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The role of red-cell distribution width (RDW) and mean platelet volume (MPV) as biomarkers of community-acquired pneumonia (CAP) severity

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Literature Review

ABSTRACT

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morbidity and mortality worldwide. Red-cell distribution width (RDW) and mean platelet volume (MPV) are two parameters included in complete blood count (CBC). It is simple, inexpensive, and widely available in any hospital. Many previous studies have shown that RDW and MPV can be used as supporting biomarkers for CAP, but the study in this area remains limited. This study aims to investigate the relationship between RDW and MPV with the severity of CAP and their potential as biomarkers. We conducted a scoping review of original articles using PubMed, Springer Link, Taylor and Francis, EBSCO, Cochrane Library, Google Scholar, Medline, Science Direct, Wiley, and Portal Garuda. Only articles published between 2012 and 2022 in English or Indonesian were included. Out of 11,852 articles reviewed, only 18 met the criteria for the focus on using RDW, MPV, or both as biomarkers for CAP. The details of these studies, including their research design, internal and external validity, and key results, are presented. The results show that increased RDW and MPV levels correlate with higher morbidity and mortality rates among CAP

patients. Elevated levels of RDW (>14%) and MPV (>8.1 fL) can predict and acts as a biomarker of CAP severity. Thus, measuring RDW and MPV may give physicians a way to anticipate the outcomes for patients with CAP, helping them make and implement decisions, either alone or in

Community-acquired pneumonia (CAP) remains a leading cause of

Pneumonia komunitas (CAP) merupakan salah satu penyebab utama morbiditas dan mortalitas di seluruh dunia. Red-cell distribution width (RDW) dan mean platelet volume (MPV) adalah dua parameter dalam pemeriksaan darah rutin yang sederhana, murah, dan tersedia hampir di seluruh rumah sakit. Banyak penelitian terdahulu menunjukan RDW dan MPV dapat digunakan sebagai biomarker keparahan pneumonia komunitas. Studi ini bertujuan mengkaji peran RDW dan MPV sebagai biomarker derajat keparahan pneumonia komunitas. Metode yang digunakan adalah scoping review. Jenis artikel yang diulas pada penelitian ini adalah original article dengan pencarian melalui sepuluh sumber data yaitu PubMed, Springer Link, Taylor and Francis, EBSCO, Cochrane Library, Google Scholar, Medline, Science Direct, Wiley, dan Portal Garuda. Artikel yang dipilih adalah artikel berbahasa Indonesia atau Bahasa Inggris yang dipublikasi pada tahun 2012-2022. Dari 11.852 artikel yang diulas, hanya 18 yang memenuhi kriteria dan fokus membahas RDW, MPV, atau keduanya sebagai biomarker untuk CAP. Hasilnya menunjukkan bahwa peningkatan kadar RDW dan MPV berkorelasi dengan, prognosis, tingkat morbiditas, dan mortalitas yang lebih tinggi di antara pasien CAP. Tingginya tingkat RDW (>14%) dan MPV (>8,1 fL) dapat memprediksi dan berfungsi sebagai biomarker keparahan CAP. Pengukuran RDW dan MPV saat pasien masuk rumah sakit dapat memberi klinisi cara untuk menyesuaikan tatalaksana CAP sesuai prognosis atau keparahan pasien CAP, baik sendiri maupun dikombinasikan dengan metode lain yang sudah ada.

combination with other established methods.

INTRODUCTION

Community-acquired pneumonia (CAP) is the world's fourth leading cause of mortality. Determining prognosis with a scoring system plays a vital role in the management of patients with CAP, and there are currently several severity scoring systems in use, such as the pneumonia severity index (PSI) and CURB-65 (confusion, urea, respiratory rate, blood pressure, age ≥65).¹ However, these severity scores have some limitations and variations. For example, CURB-65 and CRB-65 are crude scores for rapid assessment in high-risk patients, while PSI is believed to help identify low-risk patients. Therefore, more efforts are needed to improve the prognostic value in managing CAP as early identification of high-risk patients with poor prognosis.²

Several biomarkers have been examined and verified for their use in the prognosis determination of community pneumonia that can improve the prognostic performance of severity scores. However, some of these biomarkers are non-specific and insensitive. Some of them, such as procalcitonin, C-reactive protein, atrial natriuretic protein (ANP), and copeptin, which are currently widely studied, are relatively expensive and not readily available. Several simpler, cheaper, and widely available biomarkers can be used to assess the severity of pneumonia, including RDW and MPV. Red-cell distribution width and MPV examinations are relatively frequently performed because they are one of the parameters in a complete blood test, but their clinical value is rarely discussed.3

Red-cell distribution width is defined as the coefficient of variation of circulating red blood cells. This parameter is calculated as the standard deviation of red cell volume/average red cell volume x 100% (expressed as a percentage). Several years earlier, RDW was used in clinical practice to diagnose various types of anemia. A higher RDW reflects abnormal red blood cell homeostasis, indicating the presence of normal red blood cell destruction. A

In addition, elevated RDW has a prognostic role in the outcome of several diseases, such as cardiovascular disease, rheumatoid arthritis, colon cancer, and metabolic syndrome. Likewise, several studies have reported RDW as a prognostic predictor of mortality in different populations. The exact mechanism of RDW variation remains

unknown, but it is mainly related to oxidative stress and inflammation processes that reflect the prognostic role of RDW. Inflammation can directly affect the survival rate of red blood cells, resulting in a mixed volume of red blood cells in the circulatory system.⁴

Meta-analysis studies by Su et al. and Hou et al. have supported the hypothesis that RDW may be one of the valuable parameters for gathering diagnostic or prognostic information in various cardiovascular and thrombotic disorders, although the relationship between RDW and cardiovascular disease is unclear. ^{5,6} Recently, RDW has been associated with community pneumonia patient outcomes, especially with 30-day and 90-day mortality and hospitalizations. ¹

A study by Lee et al. shows that change in RDW from day 1 to day 4 is an independent predictor of mortality in CAP patients. There were no significant differences in RDW changes between survivors and non-survivors on the second and third days. However, RDW levels decreased in survivors and increased in non-survivors over four days in the hospital.^{6,7}

On the other hand, MPV is a routine laboratory test measured in a complete blood count and is considered a marker of platelet function and activation.⁸ Platelets also play an essential role in homeostasis, inflammation, and immune processes. Elevated MPV is associated with increased morbidity and mortality in various patient populations. Based on studies, there is an increased risk of in-hospital mortality and outcomes in patients with hospitalized community pneumonia.^{1,9}

The prognostic significance of MPV has been studied in only two small studies in CAP patients based on a single MPV determination. MPV is a dynamic parameter that can change significantly within days or weeks. Several previous studies identified an increase in MPV over time as a strong predictor of morbidity and mortality in patients with critical illness, bacteremia, coronary artery disease, and heterogeneous disorders. We hypothesized that MPV may reflect platelet activity and may be associated with impaired host body response. According to this hypothesis, elevated MPV may be related to poor outcomes and may predict in-hospital mortality in ICU patients with severe pneumonia. 1,10

Many studies have shown the prognostic

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significance of RDW and MPV as biomarkers of community pneumonia severity. However, the review articles related to this topic remain to be developed. Therefore, we are interested in reviewing existing articles using a scoping review scheme. This study aims to investigate the relationship between RDW and MPV with the severity of CAP and their potential as biomarkers.

METHODS

The data sources used are research journals published in several databases: PubMed, Google Scholar, Garuda Portal, Science Direct, Springer Link, Wiley, and Taylor and Francis. Literature searches were conducted in September-November 2022 and published between 2012 to 2022 in English or Bahasa Indonesia. Based on the PICO (population, intervention, comparison, and outcomes) analysis, the keywords were "community pneumonia" or "Community-acquired pneumonia" or "CAP" and "RDW" or "Red-cell distribution width" and "MPV" or "Mean platelet volume" and "Severity" or "Outcome." In addition to using keywords, there were restrictions placed on each data source, namely year, language, article type, publication title type, subject area, and full-text accessible articles. Article selection was carried out based on the specified inclusion criteria. The article selection process was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR). Data analysis was performed using Google Sheets by Google LLC.

RESULT

Article searches were conducted by entering the keywords compiled based on PICO analysis into 10 data sources: PubMed, Springer Link, Taylor and Francis, Google Scholar, Medline, Science Direct, EBSCO, Cochrane Library, Wiley, and Garuda Portal. The number of search results from all data sources is 11,852 articles. Based on PRISMA-ScR, we eliminated duplicated articles and retrieved 7,341 articles. Next, screening was carried out, and 1,582 articles were obtained. Furthermore, eligibility was carefully reviewed, and 28 articles were chosen. Finally, 18 articles with relevant titles were selected (Figure 1).

Table 1 summarizes all the extracted data, including the duration of each research and essential statistics values. Out of the 18 selected articles, 33% were cohort studies, 11% were crosssectional, 11% were case-control, 5% descriptive, and the remaining 40% combined prospective and retrospective studies. The studies were conducted over durations ranging from 6 months to 6 years in various countries: Israel, Iran, Turkey, Thailand, China, Egypt, Italy, Spain, the United States of America, and South Korea. Among these articles, 12 supported the relationship between RDW and CAP severity, while 5 supported the relationship between MPV and CAP severity. Only one article contradicted the association between RDW and CAP severity.

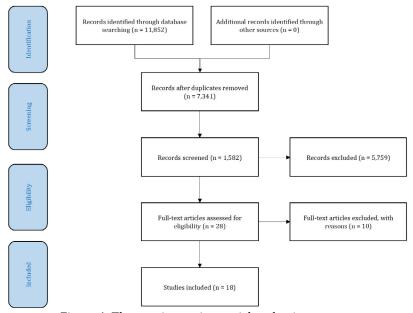


Figure 1. The scoping review article selection process

Table 1. Sources of Evidence for Search and Results

No	Title	Authors	Year	Method	Place	Duration	Aim	Results
1	A rise in mean plate- let volume during hospitalization for community-acquired pneumonia predicts poor prognosis: a retrospective obser- vational cohort study.	Gorelik, et al. ¹¹	2017	Cohort retro- spective	Israel	3 year	Comparing demographic, clinical, laboratory, and radiographic characteristics, as well as short-term and long-term outcomes of CAP patients, with changes in MPV.	An increased MPV strongly predicted the need for mechanical ventilation and in-hospital death (RR: 2.62 and 6.79, 95% CI: 1.54–4.45 and 3.48–13.20). Elevation of MPV also strongly predicts all cause of mortality (RR 1.26 and 95% CI 1.11–1.43).
2	Association between community-acquired pneumonia and plate- let indices: A case-con- trol study	Motamed, et al. ¹²	2021	Case- control	Iran	1 year	Evaluating the role of the platelet index in diagnosing CAP.	One index is not accurate enough to predict CAP. The median neutrophil count of the case group was higher than the control group (p=0.00), while the lymphocyte of the case group was lower (p=0.00).
3	C-reactive protein (CRP)/mean platelet volume (MPV) ratio as a new biomarker for community-acquired pneumonia in children	Güzel, et al. ¹³	2017	Case- control	Turki- ye	6 month	Evaluating the re- lationship between the CRP/MPV ratio and WBC/MPV and the diagnosis and severity of disease in children with CAP.	The ratio of CRP/MPV and WBC/MPV can be used as biomarkers for evaluating the diagnosis of CAP (p<0.05 with r=0.761 and 0.731). The CRP/MPV ratio can be a predictive marker of disease activity.
4	Combination of mean platelet volume and the CURB-65 score better predicts 28-day mortality in patients with community-acquired pneumonia	Golcuk, et al. ¹⁴	2015	Cross- sectional prospec- tive	Turki- ye	10 month	Investigate the correlation between MPV and the CURB-65 score and determine whether the combination of the CURB-65 score with MPV can better predict 28-day mortality in patients with CAP.	MPV have inverse correlation with CURB-65 (R=-0.58, P<0.001). The combination of the CURB-65 score and MPV (with cut off 8.55 fL) can improve the prediction of 28-day mortality.
5	Comparison of Red Cell Distribution Width with the Severity and Outcomes in Children with Community-Ac- quired Pneumonia	Kriang- burapa, et al. ¹⁵	2021	Cross- sectional retro- spective	Thai- land	5 year	Comparing the increase in RDW with the severity and outcome of CAP in children.	High RDW indicates a far higher clinical respiratory score in children with CAP (p<0.001)
6	Cell Distribution Width Combined White Blood Cells in Peripheral Blood Routine Have a Better Sensitivity than CURB-65 Scores in Pre- dicting ICU Admission and Mortality in Adult Community-Acquired Pneumonia Patients	Ge, et al. ¹⁶	2019	Retro- spective	China	-	Understanding the usefulness of routine blood tests in predicting CAP patients in ICU and 30-day mortality.	RDW, WBC, and CURB-65 ≥ 3 scores increased 30-day mortality risk (RDW: 4.01x, WBC: 1.65x, CURB-65: 3.43x). The combined RDW with WBC had an AUC of 0.786 (95% CI 0.701-0.876) in the ROC curve, while RDW with CURB-65 had an AUC of 0.836 (95% CI 0.764-0.908).
7	Mean platelet volume change (Δ MPV) and red blood cell distribution width (RDW) as promising markers of community-acquired pneumonia (CAP) outcome	Farghly, et al. ¹⁷	2020	Cohort prospec- tive	Egypt	2 year	Evaluating the relationship between RDW and/or MPV and mortality and morbidity in CAP patients to improve the prognostic scoring system that is already in use.	Delta MPV and RDW showed significant positive correlations with PSI and CURB-65 (p<0.001). Patients who died had significantly higher delta MPV (2.61 \pm 1.01 vs. 1.78 \pm 0.76; p=0.01) and RDW (16.50 \pm 3.54 vs. 15.50 \pm 2.81; p=0.02).

No	Title	Authors	Year	Method	Place	Duration	Aim	Results
8	Prognostic value of albumin-red cell dis- tribution width score in patients with severe community-acquired pneumonia	Chen, et al. ¹⁸	2020	Retro- spective	China	5 year	Investigate the correlation between the Albumin-RDW score and 90-day mortality of severe CAP patients.	The Albumin-RDW score and invasive ventilation were independent risk factors for 90-day mortality (P<0.05). The AUC of the ALB-RDW score was 0.742 (95% CI: 0.667-0.817), surpassing the CURB-65 score of 0.725 (95% CI: 0.651-0.798). When combined with the CURB-65 score, the AUC increased to 0.798 (95% CI: 0.733-0.862).
9	RDW-based clinical score to predict long-term survival in community-acquired pneumonia: a European derivation and validation study	Melchio, et al. ¹⁹	2021	Cohort	Italia	2 year	Obtaining and validating a risk prediction score to estimate 18-month mortality in patients who have had an episode of CAP and have been discharged from the general ward.	Multivariate analysis revealed independent predictors for long-term mortality in patients discharged for CAP from a general ward, including RDW, temperature, altered mental status, and Charlson Comorbidity Index. The derived score demonstrated good discrimination (c-index 0.76, 95% CI 0.70-0.81; and 0.83, 95% CI 0.78-0.87, in the derivation and validation cohort, respectively) and calibration.
10	Red blood cell distribu- tion width [RDW] and long-term mortality after community-ac- quired pneumonia. A comparison with proadrenomedullin	Bello, et al. ²⁰	2015	Cohort	Spain	5 year	Assessing the accuracy of both biomarkers (Pro-ADM and RDW) for long-term mortality in CAP (>90 days).	RDW > 14% increased the prediction power of PSI and CURB65 scores, as did proADM. The associations of RDW > 14 + PSI and RDW > 14 + CURB65 showed a sensitivity for long-term mortality of 80.8%-90% and 74%-90%, and a specificity of 56.7%-61.5% and 59.3%-64.2%, respectively.
11	Red Blood Cell Distribution Width and Pediatric Community-Acquired Pneumonia Disease Severity	Lee, et al. ²¹	2022	Prospective	America	2 year	Investigating the relationship between the red blood cell distribution width (RDW) and pediatric CAP.	The analysis using restricted cubic splines revealed that there is an independent and nonlinear positive association between RDW and the severity of CAP (p=0.027). The risk of severe CAP rapidly increases with RDW values up to 15%.
12	Red cell distribution width as a prognostic marker in patients with community-ac- quired pneumonia	Lee, et al. ²²	2012	Retro- spective	Korea	3 year	Evaluating the association between RDW and death in patients with CAP.	RDW is associated with 30-day mortality, length of hospital stay, and use of vasopressors in patients with inpatient CAP (p<0.05). RDW improves the prognostic performance of PSI and CURB-65.
13	Role of red cell dis- tribution width in assessing response to treatment and progno- sis in community-ac- quired pneumonia: A prospective study	Cinarka, et al. ²³	2019	Cohort	Turki- ye	8 month	Investigating the prognostic role of RDW in CAP at presentation and its current role in assessing response to treatment.	In nonsurviving CAP patients, the RDW level was $17.7\% \pm 2.1\%$, while in surviving CAP patients, it was $15.9\% \pm 1.8\%$ (P=0.01). The pretreatment RDW level was $16.2\% \pm 1.9\%$, which decreased to $15.3\% \pm 2.2\%$ on the 7th day (P=0.002). An RDW cutoff of >16.5% predicted 30-day mortality with 78% sensitivity and 70% specificity.

No	Title	Authors	Year	Method	Place	Duration	Aim	Results
14	The clinical signifi- cance of changes in red blood cell distribution width in communi- ty-acquired pneumo- nia patient	Lee, et al. ⁷	2016	Retro- spective	Korea	4 year	Evaluating the re- lationship between changes in RDW and mortality in hospitalized pa- tients with CAP	There's a significant relationship between ΔRDW and 30-day mortality risk in the multivariate Cox regression analysis (p<0.05).
15	The relationship between level of the red cell distribution width and the outcomes of patients who acquired pneumonia from the community	Yousef A, et al. ²⁴	2020	Descriptive and Prospective	Egypt	1 year	Assessing the importance of RDW as a prognostic test in patients with CAP.	RDW level was higher in non survivors compared to survivors (18.52±3.07 vs. 12.76±2.08; P=0.022). There was a positive relationship between RDW level and PSI points (r=0.664; P=0.000). An RDW level above 16.1% had a sensitivity of 94.12% and specificity of 98.70% for predicting in-hospital mortality in CAP patients.
16	The role of red blood cell distribution width in the severity and prognosis of commu- nity-acquired pneu- monia	Ren, et al. ²⁵	2021	Retro- spective	China	3 year	Investigating the correlation between RDW and the severity and prognosis of CAP	Higher RDW values ≥ 12.987 are associated with poor short-term outcomes in CAP patients (p<0.01). When RDW, PSI, and CURB-65 were combined, the best performance was achieved in predicting 90-day CAP mortality risk.
17	The value of mean platelet volume in the determination of community-acquired pneumonia in children	Karadag- Oncel, et al. ²⁶	2013	Retro- spective	Turki- ye	3 year	Evaluating whether MPV can be used as a diagnostic tool for community-acquired pneumonia (CAP) and for making inpatient decisions.	CAP patients had lower MPV values compared to healthy individuals (7.1±0.68 vs. 8.31±1.2 fL; p<0.001). Hospitalized CAP patients had significantly higher MPV values compared to outpatients (7.32±0.71 vs. 6.83±0.5 fL; p=0.012). The MPV level cutoff point for diagnosing CAP was determined to be 8.1 fL, with a sensitivity of 91%, specificity of 51%, positive predictive value (PPV) of 80.8%, and negative predictive value (NPV) of 70.5%.
18	Is elevated Red cell distribution width a prognostic predictor in adult patients with community-acquired Pneumonia?	Braun, et al. ²⁷	2014	Cohort	Israel	6 year	Determining the prognostic predic- tive value of RDW in patients with CAP in the general inpa- tient population	Patients with increased RDW had significantly higher mortality rates (p<0.001) and rates of complicated hospitalization (p=0.000).

Based on the review of journal articles, it was found that early measurement of RDW at hospital admission and increased MPV during hospitalization of CAP patients were associated with more severe clinical characteristics and high mortality, so these two peripheral blood tests can improve the performance of prognostic scales.17,19 An MPV level cutoff point of 8.1 fL offers high sensitivity, positive predictive value (PPV), and negative predictive value (NPV) for diagnosing CAP. At the same time, RDW > 14% improved the prediction power of PSI and CURB65 scores for long-term mortality.^{21,26}

DISCUSSION

Most of the articles we found show the relation between RDW and MPV with the severity of CAP, hospital admission, and mortality caused by CAP. These findings also indicate the potential of RDW and MPV as biomarkers to help assess the clinical characteristics besides CURB-65, alone or together. Increased MPV in CAP patients is associated with its severity.

Change in RDW from day 1 to day 4 is an independent predictor of mortality in patients with CAP.⁷ Measuring the RDW of CAP patients at hospital admission can help clinicians determine short- and long-term prognoses.^{24,25} High RDW

values at admission were also associated with significantly higher mortality and morbidity rates in adult patients with CAP.²⁷

In adult patients, an increase in both RDW and WBC is associated with increased mortality. Together with CURB-65 and PSI, RDW values may improve the accuracy of long-term mortality of CAP.²⁰ In fact, RDW and WBC have better sensitivity than the CURB-65 score in predicting ICU admission mortality in CAP patients.¹⁶ In contrast, a high RDW value in pediatric patients indicates a significantly higher clinical respiratory score.^{15,22} A high value of RDW with a high Albumin value is also an independent risk factor for 90-day mortality in CAP patients and is even stronger when combined with the CURB-65 score.¹⁸ RDW can also be used as an effective parameter in assessing antibiotic response.²³

A study by Braun et al. on hospitalized CAP patients showed that RDW >14.5% was an independent risk factor of 90-day mortality.²⁷ A study by Lee et al. showed that RDW >15.2% was associated with 30-day mortality and improved the prognostic performance of PSI and CURB-65.7 A long-term study in 2015 showed that RDW (>14%) improved the accuracy of PSI and CURB-65 at 2 and 3 years and was associated with cardiovascular disorders.²⁰

Red-cell distribution width may act as an independent risk factor for inflammation and infection and an independent predictor of mortality in Gram-negative bacteremia and sepsis.⁷ Elevated RDW is also associated with acute and chronic hepatitis B and inflammatory bowel disease. There is a strong correlation between a high-value RDW and an elevated index of inflammation, including the Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP).²³

Inflammation and oxidative stress in CAP patients may affect red blood cell homeostasis. RDW may act as an inflammatory biomarker. Serum levels of antioxidants such as selenium and carotenoids are associated with RDW. Patients with a high value of RDW tend to have a higher CAP severity index score and higher overall mortality. Anisocytosis can act as a marker of cellular aging, inflammation, oxidative stress, hypoxia, immune dysregulation of the spleen, or poor nutritional status, all of which are associated with abnormalities of erythropoiesis or hemochromatosis. Moreover, damaged

erythrocytes can also deform and impair tissue oxygenation.¹⁹

The higher the MPV value, the more severe the clinical severity of CAP patients and the prognosis. The increase in MPV can also be used to predict mortality and long-term effects. ¹¹ Besides, combining the CURB-65 score with the MPV value can improve the prediction of 28-day mortality. ¹⁴ In addition, WBC/MPV ratio can also be used as a biomarker to evaluate the diagnosis of CAP, and the CRP/MPV ratio can be a biomarker of disease activity. ¹³ However, MPV alone cannot be used to diagnose CAP. ¹²

The main mechanism for the increase of MPV is the severe inflammation caused by CAP. In severe infection, increased release of thrombopoietin and various inflammatory cytokines, such as interleukin-1, -3, and -6 and tumor necrosis factor- α , promotes thrombopoiesis and increased expression of giant immature platelets into the blood circulation. The elevated MPV increases platelet consumption in peripheral tissues and the spleen, induced by severe inflammatory status. Oxidative stress due to CAP infection may also occur, causing inflammation in patients. 11,17

Larger platelets are known to be functionally, metabolically, and enzymatically more active than smaller ones. Activation of large platelets increases the release of procoagulant substances such as thromboxane A2, β -thrombomodulin, and proteins. Platelet hyperaggregability, vasoconstriction, and endothelial dysfunction may increase the short-term risk of cardiovascular thrombosis and death in patients with elevated MPV. 17

Other factors contributing to the increased MPV are renal dysfunction which is known to be associated with increased MPV. Hypoxemia can also lead to increased platelet consumption, and bone marrow stimulation can also increase MPV.^{11,13}

In contrast to the findings of Gorelik et al., a study by Golcuk et al. showed a significant inverse relationship between MPV and CAP severity. The higher the severity of CAP, the smaller the MPV size. Patients with pneumonia have systemic inflammation, with various elevated proinflammatory cytokines, including IL-6. When the inflammatory process starts, IL-6 stimulates thrombopoiesis through thrombopoietin, which decreases platelet size; hence smaller platelets are released from the bone marrow. The lower

MPV in patients with CAP may be explained by this relationship. 14

A case-control study by Hajar et al. showed lower MPV values in CAP patients than in controls. However, this discrepancy was not statistically significant. Although the MPV value cannot be used as a diagnostic tool for CAP, the number of MPV varies depending on the severity of the infection, which indicates a good indicator for the diagnosis of CAP.¹²

Measuring RDW and MPV could aid in early risk stratification and improve prognostic assessments, supporting clinicians in optimizing patient management and outcomes. Further research and integration of RDW and MPV as additional tools in CAP assessment are warranted to enhance clinical practice and patient care.

CONCLUSION

In conclusion, we found that most articles show the relationship between RDW and MPV with the severity of CAP. Moreover, we found that RDW and MPV have the potential to be used as biomarkers since elevated levels of RDW (>14%) and MPV (>8.1 fL). The measurement of RDW and MPV at hospital admission can provide clinicians with a way to predict the severity and prognosis of deterioration of patients with CAP, enabling them to plan and implement subsequent actions in combination with other existing methods. It should be noted that RDW or MPV testing is a simple, affordable, and ubiquitous peripheral blood test that is widely used. Further research could lead to incorporing RDW and MPV into routine CAP management protocols, offering better patient care and prognosis prediction.

CONFLICT OF INTEREST

The authors declare that there are no potential conflicts of interest in association with the authorship and publication of this article.

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None.

REFERENCES

 Farghly S, Abd-Elkader R, El Zohne RA, Abd El-Kareem DM. Mean platelet volume change (ΔMPV) and red blood cell distribution width (RDW) as promising markers of community-acquired pneumonia (CAP) out-

- come. The Egyptian Journal of Bronchology. 2020;14(1).
- 2. Lee JH, Chung HJ, Kim K, Jo YH, Rhee JE, Kim YJ, et al. Red cell distribution width as a prognostic marker in patients with community-acquired pneumonia. American Journal of Emergency Medicine. 2013;31(1):72–9.
- 3. Kristianto W, Setyoningrum RA, Boediono A. Red-Cell Distribution Width (RDW) dan Mean Platelet Volume (MPV) sebagai Biomarker Keparahan Pneumonia Anak. Sari Pediatri. 2018;19(6):335.
- 4. Ren Q, Liu H, Wang Y, Dai D, Tian Z, Jiao G, et al. The Role of Red Blood Cell Distribution Width in the Severity and Prognosis of Community-Acquired Pneumonia. Can Respir J. 2021;2021(1).
- 5. Su C, Liao LZ, Song Y, Xu ZW, Mei WY. The role of red blood cell distribution width in mortality and cardiovascular risk among patients with coronary artery diseases: A systematic review and meta-analysis. J Thorac Dis. 2014;6(10):1429–40.
- 6. Hou H, Sun T, Li C, Li Y, Guo Z, Wang W, et al. An overall and dose-response meta-analysis of red blood cell distribution width and CVD outcomes. Sci Rep. 2017 Feb 24;7.
- 7. Lee SM, Lee JH, Kim K, Jo YH, Lee J, Kim J, et al. The clinical significance of changes in red blood cell distribution width in patients with community-acquired pneumonia. Clin Exp Emerg Med. 2016 Sep 30;3(3):139–47.
- 8. May JE, Marques MB, Reddy VVB, Gangaraju R. Three neglected numbers in the CBC: The RDW, MPV, and NRBC count. Vol. 86, Cleveland Clinic Journal of Medicine. Cleveland Clinic Educational Foundation; 2019. p. 167–72.
- 9. Gorelik O, Izhakian S, Barchel D, Almoznino-Sarafian D, Tzur I, Swarka M, et al. Prognostic significance of platelet count changes during hospitalization for community-acquired pneumonia. Platelets. 2017;28(4):380–6.
- 10. Tzur I, Barchel D, Izhakian S, et al. Platelet distribution width: a novel prognostic marker in an internal medicine ward. J Community Hosp Intern Med Perspect. 2019;9(6):464-470
- 11. Gorelik O, Tzur I, Barchel D, Almoznino-Sarafian D, Swarka M, Beberashvili I, et al. A rise in mean platelet volume during hospitalization for community-acquired pneumonia

- predicts poor prognosis: A retrospective observational cohort study. BMC Pulm Med. 2017;17(1):1–8.
- 12. Motamed H, Bashiri H, Yari F, Bozorgomid A, Rostamian M, Azarakhsh Y, et al. Association between community-acquired pneumonia and platelet indices: A case-control study. Journal of Acute Disease. 2021;10(1):23.
- 13. Çelik Güzel E, Fidan Ç, Güzel S, Paketçi C. C-reactive protein (CRP)/mean platelet volume (MPV) ratio as a new biomarker for community-acquired pneumonia in children. Cukurova Medical Journal (Çukurova Üniversitesi Tıp Fakültesi Dergisi). 2017;42(3):451–8.
- 14. Golcuk Y, Golcuk B, Bilge A, Irik M, Dikmen O. Combination of mean platelet volume and the CURB-65 score better predicts 28-day mortality in patients with community-acquired pneumonia. American Journal of Emergency Medicine [Internet]. 2015;33(5):648–52.
- 15. Kriangburapa. Comparison of Red Cell Distribution Width with the Severity and Outcomes. The Journal of Prapokklao Hospital Clinical Medical Education Center. 2021;38(2):133–43.
- 16. Ge Y, Liu C. Elevated Red Blood Cell Distribution Width Combined White Blood Cell in Peripheral Blood Routine Have a Better Sensitivity than CURB-65 Scores in Predicting ICU Admission and Mortality in Adult Community-Acquired Pneumonia Patients. Clin Lab [Internet]. 2018 [cited 2023 Jun 7]; Available from: www.clin-lab-publications.com/article/2942
- 17. Farghly S, Abd-Elkader R, El Zohne RA, Abd El-Kareem DM. Mean platelet volume change (ΔMPV) and red blood cell distribution width (RDW) as promising markers of community-acquired pneumonia (CAP) outcome. The Egyptian Journal of Bronchology. 2020;14(1).
- 18. Chen L, Lu XY, Zhu CQ. Prognostic value of albumin-red cell distribution width score in patients with severe community-acquired pneumonia. Ann Cardiothorac Surg. 2020 May 1;9(3):759–65.
- 19. Melchio R, Giamello JD, Testa E, Ruiz Iturriaga LA, Falcetta A, Serraino C, et al. RDW-based clinical score to predict long-term survival in community-acquired pneumonia: a European derivation and validation study. Intern Emerg Med. 2021 Sep 1;16(6):1547–57.

- 20. Bello S, Fandos S, Lasierra AB, Mincholé E, Panadero C, Simon AL, et al. Red blood cell distribution width [RDW] and long-term mortality after community-acquired pneumonia. A comparison with proadrenomedullin. Respir Med. 2015 Sep 1;109(9):1193–206.
- 21. Lee J, Zhu Y, Williams DJ, Self WH, Arnold SR, McCullers JA, et al. Red Blood Cell Distribution Width and Pediatric Community-Acquired Pneumonia Disease Severity. Hosp Pediatr. 2022 Aug 4;12(9):798–805.
- 22. Lee JH, Chung HJ, Kim K, Jo YH, Rhee JE, Kim YJ, et al. Red cell distribution width as a prognostic marker in patients with community-acquired pneumonia. Am J Emerg Med. 2013;31(1):72–9.
- 23. Cinarka H, Gümüş A, Özyurt S, Karataş M, Gıakoup D, Cüre M, et al. Role of red cell distribution width in assessing response to treatment and prognosis in community-acquired pneumonia: A prospective study. Eurasian Journal of Pulmonology. 2019;21(3):182.
- 24. Yousef YA, Manal MA. The relationship between level of the red cell distribution width and the outcomes of patients who acquired pneumonia from community. Egyptian Journal of Bronchology. 2019 Dec;13(5):738–42.
- 25. Ren Q, Liu H, Wang Y, Dai D, Tian Z, Jiao G, et al. The Role of Red Blood Cell Distribution Width in the Severity and Prognosis of Community-Acquired Pneumonia. Can Respir J. 2021;2021.
- 26. Karadag-Oncel E, Ozsurekci Y, Kara A, Karahan S, Cengiz AB, Ceyhan M. The value of mean platelet volume in the determination of community acquired pneumonia in children. Ital J Pediatr. 2013;39.
- 27. Braun E, Kheir J, Mashiach T, Naffaa M, Azzam ZS. Is elevated Red cell distribution width a prognostic predictor in adult patients with community acquired Pneumonia? BMC Infect Dis. 2014 Mar 5;14(1).