Availability: The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.
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