Journal of Medicine, Physiology and Biophysics
ISSN 2422-8427 An International Peer-reviewed Journal
Vol.44, 2018

Frequency of raised red cell distribution width in acute exacerbation of COPD patients

Dr Maham Khan
MBBS
House Officer
Bahawal Victoria Hospital, Bahawalpur.
House No. 7 Street No.1,Faisal Awan Colony Sajjid Awan Town Bahawalpur.

Dr Maria Batool
MBBS
House Officer
Bahawal Victoria Hospital, Bahawalpur.
Alshifa Eye Clinic JalalpurMor Lodhran.

Dr Hina Rashid
MBBS
House Officer
Bahawal Victoria Hospital, Bahawalpur
House No. 636/627 ,Sajid awan colony satellite town Bahawalpur

Dr Ammad Saddique
MBBS
House Officer
Bahawal Victoria Hospital, Bahawalpur.
24/A Muhammadia Colony, Bahawalpur.

Dr Haseeb Ahmad
MBBS
House Officer
Bahawal Victoria Hospital, Bahawalpur.
House No. 38 New Sadiq Colony near Haroon Town Bahawalpur.

Dr Waleed Abdullah
MBBS
House Officer
Bahawal Victoria Hospital, Bahawalpur.
House No. 6/Kb, V.J House, Riaz Colony, Street No. 1, Bahawalpur.

Corresponding Author:
Dr Haseeb Ahmad
House No. 38 New Sadiq Colony near Haroon Town Bahawalpur.

Abstract

Objective: objective of our study is to investigate and establish the frequency of raised red cell distribution width in acute exacerbation of COPD patients.

Study design: Cross sectional study

Place and Duration of study: This study was conducted in pulmonology department of Nishtar Hospital Multan from January 2016 to December 2017.

Methods: Total 384 patients were selected by non-probability consecutive sampling and approval of study was taken from ethical committee of the institution. Written permission of study was signed by every patient enrolled in study. Numerical variables like age, weight, white blood cells, platelets, MCV, hemoglobin (Hb) and duration of COPD were analyzed statically by taking their mean and standard deviation and t-test was applied to test their significance. Non numerical variables like gender, anemia, thrombocytopenia, income and area of living were statistically analyzed by taking their frequency and chi square test was applied to test their significance. While the outcome variable red cell distribution width was assessed by 3-part hematology chamber.

Results: Overall, there were 100% (n=384) patients were included, in this study, both genders. There were 60.7% (n=233) males and 39.3% (n=151) females. 72.1% (n=277) patients belonged to urban areas while 27.9% (n=107) belonged to rural areas. 69% (n=265) had good income and 31% (n=119) had low income. The mean age and BMI of the patients was 65.22±6.45 years and 26.21±2.18 kg/m^2 respectively. There were 26% (n=100) patients between 40-60 years while majority of the patients i.e. 74% (n=284) between 61-80 years of age. The distribution of BMI of the patients observed as; 39.3% (n=151) patients between 18-25 kg/m^2 and 60.7% (n=233) patients between 26-32 kg/m^2. The main outcome variable of this study was red cell distribution width. The Mean±S.D of red cell distribution width was 14.03±1.62%. While, red cell distribution width noted as normal and raised; 54.9% (n=211) and 45.1% (n=173) respectively.

Conclusion: Study concluded that there was significant prevalence of raised red cell distribution width (RDW) in acute exacerbation of COPD patients. This easy, inexpensive and quick parameter should be investigated further. So it can be used as prognostic marker and predictor of mortality in acute exacerbation of COPD patients.

Key words: Acute exacerbation of COPD (AECOPD), red cell distribution width (RDW), COPD, Inflammation.

Introduction

Chronic obstructive pulmonary disease (COPD)is irreversible chronic air flow limitation and inflammatory obstructive disease of lung {1}. It is third most common cause of death {2} after ischemic heart disease and stroke in whole world in 2010. Most cases of COPD are caused by smoking {3}. Other contributing factors for many individuals, who developed COPD are environmental pollution, bio-fuel exposure and chemicals found in many work environments {4-5}. Not every smoker develops COPD {6} but most COPD cases (about 90% of them) have smoked. In the course of disease acute exacerbations of COPD are most significant events and its mortality in hospital is recorded as 5.8%, 7.25%, 7.4% and 10% {7-10}. Acute exacerbation of COPD (AECOPD) are responsible for approximately 50-70% of the cost associated with COPD. Many biomarkers are used for predicting their association with AECOPD and they are also used for predicting the outcome in AECOPD patients after hospitalization. It helps the clinicians in better management and making good decisions.

The red cell distribution width (RDW) represents the variability in the size of erythrocytes in blood circulation {11}. Red cell distribution width (RDW) is mainly used in differential diagnosis of microcytic anemia {12}. It has been reported that increased values of red cell distribution width are related with chronic inflammation which changes erythropoiesis and red cell membrane. It is reported that red cell distribution width is good predictor of mortality in older adults and general population {13}. Red cell distribution width has been defined as prognostic factor {14} in many clinical situations like congestive heart failure, coronary heart disease and pulmonary hypertension. Mortality rates increased 5 fold from the lowest to the highest quartile of RDW. Many diseases in pulmonology like pulmonary embolism, lung cancer, community acquired pneumonia, stable COPD and AECOPD have shown relationship of mortality with higher red cell distribution width values. Few studies have described red cell distribution width as predictor of mortality in many conditions. We want to investigate the frequency of raised red cell distribution width in AECOPD patients so that it can help to determine the outcome in AECOPD patients. Our study will provide a ground to establish the prevalence of raised red cell distribution width in acute exacerbation of COPD patients in our geographical area of South Punjab. It will provide bases to further investigate the issue in this area. Study done by Shaghayegh Rahimyar et al. was taken as reference study {19}.

Material and methods

We conducted cross sectional study at Nishtar Hospital Multan from January 2016 to December 2017. Total 128 patients, who were known cases of COPD, diagnosed as AECOPD clinically by chest consultants, having at least five years of experience of working as consultant in pulmonology, at the time of admission were enrolled by non-probability consecutive sampling. Approval of study was obtained from ethical committee of the institution. Performa for the permission of study was signed by each patient. Exclusion criteria were the following:1) patients having history of autoimmune disorders 2) sever immune depression (HIV infection or sever hematological diseases) 3) patients who were taking any medications for systemic diseases like diabetes and hypertension. For our study sample size was calculated using reference from a previous study by Shaghayegh Rahimyar et al. For which confidence interval was taken as 95 %, power of study 80, 48.2% of all acute exacerbation of COPD patients have elevated red cell distribution width (www.openepi.com).

All patients of acute exacerbation of COPD were enrolled by diagnosing and admitting them in ward from emergency department and outdoor department. A detailed history of symptoms, duration of COPD, smoking status, previous drug history, professional history and history of allergy was taken. It was asked about any history of systemic diseases like diabetes, hypertension and cardiovascular diseases. Through clinical examination was conducted in each patient to check the severity of disease, its complication and presence of any other systemic disease. Personal information like age gender, area of living, income status and BMI was taken by filling the Performa.

Whole blood count including red cell distribution width, MCV, hemoglobin, platelets, WBC were measured from venous blood samples taken at the time of admission in ward within 6 hours. FEV1/FVC were taken on first day. Best of three values were taken.

RDW is measured in 3-part hematology cell counter. RDW normal range was between 11.3% to 13.9% in our laboratory. Red cell distribution width >13.9% was considered as raised level.

Data was analyzed by using software SPSS vol.23.Numerical variables like age, BMI, platelets, white blood cells, MCV, hemoglobin and duration of COPD were statistically analyzed by using their mean and standard deviation. Non numerical variables like gender, thrombocytopenia, anemia and area of living were statistically analyzed by using their frequency. Chi-square and t-test were applied to check the significance of these variables accordingly. P value <0.05 was taken as significant.

Results:

Overall, there were 100% (n=384) patients were included, in this study, both genders. There were 60.7% (n=233) males and 39.3% (n=151) females. 72.1% (n=277) patients belonged to urban areas while 27.9% (n=107) belonged to rural areas. 69% (n=265) had good income and 31% (n=119) had low income. The mean age and BMI of the patients was 65.22±6.45 years and 26.21±2.18 kg/m^2 respectively. There were 26% (n=100) patients between 40-60 years while majority of the patients i.e. 74% (n=284) between 61-80 years of age. The distribution of BMI of the patients observed as; 39.3% (n=151) patients between 18-25 kg/m^2 and 60.7% (n=233) patients between 26-32 kg/m^2. (Table. 1).

The main outcome variable of this study was red cell distribution width. The Mean±S.D of RDW was 14.03±1.62%. While, red cell distribution width noted as normal and raised; 54.9% (n=211) and 45.1% (n=173) respectively (Table. 3). Anemia was noted as 37% (n=142) patients and thrombocytopenia noted as 39.8% (n=153). The Mean±S.D MCV, WBC, platelets, Hb and duration of COPD of the patients was 89.82±4.57fL, 9355.84±465.68, 150319.1±831.83, 13.17±3.76g/dl and 57.81±1.88 months respectively. (Table. 2).

No association was found between red cell distribution width and gender (p=0.140), area of living (p=0.076), Smoking status (p=0.125), stratified age (p=0.344), stratified BMI (p=0.060), anemia (p=0.392), Thrombocytopenia (p=0.664), MCV (p=0.073), WBC (p=0.639), Platelets (p=0.266), Hb (p=0.629), duration of COPD (p=0.402) except income (p=0.033), after applying chi-square and independent samples t test. (Table. 1-2).

Table. 1

Demographic Variables

Characteristics	Frequency	Percentage (%)	Test of Sig.
Gender			
Male	233	60.7	χ^2 **=2.178** **p=0.140**
Female	151	39.3	
Total	**384**	**100.0**	
Area			
Rural	107	27.9	χ^2 **=0.076** **p=0.783**
Urban	277	72.1	
Total	**384**	**100.0**	
Income			
Low	119	31.0	χ^2 **=4.54** **p=0.033**
Good	265	69.0	
Total	**384**	**100.0**	
Smoking Status			
Smoker	119	31.0	χ^2 **=4.15** **p=0.125**
Non-Smoker	50	13.0	
Ex-Smoker	215	56.0	
Total	**384**	**100.0**	
Stratified Age			
40-60 Years	100	26.0	χ^2 **=0.897** **p=0.344**
61-80 Years	284	74.0	
Total	**384**	**100.0**	
Stratified BMI			
18-25 kg/m^2	151	39.3	χ^2 **=3.54** **p=0.060**
26-32 kg/m^2	233	60.7	
Total	**384**	**100.0**	
Descriptive Statistics			
Age	65.22±6.45 years		
BMI	26.21±2.18 kg/m^2		

Table. 2

Hematological and variables having impact on COPD severity.

Characteristics	Frequency	Percentage (%)	Test of Sig.
Anemia			
Yes	142	37.0	χ^2 =0.73 p=0.392
No	242	63.0	
Total	**384**	**100.0**	
Thrombocytopenia			
Yes	153	39.8	χ^2 =0.188 p=0.664
No	231	60.2	
Total	**384**	**100.0**	
Descriptive Statistics (Mean±S.D)			
MCV	**89.82±4.57fL**		**t=1.79 p=0.073**
WBC	**9355.84±465.68**		**t=0.473 p=0.637**
Platelets	**150319.1±831.83**		**t=1.114 p=0.266**
Hb	**13.17±3.76 g/dl**		**t=0.483 p=0.629**
Duration of COPD	**57.81±1.88 months**		**t=-0.839 p=0.402**

Table. 3

RDW

Characteristics	Frequency	Percentage (%)
Normal	211	54.9
Raised	173	45.1
Total	**384**	**100.0**
Mean±S.D	14.03±1.62%	

Discussion

Red cell distribution width (RDW) had been studied and found associated with many clinical conditions. Importance of knowing the association is that it can be used as prognostic marker in diseases and also predictor of clinical outcomes, such as mortality and morbidity, in these conditions.

The main finding of study was that raised red cell distribution width was significantly prevalent in acute exacerbation of COPD patients. Study found that 45.1% of all acute exacerbation of COPD patients had higher than normal red cell distribution width values. These results were closely resembling to another study done by Shaghayegh Rahimirad et al. {19}.

In previous study red cell distribution width had been found associated with ischemic strokes in younger adults age less than 55 years {15}. In JUPITER trial among others red cell distribution width was one important component in predicting mortality {16}. In study done by Syed Atif Safder et al. red cell distribution width was found independent predictor of mortality in critical ill patients in ICU {17}. Red cell distribution width as

prognostic factor had been investigated and found that it is prognostic factor in sepsis and septic shock patients {18}.

So by establishing significant prevalence of elevated red cell distribution width. It can be investigated that red cell distribution width is predictor of mortality and can be compared with other markers of prediction. Red cell distribution width reported as superior marker of predicting mortality as compared to N-terminal-pro-B-type natriuretic peptide in pulmonary hypertension {20}. Red cell distribution width was reported in cohort study a significant predictor of mortality {21}.

Study of 109,675 patients on dialysis, higher mortality found in patients with high red cell distribution width {22}.

Dharmeshkumar Patel et al. investigated association of red cell distribution width and severity of disease {23}. In stable COPD it had been reported as predictor of mortality {24}.

Exact mechanism of significant prevalence of raised red cell distribution width in acute exacerbation of COPD patients is unclear. It might be due to chronic inflammation that causes anisocytosis and interferes with erythropoiesis. A positive correlation found between red cell distribution width and other inflammatory markers such as CRP, ESR and inflammatory cytokines done on systemic lupus erythematous patients, rheumatoid arthritis patients. It had been established that COPD is associated with oxidative stress {25}.

Independent to the iron status, red cell distribution width level increased in anemia of chronic diseases. It had been reported that inflammation causes red blood cells membrane deformability, promotes death of RBCs and alters erythropoiesis. COPD is also chronic inflammatory disease. So it can be thought that RDW is reflection of inflammation in AECOPD. Another rationale of raised RDW in COPD patients can be the malnutrition in these patients. Malnutrition is comorbidity in COPD and it is directly associated with the disease {26}. It leads to impaired erythrocytes formation, which result in heterogeneous RBCs and increased red cell distribution width.

There are two advantages of considering RDW as prognostic marker. First, it is quick, easy and inexpensive test and can be tested even in community. Second, as compared to ESR, CRP and platelets, life span of RBC is approximately 120 days. So it may reflect long duration of patient's condition.

As study had found a significant prevalence of raised red cell distribution width in acute exacerbation of COPD patients so it should be researched further. So that it could be considered as prognostic inflammatory marker in AECOPD.

Major limitation of study was its cross sectional design. Second the sample size of study was relatively small. Finally, it did not measure and compare other inflammatory markers association in AECOPD.

Conclusion

Study concluded that there was significant prevalence of raised red cell distribution width (RDW) in acute exacerbation of COPD patients. This easy, inexpensive and quick parameter should be investigated further. So it can be used as prognostic marker and predictor of mortality in acute exacerbation of COPD patients.

References

1. Nie Y, Chen V, Shannon CP, Andiappan AK, Lee B, Rotzschke O, Castaldi PJ, Hersh CP, Fishbane N, Ng RT, McManus B. Network-based analysis reveals novel gene signatures in peripheral blood of patients with chronic obstructive pulmonary disease. Respiratory research. 2017 Apr 24;18(1):72.
2. Currie GP. ABC of COPD. John Wiley & Sons; 2017 Aug 14.
3. Golpe R, López PS, Jiménez EC, Anón OC, de Llano LA. Distribution of clinical phenotypes in patients with chronic obstructive pulmonary disease caused by biomass and tobacco smoke. Archivos de Bronconeumología (English Edition). 2014 Aug 31;50(8):318-24.
4. Künzli N. Does Air Pollution Cause a Threefold Increase in Chronic Obstructive Pulmonary Disease among Patients with Asthma?.

5. Ramírez-Venegas A, Sansores RH, Velázquez-Uncal M, Pérez-Bautista O. Tobacco smoking is the most common and best known cause of COPD [1]. But it is not theonly cause of COPD. Increasing evidence suggests that an important number of subjects with COPD are never-smokers [2]. The prevalence of COPD among nonsmokers shows significant variation across geographic regions and between epidemiological studies. Such variation may be the result of several different aspects, including study design, definition of COPD, diagnostic criteria (spirometrically confirmed Global Initiative .... Controversies in COPD. 2015 Sep 1;69:35.
6. Popper H. Smoking-Related Lung Diseases. InPathology of Lung Disease 2017 (pp. 103-119). Springer Berlin Heidelberg.
7. Slenter RH, Sprooten RT, Kotz D, Wesseling G, Wouters EF, Rohde GG. Predictors of 1-year mortality at hospital admission for acute exacerbations of chronic obstructive pulmonary disease. Respiration. 2013;85(1):15-26.
8. Fruchter O, Yigla M. Predictors of long-term survival in elderly patients hospitalized for acute exacerbations of chronic obstructive pulmonary disease. Respirology. 2008 Sep 1;13(6):851-5.
9. Roche N, Zureik M, Soussan D, Neukirch F, Perrotin D. Predictors of outcomes in COPD exacerbation cases presenting to the emergency department. European Respiratory Journal. 2008 Oct 1;32(4):953-61.
10. Gaude GS, Rajesh BP, Chaudhury A, Hattiholi J. Outcomes associated with acute exacerbations of chronic obstructive pulmonary disorder requiring hospitalization. Lung India: official organ of Indian Chest Society. 2015 Sep;32(5):465.
11. Calabria M, Bruno C, Tripolino C, Ursini F, Naty S, Grembiale RD. AB0344 Association between Red Blood Cells Distribution Width and Disease Activity Score in Rheumatoid Arthritis. Annals of the Rheumatic Diseases. 2014 Jun 1;73(Suppl 2):918-.
12. Khan H, Khan K, Raziq F, Naseem A. IRON DEFICIENCY ANEMIA; RED CELL DISTRIBUTION WIDTH (RDW) AND RED CELL INDICES IN THE PREDICTION OF AMONG HEALTHY WOMEN IN THIRD TRIMESTER OF PREGNANCY. Professional Medical Journal. 2014 Jan 1;21(1).
13. Kim SH, Yeon JH, Park KN, Oh SH, Choi SP, Kim YM, Kim HJ, Youn CS. The association of Red cell distribution width and in-hospital mortality in older adults admitted to the emergency department. Scandinavian journal of trauma, resuscitation and emergency medicine. 2016 Jun 6;24(1):81.
14. Lee H, Kong SY, Sohn JY, Shim H, Youn HS, Lee S, Kim HJ, Eom HS. Elevated red blood cell distribution width as a simple prognostic factor in patients with symptomatic multiple myeloma. BioMed research international. 2014 May 21;2014.
15. Alimehmeti I, Grabova S, Lekli E, Keri D, Doçi H, Konda E, Zekja I, Xhaxho S, Kruja J. Red blood cell distribution width (RDW) association with ischemic stroke among adults younger than 55 years. Journal of the Neurological Sciences. 2013 Oct 15;333:e250.
16. Horne BD, Anderson JL, Muhlestein JB, Ridker PM, Paynter NP. Complete blood count risk score and its components, including RDW, are associated with mortality in the JUPITER trial. European journal of preventive cardiology. 2015 Apr;22(4):519-26.
17. Safdar SA, Modi T, Sriramulu LD, Shaaban H, Sison R, Modi V, Adelman M, Guron G. The role of red cell distribution width as a predictor of mortality for critically ill patients in an inner-city hospital. Journal of natural science, biology, and medicine. 2017 Jul;8(2):154.
18. Jo YH, Kim K, Lee JH, Kang C, Kim T, Park HM, Kang KW, Kim J, Rhee JE. Red cell distribution width is a prognostic factor in severe sepsis and septic shock. The American journal of emergency medicine. 2013 Mar 31;31(3):545-8.
19. Rahimirad S, Ghafari M, Ansarin K, Rashidi F, Rahimi-Rad MH. Elevated Red blood cell distribution width predicts mortality in acute exacerbation of COPD. Pneumologia. 2016;65(2):85-9.
20. Hampole CV, Mehrotra AK, Thenappan T, Gomberg-Maitland M, Shah SJ. Usefulness of red cell distribution width as a prognostic marker in pulmonary hypertension. The American journal of cardiology. 2009 Sep 15;104(6):868-72.
21. Riedl J, Posch F, Königsbrügge O, Lötsch F, Reitter EM, Eigenbauer E, Marosi C, Schwarzinger I, Zielinski C, Pabinger I, Ay C. Red cell distribution width and other red blood cell parameters in patients with cancer: association with risk of venous thromboembolism and mortality. PloS one. 2014 Oct 27;9(10):e111440.

22. Vashistha T, Streja E, Molnar MZ, Rhee CM, Moradi H, Soohoo M, Kovesdy CP, Kalantar-Zadeh K. Red cell distribution width and mortality in hemodialysis patients. American Journal of Kidney Diseases. 2016 Jul 31;68(1):110-21.
23. Patel D, Kamdar DJ. Prediction of severity of COPD based on red cell distribution width value. Indian Journal of Immunology and Respiratory Medicine. 2016 Oct;1(4):84-7.
24. Seyhan EC, Özgül MA, Tutar N, Ömür IM, Uysal A, Altın S. Red blood cell distribution and survival in patients with chronic obstructive pulmonary disease. COPD: Journal of Chronic Obstructive Pulmonary Disease. 2013 Aug 1;10(4):416-24.
25. Wiegman CH, Michaeloudes C, Haji G, Narang P, Clarke CJ, Russell KE, Bao W, Pavlidis S, Barnes PJ, Kanerva J, Bittner A. Oxidative stress–induced mitochondrial dysfunction drives inflammation and airway smooth muscle remodeling in patients with chronic obstructive pulmonary disease. Journal of Allergy and Clinical Immunology. 2015 Sep 1;136(3):769-80.