



The Role of Mean Platelet Volume as a Predictor of Mortality in Mechanically Ventilated Patients

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

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List of Contents

Title	Page No.
List of Tables.....	5
List of Figures	7
List of Abbreviations.....	9
Introduction	- 1 -
Aim of the Work	13
Review of Literature	
📖 Physiology of Platelets	14
📖 Mean Platelet Volume in Health and Disease	37
📖 Mechanical Ventilation	43
📖 Role of Mean Platelet Volume as A Predictor of Mortality in Ventilated Patients	59
Patients and Methods.....	63
Results.....	70
Discussion	88
Summary.....	98
Conclusion and Recommendations.....	102
References	103
Arabic Summary	--

List of Tables

Table No.	Title	Page No.
Table (1):	Platelet receptors recruitment, adhesion, and aggregation	25
Table (2):	Platelet receptors in the amplification in phase	26
Table (3):	Platelet receptors in the stabilization phase and in the negative regulation of platelet activation.....	27
Table (4):	Comparison between the studied groups regarding demographic characteristics	70
Table (5):	Comparison between the studied groups regarding special habits	71
Table (6):	Comparison between the studied groups regarding comorbidities	72
Table (7):	Comparison between the studied groups regarding diagnosis	73
Table (8):	Distribution of the studied patients according to past history	75
Table (9):	Distribution of the studied patients according to signs	76
Table (10):	Comparison between the studied groups regarding vital signs	77
Table (11):	Distribution of the studied patients according to x ray findings.....	78
Table (12):	Distribution of the studied patients according to ECG findings	79
Table (13):	Distribution of the studied patients according to ECHO findings	80
Table (14):	Comparison between the studied groups regarding CBC findings	81
Table (15):	Comparison between the studied groups regarding MPV over time.....	82

List of Tables cont...

Table No.	Title	Page No.
Table (16):	Comparison between the studied groups regarding percent change of MPV over time	83
Table (17):	Comparison between the studied groups regarding liver and kidney function test	84
Table (18):	Comparison between the studied groups regarding ABG.....	85
Table (19):	Multivariate analysis of factors associated with mortality among mechanically ventilated patients.....	86
Table (20):	Correlation between platelet count and MPV over time among the studied patients	86
Table (21):	Correlation between TLC and MPV over time among the studied patients	87
Table (22):	Correlation between hemoglobin level and MPV over time among the studied patients	87

List of Figures

Fig. No.	Title	Page No.
Figure (1):	The three stages of platelet activation.	16
Figure (2):	Platelet-activation mechanisms and role of the P2Y ₁₂ receptor	20
Figure (3):	Mechanism of vascular changes by platelet-derived microparticles (PMPs)	31
Figure (4):	Pathway illustrating hemostasis.....	32
Figure (5):	Thromboxane biosynthesis pathway.	32
Figure (6):	After an injury in the vessel wall, activation of platelets begins to start.....	33
Figure (7):	Diagram illustrating the role of von Willebrand factor (vWf) in platelet adhesion.	33
Figure (8):	Schematic representation of the main functions of platelets.	36
Figure (9):	Platelets.....	37
Figure (10):	Possible factors affecting platelet size and its association with thrombosis and inflammation.	39
Figure (11):	Combined bar chart showing relation between patient outcome and comorbid hypertension and diabetes	72
Figure (12):	Combined bar chart showing comparison between the studied groups regarding diagnosis.	74
Figure (13):	Combined bar chart showing relation between patient outcome and history of ICU admission and MV.....	75

List of Figures *(Cont...)*

Fig. No.	Title	Page No.
Figure (14):	Combined bar chart showing relation between patient outcome and signs.....	76
Figure (15):	Combined bar chart showing relation between patient outcome and x ray findings.	78
Figure (16):	Combined bar chart showing relation between patient outcome and ECG findings.....	79
Figure (17):	Multiple line graph showing change in MPV over time among the studied groups.	82
Figure (18):	Combined bar chart showing percent change in MPV over time among the studied groups.....	83
Figure (19):	Simple bar chart showing comparison between the studied groups regarding PCO2. ...	85

List of Abbreviations

Abb.	Full term
AA	<i>Arachidonic acid</i>
ADP	<i>Adenosine diphosphate</i>
APACHE II	<i>Acute Physiology and Chronic Health Evaluation II</i>
ASV	<i>Adaptive support ventilation</i>
ATC	<i>Automatic tube compensation</i>
ATP	<i>Adenosine 5'-triphosphate</i>
CPAP	<i>Continuous positive airway pressure</i>
EDTA	<i>Ethylenediaminetetraacetic acid</i>
EMPs	<i>Endothelial cell-derived microparticles</i>
FiO₂	<i>Fraction of inspired oxygen</i>
FITC	<i>Fluorescein isothiocyanate</i>
GP	<i>Glycoprotein</i>
I: E	<i>Inspiratory to expiratory</i>
ICUs	<i>Intensive care units</i>
ITP	<i>Immune thrombocytopenic purpura</i>
MAPK	<i>Mitogen-activated protein kinase</i>
MGDF	<i>Megakaryocyte growth and development factor</i>
MPC	<i>Mean platelet component</i>
MPV	<i>Mean Platelet Volume</i>
NO	<i>Nitric oxide</i>
OCS	<i>Open canalicular system</i>
PAV	<i>Proportional assist ventilation</i>

List of Abbreviations (Cont...)

Abb.	Full term
<i>PCT</i>	<i>Plateletcrit</i>
<i>PCV</i>	<i>Pressure-controlled ventilation</i>
<i>PDW</i>	<i>Platelet distribution width</i>
<i>PE</i>	<i>Phycoerythrin</i>
<i>PEEP</i>	<i>Positive end-expiratory pressure</i>
<i>PKC</i>	<i>Protein kinase C</i>
<i>PLT</i>	<i>Platelet</i>
<i>PSV</i>	<i>Pressure Support Ventilation</i>
<i>RA</i>	<i>Rheumatoid arthritis</i>
<i>RDS</i>	<i>Respiratory distress syndrome</i>
<i>SIMV</i>	<i>Synchronized intermittent mandatory ventilation</i>
<i>SLE</i>	<i>Systemic lupus erythematosus</i>
<i>TF</i>	<i>Tissue factor</i>
<i>THPO</i>	<i>Thrombopoietin</i>
<i>TXA₂</i>	<i>Thromboxane A₂</i>
<i>VC</i>	<i>Volume-cycled</i>
<i>vWf</i>	<i>von Willebrand factor</i>

INTRODUCTION

Mechanical ventilation is frequently used for life support in intensive care units (ICUs). When initial attempts of spontaneous breathing fail to achieve the goal of liberation from mechanical ventilation, clinicians must choose appropriate mode(s) of ventilatory support. Different ventilatory modes may be used during weaning from mechanical ventilation. The most common ones are: pressure support ventilation (PSV), synchronized intermittent mandatory ventilation (SIMV), continuous positive airway pressure (CPAP) and spontaneous breathing with a T-tube. But, there are other modes which have a role in weaning process such as automatic tube compensation (ATC), proportional assist ventilation (PAV), servocontrolled ventilation and adaptive support ventilation (ASV) (*Krmpotic and Lobos, 2013*).

Mean Platelet Volume (MPV) is a reflection of both proinflammatory and prothrombotic conditions, where thrombopoietin and numerous inflammatory cytokines regulate thrombopoiesis. MPV is higher when there is destruction of platelets. This may be seen as in inflammatory bowel disease, and in immune thrombocytopenic purpura (ITP), and in myeloproliferative diseases and Bernard-Soulier syndrome. It may also be related to pre-eclampsia, and recovery from transient hypoplasia (*Liu et al., 2012*).

Ye et al. (2018) investigated platelet volume indices and in-hospital mortality in children on mechanical ventilation. They revealed that risk factors for mortality in critically ill children may differ at different ages. Increased lactic acid levels appear to be the main risk factor for mortality in all critically ill children, and platelet count was found to be associated with mortality in patients aged >3 years only.

AIM OF THE WORK

To compare whether there is an association between MPV and mortality in mechanically ventilated patients as regard:

- What is the mechanical ventilation?
- What is the mean platelet volume (MPV)?
- Association between them.

Chapter 1

PHYSIOLOGY OF PLATELETS

Platelets were discovered by Giulio Bizzozero in 1882, but for many decades the dynamic and multifunctional nature of platelets remained a field of interest only for biologists. Anucleate, discoid platelets are the smallest blood particles which unveil their dynamicity through their morphology (*Ribatti and Crivellato, 2007*).

Primarily they are associated with hemostasis, which is to initiate blood coagulation. Although very dynamic, they usually prefer to remain in inactive state and get activated only when a blood vessel is damaged. But hemostasis or blood coagulation is not the sole function of platelets; rather it is employed in several multifunctional attributes monitoring the homeostasis of the body. Its high sensitivity to different disease states eventually assigned it to be one of the most accessible markers. While keeping interactions with leukocytes and endothelial cells, it restores its behaviour as an important inflammatory marker (*Cerletti et al., 2012*).

Platelet reactivity for different disease pathogenesis is widely dependent upon some biologically active markers like CD36, CD41, CD42a, CD42b, and CD61. These include some active surface receptors and platelet secretory products. Platelet

tends to alter the expression and signaling of these markers in different disease diagnosis and prognosis, providing a huge field to explore disease progression.

Primarily, platelet activity is associated with the initiation of coagulation cascades. Damage in blood vessel makes the subendothelial surface the primary target site of platelet action, where it establishes the hemostasis. Various proaggregatory stimuli also known as platelet agonists promote the action of platelet adhesion to the subendothelial surfaces. During this process, platelet changes its shape, releases its granule contents, and gradually forms aggregates by adhering with each other. Thus its primary activity remains associated with minimizing blood loss. However, as discussed earlier platelets are not only confined in regulating hemostasis and thrombosis, but they also play many pivotal roles in disease pathophysiology (*Vinik et al., 2001*).

Platelet interaction and cardiovascular disease progression remain an unsolved riddle for many years. Platelet hyperaggregation among the diabetic patients with CVD remains another striking area to explore. Platelet hyperactivity in various diseases provokes adverse effects in some cases, especially in coronary artery disease where hyperaggregation obstructs blood circulation. Expression of platelet markers can be well studied by ELISA or Western blot. However, till date flow cytometry is the best standardized method to study platelet function (*Sharma and Berger, 2011*).