# Assessment of Hemodynamic Status and Perfusion Markers in Critically III Children with Septic Shock

#### Thesis

Submitted for partial fulfillment of Master Degree in Pediatrics

By

#### Mina Karem Khallaf

M.B.B.CH

Faculty of Medicine, Assuit University

Supervised by

### **Prof. Dr. Tarek Abdel Gawad**

Professor of Pediatrics
Faculty of Medicine – Ain Shams University

## **Prof. Dr. Mervat Gamal El-Din Mansour**

Professor of Pediatrics
Faculty of Medicine – Ain Shams University

# **Dr. Waleed Mohamed Elguindy**

Assistant Professor of Pediatrics
Faculty of Medicine – Ain Shams University

Faculty of Medicine

Ain Shams University

2018

# Acknowledgments

First and foremost, I feel always indebted to Allah, the Most Beneficent and Merciful who gave me the strength to accomplish this work,

My deepest gratitude to my supervisor, **Prof. Dr. Tarek Abdel Gawad,** Professor of Pediatrics, Faculty of Medicine – Ain Shams University, for his valuable guidance and expert supervision, in addition to his great deal of support and encouragement. I really have the honor to complete this work under his supervision.

I would like to express my great and deep appreciation and thanks to **Dr. Mervat Gamal El-Din Mansour,**Professor of Pediatrics, Faculty of Medicine – Ain Shams University, for her meticulous supervision, and her patience in reviewing and correcting this work.

I must express my deepest thanks to **Dr. Waleed Mohamed Elguindy,** Assistant Professor of Pediatrics,
Faculty of Medicine – Ain Shams University for guiding me
throughout this work and for granting me much of his time. I
greatly appreciate his efforts.

Thanks a lot to all my professors and colleagues for their considerable care and support.

Mina Karem Khallaf

# **List of Contents**

Subject	Page No.
List of Abbreviations	i
List of Tables	ii
List of Figures	vii
Introduction	1
Aim of the Study	3
<b>Review of Literature</b>	
Sepsis and septic shock in pediatrics	4
Hemodynamic changes during sepsis	38
Lactate: An important biomarker of tissue perfusion in sepsis and septic shock	59
Patients and Methods	68
Results	80
Discussion	125
Summary	148
Conclusions	152
Recommendations	153
References	154
Arabic Summary	

#### **List of Abbreviations**

# Full-term

**ACCM**: American College of Critical Care Medicine

**AIDS** : Acquired immune-deficiency syndrome

**ALT** : Alanine transaminase

**BP** : Blood pressure

466r.

**COPD** : Chronic Obstructive Pulmonary Disease

**CRP** : C-reactive protein

**CT** : Computed Tomography

**CVP** : Central venous pressure

**ECG** : Electrocardiogram

**ED** : Emergency Department

**EF** : Ejection fraction (EF

**ESR** : Erythrocyte Sedimentation Rate

GIT : Gastrointestinal tract

**ICU** : Intensive care unit

**ILs**: Interleukins

iNOS : Inducible NOS

**MAP** : Mean arterial pressure

NO : Nitric oxide

**PAF** : Platelet-Activating Factor

PALS : Pediatric Advanced Life Support

**PICUs** : Pediatric intensive care units

**Pmx B** : Polymyxin B

**PSCC**: Pediatric Sepsis Consensus Congress

**RCTs** : Randomized control studies

**SD** : Standard deviation

**SIMD** : Sepsis-induced myocardial dysfunction

**SPSS** : Statistical Package for Social Sciences

**SvO2** : Venous oxygen saturation

**TNF**: Tumor Necrosis Factor

**WHO** : World Health Organization

# **List of Tables**

Table No.	. Title Page	No.
<b>Table</b> (1):	International Consensus Definitions for Pediatric Sepsis	5
<b>Table (2):</b>	Age-specific vital signs and laboratory variables	15
<b>Table (3):</b>	Pediatric organ dysfunction criteria	16
<b>Table (4):</b>	Antibiotic choice based on risk factors of sepsis	23
<b>Table (5):</b>	Vasopressor agents	26
<b>Table (6):</b>	Summary of cardiac effects of inotropes used in sepsis and shock.	27
<b>Table (7):</b>	Dempgraphic and clinical characteristics among the studied patients	80
<b>Table (8):</b>	Vital data among the studied patients	81
<b>Table (9):</b>	Serum lactate levels and lactate clearance among the studied patients	82
<b>Table (10):</b>	Hemodynamic measure among the studied patients (2/2)	83
<b>Table (11):</b>	Hemodynamic and respiratory support modalities among the studied patients	84
<b>Table (12):</b>	Length of PICU stay and mortality among the studied patients	85
<b>Table (13):</b>	Demographic and clinical characteristics of patients with sepsis and septic shock	87

<b>Table (14):</b>	Comparison between sepsis and septic shock patients regarding clinical scores 87
<b>Table (15):</b>	Comparison between sepsis and septic shock patients regarding source of infection
<b>Table (16):</b>	Comparison between sepsis and septic shock patients regarding vital data
<b>Table (17):</b>	Comparison between sepsis and septic shock patients regarding lactate
<b>Table (18):</b>	Comparison between sepsis and septic shock patients regarding hemodynamic measures (1/2)
<b>Table (19):</b>	Comparison between sepsis and septic shock patients regarding hemodynamic measures (2/2)
<b>Table (20):</b>	Comparison between sepsis and septic shock patients regarding hemodynamic and respiratory support modalities used
<b>Table (21):</b>	Comparison between sepsis and septic shock patients regarding length of PICU stay and mortality
Table (22):	Comparison between non-survivors and survivors regarding demographic and clinical characteristics
<b>Table (23):</b>	Comparison between non-survivors and survivors regarding clinical scores99
<b>Table (24):</b>	Comparison between non-survivors and survivors regarding source of infection 99

Comparison between non-survivors and survivors regarding vital data 100
Comparison between non-survivors and survivors regarding lactate
Comparison between non-survivors and survivors regarding hemodynamic measures (1/2)
Comparison between non-survivors and survivors regarding hemodynamic measures (2/2)
Comparison between non-survivors and survivors regarding hemodynamic and respiratory support modalities used
Correlations of COP among the studied patients
Correlations of CI among the studied patients
Correlations of SVRI among the studied patients
Correlations of EF among the studied patients
Correlations of EDVLV among the studied patients
Correlations of ESVLV among the studied patients
Correlations of IVC-Min among the studied patients
Correlations of lactate clearance among the studied patients

List of Table
---------------

<b>Table (38):</b>	Diagnostic performance in predicting non- survivorship	122
<b>Table (39):</b>	Diagnostic characteristics of lactate-24 ≥2.0 (mmoL/L) in prediction of death	124

# **List of Figures**

Figure No.	. Title	Page No.
Figure (1):	Diagram illustrating criteria for definitions sepsis and septic shock	
Figure (2):	ACCM/PALS algorithm for the man of pediatric septic shock	•
Figure (3):	Pathophysiology of septic sho secondary myocardial dysfunction	
Figure (4):	Direct myocardial depression in sepsis	s 53
•	Management of myocardial dysfur septic shock.	
Figure (6):	Pathway of glycolysis	62
<b>Figure (7):</b>	Diagnosis among the studied patient	s 80
Figure (8):	Mortality among the studied patients	8585
Figure (9):	Comparison between sepsis and separations regarding lactate	
	Comparison between sepsis and separation patients regarding cardiac output	
•	Comparison between sepsis and separation of the comparison o	
• , ,	Comparison between sepsis and separation of	
	Comparison between sepsis and separation separation SVRI	
<b>Figure (14):</b>	Comparison between sepsis and separations regarding EF%	
	Comparison between sepsis and septentients regarding EDVLV	

<b>Figure (16):</b>	Comparison between sepsis and septic shock patients regarding ESVLV
<b>Figure (17):</b>	Comparison between sepsis and septic shock patients regarding IVC-Max
<b>Figure (18):</b>	Comparison between sepsis and septic shock patients regarding IVC-Min
<b>Figure (19):</b>	Comparison between sepsis and septic shock patients regarding mortality
<b>Figure (20):</b>	Comparison between non-survivors and survivors patients regarding lactate
<b>Figure</b> (21):	Comparison between non-survivors and survivors regarding cardiac output
<b>Figure (22):</b>	Comparison between non-survivors and survivors regarding CI
<b>Figure (23):</b>	Comparison between non-survivors and survivors regarding SV
<b>Figure (24):</b>	Comparison between non-survivors and survivors regarding SVRI
<b>Figure (25):</b>	Comparison between sepsis and non- survivors and survivors regarding EF
<b>Figure (26):</b>	Comparison between sepsis and septic shock patients regarding EDVLV
<b>Figure (27):</b>	Comparison between sepsis and septic shock patients regarding ESVLV
<b>Figure (28):</b>	Comparison between sepsis and septic shock patients regarding IVC-Max
<b>Figure (29):</b>	Comparison between sepsis and septic shock patients regarding IVC-Min
<b>Figure (30):</b>	ROC curve for lactate-24 in predicting death 123

#### **Abstract**

#### **Abstract**

Background: Severe sepsis causes release of inflammatory mediators and an associated redistribution of intravascular volume together with depression of myocardial function which manifests as hemodynamic pattern of low cardiac output, low systemic vascular resistance, hypotension, hyperlactatemia and signs of altered tissue perfusion such as oliguria and prolonged capillary refill time. Aim of the Work: To assess hemodynamic status together with the perfusion markers (lactate) in critically ill children with septic shock. Patients and Methods: This single cohort study was conducted on 40 patients recruited from the pediatric intensive care units (PICU) at: Ain Shams university hospital, Al-Galaa Military medical complex and Ghamra Military hospital From December 2017 to August 2018. Results: Only four cases of cases with septic shock developed ejection fraction below 55% denoting myocardial dysfunction during the duration of assessment (first 24 hours of diagnosis). There was negative correlation between cardiac functions represented by hemodynamic measures on one side and SOFA score, PIM 2 score and serum lactate levels on the other side. However, by studying the performance of the parameters included in our study in predicting death; only lactate-24 ≥2.0 (mmoL/L) had statistically significant moderate diagnostic performance, other studied measurements had weak diagnostic performance. Conclusion: Myocardial dysfunction was found to be common in children having septic shock. Close monitoring and hemodynamic assessment is important to avoid missing these cases. In addition, serum blood lactate level is an important biomarker that should be carefully monitored as it is a good prognostic tool that can predict outcome in pediatric sepsis and septic shock.

**Key words:** hemodynamic status, perfusion, critically ill children, septic shock

#### Introduction

Sepsis is defined as life-threatening organ dysfunction due to dysregulated host response to infection (Abraham, 2016). Severe sepsis causes release of inflammatory mediators and an associated redistribution of intravascular volume together with depression of myocardial function which manifests as hemodynamic pattern of low cardiac output, low systemic vascular resistance, hypotension refractory to vasopressors, hyperlactemia and signs of altered tissue perfusion such as oliguria and prolonged capillary refill time which considered significant cause of pediatric morbidity and mortality (Mickiewicz et al., 2015).

The rapid determination of hemodynamic status would allow tailoring of vaso-active drugs in what is known to be dynamic situation. Determination of hemodynamic status is the best discriminator of survivors from non survivors in childhood sepsis (*Proulx et al.*, 2011).

Hence, determination of hemodynamic status includes monitoring of cardiac output and markers of perfusion. Cardiac output assessment is essential for

assessment of cardiac function to maintain adequate tissue perfusion (*Nusmeier et al.*, 2010).

The technology for cardiac output assessment should be non-invasive, accurate, rapid and compatible so, echocardiography has been widely used for cardiac output assessment due to its ability to provide non-invasive measurement with minimal discomfort or risk together with its portability, immediate availability and repeatability (*Larsen et al.*, 2011).

As regards perfusion markers, the inflammatory mediators of sepsis may worsen tissue hypoxia by increasing cellular oxygen demand, thereby altering the oxygen extraction and reducing myocardial contractility. Thus, an interrelation between sepsis and hypoxia may occur (*Jat et al.*, 2011).

Blood lactate levels supposed to reflect the magnitude of anaerobic metabolism related to cellular hypoxia. Blood lactate levels have been well correlated to survival forms of acute circulatory failure (*Munde et al.*, 2014). Blood lactate levels is the earliest discriminator of survival, survivors had an early reduction of lactate level and better lactate clearance (*Bai et al.*, 2014).

# **Aim of the Study**

To assess hemodynamic status together with the perfusion markers (lactate) in critically ill children with septic shock.