

Potential Biochemical Markers in Egyptian Children with Autistic Disorder

A thesis For Partial Fulfillment of the Requirements
For Master Degree of Science In Biochemistry

By
Eman Abd El fattah Megahed

Under Supervision of
Prof. Dr. Fahmy T. Ali
Professor of Biochemistry
Faculty of Science
Ain Shams University

Prof. Dr. Azza A. El Bakry
Head of child psychiatry unit
Cairo university

Dr. Mostafa M. El Hady
Lecture of Biochemistry
Faculty of Science
Ain Shams University

Faculty of Science
Biochemistry Department

2016

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

اسبغناك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدقة الله العظيم

سورة البقرة الآية: ٢٢

Dedication

We must love them both, whose opinions we share and whose opinions we reject. For both have labored in the search for truth and have helped us in the finding of it. Finally, Success comes when passion and talent are combined with a heavy dose of perseverance and a bit of luck.

Eman Abd Elfattah Megahed

Declaration

This thesis has not been submitted to this or
any other university

Eman Abd Elfattah Megahed

Acknowledgements

First and foremost, my deep praises to “**Allah**” who had guided us to this: never could we have found guidance, had it not been for the guidance of **Allah**. Thanks to **Allah** of all gifts given to me.

I express my deepest thanks to ***Prof. Dr. Fahmy T. Ali***, for his valuable supervision, sincere guidance, meticulous advice, constructive suggestion and wholehearted support throughout this work and above all for his moral support and fatherly attitude.

My sincere appreciation and gratitude to ***Prof. Dr. Azza A. El Bakry*** Professor of psychiatry, Head of child psychiatry unit, Cairo University. For her kind, sincere, valuable instructions, careful reading and unlimited advisement and encouragement throughout the work.

I would like also to express my deep gratitude to ***Dr. Mostafa M. El Hady*** Lecturer of Biochemistry, Faculty of Science, Ain Shams University, for his continuous support, his valuable advises, encouragement and guidance at every stage of this work.

I would like to convey my thanks to my family and also to my colleagues for their encouragement.

Eman Abd Elfattah Megahed

Contents

Contents	Page
Abbreviations.	I
List of figures.	IV
List of tables.	VII
Abstract.	VIII
Introduction.	1
Aim of the work.	5
Review of literature	6
➤ Epidemiology.	9
➤ Autism prevalence among Egyptian children.	10
➤ Economic Cost.	11
➤ Causes.	11
➤ ASD: EARLY DEVELOPMENTAL ETIOLOGY.	19
➤ The role of maternal prenatal infection in ASD risk.	20
➤ Oxidative stress and autism spectrum disorder.	22
➤ Glutathione peroxidase.	30
➤ Isoprostane.	32
➤ Nitric oxide.	35
➤ Ceruloplasmin	38
➤ Transferrin	42
➤ Brain-derived neurotrophic factor (BDNF)	44
➤ Zinc	47
➤ Symptoms	50
➤ Diagnosis	52
➤ Classification criteria for Autism Spectrum Disorders from DSM-IV	60
➤ Childhood Autism Rating Scale	62

Subjects and Methods	65
➤ <i>Subjects</i>	65
➤ <i>Chemicals and Kits</i>	66
➤ <i>Investigated Parameters</i>	77
➤ <i>Methods</i>	78
➤ <i>Statistical Analysis</i>	90
Results	91
➤ <i>Descriptive data and mean plots</i>	91
➤ <i>Evaluate the Accuracy of Parameters of Diagnostic Performance.</i>	114
➤ <i>Significant Correlations between the Estimated Parameters</i>	122
Discussion.	131
Summary.	148
References.	152
الملخص العربي	

ABBREVIATIONS

AGC	: Aspartate /glutamate carrier
APA	: American psychiatric Association.
APOP	: Advance protein oxidation product.
AS	: Asperger's syndrome.
ASDs	: Autism spectrum disorders.
ATP	: Adenosine triphosphate.
BDNF	: Brain-derived neurotrophic factor.
CARS	: Childhood Autism Rating Scale.
CARS2-HF	: Childhood Autism Rating Scale second edition High-Functioning Version Rating Booklet
CARS2- QPC	: Childhood Autism Rating Scale second edition Questionnaire of Parent Concerns.
CARS2-ST	: Childhood Autism Rating Scale second edition Standard Version Rating Booklet.
CAT	: Catalase.
CML	: Chronic myeloid leukemia.
DSM-5	: Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5).
EAS	: The Egyptian Autistic Society.
ELISA	: Enzyme-linked immunosorbent assay.
eNOS	: Endothelial nitric oxide.
GABA	: Gamma-amino butyric acid.
GPX	: Glutathione peroxidase.
GSH	: Glutathione reductase.

GWAS	: Genome-wide association studies.
HFA	: High function autism.
iNOS	: Inducible nitric oxide.
IP	: Isoprostane.
LFA	: Low function autism.
MT	: Metallothionein.
NAA	: N-acetyl aspartate.
NCCM	: National Council for Motherhood and Childhood
nNOS	: Neuronal nitric oxide.
NO	: Nitric oxide.
NOS	: Nitric oxide synthase.
PDD-NOS	: Pervasive developmental disorder–not otherwise specified.
PUFAs	: Polyunsaturated fatty acids.
RNS	: Reactive nitrogen species.
SNPs	: Single nucleotide polymorphisms.
SOD	: Superoxide dismutase.
Zn	: Zinc.
ROS	: Reactive oxygen species.
VPA	: Valporic acid.
Cu	: Copper.
CNS	: Central nervous system.
Hg	: Mercury.
ADHD	: Attention deficient hyper active disorder.
TMB	: Tetra methyl benzadine.

HRP	: Horseradish peroxidase.
NIMH	: National institute of mental health.
ID	: Iron deficiency.
TIBC	: Total iron binding capacity.
NGF	: Neurotrophin growth factor.