The relationship between mean platelet volume and dyslipidaemia in patients with metabolic syndrome and newly detected diabetes mellitus

Anar F\textsuperscript{a*}, Amin MF\textsuperscript{b*}, Pathan MF\textsuperscript{c}, Afsana F\textsuperscript{d}

ABSTRACT

\textbf{Background:} High mean platelet volume (MPV) is considered as one of the most emerging cardiovascular risk factors in patients with diabetes mellitus and metabolic syndrome. The aim of this study was to find association between MPV and dyslipidaemia in both newly detected diabetes mellitus and metabolic syndrome patients.

\textbf{Methods:} This cross-sectional study was carried out from July to December 2019, at BIRDEM General Hospital and total 115 patients were enrolled in the study. Newly detected diabetes mellitus patients (n=50) were considered in one group, whereas patients with metabolic syndrome (n=65) were in another group. Detailed history, clinical examination and biochemical parameters of the two groups were recorded. MPV was compared between the two groups and also correlated with the components of the metabolic syndrome separately.

\textbf{Results:} Mean age of patients with metabolic syndrome and newly detected diabetes mellitus were 48.65±15.09 and 38.12±16.53 years respectively. Male were predominant in diabetic group (62%) but in metabolic syndrome group female were predominant (57%). MPV was higher in patients with metabolic syndrome (12.06±1.19 fl) than those of newly detected diabetes mellitus (10.51±1.19 fl) and this difference was statistically significant (p=0.000). Total cholesterol (213.18±82 mg/dl) and triglyceride (410.71±416.79mg/dl) in metabolic syndrome were higher than that of diabetes group (total cholesterol-156.62±49.29, triglyceride-191.10±176.18) and this was significant statistically (p=0.000, p=0.001 respectively). Positive correlation was found between MPV and total cholesterol (p=0.002) and triglyceride level (p=0.000) in metabolic syndrome.

\textbf{Conclusion:} Higher value of MPV was observed in patients with metabolic syndrome. Hypercholesterolaemia and hypertriglyceridaemia was also significantly associated with high MPV.

\textbf{Key words:} mean platelet volume, dyslipidaemia, diabetes mellitus, metabolic syndrome.

\textbf{INTRODUCTION}

Coronary artery disease (CAD) is the leading cause of mortality and morbidity worldwide. It is estimated that CAD will be the leading cause of death in the developing countries by 2020.\textsuperscript{1-3} A number of risk factors for atherosclerotic cardiovascular disease have become reasonably well established on the basis of their relation to the clinically manifest disease. Among many factors that have been shown to be important are diabetes mellitus (DM), metabolic syndrome and its components, like abdominal obesity, dyslipidaemia, hypertension etc. Platelets play a vital role in the pathogenesis of atherothrombosis, which is a major contributing factor in CAD. Platelets secrete a large number of substances that mediate the process of atherosclerosis, thrombosis, coagulation and inflammation.\textsuperscript{4,5} Activation of platelets at the site of vascular endothelium injury initiates occlusive arterial disease.\textsuperscript{4,5}
Mean platelet volume (MPV) is a marker of platelet size that is easily determined on routine automated analyzer and available at a relatively low cost. Elevated MPV is associated with other markers of platelet activity, including increased platelet aggregation, increased thromboxane synthesis and α-thromboglobulin release and increased expression of adhesion molecules.\(^6,7\) Furthermore, higher MPV is observed in patients with DM, hypertension, hypercholesterolemia, smoking and obesity, suggesting a common mechanism by which these factors may increase the risk of cardiovascular and cerebrovascular disease.\(^8-12\) So, MPV has recently emerged as a potential, independent cardiovascular risk factor both in diabetic and metabolic syndrome patients.

In Bangladesh, most of the diabetic patients are of type 2 DM with insulin resistance. As MPV is another parameter of insulin resistance, so measuring MPV can guide us for primary prevention of cardiovascular disease in DM as well as metabolic syndrome. So, the purpose of this study was to find out the relationship between MPV and dyslipidaemia in both newly detected diabetes mellitus and metabolic syndrome.

**METHODS**

This cross-sectional study was conducted in BIRDEM General Hospital from July to December 2019. Newly detected DM patients and patients with metabolic syndrome who visited outdoor and admitted in various departments of BIRDEM General Hospital were considered our study population. In one group there were newly detected DM patients without metabolic syndrome (n=50). In other group there were patients with metabolic syndrome (n=65) with impaired glucose tolerance (IGT) or impaired fasting glucose (IFG) excluding diabetes.\(^13,14\)

Patients with age <18 years, diabetic patients on anti-diabetic agents, patients on anti-platelet drugs, subjects having idiopathic thrombocytopenic purpura, iron deficiency anaemia, platelet count <100 and >450 x 10\(^3\) µL, acute myocardial infarction or any emergency and pregnant patients were excluded from the study.

After obtaining informed written consent from patients, detailed history including family and drug history, clinical examination with biochemical parameters was recorded for newly detected diabetic patients. Non-diabetic patients with body mass index >23 kg/m\(^2\) were further evaluated for the presence of other components of metabolic syndrome. Data were collected by using a structured questionnaire containing all the variables of interest by convenient sampling. MPV was compared between these two groups and also association with components of metabolic syndrome was evaluated.

Data was processed manually and analyzed with the help of statistical package for social sciences (SPSS) version 23.0. Quantitative data was expressed as mean and standard deviation and compared between metabolic syndrome and newly detected diabetes group by ANOVA test or student’s t test. Qualitative data was expressed as frequency and percentage and comparison carried by Chi-square (χ²) test. Pearson’s correlation was done to see the relationship between clinical and biochemical parameters with MPV. A p value of <0.05 was considered statistically significant and p<0.01 was considered highly significant.

**RESULTS**

Total patients were 115, 50 were newly detected diabetic patients without metabolic syndrome and 65 had metabolic syndrome without diabetes. Mean age of study participants in newly detected diabetic group was 38.12±16.53 years and that of metabolic syndrome group was 48.65±15.09 years. Men were predominant in diabetic group (62%) but in metabolic syndrome group women were predominant (57%). Family history of diabetes was present in 66% patients having metabolic syndrome, whereas it was 52% in diabetic group. Hypertension was present in patients with metabolic syndrome (27) whereas a small number of newly detected diabetic patients (10) were found to be hypertensive (Table I).

| Factors                  | Newly detected diabetes mellitus (n=50) | Metabolic syndrome (n=65) | p value |
|--------------------------|----------------------------------------|---------------------------|---------|
| Age (years)              | 38.12±16.53                            | 48.65±15.09               | 0.001*  |
| Gender                   |                                        |                           |         |
| Male                     | 31 (62%)                               | 28 (43%)                  | 0.045*  |
| Female                   | 19 (38%)                               | 37 (57%)                  |         |
| Family history of diabetes |                                       |                           |         |
| Present                  | 26 (52%)                               | 43 (66%)                  | 0.131   |
| Absent                   | 24 (48%)                               | 22 (34%)                  |         |
| Hypertension             |                                        |                           |         |
| Present                  | 10 (20%)                               | 27 (42%)                  | 0.016*  |
| Absent                   | 40 (80%)                               | 38 (58%)                  |         |
Mean body mass index (BMI) (30.69±7.35 kg/m$^2$) was greater in metabolic syndrome group than diabetic group (22.77±5.73 kg/m$^2$) and the difference was statistically significant (p=0.000). Mean HbA1C was greater in newly detected diabetes group (12.48±3.32%) than metabolic syndrome group (5.49±.69%) and this result was also significant (p=0.000).

In this study, it was found that MPV in metabolic syndrome group (12.07±1.19 fl) has higher values than newly detected DM patients (10.51±1.19 fl) and this result was statistically significant (p=0.000).

Mean total cholesterol (213.18±82 mg/dl), triglyceride (410.71±416.79 mg/dl), low density lipoprotein (102.73±38.37 mg/dl) and high density lipoprotein (31.85±10.64 mg/dl) were greater in metabolic group than that of diabetic patients which is shown in Table II. Among the values the difference of mean total cholesterol (p=0.002) and triglyceride (p=0.001) was statistically significant in between two groups.

| Factors                        | Newly detected diabetes mellitus (n=50) | Metabolic syndrome (n=65) | p value |
|--------------------------------|----------------------------------------|---------------------------|---------|
| Weight (kg)                    | 56.50±13.63                            | 78.20±18.49               | 0.000*  |
| Body mass index (kg/m$^2$)     | 22.77±5.73                             | 30.69±7.35               | 0.000*  |
| HbA1c (%)                      | 12.48±3.32                             | 5.49±.69                 | 0.000*  |
| Total cholesterol (mg/dl)      | 156.62±49.29                           | 213.18±82                | 0.000*  |
| Triglyceride (mg/dl)           | 191.10±176.18                          | 410.71±416.79            | 0.001*  |
| High density lipoprotein (mg/dl)| 30.12±12.61                           | 31.85±10.64              | 0.428   |
| Low density lipoprotein (mg/dl)| 93.34±39.98                            | 102.73±38.37             | 0.206   |

By Pearson’s correlation significantly positive correlation was found between MPV dyslipidaemia in metabolic syndrome group. In this study, total cholesterol (p=.002, r =0.282) and triglyceride level (p=.000, r =0.272) showed significant positive correlation with MPV which is evident in Figure 1 and Figure 2 respectively.

![Figure 1](https://example.com/figure1.png)  
**Figure 1** Correlation between MPV and total cholesterol level in metabolic syndrome

![Figure 2](https://example.com/figure2.png)  
**Figure 2** Correlation between MPV and triglyceride level in metabolic syndrome
DISCUSSION

In this study, men were predominant in the diabetic group and women were predominant in the metabolic syndrome group. This finding is consistent with the findings of the study Jain S. et al where metabolic syndrome was present both in women and men corresponding to 29% and 23% respectively. The prevalence was higher in women than in men.\textsuperscript{15}

Mean BMI in metabolic group was greater than that of diabetic group. This finding was consistent with the classical finding of obesity in metabolic syndrome which was evident in the study of Schillaci G et al.\textsuperscript{16}

In this study, among the components of dyslipidaemia, the difference of mean total cholesterol and triglyceride was found to be higher in metabolic syndrome and this was statistically significant in between two groups. Han TS et al found that hypertriglyceridaemia was significantly associated in metabolic syndrome group than the control group.\textsuperscript{17}

It was evident from this study that MPV was higher in patients with metabolic syndrome than that of newly detected diabetes mellitus. Scott M et al and Sansanayudh N et al. found that MPV was significantly higher in patients with metabolic syndrome than the control group which was consistent with our findings.\textsuperscript{18,19} On the contrary, Shah B et al found that MPV was significantly higher in subjects with diabetes but not in subjects with metabolic syndrome.\textsuperscript{20}

Dyslipidaemia is one of the essential components of metabolic syndrome. In previous literature, it was already proven that hypertriglyceridaemia, low HDL, high LDL are responsible for adverse coronary event.\textsuperscript{21,23} In our study, positive correlation was found between MPV and hypertriglyceridaemia in metabolic syndrome. Although hypercholesterolaemia is not a component of metabolic syndrome, in this study it was positively correlated with MPV in metabolic syndrome patients. No significant correlation was found with MPV and high LDL, low HDL here. To support this finding there was another study done by Kutluca A et al. where total cholesterol (p = <0.001) and triglyceride (p= <0.001) was significantly correlated with MPV.\textsuperscript{24} In a study, higher MPV values were found in patients with hypercholesterolemia than that of control group. Moreover, these authors noted an MPV decrement after 12 weeks of rosuvastatin treatment.\textsuperscript{25}

In our study, no significant association was found between BMI and MPV. Coban E et al. found that MPV showed positive correlations with BMI level in the obese group (r = 0.430, p = 0.017) which is contradictory to our finding.\textsuperscript{26} Regarding hypertension and glycaemic status which are important components of metabolic syndrome, no significant correlation was found between MPV and these two variables in this study. Babic N et al. also found no correlation between MPV and HbA1c.\textsuperscript{27} On the contrary, Shah B et al. found significant correlation between them. They found a positive correlation between MPV and hyperglycaemia (P<0.0001) and between MPV and hemoglobinA1C (P<0.0001) in subjects with diabetes.\textsuperscript{20}

Ulutas KT et al. shows MPV was significantly higher in HbA1c > 7% as compared to both HbA1c <7% and non-diabetic people. MPV had a high positive correlation with HbA1c and fasting blood glucose, as with diabetes duration. It is found that MPV was increased in type 2 DM.\textsuperscript{28}

There are several studies about the association between MPV and cardiovascular risk factors.\textsuperscript{8-12} But this kind of study which reveals the comparison between newly detected DM and metabolic syndrome in terms of MPV and also correlation between dyslipidaemia and MPV is done first time in Bangladesh.

Limitation

The limitation of this study was that the MPV value evaluated represented only one point in time. We were unable to determine time-sensitive EDTA induced platelet swelling. Potential reasons for an increased platelet volume other than platelet activation, such as inherited giant platelet disorders, May Hegglin syndrome, Mediterranean macrothrombocytopenia, Bernard-Soulier syndrome etc. could not be differentiated. A comparison with a control group without metabolic syndrome and any level of glucose intolerance (diabetes, IFG, IGT) could be more helpful in this kind of research.

Conclusion

MPV was higher in patients with metabolic syndrome than newly detected diabetic patients and further higher with increasing numbers of components of metabolic syndrome. Hypertriglyceridaemia and hypercholesterolaemia had significant association with high MPV. For prevention of cardiovascular disease, more extensive search for risk factors should be done in patients with metabolic syndrome and more emphasis
should be given on lifestyle modification and control of dyslipidaemia.

**Authors’ contribution:** FA conceived the idea and designed the study. FP was in-charge of supervision. FA contributed in organizing data and literature search. FA collected data, performed the analysis and drafted the manuscript. All authors read and approved final manuscript for publication.

**Conflicts of interest:** Nothing to declare.

**REFERENCES**

1. The World Health Report 1999: The double burden: Emerging epidemics and persistent problems. WHO 1999.
2. Howson CP, Reddy KS, Ryan TJ, Bale JR. Control of cardiovascular diseases in developing countries: Research, development and institutional strengthening. HeartBeat: Bulletin of the World Heart Federation 1999. Available at: http://www.who.heart.org/new/ Mar99/control.html.
3. Murray CJL, Lopez AD. The global burden of disease. In: Murray CJL, Lopez AD, editors. The global burden of disease: a comprehensive assessment of mortality and disability from disease, injuries and risk factors in 1990 and projected to 2020. Boston (Mass): Harvard School of Health; 1996.
4. Bath P, Algert C, Chapman N PROGRESS Collaborative Group. Association of mean platelet volume with risk of stroke among 3134 individuals with history of cerebrovascular disease. Stroke 2004; 35: 622–626.
5. Coppinger JA, Cagney G, Toomey S, Kislinger T, Belton O, McRedmond JP et al. Characterization of the proteins released from activated platelets leads to localization of novel platelet proteins in human atherosclerotic lesions. Blood 2004; 103: 2096–104.
6. Bath PM, Butherword RJ. Platelet size: Measurement, physiology and vascular disease.Bloodcoagul Fibrinolysis 1996; 157-161.
7. Thompson CB, Jakubowski JA, Quinn PG, Daykin D, Valeri CR. Platelet size as a determinant of platelet function. J lab clin Med 1983;101: 205-213.
8. 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; 15:475–478. [PubMed: 15763888]
9. Nadar S, Blann AD, Lip GY. Platelet morphology and plasma indices of platelet activation in essential hypertension: effects of amiodipine-based antihypertensive therapy. Ann Med. 2004; 36:552–557. [PubMed: 15513305]
10. Pathansali R, Smith N, Bath P. Altered megakaryocyte–platelet haemostatic axis in hypercholesterolaemia. Platelets. 2001; 12:292–297. [PubMed: 11487381]
11. Kario K, Matsuo T, Nakao K. Cigarette smoking increases the mean platelet volume in elderly patients with risk factors for atherosclerosis. Clin Lab Haematol. 1992; 14:281–287. [PubMed: 14780077]
12. Coban E, Ozdogan M, Yazicioglu G, Akcif F. The mean platelet volume in patients with obesity. Int J Clin Pract. 2005; 59:981–982. [PubMed: 16033624].
13. American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes—2019. Diabetes care. 2019 Jan 1;42(Supplement 1):S13-28.
14. Alberti KG, Zimmet P, Shaw J. The metabolic syndrome— a new worldwide definition. The Lancet. 2005 Sep 24;366(9491):1059-62.
15. Beigh SH, Jain S. Prevalence of metabolic syndrome and gender differences. Bioinformation. 2012;8(13):613.
16. Schillaci G, Pirro M, Vaudo G, Gemelli F, Marchesi S, PorcellatiC, et al. Prognostic value of the metabolic syndrome in essential hypertension. J Am CollCardiol 2004, 43:1817-1822.
17. Han TS, Lean ME. A clinical perspective of obesity, metabolic syndrome and cardiovascular disease. JRS Cardiovasc Dis. 2016; 25:5-12.
18. Scott M. Grundy, Obesity, Metabolic Syndrome, and Cardiovascular Disease, The Journal of Clinical Endocrinology & Metabolism 2004; 89: 2595–2600.
19. Sansanayudh N. The association between mean platelet volume and cardiovascular risk factors, Eur J Intern Med 2015;4:43-45.
20. Shah B, Sha D, Xie D, Mohler ER 3rd, Berger JS. The relationship between diabetes, metabolic syndrome, and platelet activity as measured by mean platelet volume: the National Health And Nutrition Examination Survey, Diabetes Care 2012;35(5):1074-1078.
21. Kreisberg RA. Diabetic dyslipidemia. The American journal of cardiology. 1998 Dec 17;82(12):67U-73U.
22. Yang SH, Du Y, Li XL, Zhang Y, Li S, Xu RX, Zhu CG, Guo YL, Wu NQ, Qing P, Gao Y. Triglyceride to high-density lipoprotein cholesterol ratio and cardiovascular events in diabetics with coronary artery disease. The American journal of the medical sciences. 2017 Aug 1;354(2):117-24.
23. Lahoz C, Mostaza JM, Tranche S, Martin-Jadraque R, Mantilla MT, López-Rodriguez I, Monteiro B, Sanchez-Zamorano MA, Taboada M. Atherogenic dyslipidemia in
patients with established coronary artery disease. Nutrition, Metabolism and Cardiovascular Diseases. 2012 Feb 1;22(2):103-8.

24. Kutlucan A, Bulur S, Kr S. The relationship between mean platelet volume with metabolic syndrome in obese individuals. Blood Coagul Fibrinolysis. 2012;23(5):388-390.

25. Coban E, Afacan B. The effect of rosuvastatin treatment on the mean platelet volume in patients with uncontrolled primary dyslipidemia with hypolipidemic diet treatment. Platelets 2008; 19: 111–4.

26. Coban E, Yilmaz A, Sari R. The effect of weight loss on the mean platelet volume in obese patients. Platelets 2007; 18: 212–6.

27. Babu N, Avdagi N, Musi M, Huski J, Dervišević A, Velija-Ašimi Z, Mujan et al. The mean platelet volume is increased in patients with type 1 and type 2 diabetes mellitus, but not in subjects with impaired glucose tolerance. Medical Journal. 2013 Jul 1;19(3).

28. Ulutas KT, Dokuyucu R, Sefil F Evaluation of mean platelet volume in patients with type 2 diabetes mellitus and blood glucose regulation: a marker for atherosclerosis?. Int J Clin Exp Med. 2014;7(4):955-961.