The Relationship between Serum Leptin and Insulin Resistance in Children and Adolescents with Obesity, Type 1 and Type 2 Diabetes Mellitus

Thesis
Submitted for partial fulfillment of Master Degree in Pediatrics

By Hany Sayed Abdel Maksoud

M.B. B.Ch., 2004, Ain Shams University

Supervised by

Prof.Dr. Mona Hussein El Samahy

Professor of Pediatrics
Faculty of Medicine-Ain Shams University

Prof. Dr. Manal Fawzy Ghozlan

Professor of Clinical Pathology Faculty of Medicine-Ain Shams University

Dr. Jonair Hussein Abdel Kafy

Lecturer of Pediatrics
Faculty of Medicine-Ain Shams University

Faculty of Medicine Ain Shams University 2013

List of Contents

	Page No.
List of Abbreviations	<i>i</i>
List of Tables	iii
List of Figures	v
Introduction and the aim of the work	1
Review of literature	
Type 1 Diabetes Mellitus	4
Type 2 Diabetes Mellitus	13
Obesity	35
Subjects and methods	45
Results	52
Discussion	74
References	85

List of Abbreviations

ACTH : Adrenocorticotropic hormone

AGRP : Agouti gene related protein

AMPK : 5-Adenosine monophosphate activated protein kinase

ARC : Hypothalamic arcuate nucleus

ASIP : Agouti signaling protein
BBB : Blood brain barrier.
BMI : Body mass index.

BDNF : Brain derived neurotrophic factor **cAMP** : Cyclic adenosine monophosphate

CART : Cocaine and amphetamine regulated transcript

CCK : Cholecystokinin

CNS : Central nervous system

CRP : C-reactive protein

DCCT: Diabetes Control and Complications Trial

DKA : Diabetic ketoacidosis

DHEAS : Dehydroepiandrosterone sulfate

DM : Diabetes mellitus

EMCL : Extra myocellular lipids

FFA : Free fatty acids.
GH : Growth hormone

GLP-1 : Glucagon like peptide-1
GLUT-4 : Glucose transporters-4.
HDL : High density lipoproteins.
HbA1c : Glycosylated hemoglobin
HSL : hormone sensitive lipase
IFG : Impaired fasting glucose.
IGF-1 : Insulin growth factor-1

IGT : Impaired glucose tolerance.

IL-1 : Interleukin-1. IL-6 : Interleukin-6.

IMCLs : Intra myocellular lipids.

IR : Insulin resistance.

IRS-1 : Insulin receptor substrate-1.

JAK-STAT3: Janus kinase signal transducerand activator of

transcription 3

LDL : Low density lipoproteins .

LHA : Lateral hypothalamus
LH : Luteinizing hormone

FSH : Follicular stimulating hormoneMAPK : Mitogen activated protein kinase.MCH : Melanin concentrating hormone.

MC3R : Melanocortin 3 receptorMC4R : Melanocortin 4 receptor

mTOR : Mammalian target of rapamycin

MS : Metabolic syndrome

NAFLD : Non alcoholic fatty liver disease

NGT : Normal glucose tolerance

NPY : Neuropeptide Y
ObRs : Leptin receptors.

OSA : Obsructive sleep apnea
PC-1 : Prohormone convertase-1
PCOS : Polycystic ovarian disease

PI3 : Phospatidylinositol 3

PI3K : Phospatidylinositol 3-kinase

PKA : Protein kinase APKC : Protein kinase C

POMC: Pro-opiomelanocortin

PVN : Para ventricular neucleus

PYY : Peptide YY

ROS : Reactive oxygen species

SOD : Superoxide dismutase
 SOB-R : Soluble leptin receptors
 T1DM : Type 1 diabetes mellitus
 T2DM : Type 2 diabetes mellitus

TG : Triglycerides

TNF : Tumor necrosis factor.

VMH : Ventromedial hypothlamus.VLDL : Very low density lipoprotein.

WHR : Waist-hip ratio

List of Tables

Cable No	. Citle 9	Page No.	
Ouete 7ta	. one 3	rage rea.	
Table (1):	Etiological classification of diabetes mellitus	5	ck not defined.
Table (2):	Demographic features of different studied groups		
Table (3):	comparison between different studied groups as regard weight, height and BMI		not defined.
Table (4):	Comparison between different studied groups as regard blood pressure		1ed.
Table (5):	Comparison between different studied groups as regard WHR		
Table (6):	Comparison between different studied groups as regard IR, metabolic syndrome and eGDR		
Table (7):	Comparison between T1DM and control groups as regard IR, eGDR and leptin		not defined.
Table (8):	Comparison between T2DM and control group as regard IR, eGDR and leptin		defined.
Table (9):	Comparison between control and obese groups as regard eGDR and leptin		defined.
Table (10):	Comparison between T1DM and T2DM groups as regard IR, eGDR and leptin		not defined.
Table (11):	Comparison between T1DM and obese groups as regard eGDR and leptin		
Table (12):	Comparison between T2DM and obese groups as regard eGDR and leptin		fined.
Table (13):	Insulin dose and anti-diabetic drugs in different studied groups		

Table (14):	Laboratory investigations in the studied groups	62	
Table (15):	Correlation between IR and different studied parameters in T1DM	63	
Table (16):	IR VS MS, leptin and microalbuminuria in T2DM	64	
Table (17):	Correlation between leptin and different studied parameters in studied groups	65	fined.
Table (18):	Correlation between eGDR and different studied parameters in studied groups	66	fined.
Table (19):	Correlation between BMI and different studied parameters in studied groups	67	fined.
Table (20):	Correlation between WHR and different studied parameters in studied groups	71	fined.

List of Figures

Figure V	la. Citle	PagoNo.
Fig. (1):	Showing Insulin binding to the insuli receptor	
Fig. (2):	Showing Leptin's action in the brain durin states of energy excess and energ deficiency.	У
Fig. (3):	Showing Insulin signalling pathway	56
Fig. (4):	Showing methods of measuring waist hip ratio	o57
Fig. (5):	Comparison between IR in different studie groups	
Fig. (6):	comparison between mean values of eGDI in different studied groups	
Fig. (7):	comparison between mean values of HAB1 in different studied groups	
Fig. (8):	comparison between mean values of leptin i different studied groups	
Fig. (9):	Showing negative correlation between eGD and insulin dose in T1DM group	
Fig. (10):	Showing negative correlation between eGD and SBP in T1DM group	
Fig (11):	Showing negative correlation between eGD and DBP in T1DM group	
Fig. (12):	Showing negative correlation between eGD and leptin in T1DM group	
Fig. (13):	Showing negative correlation between eGD and leptin in obese group	

ined.

not defined.

Fig. (14):	and SBP in T1DM		•	.73
	Showing positive and DBP in T1DM			.73

بسم الله الرحن الرحيم وَأَنْزَلَ اللهُ عَلَيْكَ الْكِتَابَ وَالْحِكْمَةُ وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ تَعْلَمُ تَعْلَمُ وَكَانَ فَضَلُ اللهِ وَكَانَ فَضَلُ اللهِ عَلَيْكَ عَظِيمًا صرق الله العظيم سورة النساء آية (١١٢)

Acknowledgement

First and foremost, I feel always indebted to **Allah**, the most kind and the most merciful.

I would like to express my sincere gratitude to **Prof. Dr. Mona Hussein El-Samahy**, Professor of Pediatrics, Faculty of Medicine—Ain Shams University, under her supervision, I had the honor to complete this work, I am deeply grateful to her for her professional advice, guidance and support.

I wish also to express my gratitude to **Prof. Dr. Manal Fawzy Ghozlan**, Professor of Clinical Pathology, Faculty of Medicine—Ain Shams University, for her great efforts, kind advice, support and encouragement throughout the whole work.

I am also greatly indebted to **Dr. Jonair Huessin Abd El Kafy**, Lecturer of Pediatrics, Faculty of Medicine —Ain Shams University, for her tremendous effort she has done, enthusiasm and help.

Also many thanks to the patients, as their cooperation was very important to accomplish this work.

Last but not least, I like to thank my beloved parents and brothers for their persistent assistance, kind care, help and encouragement. They are the candle of my life.



Introduction and the Aim of the work





Review of Literature





Subjects and Methods





Results

