

Study of Platelet Indices in Patients with Metabolic Syndrome

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Int J Recent Surg Med Sci 2019;5:10–14

Abstract

Introduction Metabolic syndrome (MetS) is a combination of abdominal obesity, atherogenic dyslipidemia, elevated blood pressure, and elevated plasma glucose. MetS patients have higher chances of developing insulin resistance, visceral adiposity, atherogenic dyslipidemia, and thus coronary artery disease and stroke. Alteration of platelet indices in diabetes mellitus, atherosclerosis, and other proinflammatory states has been described in multiple studies. Thus, this study was carried out to assess platelet indices in MetS.

Objectives This study was carried out to assess platelet indices in MetS.

Methods A cross-sectional study was carried out at Acharya Vinoba Bhave Rural Hospital, a tertiary care center over a period of 2 months from June 1, 2018 to July 31, 2018. Fifty patients diagnosed as having MetS, and 50 healthy controls were chosen. Estimation of anthropometric parameters including waist circumference; measurement of blood pressure; biochemical parameters including lipid profile; and platelet indices including platelet-crit, mean platelet volume (MPV), and platelet distribution width (PDW) were carried out.

Statistical Analysis Statistical analyses were carried out using inferential statistics, including chi-square test and Student's unpaired *t*-test, and software SPSS version 22.0 (IBM Corporation, Armonk, New York, United States) with GraphPad Prism version 6.0 (Informer Technologies, Inc. Los Angeles, California, United States) was used, with $p < 0.05$ being considered as significant.

Results A statistically significant, positive correlation was found between the waist circumference, systolic blood pressure, serum triglyceride levels, and plateletcrit, with the MetS status of patients ($p < 0.05$).

Conclusion This study revealed that MetS is a proinflammatory and prothrombotic state, characterized by alteration of platelet indices. Plateletcrit was shown to be a statistically significant biomarker along with other parameters such as waist circumference, systolic blood pressure, and serum triglyceride levels. Early detection and follow-up of patients using these markers can lead to an overall decline in morbidity and mortality owing to MetS.

Keywords

- ▶ metabolic syndrome
- ▶ atherosclerosis
- ▶ platelet indices
- ▶ triglycerides

Introduction

Metabolic syndrome (MetS) is a combination of abdominal obesity, atherogenic dyslipidemia, elevated blood pressure

(BP), and elevated plasma glucose.¹ Prevalence of the MetS in India varies according to extent of urbanization, with some studies reporting that up to one-third of the urban population

received
November 2, 2018
accepted
February 19, 2019

DOI <https://doi.org/10.1055/s-0039-1688542>
ISSN 2455-7420.

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in large cities in India have MetS.^{2,3} Studies from South India have shown the prevalence of classic risk factors for MetS to be 31.4% for abdominal obesity, 45.6% for hypertriglyceridemia, 65.5% for low high-density lipoprotein (HDL), 55.4% for hypertension, and 26.7% having raised fasting plasma glucose.^{4,5} Some of the studies from eastern India have estimated a prevalence of MetS to be 31.4% in their study population, with female population having a higher prevalence than male population.⁶ The rural prevalence of MetS is found to be reasonably low when compared with the urban prevalence.⁷

Recent studies on platelet volume indices in the spectrum of ischemic heart diseases show that all platelet indices—plateletcrit, mean platelet volume (MPV) and platelet distribution width (PDW)—were significantly raised in patients who had suffered from acute myocardial ischemia. A key component of vaso-occlusion is believed to be increased platelet activation and reactivity, and thus an increased platelet volume resulting in an elevated PDW. Also, higher concentrations of platelet microparticles have been detected in proinflammatory disorders such as sickle cell anemia. Studies on diabetes mellitus (DM), which too is considered to be a prothrombotic state with enhanced platelet reactivity, found a statistical rise in MPV and PDW, yet very few studies have been carried out regarding platelet indices for MetS patients.

MetS patients have been found to be at a greater risk for developing insulin resistance, visceral adiposity, atherogenic dyslipidemia, and endothelial dysfunction. Patients with insulin resistance tend to develop hypertriglyceridemia and are prone for developing atheromas in vascular lumen, leading to an increased incidence of coronary artery disease and stroke.⁸ Hypertriglyceridemia too leads to endothelial dysfunction that predisposes to the development of atherosclerotic depositions along vessel lumina. Visceral adiposity has been implicated in dysregulation of adiponectin levels, which too eventually causes vascular dysfunction.⁹

Thus, in multiple recent studies, it has been shown that platelet indices are higher in patients suffering from DM, impaired fasting glucose, and dyslipidemia, as compared with normal, healthy individuals. Thus, the aim of this study was to analyze the platelet indices in MetS patients.

Objectives

- To assess various platelet indices in MetS patients including plateletcrit, MPV, and PDW.
- To correlate platelet indices with other parameters of MetS, including waist circumference, BP, and lipid profile.

Methods

After obtaining due consent from the institutional ethics committee, a cross-sectional study was conducted in the Department of Medicine, and Central Clinical Laboratory, Acharya Vinoba Bhave Rural Hospital (AVBRH), Sawangi (Meghe), Wardha, for a period of 2 months from June 1, 2018 to July 31, 2018.

Study participants selected were 50 MetS patients aged between 18 and 60 years, attending the medicine OPD and/

or admitted to the medicine ward/intensive care unit (ICU). A control group of 50 healthy, non-MetS participants was also chosen. Participants were selected on the basis of simple random sampling to eliminate any bias.

Diagnostic Criteria

Diagnostic criteria used to classify MetS patients included the American College of Cardiology and American Health Association's National Cholesterol Education Program: modified Adult Treatment Plan III (NCEP-ATP III) criteria,¹⁰ which includes the following, and requires three or more positive findings to confirm a diagnosis:

- Abdominal obesity: Waist circumference > 80 cm in women and > 90 cm in men
- Body mass index (BMI): > 30 kg/m², and/or waist/hip ratio > 0.09 in men and > 0.85 in women
- Raised triglyceride levels: ≥ 150 mg/dL
- Reduced HDL levels: < 40 mg/dL in men and < 50 mg/dL in women
- Raised BP: ≥ 130 mm Hg systolic or ≥ 85 mm Hg diastolic
- Raised fasting glucose levels: 110–125 mg/dL, type 2 DM or impaired glucose tolerance and/or insulin resistance, denoted by hyperinsulinemia relative to glucose levels

Exclusion criteria considered were

- Patients suffering from coronary artery disease, stroke, or DM
- Patients having blood dyscrasias such as sickle cell trait or thalassemia
- Patients on treatment including glucocorticoids, anticoagulants, or antiplatelet drugs

Written consent of participants was then obtained, which explained in detail about the purpose, methodology, and implications of this study. Next, a proforma detailing relevant clinical history was taken.

Measurement of Blood Pressure

According to American Heart Association (AHA) guidelines, high BP is defined as readings of ≥ 130 mm Hg for systolic blood pressure (SBP) measurement, or readings of ≥ 80 for the diastolic blood pressure (DBP) measurement. BP of each patient was thus taken based on AHA-recommended protocol.¹¹

Measurement of Waist Circumference

Waist circumference was measured at the midpoint between the lower margin of least palpable rib and the top of the iliac crest, using a stretch resistant tape that provided a constant 100-g tension. The tape was fitted to be snug around the body, but not pulled so tight that it was constricting. The patient was made to stand with arms at the sides, feet positioned close together, and weight evenly distributed across the feet. Waist circumference was measured at the end of a normal expiration, when the lungs are at their functional residual capacity. The patient was advised to relax and take a few deep, natural breaths before the actual measurement was made, to minimize the pull of abdominal contents during the waist measurement.

Collection of Blood Sample

Skin over the median cubital vein was first disinfected by applying surgical spirit over the cubital fossa, along with the application of a tourniquet proximal to the fossa. Then using a sterile standard venipuncture needle, blood was collected in a potassium ethylene diamine tetra acetate bulb for sampling and complete blood count, and was analyzed within 15 minutes of collection.

Calculation of Mean Platelet Volume

The blood collected was placed in a siliconed, graduated centrifuge tube containing 0.3 mL of 45% disodium ethylene diamine tetraacetic acid and mixed. Then the sample was spun at 900 rpm (revolution per minute) for 15 minutes and supernatant plasma separated 20 mm of platelet-rich plasma obtained was then diluted in 100 mL of 0.85% saline giving a dilution ratio of 1/5,000.

Electronic Counting of Platelet Indices

Based on the principle of detection of electrolyte displacement, platelet indices were then obtained from the 1/5,000 dilution using a coulter counter (Beckman coulter Z series: Z counter manufactured by Beckman Coulter, Germany), with a 0.50 orifice, aperture current setting 7, and threshold 25.

Calculation of Triglycerides

Quantitative in vitro determination of triglycerides in serum or plasma was done by colorimetric method. The triglycerides were determined after enzymatic hydrolysis with lipases. The indicator used was a quinone imine formed from hydrogen peroxide, 4-aminophenazone, and 4-chlorophenol under the influence of peroxidase.

Statistical Analysis

Statistical analyses were carried out using inferential statistics, including chi-square test and Student's *t*-test. Software used for the analysis was SPSS version 22.0 (IBM Corporation, Armonk, New York, United States) and GraphPad Prism version 6.0 (Informer Technologies, Inc. Los Angeles, United States), with $p < 0.05$ being considered as significant.

Results

This study assessed morphologic, hematologic, and biochemical parameters of 100 candidates who were chosen by simple

random sampling. Category I comprised 50 participants who were diagnosed with MetS, and category II comprised 50 participants who served as healthy counterparts of the control group. Criteria assessed to make the diagnosis of MetS were the NCEP-ATP III criteria,¹⁰ with diagnostic components previously mentioned.

On assessment of waist circumference of categories I and II patients, category I patients had a mean waist circumference of 92.65 ± 6.97 cm whereas category II patients had a mean waist circumference of 84.72 ± 5.26 cm (► **Table 1**). On assessment by Student's unpaired *t*-test, a positive, significant correlation of waist circumference and MetS status of patients was obtained ($p = 0.036$) (► **Table 1**).

BP was the parameter assessed next. Mean SBP of category I patients was found to be 136.96 ± 14.32 mm Hg, whereas mean SBP of category II patients was found to be 128.12 ± 8.76 mm Hg. On applying Student's unpaired *t*-test, there was a positive, significant correlation found in relation to their MetS status ($p = 0.022$) (► **Table 2**). On comparison of mean DBP, mean DBP of category I patients was found to be 89.20 ± 07.32 mm Hg, whereas mean DBP of category II patients was found to be 85.92 ± 05.28 mm Hg. On assessment by Student's unpaired *t*-test, there was no correlation found between DBP of patients and their MetS status.

Lipid profile of patients was then assessed. When serum triglyceride levels of categories I and II patients were compared, mean serum triglyceride levels of category I patients were found to be 178.53 ± 68.91 mg/dL, whereas mean serum triglyceride levels of category II patients were found to be 140.57 ± 49.82 mg/dL. On applying *t*-test, a positive, significant correlation was found in relation to their MetS status ($p = 0.035$) (► **Table 3**). When mean serum HDL levels were compared among the two categories, mean serum HDL levels of category I patients were found to be 28.95 ± 7.40 mg/dL, whereas mean serum HDL levels of category II patients were found to be 34.16 ± 8.06 mg/dL. On assessment by Student's unpaired *t*-test, no correlation was found between mean serum HDL levels of patients and their MetS status.

Fasting blood glucose levels of patients was the subsequent parameter taken into consideration. When fasting blood glucose of the two categories was compared, mean fasting blood glucose levels of category I patients were found to be 143.34 ± 72.86 mg/dL, whereas mean fasting blood glucose levels of category II patients were found to be 123.39 ± 40.04 mg/dL. On assessment by Student's unpaired *t*-test, there was no

Table 1 Correlation of metabolic syndrome status and waist circumference of study population

Category	N	Mean	Standard deviation	Standard error mean	t-Value	p-Value
I	50	92.65	6.97	1.50	2.12	0.036, S
II	50	84.72	5.26	1.42		

Table 2 Correlation of metabolic syndrome status and systolic blood pressure of study population

Category	N	Mean	Standard deviation	Standard error mean	t-Value	p-Value
I	50	136.96	14.32	1.86	2.33	0.022, S
II	50	128.12	8.76	1.40		

Table 3 Correlation of metabolic syndrome status and serum triglyceride levels of study population

Category	N	Mean	Standard deviation	Standard error mean	t-Value	p-Value
I	50	178.53	68.91	9.69	2.09	0.035, S
II	50	140.57	49.82	5.97		

correlation found between fasting blood glucose of patients and their MetS status.

Platelet indices of patients, comprising plateletcrit, MPV, and PDW, were then taken into consideration. The first parameter taken into consideration was the patient's plateletcrit. When mean plateletcrit of the two categories was compared, mean plateletcrit levels of category I patients were found to be $0.25 \pm 0.08\%$, whereas mean plateletcrit levels of category II patients were found to be $0.21 \pm 0.02\%$. When these values were assessed using Student's unpaired *t*-test, a positive, significant correlation was found between mean plateletcrit of patients in correlation to their MetS status ($p = 0.019, S$) (► **Table 4**). When MPV of the two categories was compared, MPV of category I patients was found to be 10.07 ± 1.05 fL, whereas MPV of category II patients was found to be 10.23 ± 0.66 fL. On assessment by Student's unpaired *t*-test, no correlation was found between MPV of patients and their MetS status. The last platelet parameter to be assessed was PDW. When mean PDW of the two categories was compared, mean PDW of category I patients was found to be $15.37 \pm 2.66\%$, whereas mean PDW of category II patients was found to be $14.82 \pm 2.15\%$. On assessment by Student's unpaired *t*-test, no correlation was found between mean PDW of patients and their MetS status.

Discussion

Out of the 100 study patients chosen by simple random sampling, category I consisted of 50 patients who were MetS patients and category II comprised 50 healthy control group participants. Thirty-four (68%) of category I patients were males, whereas 16 (32%) were females. Twenty-eight (56%) of category II patients were males, whereas 22 (44%) were females. On assessment by Student's unpaired *t*-test, no statistical significance was found in correlation of sex of patients to MetS status ($p < 0.05$). When patients' age was assessed, 5 (10%) category I patients were from the age group of 18 to 30 years, 14 (28%) belonged to the age group of 30 to 40 years, a maximum of 19 (38%) were between 40 and 50 years, whereas 12 (24%) lay in the age group of 50 to 60 years. Out of category II patients, 11 patients (22%) belonged to the age group of 18 to 30 years, 18 (36%) belonged to the age group of 30 to 40 years, 14 (28%) were between 40 and 50 years of age, whereas 7 (14%) lay in the age group of 50 to 60 years. On assessment by Student's unpaired *t*-test, no statistical

significance was found in correlation of patients' age to their MetS status ($p < 0.05$).

The findings we obtained in this study have been similar to those obtained by various other authors regarding work on both, MetS, and platelet indices in national and international literature. We obtained a significant, positive correlation of the MetS status of patients to their waist circumference, SBP, serum triglyceride levels, and plateletcrit, as confirmed using independent Student's unpaired *t*-tests.

Fan et al demonstrated that the levels of endothelial microparticles, PMPs (platelet-derived microparticles), and microparticle-carried protein disulfide isomerase (PDI) activity are found to be significantly increased in MetS patients.¹² The role of platelet-activation pathways has also been widely studied in causation of complications in MetS.^{13,14} Studies have shown that platelet aggregation is controlled by the activity of PDI. This relationship between PDI and platelet hyperreactivity in MetS and its role in the causation of insulin resistance and nitric oxide dysfunction were studied by Gaspar et al.¹⁵

Further pathophysiology of platelet dysfunction and other biochemical abnormalities in MetS patients was studied by Santilli et al, who documented sex-based differences in cardiovascular risk factors and predisposition to DM.¹⁶ This sex-based female predisposition was noted by authors Zhou et al as well, who have shown that increasing plateletcrit acts as a predisposing factor to development of cardiovascular complications in MetS patients, and also noted an increased risk of developing MetS among patients with increased leucocyte and erythrocyte counts.^{17,18} Furman et al noted that elevated platelet indices correlated statistically with waist circumferences of patients and acted as a determinant of abdominal obesity, a major factor implicated in the development of MetS, with similar results shown by authors Barzin et al as well.^{19,20}

Other platelet indices studied include platelet-to-lymphocyte ratio, which was found to be elevated in MetS patients, as well as shown to be a marker for cardiovascular dysfunction in MetS patients by Akboga et al.^{21,22} A large multicenter study based in South Korea, spanning 2 years from 2010 to 2012 and involving 2,228 patients by Lim et al, showed that elevated platelet indices were a risk stratification marker for development of MetS not only in adults but in the pediatric and adolescent population as well.²³ Similar results on proinflammatory biomarkers in MetS patients in the adolescent age group were documented by Can et al.²⁴

Table 4 Correlation of metabolic syndrome status and plateletcrit of study population

Category	N	Mean	Standard deviation	Standard error mean	t-Value	p-Value
I	50	0.25	0.08	0.014	2.49	0.019, S
II	50	0.21	0.02	0.003		

On comparison with controls, Zaccardi et al found that MPV was significantly higher in patients with type 2 DM but not in MetS patients, findings similar to what were obtained in our study as well.^{25,26}

Conclusion

Thus, this study demonstrated that MetS is a proinflammatory and prothrombotic state, characterized by alteration of platelet indices. Plateletcrit was shown to be a significant biomarker along with other parameters, including waist circumference, SBP, and serum triglyceride levels. Early detection using these markers can lead to an overall decline in morbidity and mortality due to MetS.

Funding

None.

Conflict of Interest

None declared.

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