Archives of Anesthesiology and Critical Care (Autumn 2023); 9(Supplement 2): 474-478.

Available online at http://aacc.tums.ac.ir

Research Article

Investigating the Relationship between Red Cell Width Distribution (RDW) and Outcome in Ventilator-Associated Pneumonia: A Prospective Cross-Sectional Study

Shervin Ramezani[1], Hesam Aldin Varpaei[2], Mostafa Mohammadi[3]*, Hamid Rahmani[4], Masoud Ramezani[3]

[1]Department of Anesthesiology, Tehran University of Medical Sciences, Tehran, Iran.

[2]College of Nursing, Michigan State University, East Lansing, USA.

[3]Department of Critical Care, Tehran University of Medical Sciences, Tehran, Iran.

[4]Department of Pharmacology, Tehran University of Medical Sciences, Tehran, Iran.

ARTICLE INFO

Article history:
Received 15 November 2022
Revised 06 December 2022
Accepted 21 December 2022

Keywords:
Ventilator associated pneumonia;
Red cell distribution width;
Mortality;
Intensive care unit;
Critical care;
Mechanical ventilation

ABSTRACT

Background: Ventilator-associated pneumonia (VAP) is a consequence of mechanical ventilation, which can be fatal. Several markers are available to predict outcomes related to VAP. Choosing a predictor that is inexpensive, affordable, and accurate is advantageous. This study aimed to examine red cell distribution width (RDW) as a predictor of mortality in patients with VAP.

Methods: This prospective cohort study was conducted among 49 patients in the intensive care unit (ICU) of Valiasr Hospital in Tehran. A researcher-made checklist was used to collect RDW and other marker data, as well as mortality outcomes and length of stay (LOS) in the ICU. The Pearson correlation coefficient in the SPSS software and the regression model in the Eviews software were used to examine the relationship between markers and different outcomes.

Results: Of a total of 49 patients (57.1% male; mean age = 54 ± 16), the length of ICU stays ranged from 7 to 14 days. According to the Pearson correlation coefficient, a significant association between RDW and mortality (P =.009) was noted. But no significant relationship between RDW and length of stay in the ICU (P =.81) was noted. Additionally, the regression model showed a positive relationship between RDW and white blood cells (WBC), lactate, and sequential organ failure assessment (SOFA).

Conclusion: Our study showed a positive but weak correlation between RDW and ICU mortality in patients with VAP. Due to its availability and low cost of measurement, RDW is an appropriate option for predicting mortality risk in patients who are admitted to the ICU and develop VAP.

Introduction

Nosocomial infections are one of the most important issues in medical centers. Acquired nosocomial infections are the most common complication among hospitalized patients. Although critical care settings (or ICUs) account for just around 5–15% of hospital beds, they are responsible for more than 30% of nosocomial infections [1].

Hospital-acquired pneumonia (HAP) accounts for 30% of all nosocomial infections. This pneumonia is the second most common nosocomial infection after urinary

The authors declare no conflicts of interest.

*Corresponding author.
E-mail address: mohammady_mm@tums.ac.ir

tract infection [3]. Now, the terms of HAP are revoluted and called health care-associated pneumonia (HCAP) [16]. Ventilator-associated pneumonia (VAP) is a subset of nosocomial pneumonia that develops 48 hours or more after intubation and connection to a mechanical ventilator [2]. In the United States, VAP is the second most prevalent source of infection in the ICU. More than 24 hours of intubation is associated with a 6-to-21-fold increase in the likelihood of VAP development [4]. The pooled incidence of VAP is high in low- and upper-middle-income countries but low in high-income countries (18.5, 15.2, and 9.0 per 1000 ventilator days, respectively) [5]. Most common causative pathogen of VAP are Acinetobacter baumannii, Pseudomonas aeruginosa, and methicillin-resistant Staphylococcus aureus (MRSA) [6]. VAP is a major challenge in the treatment sector from the past to the present, with many fatal consequences. Therefore, predicting the outcome of mortality due to VAP can be very effective [7].

Red Cell Distribution Width is a quantitative index of anisocytosis, the variability in size of the circulating erythrocytes [9] and it seems to be one of these predictors. Today, information on the mortality of chronic diseases shows that RDW is a predictor of disease progression and response to treatment [8]. Although mechanisms have not been identified clearly, RDW is an emerging marker of chronic inflammation, oxidative stress, and coronary artery disease [10-11]. Recent evidence suggests that increase changes in red blood cell size in cardiovascular disease, thromboembolism, diabetes, cancer, obstructive pulmonary disease, liver, and kidney disease are strong and independent risk factors for predicting mortality [12-15].

Therefore, due to the high power of RDW, as a marker in predicting various clinical outcomes, it can use as a key tool in the treatment of patients who diagnosed with VAP. Recently some studies were performed to investigate relationship between biomarkers such as RDW and prognosis of VAP but there is no domestic study has been studied the, this study examined this issue.

Methods

Study design

This study was a prospective cohort study conducted to evaluate the relationship between RDW with mortality outcomes and other inflammatory markers. Ethical approval of this study was obtained from the local ethics committee (ethic code = IR.TUMS.IKHC.REC.1397.242).

Data collection

A researcher-made checklist was used to gather data. RDW, Sequential Organ Failure Assessment (SOFA), and white blood cell (WBC) daily data were measured and entered into the checklist. APACHE score was measured only at the beginning of admission to the ICU. Lactate and C-reactive protein (CRP) were measured at the beginning of the study and then every 72 hours. Also, the checklist included demographic information as well as mortality data and LOS.

Patient selection

Patients who were admitted to the ICU during the study period were screened for eligibility. Patients aged 18 to 65 years old with diagnosis of VAP (clinical pulmonary infection score> 6) were included. Exclusion criteria of the study included the following: patients with active malignancy and patients receiving immunosuppressive drugs and corticosteroids. Informed consent forms were taken from the patients or their caregivers.

Statistical analysis

Descriptive statistics are presented as frequency (percentage) for categorical variables whereas.

Continuous data are presented as mean ± standard deviation for normally distributed data. Statistical Package for the Social Sciences (SPSS) 26.0 (SPSS Inc., Chicago, IL) was used for statistical analysis and $p<0.05$ considered as statistically significant.

Association between RDW and mortality and LOS were assessed with Pearson correlation coefficient.

Also, regression model in Eviews software was used to analysis the relationship between RDW with WBC, SOFA score, and Lactate variables.

Results

Of a total of 49 enrolled patients (n = 29, 57.1% male; mean age = 54±16 years), the average LOS in the ICU was approximately 11 days, with a minimum of 7 days and a maximum of 14 days. Also, 10.2% (n= 5) of the patients died and 89.8% (n= 44) were discharged from the ICU. The Baseline characteristics, laboratory data and outcomes of the patients are shown in (Table 1).

Results of Pearson coefficient showed that there was a positive correlation between RDW and mortality and LOS ($\boldsymbol{\lambda}$= 0.07 and 0.049, respectively). However, only the relationship between RDW and mortality was significant (P=0.009). Results of Pearson coefficient are shown in (Table 2).

Results of regression model showed that there was a positive correlation between RDW and WBC, Lactate, and SOFA (β=0.06, 0.008, 0.006 respectively). However, all the relationship between RDW and variables were not significant (P-value>0.05). Results of regression model are shown in (Table 3).

Table 1- Baseline characteristics, laboratory data and outcomes of the patients

Demographic	(mean ± SD)
Age (year)	54 ±16
Gender, n (%)	Male: 28 (57.1)
	Female: 21(42.9)
Laboratory data	(mean ± SD)
White Blood Cell (cells /μl)	13900 ± 7355
Polymorhphonuclear cells (%)	84 ± 9
Absolute Lymphocyte count (%)	10 ± 6
Red cell distribution width (femtoliter)	17 ± 3
C-reactive protein(mg/dl)	76 ± 55
Lactate (mg/dl)	17 ± 9
APACHE	16 ±5
SOFA	6 ± 2
Outcomes	
Length of stay (days) (mean ± SD)	11 ±5
Mortality in ICU, n (%)	5 (10.2)

Table 2- Results of Pearson coefficient

	RDW	
	λ	**P value**
Mortality	0.07	0.009
LOS	0.049	0.81

Table 3- Results of regression model

	RDW	
	Coefficient (β)	**P value**
WBC	0.06	0.3
Lactate	0.008	0.9
SOFA	0.006	0.1

Discussion

The present study examined red cell distribution width (RDW) as a predictor of mortality in patients with VAP. Current study showed that RDW has a positive correlation with mortality, so it can used as a value to prediction of mortality. In other words, greater RDW was shown to be related with an increased risk of hospital death. Several studies have shown that RDW is independently related with a variety of negative outcomes [6, 16-18], and the findings of our study showed that RDW was an independent predictor of death in VAP patients admitted to the ICU. Patel et al demonstrated that the risk of all-cause mortality increases by 14% for every 1% increase in RDW. Also, they showed that a strong association between RDW and death from cancer and cardiovascular diseases [6]. Bazick et al. [18] investigated the relationship between RDW and all-cause death in 51413 ICU patients. The relationship between RDW and bloodstream infections was also investigated. The risk of 30-day death in individuals with RDW greater than 15.8% was about 5 times higher than in those with RDW less than 13.3%. This value was 2.61 after adjusting for confounding factors [18]. In our study, there is no statistical difference between survivors and non-survivors in terms of RDW. The risk of blood stream infection doubles in the patients with RDW > 15.8%. Of note, we did not assess the relationship between RDW and the risk of VAP development. RDW is a simple measure that has been shown to be an effective predictor of a variety of illnesses and mortality [19-20]. Regression results by Wang et al. revealed a positive and substantial association between RDW and mortality outcome, which is similar with the findings of the current study [21].

Additionally, Van Kimmenade et al. [22] found that after one year of monitoring patients with acute heart failure, the RDW might be used as a marker in predicting mortality outcomes. In other words, patients with a high RDW index died at a much greater rate [22].

It should be noted that the inflammatory response, which can be navigated by tracking different biomarkers such as RDW, plays a crucial role in the development of VAP [23]. This implies the importance of monitoring RDW for patients in critical care settings and/or patients who may experience inflammatory reactions.

Furthermore, our findings demonstrated a favorable connection between RDW and other parameters such SOFA, lactate, and WBC. Wang et al. found that RDW, together with SOFA and APACHE, might be greater predictors of mortality outcomes, despite the fact that RDW is less expensive and easier to use [24]. In the study

of Ju et al., by examining the two experimental and control groups, and by examining the daily relationship between SOFA and RDW, the results showed a positive and significant relationship between these two variables [25]. In a retrospective study, it was shown that initial RDW value could be used as an independent variable in the prediction of in-hospital mortality beyond corrected APACHE II score according to age, mechanical ventilator, sepsis, and hospital admission type in ICU patients [26]. In another study by Wang, RDW was an independent predictor of ICU-induced mortality and LOS in ICU patients [23] [27].

Our study had several limitations. The sample size of the study was small. Although, there was the positive correlation between RDW and mortality but it was a weak correlation. If a study with large sample size was designed, it may be found a strong correlation between two variables. Also, small sample size did not allow us to perform the survival analysis and predict the mortality risk according to RDW value. In our study, the period of follow-up was brief. It is preferable to follow critically ill patients beyond their ICU stay and at least during their hospitalization duration.

This was a single-centre study and limited to 49 patients, it is suggested to conduct another study with a large sample size to confirm the result of the study. Besides, this study aimed to investigate VAP in non-COVID-19 patients. Since the pathophysiology of COVID-19 [28] and COVID vaccination [29] is not clear, therefore a comparative study between VAP in COVID-19 and non-COVID-19 patients regarding RDW and mortality is suggested.

Conclusion

In conclusion, our study showed a positive but weak correlation between RDW and mortality in the ICU among patients with VAP. According to the routine check of RDW as an index in the complete blood count, its availability and low cost of measurement make it an appropriate option for predicting mortality risk in patients who are admitted to the ICU and develop VAP. Prospective and large-scale studies are required to find a strong association between RDW and mortality risk.

References

[1] Afkhamzadeh A, Lahoorpour F, Delpisheh A, Janmardi R. Incidence of ventilator- associated pneumonia (VAP) and bacterial resistance pattern in adult patients hospitalised at the intensive care unit of Besat Hospital in Sanandaj. SJKU. 2011; 16 (1):20-26.

[2] Nadi E, Nekoie B, Mobaien A, Moghimbeigi A, Nekoie A. Evaluation of the Etiology of Nosocomial Pneumonia in the ICUs of the Teaching Hospitals of Hamadan University of Medical Sciences. Avicenna J Clin Med. 2011; 18 (1):26-32.

[3] Chastre J, Fagon JY. Ventilator-associated pneumonia. Am J Respir Crit Care Med. 2002; 165(7):867-903.

[4] American Association of Critical-Care Nurses. AACN practice alert: ventilator-associated pneumonia. AACN Advanced Critical Care. 2005; 16(1):105-9.

[5] Ana Bonell, Ryan Azarrafiy, Vu Thi Lan Huong, Thanh Le Viet, Vu Dinh Phu, Vu Quoc Dat, et al. A Systematic Review and Meta-analysis of Ventilator-associated Pneumonia in Adults in Asia: An Analysis of National Income Level on Incidence and Etiology. Clinical Infectious Diseases. 2019; 68(3):511-518.

[6] Karakuzu Z, Iscimen R, Akalin H, Girgin NK, Kahveci F, Sinirtas M. Prognostic risk factors in ventilator-associated pneumonia. Med Sci Monit. 2018; 24:1321.

[7] Craven DE, Steger KA. Ventilator-associated bacterial pneumonia: challenges in diagnosis, treatment, and prevention. New Horiz. 1998 May; 6(2 Suppl):S30-45.(5 gha)

[8] Patel KV, Semba RD, Ferrucci L, Newman AB, Fried LP, Wallace RB, Bandinelli S, Phillips CS, Yu B, Connelly S, Shlipak MG, Chaves PH, Launer LJ, Ershler WB, Harris TB, Longo DL, Guralnik JM. Red cell distribution width and mortality in older adults: a meta-analysis. J Gerontol A Biol Sci Med Sci. 2010 Mar;65(3):258-65.

[9] McPherson RA, Pincus MR. Henry's clinical diagnosis and management by laboratory methods. 24th ed. Philadelphia, PA: Elsevier - Health Sciences Division; 2021.

[10] Allen LA, Felker GM, Mehra MR, Chiong JR, Dunlap SH, Ghali JK, Lenihan DJ, Oren RM, Wagoner LE, Schwartz TA, Adams KF Jr. Validation and potential mechanisms of red cell distribution width as a prognostic marker in heart failure. J Card Fail. 2010 Mar;16(3):230-8.

[11] Lippi G, Targher G, Montagnana M, Salvagno GL, Zoppini G, Guidi GC. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Arch Pathol Lab Med. 2009 Apr;133(4):628-32.

[12] Golafshan H, Hajizamani S, Khedmati ME. Clinical applications of RDW (Red Cells Distribution Width). Journal of Laboratory & Diagnosis. 2016;8(31):5-10.

[13] Förhécz Z, Gombos T, Borgulya G, Pozsonyi Z, Prohászka Z, Jánoskuti L. Red cell distribution width in heart failure: prediction of clinical events and relationship with markers of ineffective erythropoiesis, inflammation, renal function, and nutritional state. Am Heart J. 2009 Oct;158(4):659-66.

[14] Hu Z, Sun Y, Wang Q, Han Z, Huang Y, Liu X, Ding C, Hu C, Qin Q, Deng A. Red blood cell distribution

width is a potential prognostic index for liver disease. Clin Chem Lab Med. 2013 Jul;51(7):1403-8.

[15] Montagnana M, Danese E. Red cell distribution width and cancer. Ann Transl Med. 2016 Oct;4(20):399.

[16] Komiya, K., Ishii, H., & Kadota, J. (2014). Healthcare-associated Pneumonia and Aspiration Pneumonia. Aging and disease, 6(1), 27–37.

[17] Ye Z, Smith C, Kullo IJ. Usefulness of red cell distribution width to predict mortality in patients with peripheral artery disease. Am J Cardiol. 2011; 107(8):1241-5.

[18] Bazick HS, Chang D, Mahadevappa K, Gibbons FK, Christopher KB. Red cell distribution width and all-cause mortality in critically ill patients. Crit Care Med. 2011; 39(8):1913-21.

[19] Hu ZD, Chen Y, Zhang L, Sun Y, Huang YL, Wang QQ, Xu YL, Chen SX, Qin Q, Deng AM. Red blood cell distribution width is a potential index to assess the disease activity of systemic lupus erythematosus. Clin Chim Acta. 2013; 425:202-5.

[20] Zhang Z, Xu X, Ni H, Deng H. Red cell distribution width is associated with hospital mortality in unselected critically ill patients. J Thorac Dis. 2013; 5(6):730-6.

[21] Wang B, Lu H, Gong Y, Ying B, Cheng B. The Association between Red Blood Cell Distribution Width and Mortality in Critically Ill Patients with Acute Kidney Injury. Biomed Res Int. 2018; 2018:9658216

[22] van Kimmenade RR, Mohammed AA, Uthamalingam S, van der Meer P, Felker GM, Januzzi JL Jr. Red blood cell distribution width and 1-year mortality in acute heart failure. Eur J Heart Fail. 2010 Feb;12(2):129-36.

[23] Deswal A, Petersen NJ, Feldman AM, Young JB, White BG, Mann DL. Cytokines and cytokine receptors in advanced heart failure: an analysis of the cytokine database from the Vesnarinone trial (VEST). Circulation. 2001 Apr 24;103(16):2055-9.

[24] Wang F, Pan W, Pan S, Ge J, Wang S, Chen M. Red cell distribution width as a novel predictor of mortality in ICU patients. Ann Med. 2011 Feb;43(1):40-6.

[25] Ju XF, Wang F, Wang L, Wu X, Jiang TT, You DL, Yang BH, Xia JJ, Hu SY. Dynamic Change of Red Cell Distribution Width Levels in Prediction of Hospital Mortality in Chinese Elderly Patients with Septic Shock. Chin Med J (Engl). 2017 May 20;130(10):1189-1195.

[26] Meynaar IA, Knook AH, Coolen S, Le H, Bos MM, van der Dijs F, von Lindern M, Steyerberg EW. Red cell distribution width as predictor for mortality in critically ill patients. Neth J Med. 2013 Nov;71(9):488-93.

[27] Hussain Khan Z , Sasaa M A, Mohammadi M , Alipour A , Hajipour A . Mortality Related to Intubation in Adult General ICUs: A Systematic Review and Meta-Analysis, Arch Neurosci. Online ahead of Print; 7(3):e89993.

[28] Hussain Khan, Z., Maki Aldulaimi, A., Varpaei, H., Mohammadi, M. Various Aspects of Non-Invasive Ventilation in COVID-19 Patients: A Narrative Review. Iranian Journal of Medical Sciences, 2022;

[29] Mohammadi M, Khafaee Pour Khamseh A, Varpaei H A. The Need for Pre-vaccination Screening. Int J Infect.In Press(In Press):e119476.