التصوير المتقدم للجهاز العصبي في تشخيص مرض الميتوكوندريا في الأطفال

بروتوكول رسالة
توطئة للحصول على درجة الماجيستير
في طب الأطفال

مقدمة من

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Advanced Neuroimaging Technique In Diagnosis of Mitochondrial Disease In Children

Thesis

Submitted for partial fulfillment of
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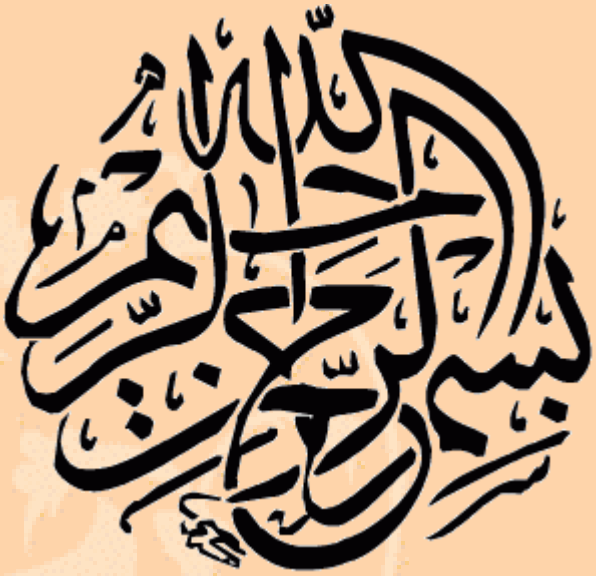

" قَالُوا سُبْحَانَكَ لَا
عِلْمَ لَنَا إِلَّا مَا
عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْحَكِيمُ "

صدق الله العظيم

البقرة الآية ٣٢

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Dedication

To my parents ,to my Husband ,to my friends , to my sisters ,to my sons Eyad and Malek
And To all suffering children .

CONTENTS

LIST OF ABBREVIATIONS

ALT	**Alanine transferase**
AST	**Aspartate transferase**
ATP	**adenosine triphosphate**
Cho	**Choline**
Co Q10	**coenzyme Q10**
CPEO	**Chronic progressive external ophthalmoplegia**
Cr	**Creatine**
Cyt c	**cytochrome c**
DPT	**Diphteria,pertussis,tetanus**
ETC	**electron transport chain**
IUGR	**Intra uterine growth retardation**
KSS	**Kearns-Sayre syndrome**
LHON	**Leber Hereditary Optic Neuropathy**
MD	**Mitochondrial disease**
MDC	**mitochondrial disease criteria**
MELAS	**Mitochondrial Encephalopathy, Lactic Acidosis and Stroke like episodes**
MERRF	**Myoclonic Epilepsy, Ragged Red Fibers**
MI	**Myo-inositol**
MILS	**Maternally inherited Leigh syndrome**
mmol	**Milli-molecule**
MnSOD	**Mitochondrial manganese superoxide dismutase**
MRI	**Magnetic Resonance Imaging**
MRS	**Magnetic Resonance spectroscopy**

msec	**millisecond**
mtDNA	**Mitochondrial DNA**
NAA	**N-acetylaspartate**
NARP	**Neuropathy, Ataxia, Retinitis Pigmentosa**
nDNA	**Nuclear DNA**
NO	**nitric oxide**
ONOO	**peroxynitrite**
OXPHOS	**oxidative phosphorylation**
PEO	**progressive external Ophthalmoplegia**
ppm	**Part per miniute**
ROS	**reactive oxygen species**
rRNAs	**ribosomal RNAs**
TE	**Time to echo**
tRNAs	**transfer RNAs**

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Introduction

The clinical recognition of mitochondrial disease is often a challenging endover. Genetically based, primary mitochondrial dysfunction presents as a heterogeneous group of disorders, which together are now recognized to constitute the most common neurometabolic disorder of childhood.**(Sanderson et al.,2006)**.

Epidemiologic studies of mitochondrial disease are limited by disease heterogeneity and underdiagnosis. Prevalence figures are less accurate than incidence figures in estimating mitochondrial disease frequency due to the high childhood mortality of these disorders. **(Dimauro and Davidzon.,2005).**

Mitochondrial diseases are usually progressive and multisystemic. Typically affected organs are those with a high energy demand, including skeletal and cardiac muscle, endocrine organs, kidney, nonmucosal components of the intestinal tract, retina, and the central nervous system. However, virtually any organ or tissue can be involved. **(Dimauro and Davidzon.,2005).**

As a general rule, the involvement of 3 or more organ systems without a unifying diagnosis should raise

suspicion for mitochondrial disease. Although effective treatments remain elusive, definitive diagnosis is crucial for permitting appropriate symptom management, as well as accurate prognostic and recurrence-risk counseling.**(Dimauro and Davidzon.,2005)**.

Mitochondrial disease may present with "any symptom in any organ at any age**,**but some symptoms and signs truly are more suggestive of a mitochondrial disorder than others. **(Munnich et al.,1996)**

These features warrant the initiation of a baseline diagnostic evaluation for mitochondrial disease. **(Richard et al.,2007)**.

In contrast, there are a multitude of nonspecific symptoms that frequently occur in infants and children with mitochondrial disease but have a broad differential diagnosis, and more often lead to other clear diagnoses. **(Richard et al.,2007)**.

Thus, the nonspecific symptoms, particularly if they occur in isolation, do not indicate a mitochondrial problem per se. **(Richard et al.,2007)**.

However, when they are present in combination, the likelihood of a mitochondrial disorder increases, particularly if the nonspecific features involve different