

Biochemical and molecular study of Maple Syrup Urine Disease among Egyptian Children

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لسبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Contents

Title	Page No.
List of Tables	i
List of Figures.....	ii
List of Abbreviations	v
Introduction	1
Aim Of Work.....	5
Review Of Literature	6
1- Inherited Metabolic Disorders	6
2- Inborn Error Of Metabolism.....	7
○ Types Of Inborn Error Of Metabolism.....	8
○ Organic Acidemia.....	9
3- Maple Syrup Urine Disease (Msud)	14
○ Molecular Studies	16
○ The Metabolic Pathway Of Msud.....	33
○ Prevalence Of (Msud).....	35
○ Clinical Manifestation Of (Msud)	36
○ Biochemical diagnosis of (MSUD)	40
○ Treatment And Clinical Management	43
Subjects And Methods.....	46
1- Subjects	46
○ Patients	46
○ Biochemical and molecular studies	47
○ Screening of IEMs by (LS/MS/MS).....	47
○ Blood samples	49
○ Ready-made kits	49
○ Primers.....	50

List of Contents

Title	Page No.
2- Methods	
○ RNA purification	52
○ Synthesis of cDNA from mRNA Template.....	56
○ Amplification of BCKDHA gene from cDNA by Polymerase Chain Reaction (PCR)	60
○ Agarose Gel Electrophoresis	62
○ Sequencing of the PCR product	65
○ Analysis of the data	65
Results	66
1- Clinical and biochemical manifestation	66
2. Mutation analysis of MSUD gene	69
○ Gel Electrophoresis of PCR products of MSUD cDNA ..	69
○ Sequence analysis and alignment results of BCKDHA gene	72
○ Analysis of the Sequencing chromatogram	73
○ Analysis of the amino acid sequence of the Predicted BCKDHA protein.....	76
○ The expected 3-dimension structure of the mutant BCKDHA protein.....	82
Discussion.....	85
Summary.....	96
References	100
Appendix	121
Arabic Summary	-
Arabic Abstract	-

List of Tables

Table No.	Title	Page No.
Table (1-1):	Classification of inborn error metabolism (IEM) different types	12
Table (1-2):	Organic acids excreted in urine in different organic acidurias.....	13
Table (1-3):	Maple Syrup Urine Disease genetics, clinical phenotype, and biochemical features	39
Table (1-4):	Selected medical foods	44
Table (2-1):	Sequence of primers used for PCR reaction covering mRNA of GCDH sequence	51
Table (2-2):	Preparation of washing buffers and lysis buffer for RNA.....	53
Table (2-3):	Genomic DNA elimination reaction components	57
Table (2-4):	Reverse-transcription reaction components	58
Table (2-5):	Contents of PCR reaction mixture.....	60
Table (2-6):	Different degrees of annealing temperatures of different sets of primers.....	61
Table (3-1):	Biochemical manifestations of MSUD patients	68
Table (3-2):	Size of PCR Products of the three sets of primers.....	69
Table (3-3):	Mutations identified in the BCKDHA gene of 6 Egyptian patients.	81

List of Figures

Fig. No.	Title	Page No.
Figure (1-1)	BCKDHA gene location on chromosome 19	16
Figure (1-2)	Structure of the BCKDHA protein	17
Figure (1-3)	BCKDHB gene location on chromosome 6	21
Figure (1-4)	Structure of the BCKDHB protein	22
Figure (1-5)	Dihydrolipoamide branched chain transacylase (DBT) gene location on chromosome 1	24
Figure (1-6)	Structure of Dihydrolipoamide branched chain transacylase (DBT) protein.....	25
Figure (1-7)	Dihydrolipoamide dehydrogenase (E3) gene location on chromosome 7	28
Figure (1-8)	Structure of Dihydrolipoamide dehydrogenase (E3) protein.....	29
Figure (1-9)	Overview of MSUD testing algorithm in NBS	34
Figure (1-10)	Algorithm for newborn screening for MSUD using allo-Ile determination in dried blood spots as a second-tier assay.....	42
Figure (2-1)	Schematic representation of electrospray ionization. The liquid sample flows through a charged capillary which produces positively charged droplets attached by a negatively charged micro droplet into the MS/MS.	48
Figure (2-2)	Schematic representation of the flow of ions in Tandem Mass Spectrometer.	49
Figure (2-3)	RNA purification from whole blood sample by using RNA Purification Mini Kit.	53
Figure (3-1)	1% Agarose gel electrophoresis of amplicons PCR products with about 550 base pair of first set of primers starts from position 17 to544 using primer sequence	70

List of Figures

Fig. No.	Title	Page No.
Figure (3-2):	1% Agarose gel electrophoresis of amplicons PCR products with about 550 base pair of third set of primers.....	70
Figure (3-3):	1% Agarose gel electrophoresis of amplicons PCR products with about 650 base pair of second set of primers.....	71
Figure (3-4):	The homozygous novel frame shift mutation of BCKDHA gene; del T 512 generating missense mutation L171Rfs*159.....	73
Figure (3-5):	The homozygous novel frame shift mutation in 10 bases of BCKDHA gene.....	74
Figure (3-6):	The homozygous frame shift mutation in 8 bases of BCKDHA gene.....	74
Figure (3-7):	The homozygous base substitution transversion mutation of BCKDHA gene; 1312T>A	75
Figure (3-8):	Deduced amino acid sequence of wild type BCKDHA protein representing 446 amino acids.....	76
Figure (3-9):	Protein predicted from c.512_512delT mutation giving p. L171Rfs*159 mutation in Bold (novel mutation).....	77
Figure (3-10):	Protein predicted from c.947_956del GGGCTGTGGC mutation giving p. R316Qfs*11 mutation in Bold (novel mutation).	78
Figure (3-11):	Protein predicted from c.859_866delCGAGGCC region generating G288Vfs*11 missense mutation in bold.....	79
Figure (3-12):	Protein predicted from c c.1312T>A base substitution transversion generating missense Y438N mutation in bold.....	80
Figure (3-13):	3D model of normal BCKDHA precursor protein.....	82

List of Figures

Fig. No.	Title	Page No.
Figure (3-14):	3D model of subunit with p.Leu 171Arg mutation (novel mutation).	83
Figure (3-15):	3D model of subunit with p. Arg316Gln mutation (novel mutation).	83
Figure (3-16):	3D model of subunit with p. Gly288Val mutation.	84
Figure (3-17):	3D model of subunit with p.Tyr438Asn mutation	84

List of Abbreviations

Abb.	Meaning
allo-Ile	allo-Isoleucine
α KGDH	α -ketoglutarate dehydrogenase complex
BCCAs	Branched chain amino acids
BCKAs	Branched chain α -keto acid
BCKDC	branched-chain alpha-ketoacid dehydrogenase complex
BCKDH	Branched chain ketoacid dehydrogenase
BCKDHA	The BCKDHA gene encodes the alpha subunit of E1
BCKDHB	The BCKDHB gene encodes the beta subunit of E1
BIA	bacterial inhibition assay
CNS	central nervous system
DBT	Dihydrolipoamide branched chain transacylase
DLD	Dihydrolipoamide dehydrogenase
DLDD	dihydrolipoamide dehydrogenase deficiency
E1	branched chain α -ketoacid decarboxylase
E2	dihydrolipoyl transacylase
E3	dihydrolipoamide dehydrogenase
HPLC	high-performance liquid chromatography
IEM	inborn errors of metabolism

List of Abbreviations

Abb.	Meaning
MSUD	Maple Syrup Urine Disease
NBS	newborn screening
OADs	Organic acid disorders
PDH	pyruvate dehydrogenase complex
PKU	phenylketonuria

INTRODUCTION

Maple syrup urine disease (MSUD), originally described by Menkes in 1954, is an inherited genetic disease with an autosomal recessive pattern affecting approximately 1 out of 120,000 infants worldwide (*Parmar et al., 2004*).

Maple syrup urine disease (MSUD), or branched chain ketonuria caused by impaired Branched chain α -ketoacid dehydrogenase (BCKDH) complex activity (*Danner and Elsas, 1989*). The biochemical basis of this disease is the inability to metabolize branched chain α -keto acid (BCKAs) derived from the essential branched chained amino acids (BCAAs): leucine, isoleucine, and valine. The elevated BCAAs and BCKAs may have severe clinical consequences including ketoacidosis, mental retardation, and neurological impairment (*Sakai et al., 2005*).

The determination of branched chain amino acids, α - keto acid derived from BCAA, methionine, phenylalanine and tyrosine is currently the most reliable approach for the diagnosis of MSUD (*Kandar et al., 2009*). Diagnosis is also made clinically based on the peculiar maple syrup odor or sugar burnt of the urine, encephalopathy, and α -ketoacids in urine. The presence of plasma L-alloisoleucine and urinary α -hydroxyisovalerate are pathognomonic for MSUD (*Sakai et al., 2005*).