بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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MONA MAGHRABY

Assessment of Nutritional Status and Glycemic Control in Patients with Hepatic Glycogenosis

Thesis

For Partial Fulfillment of Master Degree
in **Pediatrics**

By

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

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Eman Nazeeh Ahmed

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List of Abbreviations

Abb.	Full term
AGL	*Amylo-alpha-1,6- glucosivase, 4-alpha-glucanocratransferase*
ALP	*Alkaline phosphatase*
ALT	*Alanine aminotransferase*
AST	*Aspartate transaminase*
ATP	*Adenosine tri phosphate*
BG	*Blood glucose*
BMI	*Body mass index*
BMIZ	*Body mass index z score*
CBC	*Complete blood count*
CHO	*Carbohydrates*
CNGDF	*Continuous nasogastric day feeding*
EEG	*Electroencephalogram*
GH	*Growth hormone*
GI	*Gastrointestinal*
GSD	*Glycogen storage disease*
HAZ	*Height for age z score*
HCC	*Hepatocellular carcinoma*
IBD	*Inflammatory bowel disease*
IQ	*Intelligence Quotient*
LDH	*Lactate dehydrogenase*
MRI	*Magnetic Resonance Imaging*
MUAC	*Mid upper arm circumference*
OGF	*Over-nights gastric feedings*
RCS	*Raw Cornstarch*
TG	*Triglycerides*

List of Abbreviations (cont...)

Abb.	Full term
UCCS	*Uncooked corn starch*
W HO	*World Health Organization*
WAZ	*Weight for age z score*
WHR	*Waist Hip ratio*

INTRODUCTION

Glycogen is most abundant in the liver and muscle. The main role of glycogen in the liver is to maintain glucose homeostasis. The liver stores glucose for release to tissues that are unable to synthesize significant amounts during fasting ***(Oldfors et al., 2014; Chen, 2001).***

Glycogen storage diseases (GSD) are inherited metabolic disorders of glycogen metabolism ***(Roach, 2002).***

In postprandial period, blood glucose level increases and endogenous glucose production is suppressed. Exogenous glucose is either metabolized to pyruvate or stored as glycogen in the liver and skeletal muscles ***(Saltik et al., 2000).*** Under aerobic conditions, pyruvate is converted to acetyl coenzyme A (acetyl-Co A), which enters the citric acid cycle, the products of which are water, carbon dioxide and adenosine tri phosphate (ATP) or used for the synthesis of fatty acids. In contrast under anaerobic conditions, pyruvate is converted to lactate which is an important alternative fuel during episodes of hypoglycemia. Different hormones including insulin, glucagon, cortisol and others regulate the relationship of glycolysis, gluconeogenesis and glycogen synthesis ***(Roach, 2002).***

There are a number of inborn errors of glucose and glycogen metabolism (dextrinosis and glycogenosis) that result from mutations in genes for virtually all of the proteins

involved in glycogen synthesis, degradation, or regulation. Those disorders that result in abnormal storage of glycogen are known as glycogen storage diseases (GSDs). They are largely categorized by number according to the chronology of recognition of the responsible enzyme defect (Table 1). The age of onset varies from in utero to adulthood ***(Chen, 2001).***

Table (1): Hepatic glycogen storage disorders

Type	Eponym	Enzyme deficiency	Gene	Gene locus	Affected tissue
0			*GYS2*	12p12.2	Liver
Ia	Von Gierke		*G6PC*	17q21	Liver, bowel, kidney
Ib		Hepatic glycogen synthase	*SLC37A4*	11q23	Liver, bowel, kidney, marrow
III	Cori/Forbe	Glucose-6-phosphatase	*AGL*	1p21	Liver (muscle, heart)
IV	Andersen	Glycogen branching enzyme	*GBE1*	3p12	Liver (generalised)
VI	Hers	Hepatic phosphorylase	*PYGL*	14q21-q22	Liver
IX		Phosphorylase kinase	*PHKA1*	Xq13.1-q21	Muscle
			PHKA2	Xp22.2-p22	Liver
			PHKB	16q12-q13	Generalised
			PHKG1	7p12-q21	Muscle
			PHKG2	16p12.1-p11.2	Liver & testis
			PHKD	Various	Generalised
X1	Fanconi-Bickel	GLUT 2 transporter	*SLC2A2*	3q26.1-q26.3	Liver, kidney

Abbreviations: GYS2, Glycogen synthase 2; G6PC, Glucose-6-phosphatase catalytic subunit; SLC37A4, Solute carrier family 37 member 4; AGL, Amylo-alpha-1,6-glucosidase,4-alpha-glucanotransferase; GBE1, 1,4-alpha- glucan branching enzyme 1; PYGL, Glycogen phosphorylase L; PHKA1, Phosphorylase kinase regulatory subunit alpha 1; PHKA2, Phosphorylase kinase regulatory subunit alpha 2; PHKB, Phosphorylase kinase regulatory subunit beta; PHKG2,, Phosphorylase kinase catalytic subunit gamma 2; GLUT 2, Solute carrier family 2 member 2.

Adapted from Wolfsdorf and Weinstein 2003, Beauchamp et al 2007., Kishnani et al.2010, Hicks et al 2011., Dagli et al.2017, Kishnani et al 2014 and Bali et al 2017.

Typically, patients with hepatic forms of GSD are referred to physicians either with recurrent hypoglycaemia, or with hepatomegaly. The severe forms of GSD in childhood are associated with very short fasting intervals of less than 4 hours (Lee et al., 1996). This is quite typical of GSD I but can also be seen in GSD III, VI and IX. Sometimes patients present in the newborn period with profound hypoglycaemia often with seizures ***(Lee et al., 1996).***

The hypoglycaemic glycogen storage diseases (GSD) include GSD 0, I, III, VI, IX and Fanconi Bickel syndrome. They are all associated with hypoglycaemia. GSD type 0 has a small liver and the other conditions have acquired hepatomegaly ***(Lee et al., 2013).***