

SIGNIFICANCE OF MEAN PLATELET VOLUME, RED CELL DISTRIBUTION WIDTH WITH THE PRESENCE AND SEVERITY OF METABOLIC SYNDROME¹Yadav Subhash L., ^{2*}Dr. Gosavi Satish V., ³Roy Swetabh, ⁴Rode Vikram, ⁵Kondeware Mayur^{1,3,4,5}Resident, Department of Medicine, Krishna Institute of Medical Sciences, Karad.²Associate Professor, Department of Medicine, Krishna Institute of Medical Sciences, Karad.***Corresponding Author: Dr. Gosavi Satish V.**

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ABSTRACT

Introduction: Metabolic syndrome (MS) is a multiplex risk factor that arises from insulin resistance accompanying abnormal adipose deposition and function. It is a risk factor for coronary heart disease, as well as for diabetes, fatty liver, and several cancers. Recent studies have demonstrated that RDW may also be an effective predictor of morbidity and mortality in various non-communicable diseases. **Materials and Methods:** The present study was an observational case control study carried out between December 2015 to November 2017 at Tertiary care hospital among patients of Metabolic syndrome is diagnosed according to the National Cholesterol Education Program Adult Treatment Panel III criteria 3 (NCEP ATP 3) attending Medicine outpatient departments. **Results:** The RDW and MPV values of patients in Group 1 were significantly lesser as compared to RDW and MPV values of patients in Group 2 and Group 3. It was also observed that patients meeting 5 MS criteria (Group 3) had significantly higher MPV and RDW than those meeting 3 MS criteria (Group 2). **Conclusions:** It is known that systemic inflammation is involved in MS and in patient with MS the risk for development CVD increases. The present study is the first report about the association of MPV and RDW with the presence and the severity MS.

KEYWORDS: Metabolic syndrome, Non Communicable diseases, Cardiovascular disorders, red cell distribution width, mean platelet volume.

INTRODUCTION

Metabolic syndrome (MS) is a multiplex risk factor that arises from insulin resistance accompanying abnormal adipose deposition and function. It is a risk factor for coronary heart disease, as well as for diabetes, fatty liver, and several cancers. Metabolic syndrome is a clustering of at least three of the five medical conditions like abdominal obesity, high blood pressure, high blood sugar, high serum triglycerides and low high-density lipoprotein levels.^[1]

One of the important factors contributing to increased prevalence of type 2 diabetes in Asian Indians is the fact that they have a greater degree of insulin resistance compared to Caucasians.^[2-4] Mohan et al first demonstrated that Asian Indians have higher insulin levels to a glucose load than Europeans.^[4]

The increased platelet activity is emphasized to play a role in the development of vascular complications of this metabolic disorder.^[5] Platelet volume, a marker of the platelet function and activation is measured as mean platelet volume (MPV) by hematology analyzers. Diabetic patients have an increased risk of developing micro- and macro vascular disease and platelets may be

involved as a causative agent with respect to altered platelet morphology and function.^[6,7] Additionally, recent studies have revealed serum uric acid level, carboxy-terminal pro-peptide and retinal venular diameter as significant indicators of diabetic complications such as diabetic nephropathy or retinopathy.^[8,9,10] RDW, defined as the heterogeneity of circulating erythrocytes (anisocytosis), was used to distinguish the variable pathogenesis of anemia together with the MPV.^[11] Malnutrition, including Fe deficiency and lack of vitamin B12 and folic acid, generates elevated RDW.^[12] Recent studies have demonstrated that RDW may also be an effective predictor of morbidity and mortality in various non-communicable diseases such as stroke,^[13] atherosclerosis,^[14] ESRD¹⁵ and heart failure.^[16]

Hence, the present study was done at our tertiary care centre to investigate the relationship between the MS and new inflammatory markers as mean platelet volume (MPV) and red blood cell distribution width (RDW), they are simple and reliable indicators of inflammation.

MATERIAL AND METHODS

The present study was an observational case control study carried out between December 2015 to November 2017 at Tertiary care hospital among patients of Metabolic syndrome is diagnosed according to the National Cholesterol Education Program Adult Treatment Panel III criteria 3 (NCEP ATP 3) attending Medicine outpatient departments and referred to Department of Medicine to determine the mean platelet volume (MPV) and Red cell distribution width (RDW) in metabolic syndrome patient and compared it to non metabolic syndrome.^[17]

Considering a confidence level of 95% and confidence interval of 6 the number of patients in our study to achieve statistical significance is 267. This was calculated by Survey System. Hence 300 subjects were included in this study and they were further divided in to 3 groups with 100 patients in each as following:

Group 1: Age and Sex-match healthy subjects.

Group 2: Patients with 3 metabolic syndrome criteria.

Group 3: Patients with 5 metabolic syndrome criteria.

Patients with Renal failure, Cardiac failure, Iron Deficiency anemia, Hepatic failure, Secondary hypertension, Coronary arterial disease, Arrhythmia, Cardiac valve disease were excluded from the study.

A detailed case history was taken with special reference to the symptoms, past history of DM, HTN, dyslipidemia, smoking, alcohol consumption and tobacco/misri chewing.

A careful physical examination was done with special reference to Blood Pressure, Waist circumference, Hip Circumference, Height and weight.

Various required blood investigations like Complete blood counts (RDW, MPV), Lipid profile (HDL Cholesterol level, Triglyceride level), Serum glucose level and Anthropometry (waist circumference, height, weight) were done.

Quantitative data is presented with the help of Mean and Standard deviation. Comparison among the study groups is done with the help of unpaired t test as per results of normality test. Qualitative data is presented with the help of frequency and percentage table. Association among the study groups is assessed with the help of Fisher test, students' test and Chi-Square test. 'p' value less than 0.05 is taken as significant. Results were graphically represented where deemed necessary. Appropriate statistical software, including but not restricted to MS Excel, SPSS ver. 20 was used for statistical analysis. Graphical representation was done in MS Excel 2010.

RESULTS

A hospital based comparative study was conducted to investigate the relationship between the Metabolic Syndrome (MS) and new inflammatory markers as mean

platelet volume (MPV) and red blood cell distribution width (RDW). The present study was carried out with following three groups of 100 patients each.

Group 1: Age and Sex-match healthy subjects.

Group 2: Patients with 3 MS criteria.

Group 3: Patients with 5 MS criteria.

Majority of the patients in Group 1 were in the age group of 51-60 years (34%) followed by 61-70 years (28%). The mean age of the patients was 51.7 ± 12.84 years. Majority of the patients in Group 2 were in the age group of 51-60 years (30%) followed by 61-70 years (24%). The mean age of the patients was 50.2 ± 12.63 years. Majority of the patients in Group 3 were in the age group of 51-60 years (28%) followed by 61-70 years (26%). The mean age of the patients was 50.4 ± 12.72 years. There was no significant difference between the groups as per Student t-test ($p > 0.05$) (Table 1). There were 56%, 54% and 55% male patients in Group 1, Group 2 and Group 3 respectively while female patients constituted 44%, 46% and 45% of the study groups respectively. The differences in proportions between the groups we're not found statistically significant as per Fisher test ($p > 0.05$) (Figure 1).

In the present study we measured their anthropometric indices, it was found that 38 (38%) patients in Group 1 were in the normal range of their body mass index, while 54 (54%) and 8 (8%) patients were overweight and obese respectively. 4 (4%) patients in Group 2 were in the normal range of BMI, while 84 (84%) and 12 (12%) patients were overweight and obese respectively. 2 (2%) patients in Group 2 were in the normal range while 87 (87%) and 11 (11%) patients were overweight and obese respectively. The mean BMI of patients in Group 1 ($25.7 \pm 3.15 \text{ kg/m}^2$) was significantly lesser as compared to mean BMI of patients in Group 2 ($27.6 \pm 1.92 \text{ kg/m}^2$) and Group 3 ($27.6 \pm 1.87 \text{ kg/m}^2$). The BMI of the patients was significantly different as per Student t-test ($p < 0.05$) (Table 2). Increased WHR was present in 53.6%, 88.9% and 94.6% of male patients in Group 1, Group 2 and Group 3 respectively. There was a significant difference in the WHR of the male patients in all the three groups ($p < 0.05$) (Table 2). Increased WHR was present in 72.7%, 95.7% and 95.6% of female patients in Group 1, Group 2 and Group 3 respectively. There was a significant difference in the WHR of the female patients in all the three groups ($p < 0.05$) (Table 2).

The SBP and DBP values of patients in Group 1 were significantly lesser as compared to SBP and DBP values of patients in Group 2 and Group 3. This difference was statistically significant as per Student t-test ($p < 0.05$) (Table 3). The FBS and PPBS values of patients in Group 1 were significantly lesser as compared to FBS and PPBS values of patients in Group 2 and Group 3. This difference was statistically significant as per Student t-test ($p < 0.05$) (Table 3). The Triglyceride value was significantly lesser and HDL value was significantly higher of patients in

Group 1 as compared to Triglyceride and HDL values of patients in Group 2 and Group 3. This difference was statistically significant as per Student t-test ($p < 0.05$) (Table 3). The RDW and MPV values of patients in Group 1 were significantly lesser as compared to RDW and MPV values of patients in Group 2 and Group 3. It was also observed that patients meeting 5 MS criteria (Group 3) had significantly higher MPV and RDW than those meeting 3 MS criteria (Group 2) (Table 3). It was observed that there were no statistically significant correlations between RDW and age, SBP, PPBS, WBC, MCV and Platelet Count. RDW was inversely correlated with DBP and FBS but the correlation was insignificant. RDW was

strongly and directly associated with the Body Mass Index ($r = 0.655$; $p < 0.05$) and WHR ($r = 0.534$; $p < 0.05$). RDW did not correlate significantly with any of the components of the lipid profile.

MPV showed direct but insignificant correlation with BMI, WHR, SBP, FBS, PPBS, WBC and MCV. MPV was inversely correlated with age and DBP but the correlation was insignificant. MPV did not correlate significantly with any of the components of the lipid profile. MPV was inversely correlating with Platelet Count ($r = -0.368$, $p < 0.05$) (Table 4, 5).

Table 1: Distribution of patients according to Age.

Age (years)	Group 1		Group 2		Group 3		p Value
	N	%	N	%	N	%	
21-30	8	8%	6	6%	5	5%	>0.05
31-40	16	16%	18	18%	20	20%	
41-50	14	14%	22	22%	21	21%	
51-60	34	34%	30	30%	28	28%	
61-70	28	28%	24	24%	26	26%	
Total	100	100%	100	100%	100	100%	
Mean \pm SD	51.7 \pm 12.78		50.2 \pm 12.56		50.4 \pm 12.72		

Table 2: Distribution of study subjects according to their anthropometric measurements.

Variables		Group 1		Group 2		Group 3		p Value
		N	%	N	%	N	%	
WHR in males	<0.9	26	46.4%	6	11.1%	3	5.4%	<0.05
	≥ 0.9	30	53.6%	48	88.9%	52	94.6%	
	Total	56	100%	54	100%	55	100%	
WHR in females	<0.8	12	27.3%	2	4.3%	2	4.4%	<0.05
	≥ 0.8	32	72.7%	44	95.7%	43	95.6%	
	Total	44	100%	46	100%	45	100%	
BMI	Normal	38	38%	4	4%	2	2%	<0.05
	Overweight	54	54%	84	84%	87	87%	
	Obese	8	8%	12	12%	11	11%	
	Total	100	100%	100	100%	100	100%	
	Mean \pm SD	25.7 \pm 3.14		27.6 \pm 1.91		27.6 \pm 1.87		

Table 3: Distribution of study subjects according to their various investigation results.

Variables		Group 1		Group 2		Group 3		p Value
		Mean	SD	Mean	SD	Mean	SD	
Blood Pressure Levels	SBP	119.8	12.89	136.4	18.16	139.8	17.91	<0.05
	DBP	76.7	9.94	86.4	3.70	87.8	3.74	<0.05
Blood Glucose Levels	FBS	103.4	15.95	163.5	15.96	166.9	15.82	<0.05
	PPBS	131.6	29.21	221.6	29.21	225.1	29.02	<0.05
Lipid Profile parameters	Cholesterol	190.9	11.24	194.2	13.02	197.7	13.19	>0.05
	Triglyceride	143.5	25.14	184.5	39.97	187.9	39.67	<0.05
	LDL	114.4	25.11	116.8	26.61	120.2	26.36	>0.05
	HDL	54.2	4.91	42.7	4.87	41.7	4.84	<0.05
blood indices	WBC ($\times 10^9/\mu\text{L}$)	6.9	0.89	7.1	0.81	7.3	0.89	>0.05
	MCV (fL)	84.1	2.23	84.9	2.88	85.2	2.86	>0.05
	RDW (%)	14.6	4.35	16.4	5.16	20.2	5.07	<0.05
	Platelet Count ($\times 10^9/\mu\text{L}$)	258.8	36.36	261.6	30.96	265.4	30.88	>0.05
	MPV (fL)	8.4	0.52	9.2	1.06	12.9	1.05	<0.05

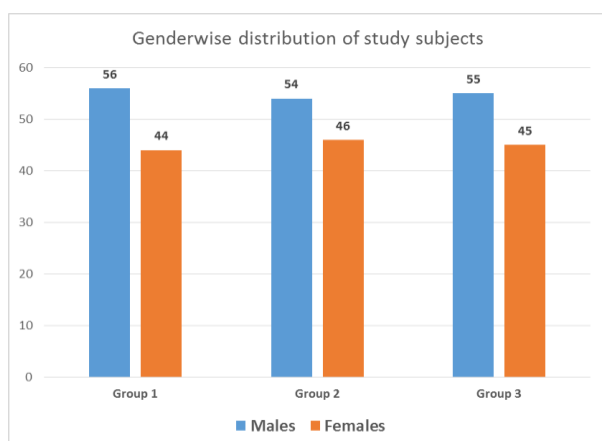
Abbreviations: WBC - white blood cell; MCV - mean corpuscular volume; RDW - red cell distribution width; MPV - mean platelet volume

Table 4: Correlation of RDW with various parameters.

Parameters	RDW	
	R	P
Age	0.086	>0.05
BMI	0.655	<0.05
WHR	0.534	<0.05
SBP	0.183	>0.05
DBP	-0.094	>0.05
FBS	-0.076	>0.05
PPBS	0.076	>0.05
Cholesterol	0.115	>0.05
Triglyceride	0.099	>0.05
LDL	0.012	>0.05
HDL	0.103	>0.05
WBC	0.073	>0.05
MCV	0.005	>0.05
Platelet Count	0.202	>0.05

Table 5: Correlation of MPV with various parameters.

Parameters	MPV	
	R	P
Age	-0.051	>0.05
BMI	0.088	>0.05
WHR	0.057	>0.05
SBP	0.042	>0.05
DBP	-0.038	>0.05
FBS	0.028	>0.05
PPBS	0.032	>0.05
Cholesterol	-0.094	>0.05
Triglyceride	0.008	>0.05
LDL	-0.023	>0.05
HDL	-0.059	>0.05
WBC	0.049	>0.05
MCV	0.023	>0.05
Platelet Count	-0.368	<0.05

**Figure 1: Gender-wise distribution of study subjects.**

DISCUSSION

It was a hospital based analytical cross sectional study conducted to investigate the relationship between the

Metabolic Syndrome (MS) and new inflammatory markers as mean platelet volume (MPV) and red blood cell distribution width (RDW). The present study was carried out with following three groups of 100 patients each:

Group 1: Age and Sex-match healthy subjects.

Group 2: Patients with 3 MS criteria.

Group 3: Patients with 5 MS criteria.

Recently the increasing prevalence of metabolic syndrome has become a global health problem. Disclosed risk factor includes age, family history of diabetes, obesity, hypertension and high triglycerides. Thus monitoring of MS in order to prevent complications is urgently needed. The RDW a widely available and inexpensive test conducted as a part of the CBC measure the degree of anisocytosis. Red cell distribution width (RDW) is considered an inflammatory marker which may reflect an underlying inflammatory process. Mean platelet volume (MPV) is considered an inflammatory marker, it's the average size of platelets. Various studies identifies the MPV and RDW 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, RDW was directly correlated with metabolic syndrome.

The present study reports that majority of study subjects belonged to age group of 51-60 years followed by >60 years among all the three groups. The mean ages of study participants in all the three groups were relatively similar. Similarly the proportion of male: female cases are somewhat similar in all the three groups and found no statistical significance between the findings. From the anthropometric findings of this study, it can be noted that frequency of overweight class of BMI subjects tends to be increasing from group 1 to group 3 and this difference proved to be statistically significant. Similar results were found when we measured their waist: hip ratio, it also tends to increase in similar fashion in both males and females and is found to be statistically significant.

We have also observed similar significant increase in levels of blood pressures, blood glucose levels, serum lipid profiles, and red cell distribution width as we analyzed their values from group 1 to group 3 respectively. It was observed in the present study that there were no statistically significant correlations between RDW and age, SBP, PPBS, WBC, MCV and Platelet Count. RDW was inversely correlated with DBP and FBS but the correlation was insignificant. RDW was strongly and directly associated with the Body Mass Index ($r=0.655$; $p<0.05$) and WHR ($r=0.534$; $p<0.05$). RDW did not correlate significantly with any of the components of the lipid profile.

Nada AM,^[11] retrospective study on indices of some elements of the complete blood count, in type 2 diabetic patients, in comparison with non-diabetic healthy controls

reported RDW was strongly and directly associated with the body mass index (P,0.0001). MCV showed to be inversely associated with BMI (P=0.016) and HbA1c (P=0.048). Tavit Y et al¹⁸ study investigating MPV values in patients MS and to interrogate the association with CAD reported Patients with metabolic syndrome had as expected higher systolic and diastolic blood pressure, BMI, waist circumference, serum triglyceride, fasting plasma glucose, lower HDL-cholesterol, and number of components of metabolic syndrome compared with control subjects. However no significant difference between groups with respect to age, gender, total cholesterol, LDL-cholesterol, and platelet counts. The previous study by Grotto HZW et al,¹⁹ had similar results to our study.

In the present study, higher RDW in MS patients than healthy controls indicate the presence of anisocytosis, which is related to impairment of erythropoiesis and degradation of erythrocytes by fragmentation or agglutination.^[20,21] This occurs in the presence of chronic inflammation and increased level of oxidative stress.^[22]

Similar to our study, Vayá et al mentioned a significant strong correlation between RDW and BMI.^[23] Obesity is associated with a low-grade inflammatory process in the white adipose tissue,^[24] so its association with RDW can be considered reasonable.

In our study, MPV showed direct but insignificant correlation with BMI, WHR, SBP, FBS, PPBS, WBC and MCV. MPV was inversely correlated with age and DBP but the correlation was insignificant. MPV did not correlate significantly with any of the components of the lipid profile. MPV was inversely correlating with Platelet Count ($r=-0.368$, $p<0.05$). In our study, an inverse correlation between MPV and platelet count is in agreement with the study conducted by Akinsegun A et al.^[25] This was explained to be as a result of small platelets being consumed in order to maintain a constant platelet functional mass.

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.^[26]

CONCLUSION

It is known that systemic inflammation is involved in MS and in patient with MS the risk for development CVD increases. The present study is the first report about the association of MPV and RDW with the presence and the severity MS. The results may have clinical importance because the parameters indicating inflammation in MS may be the early markers of developing cardiovascular events. MPV and RDW are important, simple, effortless and cost effective tools that should be used more

extensively to predict impending acute events. Patients with metabolic syndrome can easily be identified during hematological analysis by looking at raised MPV and RDW and could possibly benefit from further mortality. Significant correlation was observed between the 3 and 5 criteria of MS and inflammation based on these new markers that should be simple and reliable indicator of inflammation.

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