

The Clinical Profile of Chronic Obstructive Lung Diseases Patients in Acute Exacerbations and Stable COPD with Age and Sex Matched Controls

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Abstract: Aim: A case control study to compare the clinical profile of chronic obstructive lung diseases patients in acute exacerbations and stable COPD with age and sex matched controls and to compare the various parameters and its relation in terms of outcome in patient with COPD stable and acute exacerbations with age and sex matched controls. **Methodology:** It includes 60 cases of stable and exacerbation COPD patients each and 60 controls. COPD diagnosed according to GOLD guidelines. Mean platelet volume and high sensitive C- reactive protein was measured in COPD patients. **Results:** The MPV in the controls, stable cases group and for exacerbation group was 9.48 ± 1.46 , 8.26 ± 0.58 and 8.21 ± 0.46 fl respectively. The mean platelet volume of the stable cases those with FEV1 less than 30% had a mean platelet volume of 7.72 ± 0.44 fl, and those within FEV1 30-50% and 50-80% had mean of MPV as 8.08 ± 0.30 fl and 8.67 ± 0.49 fl respectively. The mean platelet volume of the exacerbation cases those with FEV1 less than 30% had a mean platelet volume of 7.56 ± 0.35 fl, and those within FEV1 30-50% and 50-80% had mean of MPV as 8.09 ± 0.41 fl and 8.4 ± 0.20 fl respectively. The p value for this comparison was observed to be 0.9301 which is non-significant **Conclusion:** Mean platelet volume is easily accessible low cost marker. The present study shows that a decrease of mean platelet volume occurs when COPD exacerbation inflammatory processes occur.

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I. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality in the world¹. Chronic Obstructive Pulmonary Disease (COPD) is characterized by the presence of airflow obstruction due to chronic bronchitis or emphysema, the air flow obstruction is generally progressive, may be accompanied by airway hyper reactivity, and may be partially reversible². The prevalence of COPD in India is on the rise. India contributes very significantly in mortality from COPD 102.3/100,000 and 6,740,000 DALYs (Disability-adjusted life year) out of world total of 27,756,000 DALYs, thus significantly affecting health related Quality of Life in the country. The COPD prevalence varied from 3% to 8% among Indian males and approximately 2.5% to 4.5% among Indian females². In India 65% of men use tobacco (35% smoke, 22% use smokeless tobacco, and 8% use both) and 3% by women^{3,4}.

Exacerbations and co morbidities contribute to the overall severity in individual patient⁵. Acute exacerbation of COPD (AECOPD) is common cause of emergency room visits and is the major cause of mortality and morbidity. Moreover, more than half of the patients discharged with the diagnosis of AECOPD often require readmission in the subsequent six months⁶. Thus, the economic and social burden of AECOPD is extremely high⁷.

COPD includes Emphysema, an anatomically defined condition of the lung characterized by destruction and enlargement of the lung alveoli; chronic bronchitis, a clinically defined condition with chronic cough and phlegm; and small airway disease, a condition in which small airways are narrowed⁸. COPD is present only if chronic obstruction occurs; chronic bronchitis without airflow obstruction is not included in COPD⁹.

It has been established that stable COPD is associated with low grade systemic inflammation as demonstrated by an increase in Blood leucocytes, Acute phase proteins such as CRP and inflammatory cytokines^{10, 11, 12}. COPD exacerbations have impaired health status, reduced physical activity, and accelerated decline of lung function. COPD exacerbations are associated with an increase in systemic inflammation^{13, 14, 15}.

Thus an increase in inflammatory markers such as blood leucocytes, CRP, Erythrocyte sedimentation rate and inflammatory cytokines is observed and most likely associated with lung function decline^{14, 15}.

Platelets are involved in inflammation, atherogenesis, and thrombosis¹⁶. Mean platelet volume is one of the platelet function indices. It reflects the platelet production rate and stimulation¹⁷. Previous studies showed inverse correlations between MPV and disease activity in inflammatory bowel disease, rheumatoid arthritis and ankylosing spondylitis¹⁸. Mean platelet volume is a parameter generated by routine complete blood count tests that is usually overlooked by clinicians¹⁹. Mean platelet volume is a marker of inflammation it is found to be increased in patients at risk for atherothrombotic disease and measurement of platelet volume has been suggested as a marker of platelet activation.²⁰ The Mean platelet volume has been investigated as an indicator of inflammation in several different diseases²¹⁻²⁶.

The association between Mean platelet Volume and chronic obstructive pulmonary disease is controversial. Some studies have shown that Stable COPD patients have higher Mean platelet volume than those in the control groups²⁷ whereas another report found that this association of increased mean platelet volume in COPD patients was not statistically significant²⁸.

Keeping these factors in mind, the present study is designed to prospectively study the clinical presentation, laboratory abnormalities, including mean platelet volume and association in terms of prognosis in patients with COPD exacerbation and stable COPD patients.

II. Methodology

An Institutional based case control prospective study was conducted in department of Medicine and PBM hospital Bikaner. Patients of COPD diagnosed according to the GOLD's criteria were consecutively enlisted and enrolled from those attending the medicine outdoor and wards. Sample size was calculated as 60 subjects (stable and exacerbation) and 60 controls at 95% confidence interval and 80% power assuming minimum detectable difference in MPV of 0.6 ± 1 . Chronic obstructive pulmonary disease stable and exacerbation patients diagnosed according to GOLD guidelines. Controls were normal healthy individuals. Exclusion criteria is other systemic illness were not included.

Blood collected from large antecubital vein in a tubes containing direct thrombin inhibitor was used. Hematological profile- Hemoglobin, complete blood count, differential count, Platelet count, MPV, ESR etc. Pulmonary function test was done when the patient is stable by RMS Helios series of spirometers. Pulmonary functions including forced vital capacity (FVC), forced expired volume in one second (FEV_1), FEV_1/FVC ratio, and peak expiratory flow rate (PEFR) were measured according to the American Thoracic Society (ATS) criteria. **Statistical analysis-** The results were obtained, noted in the Performa and data was analyzed on SPSS20 statistical software. Unpaired t-test was used to calculate p value. P-value at 95% confidence level or ≤ 0.05 was taken as highly significant.

III. Results

The study included 120 patients of COPD and 60 controls. The mean age for the control group was 64.46 ± 11.66 years, for the stable cases were 65.01 ± 11.55 years and that for the exacerbation cases was 65.06 ± 11.52 years. The mean number of pack years of cigarettes smoked for controls was 23.85 ± 8.02 pack years, for the stable cases group was 24.48 ± 12.06 pack years and that for the exacerbation cases group was 32.6 ± 18.46 pack years. The BMI for the controls was 24.23 ± 2.83 for the stable cases group was 23.9 ± 2.77 and that for the exacerbation cases group was 23.2 ± 2.72 (Table: 1). A comparison of the cases (stable and exacerbation) and the control groups based on the pulse rate the mean for which is 78.31 ± 6.72 bpm in the control group and 80.56 ± 17.86 bpm in the stable cases and 106.93 ± 12.11 bpm in exacerbation cases. . The mean of the respiratory rate in the control group was 16.18 ± 13.28 breaths / min, the mean was 20.2 ± 2.55 breaths/ min for the stable cases and 24.45 ± 2.89 breaths/ min for the exacerbation cases. The total leucocyte count in the control group was $5.9 \pm 1.79 \times 10^9$ cells/L, for the stable cases it was $7.5 \pm 2.45 \times 10^9$ cells/L, and , for exacerbation cases it was $14.46 \pm 4.87 \times 10^9$ cells/L . The MPV in the controls, stable cases group and for exacerbation group was 9.48 ± 1.46 , 8.26 ± 0.58 and 8.21 ± 0.46 fl respectively. The total platelet count in the controls was 2.44 ± 0.66 lacs, for stable was 3.01 ± 1.05 lacs whereas that in the exacerbation cases was 5.6 ± 2 lacs. The Blood oxygen saturation in the controls, stable cases group and for exacerbation group was $97.43 \pm 1.0\%$, $90.14 \pm 5.45\%$ and $82.6 \pm 9.17\%$ respectively. The p values of the controls- stable and controls exacerbation with respect to the PR, Blood saturation, the RR, TLC and MPV was 0.0001 respectively which is statistically significant (Table: 2, Fig: 1).

Table: 1 the comparison of the case and control population based on age, number of pack years of cigarette smoked and BMI.

Parameter	Control		Stable		Exacerbation	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	64.46	11.66	65.01	11.55	65.06	11.52
Smoke Pack years	23.85	8.02	24.48	12.06	32.6	18.46
BMI (kg/m ²)	24.23	2.83	23.9	2.77	23.2	2.72
Total no. of patients	60		60		60	

Table: 2 shows the comparison of cases and control population based on the Pulse rate, Respiratory rate, Total Leucocyte Count, Mean Platelet Volume and platelet count

Parameters	Controls		Stable		Exacerbation		p-value between control and stable	p-value between control and exacerbation
	Mean	SD	Mean	SD	Mean	SD		
PR(beats/min)	78.31	6.72	80.56	17.86	106.93	12.11	0.36	0.0001
Blood oxygen saturation	97.43	1.0	90.14	5.458-	82.6	9.179	0.0001	0.0001
TLC(x10 ⁹ /L)	5.9	1.79	7.5	2.45	14.46	4.87	0.0001	0.0001
MPV(fl)	9.48	1.46	8.26	0.58	8.21	0.46	0.0001	0.0001
Respiratory Rate (per min)	16.18	1.32	20.2	2.55	24.45	2.89	0.0231	0.0001
Platelets (lacs)	2.44	0.66	3.01	1.05	5.6	2.97	0.6602	0.2938

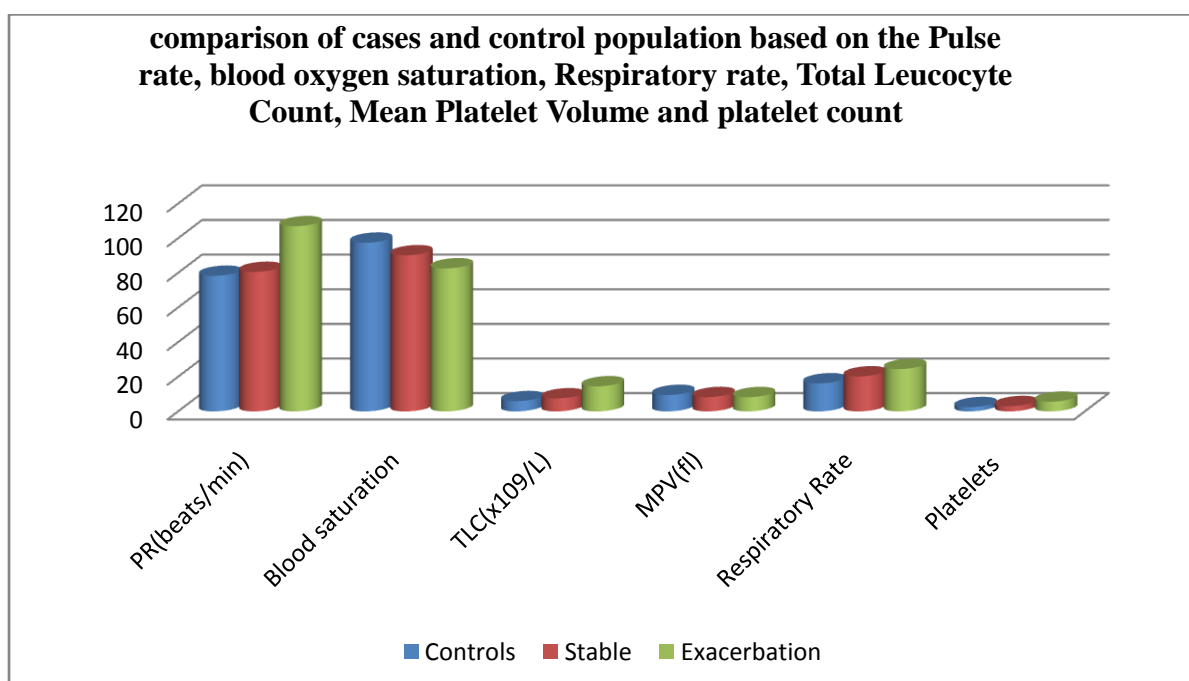


Fig: 1 showing the comparison of cases and control population based on the Pulse rate, blood oxygen saturation, Respiratory rate, Total Leucocyte Count, Mean Platelet Volume and platelet count.

Table: 3 Comparison of ABG parameters in the cases and control groups.

ABG parameter	Controls		Stables		Exacerbation		p-value between control and stable	p-value between control and exacerbation
	Mean	SD	Mean	SD	Mean	SD		
pH	7.41	0.04	7.34	0.08	7.24	0.13	0.0001	0.0001
po ₂ (mm of Hg)	96.49	1.71	76.06	7.53	71.3	6.29	0.0001	0.0001
pco ₂ (mm of Hg)	31.83	2.33	49.85	10.79	59.76	14.0	0.0001	0.0001

Table: 4 Comparison MPV and FEV1 in the cases (Stable and exacerbation).

FEV1 %	MPV in Stable		MPV in Exacerbation		p-value
	Mean	SD	Mean	SD	
<30%	7.72	0.44	7.56	0.35	0.9301
30-50	8.08	0.30	8.09	0.41	
50-80	8.67	0.49	8.4	0.20	

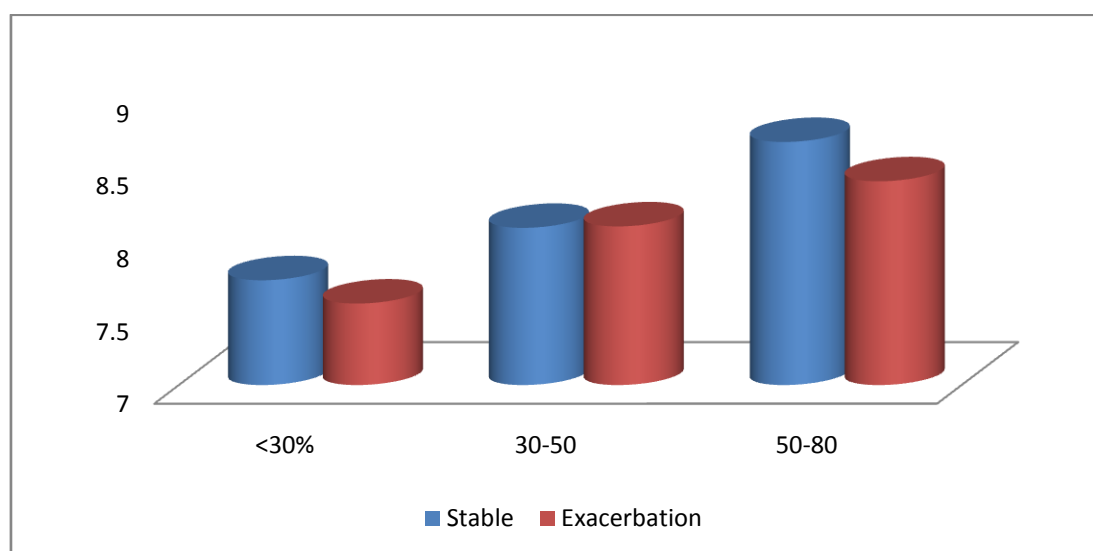


Fig: 2 Chart showing a comparison of MPV among the cases divided on the basis of FEV1.

Table: 5 Comparison of MPV and TLC in the cases (Stable and exacerbation).

TLC	MPV in Stable			MPV in Exacerbation			p-value
	No.	Mean	SD	No.	Mean	SD	
<11	52	8.34	0.55	24	8.05	0.44	0.0269
>11	8	7.75	0.59	36	7.8	0.45	

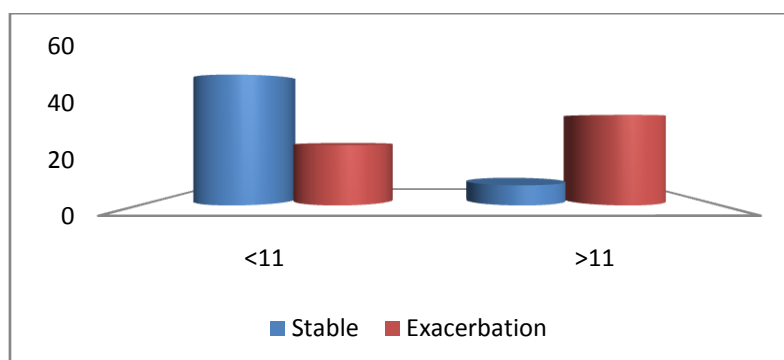


Fig: 3 Graph showing the comparison of MPV and TLC. In this graph the TLC is taken on the x-axis and MPV is taken on the y-axis.

The mean pH in the controls was 7.41 ± 0.04 , in stable 7.34 ± 0.08 whereas that in the exacerbation cases it was 7.24 ± 0.13 whereas the pO₂ and pCO₂ in the controls was 96.49 ± 1.71 mm of Hg and 31.83 ± 2.33 mm of Hg respectively, in the stable cases group the pO₂ was 76.06 ± 7.53 mm of Hg and the mean pCO₂ was 49.85 ± 10.79 mm of Hg and in exacerbation group the pO₂ was 71.3 ± 6.29 mm of Hg and the mean pCO₂ was 59.76 ± 14.0 mm of Hg. The difference between the two groups with respect to the different parameters of ABG was also significant. The p value being <0.001 in each case (Table: 3).

The comparison between the said groups among the cases made on the basis of FEV₁ and the MPV in the three groups. The mean platelet volume of the stable cases those with FEV₁ less than 30% had a mean platelet volume of 7.72 ± 0.44 fl, and those within FEV₁ 30-50% and 50-80% had mean of MPV as 8.08 ± 0.30 fl and 8.67 ± 0.49 fl respectively. The mean platelet volume of the exacerbation cases those with FEV₁ less than 30% had a mean platelet volume of 7.56 ± 0.35 fl, and those within FEV₁ 30-50% and 50-80% had mean of MPV as 8.09 ± 0.41 fl and 8.4 ± 0.20 fl respectively. The p value for this comparison was observed to be 0.9301 which is non-significant (Table: 4; Fig: 2).

We divided the cases into two groups based on the TLC one group was with $TLC < 11 \times 10^9$ cells/L and the other group was $TLC > 11 \times 10^9$ cells/L and compared the MPV in the two groups. We found that the MPV in the stable group with $TLC < 11 \times 10^9$ cells/L was 8.34 ± 0.55 fl whereas that in the group $> 11 \times 10^9$ cells/L was 7.75 ± 0.59 fl. The MPV in the exacerbation group with $TLC < 11 \times 10^9$ cells/L was 8.05 ± 0.44 fl whereas that in the group $> 11 \times 10^9$ cells/L was 7.8 ± 0.45 fl. The p-value for this Comparison was 0.0269 showing a significant difference (Table: 5; Fig: 3).

IV. Discussion

The age range in cases was 33-90 years whereas the age range in the controls was 39-90 years. The youngest patient of the cases group was 33 years old whereas the youngest control was 39 years. The mean age in our cases was 65 years which was similar to the mean age of cases in study done by Rui Tao Wang et al²⁹ where the mean age was 69 for cases and also in the study done by P. steriopoulos et al³⁰ where the mean age of the cases was 70 years. Similarly, in the study done by Sevinc S. Ulasli³¹ et al the mean age of the cases was 70.6 years and that of the control group was 68.7 years. The range of pack years of cigarette smoked was 7.5-60 pack years in stable and 7.5-100 pack years in exacerbation group whereas the range of pack years of cigarette smoked in control group was 2-40 pack years. In other studies the number of pack years of cigarette smoked was 56.4 and 54.3 for cases and controls respectively in the study conducted by Wang RT et al²⁹. Whereas in the study conducted by Ulasli SS et al the smoking pack years were 19.5 for the cases and none for the control³⁴. As expected the mean heart rate in COPD patients is higher than controls this reflects a basic state of increased basal metabolism possibly due to increased respiratory effort to maintain minimum oxygen saturation.

The study done by Jensen MT et al found that with the increasing severity of COPD the resting heart rate increased and that the COPD patients in general had a higher resting heart rate than the non COPD controls. They even used this as a predictor of mortality in COPD patients³². The higher mean respiratory value in the cases than controls reflects an increase respiratory effort possibly as a result of hypoxemia due to chronic obstructive state. Raupach T et al found a higher resting respiratory rate in patients diagnosed with COPD as compared to healthy controls they however in their study attributed this to increased sympathetic excitation in the COPD patients³³.

The finding observed by Wang RT et al²⁹ where the mean platelet volume was 9.7fl in the cases and 10.4fl in the controls. Also in the study by Biljak et al³⁴ the MPV in the cases group was 8.7 fl and the MPV in the control group was 9.6 fl. In the study done by Ulasli SS. et al³¹ they found that the MPV in the COPD patients was 8.6 fl as compared to 9.3 in the healthy controls.

However some studies contradict our findings like the one done by Cui H et al³⁵ found that in COPD patients the Mean Platelet Volume increased. Another study done by Rajeev bansal et al³⁶ also showed that in COPD patients the MPV was significantly higher (10.8 fl) as compared to controls (7.96 fl). In the study by Steriopoulos P³⁷ et al the MPV in COPD patients was 10.69 fl and that in the control was 9.96 fl.

A reason for this conflicting data result is possibly due to the failure to rule out the confounding factors such as Body Mass Index, Smoking Status and medication use³⁸. Obesity and cigarette smoking increase Mean platelet volume and weight loss and smoking cessation decreased Mean platelet Volume^{39, 40, 41}. Medications such as Statins and Angiotensin converting enzyme inhibitors exert anti-inflammatory effect in COPD⁴².

Our observation of the blood pH was similar to that of Wang RT et al who found the mean pH in COPD (7.32) patients to be lower than the control group. The reason for the fall in blood pH is probably due to the rise of blood pCO₂ which causes a fall in blood pH. This observation of a statistically significant decreased pO₂ in COPD patients is similar to the finding in the Wang et al study where the mean pO₂ in the study group i.e the COPD patients was 72.4 mm of Hg as compared to 90.9 mm of Hg in the control group. In the study done Rajeev Bansal et al the pO₂ in the COPD patients was found to be 70.8 mm of Hg whereas that in the control group was found to be 90.7mm of Hg and the p-value of less than 0.05 suggested a significant difference³⁶. The

decrease in pO₂ in COPD patients is also attributed to the chronic and irreversible narrowing of airways leading to a state of chronic hypoxemia.

It is shown that in COPD patients as the TLC increased the mean platelet volume decreased. A Pearson's correlation coefficient of -0.377 also suggests a negative correlation between the two values. This observation was similar to the observation in the study done by Wang et al²⁹, Biljak et al who in their study found a negative correlation between TLC and MPV in COPD patients. Studies like those done by Suvak B et al⁴³, Ekiz O et al⁴⁴ found that in certain diseases causing systemic inflammation like Behcet's disease etc the MPV increased with increased TLC. However other studies like Kisacik B et al⁴⁵ found that in certain inflammatory diseases like Rheumatic arthritis etc increased TLC was associated with relatively decreased MPV. Banerjee et al also showed increased platelet and TLC and decreased MPV in COPD patients. The results indicated that the increased thrombotic risk in COPD might be still induced by the activated platelet⁴⁶.

In this study a correlation and comparison of Mean Platelet Volume an established marker of inflammation was made between COPD and controls. The Mean Platelet Volume in COPD patients was found to be decreased as compared to healthy age, sex and smoking habits matched controls. There was a negative correlation between Mean Platelet Volume and various markers of inflammation in COPD patients in the study. This correlated with the previous studies done by Wang RT et al, Biljak et al, Ulasli et al.

V. Conclusion

In conclusion, mean platelet volume is easily accessible low cost marker. The present study shows that a decrease of mean platelet volume occurs when COPD exacerbation inflammatory processes occur. Moreover, the decrease of mean platelet volume correlated with clinical and laboratory features that accompany COPD exacerbation. Thus, a decrease in mean platelet volume values may indicate exacerbations of COPD. Future studies should investigate whether mean platelet volume obtained as part of routine laboratory testing could identify patients at risk for an exacerbation event in subjects with COPD.

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