ASSOCIATION OF RED BLOOD CELL INDICES AND ERYTHROCYTE SEDIMENTATION RATE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) PATIENTS

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ABSTRACT

Objective: To find association of red blood cell indices and erythrocyte sedimentation rate (ESR) in COPD patients.
Study Design: Retrospective case control study.
Place and Duration of Study: University of Health Sciences Lahore, from Oct to Dec 2019.
Methodology: This study was conducted at University of Health Sciences Lahore after approval from Institutional Review Board of University of Health Sciences Lahore. The Data was assessed by IBM-SPSS version 24. Significance of the associations was assessed by Fisher's Exact test and independent sample t-test.
Results: The continuous variables of our data were having normal distribution hence their mean ± standard deviations were calculated. Mean age of the cases with COPD was 56.22 ± 11.34. Mostly were males (91%). The prevalence of the cases and the controls was also calculated by comparing them with different demographic variables. It was found to be highly statistically significant when compared with age (p=0.04). Age group of 51-65 was also more affected with COPD then the other age groups. Patients with lower socio-economic group were found to be more affected by COPD then those from other socio economic groups. When association of COPD was seen with different red blood cell indices then it was striking to find out that the mean corpuscular hemoglobin concentration (MCHC) was significantly associated (p=0.03). Erythrocyte sedimentation rate was also found to be strongly associated with COPD cases (p=0.001).
Conclusion: Hence it is concluded that the red blood cell indices and ESR have a strong association with COPD.

Keywords: COPD, ESR, Red blood cell indices.

INTRODUCTION

COPD is a global public health concern and is currently the third leading cause of death worldwide. It is a common, complex, and heterogeneous condition, which is responsible for considerable and growing morbidity, mortality, and health care expenses worldwide[1]. Exacerbations of COPD indicate instability or worsening of the patient's clinical status and progression of the disease and have been associated with the development of complications, an increased risk of subsequent exacerbations, a worsening of coexisting conditions, reduced health status and physical activity, deterioration of lung function, and an increased risk of death. Once the diagnosis of COPD has been made, the prediction of the prognosis such as exacerbation or mortality seems to be of vital importance; however, in some primary health care settings with inferior approach of examination, the evaluation of prognosis seems to be a mission impossible.

Recent systematic review indicated that anemia and inflammatory markers are becoming increasingly recognized as factors that contribute to the COPD pathogenesis[2]. The markers arelinked with an increased risk of hospitalization and mortality[3]. Since RF limits the occurrence of meals per day to only two, it may cause numerous biochemical and hematological changes in individuals who fast. Similarly, for the spirometry test, the inflammatory and hematological markers continue to be normally interpreted.

Red blood cell distribution width (RDW) in complete blood count (CBC) shows variations in size of circulating red blood cells (anisocytosis). RDW is used for the differential diagnosis of anemia. RDW has also been shown as a possible marker for all cause mortality[4]. In the Third National Health and Nutrition Examination Survey of 15,852 adults, mortality rates increased 5-fold from the lowest to the highest quintile of RDW[5]. Prior studies have investigated the association of RDW with mortality in internal medicine ward, critical careunites (adult and pediatric)[12,13] and emergency department[6].

The ESR is commonly considered a non-specific index of disease activity proved useful in the follow up of patients with selected chronic conditions such as polymyalgia rheumatica, temporal arteritis or rheumatoid arthritis[7]. Indeed, ESR increases in response to rising serum levels of acute phase proteins, fibrinogen and immunoglobulin, as well as in response to anemia. Thus, at variance from CRP, it is not a pure indirect

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inflammatory index. This might be an advantage rather than a limitation in the assessment of COPD patients because COPD, mainly if severe, is frequently associated with hyperfibrinogenemia and anemia[8]. Accordingly, ESR seems worthy of exploitation as potential index of COPD severity if we consider COPD a systemic more than a merely respiratory condition. The very easy, well standardized and reproducible procedure of measurement further strengths this perspective (International Committee for Standardization in Hematology (expert panel on blood rheology). In addition, this is an almost costless procedure, well suited then for low-income countries, where COPD prevalence is dramatically rising[9].

So this study is aimed at finding out the changes in the red cell indices in COPD in the local population of Lahore, Pakistan.

METHODOLOGY

Thisretrospective case control study was conducted at University of Health Sciences Lahore, from October to December 2019 after approval from Institutional Review Board of University of Health Sciences Lahore. A validated questionnaire was filled by the patients after taking informed consent from them. Convenient sampling technique was used.

Sample size was calculated according to following formula:

$$n_1 = \frac{\left(Z_{1-\beta} + Z_{1-\alpha/2}\right)^2 (\sigma_1 2 + \sigma_2 2)}{(\square 1 - \square 2)^2}$$

Z1-a/2= is standard normal variant (at 5% type 1 error (p<0.05) it is 1.96. As in majority of studies.

p-values are considered significant below 0.05 hence 1.96 is used in formula.

Sample size = 160[10].

The patients presenting to medical outpatient department of Tertiary care hospitals of Lahore with diagnosed COPD were included in the study and the normal population was taken from different students of the universities. The patients with disorders other than COPD were excluded.

Total RBC and WBC were counted via an automatized. According to the staining and morphological criteria, differential cell analysis was carried out under a light microscope by counting 100 cells, and the percentage of each cell type was calculated. The ESR analysis was performed according to the method of Westergren. ESR values >20 mm/hr were considered abnormal.

The data was assessed by SPSS-24. Frequency distributions of study participants were calculated. Significance of the associations was assessed by Fisher's Exact test and independent sample t-test. p-value <0.05 was taken as statistically significant.

RESULTS

The continuous variables of our data were having normal distribution hence their mean ± standard deviations were calculated. Mean age of the cases with COPD was 56.22 ± 11.34. Mostly were males (91%). The prevalence of the cases and the controls was also calculated by comparing them with different demographic variables. It was found to be highly statistically significant when compared with age (p=0.04). Though other demographic variables were not statistically significant but the males were found to be having affected more from COPD then the females. Age group of 51-65 was also more affected with COPD then the other age groups. Patients with lower socioeconomic group were found to be more affected by COPD then those from other socio economic groups (table-I).

Table-I: Prevalence of chronic obstructive pulmonary disease patients according to demographic variables (n=162).

Variables	Groups	Cases	Controls	*p*-value
Gender	Male	70	40	0.78
	Female	12	40	
Age Groups	35-50	6	28	0.04
	51-65	66	30	
	>65	10	22	
Socio-economic Group	Lower Class	61	10	0.08
	Middle Class	20	64	
	Upper Class	1	6	
Comorbidity	Yes	51	19	0.19
	No	31	61	

**Calculated by Fisher's Exact test*

When association of COPD was seen with different red blood cell indices then it was striking to find out that the mean corpuscular hemoglobin concentration (MCHC) was significantly associated (p=0.03). Erythrocyte sedimentation rate was also found to be strongly associated with COPD cases (p=0.001). Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Volume (MCV) and Red Cell Distribution Width (RCDW) were non-significantly associated with cases of COPD (table-II).

Table-II: Prevalence of chronic obstructive pulmonary disease patients according to red blood cells indices (n=162).

Variables	COPD		*p*-value
	Cases	Controls	
Mean Corpuscular Hemoglobin	28.9 ± 3.9	34.2 ± 1.8	0.44
Mean Corpuscular Hemoglobin Concentration	22.7 ± 3.23	29.2 ± 0.9	0.03
Mean Corpuscular Volume	69.3 ± 4.20	81.1 ± 1.2	0.18
Red Cell Distribution Width	62.4 ± 2.81	65.2 ± 3.9	0.07
Erythrocyte Sedimentation Rate	53.1 ± 18.2	7.1 ± 0.4	0.001

**Calculated by independent sample t-test*

DISCUSSION

The major finding of the present study was that ESR and MCHC were higher and significantly associated in patients with in-hospital presentation of COPD. To the best of our knowledge, this is the first report on the diagnostic significance of red cell indices in COPD. Koma *et al*[11] carried out a retrospective study of 332 patients with lung cancer reported that the survival rates were lower in the high RDW group than in the low RDW group but that study did not bring into account the cases of COPD as the cause of lung cancer. In a prospective study of 136 patients with acute pulmonary thromboembolism, high ESR was independently associated with increased acute pulmonary embolism related mortality (Hazard ratio 15.5)[12]. In a cohort study in which RDW and ESR was measured in 1,840 patients with various forms of newly diagnosed or progressive COPD, high ESR value was found to be a significant predictor of progression of COPD (37) Vashistha *et al*[13] with studying of 109,675 adult on haemodialysis reported higher mortality in patients with elevated RDW and RDW was stronger predictor of death in COPD than anemia though our study found the association of COPD with RCDW non-significant.

In Zhang *et al*[14] study of 122 patients with traumatic brain injury, high RDW had a positive predictive value (PPV), negative predictive value (NPV) 65.4%, 95.7%. Shteinshnaider *et al*[15] reported that among 586 internal medicine inpatients, the mortality rates were 51.1% in elevated RDW vs. 20.3% (p<0.001) in patients with normal RDW. Every 1% increment of RDW on admission was associated with relative risk of 1.21 for predicting mortality.

In a retrospective analysis of 907 patients with acutedyspnea who visited an emergency department, there wasa step-wise increase of 30 day mortality risk from lowest tohighest RDW tertiles[16]. The precise mechanism for the association between high RDW and mortality in these COPD remains unclear, however, it is assumed to be related to chronic inflammation, which interferes with erythropoiesis[17]. Studies showed that COPD positively correlated with inflammatory indices such as C-reactive protein(CRP), erythrocyte sedimentation rate (ESR), and inflammatory cytokines in a large cohort of unselected outpatients[18], systemic lupus erythematous patients[19], rheumatoidarthritis[20], and obese adolescents[21]. It is proposed that RBCs as biomarker of progression inchronic or acute diseases with oxidative alterations[22]. It iswell recognized that COPD is associated with oxidativestress imbalance. RDW increases in the anemia of chronic diseases, independent of iron status. It is explained that inflammation processes promote deaths of RBCs and alter erythropoiesis and RBCs membrane deformability[23]. Some inflammatory mediators influence iron metabolism and suppress erythropoietin-induced maturation of RBCs. COPD is considered an inflammatory disease. Therefore, it can be assumed MCHC, RDW and ESR values reflect the inflammation status of COPD.

The major limitation of this study is its retrospective design. The other weakness of our study is that we did notuse the Charlson comorbidity index[24] for evaluation of comorbid conditions. Finally, we didn't measure well recognized inflammatory markers. Future studies are suggested with prospective design with measurement of inflammatory markers, such as Procalcitonin, IL-6, and CRP with evaluation of comorbidities with Charlson index.

CONCLUSION

Hence it is concluded that the red blood cell indices and ESR have a strong association with COPD. As we had limited sample size so a detailed study in future can be done with extended sample size.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any authors.

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