DIAGNOSIS OF DUCHENNE MUSCULAR DYSTROPHY BY MLPA AND EVALUATING THE EFFECT OF NEGATIVE SMOKING ON PATIENT`S BEHAVIOR

Submitted By
Nermeen Hamdy El-Azhary Ahmed
M.B.B.Ch., Faculty of Medicine, Cairo University, 2004
Master in (Clinical & Chemical Pathology), Faculty of Medicine,
Ain Shams University, 2015

A Thesis Submitted in Partial Fulfillment
Of
The Requirement for the Doctor of Philosophy Degree
In
Environmental Sciences

Department of Environmental Medical Sciences
Institute of Environmental Studies and Research
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APPROVAL SHEET

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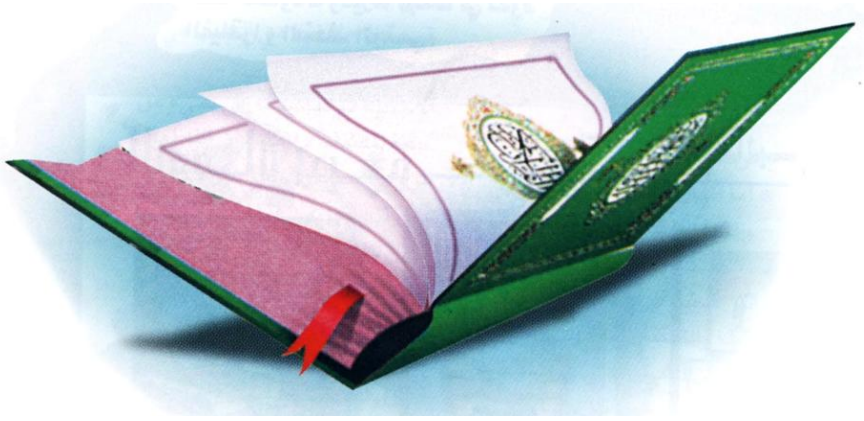
Dedication

I would like to thank **My Husband** *for his actual help and support received in many ways,* **My Mother** *and* **My Father** *for their constant support.*

I wish to thank all my professors, staff members and my colleagues for their kind help and support.

بسم الله الرحمن الرحيم

وَقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ
عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ



صدق الله العظيم

[سورة: التوبة - الآية: ١٠٥]

Abstract

Introduction: Duchenne Muscular Dystrophy (DMD) is the most common x-linked disease caused by mutations in the dystrophin gene. It is characterized by muscle weakness in early childhood, causing death before the age of 20 years. Multiplex ligation-dependent probe amplification (MLPA) had been reported to be a simple, rapid and reliable tool for detection of deletions and duplications in the DMD gene. Attention Deficit Hyperactivity Disorder (ADHD) had been reported in DMD patients. Tobacco smoking exposure is related to offspring behaviour.

Aim: This study aimed to characterize the mutational pattern among DMD patients by MLPA technique and to study the association of exposure to tobacco smoking and behavioral disorders among DMD patients.

Patients and methods: The study was carried out on 30 DMD patients. Peripheral blood was collected for MLPA and karyotype analysis. All patients were subjected to SWAN scale to diagnose ADHD and smoking questionnaire.

Results: According to the types of mutations found in the studied patients, Mutation analysis showed 65% deletion and 10% duplication, while 25% of the patients had neither deletion nor duplication. We found no statistical significance for negative smoking as a contributing factor for ADHD in DMD patients.

Conclusion: Accurate genetic and prenatal diagnosis are needed for families with history of muscular dystrophy to avoid having children with DMD. MLPA should be the initial diagnostic tool for detection of deletion or duplication. ADHD is the most common neurobehavioral comorbidity associated with DMD. Smoking during pregnancy has no direct effect on outcomes of all offspring, including ADHD, and alternative risk factors should be considered.

Keywords: Duchenne Muscular Dystrophy, MLPA, Negative smoking, Attention deficit hyperactivity disease

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ABI	An automated single-capillary genetic analyzer designed for a wide range of sequencing and fragment analysis applications.
ACE	Angiotensin converting enzyme
ADD	Attention Deficit Disorder
ADHD	Attention-Deficit/Hyperactivity Disorder
Array CGH	Array Comparative Genomic Hybridization
ASD	Autistic Spectrum Disorder
ASOT	Antistreptolysin O titre
BMI	Body Mass Index
CCA	Conventional Cytogenetic Analysis
cDNA	Complementary DNA
CK	Creatine Kinase
CPK	Creatine Phosphokinase
DHPLC	Denaturing High Pressure Liquid Chromatography
DMD	Duchenne Muscular Dystrophy disease
DNA	Double Stranded Nucleic Acid
Dp	Dystrophin Isoform
ECG	Electrocardiography
EDTA	Ethylenediamine Tetra-acetic Acid
EMG	Electromyography
ESR	Erythrocyte Sedimentation Rate
FISH	Fluorescence In Situ Hybridization
GTG	Giemsa Banding
ID	Intellectual Disability
Inv	Inversion
IQ	Intelligence Quotient