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List of Abbreviations

AGEs	:	Advanced glycation end products
Akt	:	The protein kinase B
ALT	:	Alanine amino transferase
AST	:	Aspartate amino transferase
ATP	:	Adenosine triphosphate
ATP/ADP	:	Adenosine triphosphate/adenosine diphosphate ratio
AUC	:	Area under the curve
BMI	:	Body mass index
CAP	:	Cbl associated protein
Cbl	:	Casitas B lineage lymphoma
CRP	:	C-reactive protein
CVD	:	Cardiovascular disease
Cyclic AMP	:	Cyclic adenosine monophosphate
DAG	:	Diacylglycerol
D.Bp	:	Diastolic blood pressure
DNA	:	Deoxyribonucleic acid
EASIA	:	Enzyme Amplified Sensitivity Immunoassay
ENPP1or PC-1	:	Ectonucleotide pyrophosphatase phosphodiesterase -1
FFAs	:	Free fatty acids
FKHR	:	Forkhead in rhabdomyosarcoma
Foxo family	:	Forkhead member of the class O
FGIR	:	Fasting glucose/insulin ratio.
G6P	:	Glucose-6-phosphate
GH	:	Growth hormone
GIP	:	Gastric inhibitory polypeptide
GIP	:	Glucose-dependent insulinotropic polypeptide,
GLP-I	:	Glucagon-like peptide-1
GLUT	:	Glucose transporter
GLUT-4	:	Glucose transport -4

List of Abbreviations (Cont.)

GLUT mRNA	:	Glucose transporter messenger ribonucleic acid
GPO	:	Glycerol-3-phosphate oxidase
GRP	:	Gastrin-releasing polypeptide
GSIS	:	Glucose stimulated insulin secretion
GSK-3	:	Glycogen synthase kinase-3
HDL	:	High density lipoprotein
HDL-C	:	High-density lipoprotein cholesterol
Ht	:	Height
HOMA	:	Homeostasis Assessment Model
HOMA-IR	:	Homeostasis Assessment Model insulin resistance
HPA	:	Hypothalamo-pituitary adrenal axis
HRP	:	Horseradish peroxidase
IGF-1	:	Insulin like growth factor-1
IGT	:	Impaired glucose tolerance
IKK-Eβ	:	Serine kinase IkB kinase-β
IL-1	:	Interleukin-1
IL-15	:	Interleukin-15
IL-1RA	:	Interleukin-1receptor antogonist
IL-6	:	Interleukin-6
IR	:	Insulin resistance
IRS	:	Insulin-receptor substrates
IRS-1	:	Insulin-receptor substrates-1
IRS-2	:	Insulin-receptor substrates-2
ITT	:	Insulin tolerance test
LDL	:	Low density liproprotien
LDL-C	:	Low-density lipoprotein cholesterol
MAbs	:	Monoclonal antibodies
MAP	:	Mitogen activated protein.
McA	:	McAuley
MCP-1	:	Monocyte chemoattractant protein-1
MIDD	:	Maternally inherited diabetes and deafness

List of Abbreviations (Cont.)

MMAMG	:	Minimal model approximation of the metabolism of glucose
MODY	:	Maturity onset diabetes of the young
NAFLD	:	Non-alcoholic fatty liver disease
NEFA	:	Non-esterified fatty acids
NF-KB	:	Nuclear transcription factor KB
NPV	:	Negative predictive value
NO	:	Nitric oxide
OGTT	:	Oral glucose tolerance test
OSA	:	Obstructive sleep apnea
P13-K	:	Phosphatidyl inositol 3-kinase
PACAP	:	Pituitary adenylate cyclase-activating polypeptide
PAI-1	:	Plasminogen activator inhibitor -1
PCOS	:	Polycystic ovary syndrome
PDK1	:	Phosphoinositide-dependent kinase 1
PIP2	:	Phosphatidylinositol 4,5-bisphosphate
PIP3	:	Phosphatidylinositol 3,4,5-trisphosphate
PK	:	Pyruvate kinase
PKA	:	Protein kinase A
PKB	:	Protein kinase B
PKC	:	Protein kinase C
PPAR –α	:	Peroxisome proliferator – activated receptor - alpha
PPAR- γ	:	Peroxisome proliferator – activated receptor - gamma
PPAR	:	Peroxisome proliferator – activated receptor
PPBS	:	Post prandial Blood sugar
PPV	:	positive predictive value
PTEN	:	Phosphatase and tensin homologue deleted on chromosome 10
PTP 1B	:	Protein-tyrosine phosphatases 1B
PTPases	:	Protein-tyrosine phosphatases
QUICKI	:	Quantitative insulin sensitivity check index

List of Abbreviations (Cont.)

RAAS	:	Rennin angitensin aldosterone system
RBP-4	:	Retinol-binding protein -4
RNS	:	Reactive nitrogen species
ROC	:	Receiver operator characteristic
ROS	:	Reactive oxygen species
S.Bp	:	Systolic blood pressure
SHBG	:	Sex-hormone binding globulin
SHIP2	:	SH-2-containihg inositol 5-phosphatase 2
SNS	:	Sympathetic nervous system
TDP	:	Time-dependent potentiation
TGs	:	Triglycerides
TIMP-l	:	Tissue inhibitors of metalloproteinases -1
TMP	:	3,3',5,5'-Teramethyl-benzidine
TNFα	:	Tumor necrosis factor-alpha
TZDs	:	Thiazolidinediones
VIP	:	Vasoactive intestinal peptide
VLDL	:	Very-low-density lipoprotein
W/H ratio	:	Waist hip ratio
WT	:	weight
4-AAP	:	Amino-4-antipyrine

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Single Versus Multiple Assessment(s) of Different Insulin Resistance Modalities (HOMA – QUICKI – McAULEY)

Thesis
Submitted for Partial Fulfillment of Master Degree
In **Endocrinology**

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مقارنة دقة التقييم لمقاومة الإنسولين مرة واحدة بالمقارنة بالتقييم عدة مرات

رسالة مقدمة

الطبيبة/ رشا كمال محمد الزهيري

توطئة للحصول على درجة الماجستير في
الغدد الصماء والأيض

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Introduction

Diabetes mellitus is the most common endocrine disorder, currently affecting over 170 million people world wide and prospectively over 365 million in the year 2030 ***(Wild et al., 2004).***

More than 90% of the diabetic patients suffer from type 2 diabetes mellitus. Besides β cell failure, the major pathophysiological event contributing to the development of type 2 diabetes mellitus is resistance of target tissues to insulin ***(Kahn, 2003)***.

Insulin lowers blood glucose levels by facilitating glucose uptake mainly in to skeletal muscle and fat tissue and by inhibiting endogenous glucose production by the liver. In insulin resistance states, these organs do not properly respond to insulin, thereby causing hyperglycemia and reactive increase in insulin secretion by the pancreatic β cells, the elevated insulin levels can compensate for the poor insulin response only for a limited time, but on the other hand impair insulin resistance ***(Kahn, 2003)***.

Insulin resistance is the object of growing interest because it is a strong predictor and plays an important role in the development of type 2 diabetes and cardiovascular disease

(Stumvoll and Gerich, 2001). The availability of methods to reliably and easily measure insulin resistance is of particular interest. Therefore, studying their accuracy is worthy being done.

Aim of the Study

The aim of the study is to compare the accuracy of assessment of insulin resistance by applying Homeostatic Model Assessment (HOMA), Quantitative Insulin Sensitivity Check Index (QUICKI), and McAuley index once in comparison with their application multiple times, and to see their correlation with clinical features of metabolic syndrome.

Insulin

Definition:

Insulin is a peptide hormone secreted by the β cells of the pancreatic islets of Langerhans and maintains normal blood glucose levels by facilitating cellular glucose uptake, regulating carbohydrate, lipid and protein metabolism and promoting cell division and growth through its mitogenic effects ***(Cefalu, 2001).***

Structure and Chemical Properties of Insulin

Insulin is a protein consisting of 51 amino acids contained within two peptide chains: an A chain, with 21 amino acids; and a B chain, with 30 amino acids. The chains are connected by two disulfide bridges. In addition, there is an intra chain disulfide bridge that links positions 6 and 11 in the A chain, as shown in fig (1).

The molecular weight of human insulin is 5808. Endogenous insulin has a circulatory half life of 3-5 minutes. It is catabolized chiefly by insulinase in liver, kidney, and placenta. Approximately 50% of insulin is removed in a single pass through the liver ***(Gadener and Shoback, 2007).***

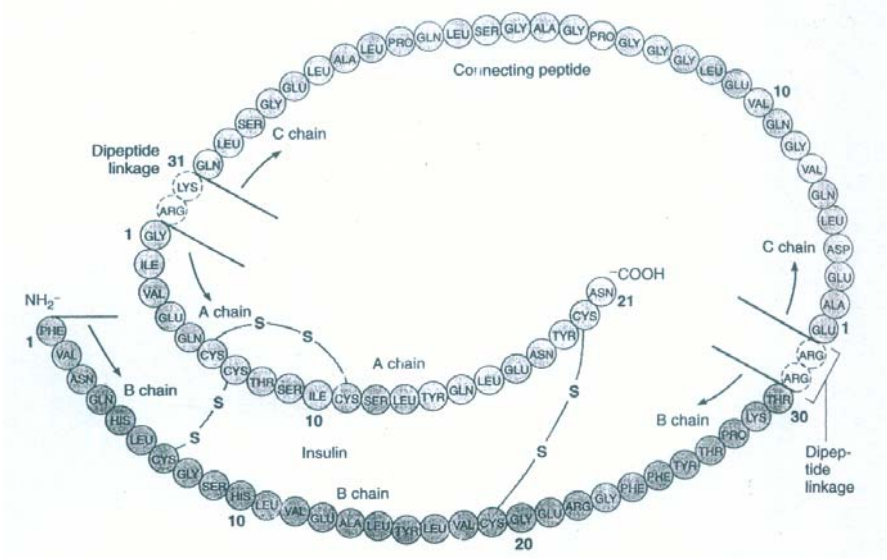

Fig1: Structure of human Insulin ***(Gadener and Shoback, 2007).***

Synthesis and Release of Insulin

The human insulin gene is located on the short arm of chromosome 11. A precursor molecule, preproinsulin, a peptide of MW 11,500, is translated from the preproinsulin messenger RNA in the rough endoplasmic reticulum of pancreatic β cells. Microsomal enzymes cleave preproinsulin to proinsulin (MW 9000) almost immediately after synthesis. Proinsulin is transported to the Golgi apparatus, where packaging into clathrin –coated secretory granules takes place. Maturation of the secretory granule is associated with loss of the clathrin coating and conversion of proinsulin into insulin and a smaller connecting peptide, or C peptide, by proteolytic cleavage at two sites along the peptide chain ***(Gadener and Shoback, 2007).***

The mature insulin molecule and C peptide are stored together and cosecreted from secretory granules in the beta cells. Because the C peptide is less susceptible than insulin to hepatic degradation, it is useful marker of insulin secretion and allows discrimination of endogenous and exogenous sources of insulin in the evaluation of hypoglycemia ***(Jameson, 2006).***

Insulin secretion from the islet cells into the portal veins is characteristically pulsatile, reflecting the summation of coordinate secretory bursts from millions of islet cells. An ultradian oscillatory pattern of insulin release, in addition to post meal variation, has been reported." In response to a stimulus such as glucose, insulin secretion is characteristically biphasic, with an initial rapid phase of insulin secretion, followed by a less intense but more sustained release of the hormone ***(Porksen et al., 2002).***