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Study of the Relationship between Insulin Resistance, Iron Status Markers and Body Weight in a Sample of Egyptian Population

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سُبْحَانَكَ لَا مَعْلَمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

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List of Contents

Title	Page No.
List of Tables	i
List of Figures	iii
List of Abbreviations	v
Introduction.....	1
Aim of the Work	3
Review of Literature	
Diabetes Mellitus	4
Insulin Resistance.....	33
Obesity and Relationship with Diabetes Mellitus and Insulin Resistance	40
Iron Markers and Relationship with DM and Insulin Resistance	52
Patients and Methods	60
Results	78
Discussion.....	108
Summary	115
Conclusion	117
Recommendations	118
References	119
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Table 1:	Etiologic Classification of Diabetes Mellitus	6
Table 2:	Staging of Type 1 DM	9
Table 3:	Diagnosis of GDM	13
Table 4:	Criteria for the diagnosis of diabetes.....	20
Table 5:	Causes of insulin resistance	35
Table 6:	Various methods to measure insulin resistance	36
Table 7:	Comparison between the three studied groups regarding age and gender.....	87
Table 8:	Insulin resistance and severity among the patients group (obese diabetic and obese non diabetic).....	88
Table 9:	Comparison between the three studied groups regarding smoking, family history of diabetes.....	90
Table 10:	Comparison between the three studied groups regarding Blood pressure, pulse, BMI, W/H Ratio.....	91
Table 11:	Comparison between the three studied groups regarding Hb, Hematocrit, MCV, MCH, RDW.....	92
Table 12:	Comparison between the three studied groups regarding iron study.....	93
Table 13:	Comparison between The three studied groups regarding FBG, 2hpp, F.insulin, T.cholesterol, LDL, HDL.TG, HOMA IR.	94

List of Tables_{cont...}

Table No.	Title	Page No.
Table 14:	Correlation between the studied parameters in patients group (obese diabetic and obese non diabetic).....	97
Table 15:	Multivariate linear regression analysis for factors affecting the level of HOMA IR.....	105
Table 16:	Comparison between patients with T.sat \leq 20% and those with T.sat $>$ 20% regarding the studied parameters.....	106

List of Figures

Fig. No.	Title	Page No.
Figure 1:	Pathogenesis of insulin resistance.....	34
Figure 2:	Pleiotropic effects of insulin to promote adipose storage	42
Figure 3:	Evolving view of the biological functions of the adipocyte.....	47
Figure 4:	Comparison between the three studied groups regarding age.....	87
Figure 5:	Insulin resistant among the patients group.....	89
Figure 6:	Severity among the patients group	89
Figure 7:	Comparison between the three studied groups regarding W/H Ratio	91
Figure 8:	Comparison between The three studied groups regarding Hematocrit.....	92
Figure 9:	Comparison between the three studiedgroups regarding T.cholesterol, LDL, HDL, TG.....	95
Figure 10:	Comparison between the threestudied groupsregarding FPG, 2hpp.....	95
Figure 11:	Comparison between the three studied groups regarding Fasting insulin.	96
Figure 12:	Comparison between the three studied groups regarding HOMA.....	96
Figure 13:	Correlation between ferritin and TIBC	98
Figure 14:	Correlation between ferritin and T. sat	98
Figure 15:	Correlation between S. iron and T. sat.....	99
Figure 16:	Correlation between S. iron and TIBC	99
Figure 17:	Correlation between S.iron, LDL.....	100

List of Figures_{cont...}

Fig. No.	Title	Page No.
Figure 18:	Correlation between TIBC and FPG	100
Figure 19:	Correlation between T.SAT, SBP	101
Figure 20:	Correlation between, HOMAIR, Age.	101
Figure 21:	Correlation between HOMAIR, Hematocrit.....	102
Figure 22:	Correlation between HOMAIR, MCV	102
Figure 23:	Correlation between HOMAIR, FPG.....	103
Figure 24:	Correlation between HOMAIR, 2hpp.	103
Figure 25:	Correlation between HOMAIR, Fasting insulin.	104
Figure 26:	Correlation between HOMAIR, LDL.....	104
Figure 27:	Comparison between patients with T.sat ≤ 20% and those with T.sat > 20% regarding ferritin level	107
Figure 28:	Comparison between patients with T.sat ≤ 20% and those with T.sat > 20% regarding iron level	107

List of Abbreviations

Abb.	Full term
ADA	American diabetes association
ASCVD	Atherosclerotic cardiovascular disease
BMI	Body mass index
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
FPG	Fasting plasma glucose
2hpp	2hour post prandial
GDM	Gestational diabetes mellitus
GLT	Glucose load test
HDL	High density lipoprotein
LDL	Low density lipoprotein
TG	Triglycerides
TIBC	Total iron binding capacity
T.SAT	Transferrin saturation
HOMA-IR	Homeostasis model assessment
WAT	White adipose tissue
BAT	Brown adipose tissue
IR	Insulin resistance
IAs	Insulin auto antibodies
IADPSG	International Association of Diabetes and Pregnancy Study Groups
ICAs	Islet cell antibodies
ICD	International classification of diseases

List of Abbreviations *cont...*

Abb.	Full term
IDDM.	Insulin dependent diabetes mellitus
LADA.	Latent autoimmune diabetes in adults
MODY.	Maturity onset diabetes in young
NHANES.	National Health and Nutrition Examination Survey
NICE.	National Institute for Clinical Excellence
NIDDM.	Non Insulin dependent diabetes mellitus
NIH.	National Institutes of Health

INTRODUCTION

Iron homeostasis is affected by obesity and obesity-related insulin resistance in a many-faceted fashion. On one hand, iron deficiency and anemia are frequent findings in subjects with progressed stages of obesity. On the other hand, hyperferritinemia with normal or mildly elevated transferrin saturation is observed in approximately one-third of patients with metabolic syndrome (MetS) or nonalcoholic fatty liver disease (NAFLD) (*Elmar Aignar et al., 2014*).

This constellation has been named the “dysmetabolic iron overload syndrome (DIOS)”. Both elevated body iron stores and iron deficiency are detrimental to health and to the course of obesity-related conditions. Iron deficiency and anemia may impair mitochondrial and cellular energy and further increase inactivity and fatigue of obese subjects.

Obesity-associated inflammation is tightly linked to iron deficiency and involves impaired duodenal iron absorption associated with low expression of duodenal ferroportin (FPN) along with elevated hepcidin concentrations (*Elmar aignar et al., 2014*).

Obesity, the most common cause of insulin resistance, is associated with a decreased number of receptors and with post receptor failure to activate tyrosine kinase. Although adiposity and insulin resistance are related, they are not necessarily synonymous, and each may make independent and different contributions to

increasing the risk of cardiovascular disease. Moreover, in obesity, inflammation, with increased accumulation and inflammatory polarization of immune cells, takes place in various tissues, including adipose tissue, skeletal muscle, liver, gut, pancreatic islet, and brain, and may contribute to obesity-linked metabolic dysfunctions, leading to insulin resistance and type 2 diabetes (*Olatunbosun et al., 2020*).

Leptin and ghrelin are two hormones that have a major influence on energy balance. Leptin is a long-term regulator of energy balance, suppressing food intake and thereby inducing weight loss, while ghrelin is a fast-acting hormone, seemingly playing a role in meal initiation. Obese individuals tend to be leptin resistant; their circulating levels of the anorexigenic hormone leptin are increased, but the levels of the orexigenic hormone ghrelin are decreased (*Cui et al., 2017*).

Iron overload is a risk factor for diabetes. The link between iron and diabetes was first recognized in pathologic conditions hemochromatosis and thalassemia, but high levels of dietary iron also impart diabetes risk. Iron plays a direct and causal role in diabetes pathogenesis mediated both by beta cell failure and insulin resistance. Iron also regulates metabolism in most tissues involved in fuel homeostasis, with adipocyte in particular serving an iron sensing role (*Simcox and McClain, 2013*).

AIM OF THE WORK

The aim of this study is to investigate the relationship between insulin Resistance, iron Status Markers and body Weight in a sample of Egyptian population.

DIABETES MELLITUS

Diabetes mellitus (DM) is a group of metabolic disorders characterized by a chronic hyperglycemic condition resulting from defects in insulin secretion, insulin action or both (*De León and Stanley, 2016*).

The number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014. The global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014 (*Balakumar et al., 2016*).

There are two main types of diabetes mellitus. Type 1 diabetes is insulin dependent diabetes mellitus (IDDM), and is caused by lack of insulin secretion by beta cells of the pancreas. Type 2 diabetes, also called non-insulin dependent diabetes mellitus (NIDDM), is caused by decreased sensitivity of target tissues to insulin which is later followed by decreased secretion of insulin (*Diaz-Valencia et al., 2015*).

Classification of Diabetes Mellitus:

Diabetes is a heterogeneous complex metabolic disorder characterized by elevated blood glucose concentration secondary to either resistance to the action of insulin, insufficient insulin secretion, or both (*Herrera et al., 2018*).

The major clinical manifestation of the diabetic state is hyperglycemia. However, insulin deficiency and/or insulin