Medicine

STUDY OF RED CELL DISTRIBUTION WIDTH IN PATIENTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT **Background-** The present study was conducted to examine the red cell distribution width (RDW) in patients of chronic obstructive pulmonary disease (COPD) and to assess its correlation with different stages. **Methodology-**This study was a cross sectional study conducted at Department of Medicine, tertiary care hospital Bhopal for a period of 2 years on stable COPD patients with no history of hospitalization or admission to emergency department for at least 8 weeks. Detailed clinical history was obtained and examination was done. Routine investigation, PS for comment along with Red cell distribution width and Pulmonary function test were also conducted.**Results-** The present study included a total of 200 patients and majority of the patients were in the age group of 51-60 years (33.5%) followed by the 61-70 years (31.5%), 41-50 years (23%). Male: Female ratio was 3:1. The present study observed that as the stage of COPD progressed, Red blood cell distribution width (RDW) increased (p<0.01). **Conclusion-** Based on the findings of present study, we conclude that RDW value increases with the stage of COPD irrespective of hemoglobin or smoking status. Hence RDW being a simple test and a good biomarker for inflammation can be considered as a predictive marker for the evaluation for the severity of COPD. It can help in assessing the prognosis even in stable COPD patients.

KEYWORDS : COPD, RDW, smoking, stages

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by progressive persisting airflow limitation and increased chronic inflammatory response in airways due to harmful particles in the air. It is reported as a part of systemic inflammatory syndrome which its mortality mostly due to cardiovascular diseases instead of respiratory insufficiency.[1]

According to WHO Global Burden of Disease Study (2016), prevalence of COPD was estimated to be 251 million in 2016. The estimated deaths due to COPD were 3.17 million contributing to 5% of all deaths globally in 2016.[2] Of them, more than 90% deaths were reported in low and middleincome countries. It was fifth leading cause of death in 2002 and estimates show that COPD becomes in 2030 the third leading cause of death worldwide.[2]

According to the Global Initiative for Chronic Obstructive Lung Disease program, the stages of COPD are based on the forced expiratory volume in 1 second (FEV1) of a standard predicted value as follows: Stage I (Very Mild COPD) is FEV1 of equal to or more than 80% of the predicted value, stage II (Moderate COPD) is FEV1 of 50% to 79% of the predicted value, stage III (severe COPD) is FEV1 of 30% to 49% of the predicted value, and stage IV (very severe COPD), also known as end-stage COPD, is FEV1 of less than 30% of the predicted value or FEV1 of less than 50% of the predicted value plus respiratory failure.[1]

The risk factors of COPD included tobacco smoke (including second-hand or passive exposure). Apart from this, indoor air pollution, outdoor air pollution, occupational dusts and chemicals (such as vapours, irritants, and fumes), frequent lower respiratory infections during childhood contribute to COPD.[2] Massive smoking, diet, sedentary lifestyle, and systemic inflammation caused by hypoxia and oxidative stress are underlying reasons of high cardiovascular morbidity and mortality rates in COPD patients.[3]

The RDW is a routine laboratory parameter that indicates the variability in the size of circulating erythrocytes. Systemic inflammation, ineffective erythropoiesis, nutritional deficiencies, bone marrow dysfunction or increased destruction can also cause a higher RDW. Recent evidences report that acute or chronic disorders such as cardiovascular diseases (CVD), cancer, sepsis, chronic obstructive pulmonary disease (COPD), pulmonary thromboembolism (PTE), diabetes mellitus, liver and kidney failure are related with increased RDW levels.[4]

The RDW is used mainly in differential diagnosis of microcytic anemia. However, it has been used as a prognostic tool in different clinical settings such as pulmonary arterial hypertension, congestive heart failure and coronary heart disease.[5]There is association between increased red cell distribution width (RDW) levels and high mortality risk in both general population and in patients with cardiovascular diseases and COPD. COPD is a systemic disease and inflammation has an important role on development of COPD. COPD-related inflammation promotes red blood cell membrane deformability, impair erythropoesis and cause increased RDW levels, as do other chronic inflammatory processes.[6,7]

As RDW is a simple test and a good marker for inflammation, its value as predictive marker for prognosis in COPD will be very useful. The present study was thus conducted with the aim to examine the red cell distribution width (RDW) in patients of chronic obstructive pulmonary disease (COPD) and to assess its correlation with different stages.

Methodology

The present study was designed as a facility based cross sectional study which was conducted at Department of Medicine Gandhi Medical College, & associated Hospitals (Hamidia Hospital) Bhopal for a period of 2 years i.e. from 1st November 2017 to 30th October 2019. All the stable COPD patients with no History of hospitalization or admission to emergency department for at least 8 weeks were included in the study. The exclusion criteria was patients with anemia of any origin; history of blood transfusion and anti-inflammatory drugs (systemic steroids/immunosuppressive drugs) usage in the last 2 months; patients with sepsis or history of cancer, heart failure, connective tissue disorder or inflammatory bowel disease, CLD, CKD. The diagnosis of COPD was based on FEV1 and GOLD criteria. The staging of COPD was done based on the guidelines of COPD GOLD 2015 Criteria as follows-

- Stage 1- FEV1 >80%
- Stage 2- FEV1 50-79%
- Stage 3- FEV1 30-49%
- Stage 4- FEV1 <30%

After approval of the study protocol by the Institutional Ethics Committee, written consent taken from all the patients fulfilling inclusion criteria. All the cases were subjected to detailed clinical history including personal and addiction history, systemic examination, routine investigation, PS for comment along with Red cell distribution width and Pulmonary function test. Normal RDW range was 11.5-14.5%. Anemia was categorized based on WHO guidelines as male- Hb <13gm% and female- Hb <12gm%.

Statistical analysis:

All the data analysis was performed using IBM SPSS ver. 20 software. Frequency distribution and cross tabulation was used to prepare the tables. Quantitative variables were expressed as the mean and standard deviation. Categorical data was expressed as percentage. PRISM and Microsoft office was used to prepare the graphs. Student t- test and ANOVA was used to compare the means. Chi Square test was used to compare the categorical data. P value of < 0.001 is considered as significant.

Results-
The present study included a total of 200 patients of COPD fulfilling the inclusion criteria.

Table 1- Distribution according to Baseline variables

Baseline variables		Frequency (n=200)	Percent
Age groups (year)	30-40	6	3.0
	41-50	46	23.0
	51-60	67	33.5
	61-70	63	31.5
	71-80	16	8.0
	>80	2	1.0
Gender	Male	154	77.0
	Female	46	23.0
Smoking history	Active smoker	81	40.5
	Ex smoker	62	31.0
	Non smoker	57	28.5

In present study majority of the patients were in the age group of 51-60 years (33.5%) followed by the 61-70 years (31.5%), 41-50 years (23%). COPD was more prevalent in male population (77%) as compared to female (23%) and Male: Female ratio was 3:1. Majority of the patients were smokers (71.5%) whereas only 28.5% cases were non smokers. (Table 1)

Figure 1: Stages of COPD
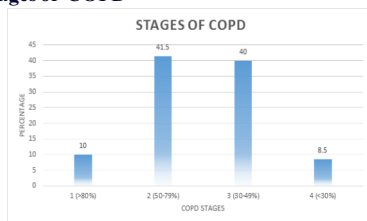
In present study on distributing patients according to COPD stages (based on FEV1 values) it was found that, majority of the COPD patients had stage 2 COPD (41.5%) followed by stage 3 (40%). There were patients who were in stage 4 of COPD (8.5%).

Table 2: Mean RDW in various COPD stages

Stage of COPD	Mean RDW
Stage 1	14.8
Stage 2	15.6
Stage 3	16.8
Stage 4	17.9
P value	0.01

As stage of COPD advances, mean RDW also tends to increase and the observed difference was statistically highly significant (p<0.01).

Table 3: Comparing RDW with COPD stages

RDW (%)	Stages of COPD				Total	P value
	1	2	3	4		
14.6-15.5	16	30	2	0	48	<0.001
15.6-16.5	3	45	33	0	81	
16.6-17.5	1	7	39	13	60	
17.6-18	0	1	6	4	11	

On comparing the Red blood cell distribution width (RDW), it was found that as the stage of COPD advances RDW increases and the difference in RDW between different stage is statistically significant. In Stage 4 COPD majority had higher RDW of 16.6 to 17.5 (76.5%) and 17.6 to18 (23.5%). In stage 3 COPD majority of the patients had

high RDW of 16.6 to17.5 (48.8%). And in that of stage 2 and 1, RDW value ranges maximum patient in between 14.6-15.5% and 15.6-16.5% respectively.

Table 4- Comparing smoking versus stages of COPD versus RDW

Stages of COPD	Smoking Status	RDW(%)				Total
		14.6-15.5	15.6-16.5	16.6-17.5	17.6-18	
1	Non smoker	14 (87.5%)	2 (12.5%)	0 (0%)	0 (0%)	16
	Active smoker	1(33.3%)	1(33.3%)	1(33.3%)	0(0%)	3
	Ex smoker	1(100%)	0(0%)	0(0%)	0(0%)	1
2	Non smoker	13(44.8%)	14(48.2%)	2 (6.8%)	0 (0%)	29
	Active smoker	6(21.4%)	19(67.8%)	3(10.7%)	0(0%)	28
	Ex smoker	11(42.3%)	12(46.1%)	2(7.6%)	1(3.8%)	26
3	Non smoker	1(9%)	7(63.6%)	3 (27.4%)	0(0%)	11
	Active smoker	1 (2.5%)	11(27.5%)	23(57.5%)	5(12.5%)	40
	Ex smoker	0(0%)	15(51.7%)	13(44.8%)	1(3.4%)	29
4	Non smoker	0 (0%)	0(0%)	0(0%)		1
	Active smoker	0(0%)	0(0%)	8 (80%)	2 (20%)	10
	Ex smoker	0(0%)	0(0%)	5(83.3%)	1(16.7%)	6

In present study, stage 3 and 4 COPD patients who are smokers had maximum RDW value and majority of patients who are non-smokers are in stage 1 and 2 who had lower RDW value.

DISCUSSION
Chronic obstructive pulmonary disease (COPD) is a frequent chronic respiratory disease identified with progressive airway limitation, which is often accompanied by chronic inflammation. Elevated RDW has been linked with inflammatory process of chronic respiratory disorders in literature.[6,7] Inflammation causes deterioration in the erythrocyte membrane and reduces the lifespan of red cells. RDW has been associated with conditions characterized with prominent amount of inflammation, such as, hashimoto's thyroiditis, rheumatoid arthritis, coeliac disease, systemic lupus erythematosus, and pneumonia.[8] In present study we tried to established the relationship between RDW and COPD and its correlation with different stages.

In present study majority of the patients were in the age group of 51-60 years (33.5%) followed by the 61-70 years (31.5%), 41-50 years (23%) i.e. COPD was more common among the patients who were in fifth to sixth decade of life. The mean age of the patients presenting with COPD in a study by Sevinc et al was 65.6±9.6 years.[9] In another study by Mehmet et al the median age of COPD patients was 65 and age range was 40-88 years.[10] COPD was more prevalent in male population (77%) as compared to female (23%) in present study. Similar findings were reported by Yilmaz et al in which majority of patients with COPD were males (54%) than females (46%).[11]

In present study, majority of the patients were smokers (71.5%) as compared to non-smokers (28.5%). Similarly, in Ozgul et al study out of 175 COPD patients, majority of the patients were smokers 166 (95%) as compared to non-smokers (5%).[12] Similarly in another study by Baris et al, of the 189 patients, majority of the patients were smokers 156 (82%) than non-smokers 18%.[13]

In present study, on distributing patients according to their Forced expiratory volume in 1 min values, it was found that majority of the COPD patients had FEV1 between 50-79% (41.5%) followed by 40 % patients with FEV1 in the range of 30-49%. There were only 8.5% patients who had FEV1 <30%. Tertemiz et al in their study observed that majority of the COPD patients had 60.2% FEV1.[14]

Upon distributing patients according to COPD stages (based on FEV1 values) it was found that majority of the COPD patients had stage 2

COPD (41.5%) followed by stage 3 (40%) in present study. Similarly Tertemiz et al in their study distributed the COPD stages of the patients and observed that majority of COPD patients (52%) were in stage 2, followed by stage 3 (26%) and stage 1 (16%). Only 6% of patients were in stage 4.[14] Similar result was observed in Sevinc et al study, where COPD stage of the patients were stage 1; 16%, stage 2; 52%, stage 3; 26%, stage 4; 6%.[9]

The present study observed that in Stage 4 COPD, majority of patients had higher RDW of 16.6 to 17.5 (76.5%) and 17.6 to18 (23.5%) which indicate greater variation in RBC size, which also proves that COPD may be the cause of high RDW. As in stage 3 COPD majority of the patients had high RDW of 16.6 to17.5 (48.8%). Study conclude that as the COPD progresses, the RDW increases which is an indicator of possible causes of the underlying chronic inflammation. Tertemiz et al noted mild association between RDW and COPD stages, the high RDW levels was observed in severe COPD stages, especially in the very severe group(p < 0.001).[14] In another study by Mehmet et al, the authors reported that RDW elevation becomes more prominent as the stage of COPD advanced. The reference study also pointed an association between RDW and mortality in stable COPD.[10] Sevinc et al found that RDW was significantly different between COPD stages, the highest RDW was in the very severe stage (p=0.000). When the patients were grouped according to the laboratory upper limit of RDW, survival rate was 31% in the RDW>14.3 group and %75 in the RDW<14.3 group.[9]

In present study, on comparing the RDW with the smoking status of the patients, it was revealed that smokers had significantly higher RDW as compared to non-smokers. Majority of the patients of stage 2 (71.6%), stage 3 (91.7%) and stage 4 (90.9%) COPD were smokers. Which proved that smoking can be cause of increase in RDW in COPD patients. Similarly, in another study of Kurtoglu et al, smokers RDW levels were found to be higher than the ones associated with non-smokers.[15] Baris et al did not observed statistically significant differences of smoking history, smoking package of years in patients with increased RDW level compared to normal ones.[13] In Ozgul et al study RDW values were significantly higher in smokers compared to non-smokers.[12]

CONCLUSION

Based on the findings of present study, we conclude that RDW value increases with the stage of COPD irrespective of hemoglobin or smoking status. Hence RDW being a simple test and a good biomarker for inflammation can be considered as a predictive marker for the evaluation for the severity of COPD. It can help in assessing the prognosis even in stable COPD patients.

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