ROLE OF CBC PARAMETERS IN COPD WITH ACUTE EXACERBATION IN A TERTIARY CARE CENTER

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is a major global health problem. It is a complex disease characterised by chronic inflammation in the airways by noxious particles. Episodes of increased symptoms called as acute exacerbations are associated with accelerated decline in the lung function. Blood cultures to find out the causative organism in these cases are time consuming. Complete Blood Count (CBC) parameters like Total leukocyte count (TLC), hemoglobin (Hb), platelet count, Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) are found to be related with COPD and its acute exacerbation. An observational hospital based descriptive study was conducted for a period of six months in the Department of Pathology and Medicine of a tertiary care centre. A total of 144 patients of COPD with acute exacerbation (AECOPD) were included in the study. The mean age of the patients was 70.47 ± 9.49 years with female preponderance (61.1%). Though mean hemoglobin level (13.25 ± 2.70 gm %), (95% CI 12.80-13.69) showed statistical significance, other CBC parameters had no obvious difference among the different groups of AECOPD patients. But we cannot deny on the clinical significance of these parameters. The TLC and platelet count were slightly lower in the AECOPD patients with cor pulmonale when compared with AECOPD patients without cor pulmonale. Similarly, platelet parameters like MPV and PDW were slightly higher in the AECOPD patients who are smokers. Though these parameters were not statistically significant, they are found to be cost effective, time saving and clinically significant which would definitely help in the management of AECOPD patients. Hence, these parameters can be used as an easily measurable AECOPD biomarker.

KEYWORDS

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a complex and heterogenous disease characterised by chronic inflammation in the airways by noxious particle such as tobacco smoking.[1] Chronic obstructive pulmonary disease is a major global health problem with an upward trend.[2] It is characterised by progressive air flow limitation that is not fully reversible and is associated with an abnormal inflammatory response of the lung to noxious particles or gases.[2,3]

In some patients there are episodes of increased symptoms called as acute exacerbations.[3] Acute exacerbations is clinically defined as increase in shortness of breathing, severity of cough and sputum volume and/or purulence of sputum. Acute exacerbation of COPD (AECOPD) have short and long term clinical implications and are associated with accelerated decline in lung function which is the hallmark of COPD.[4]

This contributes to disease severity and is implicated in the quality of life, morbidity and mortality of these patients.[2] Assessment of COPD is based primarily on clinical presentations which can be variable and due to these, many biomarkers are also assessed.[2,5] Blood culture has been commonly used as a traditional approach for the detection of any infectious cause. However, blood cultures are time consuming and it takes days to weeks to identify the bacterial or fungal organism in the blood. Blood analysis like Total leukocyte count (TLC) and neutrophil count are performed in all exacerbation cases and have a limited value in the early detection of community acquired bacteremia.[5] The search therefore continues for additional infection markers that may facilitate the prediction of bacteremia. Although new markers (procalcitonin and pro-adrenomedullin) are being evaluated, the swift implementation of these markers is hampered by validation, costs and accessibility.[6]

Elevation of TLC is seen in any other inflammatory conditions.[1] From Complete blood count (CBC), different parameters can be measured and can be used for the evaluation of AECOPD. Red Cell Distribution Width (RDW) is a routine hemogram test which refers to the variation in size of erythrocytes. It is also considered as a prognostic factor in certain inflammatory conditions.[7]

Studies done in different parts of the world has shown the association of TLC, Hemoglobin (Hb), platelet count, Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and RDW with COPD.[7-10] This study was conducted to find out the role of CBC parameters in AECOPD. All the patients of AECOPD coming to Nepal Medical College Teaching Hospital (NMCTH) were included in the study.

MATERIALS AND METHODS

An observational hospital based descriptive study was carried out in the Department of Pathology in collaboration with Department of Medicine of a tertiary care centre (NMCTH) for a period of six months (November 2018 to April 2019). Ethical approval was taken from Institutional Review Committee (IRC) of NMCTH. A total of 144 patients of AECOPD who are diagnosed clinically in Medicine Out Patient Department (OPD)/ Emergency (ER) was included in the study where the diagnosis of COPD was made based on Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.

After the written consent from the patient/ patient party, blood sample of patients from OPD, ward and ER patients was sent to the Clinical Lab. Sample which was collected in Ethylene diamine tetra acetic acid (EDTA) vial was run in Sysmex 5 parts hematology automatic cell counter- XS-500i. The CBC parameters- TLC, Hb level, platelet count, MPV, PDW and RDW were obtained from the computer. Relevant clinical history of the patients was also taken. Patients less than 40 years, patient with bleeding disorder and hematological malignancies were excluded from the study.

Data were entered in Microsoft Excel 2003 and then analyzed by using (Statistical Package for Social Sciences) SPSS version 16. Mean age of the patients and sex wise distribution was reported. Mean of each variable was compared with sex and associated disease conditions like cor pulmonale and systemic diseases like hypertension, diabetes and renal failure. Variables were compared among COPD patients who are smokers and nonsmokers. The level of significance (∞) was set at 5.0% and p value <0.05 was considered significant.

RESULTS

There were a total of 144 patients of AECOPD in this study. The age of the patient ranged from 43 years to 93 years with the mean age of 70.47 ± 9.49 years. Females (61.1%) with AECOPD were more in number compared to male (38.9%). Mean age of male patients was 72.62 ± 8.86 years and mean age of female patients was 69.09 ± 9.67 years (Table 1).

Out of the total number of patients, 93 (64.58%) of them were smokers. Cor pulmonale was seen in 62 patients (43.05%) and other systemic diseases like hypertension, diabetes and renal failure was seen in 56 patients (38.89%).

Table 1: Sex wise distribution of AECOPD				
Sex	**n**	**Age (years)**		
		Mean ± SD	**Min**	**Max**
Male	56 (38.9%)	72.62 ± 8.86	50	95
Female	88 (61.1%)	69.09 ± 9.67	43	85

Mean Hb level in male and female patients were 12.82 ± 2.38gm % and 13.52 ± 2.87gm % (95% CI of mean difference, -1.61- 0.21) respectively. There was no significant difference in Hb level among male and female patients and in different groups- AECOPD with cor pulmonale, systemic diseases and AECOPD patients who were smokers (Table 2).

Table 2: Comparison of Hb in different groups							
Hb (gm%)		**Mean**	**Standard Deviation**	**Mean Difference**	**95% CI of Mean difference**		**P value**
					Upper limit	**Lower limit**	
Sex	Male	12.82	2.38	-0.70	-1.61	0.21	0.129
	Female	13.52	2.87				
Cor Pulmonale (CP)	Absent	12.95	2.68	0.70	-0.19	1.60	0.123
	Present	13.65	2.70				
Other Systemic Disease	Absent	13.55	2.84	-0.78	-1.69	0.12	0.090
	Present	12.77	2.41				
Smoker	Yes	13.56	2.75	0.89	-0.03	1.81	0.059
	No	12.68	2.54				

Table 3: Comparison of TLC in different groups							
TLC (x 10³/µl)		**Mean**	**Standard Deviation**	**Mean Difference**	**95% CI of Mean difference**		**P value**
					Upper limit	**Lower limit**	
Sex	Male	11.12	5.10	1.77	0.25	3.29	0.023
	Female	9.35	4.07				
Cor Pulmonale (CP)	Absent	11.71	4.97	-3.88	-5.26	-2.50	0.000
	Present	7.83	2.69				
Other Systemic Disease	Absent	9.52	4.30	1.32	-0.21	2.85	0.090
	Present	10.85	4.87				
Smoker	Yes	9.90	4.52	-0.38	-1.95	1.20	0.638
	No	10.28	4.68				

Table 4: Comparison of platelet count in different groups							
Platelet count (x 10³/µl)		**Mean**	**Standard Deviation**	**Mean Difference**	**95% CI of Mean difference**		**P value**
					Upper limit	**Lower limit**	
Sex	Male	225.59	81.26	12.62	-12.77	38.01	0.327
	Female	212.97	70.99				
Cor Pulmonale	Absent	233.77	78.03	-36.91	-61.24	-12.59	0.003
	Present	196.85	66.01				
Other Systemic Disease	Absent	213.66	70.09	10.84	-14.57	36.25	0.400
	Present	224.50	82.64				
Smoker	Yes	215.39	68.51	-7.02	-32.97	18.92	0.593
	No	222.41	86.44				

Table 5: Comparison of MPV in different groups						
MPV (fL)		Mean	Standard Deviation	Mean Difference	95% CI of Mean difference		P value
					Upper limit	Lower limit	
Sex	Male	10.57	1.38	0.09	-0.35	0.53	0.701
	Female	10.49	1.25				
Cor Pulmonale	Absent	10.64	1.28	-0.28	-0.71	0.15	0.196
	Present	10.36	1.31				
Other Systemic Disease	Absent	10.63	1.40	-0.29	-0.73	0.15	0.190
	Present	10.34	1.11				
Smoker	Yes	10.73	1.43	0.58	0.15	1.02	0.009
	No	10.14	0.92				

Table 6: Comparison of PDW in different groups						
PDW (%)		Mean	Standard Deviation	Mean Difference	95% CI of Mean difference		P value
					Upper limit	Lower limit	
Sex	Male	12.16	2.78	-0.16	-1.06	0.74	0.720
	Female	12.33	2.58				
Cor Pulmonale	Absent	12.55	2.92	-0.65	-1.53	0.23	0.144
	Present	11.89	2.21				
Other Systemic Disease	Absent	12.43	2.78	-0.42	-1.32	0.48	0.356
	Present	12.01	2.44				
Smoker	Yes	12.72	2.89	1.28	0.39	2.17	0.005
	No	11.44	1.92				

Table 7: Comparison of RDW in different groups						
RDW (%)		Mean	Standard Deviation	Mean Difference	95% CI of Mean difference		P value
					Upper limit	Lower limit	
Sex	Male	15.04	1.87	-0.42	-1.35	0.51	0.369
	Female	15.46	3.18				
Cor Pulmonale	Absent	14.93	2.64	0.85	-0.05	1.76	0.065
	Present	15.78	2.84				
Other Systemic Disease	Absent	15.18	2.71	0.29	-0.64	1.22	0.539
	Present	15.47	2.82				
Smoker	Yes	15.37	2.90	0.22	-0.73	1.17	0.644
	No	15.15	2.48				

Mean TLC between male ($11.12 \times 10^3 \pm 5.10$) and female ($9.35 \times 10^3 \pm 4.07$) patients with 95% CI of mean difference, 0.25-3.29 was found to be statistically significant. Similarly, there was significant difference in the mean TLC and platelet count among AECOPD patients with cor pulmonale and AECOPD patients without cor pulmonale. (Table 3 and 4)

The comparison of MPV and PDW among AECOPD patients with and without cor pulmonale, with and without systemic diseases and who were smokers and non smokers was shown in Table 5 and 6. Patients who were smokers had significantly higher level of MPV and PDW. The mean difference in RDW in AECOPD patients in different groups was not significant. (Table 7)

DISCUSSION

This study showed the mean age of the patients with AECOPD was 70.47 ± 9.49 years where mean age of male patients was more than mean age of female patients. Females were found to be younger as compared to males in a study done by Jain *et al*.[11] Milacic *et al*[12] and Agapakis *et al*[2] showed the mean age of 67.76 ± 9.39 and 65.3 ± 11.1 years respectively. In one study done in India, COPD patients were much younger where the mean age was 60.61±10.36 years.[11] Majority of the patients in our study were females. In contrast to our study, several other studies showed that AECOPD were more commonly seen in males.[1,2,11-14] The gender difference was not significant in our study. Anecchino *et al*[13] showed no gender difference in the occurrence of the disease before 75 years of age but the difference was evident in patients more than 75 years. Milacic *et al*[12] also showed no gender difference in AECOPD. In a study done in India, it was observed that the gender related difference do exist in AECOPD patients. Increased tobacco use in women likely explains some of the increase in the prevalence of COPD in women but data suggests that women may actually be at greater risk of smoking induced lung function impairment and severe dyspnoea for the same level of tobacco exposure. Non smokers with AECOPD are more likely to be females. Evidence also suggests that men are more prone to emphysematous phenotype.[15] Apart from tobacco smoke, the indoor air pollution from biomass fuel plays an important role in the development of COPD in women.[11]

Most of the patients were smokers (64.58%) in our study like in other studies.[11,12,14] Study has shown that smoking is a major factor in AECOPD and most smokers admitted for exacerbation of COPD were included in the severe COPD group.[16] Cor pulmonale was seen in 43.05% patients in our study. Cardiac co morbidity like cor pulmonale increases with the severity of AECOPD. Kaushal *et al*[17] found that 32% of COPD patients in their study had cor pulmonale. Cor pulmonale can be seen as high as 79% in cases of AECOPD.[18]

Other systemic diseases like hypertension, diabetes and renal failure was seen in 38.89% patients. Studies have shown the coexisting illness like diabetes and hypertension in COPD as well as AECOPD patients.[1,11,13,14] Diabetes among COPD was seen in 3.1% patients in a study done by Jain *et al*.[11] Ittyachen *et al*[14] also showed diabetes in 27.1% and hypertension in 28.6% of COPD patients. Koo *et al*[1] showed coexisting diabetes in 18.0% and hypertension in 52.6% of COPD cases. In a study done by Anecchino *et al*[13], diabetes was seen in 12.4% of COPD patients and cardiovascular disease (64.4%) was the most common condition coexisting in COPD patients.

Anemia has been recognized as a frequent comorbidity in COPD patients.[19,20] The prevalence of anemia in patients with COPD varies from 7.5% to 33%. Anemia of chronic disease is probably the most common type of anemia associated with COPD.[19] Male patients had mean Hb level slightly lower than the normal in our study. The difference in the Hb level was neither significant among male and female groups nor in other groups like AECOPD with cor pulmonale, systemic diseases and AECOPD patients who were smokers. Toft-Peterson *et al*[21] also showed that male COPD patients had lower level of hemoglobin than female patients and concluded that low Hb were frequent in COPD patients with acute exacerbations.

Increased in TLC has been reported in COPD patients.[1] Our study showed slightly higher mean TLC in male patients and normal TLC in female patients and the difference was statistically significant. Similar to our finding, Alkadi *et al*[22] and Karadeniz *et al*[8] also showed significant increase in TLC in AECOPD patients. Our study showed significant low TLC in AECOPD patients with cor pulmonale than AECOPD patients without cor pulmonale. Similar correlation with TLC, smoking and AECOPD severity was found in a study done by Koo *et al*[1] in Korea.

Mean platelet count in AECOPD patients with cor pulmonale was comparatively less than the patients in other groups and the difference was significant in our study. Studies had shown significant increase in the platelet count in AECOPD.[23,24] Platelet count, a commonly measured clinical assay, may be a biomarker for moderate-severe COPD symptoms.[24] In contrast to this, Skoczynski *et al*[25] showed that COPD has no influence in the platelet count.

The MPV and PDW indicates the severity of inflammation as inflammation plays an important role in AECOPD.[10] According to our study, there exists a statistical significance among smokers and non smokers AECOPD patients with respect to MPV and PDW. Studies conducted in different parts of the world had shown that MPV values were significantly lower in patients AECOPD.[8,10,26-28] Ragulan *et al*[10] explained that negative correlation occurs between MPV and severity of COPD.[10] Cigarette smoking was proved to be associated with an increased MPV.[28] This was supported by our finding which showed slightly higher MPV level in smoker COPD patients than

the non smoker patients though it was within the normal range. In our study, PDW was within normal range which was similar to a study done by Ragulan *et al.*[10] However, in a study done by Karadeniz *et al*,[8] higher PDW was seen in AECOPD.

The mean RDW was slightly higher in our study but statistically no difference was identified with respect to different groups of AECOPD but finding of Ragulan *et al*[10] showed statistical significance among male and female AECOPD with respect to RDW. In their study, RDW was higher in male which was in contrast to our study where female had a slightly higher RDW. Elevated RDW has been linked with inflammatory process of chronic disorders. It is a well known fact that inflammation causes deterioration in the erythrocyte membrane and reduces the lifespan of red cells. Studies had revealed that RDW significantly increases with COPD.[7,29] It was also seen that RDW elevation becomes more prominent as the stage of COPD advanced.[7]

In conclusion, chronic obstructive pulmonary disease is quite common in our part of the world and acute exacerbations are very common. Though inflammatory markers are readily available, some are not cost-effective and other tests like culture takes time. Tests like Hb, Platelet count, MPV, PDW and RDW is easily available while performing CBC in the coulter counter. These tests were associated with AECOPD and showed clinical significance in parameters like Hb among male and female patients and TLC and platelet count among patients with cor pulmonale and without cor pulmonale. Platelet parameters like MPV and PDW among smokers were slightly higher than non smokers AECOPD patients. Our study also showed that CBC counts were within the normal range and had weak statistical power. Based on our study, we can conclude that CBC parameters provide the additional information for treatment selection in AECOPD patients. Hence, these parameters can be considered as simple and convenient AECOPD biomarkers.

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