ejpmr, 2024, 11(8), 245-254

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

RED BLOOD CELL DISTRIBUTION WIDTH (RDW) AS A PROGNOSTIC FACTOR IN PATIENTSWITH COMMUNITY-ACQUIRED PNEUMONIA IN DAMASCUS HOSPITAL

Rafah Jumaa[1]*, Asmaa Alashkar[2] and PhD. Hussam Al-Bardan[3]

[1,2]Faculty of Medicine, Syrian Private University.
Damascus University.

***Corresponding Author: Rafah Jumaa**

Faculty of Medicine, Syrian Private University.

Article Received on 04/06/2024 **Article Revised on 25/06/2024** **Article Accepted on 15/07/2024**

ABSTRACT

Background: Pneumonia is a common acute respiratory infection that affects the alveoli and distal airways; it isa major health problem and associated with high morbidity and short-term and long-term mortalityin all age groups worldwide. Pneumonia is broadly divided into community-acquired pneumonia or hospital-acquired pneumonia.[1] Community-acquired pneumonia (CAP) is a global disease responsible for a large proportion of deaths and having significant economic cost.[2] Streptococcus Pneumoniae remains the most common cause of CAP across all severities. Mycoplasma pneumonia, Haemophilus Influenzae, and Chlamydophila Pneumoniae are associated with mild-to-moderate CAP and Staphylococcus aureus, Legionella species, and gram- negative pathogens, including Klebsiella Pneumoniae and Pseudomonas aeruginosa, are more likely to be associated with severe CAP.[3] However, Viruses can also infect the low respiratorytract and cause pneumonia. The most common viral pathogens are influenza A and B; parainfluenza 1, 2 and 3; respiratory syncytial virus; or adenovirus.[4] Red cell distribution width(RDW) is associated with mortality in patients with community-acquired pneumonia (CAP). Although The relationship between morbidity, mortality and RDW value is weak. The objective of this study was to evaluate the association between RDW changes and mortality in hospitalized patients with CAP.[5] **Methods:** Retrospective analyses were performed using medical records of patients hospitalized for CAPfrom April 2019 to June 2024 in Damascus hospital in Damascus, Syria. The abstracted values included Age, Gender, Length of stay in hospital, ICU admission, Length of stay in ICU, Need for mechanical ventilation, Mortality. RDW was measured using an automated hematology analyzer. **Results:** A total of 122 patients were included. The results show that there was no significant difference in the distribution of RDW values between males and females (P=0.38). Also, there was no statistically significant relationship between age and RDW values (P=0.09). Patients with higher RDW values (14-15) were more likely to need ICU admission (53.3%, P =0.011) and mechanical ventilation (46.7%, P =0.019) compared to those with low RDW values but still RDW is not a reliable predictor of ICU admission and mechanical ventilation. Length of hospitalization was significantly associated with higher levels of RDW value (P = 0.02). There was no significant difference in Length of stay in the ICU (P = 0.67) and mortality rates (P = 0.16) between the different RDW value groups. **Conclusion:** Higher RDW value is associated with some of the more severe clinical outcomes, such as increased ICU admission and need for mechanical ventilation, in this sample of patients withpneumonia but its not a reliable predictor.

KEYWORDS: Red blood cells distribution width, Community-acquired pneumonia, RDW as a prognostic factor, ICU admission, Mechanical ventilation.

INTRODUCTION

Community-acquired pneumonia (CAP) is the most leading cause of death among infectious diseases and an important health problem.[6] Predicting the prognosis of patients with pneumonia is essential for the optimal treatment.[7] Traditional pneumonia severity indicators recommended by guidelines such as CURB-65 (Confusion, Urea, Respiratory rate, Blood pressure, Age ≥65), pneumonia severity index (PSI), and A-DROP (Age, Dehydration, Respiratory failure, Orientation disturbance, blood Pressure)[8] have been reported to be less useful in some populations.[7]

However, these biomarkers are somewhat expensive to obtain and are not always available immediately.[9] For this reason, there is orientation to find new prognostic factors to raise the level of these scales Red cell distribution width (RDW) is a measurement of the variability of red cell sizes and it increases in response to inflammatory stimulation or poor nutritional status,[10]

that is routinely reported as part of a complete blood count.

Many researchers have studied RDW as a prognostic marker in various diseases such as septic shock, acute kidney injury, pulmonary hypertension, pulmonary embolism and community- acquired pneumonia[11] but still no mechanism for this correlation has been found.[12] However, it is thought that acute hypoxia causes a significant increase in serum erythropoietin levels, thus, being able to induce the formation of enlarged erythrocytes, which in turn causes anincrease in RDW.[13]

At the time of hospital admission, a CBC is routinely performed when pneumonia is suspected, and it is relatively beneficial and inexpensive, especially for a developing country like Syria.

This study was designed to evaluate the association of RDW with mortality and to determine the prognostic significance of RDW in patients with CAP. We hypothesized that RDW would be associated with mortality and morbidity and would exhibit prognostic significance in patients with CAP.

METHODS

Study design and setting

Retrospective study: A retrospective study was conducted

- Hospital consent was obtained to access patient data and samples were collected from patient records in Internal Thoracic Department of the hospital.
- The questionnaire was created electronically and automatedly via Google Form, and The data was archived using Microsoft Excel 2019
- The study included 122 patients with a previous admission to the internal thoracic department with a diagnosis of pneumonia.
- The RDW was evaluated as an indicator of poor prognosis in pneumonia patients, by evaluating the relationship with and its prediction of the following variables.

(1) The need for admission to the intensive care unit, (2) the need for mechanical ventilation,(3)Duration of stay in the hospital, (4) Duration of stay in the intensive care unit, (5) Occurrence of death.

Exclusion Criteria

- Archiving mistakes.
- Cases having loss of data in a way that makes it unable to include in the study.

Ethical consideration

The study protocol was approved by the Research Ethics Committee at the Syrian Private University.

Statistical Analysis

Patient data were tabulated and entered into the computer, and then the Statistical Package for Science program SPSS version[16] was used in analyzing this data, the following statistical methods were relied upon.

1) Descriptive statistics: It consists of finding the relative frequency distributions of categorical study variables.

2) Analytical (inferential) statistics: This part of the analysis aims to present and interpret the results and infer them in order to reach the goal of the study, by conducting the Chi Square (independence test) to study whether a relationship exists between two descriptive variables by applying the Chi Square statistic. The estimation of statistical differences and relationships was based on a level of statistical significance of 0.05, which is the level approved in studies, and therefore the statistical decision can be given through the P-value as follows: If the statistical significance value of the P-Value is greater than 0.05, then there are no fundamental differences in evaluating Differences and relationships. However, if the statistical significance value is smaller than 0.05, there are significant statistical differences in evaluating the differences and relationships.

3) Receiver Operating Characteristic curve (ROC) and Area Under the Curve (AUC) analysis were used to evaluate the ability of RDW to predict outcome. ROC describes the relationship between the true positive rate (correct prediction of a positive result) and the false positive rate (false prediction of a positive result). The AUC value, which represents the area under the ROC curve, was also calculated. A higher AUC value indicates a better ability of the model to distinguish between positive and negative groups. An AUC value of 0.5 indicates no predictability, while a value of 1.0 indicates perfect prediction.

RESULT

Part One: Descriptive analysis of the variables

Males made up the majority of the patients (60.7%), with youngsters accounting for the greatest age group (47.5 percent). The majority of patients (80.3%) were community-acquired pneumonia; 25.4% were hospitalised to the critical care unit, and 23% required ventilatory therapy. In terms of hospital stay, 27% of patients spent 5 to 8 days, while 23% spent more than13 days. In the intensive care unit, 32.3% of patients spent between two and five days. Finally, the death rate for these individuals reached 18% (Table 1). (Figures 1-9).

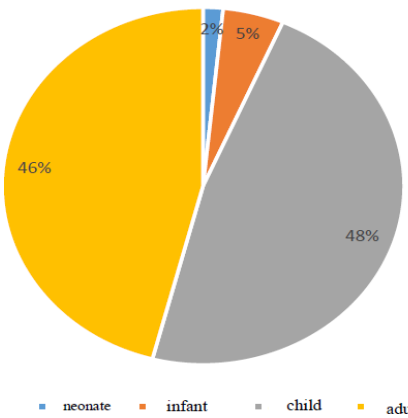


Figure 1: Gender Distribution of Sample.

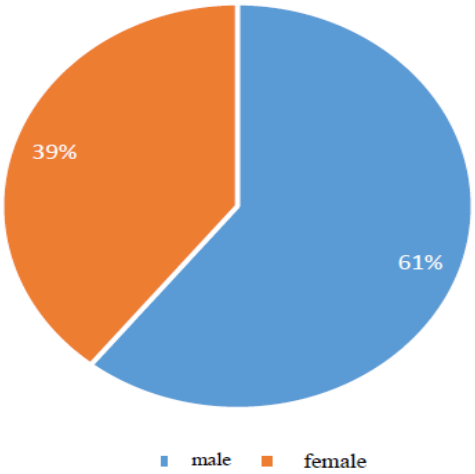


Figure 2: Age Distribution of Sample.

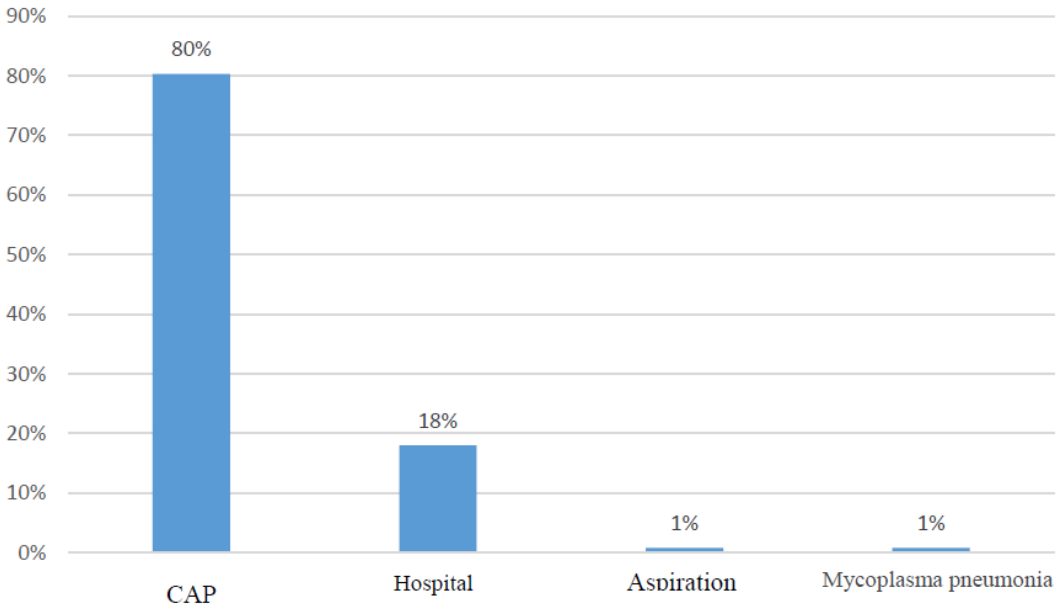


Figure 3: Distribution of the sample based on the type of pneumonia.

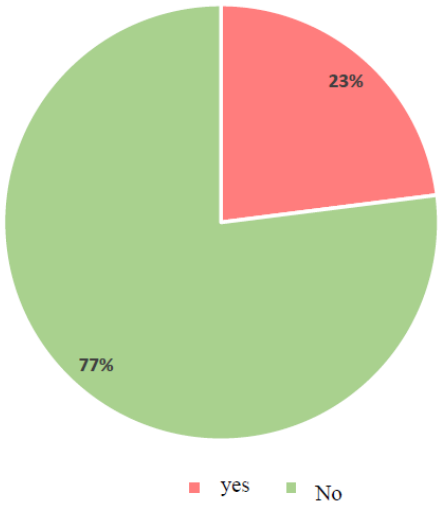


Figure 4: Sample distribution regarding the need for mechanical ventilation.

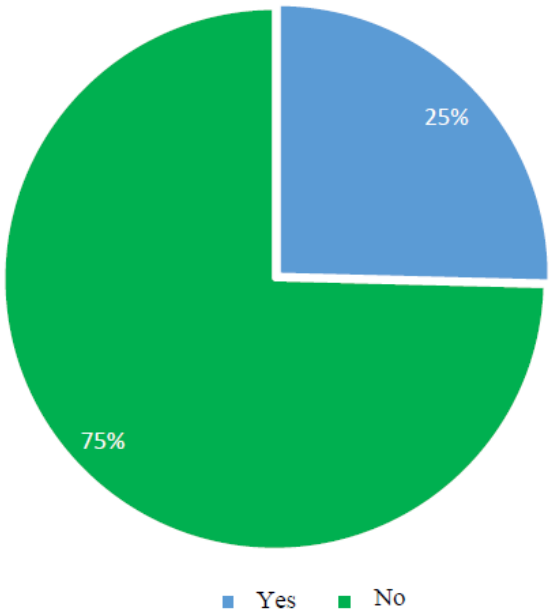


Figure 5: Sample distribution In terms of the need for admission to the intensive care unit.

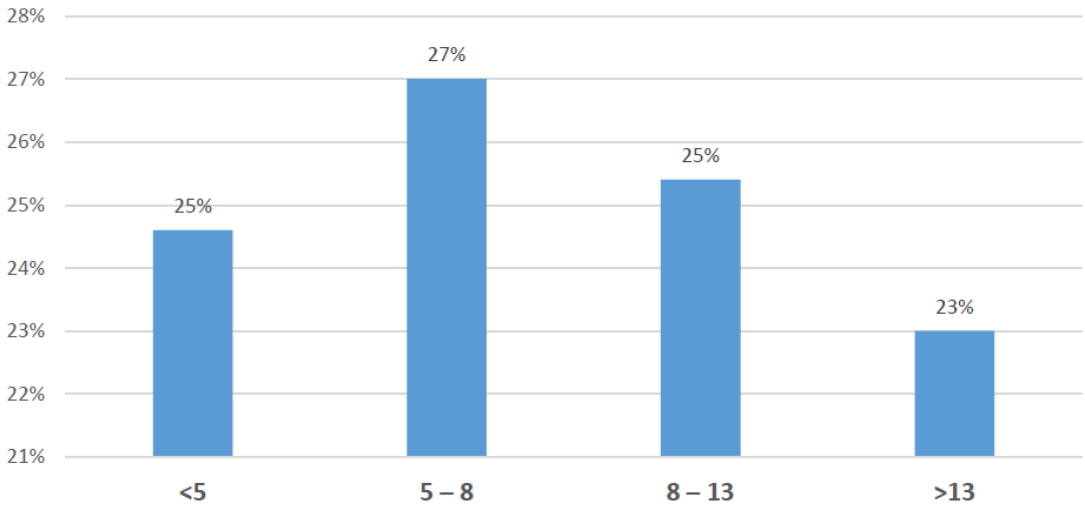


Figure 6: Sample distribution in terms of length of stay in the hospital.

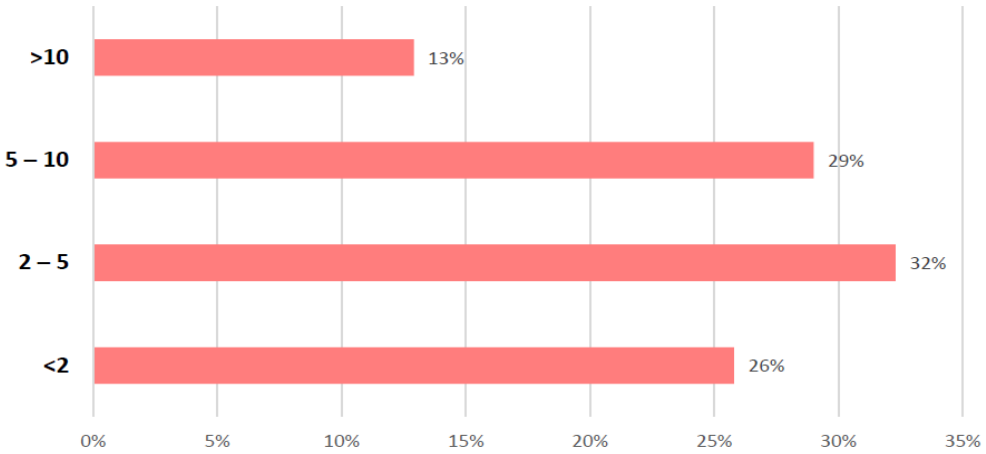


Figure 7: Sample distribution in terms of length ofstay in intensive care.

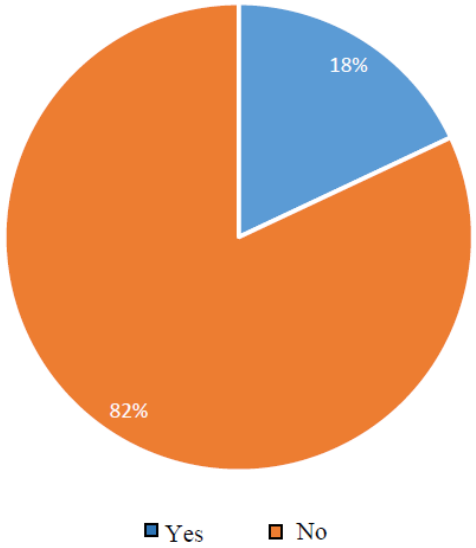


Figure 8: Death rate.

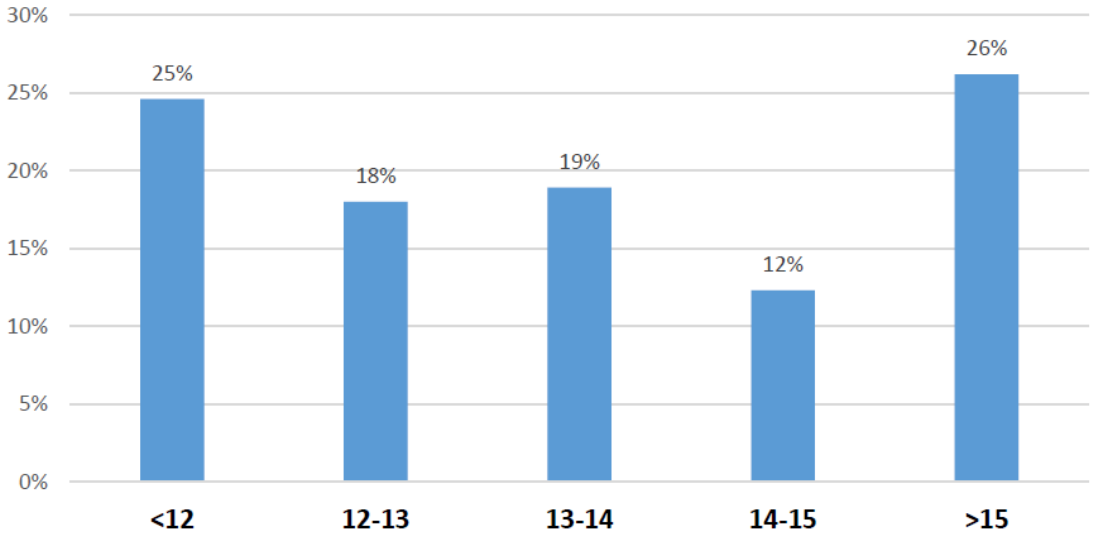


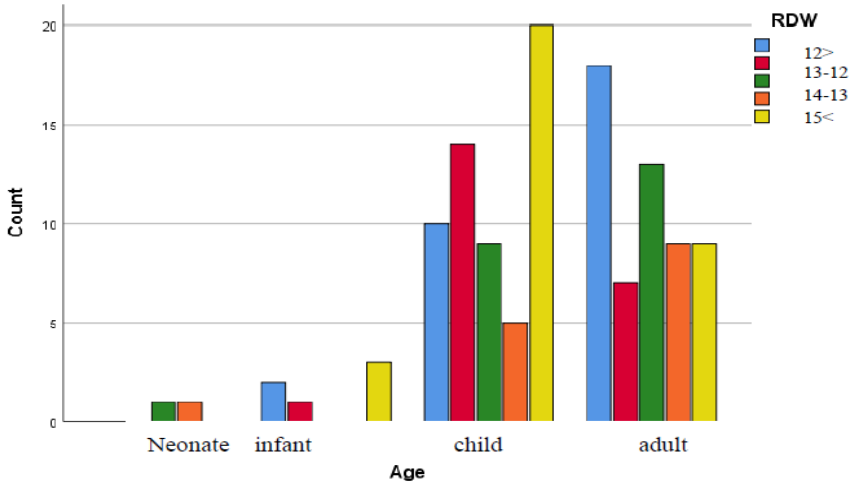
Figure 9: Sample distribution in terms of RDW levels.

Patients characteristics (N=122): n(%)		
Sex	Men	74 (60.7)
	Female	48 (39.3)
Age	Newborn	2 (1.6)
	Infant	6 (4.9)
	Child	58 (47.5)
	Adult	56 (45.9)
Type of Pneumonia	Community- acquired pneumonia	98 (80.3)
	Hospital acquired pneumonia	22 (18)
	Aspiration pneumonia	1 (0.8)
	Tuberculous pneumonia	1 (0.8)
The need for ICUhospitalization	Yes	31 (25.4)
	No	91 (74.6)
The need for Ventilation	Yes	28 (23)
	No	94 (77)
Length of hospital stay	Less than 5 days	30 (24.6)
	days 8 - 5	33 (27)
	days 13 - 8	31 (25.4)
	More than 13 days	28 (23)

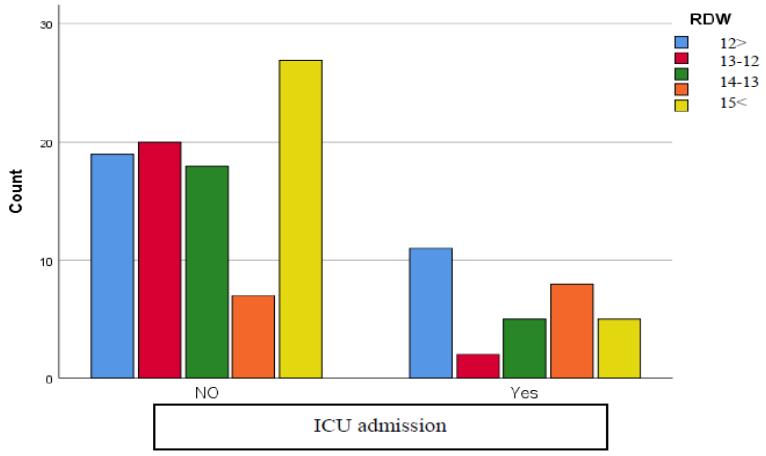
Length of ICU stay (N=31)	Less than 2 days	8 (25.8)
	5-2	10 (32.3)
	10-5	9 (29)
	More than 10 days	4 (12.9)
Death	Yes	22 (18)
	No	100 (82)
Patients characteristics (N=122): n(%)		
RDW Value	Less than 12	30 (24.6)
	13-12	22 (18)
	14-13	23 (18.9)
	15-14	15 (12.3)
	More than 15	32 (26.2)

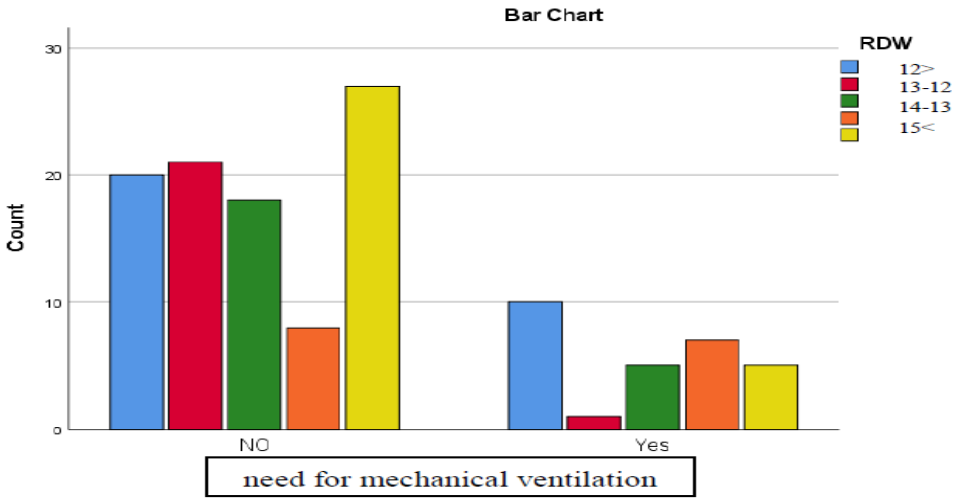
Part Two: Semantic analysis of the study variables.
Firstly: This study investigated the relationship between patient factors and RDW values, and the findings were as follows

- **Age:** There was no statistically significant relationship between age and RDW values (P=0.09). Despite this, a higher proportion of children (39.1%) had RDW values between 13-14, while a greater proportion of adults (60%) had RDW values less than 12 (Figure 10).



- **Sex:** There was no significant difference in the distribution of RDW values between males and females (P=0.38).
- **Pneumonia type:** The majority of patients (80.3%) had community-acquired pneumonia, and the pneumonia type was not significantly associated with RDW values (P=0.36).
- **ICU admission and need for mechanical ventilation:** Patients with higher RDW values (14-15) were more likely to need ICU admission (53.3%, P =0.011) and mechanical ventilation (46.7%, P =0.019) compared to those with low RDW values.





- **Length of hospital stay:** Length of hospitalization was significantly associated with higher levels of RDW value (P = 0.02), with patients whom RDW values were between 12-13 and 13-14 tending to have a longer hospital stay ((56.5%) and (33.3%) They had a longer stay (5-8days in a row).
- **Length of stay in the ICU:** was not associated with the RDW value (P = 0.67).
- **Mortality:** There was no significant difference in mortality rates between the different RDW value groups (P = 0.16).

Overall, the results suggest that higher RDW values were associated with some of the more severe clinical outcomes, such as increased ICU admission and need for mechanical ventilation, in this sample of patients with pneumonia (Table 2).

Table 2: Relationship between patients' characteristics and RDW values (N=122): n(%)

Variables		RDW Values					Totals	P-value
		Less than 12	12-13	13-14	14-15	More than 15		
Age	Newborn	0	0	1 (4.3)	1 (6.7)	0	2 (1.6)	0.09
	Infant	2 (6.7)	1 (4.5)	0	0	3 (9.4)	6 (4.9	
	Child	10 (33.3)	14 (63.6)	9 (39.1)	5 (33.3)	20 (62.5)	58 (47.5)	
	Adult	18 (60)	7 (31.8)	13 (56.5)	9 (60)	9 (28.1)	56 (45.9)	
Sex	Men	21 (70)	11 (50)	16 (69.6)	7 (46.7)	19 (59.4)	74 (60.7)	0.38
	Female	9 (30)	11 (50)	7 (30.4)	8 (53.3)	13 (40.6)	48 (39.3)	
Type of Pneumonia	Community-acquired	23 (76.7)	20 (90.9)	17 (73.9)	13 (86.7)	25 (78.1)	98 (80.3)	0.36
	Hospital acquired	7 (23.3)	2 (9.1)	6 (26.1)	2 (13.3)	5 (15.6)	22 (18)	
	Others	0	0	0	0	2 (6.3)	2 (1.6)	
ICU Hospitalization	Yes	11 (36.7)	2 (9.1)	5 (21.7)	8 (53.3)	5 (15.6)	31 (25.4)	**0.011***
	No	19 (63.3)	20 (90.9)	18 (78.3)	7 (46.7)	27 (84.4)	91 (74.6)	
	Yes	10 (33.3)	1 (4.5)	5 (21.7)	7 (46.7)	5 (15.6)	28 (23)	**0.019***
Ventilation required	No	20 (66.7)	21(95.5)	18(78.3)	8 (53.3)	27(84.4)	94 (77)	
Length of hospital stay	Less than 5	10 (33.3)	7 (31.8)	4 (17.4)	5 (33.3)	4 (12.5)	30(24.6)	**0.02***
	8 – 5	8 (26.7)	5 (22.7)	13(56.5)	0	7 (21.9)	23 (27)	
	13 – 8	6 (20)	5 (22.7)	2 (8.7)	5 (33.3)	13(40.6)	31(25.4)	
	More than 13	6 (20)	5 (22.7)	4 (17.4)	5 (33.3)	8 (25)	28 (23)	
Length of ICU stay (N=31)	Less than 2days	1 (9.1)	0	2 (40)	3 (37.5)	2 (40)	8 (25.8)	0.67
	5-2	5 (45.5)	1 (50)	2 (40)	1 (12.5)	1 (20)	10 (32.3)	
	10-5	4 (36.4)	1 (50)	0	2 (25)	2 (40)	9 (29)	
	More thandays 10	1 (9.1)	0	1 (20)	2 (25)	0	4 (12.9)	
Mortality	Yes	7 (23.3)	1 (4.5)	5 (21.7)	5 (33.3)	4 (12.5)	22 (18)	0.16
	No	23 (76.7)	21 (95.5)	18 (78.3)	10 (66.7)	28 (87.5)	100 (82)	

*significant p- value (P<0.05)

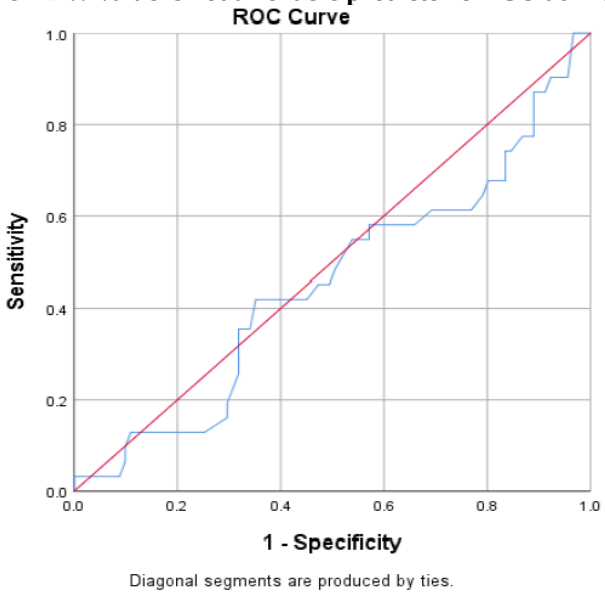
Secondly: Evaluating the ability of RDW to predict pneumoniaoutcomes.

A. Evaluating the ability of the RDW value to predict the need for admission to the ICU.

Area Under the Curve				
Test Result Variable(s): RDW				
Area	Std. Error	Sig.	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.453	.062	.434	.332	.574

The AUC value of 0.453 suggests that the RDW performs poorly in distinguishing between the positive (ICU admission) and negative groups. The P value of 0.434 is far higher than the conventional significance level of 0.05, indicating that this finding is not statistically significant. This suggests there's is no significant association between RDW and ICU admission. The 95% confidence range for the area under the curve is relatively large, ranging from 0.332 to 0.574, indicating that the RDW has poor predictive power for ICU admissions.

These findings indicatethat the RDW value is not a reliable predictor of ICU admission.



B. Evaluating the ability of RDW to predict the need for mechanical ventilation.

Area Under the Curve				
Test Result Variable(s): RDW				
Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
			LowerBound	UpperBound
.468	.064	.605	.342	.593

The area under the curve (AUC) is 0.468, while the standard error is 0.064. This AUC result demonstrates that RDW discriminates poorly between groups that require mechanical ventilationand those that do not.

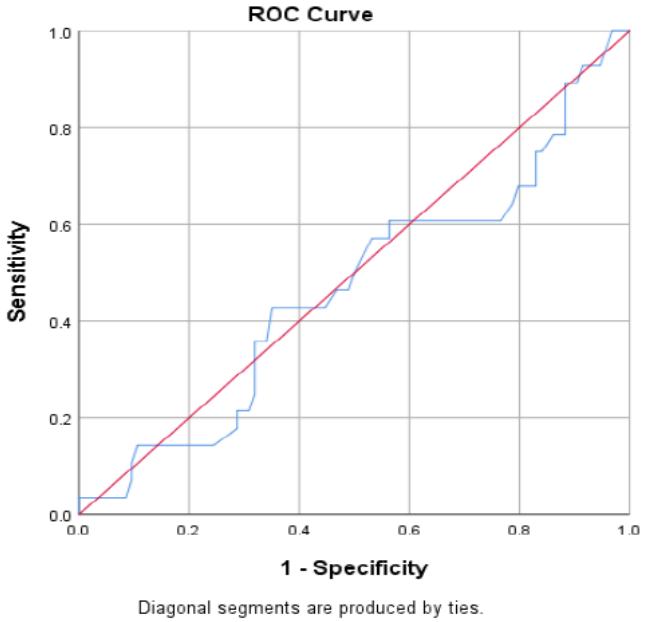
The asymptotic significance (P-value) is 0.605, well beyond the normal significance threshold of 0.05. This signifies that the result isn't statistically significant, implying that there is no valuable relationship between RDW and the need for mechanical ventilation. The 95% confidence rangefor the area under the curve is relatively large, ranging from 0.342 to 0.593, indicating the RDW's poor forecasting performance for mechanical ventilation requirements.

Overall, these findings show that the RDW value is not a reliable predictor of the requirement for mechanical ventilation.

C. Evaluating the ability of RDW to predict death in patients with pneumonia.

Area Under the Curve				
Test Result Variable(s): RDW				
Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.473	.067	.692	.341	.605

The area under the curve (AUC) for the test variable "RDW value" is 0.473, with a standard error of 0.067. The asymptotic significance (p-value) is 0.692, which is not statistically significant at the typical level of 0.05. The 95% confidence interval for the AUC ranges from 0.341 to 0.605. Interpretation of these results leads to the conclusion that the RDW value is not a reliable marker for predicting mortality.



DISCUSSION

The results of this study show that some poor clinical outcomes of pneumonia are associated with higher RDW values, specifically those exceeding 13%. Despite this, these high values were more associated with secondary outcomes such as longer hospital stays and the need for ICU admission rather than primary outcomes like mortality. Few studies have examined RDW valuesas an indicator of poor prognosis in this patient group.

Previous studies have indicated that RDW can be an important predictor of mortality among populations aged 45 and older; outpatients with cardiovascular diseases, cancer, or chronic lowerrespiratory diseases; and in heart failure groups. Additionally, among critically ill patients, RDWhas also been significantly associated with the risk of death and sepsis.[14,15] A 2012 study in Korea reported that higher RDW values were associated with 30-day mortality rates in patients with community-acquired pneumonia (CAP), with this effect being more pronounced at RDW values above 15%.[9] Other previous studies have also reported an association between high RDW values and mortality, especially among non-elderly adult patients.[9]

In our study, various proportions of patients with high RDW values experienced death, with a non-statistically significant relationship. This result can be explained by the small sample size, as well as the non-normally distributed age groups among children, younger age groups, and older adults. Additionally, the time between hospital admission and death could not be determined.

This study showed a significant relationship between RDW values and the length of hospital stay, consistent with the previous study in 2011.[9] Previous studies suggested that inflammation and oxidative stress affect RDW. A previous study showed that RDW had a strong, graded association with inflammatory markers in outpatient groups.[16] Pneumonia is an infectious disease that leads to inflammatory and oxidative stress on the host. If these stresses are severe, the mortality rate will increase. This could explain the association between RDW and other poor pneumonia outcomes in this study, such as the need for mechanical ventilation and ICU admission, as these are results of severe disease conditions. However, when RDW values were evaluated as a predictor for these outcomes (and even for death), the analysis showed no statistically significant results, and higher RDW values were not significant in predicting theseoutcomes (AUC value > 0.5).

On the other hand, scales that assess pneumonia severity, including PSI and CURB-65, have proven useful in identifying low and high risk of death among patients with community-acquired pneumonia (CAP). However, PSI was created from hospitalized CAP patients to identify low- risk patients who can be safely treated as outpatients, while CURB-65 was designed to identify patients at high risk of death. Therefore, the predictive capabilities of PSI and CURB-65 alone may be limited. Several studies have reported that adding biomarkers can improve the performance of these severity scales. In the 2011 Korean study, mortality prediction was improved for both PSI and CURB-65 by adding RDW as a severity criterion.[9] Most previous studies recommend that for

patients presenting to the emergency department with CAP, a CBC test, which is relatively inexpensive and commonly reported as part of a CBC, should almost universally be performed. Thus, RDW can be used as a biomarker in predicting outcomes in patients with CAP without incurring additional costs.[9]

Additionally, in a 2018 prospective cohort study conducted on pediatric pneumonia patients, it was found that adding RDW improved the sensitivity and specificity of the severity score, along with other biomarkers like CRP.[11] One of the main limitations of this study is considering RDW as the sole predictor of poor prognosis in this patient group. However, our results highlight the insignificance of relying solely on RDW laboratory values for prognostic evaluation.

CONCLUSION

Higher RDW value is associated with some of the more severe clinical outcomes, such as increased ICU admission and need for mechanical ventilation, in this sample of patients with pneumonia but its not a reliable predictor.

ACKNOWLEDGMENTS: Not applicable.

REFERENCES

1. Torres, A., Cilloniz, C., Niederman, M.S. et al. Pneumonia. Nat Rev Dis Primers, 2021; 7: 25.
2. Waterer, Grant W. "Community-acquired pneumonia: a global perspective." Seminars in respiratory and critical care medicine. Vol. 37. No. 06. Thieme Medical Publishers, 2016.
3. File, Thomas M. "The science of selecting antimicrobials for community-acquired pneumonia (CAP)." Journal of Managed Care Pharmacy 15.2 Supp A., 2009; 5-11.
4. Figueiredo, Luiz Tadeu Moraes. "Viral pneumonia: epidemiological, clinical, pathophysiological and therapeutic aspects." Jornal Brasileiro de Pneumologia, 2009; 35: 899-906.
5. Lee, S. M., Lee, J. H., Kim, K., Jo, Y. H., Lee, J., Kim, J., & Park, H. (2016). The clinical significance of changes in red blood cell distribution width in patients with community-acquired pneumonia. Clinical and Experimental Emergency Medicine, 3(3): 139.
6. Ferreira-Coimbra, Joao, Cristina Sarda, and Jordi Rello. "Burden of community-acquired pneumonia and unmet clinical needs." Advances in therapy, 2020; 37.4: 1302-1318.
7. Yoshimatsu, Yuki, et al. "Prognostic factors of poor outcomes in pneumonia in older adults: aspiration or frailty?." European Geriatric Medicine, 2024’; 1-8.
8. Shindo, Yuichiro, et al. "Comparison of severity scoring systems A-DROP and CURB-65 for community-acquired pneumonia." Respirology, 2008; 13.5: 731-735.
9. Lee JH, Chung HJ, Kim K, Jo YH, Rhee JE, Kim YJ, Kang KW. Red cell distribution width as a prognostic marker in patients with community-acquired pneumonia. Am J Emerg Med, 2013 Jan; 31(1): 72-9. doi: 10.1016/j.ajem.2012.06.004. Epub 2012 Aug 3. PMID: 22867824.
10. Zhang, Zhongheng, et al. "Red cell distribution width is associated with hospital mortality in unselected critically ill patients." Journal of thoracic disease, 2013; 5.6: 730.
11. Moustafa, Asmaa N., Hend M. Moness, and Marwa Waly Eldin Ali. "Red cell distribution width as a prognostic marker for complications of community-acquired pneumonia in children: a comparison with Proadrenomedullin and Copeptin." BMC Pulmonary Medicine, 2023; 23.1: 371.
12. Dugdale, Alan E., and Tony Badrick. "Red blood cell distribution width (RDW)—a mechanism for normal variation and changes in pathological states." Journal of Laboratory and Precision Medicine, 2018; 3.
13. Eraslan, Berrin Z., et al. "The importance of the erythrocyte distribution width/albumin ratio in patients with chronic obstructive pulmonary disease exacerbation." Saudi Medical Journal, 2024; 45.1: 27.
14. Perlstein TS, Weuve J, Pfeffer MA, et al. Red blood cell distribution width and mortality risk in a community-based prospective cohort. Arch Intern Med, 2009; 169(6): 588-94.
15. Bazick HS, Chang D, Mahadevappa K, et al. Red cell distribution width and all-cause mortality in critically ill patients. Crit Care Med, 2011; 39(8): 1913-21.
16. Lippi G, Targher G, Montagnana M, et al. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Arch Pathol Lab Med, 2009; 133(4): 628-32.
17.