

ELECTROCARDIOGRAPHIC CHANGES IN SEPSIS AND SEPTIC SHOCK IN PEDIATRIC ICU

Thesis

*Submitted for Partial Fulfillment of Master Degree
(M.SC.) In Pediatrics*

By

Radwa Hassaan Mahmoud

MB.B.Ch (2010)

Ain Shams University

Under the Supervision of

Prof. Dr. Tarek Ahmed Abd El Gawad

Professor of Pediatrics

Faculty of Medicine, Ain Shams University

Dr. Marwa Moustapha Attia Al-Fahham

Lecturer of Pediatrics

Faculty of Medicine, Ain Shams University

Faculty of Medicine

Ain Shams University

2015

List of Contents

Title	Page No.
List of Tables	II
List of Figures	IV
List of Abbreviations	V
Introduction.....	1
Aim of the work	3
<u>Review of Literature</u>	
• <u>Chapter (1):</u> Sepsis an+d septic shock	4
• <u>Chapter (2):</u> Sepsis induced myocardial dysfuction.....	15
• <u>Chapter (3):</u> Sepsis - induced ECG changes	22
• <u>Chapter (4):</u> Management strategies of sepsis and septic shock.....	36
Patients and methods.....	55
Results	61
Conclusion	97
Recommendations.....	99
Summary.....	100
References.....	106
Arabic Summary	-

List of Tables

Table No.	Title	Page No.
Table (1):	Modified table showing the international pediatric sepsis consensus derived definitions for sepsis and organ dysfunction among children.....	5
Table (2):	Modified table showing criteria for multiple organ dysfunction.....	9
Table (3):	Modified table showing the parameters used in PRISM score.....	13
Table (4):	Antibiotic choice based on risk factors of sepsis.....	42
Table (5):	Age, weight and height distribution among cases:.....	61
Table (6):	Clinical causes of sepsis among study cases:.....	61
Table (7):	Causes of sepsis among cases.....	62
Table (8):	The most serious complications occurred among study cases:.....	63
Table (9):	Ventilation status among the study cases:.....	64
Table (10):	Risk of mortality by PRISM score among cases:.....	65
Table (11):	Lab data among study cases:.....	65
Table (12):	Lab data among study cases (cont.).....	65
Table (13):	Duration of ICU stay (days) and fate among study cases:.....	67
Table (14):	Echo finding among study cases:.....	68
Table (15):	Holter finding among study cases:.....	69
Table (16):	Holter finding among study cases (cont.):.....	71
Table (17):	Correlations between echo findings and PRISM score:.....	73
Table (18):	Relation between Holter findings and PRISM score:.....	75
Table (19):	Correlation between Holter findings and PRISM score (cont.).....	76

List of Tables cont...

Table No.	Title	Page No.
Table (20):	Correlation between echo findings and number of tachycardia by Holter:.....	78
Table (21):	Correlation between echo findings and number of bradycardia by Holter:	78
Table (22):	Correlation between echo findings and number of PVCs by Holter:	79
Table (23):	Correlation between echo findings and number of couplets by Holter:.....	81
Table (24):	Correlation between echo findings and number of triplets by Holter:	82
Table (25):	Correlation between echo findings and number of V-Tach by Holter:	85

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Synopsis of potential underlying mechanisms in septic myocardial dysfunction CAD.....	20
Figure (2):	Autonomic nervous system control of heart rate characteristics in sepsis (Fairchild et al., 2011)	27
Figure (3):	ACCM/PALS algorithm for the management of pediatric septic shock.....	40
Figure (4):	Sex distribution among cases.	62
Figure (5):	Percentage of DIC, renal failure and mechanical ventilation among cases.	64
Figure (6):	Comparison between levels of blood sugar, calcium, potassium and sodium levels among cases.	66
Figure (7):	Fate of the cases.....	67
Figure (8):	Heart rate and ST segment changes among patients.	70
Figure (9):	PVCs and supra ventricular tachycardia episodes among patients.....	72
Figure (10):	Bigeminy and trigeminy episodes among cases.	72
Figure (11):	Scatter diagram showing significant positive correlation between AO/LA and PRISM score in the patient subjects	74
Figure (12):	Scatter diagram showing significant negative correlation between AO and PRISM score in the patient subjects.	74
Figure (13):	Correlation between couplet episodes and mean PRISM score.	75
Figure (14):	Correlation between minimum heart rate and PRISM score.	77
Figure (15):	Correlation between PVC episodes and PRISM score.	77
Figure (16):	Correlation between AO/LA and number of PVC by holter.	80
Figure (17):	Correlation between LVIDd and number of PVC by holter.	80
Figure (18):	Correlation between AO/LA and number of couplet by Holter	82
Figure (19):	Correlation between AO/LA and number of triplet by Holter.	83
Figure (20):	Correlation between IVSs and number of triplet by Holter.	84
Figure (21):	Correlation between SV and number of triplet by Holter.....	84

LIST OF ABBREVIATIONS

Abb.	Meaning
AF	: Atrial fibrillation
ALT	: Alanine transaminase
AO	: Aortic annulus diameter in diastole
APACHE	: The acute physiology and chronic health evaluation
ARDS	: Acute respiratory distress syndrome
AVP	: Vasopressin
BNP	: B-type natriuretic peptide
CAD	: Coronary artery disease
CBC	: Complete blood count
CI	: Cardiac index
CO	: Cardiac output
CRP	: C- Reactive protein
CVP	: Central venous pressure
DIC	: Disseminated Intravascular Coagulopathy
ECG	: Electrocardiogram
ECMO	: Extracorporeal membrane oxygenation
ED	: Emergency department
EDS	: End Systolic Volume
EDV	: End Diastolic Volume
EF	: Ejection Fraction
EGDT	: Early, goal-directed therapy
ET-1	: Endothelin-1
FATD	: Femoral artery thermodilution
FIO2	: Fractional inspired oxygen
HM	: Holter monitoring
HRC	: Heart rate characteristics
HRV	: Heart Rate Variability
ICU	: Intensive care unit

LIST OF ABBREVIATIONS (CONT.)

Abb.	Meaning
IL-1	: Leukocytes such as interleukin-1
iNOS	: inducible NO synthase
IO	: Intraoral
IV	: Intravenous
IVSd	: Interventricular septal thickness in diastole
IVSs	: Interventricular septal thickness in systole
LA	: Left atrial antro-posterior diameter in diastole
LPS	: Lipopolysaccharide
LPWd	: Left posterior wall thickness in diastole
LPWs	: Left posterior wall thickness in systole
LV	: Left ventricular
LVIDd	: Left ventricular internal diameter diastole
LVIDs	: Left ventricular internal diameter in systole
MAP	: Mean arterial pressure
Mb	: Scavenger myoglobin
MDS	: Myocardial depressant substance
M-LVDP	: Left ventricle diastolic pressure
MODS	: Multiorgan dysfunction syndrome
MSP	: Mean arterial pressure
NO	: Nitric Oxide
PAC	: Premature atrial contractions
PaCO ₂	: Arterial carbon dioxide Partial pressure
PaO ₂	: Arterial oxygen partial pressure
PICUs	: Pediatric Intensive Care Units
Pmx B	: Polymyxin B
PRISM	: Pediatric risk of mortality
PSI	: Physiologic Stability Index
PVC	: Premature ventricular contractions
RAD	: Right axis deviation
RAE	: Right atrial enlargement
RCTs	: Randomized control studies

LIST OF ABBREVIATIONS (CONT.)

Abb.	Meaning
RVH	: Right ventricular hypertrophy
SIRS	: Systemic inflammatory response syndrome
ScvO ₂	: Central venous oxygen saturation
SE	: Septic encephalopathy
SIMD	: Sepsis-induced myocardial dysfunction
SIMV	: Spontaneous Intermittent Mandatory Ventilation Mode
SV	: Stroke Volume
SvO ₂	: Venous oxygen saturation
SVR	: Systemic vascular resistance
SVT	: Supraventricular tachycardia
TISS	: Therapeutic intervention scoring system
TLR-4	: Toll-like receptor -4
TNF- α	: Tumor necrosis factor-alpha
VT	: Ventricular tachycardia
β -AR	: β - adrenoceptor

Acknowledgement

*First of all, thanks to **Allah** the most merciful for guiding me through and giving me the strength to complete this work the way it is.*

*I would like to express my sincere appreciation and my deep gratitude to **Prof. Dr. Tarek Ahmed Abd El Gawad**, Professor of Pediatrics, Faculty of Medicine, Ain Shams University, for me It was indeed an honor to have been supervised by him spending a lot of his time and much effort to accomplish this work. I owe much to his guidance, and this work owed a lot to his insight and support.*

*I would like to express my sincere appreciation and my deep gratitude to **Dr. Marwa Moustapha Attia Al-Fahham** Lecturer of Pediatrics, Faculty of Medicine, Ain Shams University, for her close observation, effective help and careful supervision. She offered me continuously with her enriching advices which helped me throughout the work,*

No words could adequately express my deepest appreciation to my family, for their continuous support and guidance. I shall remain indebted to them all my life.

Radwa Hassaan Mahmoud

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سَبِّحْكَ لَا إِلَهَ إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢



Introduction

INTRODUCTION

Sepsis is one of the leading causes of death in children whose mortality ranges from 4% to 20% (*Odetola et al., 2007*). The incidence of sepsis and sepsis-related deaths appears to be increasing by 1.5% per year (*Angus et al., 2001*). Moreover, morbidity and mortality from sepsis and septic shock are high resulting in their being the 10th most common cause of death in the United States (*Martin et al., 2003*).

Sepsis is defined by the consensus conference as “the systemic inflammatory response syndrome (SIRS) that occurs during infection”. It is generally viewed as a disease aggravated by the inappropriate immune response encountered in the affected individual (*Hotchkiss and Karl, 2003*).

The international consensus panel proposed the term “severe sepsis” to describe instances in which sepsis is complicated by acute organ dysfunction, and they codified “septic shock” as sepsis complicated by either hypotension that is refractory to fluid resuscitation or by hyperlactatemia (*Angus and Poll, 2013*).

Septic shock is characterized by myocardial dysfunction, loss of vascular tone, and capillary leak leading to diminished organ perfusion and the development of multiple organ system failure (*Rudiger and singer, 2007*).

Electrocardiogram (ECG) is the cardiovascular most frequently monitored physiologic signal in the intensive care unit (ICU) environment.

ECG remains the gold standard for diagnosis in spite of the advance of many other diagnostic techniques as it is a noninvasive, inexpensive, simple, and reproducible technique. Moreover, it is one of the most commonly used diagnostic tests that can be rapidly recorded with extremely portable equipment and is in general always obtainable (*Drew et al., 2004*).

Studies of children with septic shock have documented various rhythm disturbances with a range of incidences. For example, premature ventricular ectopics (PVCs) and other types of rhythm abnormalities that may form a risk for ventricular tachycardia and sudden cardiac death (*Knoester et al., 2008*).

Moreover, ECG is used to diagnose cardiac ischemia in critically ill patients who are unable to communicate symptoms. It was found that fourthy eight percent of patients with septic shock had possible or probable ECG -ischemia (*Mehta et al., 2013*).

AIM OF THE WORK

The aim of this study is to test the hypothesis that routine Holter analysis in non cardiac pediatric ICU septic patients could reveal important electrocardiographic disturbances that might go undetected.

SEPSIS AND SEPTIC SHOCK

Sepsis remains a major cause of morbidity and mortality among children in pediatric intensive care units (PICUs). It represents a clinical challenge even in developed countries, being a leading cause of admissions to the pediatric emergency department and the pediatric intensive care unit (**Lawrence, 2011**).

Initially, only adult definitions were applied to the pediatric studies. However, definitions of sepsis, severe sepsis, septic shock and multiple organ dysfunction/failure syndromes in children are slightly different when compared to those used for adults (**Biban et al., 2012**).

An international panel of 20 experts in sepsis and clinical research from five countries (Canada, France, Netherlands, United Kingdom, and United States) was convened to modify the published adult consensus definitions of infection, sepsis, severe sepsis, septic shock, and organ dysfunction for children. These definitions are illustrated in table (1) (**Mehra and Bakshi, 2007**).