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Mean Platelet Volume and Red Cell Distribution Width as Simple Biomarkers of Pulmonary Hypertension and Clinical Outcome: A Prospective Observational Study.

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Abstract

Background: Pulmonary hypertension (PH) is a progressive cardiopulmonary disorder associated with increased pulmonary vascular resistance, right ventricular dysfunction and significant morbidity and mortality. Mean platelet volume (MPV) and red cell distribution width (RDW) are routinely available parameters derived from the complete blood count and have been proposed as markers of inflammation, endothelial dysfunction and disease severity. This study evaluated the association of MPV and RDW with pulmonary artery systolic pressure (PASP) and clinical outcome in patients with pulmonary hypertension. ***Methods:*** A prospective observational study was conducted among 40 patients aged >18 years with pulmonary hypertension attending or admitted to the Department of General Medicine at K R Hospital, Mysuru. Patients receiving antiplatelet or antithrombotic therapy, those with chronic kidney disease or chronic liver disease, and those with a history of recent blood transfusion were excluded. Clinical evaluation, routine laboratory investigations, arterial blood gas analysis, chest imaging and transthoracic echocardiography were performed. Pulmonary artery systolic pressure was assessed by echocardiography, with PASP >30 mmHg considered indicative of pulmonary hypertension for the study. MPV and RDW were obtained from complete blood counts. Data were analysed using SPSS version 24.0. Associations between variables and outcome were assessed using unpaired t-test and chi-square test, while correlation analysis was used for continuous variables. ***Results:*** The study included 40 patients with a mean age of 57.93 ± 14.62 years; 25 (62.5%) were women and 15 (37.5%) were men. The mean MPV was 9.62 ± 0.87 fL, mean RDW was 14.74 ± 1.75%, and mean PASP was 55.88 ± 12.44 mmHg. Fifteen patients (37.5%) died, while 25 (62.5%) were discharged. MPV and RDW showed significant positive correlations with PASP, with correlation coefficients of 0.989 ($p<0.001$) and 0.715 ($p<0.01$), respectively. RDW was significantly higher among patients who died compared with survivors (16.38% vs. 13.76%, $p<0.001$), whereas MPV did not differ significantly between outcome groups. Mean PASP was significantly higher among patients who died than among survivors (67.93 ± 5.79 vs. 48.64 ± 9.29 mmHg, $p<0.001$). On ROC analysis, MPV had an area under the curve (AUC) of 0.863 at a cutoff of 9.65 fL, with 66.7% sensitivity and 84% specificity. RDW had an AUC of 0.924 at a cutoff of 14.85%, with 80% sensitivity and 80% specificity. PASP had an AUC of 0.937. ***Conclusion:*** Both MPV and RDW showed significant positive correlations with PASP in patients with pulmonary hypertension. RDW was significantly associated with mortality, whereas MPV was not significantly different between outcome groups. The diagnostic performance of RDW and MPV for adverse outcome was comparable with that of PASP in this cohort. These inexpensive and routinely available hematological parameters may have potential utility as adjunctive markers of disease severity and outcome in pulmonary hypertension. Larger prospective studies using right heart catheterization are required for validation.

Keywords: Pulmonary hypertension; mean platelet volume; red cell distribution width; pulmonary artery systolic pressure; mortality; biomarkers; ROC analysis.

INTRODUCTION

Pulmonary hypertension (PH) is a progressive clinical syndrome characterized by elevated pulmonary arterial pressure and increased pulmonary vascular resistance. Progressive elevation of pulmonary vascular resistance increases right ventricular afterload and may ultimately result in right ventricular dysfunction, right heart failure and death. The clinical manifestations of PH are often nonspecific, with exertional dyspnoea, fatigue, chest discomfort and syncope being common presenting symptoms.

The evaluation of pulmonary hypertension involves clinical assessment, imaging, echocardiography and, when indicated, right heart catheterization. Although right heart catheterization remains the definitive method for hemodynamic assessment, echocardiography is widely used for initial assessment and estimation of pulmonary artery pressures. The present study used echocardiographically estimated pulmonary artery systolic pressure (PASP) for assessment.

Hematological indices obtained from the routinely performed complete blood count have attracted increasing interest as potential biomarkers in cardiopulmonary disease. Mean platelet volume (MPV), a measure of platelet size, has been associated with platelet activation and inflammatory processes. Similarly, red cell distribution width (RDW), which reflects heterogeneity in erythrocyte size, may be influenced by inflammation, oxidative stress, nutritional abnormalities and impaired erythropoiesis.

Previous studies have reported increased MPV and RDW in different forms of pulmonary hypertension. Proposed mechanisms include inflammation, oxidative stress and endothelial dysfunction. However, data regarding the relationship of these inexpensive hematological parameters with pulmonary artery pressure and clinical outcome remain limited.
Therefore, the present study was undertaken to evaluate MPV and RDW in patients with pulmonary hypertension and to determine their relationship with PASP and clinical outcome.

Objectives

1. To evaluate MPV and RDW in patients with pulmonary hypertension.
2. To determine the correlation of MPV and RDW with PASP.
3. To assess the association of MPV and RDW with clinical outcome.
4. To evaluate the ability of MPV and RDW to discriminate patients with adverse outcome using receiver operating characteristic (ROC) analysis.

MATERIALS AND METHODS

Study design and setting

This was a prospective observational study conducted in the Department of General Medicine at K R Hospital, Mysuru Medical College and Research Institute, Mysuru, Karnataka. The study was conducted after obtaining institutional ethical clearance and written informed consent from the participants.

Study population

Patients attending the outpatient department or admitted to the Department of General Medicine at K R Hospital were considered for inclusion.

Sample size

The calculated sample size was 40 participants, based on an assumed prevalence of 2.6%, 5% margin of error and a 95% confidence level.

Inclusion criteria DX

1. Patients aged >18 years with pulmonary hypertension.

Exclusion criteria

1. Patients receiving antiplatelet or antithrombotic therapy.
2. Patients with chronic kidney disease.
3. Patients with chronic liver disease.
4. Patients with a history of recent blood transfusion.

Clinical and laboratory assessment

Relevant clinical history and physical examination findings were recorded in a preformed proforma. Cardiac evaluation and laboratory investigations included complete blood count with MPV and RDW, renal function tests, serum electrolytes, liver function tests, fasting and postprandial blood glucose, HbA1c, urine routine examination and ultrasonography of the abdomen.

Additional investigations including high-resolution computed tomography of the thorax, electrocardiography, chest radiography and arterial blood gas analysis were performed to assess the underlying cause and clinical status. Transthoracic echocardiography was performed to estimate PASP. For the purposes of this study, PASP >30 mmHg was considered evidence of pulmonary hypertension.

Outcome assessment

The clinical outcome was categorized as discharge or death.

Statistical analysis

Data were entered into Microsoft Excel, double-checked and analysed using SPSS version 24.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and proportions. The unpaired t-test was used for comparison of continuous variables between outcome groups and the chi-square test was used for categorical variables. Correlation analysis was performed to assess relationships between continuous variables. A p-value <0.05 was considered statistically significant. ROC curve analysis was performed to evaluate the discriminatory ability of MPV, RDW and PASP for clinical outcome.

RESULTS

Baseline characteristics

A total of 40 patients were included. The mean age was 57.93 ± 14.62 years. Women constituted 62.5% (n=25) and men 37.5% (n=15) of the study population.

The most frequent underlying comorbidity was chronic obstructive pulmonary disease (COPD), present in 14 patients (35%), followed by interstitial lung disease (ILD) in 9 patients (22.5%) and previous pulmonary tuberculosis in 7 patients (17.5%). Obstructive sleep apnea was present in 3 patients (7.5%) and rheumatoid arthritis in 1 patient (2.5%). Six participants had no recorded comorbidity.

Eleven patients (27.5%) were smokers and 13 (32.5%) reported alcohol consumption.

Parameter	Mean ± SD / n (%)
Age, years	57.93 ± 14.62
Female sex	25 (62.5%)
Male sex	15 (37.5%)
Smoking	11 (27.5%)
Alcohol consumption	13 (32.5%)
SpO_2, %	79.25 ± 13.24
$PaCO_2$, mmHg	56.85 ± 10.12
MPV, fL	9.62 ± 0.87
RDW, %	14.74 ± 1.75
PASP, mmHg	55.88 ± 12.44
Hemoglobin, g/dL	13.34 ± 1.95
Platelet count, lakh/µL	3.42 ± 0.38
Systolic BP, mmHg	119.0 ± 8.10
Diastolic BP, mmHg	78.9 ± 4.96

Clinical outcome

Twenty-five patients (62.5%) were discharged, whereas 15 patients (37.5%) died. Among the 15 patients who died, respiratory failure accounted for 13 deaths (86.67%), while myocardial infarction accounted for 2 deaths (13.33%).

Association of clinical variables with outcome

Patients who died had significantly lower mean SpO_2 than those who were discharged (65.47 ± 3.52% vs. 87.52 ± 9.37%, p<0.001). The mean PASP was significantly higher among patients who died compared with survivors (67.93 ± 5.79 vs. 48.64 ± 9.29 mmHg; p<0.001). There were no statistically significant associations between outcome and age, sex, smoking, alcohol consumption or underlying comorbidities.

MPV, RDW and outcome

The mean RDW was substantially higher among patients who died compared with those who survived (16.38% vs. 13.76%), and this difference was statistically significant (p<0.001). In contrast, MPV did not demonstrate a statistically significant difference between the two outcome groups.

Parameter	Death	Survival	P value
MPV, fL	No significant difference	No significant difference	>0.05
RDW, %	16.38	13.76	<0.001
PASP, mmHg	67.93 ± 5.79	48.64 ± 9.29	<0.001

Correlation with PASP

Both hematological parameters demonstrated significant positive correlations with PASP. MPV showed a correlation coefficient of 0.989 ($p<0.001$), while RDW showed a correlation coefficient of 0.715 ($p<0.01$). These findings indicate that increasing values of MPV and RDW were associated with higher echocardiographically estimated pulmonary artery systolic pressure.

ROC analysis

ROC analysis demonstrated good discriminatory performance of both MPV and RDW for adverse outcome. MPV demonstrated an AUC of 0.863 at a cutoff of 9.65 fL, with 66.7% sensitivity and 84% specificity. RDW demonstrated an AUC of 0.924 at a cutoff of 14.85%, with 80% sensitivity and 80% specificity. PASP had an AUC of 0.937, with 73.3% sensitivity and 88% specificity. All three parameters were statistically significant ($p<0.001$).

Variable	AUC	Cutoff	Sensitivity	Specificity	P value
MPV	0.863	9.65 fL	66.7%	84%	<0.001
RDW	0.924	14.85%	80%	80%	<0.001
PASP	0.937	62.50 mmHg	73.3%	88%	<0.001

DISCUSSION

The present study evaluated two routinely available hematological indices, MPV and RDW, in patients with pulmonary hypertension and examined their relationship with PASP and clinical outcome. The principal findings were that both MPV and RDW showed significant positive correlations with PASP, while RDW was significantly associated with mortality. MPV, despite demonstrating a strong positive correlation with PASP and good ROC performance, did not differ significantly between patients who died and those who survived.

The mean MPV in the present study was 9.62 fL. This is broadly comparable with values reported in previous studies of pulmonary hypertension. Varol et al. reported significantly higher MPV among patients with pulmonary arterial hypertension compared with controls, while Zheng et al. reported an MPV of approximately 11.4 fL in idiopathic pulmonary arterial hypertension.

The mean RDW in the present cohort was 14.74%. Previous investigations have similarly demonstrated increased RDW in pulmonary hypertension and in conditions associated with pulmonary vascular disease.

The biological basis for elevation of MPV and RDW in pulmonary hypertension is likely multifactorial. Chronic inflammation, oxidative stress and endothelial dysfunction may influence platelet activation and erythrocyte maturation, thereby altering MPV and RDW.

A particularly important finding of the present study was the significant positive correlation between MPV and PASP and between RDW and PASP. The correlation coefficients were 0.989 and 0.715, respectively. This suggests that these inexpensive hematological parameters may reflect, at least in part, the severity of pulmonary vascular disease.

RDW showed a significant association with clinical outcome. Patients who died had a mean RDW of 16.38%, compared with 13.76% among survivors, with $p<0.001$. This observation is consistent with previous literature describing higher RDW in patients with pulmonary hypertension and other cardiopulmonary conditions associated with poor outcomes.

In contrast, MPV did not demonstrate a statistically significant difference between patients who died and survivors. Therefore, although MPV showed a strong correlation with PASP, its relationship with mortality in this cohort was less consistent than that of RDW. This distinction is important because correlation with disease severity does not necessarily establish independent prognostic value.

The ROC analysis provided additional information regarding the potential clinical utility of these parameters. RDW demonstrated an AUC of 0.924, while MPV demonstrated an AUC of 0.863. PASP demonstrated an AUC of 0.937. Thus, the discriminatory performance of RDW and MPV approached that of PASP in this small cohort.

The clinical relevance of these findings lies in the accessibility of these parameters. MPV and RDW are automatically reported as part of routine hematological testing and require no additional expenditure or specialized investigation. If validated in larger cohorts, they could potentially serve as adjunctive markers for identifying patients requiring closer clinical assessment.

However, these results should be interpreted cautiously. The sample size was small, and the study was conducted at a single centre. More importantly, pulmonary hypertension was identified using echocardiographic PASP rather than right heart catheterization, which remains the gold-standard method for hemodynamic diagnosis and classification. Furthermore, the observational design does not establish a causal relationship between elevated MPV/RDW and pulmonary hypertension or mortality.

Strengths

The major strength of the study is its evaluation of inexpensive and routinely available hematological parameters in relation to an objective hemodynamic surrogate, PASP. The study also evaluated clinical outcome and incorporated ROC analysis, allowing assessment of the discriminatory performance of MPV and RDW.

Limitations

1. The study was conducted at a single tertiary-care centre.
2. The sample size was limited to 40 participants.
3. Pulmonary hypertension was assessed using echocardiographic PASP rather than right heart catheterization.
4. The study population included patients with different underlying pulmonary and systemic conditions, potentially introducing heterogeneity.
5. The observational design limits conclusions regarding causality.
6. Multivariable analysis was not performed; therefore, the independent association of MPV and RDW with mortality could not be established.

CONCLUSION

In this prospective observational study of patients with pulmonary hypertension, both MPV and RDW demonstrated significant positive correlations with pulmonary artery systolic pressure. RDW was significantly higher among patients who died, whereas MPV did not show a statistically significant difference according to clinical outcome.

ROC analysis demonstrated good discriminatory ability for both RDW and MPV, with AUC values of 0.924 and 0.863, respectively, approaching the performance of PASP (AUC 0.937). These findings suggest that RDW and MPV may have potential as inexpensive and readily available adjunctive markers of pulmonary hypertension severity and adverse clinical outcome.

However, given the small sample size, single-centre design and use of echocardiographic rather than catheter-based hemodynamic assessment, these findings should be considered preliminary. Larger prospective multicentre studies using right heart catheterization and multivariable prognostic models are warranted to determine the independent clinical utility of MPV and RDW in pulmonary hypertension.

DECLARATIONS

Ethics approval: The study was conducted after obtaining institutional ethical clearance, and written informed consent was obtained from all participants.

Consent for participation: Written informed consent was obtained from all participants.

Funding: No external funding information was reported in the dissertation.

Conflict of interest: No conflict-of-interest information was reported in the dissertation.

Data availability: The data underlying this study were obtained from the study records and are subject to institutional and ethical requirements.

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