Original Research Article

The Diagnostic Utility of Mean Platelet Volume as a Marker of Pulmonary Hypertension in COPD Patients

Abstract

Background: Chronic Obstructive Pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide that induces an economic and social burden.The aim of this work was to assess mean platelet volume (MPV), as a marker of platelet activation, predicting pulmonary hypertension (PAH) in COPD patients and its correlation with severity of PAH.

Methods: This prospective observational control cross-sectional study was carried out on 80 subjects who divided in to three groups: Group I: 30 mild to moderate COPD patients, group II: 30 severe COPD patients and group III (control): included 20 healthy age-matched individuals. All patients were subjected toradiological investigation (chest x-ray (PA) and CT chest), spirometry, transthoracic echocardiography and laboratory investigations [CBCand MPV].

Results: The best cut-off value of MPV in diagnosis of moderate PH is ≥9.65 to <9.95 fL with area under curve 0.922, sensitivity 90.5%, specificity 63.6%, Positive predictive value 35.1%, negative predictive value 94.4% and accuracy 68.8%. The best cut-off value of MPV in diagnosis of severe PH is ≥9.95 fL with area under curve 0.968, sensitivity 92.9%, specificity 75.6%, positive predictive value 63.3%, negative predictive value 97.7% and accuracy 80.3 %.

Conclusions:MPV was increased in COPD patients who developed PAH. MPV was positively correlated with severity of PAH.

Keywords: Diagnostic Utility, Mean Platelet Volume, Pulmonary Hypertension, COPD Patients

Introduction:

Chronic Obstructive Pulmonary Disease (COPD) is a prevalent, preventable, and treatable disease that is characterised by persistent respiratory symptoms and flow of air restriction due to airway and/or alveolar abnormalities that are typically caused by significant exposure to noxious particles or gases [1]. COPD is the largest cause of death and morbidity in the globe, resulting in a significant economic and social cost[2].

Morbidity from COPD may be affected with concomitant chronic conditions (e.g., cardiovascular disease) that may significantly impair patient's health status [3]. The incidence of pulmonary hypertension (PAH) in COPD is estimated to be 20 – 91%, pulmonary thrombosis is reported in 25% of COPD patients that may be due to platelets activation [4].

Platelets play an important role in several systemic inflammatory conditions by secreting different cytokines and mediators that regulate activation of immune cells and their adhesion to the endothelial barrier, thus presenting an active role in the modulation of inflammatory immune responses [5]. Mean Platelet Volume (MPV) is a reasonably easy and affordable instrument for determining the platelet size and platelet production rate in bone marrow. It shows platelet activity and inflammation intensity, as inflammation plays a crucial role in COPD[6].

Platelets are involved in PAH pathophysiology by different mechanisms of action; endothelial dysfunction, inflammatory cytokines release, The generation of serotonin was responsible for the aggregation of neutrophils, which resulted in multiple cycles of the inflammatory process[7].

The aim of this work wasto assess MPV, as a marker of platelet activation, predicting PAH in COPD patients and its correlation with severity of PAH.

Patients and Methods:

This prospective observational control cross-sectional study was carried outon 80 subjects at Chest Department, Tanta University and Kafr El- Sheikh Chest Hospitals, during the period from August 2019 till October 2021.

The study was done after approval from the Ethical CommitteeTanta University.An informed written consent was obtained from all patients 'relatives or legal representatives.

Exclusion criteria were acute exacerbations and systemic corticosteroids during the previous 8 weeks, haematological disorders, pulmonary embolism, malignancies, peripheral arterial diseases, heart diseases, respiratory, heart, hepatic and renal failure.

Subjects were divided in to three groups: Group I: 30 mild to moderate COPD patients, group II: 30 severe COPD patients and group III (control): included 20 healthy age-matched individuals. All patients were subjected to full history taking, clinical examination, radiological investigation (chest x-ray (PA) and CT chest), spirometry, transthoracic echocardiography andlaboratory investigations [CBC: including TLC, PLT, HG and MPV].

Spirometry

It was carried out using (Masterscreen 2011, Enrich Jaeger GMBH, Germany). which gives the actual value, FEV1, FVC, FEV1%.

First, prepare patients to closure his nose by clip and make sure about patient's lips to be sealed around mouthpiece, sitting position with head slightly elevated. The patient asked to inhale completely and rapidly with a pause of < 1 s followed by forced and rapid exhalation until no more air is expelled in about 6sc., repeated this manoeuvre for minimum three times, the highest value was recorded. Also, the difference between the two highest FEV1 readings should be around 150 mL. This test typically takes less than 10 minutes but will take around 30 minutes if reversibility testing is included.

Measuring pulmonary mechanics identifies airway blockage by determining the capacity of the lungs to rapidly transport large quantities of air across the airways.

Transthoracic echocardiography

It’s performed while the patient is lying either on his side or his back, depending on what kind of pictures need to be taken. The patient needs to undress from the waist up. An ultrasound technician will place some gel on the chest. The technician attachedelectrodes to patient's chest. The technician moved a transducer back and forth on the chest to record the sound waves of patient's heart as an image. The patient may be asked to breathe or move in a certain way.

Mean platelet volume:

As part of a CBC, a sample is collected in a Lavender-Top EDTA tube. The volume of platelets has been determined using three distinct methods in normal laboratories [8]. Coulter's theory is the foundation for the electrical impedance approach. When a diluted suspension of cells passes through a tiny aperture, the resistance of the electrical current between two electrodes on opposite sides of the aperture is momentarily altered by each cell. Due to the fact that electrical impedance is proportional to the volume of the particle through the aperture, this technique may determine cell size and count. The inability of cell size analysis to distinguish between big platelets and other similarly sized particles, such as tiny or fragmented red cells, is a significant limitation of the impedance approach.

In the optical approach, a diluted blood sample passes through the sensing zone, where a laser light beam is concentrated. At a given angle (one-dimensional) or two specific angles (two-dimensional), scattered light is detected and transformed into an electric impulse. The number of impulses produced is related to the number of cells and their volume [9]. Optical fluorescence, which was recently introduced on Sysmex analysers, is the third and newest method for measuring platelet count and platelet volume. This method uses a polymethine dye to stain platelets and simultaneously count fluorescent platelets. Even for platelet

transfusion, the optical fluorescence count is more accurate at low platelet counts and more suited for clinical decision-making [10].

Various anticoagulants and reagents are utilised to reduce in vitro preanalytical activation [11]. After two hours of blood drowning, Hompson et al. found K3EDTA to be a reliable anticoagulant for evaluating MPV, but Na-citrate proved unreliable [12].

MPV may be tested in sodium citrate (at a v/v ratio of 1:4 with blood) with more accuracy and repeatability than in EDTA. In addition, these measurements are not affected by incubation time, unlike EDTA. In the first two hours, MPV increased in blood taken with K3EDTA, however sodium citrate proved unreliable for measuring MPV. The International Council for Standardization in Haematology recommends K3EDTA as the anticoagulant of choice for full blood count.

Statistical analysis

Statistical analysis was performed using SPSS version 25 (IBM Inc., Chicago, IL, USA).

Results:

There was no statistically significant difference between the studied groups regarding age, gender, and smoking index. There was statistically significant difference between the studied groups regarding smoking (P =0.001).

Table 1: Statistical comparison of age, gender, smoking, and smoking indexin the studied groups

	Mild to moderate COPDgroup (I)(N=30)	SevereCOPD Group(II)(N=30)	Healthy control group(III) (N=30)	P value
Age (year)	62.57 ± 6.72	65.97 ± 8.96	62.95 ± 6.81	0.19
Gender: Male Female	 27 (90%) 3 (10%)	 26 (86.7%) 4 (13.3%)	 13 (65%) 7 (35%)	0.075
Smoking	20 (66.7%)	24 (80%)	0 (0%)	0.001* P1 =0.243 P2 =0.001* P3=0.011*
Smoking index	25.85 ± 7.69	27.21 ± 4.23	----	0.401

Data are presented as mean ± SD or frequency (%).

FEV1, FVC, FEV1/FVC (FEV1%), presence of PAH, PASP were statistically significant difference between the studied groups (P <0.001). FEV1, FVC, FEV1/FVC (FEV1%) and presence of PAH were significantly lower in group II when in comparison to group I and group III (P<0.05) and it was significantly lower in group I when in comparison to group III (P3 <0.001). PASP was significantly higher in group II when in comparison to group I (P1= 0.033) and group III and was significantly higher in group I when in comparison to group III (p3<0.001). Table 2

Table 2: Statistical comparison of FEV1, FVC, presence of pulmonary hypertension, severity of pulmonary hypertension in the studied groups

		Mild to moderate COPD group (I)(N=30)	Severe COPD group (II)(N=30)	Healthy control group (III) (N=30)	P value
FEV1 (L)		1.89 ± 0.71	1.51 ± 0.42	3.51 ± 1.11	<0.001* P1 =0.123 P2 <0.001* P3 <0.001*
FVC (L)		2.79 ± 0.71	2.58 ± 0.74	4.24 ± 1.14	<0.001* P1 =0.596 P2 <0.001* P3 <0.001*
FEV1/FVC (FEV1%)		66.12 ± 9.82	46.0 ± 8.61	87.55± 4.95	<0.001* P1 <0.001* P2 <0.001* P3 <0.001*
Pulmonary HTN	**Absent**	0 (0%)	0 (0%)	20 (100%)	<0.001*
	Mild	17 (56.7%)	8 (26.7%)	0 (0%)	
	Moderate	7 (23.3%)	14 (46.7%)	0 (0%)	
	Severe	6 (20%)	8 (26.7%)	0 (0%)	
PASP		51.97 ±14.81	59.13±14.43	20.3 ± 2.87	<0.001* P1 =0.033* P2 <0.001* P3 <0.001*

Data are presented as mean ± SD or frequency (%)

Hb, platelet count, TLC, MPV were statistically significant difference between the studied groups (P<0.05). It was significantly higher in group II when in comparison to groups I and group III. Group I showed increase in platelet count and MPV when in comparison to group III (P3 <0.001).COPD groups showed a significant increase in TLC count more than healthy control group. Table 3

Table 3: Statistical comparison of haemoglobin, platelet count and TLC, in the studied groups

	Mild to moderate COPDgroup (I)(N=30)	SevereCOPD group (II) (N=30)	Healthy control group(III) (N=30)	P value
Hemoglobin	13.81 ± 1.62	14.65 ± 1.41	12.84 ± 1.51	0.004* P1 =0.001* P2 =0.036* P3 =0.038*
Platelet	324.1 ± 134.88	395.53±102.21	196.60 ± 48.05	<0.001* P1 =0.011* P2 <0.001* P3 <0.001*
TLC	9.69 ± 2.15	9.59 ± 2.48	7.69 ± 2.22	0.006* P1 =0.9841* P2 =0.015* P3 =0.01*
MPV	9.92 ±1.34	10.65 ± 1.27	8.4 ± 0.82	<0.001* P1 =0.031* P2 <0.001* P3 <0.001*

Data are presented as mean ± SD or frequency (%)

There was positive significant correlation between MPV and severity of pulmonary hypertension(PAH). There was negative correlation between MPV and FEV1% (when FEV1% decreased, MPV increased). Table 4

Table 4: Correlation between Mean Platelet Volume and (severity of PH and FEV1%)

	Mean Platelet Volume	
	r	**p**
Severity of Pulmonary Hypertension	0.853	0.001*
FEV1 %	-0.520	0.001*

The best cut-off value of MPV in diagnosis of moderate PH is ≥9.65 to <9.95 fL with area under curve 0.922, sensitivity 90.5%, specificity 63.6%, positive predictive value (PPV) 35.1%, negative predictive value (NPV) 94.4% and accuracy 68.8%. The best cut-off value of MPV in diagnosis of severe PH is ≥9.95 fL with area under curve 0.968, sensitivity 92.9%, specificity 75.6%, PPV 63.3%, NPV 97.7% and accuracy 80.3 %.Figure 1

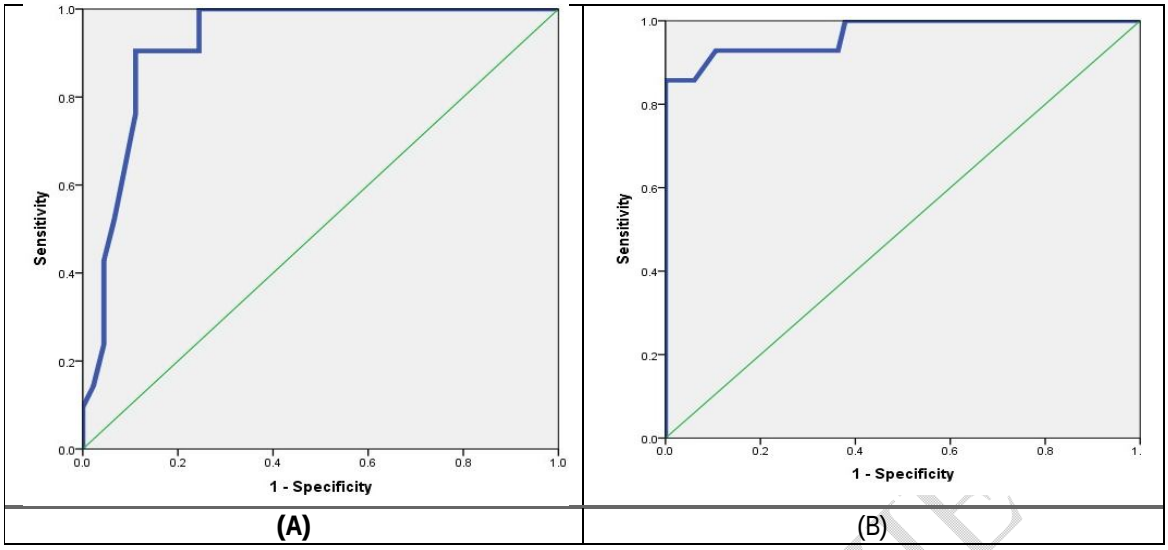

Figure 1: ROC curve showing Performance of MPV in diagnosis of(A) moderate pulmonary hypertension(B) severe pulmonary hypertension among the studied participants

Discussion

Chronic obstructive pulmonary disease (COPD) is a progressive and permanent inflammation of the airways that causes a persistent restriction of airflow. Depending on the severity of the disease and the frequency of the inflammatory response, it is also associated with several side effects[13].

In this study, there is statistically significant difference between the studied groups regarding MPV (highest in severe COPD group and lowest in healthy control group).Our results were in agreement with study of Mohamed et al., [14] as they reported that their study examined the MPV and its correlation with COPD severity grades, it was established that the MPV was significantly increased by increasing the severity of COPD.

However, in the research by Helmy et al. [15], the MPV values for patients with acute exacerbation of COPD, smokers, and the controls were 8.34, 9.28, and 9.12 fl, respectively. The MPV values of patients with acute exacerbation were substantially lower than those of smokers and controls. In terms of the presence and severity of PAH, our findings revealed statistically significant differences between the analyzed groups.No one within control group

had PAH. Severe PAH occurred in 20% and 26.7% of those with mild/moderate and severe COPD group respectively.

Our results showed that there is statistically significant difference between the studied groups regarding presence and severity of PAH. No one within control group had PAH. Severe PAH occurred in 20% and 26.7% of those with mild/moderate and severe COPD group respectively.

A higher prevalence was reported by the study of Mohamed et al.,[14] as they reported a 63% prevalence of PH in the studied COPD patients, mild PH represented 33%, while moderate and severe PH represented 15% each.

The present study showed that there is statistically significant positive correlation between MPV and both presence and severity of PAH. The difference is significantbetween each two individual groups. Mean MPV in patients with no PAH and in mild, moderate and severe PH were 8.4, 9.18, 10.34 and 12.06 respectively.

Malerba et al. [16] found in a retrospective analysis of 478 COPD patients and 72 healthy controls that the MPV in COPD patients was considerably greater than in the control group. This research also found that MPV rose with illness severity and that MPV 10.5 was connected with at least one cardiovascular disease. There is a significant statistical positive correlation between the severity of PAH and the MPV in this investigation. Our results showed that using ROC curve, the best cut-off value of MPV in diagnosis of moderate PH is ≥9.65 to <9.95 fL with area under curve 0.922, sensitivity 90.5%, specificity 63.6%, PPV 35.1%, NPV 94.4% and accuracy 68.8%. The best cut-off of MPV in diagnosis of severe PH is ≥9.95 fL with area under curve 0.968, sensitivity 92.9%, specificity 75.6%, PPV 63.3%, NPV 97.7% and accuracy 80.3%.

In this study, there is statistically significant positive correlation between severity of PAH and MPV Our results showed that using ROC curve, the best cut-off value of MPV in

diagnosis of moderate PH is ≥9.65 to <9.95 fL with area under curve 0.922, sensitivity 90.5%, specificity 63.6%, PPV 35.1%, NPV 94.4% and accuracy 68.8%.The best cut-off of MPV in diagnosis of severe PH is ≥9.95 fL with area under curve 0.968, sensitivity 92.9%, specificity 75.6%, PPV 63.3%, NPV 97.7% and accuracy 80.3%.

Limitations: The sample size was relatively small. The study was in a single centre.

Conclusions:

MPV was increased in COPD patients who developed PAH. MPV was positively correlated with severity of PAH.

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