## Evaluation of von Willebrand factor as a Marker For early diagnosis of Acute Respiratory Distress Syndrome (A.R.D.S) in comparison to Interleukin 6

Thesis Submitted for Partial Fulfillment of MD Degree in general Intensive care medicine

By

#### Samar Ibrahem Mahmoud Aimer

M.B. B.Ch., M. Sc intensive care Faculty of Medicine, Ain Shams University

# Supervised By

## Prof. Mohammed Abd El Khalek Mohammed Ali

Professor of Anesthesiology and General Intensive Care medicine Faculty of Medicine, Ain Shams University

### Assist. Prof. Ehab Hamed Abd El-Salam

Assistant Professor of Anesthesiology and General Intensive Care medicine Faculty of Medicine, Ain Shams University

#### Dr. Walid Abdallah Ibrahem

Lecturer of Anesthesiology and General Intensive Care medicine Faculty of Medicine, AinShams University

### Dr. Dalia Mahmoud Ahmed El Fawy

Lecturer of Anesthesiology and General Intensive Care medicine Faculty of Medicine, AinShams University

# 2016

فَالُوا سُبْحَانَك لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْنَنَا إِنَّكَ أَنتَ الْعَلِبِمُ الْحَلِبِمُ صرق الله العظيم سورة (لبقرة (لآية (32)



I would like to express my sincere gratitude to **Prof. Mohammed Abd el Khalek Mohammed Ali** Professor of Anesthesiology and general Intensive Care medicine, Ain Shams University Faculty of Medicine, for his continuous support and guidance for me to present this work. It really has been an honor to work under his generous supervision.

I acknowledge with much gratitude to Dr. Ehab Hamed Abd El-Salam Assistant Professor of Anesthesiology and general Intensive Care medicine, Ain Shams University Faculty of Medicine for his great supervision, efforts and unlimited help to provide all facilities in the whole work.

My deepest appreciation is to Dr. Walid Abdallah Ibrahem, and Dr. Dalia El Fawy Lecturers of Anesthesiology and general Intensive Care medicine, Faculty of Medicine, Ain Shams University for their kind advices and great efforts throughout this work they never ending determination to bring the best out of this work.

Samar Ibrahem Mahmoud aimer

# Dedication

To soul of my father, who didn't deprive me his pray for the length of his life

To every patient who may need my help

Samar ibrahem mahmoud aimer

# Content

List of Content	Ι
List of Abbreviations	II
List of Tables	VI
List of Figures	IX
Introduction	1
Review of literature :	
Chapter 1 : Physiological Respiratory	
Considerations	4
Chapter 2: Clinical bases of A.R.D.S	14
Chapter 3:Biomarkers of A.R.D.S	50
Patients and methods	65
Results	75
Discussion	118
Recommendation	132
References	133
English summary	
Arabic summary	

#### Abbreviations

- ADAMTS : A Disintegrin And Metalloproteinase with Thrombo Spondin
- **AECC** : American European Consensus Conference
- ALVEOLI trials: Assessment of Low Tidal Volume and Elevated End-Expiratory Pressure to Obviate Lung Injury
- **APC** : Activated protein C
- **APRV** : Airway pressure-release ventilation
- **ARDS** : Acute respiratory distress syndrome
- **ARM** : Alveolar recruitment maneuvers.
- **ATI** : Type I pneumocytes
- **ATII** : Type II pneumocytes
- **AUC** : Area under the curve
- **BALF** : Broncho -alveolar lavage fluid
- **BIPAP** : Bi-level positive airway pressure
- **CAPs** : Channel activating proteases

- **COP** : Critical opening pressure
- **CPAP** : Continuous positive airway pressure
- **CPS** : Child Pugh score
- **DAD** : Diffuse alveolar damage-
- **ECMO** : Extracorporeal membrane oxygenation
- **ENaC** : Epithelial sodium channel
- **EVLW** : Extra-vascular lung water
- **GMCSF** : Granulocyte-macrophage colony stimulating factor
- **GP Ib, IIb** : Glycol protein Ib, IIb.
- **HARP study** : Hydroxymethylglutaryl-CoA reductase inhibition with simvastatin in Acute lung injury to Reduce Pulmonary dysfunction
- **HFOV** : High-frequency oscillatory ventilation),
- HMGB1 : High Mobility Box-1 protein
- **HMGB-1** : Mobility group box-1 protein
- **ICAM-1** : Intercellular adhesion molecule-1
- **IIT** : Intensive insulin therapy

IPAP	: inspiratory positive airway pressure
IPF	: interstitial pulmonary fibrosis
IRDS	: Infant respiratory distress syndrome
KL-6	: Krebs von den Lungen 6
LBP	: Lipopolysaccharide binding protein
LPVS	: Lung-protective ventilatory strategy
MELD	: Model for End-Stage Liver Disease
MMP	: Matrix Metalloprotease
MMP-9	: Metallo-proteinases
NIH	: National Institutes of Health
NIV	: Noninvasive ventilation
NMBs	: Neuromuscular blockers
NO	: Nitric oxide
PAI-1	: Plasminogen activator inhibitor-1
РСР	: Procollagen peptide
PCWP	: Pulmonary capillary wedge pressure
RAGE	: Receptor for advanced glycation end-products

- RMA : Respiratory Management in Acute Lung Injury/Acute Respiratory Distress Syndrome
  ROC curve : Receiver operating characteristic curve
  RR : Respiratory rate
  SPs : Surfactant proteins
  TFPI : Tissue factor pathway inhibitor
  TRALI : Transfusion related acute lung injury
- **VEGF** : Vascular endothelial growth factor
- **VILI** : Ventilator-Induced Lung Injury
- **VOCs** : Volatile organic compounds
- **VWF** : Von Willebrand Factor

# List of Table

Table		Page
<b>Table (1):</b>	The Berlin definition of ARDS	15
Table( 2 ):	Underlying etiologies of pulmonary and extra	
	pulmonary acute respiratory distress	16
	syndrome	
<b>Table (3):</b>	Lung Injury Prediction Score calculation	
	worksheet	17
<b>Table (4):</b>	Average LIPS for patients with and without	
	the development of ARDS	18
<b>Table (5):</b>	Current therapeutic strategies available for	
	the management of patients with ARDS/ALI	24
table (6)	FIO2 and PEEP adjustment table in A.R.D.S	
	patients	27
<b>Table (7):</b>	Modalities to treat refractory hypoxemia in	
	Patients With ARDS	30
<b>Table (8):</b>	Advantages and disadvantages of each of the	
	components of airway pressure release	
	ventilation	34
<b>Table (9) :</b>	List of studied serum biomarkers in ARDS	56
<b>Table (10):</b>	Murray score of acute lung injury	68
<b>Table (11):</b>	Patients characteristics at day of enrollment	75
Table (12):	Comparison between the two groups as	