

بسم الله الرحمن الرحيم





شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار





بعض الوثائق الأصلية تالفة





بالرسالة صفحات
لم ترد بالأصل





Faculty of Postgraduate Childhood Studies
Department of Medical Studies for Children
Ain Shams University

Effect of Compliance to therapy of Congenital Hypothyroidism on the Neurodevelopmental outcome

A Thesis

*Submitted for Partial fulfillment of Master Degree in
Childhood Studies Department of Medical Studies for
Children*

By

Ahmed Ehab Ramzy Bedir

Supervised By

Prof. Hayam Kamal Nazif

Professor of Pediatrics

*Department of Medical Studies
for Children*

Faculty of Postgraduate

Childhood Studies

Ain Shams University

Prof. Howyda Mohamed

Kamal Shaaban

*Professor of clinical and
Chemical Pathology*

Benha Faculty of Medicine

Benha University

Ain Shams University

2021

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سَبَّحَانَكَ لَا إِلَهَ إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, thanks to **ALLAH** for helping me to achieve this work.

Special thanks to **Prof. Hayam Kamal Nazif**, Professor of Pediatrics Department of Medical Studies, Faculty of Postgraduate Childhood Studies, Ain Shams University, for her continuous support, sincere advice, planning, continuous guidance, encouragement and help which made the accomplishment of this work possible and easy.

I would like to express my deep gratitude to **Prof. Howyda Mohamed Kamal Shaaban**, Professor of clinical and Chemical Pathology Benha Faculty of Medicine, for her continuous guidance, and encouragement, supervision and her moral support which put the work on the correct path.

I am deeply indebted to **Dr. Dina Mohamed Fouad Khaled**, Lecturer of Phoniatics, Department of Medical Studies Faculty of Postgraduate Childhood Studies, Ain Shams University for her generous help and cooperation in offering her advice for achieving this work.

I would to thank **Dr. Samer Hamed Elkhayat**, Lecturer of Pediatric Neurology, Department of Medical Studies Faculty of Postgraduate Childhood Studies, Ain Shams University for his great efforts to guide me through this thesis.

Also, I am much thankful to **all patients and volunteers** included in this study and their parents and to the health care providers for their cooperation.

List of Contents

Title	Page No.
List of Abbreviations.....	i
List of Tables	iii
List of Figures	vii
Abstract	x
Introduction	1
Aim of the Study	4
Review of Literature	
Chapter 1: Thyroid Gland.....	5
Chapter 2: Compliance to Therapy	126
Chapter 3: Neurodevelopment Outcomes in Children with Congenital Hypothyroidism	143
Subjects and Methods.....	198
Results	204
Discussion	240
Summary	257
Conclusion	260
Recommendations	261
References	262
Appendices	334
Arabic Summary	—

List of Abbreviations

Abb.	Full term
99mTc.....	Technetium-99m
AAP.....	American Academy of Pediatrics
ACTH.....	Adrenocorticotrophic hormone
ADH.....	Antidiuretic hormone
BIA.....	Bacterial inhibition assay
BMQ	Beliefs About Medicines Questionnaire.
CH.....	Congenital hypothyroidism
DBS.....	Dried blood spot
DH	Dyshormonogenesis
DIT.....	Diiodotyrosine
DM	Diabetes Mellitus
DUOX2	Dual oxidase 2
ESPE	European Society for Pediatric Endocrinology
FT3	Free T3
FT4	Free T4
GH	Growth hormone
GPAS.....	G-protein alpha subunit
HPT	Hypothalamic-pituitary-thyroid
HRQoL.....	Health-related quality of life
ICU	Intensive care unit
IQ.....	Intellectual Quotient
LBW.....	Low birth weight
L-T4	Levothyroxine
MCT8.....	Monocarboxylase transporter 8
MEMS.....	Medication event monitoring system
MIT	Monoiodotyrosine
MOHP.....	Ministry of Health and Population
NBS	Newborn Screening
NICU	Neonatal intensive care unit
PAX8.....	Paired box gene eight
PCH	Permanent congenital hypothyroidism
PIOD.....	Partial iodide organification defects
PKU	Phenylketonuria
PSIS.....	Pituitary stalk interruption syndrome

PTH	Parathyroid hormone
QoL	Quality of life
RAI.....	Radioactive iodine
SBP2.....	Sequence binding protein 2
SMR.....	Standardized Mortality Ratio.
T3.....	Triiodothyronine
T4.....	Thyroxine
TBG	Thyroid binding globulin
TBG	Thyroxine-binding globulin
TD	Thyroid dysgenesis
Tg.....	Thyroglobulin
TH.....	Thyroid hormone
TH.....	Transient hypothyroidism
THOX2	Thyroid oxidase 2
TIOD.....	Total iodide organification defects
TPO.....	Thyroid peroxidase
TRBAbs	Thyroid receptor blocking Abs
TRH	Thyrotropin-releasing hormone
TSH.....	Thyroid-stimulating hormone
TTF-1.....	Thyroid transcription factor-1
TTF-2.....	Thyroid transcription factor-2
UI.....	Urinary iodine
US.....	United States
VLBW	Very low birth weight
WHO	World Health Organization

List of Tables

Table No.	Title	Page No.
Table (1):	Comparison of Triiodothyronine (T3) and Thyroxine (T4) in Humans.....	14
Table (2):	Incidence rates of primary congenital hypothyroidism (confirmed at birth) reported worldwide.....	26
Table (3):	Causes of hypothyroidism in the pediatric population	35
Table (4):	Causes of Congenital Hypothyroidism with transcription factor gene mutations and associated clinical finding	41
Table (5):	Maternal or Neonatal Causes of Transient Neonatal Hypothyroidism.....	48
Table (6):	Etiology of subclinical hypothyroidism in children.....	59
Table (7):	Prevalence of individual symptoms of hypothyroidism at the time of diagnosis.....	64
Table (8):	Score system for predicting congenital hypothyroidism using primary TSH measurement.....	66
Table (9):	Congenital hypothyroidism index.....	67
Table (10):	A comparison of the thyroid disorders detected by primary T4- vs. primary TSH testing	78
Table (11):	Reference ranges for thyroid function tests at ages 1-4 days and 2-4 weeks.....	85
Table (12):	Laboratory studies of thyroid function.....	89
Table (13):	Interpreting thyroid imaging	96
Table (14):	Thyroid Ultrasound, Scintigraphy, and Serum Thyroglobulin Findings in Thyroid Dysgenesis, Dyshormonogenesis, and Some Forms of Transient CH	102

List of Tables cont...

Table No.	Title	Page No.
Table (15):	Summary of the suggestion during the follow up	124
Table (16):	Screening Program the recommended starting l-thyroxine correct the hypothyroxinemia and raise the serum T4 into the "target range" and lower serum TSH levels into the normal range .	150
Table (17):	Dimensions of Adaptive Behavior Identified by AAMR and NRC	188
Table (18):	American Association on Intellectual and Developmental Disabilities adaptive skills and domains	189
Table (19):	Content of the Vineland-II Scales showing the domains and sub-domains assessed with example items for each sub-domain.....	197
Table (20):	Socio demographic data of the studied groups ...	204
Table (21):	Clinical presentation of the studied cases:	205
Table (22):	The most frequent symptoms in CH cases	206
Table (23):	Associated congenital anomalies among the studied cases.....	207
Table (24):	Causes of congenital hypothyroidism in the studied patients.....	208
Table (25):	Patient's compliance distribution according to (MMAS-8)	208
Table (26):	Severity level of congenital hypothyrodism (according to the initial "pre-treatment" FT4 levels) at time of diagnosis.....	209
Table (28):	Initial Vineland-II in the studied patients.....	211
Table (29):	Vineland-II after 6 months in the studied patients.....	213

Table No.	Title	Page No.
Table (30):	Comparison between Initial Vineland-II and after 6 months in the studied patients.....	214
Table (31):	Correlation between the compliance score and the TSH levels.....	215
Table (32):	Comparison between Initial Vineland-II and after 6 months in the studied patients and controls	215
Table (33):	Correlation between the compliance score and the T4 levels.	217
Table (34):	Correlation between the compliance score and the initiation time of hormone replacement, Initial L-thyroxine dose, L-thyroxine dose after 3 months, L-thyroxine dose after 6 months.....	220
Table (35):	Relation between patient's compliance and TSH level.....	221
Table (36):	Correlation between the compliance score and anthropometric measurement.....	2234
Table (37):	Relation between patient's compliance and occupation of the parents	228
Table (38):	Relation between patient's compliance and residence and social class of studied group.....	229
Table (39):	Relation between compliance and age, sex, symptoms and congenital malformation.....	230
Table (40):	Relation between compliance and initial Vineland-II in the studied patients.	231
Table (41):	Relation between compliance and Vineland-II after 6 months in the studied patients.....	232
Table (42):	Relation between compliance and severity level of CH.....	233
Table (43):	Relation between compliance and Length of normalization period of TSH	233
Table (44):	Relation between compliance and follow up Free T4 levels.....	234

List of Tables Cont...

Table No.	Title	Page No.
Table (45):	Relation between compliance and the severity of congenital hypothyroidism (according to Bone age).....	235
Table (46):	Correlation between the compliance score and Length of normalization period of TSH	235
Table (47):	Relation between initial Vineland-II and the severity of congenital hypothyroidism (according to Bone age)	236
Table (48):	Relation between initial Vineland-II and the Length of normalization period of TSH.	237
Table (49):	Relation between Vineland-II after 6 months and follow up Free T4.	238
Table (50):	Correlation between the compliance score and Vineland score.....	238
Table (51):	Types of congenital hypothyroidism in the studied patients	239