

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

Submitted By

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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
Ain Shams University

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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.

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَقُلْ اَعْمَلُوا 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

List of Contents

Title	Page No
List of Tables	III
List of Figures	V
List of Photos	VII
List of Abbreviations	VIII
Introduction	2
Aim of the Work	5
Review of the Literature	6
Chapter 1: Duchenne muscular dystrophy	7
Introduction	8
History	9
Definition	10
Prevalence	11
Inheritance	11
Causes	13
Cytogenetics	15
Risk factors	17
Clinical features	17
Diagnosis	22
Investigations	23
Differential diagnosis	30
Management	32

Title	Page No
Chapter 2: Importance of MLPA in diagnosis of DMD	39
Establishing a genetic diagnosis	40
Advantages of MLPA	43
Comparing MLPA to other techniques	44
Limitations of the procedures	47
Confirmation of results	48
Chapter 3: Behavioral problems of DMD and its relation to negative smoking	50
Risk factors of ADHD	60
Diagnosis of ADHD	61
Pathogenesis	63
Other medical and psychosocial conditions	63
Management	64
Patients & Methods	66
Results	87
Discussion	118
Summary & Conclusions	129
Recommendations	133
References	135
Arabic Summary	1-4

List of Tables

Table No.	Title	Page No
Table (1):	SWAN Scale for ADHD patients	70
Table (2):	History and Anthropometric Measurements of the Studied DMD Patients	89
Table (3):	Anthropometric measurements of the studied DMD patients	91
Table (4):	Family history of the studied DMD patients	93
Table (5):	The motor clinical features of the studied DMD patients	96
Table (6):	Frequency and distribution of clinical features 9 of the studied patients	98
Table (7):	Other clinical features of the studied DMD patients	99
Table (8):	Other investigations of the Studied Patients	100
Table (9):	The MLPA results of the studied DMD patients	105
Table (10):	Comparisons between DMD patients with ADHD & others without ADHD according to their negative smoking..	111
Table (11):	Comparisons between DMD patients with ADHD & others without ADHD according to their consanguinity	111
Table (12):	Comparisons between patients with ADHD & others without ADHD according to their mentality	112

Table No.	Title	Page No
Table (13):	Comparisons between patients with ADHD & others without ADHD according to their reflexes	112
Table (14):	Comparisons between patients with ADHD & others without ADHD according to the type of mutations	113
Table (15):	Comparisons between patients with ADHD & others without ADHD according to their steroids treatment	114
Table (16):	Relations of numeric variables in the studied DMD patients with mutations in the dystrophin gene	116
Table (17):	Comparisons between patients with ADHD & others without ADHD according to their motor ability	117

List of Figures

Fig. No.	Title	Page No
Figure (1):	X-linked recessive inheritance	12
Figure (2):	The Components of Dystrophin Protein	14
Figure (3):	Genomic organization of the dystrophin gene	16
Figure (4):	Diagnosis of suspected case of DMD	29
Figure (5):	Multiplex ligation-dependent probe amplification technique	42
Figure (6):	Multiplex ligation-dependent probe amplification (MLPA) reactions	79
Figure (7):	Sex distribution in the studied DMD patients	90
Figure (8):	Age distribution in the studied DMD patient	91
Figure (9):	Positive consanguinity in the studied DMD patients	92
Figure (10):	Degree of family history in the studied DMD patients	93
Figure (11):	Normal vaginal delivery in the studied DMD patients	94
Figure (12):	Onset of clinical picture in the studied DMD patients	95
Figure (13):	Clinical features of the studied DMD patients	97
Figure (14):	Steroids treatment in the studied DMD patients	100

Fig. No.	Title	Page No
Figure (15):	Electromyography in the studied DMD patients	101
Figure (16):	Normal karyotype of DMD male patient	103
Figure (17):	Normal karyotype of DMD female patient	104
Figure (18):	The MLPA Results of the Studied DMD Patients	106
Figure (19):	Frequency of Exons Mutations in MLPA Results of the Studied DMD Patients	107
Figure (20):	Multiplex Ligation-Dependent Probe Amplification analysis by Coffalyser showing no exon deletion of the dystrophin gene	108
Figure (21):	Multiplex Ligation-Dependent Probe Amplification analysis by Coffalyser showing deletion in exon 48-50 of the dystrophin gene	108
Figure (22):	Negative smoking in the Studied DMD Patients	109
Figure (23):	ADHD in the Studied DMD Patients	110

List of Photos

photo. No.	Title	Page No
Photo (1):	Egyptian relief painting from the Egyptian Dynasty	9
Photo (2):	Drawing from a tomb at Beni Hasan (circa 2800-2500 BC)	10
Photo (3):	Gowers' sign	19
Photo (4):	Automatic cell imaging system for karyotyping	77
Photo (5):	PCR Thermocycler	83
Photo (6):	Thermocycler program for the MLPA reaction	84
Photo (7):	Coffalyser® software analysis	86

List of Abbreviations

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