

بسم الله الرحمن الرحيم

 $\infty\infty\infty$

تم رفع هذه الرسالة بواسطة / مني مغربي أحمد

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

AIN SHAMS UNIVERSITY

1992

1992

ملاحظات: لا يوجد



Frequency of Non-Thyroidal Illness Syndrome in Pediatric Patients with Sepsis and Septic Shock

Thesis

Submitted for partial Fulfillment of the Master Degree in Pediatrics

By

Safaa Yossef Abd Elhameed Ali

M.B., B.Ch. (2015)
Faculty of Medicine- Minya University

Under Supervision of

Prof. Dr. Tarek Ahmed Abdelgawad

Professor of Pediatrics
Faculty of Medicine, Ain Shams University

Dr. Sondos Mohamed Magdy

Lecturer of Pediatrics Faculty of Medicine, Ain Shams University

Dr. Rana Abdelhakaim Ahmed Mahmoud

Lecturer of Pediatrics Faculty of Medicine, Ain Shams University

Dr. Sara Ibrahim Abdelfatah Taha

Lecturer of Clinical Pathology Faculty of Medicine, Ain Shams University

> Faculty of Medicine Ain Shams University 2022



سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to **ALLAH**, the Most Kind and Most Merciful.

I'd like to express my respectful thanks and profound gratitude to **Prof. Dr. Tarek Ahmed Abdelgawad,**Professor of Pediatrics, Faculty of Medicine, Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.

I am also delighted to express my deepest gratitude and thanks to **Dr. Sondos Mohamed Magdy**, Lecturer of Pediatrics, Faculty of Medicine, Ain Shams University, for her kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.

I am deeply thankful to **Dr. Rana Abdelhakaim Ahmed Mahmoud,** Lecturer of Pediatrics, Faculty of

Medicine, Ain Shams University, for her great help, active

participation and guidance.

I wish to introduce my deep respect and thanks to **Dr. Sara Ibrahim Abdelfatah Taha**, Lecturer of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her kindness, supervision and cooperation in this work.

Safaa Yossef

Dedication

Words can never express my sincere thanks to My Family and My Parents for their generous emotional support and continuous encouragement, which brought the best out of me. I owe them all every achievement throughout my life.

I would like to express my everlasting gratitude to all My Friends (Shaza Fadel & Amna Ali), so many of them influenced, encouraged and inspired me throughout the years. I wish them the best of all.

I would like also to thank the **Patients** who agreed willingly to be part of my study and without them; I would not have been able to accomplish this work.

List of Contents

Title	Page No.
List of Abbreviations	i
List of Tables	iv
List of Figures	vii
Introduction	1
Aim of the Work	4
Review of Literature	
Thyroid Gland Normal Function	5
Sepsis and Septic Shock	12
Non-Thyroidal Illness Syndrome	24
Prognosis, Outcome and Treatment of NTIS	36
Patients and Methods	41
Results	50
Discussion	80
Summary	87
Conclusion	91
Recommendations	92
References	93
Arabic Summary	

List of Abbreviations

Abb.	Full term
ALT	Alanine aminotransferase
	Acute respiratory distress syndrome
	Aspartate aminotransferase
AUC	•
CBC	Complete blood count
CRP	_
DVT	Deep vein thrombosis
ECMO	Extracorporeal membrane oxygenation
ELISA	Enzyme Linked Immunosorbent Assay
ESS	Euthyroid Sick Syndrome
FiO2	Fraction of inspired oxygen
FT3	Free triiodothyronine
FT4	Free Thyroxine
GRV	Gastric residual volumes
HB	Hemoglobin level
HBP	Heparin binding protein
HIV	Human immunodeficiency virus
IL6	Interleukin 6
iNO	Nitric Oxide, Inhalational
IVIG	Intravenous immune globulin
LPS	Lipopolysaccharide
LT3	Liothyronine
LT4	Levothyroxine
MAP	Mean arterial pressure

List of Abbreviations Cont...

Abb.	Full term
MCP	Monocyte chemoattractant protein
	Monocarboxylate transporter
mRNA	
	Non-Esterified Fatty Acids
	-
	Nuclear factor kappa B
	Na-iodine symporter
NTIS	Nonthyroidal illness syndrome
NTIS	Non-Thyroidal Illness Syndrome
OATP1C1	Organic anion-transporting polypeptide 1C1
PaCO2	Partial pressure of carbon dioxide
PaO2	Partial pressure of oxygen
PaO2/fiO2	Partial pressure of oxygen to fractional oxygen content
PARDS	Pediatric acute respiratory distress syndrome
PCT	Procalcitonin
PEEP	Positive end-expiratory pressure
PICU	Pediatric intensive care unit
PLT	Platelet
pSOFA	Pediatric sequential sepsis related organ failure assessment score
ROC	Receiver operating characteristic curve
rT3	Reverse T3
sIL-2R	Soluble interleukin-2 receptor
SOFA score	Sequential Organ Failure Assessment score

List of Abbreviations Cont...

Abb.	Full term
Spo2	Peripheral arterial oxygen saturation
TAMOF	Thrombocytopenia-associated multiple organ failure
TBG	Thyroid-binding globulin
TLC	Total Leucocytic count
TNF- α	Tumor necrosis factor- $lpha$
TPO	Thyroid peroxidase
TSH	Thyroid stimulating hormone
VA	Veno-arterial
VBG	Venous blood gases
VDD	Vitamin D deficiency
VV	Veno-venous

List of Tables

Table No.	Title	Page No.
Table (1): Table (2):	Organ dysfunction criteria Pediatric Sequential Sepsis-torgan Failure Assessment (pSOFA)	related
Table (3):	Impact of critical illness on the hormone concentrations upon admission	PICU
Table (4):	Role of commonly used medication thyroid physiology	
Table (5):	Potential pathophysiological mecha in nonthyroidal illness syndrome (N	
Table (6):	Descriptive characteristics of spatients regarding age and sex	
Table (7):	Descriptive characteristics of s patients regarding causes of admission	PICU
Table (8):	Descriptive Characteristics of spatients regarding ventilation and PICU.	stay in
Table (9):	Descriptive Characteristics of s patients regarding receiving s (inotropes or/and vasopressor)	upport
Table (10):	Descriptive Characteristics of spatients regarding blood culture	studied
Table (11):	Descriptive Characteristics of spatients regarding laborative stigations and SOFA score	oratory
Table (12):	Descriptive Characteristics of spatients regarding outcome	studied
Table (13):	Descriptive Characteristics of s patients regarding NTIS frequency	

List of Tables Cont...

Table No.	Title	Page No.	
Table (14):	NTIS among survivors and non sur	vivors5	55
Table (15):	Relations with NTIS reg descriptive Characteristics of patients (age and sex)	studied	66
Table (16):	Relations with NTIS reg descriptive characteristics of patients (ventilation, days of ven and stay in PICU)	studied tilation	56
Table (17):	Relations with NTIS reg descriptive Characteristics of patients (patients on support)	studied	57
Table (18):	Relations with NTIS reg descriptive Characteristics of patient (SOFA score CRP)	studied	57
Table (19):	Comparison between day 1 and regarding thyroid hormone levels	day 5	
Table (20):	Comparison between survivors as survivors regarding descriptive of studied patients	data of	60
Table (21):	Basic laboratory investigation survivors and non-survivors in dillness	ay 1 of	31
Table (22):	CRP and SOFA score of survivor non-survivors in day 1 of illness	ors and	
Table (23):	Comparison between sepsis and shock regarding thyroid hormone leday 1 of illness	evels in	32
Table (24):	Basic laboratory investigation survivors and non-survivors in dillness	ay 5 of	32

List of Tables Cont...

Table No.	Title	Page	No.
Table (25):	CRP and SOFA score of survivors non-survivors in day 5 of illness		63
Table (26):	Comparison between sepsis group septic shock regarding thyroid horr levels in day 5 of illness	none	63
Table (27):	Comparison between survivors and survivors regarding thyroid horr levels in day 1 and day 5	none	66
Table (28):	Correlations between thyroid horm in non-survivor in day 5 of illness days of ventilation, days of stay in P SOFA score and CRP	and ICU,	68
Table (29):	Correlations between thyroid horr levels in day 5 and receiving sup among non-survivors	port	73
Table (30):	Value of indicators in predicting F mortality		74
Table (31):	Univariate and multivariate log regression analysis for risk factor mortality	s of	76
Table (32):	Frequency and distribution pattern NTIS in day 1 among survivors and survivors	non-	77
Table (33):	Frequency and patterns of NTIS in among sepsis and septic group		78

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Thyroid hormones metabolism deiodinases	-
Figure (2):	Normal hypothalamic-pituitary-thyro	id-axis27
Figure (3):	Changes in the thyroid axis during and chronic critical illness	
Figure (4):	Thyroid hormones changes accord severity of illness	•
Figure (5):	Illustrate difference in percenta survivors and non-survivors among and septic shock groups	sepsis
Figure (6):	Courses of FT3, FT4, and TSH levels day 1 and day 5 of illness	•
Figure (7):	Course of rT3 levels among day 1 and of illness.	•
Figure (8):	Illustrates median difference in FT3 1 and day 5 among sepsis and seption groups	c shock
Figure (9):	Illustrates median difference in FT4 1 and day 5 among sepsis and seption groups	c shock
Figure (10):	Illustrates median difference in rT3 is and day 5 among sepsis and seption groups	shock
Figure (11):	Illustrate median difference in FT3 in and FT3 in day 5 between survivor non-survivors	n day 1 ors and
Figure (12):	Illustrate median difference in rT3 in and day 5of illness between survivonon-survivors.	n day 1 ors and

List of Figures Cont...

Fig. No.	Title	Page No.
Figure (13):	Shows negative correlation betw levels and days of ventilation	
Figure (14):	Shows negative correlations betweels and days of stay in PICU	
Figure (15):	Shows negative correlations between levels and SOFA score	
Figure (16):	Shows negative correlation betw levels and CRP.	
Figure (17):	Shows positive correlation betweels and days of ventilation	
Figure (18):	Shows positive correlation betweels and days of stay in PICU	
Figure (19):	Shows positive correlation betweels and SOFA score	
Figure (20):	Shows positive correlation betweels and CRP.	
Figure (21):	ROC curve analysis to predict morta	ality75
Figure (22):	Thyroid hormone levels amon patients.	•
Figure (23):	Illustrates frequency and patterns among sepsis and septic shock grou	of NTIS

Introduction

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection and "septic shock" the subset of sepsis with circulatory an cellular/metabolic dysfunction associated with a higher risk of mortality (*Weiss et al., 2020*), Determination of an acute prognosis in the early stage of sepsis and septic shock is of great importance to aid in the development of adapted strategies and improve patient outcomes(*Investigators, 2017*). Many studies have been devoted to biomarkers and clinical scores that could evaluate the severity and prognosis of patients with septic shock; however, none of them are widely used clinically(*Liu et al., 2019*). Thus, new biomarkers for reliable early prognosis are still urgently needed.

Pediatric Patients suffering from critical illnesses who require treatment in pediatric intensive care unit (PICU) present with alterations in circulating thyroid hormone levels that are referred to with several names such as Non-Thyroidal Illness Syndrome (NTIS), Euthyroid Sick Syndrome (ESS) also known as the low T3 syndrome. NTIS demonstrate abnormal thyroid functions (low serum FT3 and TT3, high rT3, normal or mildly increased FT4 and TT4, and normal low TSH or concentrations. In cases. the TT4 and FT4 severe concentrations might be low and that of TSH normal) (Feng et al., 2020; Langouche et al., 2019).