



Study of Neuro- Psychological Complications of Children with Beta-Thalassemia: Relation to Growth Pattern and Hematological Parameters.

Thesis Submitted for the Fulfillment of the Ph.D
Degree in Childhood Studies
[Care of Children with Special Needs]

Prepared by
Dr. Hanan Galal Azouz
M.B.B.Ch, Ms.Pediatrics
MD.Pediatrics [Alexandria University]

Supervised by
Dr. Hayam Nazif
Professor of Pediatrics
Institute of Post-Graduate Childhood Studies
Ain- Shams University

Dr. Akram Deghidy
Professor of Clinical Pathology
Alexandria University

Dr. Tarek Molokhia
Professor of Neuropsychiatry
Alexandria University



**دراسة المضاعفات العصبية و النفسية فى الأطفال
المصابين بأنيميا البحر المتوسط :
علاقته بنمط النمو و مقاييس الدم**

رسالة

مقدمة للحصول على درجة دكتوراه الفلسفة في الدراسات الطبية

(الاطفال ذوي الاحتياجات الخاصة)

مقدمة من الدكتورة

حنان جلال عزوز

ماجستير طب الاطفال ودكتوراه طب الاطفال

جامعة الاسكندرية

تحت إشراف

الدكتور/هيام نظيف

استاذ طب الاطفال

قسم الدراسات الطبية للأطفال

معهد الدراسات العليا للطب

جامعة عين شمس

الدكتور/طارق ملوخية

استاذ الامراض النفسية و العصبية

كلية الطب

جامعة الاسكندرية

الدكتور/أكرم دغدي

استاذ الباثولوجيا الاكلينيكية

كلية الطب

جامعة الاسكندرية

2015



صفحة العنوان

اسم الطالب : حنان جلال عزوز

الدرجة العلمية : دكتوراه الفلسفة

القسم التابع له : الدراسات الطبية للأطفال (الاطفال ذوي الاحتياجات الخاصة)

اسم المعهد : معهد الدراسات العليا للطفولة

الجامعة : عين شمس

سنة التخرج : 2015



صفحة الموافقة

اسم الطالبة : حنان جلال علي عزوز

عنوان الرسالة : دراسة المضاعفات العصبية و النفسية فى الأطفال المصابين بأنيميا البحر المتوسط : علاقته بنمط النمو و مقاييس الدم

اسم الدرجة : دكتوراه

لجنة الحكم و المناقشة :

استاذ طب الاطفال- بقسم الدراسات الطبية للأطفال و عميد المعهد
أستاذ و رئيس قسم طب الاطفال – كلية الطب- جامعة الاسكندرية
أستاذ الصحة العامة- بقسم الدراسات الطبية للأطفال و وكيل المعهد

إ.د / هيام كمال نظيف
إ.د / مصطفى أحمد سعيد سلامة
إ.د / ايهاب محمد عبد العزيز عيد

تاريخ البحث : / / 2009

الدراسات العليا

اجيزت الرسالة بتاريخ : / /

ختم الاجازة :

موافقة مجلس الجامعة

موافقة مجلس المعهد



شكر

أشكر السادة الأساتذة الذين قاموا بالاشراف وهم :

- | | |
|---|-----------------------------|
| استاذ طب الاطفال – بقسم الدراسات الطبية - معهد دراسات الطفولة | ا.د / هيام كمال نظيف |
| أستاذ الأمراض النفسية والعصبية – كلية الطب – جامعة الإسكندرية | ا.د / طارق كمال ملوخية |
| أستاذ الباثولوجيا الاكلينيكية – كلية الطب – جامعة الاسكندرية | ا.د / أكرم عبد المنعم دغيدي |

ثم الأشخاص الذين تعاونوا معي البحث و هم:

- ١.
- ٢.
- ٣.

و كذلك الهيئات الأتية :

- ١.
- ٢.
- ٣.



Study of Neuro- Psychological Complications of Children with Beta-Thalassemia: Relation to Growth Pattern and Hematological Parameters.

Thesis Submitted for the Fulfillment of the Ph.D
Degree in Childhood Studies
[Care of Children with Special Needs]

Prepared by

Dr. Hanan Galal Azouz

M.B.B.Ch, Ms.Pediatrics

MD.Pediatrics [Alexandria University]

Supervised by

Dr. Hayam Nazif

Professor of Pediatrics

Institute of Post-Graduate Childhood Studies

Ain- Shams University

Dr. Akram Deghidy
Professor of Clinical Pathology
Alexandria University

Dr. Tarek Molokhia
Professor of Neuropsychiatry
Alexandria University

2015



دراسة المضاعفات العصبية و النفسية فى الأطفال المصابين بأنيميا البحر المتوسط : علاقته بنمط النمو و مقاييس الدم

رسالة

مقدمة للحصول على درجة دكتوراه الفلسفة في الدراسات الطبية

(الاطفال ذوي الاحتياجات الخاصة)

مقدمة من الدكتورة

حنان جلال عزوز

ماجستير طب الاطفال ودكتوراه طب الاطفال

جامعة الاسكندرية

تحت إشراف

الدكتور/هيام نظيف

استاذ طب الاطفال

قسم الدراسات الطبية للأطفال

معهد الدراسات العليا للطب

جامعة عين شمس

الدكتور/طارق ملوخية

استاذ الامراض النفسية و العصبية

كلية الطب

جامعة الاسكندرية

الدكتور/أكرم دغدي

استاذ الباثولوجيا الاكلينيكية

كلية الطب

جامعة الاسكندرية

ACKNOWLEDGEMENT

Praise to "Allah", the Most Gracious and the Most Merciful Who Guides Me to the Right Way

*I would like to express my sincere gratitude to **Prof. Dr. Hayam Nazif**, Professor of Pediatrics, Institute of Post-Graduate Childhood Studies, Ain- Shams University, who gave me much of her effort, experience and close supervision throughout the work. Her generous assistance and guidance had a pivotal role in this study.*

*My deep and endless thanks to **Prof. Dr. Tarek Molokhia**, Professor of neuropsychiatry, Faculty of Medicine, Alexandria University, for the time he gave to me, his support and sincere help. I am extremely grateful to his kind supervision and inspiration throughout the work.*

*Special thanks to **Prof. Dr. Akram Deghidy**, Professor of Clinical Pathology, Faculty of Medicine, Alexandria University for his great kindness, valuable guidance and help during the progress of this work.*

I am also thankful to all staff members, my colleagues in the Pediatrics department, all children and their caregivers who participated in the study.

Last but not least, I owe special thanks and gratitude to my family who nurtured, loved and faithfully supported me throughout this entire work.

LIST OF CONTENTS

ACKNOWLEDGMENT.....	i
LIST OF CONTENTS.....	ii
LIST OF TABLES.....	iii
LIST OF FIGURES.....	vii
LIST OF ABBREVIATIONS.....	ix
I. INTRODUCTION.....	1
II. REVIEW OF LITERATURE	5
III. PATIENTS & METHODS.....	77
IV. RESULTS.....	99
V. DISCUSSION.....	165
VI. SUMMARY.....	201
VII. CONCLUSIONS	208
VIII. RECOMMENDATIONS.....	210
IX. REFERENCES	212
APPENDICES	
PROTOCOL	

ARABIC SUMMARY

LIST OF TABLES

Table	Page
(I) Genetic Basis and Clinical Manifestations of Common Beta Thalassemia Syndromes (Rund & Rachmilewitz 2005)	16
(II) Chelator characteristics (Cianciulli 2009)	46
1) Distribution of the studied patients according to sex and age (n = 40)	99
2) Distribution of the studied patients regarding Socio-economic status.	101
3) Distribution of the studied patients according to disease parameters	104
4) Distribution of the studied patients according to chelation therapy (n = 40)	105
5) Distribution of the studied patients according to growth parameters	106
6) Comparison between male and female patients according to tanner staging	108
7) Complete Blood Count Results of the Studied Patients	111
8) Iron Profile and Serum Zinc Results of the Studied Patients	112
9) Distribution of the studied patients according to Motor System Examination	113
10) Distribution of the patients according EEG study	114
11) Distribution of the studied cases according to IQ	116

12)	Intelligence quotients subscales in the studied thalassemic children	117
13)	The studied cases raw and T-scorescores according to CBCL Complaints	122
14)	Distribution of the studied cases according to CBCL Complaints Items T-score categories	123
15)	CBCL syndrome items T-score categories in the studied patients as regard gender	124
16)	Distribution of the studied cases according to Externalization problems, internalization problems and total problems	125
17)	CBCL broad categories t-score according to gender	125
18)	Comparison between the two ages groups according to CBCL complaints raw score in each of boys, girls and total children	126
19)	Distribution of the studied patients according to Child Manifest Anxiety Scale (CMAS)	127
20)	Comparison between male and female patients according to child manifest anxiety scale (CMAS)	128
21)	Distribution of patients according to Child Depression Inventory (CDI)	129
22)	Comparison between male and female patients according to child depression inventory (CDI)	130
23)	Relation between motor system examination with disease and chelation characteristics	132
24)	Relation between motor system examination with growth parameters	134
25)	Relation between motor system examination with Tanner Staging	135

26)	Relation between motor system examination with hematological and serum zinc findings	136
27)	Relation between EEG Background with disease and chelation characteristics	138
28)	Relation between EEG Background with growth parameters	139
29)	Relation between EEG Background with Tanner Staging	140
30)	Relation between EEG Background with hematological and serum zinc findings	140
31)	Correlation between IQ with different parameters	143
32)	Relation between IQ Categories with Tanner Staging	144
33)	Relation between IQ categories with disease duration	146
34)	Relation between IQ categories with mean serum iron level	146
35)	Correlation between disease and chelation therapy characteristics with CBCL Complaints	148
36)	Correlation between growth with different parameters	150
37)	Correlation between growth parameters with CBCL Complaints Items in studied patients	152
38)	Correlation between hematologic findings with CBCL Complaints Items	152
39)	Relation between CMAS grade with disease and chelation therapy characteristics	155
40)	Relation between CMAS grade with growth parameters in total group	156
41)	Relation between CMAS grade with Tanners staging in studied patients	157

42)	Relation between CMAS grade with hematological findings	158
43)	Relation between CDI grade with disease and chelation therapy characteristics	160
44)	Relation between CDI grade with growth parameters	162
45)	Relation between CDI grade with Tanner Staging in studied patients	162
46)	Relation between CDI grade with hematological findings in studied patients	164

LIST OF FIGURES

Figure	Page
(I) b-Globin gene cluster and a globin-gene cluster (Nussbaum et al 2007).	10
(II) Child with BTM	15
(III) Mechanism of iron toxicity in iron overload (Porter JB (2007))	22
(IV) Role of hepcidin in iron overload (Kroot et al 2011)	22
1) Distribution of the studied patients according to age	100
2) Distribution of the studied patients according to sex	100
3) Distribution of the studied patients according to Age beginning transfusion	102
4) Distribution of the studied patients according to Splenectomy	103
5) Transfusion Frequency in the Studied Patients	103
6) Distribution of studied patients according to height z-score	107
7) Distriburion of studied patients according to BMI z-score	107
8) Comparison between male and female patients according to Tanner staging	109
9) Distribution of patients according to serum Ferritn level	112
10) Distribution of the studied patients according to EEG findings	115
11) Distribution of the studied cases according to IQ	117