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ORIGINAL ARTICLE

Role of Mean Platelet Volume in the Prognosis of Acute Exacerbation of Chronic Obstructive Pulmonary Disease Patients

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ABSTRACT

Background: COPD is a great challenge as it is a main cause of morbidity and mortality around the world. COPD exacerbations increasing airway and systemic inflammation. **Aim of this study**: the study aimed to assess the role of MPV as a marker of inflammation in COPD patients and to evaluate its role as a prognosis parameter in AE COPD. **Patients and Methods**: This study was conducted at Zagazig University Hospitals, Chest Department, during the period from April 2017 till October 2017, the study included 25 stable and 25 exacerbated chronic obstructive pulmonary disease (COPD) patients, selected in non randomized manner. **Results:** showed that there was no significant statistical difference in RBCs, hemoglobin and hematocrit content and a highly statistical significant increase in white blood cells (WBCs) count, neutrophils count, while lymphocytes shows significant statistical increase among stable COPD group among studied groups. The results showed that the Validity of MPV cutoff value, Sensitivity was 76.0%, Specificity was 80.0%, +VE predictive was 79.1%, -VE predictive was 76.9% and the accuracy was 78.0%.**Conclusion**: MPV is an easily accessible low cost marker of inflammation in AECOPD. Decreased MPV values can be used as indicator for negative acute-phase reaction in the exacerbated COPD patients. Cut off-point of MPV<9.4 fl can be used as a threshold mean of bad outcome.

Keywords; Mean Platelet volume, COPD exacebations, prognosis

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive, associated with an abnormal inflammatory response of the lungs to noxious particles or gases and associated with systemic manifestations. [1].

COPD is a serious disease cause airflow obstruction. COPD also, associated with systemic inflammation such as blood leukocytes increase, inflammatory cytokines and C. reactive protein (CRP) [2].

The Mean platelet volume (MPV), blood count test which is important indicator the production rate of platelet and stimulation [3].

Many authors have reported that the increase in MPV can be considered as prognostic factor for pulmonary hypertension and thromboembolism in COPD patients. [4, 5]

However the association between Mean platelet Volume and Chronic Obstructive Pulmonary Disease is still controversial. Some authors reported that there were an

increase in Mean platelet volume for COPD patients than those in the control groups[6]. Whereas another report found that this increased in MPV in COPD patients was not statistically significant[7].

So, the aim of this study was to assess the role of MPV as a marker of inflammation in COPD patients and to evaluate its role as a prognosis parameter in AE COPD.

PATIENTS AND METHODS

This study was conducted at Chest Department, Zagazig University Hospitals, Out Patient Clinic, Faculty of Medicine, Zagazig University Hospitals from April 2017 to October 2017 after approval of Institutional Review Board-Zagazig University (IRB-ZU). This study included 25 stable and 25 exacerbated COPD patients, they were diagnosed according to **GOLD [1].**

Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

b):Inclusion criteria:-

1. **- patients of stable COPD**

Patients have constant symptoms (dyspnea, volume and colour of sputum), Free of serum signs of inflammation and radiological signs of pneumonia, 2 weeks free from chest infections and 4 weeks free from exacerbation. **(8)**

2- patients Exacerbation COPD:-

The exacerbation COPD can be defined as acute clinical deterioration in patient's respiratory status, Infections in airways or lungs were deemed to be exacerbations. It includes some combination of the followings; Worsening dysppea, Increase in sputum purulence , Increase in sputum production. **(8)**

Exclusion criteria:-

COPD patient with the following concomitent comorbidities were excluded:

- On anticoagulant or anti platelets therapy (eg. cerebro-vascular event, acute coronary syndrome and pulmonary embolism).
- Hematological disease.
- Rheumatological disease.
- Liver disease.
- Renal disease.
- Thrombocytopenia.

c): Study design

The patients were categorized into 2 groups;

Group (A): 25 Stable COPD patients as a control group.

Group (B): 25 patients diagnosed as Exacerbated COPD patients.

All patients subjected to the followings:

- Complete history taking, especially history of smoking, Cough, sputum production and chest wheezes, History of dyspnea
- Full clinical examination included general examination and Local chest examination.
- Plain chest X ray: **(posteroanterior & lateral view).**
- analysis **of Arterial blood gases** (ABGs): by means of a blood gas analyzer, Siemens_RAPID Lab® 348EX.
- Electrocardiography (ECG).
- Spirometric Pulmonary function tests:
- Echocardiogram (ECHO): performed to the patients with suspected "heart failure, cardiomyopathies (done for 15 patients).
- Laboratory investigations including total blood count (count of hemoglobin, white blood cell, red blood cell, platelet count, and mean platelet volume (MPV).
- Mean platelet volume (MPV) is an accurate measure of platelet size, which is routinely reported during a complete blood count (CBC) analysis were measured by using Sysmex-Kx-21N, anticoagulated with Ethlene diamine tetra acetic acid (EDTA) and rapid processing (with in 1 hour).
- Liver and Kidney function tests to exclude renal, hepatic and haematological disorders.
- Test of COPD assessment (CAT score) **(9)** to measures health state assessment of COPD.
- Assessment of all patients in the study groups **(**AECOPD **after one month)**

a) Improved.
b) Complicated.
c) Died.

Statistical analysis

Data were collected, tabulated and statistically analyzed using SPSS 20, software for Windows.

RESULTS

The current study included (25) stable and (25) exacerbated chronic obstructive pulmonary disease (COPD) patients diagnosed according to **GOLD**[9] from the outpatient clinic, Chest Department, Faculty of Medicine, Zagazig University, the results is tabulated in the following tables.

Table (1), showed that there is no statistical significant difference between exacerbated COPD group and stable COPD group as regard: Age, Sex and Smoking (P<0.05). **Table (2),** showed that the statistical significant difference was decreased in pH, SaO_2, PaO_2, HCO3 and serum calcium, while it was increased in $PACO_2$ among exacerbated COPD patients group in comparison with stable COPD patients group (P <0.05)**. Table (3),** showed that there was no significant statistical difference in RBCs, hemoglobin and hematocrit content among studied groups (P>0.05). **Table (4),** showed that there was a highly statistical significant according to white blood cells (WBCs) count, neutrophils count among exacerbated COPD group, while in stable COPD patients group there was statistical significant difference according to lymphocytes increase. **Table (5),** showed that their was a statistical significant difference according to mean Platelet count and highly statistical significant difference according to mean MPV in both groups. **Table (6),** showed the Outcome results among AECOPD patients, where 84% of patients were improved **,** 12% were complicated and 4% were died. **Table (7),** showed that there was no significant Correlation between platelets count and Quality of life in COPD patients (QOL) by CAT score; **Table (8),** shoed that there was no significant correlation between platelets count in exacerbated patients (group B) regarding spirometric pulmonary function parameters (FVC, FEV_1 , FEV_1/ FVC and FEF 25-75). **Table (9),** showed the Validity of MPV cutoff value, which the Sensitivity was 76.0%, Specificity was 80.0%, +VE predictive was 79.1%, -VE predictive was 76.9% and the accuracy was 78.0%.

Fig. (1) showed that the cutoff value < 9.4 fl with highly Significant area under-curve (P=0.00) and highly significant association and agreement between MPV cutoff values < 9.4 fl and COPD exacerbation with (P=0.00).

Table (1):Demographic characteristics of the studied patients

Variables	**AECOPD (n = 25)**		**Stable COPD (n = 25)**		t-test	p-value
Age (Mean ± S.D)	61.36±8.29		60.44±13.82		0.285	0.77
Sex:	n	%	n	%	**χ2**	**p-value**
Male	18	72%	13	52%		
Female	7	28%	12	48%	2.12	0.14
Smoking						
Ex-smokers	3	12%	4	16%	6.9	0.07
Non-smokers	10	40%	10	40%		
Passive smokers	2	8%	3	12%		
Current smokers	10	40%	8	32%		

Table (2): ABG and Electrolytes in both groups (n=25 for each group)

	Group	Mean	S.D	t	P
pH	A	**7.3**	**.05**	**-2.75**	**0.002***
	B	**7.4**	**.12**		
$PaCO_{2*}$	A	**48.3**	**11.64**	**2.18**	**0.041***
	B	**41.2**	**11.34**		
SO_2	A	**83.6**	**12.43**	**-2.044**	**0.045***
	B	**92.32**	**4.2**		
PaO2	A	**52.64**	**7.7**	**-2.007**	**0.047***
	B	**59.7**	**11.1**		
HCO_3	A	**23.2**	**4.86**	**-2.33**	**0.031***
	B	**28.84**	**3.65**		
Na^+	A	**140.6**	**8.94**	**1.09**	**0.280**
	B	**143.32**	**8.66**		
K^+	A	**3.4**	**0.5**	**0.67**	**0.502**
	B	**3.5**	**0.6**		
Calcium	A	**7.27**	**1.37**	**-2.4**	**0.028***
	B	**8.8**	**0.94**		

pH: Arterial acid-base, PaCO2: Partial pressure of carbon dioxide in arterial blood, **SO2**: Oxygen saturation in peripheral blood, **PaO2**: Partial pressure of oxygen in arterial blood, HCO3: Bicarbonate, Na+: Sodium , K+: potassium.

Table (3): Red blood cell count and different parameters of heamoglobin in AECOPD and stable COPD groups (n=25 for each group)

	Group	Mean	S.D	t/ Mann Whitney	P
RBCs	A	**5.00**	**0.65**	**0.811**	**0.422**
	B	**4.84**	**0.72**		
HCT	A	**41.45**	**6.83**	**0.371**	**0.712**
	B	**40.76**	**5.90**		
Hb	A	**13.19**	**2.01**	**0.430**	**0.669**
	B	**12.94**	**2.01**		
MCV	A	**83.02**	**6.83**	**-1.308**	**0.198**
	B	**85.89**	**8.15**		
MCH	A	**26.47**	**3.24**	**-1.623**	**0.112**
	B	**28.12**	**3.68**		
MCHC	A	**31.91**	**2.88**	**-0.966**	**0.339**
	B	**32.70**	**2.72**		

RBCs: Red blood cell count**, HCT:** Hematocrit**, Hb:** Hemoglobin **, MCV:** Mean corpuscular volume**, MCH:** Mean corpuscular hemoglobin**, MCHC:** Mean corpuscular hemoglobin concentration

Table (4):Hematological Inflammatory parameters in both groups (n=25 for each group)

	Groups	Mean ± S.D	t/ Mann Whitney	P
WBC(total)	A	**13.14 ± 3.87**	**3.16**	**0.0016***
	B	**10.35 ± 4.74**		
Neut	A	**11.02 ± 2.70**	**2.8**	**0.003***
	B	**8.23 ± 7.54**		
Mono	A	**0.76 ± 0.13**	**-0.6**	**0.565**
	B	**0.92 ± 0.58**		
EOS	A	**0.26 ± 0.11**	**-0.06**	**0.954**
	B	**0.27 ± 0.30**		
LYM	A	**2.13 ± 1.08**	**-2.15**	**0.036***
	B	**3.51 ± 1.88**		
ESR_1ST	A	**38.15 ± 13.69**	**2.9**	**0.003***
	B	**28.36 ± 15.43**		
ESR_2ND	A	**52.63 ± 16.85**	**4.1**	**0.00***
	B	**35.89 ± 14.95**		
CRP	A	**58.05 ± 15.89**	**12.28**	**0.00****
	B	**9.90 ± 14.66**		

WBC: white blood cells, Neut: neutrophils, Mono: monocytes, Eos: eosinophils, Lym: lymphocytes, ESR-1ST: erythrocyte cedimentation rate in first hour, ESR-2nd: erythrocyte cedimentation rate in second hour CRP: C- reactive protein

Table (5): Platelets count (per µl) **and Mean Platelet Volume** (fl) **in both studied groups**

	Group	**Mean**	**S.D**	**t/ Mann Whitney**	**P**
Platelet count	A	**311.62**	**123.65**	**2.24**	**0.029***
	B	**243.0**	**87.63**		
MPV	A	**8.81**	**0.73**	**-4.34**	**0.00****
	B	**9.92**	**1.04**		

Table (6): Outcome among exacerbated COPD patients

Outcome	**AE COPD (n=25)**	
	n	%
Improved	21	84%
Complicated (ICU)	3	12%
Died	1	4%

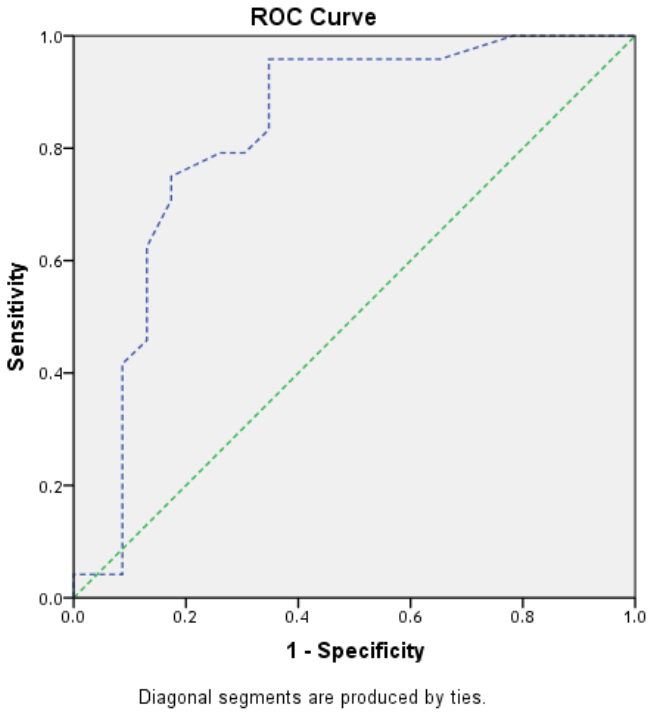

Fig. (1) :ROC Curve for detection of MPV cutoff value in exacerbated COPD patients

DISCUSSION

In the current study there were no significant statistical difference in RBCs, hemoglobin and hematocrit content among studied groups (P>0.05).On the other hand, **Weiss and Goodnough** [10] had explained that inspite of COPD is accompanied with low PO2 with compensatory increase in RBC content, but some patients presented with anaemia due to presence of inflammatory cytokines which play a significant role in producing a picture of anemia of chronic disease (ACD).

Also, in this study a highly statistical significant increase in white blood cells (WBCs) count, neutrophils count were found among exacerbated COPD group, while lymphocytes shows significant statistical increase among stable COPD group and this matched with the study of **Agapakis et al.** [11] who stated that levels of WBC count and and neutrophil percent increased significantly the exacerbation period of COPD, than in the period of stable disease .

A main finding in this study is a significantly lower MPV values in patients with AECOPD than in stable COPD (p<0.00). It is widely known that this may be due to systemic inflammation observed during an exacerbation of COPD, overproduction of inflammatory mediators as CRP, tumor necrosis factor-α and other proinflammatory cytokines takes place this is coincide with studies of **Wedzicha et al.** [12] and **Dentener et al.** [13].

In contrast with **Zhang et al.,** [14] results, they found that MPV is correlated negatively with predicted FEV_1 % and FEV_1/FVC in the stable COPD patients than healthy control. **Cui et al.,** [15] reported that the correlation between MPV and predicted FEV_1 was significantly negative (P= 0.0001), suggesting that severe obstruction had higher MPV. This was stated in stable COPD patients rather than during exacerbation.

In this study there was a significantly positive correlation between value of MPV and spirometric pulmonary function parameters FEV_1 (P= 0.001), FEV_1/ FVC (P= 0.003), and FEF 25-75 (P= 0.004). They found that there was an negative correlation between MPV value and the predicted FEV_1 % and FEV_1/FVC in the exacerbated patients than stable COPD (control group). MPV and predicted FEV_1 (P= 0.0001), suggesting increasing the MPV values in the exacerbated COPD patients.

Bruno and Valenti [16] stated that respiratory acidosis due to hypercapnia is a common and severe complication observed in patients with chronic obstructive pulmonary disease in advanced phase. Development of acidosis worsens the prognosis and is associated with higher mortality rate, while in the present study there were no statistical significant differences in electrolyte except for calcium level (P< 0.05) where it was decreased in AECOPD group, which may be referred to malnutrition.

The present work illustrated in fig. (1) showed that the cutoff value < 9.4 fl with highly Significant area under-curve (P=0.00) and highly significant difference between MPV cutoff values < 9.4 fl and COPD exacerbation with (P=0.00). With 76.0% Sensitivity, 80% Specificity and 78% accuracy of MPV at <9.4 fl in predicting COPD exacerbation, +ve predictive 79.1% and -ve predictive 76.9%. The mean platelet volume levels were significantly lower in the exacerbation period compared with stable COPD (P = 0.001). **Ragulan et al.,** [17] reported that there was an statistical significant difference between exacerbated COPD patients with MPV (P=<0.0001) and Distribution of Red Cell (P=<0.0001).

CONCLUSION

MPV is an easily accessible low cost marker of inflammation in AECOPD. Decreased MPV values can be used as indicator for negative acute-phase reaction in the exacerbated COPD patients. Cut off-point of MPV<9.4 fl can be used as a threshold mean of bad outcome

Declaration of interest :
The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.
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