



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



MONA MAGHRABY



شبكة المعلومات الجامعية
التوثيق الإلكتروني 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



MONA MAGHRABY



Efficacy of Vitamin D Supplementation on Bone Mineral Density and Vitamin D Binding Protein in Children with Autism

Thesis

Submitted for Fulfillment of Ph.D in Childhood Studies

(Care of Children with special needs)

Medical Studies Department for Children

By

Gina Huessin Ahmed Ahmed Elpatrik

M.Sc Ain Shams University

Assistant Researcher of Department at Research on Children with Special Needs

Under Supervision of

Dr. Maisa Nasr Farid

Professor of Pediatrics

Head of medical Studies Department for children

Faculty of Postgraduate Childhood Studies

Ain Shams University

Dr. Howida Hosny Al-Gebaly

Professor of Pediatrics

Dean of Faculty of Postgraduate Childhood Studies

Ain Shams University

Dr. Nagwa Abdel-Meguid Mohamed

Professor of Human Genetics

Research on Children with Special Needs

NRC

Faculty of Postgraduate Childhood Studies

Ain Shams University

2020



صفحة الموافقة

اسم الطالب : جينا حسين احمد احمد البطريق
عنوان الرسالة : تأثير فيتامين (د) على كثافة العظام و البروتين الرابط لفيتامين (د) في الأطفال الذين يعانون من اضطرابات التوحد
اسم الدرجة : دكتوراة الفلسفة في دراسات الطفولة قسم الدراسات الطبية للأطفال (رعاية الاطفال ذوي الاحتياجات الخاصة)

لجنة الحكم:

١ - أ.د/نجوى عبد المجيد محمد (رئيساً و مشرفاً)

أستاذ الوراثة البشرية - المركز القومى للبحوث

كلية الدراسات العليا للطفولة - جامعة عين شمس

٢ - أ.د/ هويد حسنى الجبالى (مناقشاً و مشرفاً)

أستاذ طب الأطفال وعميد كلية الدراسات العليا للطفولة

جامعة عين شمس

٣ - أ.د/ مایسة نصر فريد (مناقشاً و مشرفاً)

أستاذ طب الأطفال و رئيس قسم الدراسات الطبية للأطفال

كلية الدراسات العليا للطفولة - جامعة عين شمس

٤ - إيهاب محمد عيد (مناقشاً من الدخل)

أستاذ الصحة العامة قسم الدراسات الطبية للأطفال

كلية الدراسات العليا للطفولة - جامعة عين شمس

٥ - محمد خالد المنباوى (مناقشاً من الخارج)

أستاذ صحة الطفل - المركز القومى للبحوث

تاريخ البحث: / / ٢٠٢٠م

الدراسات العليا

أجيزت الرسالة بتاريخ

/ / ٢٠٢٠م

موافقة مجلس الجامعة

/ / ٢٠٢٠م

موافقة مجلس الكلية

/ / ٢٠٢٠م



صفحة العنوان

عنوان الرسالة : تأثير فيتامين (د) على كثافة العظام و البروتين الرابط لفيتامين (د) في الأطفال الذين يعانون من اضطرابات التوحد "

اسم الطالبة : جينا حسين أحمد أحمد البطريق

الدرجة العلمية : دكتوراة الفلسفة في دراسات الطفولة

القسم التابع له : قسم الدراسات الطبية

اسم الكلية : كلية الدراسات العليا للطفولة

الجامعة : جامعة عين شمس

سنة التخرج :

سنة المنح :

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدقة الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

First of all, I thank Allah to whom I relate any success I have reached and might reach in the future.

I have great pleasure in expressing my deep sense of gratitude and indebtedness to **Dr. Howida Hosny Al-Gebaly**, Professor of Pediatrics, Dean of Faculty of Postgraduate Childhood Studies and, **Dr. Maisa Nasr Farid**, Professor of Pediatrics, Head of medical Studies Department for children, Ain Shams University, for their expert supervision and constant encouragement to produce this work.

I am heartily thankful to my supervisor **Dr. Nagwa Abdel-Meguid Mohamed**, Professor of Human Genetics, Research on Children with Special Needs Department, National Research Centre, whose encouragement; guidance and support from the initial to the final level of the work enabled me to develop a better understanding of the subject.

My deep gratitude and appreciation for **Dr. Rokia Abd El-shafy El-Banna**, Professor of Biological Anthropology, Clinical anthropometric Department, National Research Centre, for her sincere help and performing the radiological part.

I would like to express my deepest gratitude to **Dr. Marwa Ibrahim Khalil Mohamed**, Researcher of Medical Molecular Genetics, National Research Centre, for providing the time to perform molecular laboratory studies for all cases.

This dissertation would not have been possible without the guidance and help of **Dr. Mona Anwer**, Professor of Clinical Pathology, National Research Centre of who in one way or another contributed and extended her valuable assistance in the preparation and completion of this study.

I would like to express my sincere thanks to all, patients with Autistic spectrum disorder and their families for their cooperation during the study.

Lastly, I offer my regards and blessings to my family especially my husband Hatem, my children (Omar and Adam) and all of those who supported me in any aspect during the completion of the study. Each of you can share in this accomplishment, for without your support it would not have been possible, thank you for everything.

Gina Huessin Elpatrik

DEDICATION

TO:

My Dear Parents especially my mum
Who give me too much
And receive too little

My Dear Husband... **Hatem Elmaraghy**
&
My lovely Sons **(Omar & Adam)**

My Patients.....

Abstract

Background: Autism spectrum disorder is a neuro-developmental disorder, which is reported to affect 1 in 59 children. Social communication deficits and restricted or repetitive interests and behaviors are main characterizing features. It is caused by the interaction of both genetic and environmental factors.

Objective: To assess vitamin D, Vitamin D Binding Protein (VDBP) and bone mineral density in autistic children, compared to typically developing children, In addition to question the benefit of using oral vitamin D daily supplementation for 4 months on autistic children's outcome.

Patients and Methods: The study was conducted on 30 autistic patients recruited from the Autism Disorders Clinic, Medical Research Centre of Excellence, National Research Centre with age ranging from 3-7 years. Patients were randomly supplemented by vitamin D in a dose of 600 IU/day for 4 months. Thirty healthy children were included as controls, with matched age and socioeconomic status to the study group. Vit D assessment was done using blood samples, VDBP was assessed using ELISA. Moreover, DEXA was done over femur neck and lumber regions.

Results: The results of the study revealed that autistic group have vitamin D deficient. However, there was no significance between patients before and after supplementation. On comparing VDBP levels of the patients and controls groups,,we discovered statistically highly significant difference of its level between before and after supplementation in autistic patients. In addition, we revealed that low bone mineral density DEXA of (neck femur and lumber) were discovered. There was no significant difference between autistic children (before and after) supplementation

Conclusion: Wrapping up, it is still premature to conclude that autism and vitamin D are both related to eachother. Although this work did not uncover any of the mysteries of autism, yet it highlighted the tight spot of vitamin D deficiency in children in general, and in autistic children in particular who are more prone to vitamin D deficiency complications as regard bone metabolism and the higher risk for immobilization. Further studies should be implemented on a larger group of autistic children, and longer duration of vitamin D supplementation to reach optimal blood vitamin D levels. We recommend vitamin D supplementation using nanotechnology to overcome associated problems with its administration.

Keywords: Vitamin D, autism spectrum disorder, vitamin D binding protein, Dual Energy X-Ray Absorptiometry

List of Contents

Title	Page No.
<i>List of Abbreviations</i>	i
<i>List of Tables</i>	iv
<i>List of Figures</i>	vi
Introduction	1
Aim of The Study	5
Review of Literature	
Autism	6
Figure (2): DSM-5 ASD diagnostic criteria and specifiers.....	14
Vitamin D.....	42
Vitamin D Binding Protein.....	65
Bone Mineral Density (BMD).....	69
Patients and Methods.....	78
Results	86
Discussion	119
Summary	131
Conclusion	134
Recommendations	135
References	137
Arabic Sumamry	—

List of Abbreviations

Abb.	Full term
1, 25 OHD.....	1 and 25 Hydroxy- vitamin D.
25 OH vitamin D....	25 hydroxy -vitamin D.
25 (OH) D	25 hydroxy vitamin D
5-HT.....	Serotonin
ABA	Applied behavior analysis
AD.....	Alzheimer's disease
ADDM.....	Autism Developmental Disabilities Monitoring
ADHD	Attention deficit hyperactive disorder
ADI-R.....	Autism Diagnostic Interview-Revised
AFM.....	α -albumin/afamin
AFP	α -fetoprotein
ALB.....	Albumin
APA.....	American psychiatric association
ASD.....	Autism spectrum disorder
BMC.....	Bone mineral content
BMD	Bone mineral density
CARS	Childhood Autism Rating Scale
CDC	Centers for Disease Control and Prevention
CDD	Childhood Disintegrative Disorder
CNS	Central nervous system
COMT.....	Catechol-O-methyl-transferase
Cu	Copper
DEXA.....	Dual Energy X-Ray Absorptiometry
DMPS	2-3-dimercaptopropane-1-sulfonate
DMSA	2-3-dimercaptosuccinic acid)

List of Abbreviations Cont...

Abb.	Full term
DSM-5.....	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.
DSM-IV.....	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition.
DTT.....	Discrete trial teaching
EEG	Electroencephalogram
ELISA.....	Enzyme linked immunosorbent assay
FDA	Food and Drug Administration
Floortime/DIR	Developmental, Individual Differences based, and Relationship based approach
GABA.....	Gamma-amino-butyric acid
GDNF	Glial neurotrophic factor
HIV/AIDS	Human immunodeficiency virus / acquired immunodeficiency syndrome
ICD-10.....	International Classification of Diseases, Tenth.
IL	Interleukin
ISCD	the International Society of Clinical Densitometry
MARRS.....	Membrane associated rapid response steroid binding
MHC1	Major Histocompatibility complex class I
MMR II.....	Measles, mumps, and rubella vaccine
NGF	Nerve growth factor
NIMH	National Institute of Mental Health Research Domain Criteria
NT3.....	Neurotrophine-3
NT-4.....	Neurotrophin-4
OT	Occupational Therapy

List of Abbreviations Cont...

Abb.	Full term
PDD	Pervasive developmental disorders.
PDD-NOS	Pervasive developmental disorder-not otherwise specified
PECS	Picture Exchange Communication System
PKU	Phenylketonuria
PTH	Parathyroid hormone
RDoC	Research Domain Criteria
RIA.....	Radioimmunoassay
ROI	Regions of interest
RS	Rett syndrome
RXR	Receptors of the retinoic X receptor
SES	Socio-economic standard
TEACCH.....	Training and Education of Autistic and Related Communication Handicapped Children
TPH2	The serotonin-synthesizing gene tryptophan hydroxylase 2.
TS	Tourette syndrome
VDBP.....	Vitamin D binding protein
VDR	Receptors for Vit D
VDRE.....	Vitamin D responsive elements
Zn.....	Zinc

List of Tables

Table No.	Title	Page No.
Table (1):	Dietary reference intakes for vitamin D	53
Table (2):	Classification of vitamin D status	57
Table (3):	Demographic characters (Age and sex) among autistics and controls (N=60) using Chi-square test; and Independent t-test.....	87
Table (4):	Descriptive data of consanguinity and type of delivery in autistics	88
Table (5):	Comparison between autistics and control groups regarding anthropometric assessment (weight, height and BMI)	90
Table (6):	Scores of autistics using C.A.R.S and A.D.I.R. assessments.....	92
Table (7):	Difference of vitamin D between patients and control groups.....	93
Table (8):	Difference of vitamin D (before and after supplementation) between autistics	93
Table (9):	Comparison of calcium level in autstics and controls:	95
Table (10):	Comparison of calcium level in autistic group before and after supplementation:.....	96
Table (11):	Comparison of vitamin D binding protein between control and autistic groups	97
Table (12):	Comparison of vitamin D binding protein between autistics (pre and post supplementation).....	98
Table (13):	Comparison of bone mineral density (DEXA)- femur neck between control and autistic groups (pre and post supplementation).....	99