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# PLATELET VOLUME INDICES (PVI) IN METABOLIC SYNDROME (MS)

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## ABSTRACT

The metabolic syndrome (MS) is characterized as the clustering of closely associated and interdependent atherosclerotic risk factors.The study was performed to analyse platelet volume indices (PVI) that are useful for identifying large platelets, which are haemostatically more active and produce more thromboxane A2. We measured PVI in 44 subjects with metabolic syndrome (age 51±10 years) and 43 subjects without metabolic syndrome (age 49±15 years). The PVI was significantly higher in patients with metabolic syndrome compared to control group ($p < 0.0001$). PVI is simple, effortless and cost effective tool for predicting the possibility of impending acute events. So, PVI may be used as a better predictor for acute complication in patients with metabolic syndrome.

**KEYWORDS: Metabolic syndrome (MS), platelet volume indices (PVI), cardiovascular disease, Platelet Large Cell Ratio (P-LCR)**

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# INTRODUCTION

Non communicable diseases which include Diabetes mellitus and cardiovascular disease are world's biggest killer diseases, estimated to cause 3.5millions death each year. Eighty percent of them are found in the low and middle income countries. The WHO has developed an action plan for implementation of global strategies in prevention and control of non-communicable diseases.[1] The alarming increases in obesity especially its central component resulting in metabolic syndrome, seems to be behind the twin epidemic of type 2 diabetes and cardiovascular disease currently sweeping the Indian subcontinent.[2] One of the objectives of this plan is to develop simple strategies to identify those at risks together with appropriate and cost effective interventions. The metabolic syndrome has been advocated as a simple clinical tool for predicting diabetes mellitus and cardiovascular diseases. It also forms a conceptual base for understanding some of the pathophysiological links between metabolic risks, DM and CVD. The clustering of metabolic syndrome risks with cardiovascular disease and DM has been recognized for more than 80 years, but the modern concept of MS began when Reaven proposed a conceptual frame work which links between biological events in a single pathophysiological construct.[3] The metabolic syndrome is a complex of interrelated risk factors for cardiovascular disease (CVD) and diabetes. These factors include dysglycemia, raised blood pressure, elevated triglyceride levels, low high-density lipoprotein levels, and obesity (particularly central adiposity) .[4] A variety of data indicate patients with metabolic syndrome have a high risk of developing cardiovascular morbidity and mortality.[5, 6] Platelets play an important role in the pathogenesis of thrombosis and atherosclerosis. Activated platelets interact with endothelium and other inflammatory cells by the action of different molecules present on the platelet surface and/or stored in platelets granules, as P-selectin.[7] Platelet volume reflects platelet reactivity [8] and has been suggested as an independent risk factor for ischemic events in cardiovascular disease .[9] Large platelets are metabolically and enzymatically more active than small platelets and produce more thromboxane A2. [10, 11] Individuals with dyslipidemia have more tendencies to form atherosclerosis plaques with a consequent increasing consumption of platelets. We have shown preliminary results on production of larger platelets by P-LCR determination in a group of patients with lipid profile abnormalities.[12] "Our aim was to study platelet parameters in the spectrum of metabolic disease."However, there is scope to make better use of the platelet parameters generated. The MPV can reflect changes in either the level of platelet stimulation or the rate of platelet production. Platelet activation is indirectly measured via MPV.

# MATERIALS AND METHODS

Subject for study was taken from healthy individuals coming to health check up department of our hospital.

### *Patients*

Individuals following criteria for metabolic syndrome have been included in this category as patients of metabolic syndrome. Criteria for metabolic syndrome have been shown in Table1 and Table2. Total 44 patients included in our study.

### *Control group*

We took 43 individuals in control group who didn't come under the criteria of metabolic syndrome we also excluded individuals with chronic diseases like carcinoma, tuberculosis, HIV etc.

**Table 1**
***Criteria for the diagnosis of metabolic syndrome*** [4]

| Waist circumference | Population or country specific |
|---|---|
| Triglycerides | ≥150 mg/dL or on treatment (fibrates or nicotinic acid) |
| HDL cholesterol | |
| Men | <40 mg/dL |
| Women | <50 mg/dL |
| Blood Pressure | ≥130/85 mmHg or on antihypertensive medications |
| Fasting blood sugar | ≥100 mg/dL or on treatment of diabetes |

- ***≥3 out of 5 criteria is required to diagnose as the metabolic syndrome.***

**Table 2**
***Country/ethnic specific values for waist circumference of South Asians:*** [4]

| Male | Female |
|---|---|
| ≥90cm | ≥80cm |

### *Blood sampling*

Blood sample was collected in plain tube for lipid profile analysis, EDTA (Ethylenediaminetetra acetic acid) vaccutainer for haematological analysis and fluoride tube for fasting glucose analysis under standard aseptic procedure. Sample was taken after 10-12 hours fasting so triglyceride and fasting glucose level doesn't get affected. All patients' and controls' samples were processed within 2 hours of sample collection. All haematological parameter were processed using Sysmex KX-21 automated cell counter. Automated cell counters, have made the platelet count (PC) and the platelet volume indices (PVI)—mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR), routinely available in most clinical laboratories. Individuals with low platelet count below 150($10^9$/L) were excluded from the study. All quality measures were taken according to NABL. Proper quality measures like internal (IQC) and external quality (EQAS) were done throughout the study. All Biochemistry parameters have been analyzed using fully automated analyzer Roche's COBAS INTEGRA 400 plus. FBS (fasting blood sugar) was measure by hexokinase method and HDL-C, Total Cholesterol and Triglycerides were measured by enzymatic methods. Blood Pressure measured in upper arm in sitting position. The waist circumference was measured at a level midway between the lowest rib and iliac crest.

### *Ethical approval*

Ethical approval was taken from human research ethical committee of our institute. Informed consent has been taken for research purpose.

### *Statistical analysis*

The obtained parameters were evaluated using descriptive statistical analysis. Statistical analyses were performed using the IBM SPSS (statistical Package for the Social Sciences v 20.0) and Microsoft Office Excel 2007 software. The p value <0.05 was taken as significant.

## RESULTS

The mean (SD) age of the patients was 51(10) and mean (SD) age of the control group was 49(15) with men and women were equally represented.

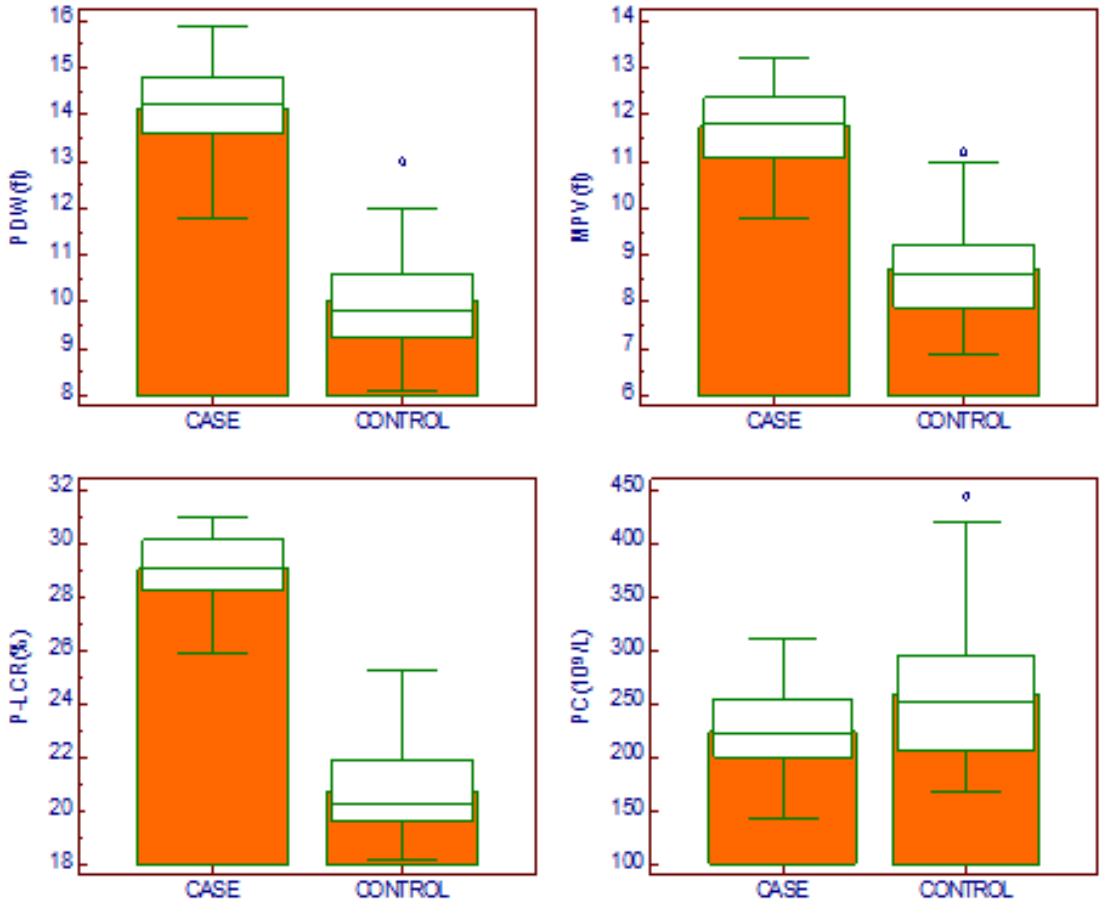
## Table 3
### *Significance of Criteria of metabolic syndrome in study groups*

| Parameter | Patients (n= 44) | Control (n= 43) | p-value |
|---|---|---|---|
| **BMI (kg/m$^2$)** | 29 (5) # | 22.5 (4.4) | <0.0001 |
| **WC(cm)** | 103.11 (8.9) | 84 (9) | <0.0001 |
| **BP (mmHg)** | 136/90 (12/8) | 116/78 (10/4) | <0.0001 |
| **FBS (mg/dl)** | 138 (41) | 95 (7) | <0.0001 |
| **TC (mg/dl)** | 188 (44) | 181 (31) | 0.377 |
| **HDL-C (mg/dl)** | 37 (6.8) | 62 (14) | <0.0001 |
| **TG (mg/dl)** | 171 (60) | 76 (24) | <0.0001 |

*#Values are mean (SD).*

***BMI-Basal Metabolic Index, WC –Waist Circumference, BP –Blood Pressure, FBS-Fasting Blood Sugar, TC- Total Cholesterol, HDL-C – High Density Lipoprotein, TG- Triglycerides Parameters included in metabolic syndrome definition[4] WC, BP, FBS, HDL-C and TG all was significantly higher in patients with metabolic syndrome compare to control group. The correlations between variables were significant in both groups (p<0.0001).Total cholesterol is not included in metabolic syndrome criteria and having no significant correlation (p=0.377).***

## Figure 1
### *Showing Box and Whisker Plot related to PC(Platelet count) ,PDW (Platelet distibution width),MPV(Mean Platelet volume) and P-LCR (Platelet Large Cell Ratio) distribution in metabolic syndrome.*




***As shown in figure1 and table4; MPV, PDW and P-LCR were significantly high and Platelet count (PC) was significantly low in patients having metabolic syndrome compare to control group. The correlations between variables were significant in both groups (p<0.005).***

**Table 4**
***Distribution of platelet volume indices (PVI) in study groups.***

| Parameter | Patient (n= 44) | Control (n= 43) | p-value |
|---|---|---|---|
| **PC ($10^9$/L)** | 224 (42.2) | 259 (65) | <0.005 |
| **MPV (fl)** | 11.73 (0.85) | 8.8 (0.98) | <0.0001 |
| **PDW (fl)** | 14.14 (0.96) | 10 (1) | <0.0001 |
| **P-LCR (%)** | 28.69 (2.84) | 20.8 (1.6) | <0.0001 |

***Values are mean (SD).***
***MPV- Mean Platelet Volume; PC- Platelet Count, PDW- Platelet Distribution Width; P-LCR- Platelet Large Cell Ratio; WBC- White Blood Cell Count***

# DISCUSSION

This report identifies the PVI to be a more useful marker of metabolic syndrome and insulin resistance than each of its individual components alone. Our data suggested that increase in MPV, PDW and P-LCR was directly correlated with metabolic syndrome. So, these indices can be used as a novel metabolic marker. As Shown above that HDL, TG, BP, FBS and WC were significantly different in both groups (p<0.0001). Though MPV, PDW and P-LCR are not included in metabolic syndrome definition, they were highly correlated with insulin resistance. One previous study by Grotto and Noronha (2004)[12] had same result as compare to our study. The importance of megakaryocyte and platelet reactivity in the development of vascular disease has been described in several studies. A practical and reliable index of platelet activation has been tested, as measurements of platelet number and size, the tendency to form aggregates and the concentration of released substances stored in platelet granules.[9] A larger MPV is an indicator of in vivo platelet activation and it is increased in vascular diseases as myocardial and cerebral infarction.[8] However, some limitations have been reported in MPV determination: age, gender and number of circulating platelets can influence MPV distribution; as well as anticoagulants used for the collection of blood, storage time and temperature; and the resolution of the cell counters, once minimal alteration in platelet size may be not detected by routine hematologic counters.[9] The roles of MPV and PDW specifically in patients with CAD (Coronary artery disease), acute coronary events and metabolic syndrome were already explored by several studies. Similarly, the P-LCR is not often quoted in the literature, probably because it is a relatively new PVI parameter.

# CONCLUSION

We have studied parameters like MPV, PDW and P-LCR, and our results showed that larger platelets are present in patients with metabolic syndrome. Because larger platelets are more reactive, they can contribute to an increased risk for cardiovascular diseases as a complication of metabolic syndrome. Further studies will elucidate the reactivity of the larger platelets and the utility of the new parameter in assessing qualitative abnormalities in platelets. Patients with larger platelets can easily be identified during routine hematological analysis and could possibly benefit from preventive treatment. Therefore, PVI are an important, simple, effortless, and cost effective tool that should be used more extensively to predict impending acute events. In spite of not included in criteria for diagnosis of metabolic syndrome, PVI can be used as a better predictor of acute complication of metabolic syndrome.

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