CLINICAL SIGNIFICANCE OF ADIPOCYTE FATTY ACID BINDING PROTEIN (A-FABP) IN GESTATIONAL DIABETES MELLITUS

Thesis

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Heba Hassan Abd El Menim

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LIST OF ABBREVIATIONS

Abbrev.	Full term
ABCA1	ATP-Binding Cassette A1.
ADA	American Diabetes Association.
A-FABP	Adipocyte Fatty Acid Binding Protein (aP2, FABP 4).
AP1	Adaptor Protein 1.
ApoE	Apolipoprotein E.
CAAT	Controlled Amino Acid Therapy.
CE	Cholesterol Esterase.
CI	Confidence Interval.
COX	Cyclo-oxygenase enzyme.
DCCT	Diabetes Control and Complications Trial.
E-FABP	Epidermal Fatty Acid binding Protein.
ELISA	Enzyme Linked Immuono Sorbant Assay.
ER	Endoplasmic Reticulm.
ESSMCD	Executive Summary: Standards of Medical Care in Diabetes.
GDG	Guide Line Development Group.
GDM	Gestational Diabetes Mellitus.
GLUT1	Glucose Transporter-1.
HAPO	Hyperglycemia and Adverse Pregnancy Outcome
HbA1c	Hemoglobin A1c (Glycoslated Hemoglobin).
HDL-C	High Density Lipoprotein -Cholesterol.
HOMA-IR	Homeostasis Model Assessment -Insulin Resistance index.
HPLC	High -Performance Liquid Chromatography.
HRP	Hypersensitive Response and Pathogenicity.
HSL	Hormone Sensitive Lipase.
IFG	Impaired Fasting Glucose.
IFN-γ	Interferon-gamma.
IGF	Insulin-Like growth Factor.

LIST OF ABBREVIATIONS (Cont...)

Abbrev.	Full term
IGF	Insulin -Like growth Factor
IGT	Impaired Glucose Tolerance.
IKK	Inhibitor of Kappa Kinase.
IL	Interleukin.
iNOS	Inducible Nitric Oxide Synthase.
IRS	Insulin Receptor Substrate.
IRS	Insulin Receptor substrate.
IVGTT	Intravenous Glucose Tolerance Test.
JNK	C-Junction N-terminal Kinase.
kDa	Kilo Dalton.
LDL-C	Low-Density Lipoprotein Cholesterol.
LXR-α	Liver X Receptor -α
MCP1	Monocyte Chemo attractant Protein 1
mRNA	Messenger Ribonucleic Acid.
NDDG	National Diabetes Data Group.
NES	Nuclear Export Signal.
NF-κB	Nuclear Factor- κB.
NGT	Normal Glucose Tolerance.
NICE	National Institute for Health and Clinical Excellence.
NLS	Nuclear Localization Signal.
OGTT	Oral Glucose Tolerance Test.
PDB	Protein Data Bank.
POS	Polycystic Ovarian Syndrome.
PPAR-γ	Peroxisome Proliferator-Activated Receptor.
RR	Relative Risk.
STAT6	Signal Transducer and Activator of Transcription 6.

LIST OF ABBREVIATIONS (Cont...)

Abbrev.	Full term
T2DM	Type 2 Diabetes Mellitus.
TG	Tri Glyceride
TH	T-Helper cell.
TMB	Tetra Methyl Benzidine.
TNFα	Tumor Necrosis Factor Alpha.
UK	United Kingdom.
VLDL	Very Low Density Lipoprotein.
WHO	World Health Organization.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a serious complication in pregnancy which is characterized by glucose intolerance with onset or first recognition during pregnancy ***(Buchanan et al., 2007).***

The 8-year postpartum diabetes mellitus risk is more than 50% in patients with previous GDM. As a consequence of a diabetic pregnancy, mother and newborn have a significantly increased future risk for metabolic and cardiovascular diseases. Fetal complications include increased fetal and neonatal morbidity and mortality due to its association with adverse outcome such as macrosomia, birth injury e.g., shoulder dystocia, neonatal hypoglycemia and fetal death ***(Lobner et al., 2006; Chenug and Byth, 2009).***

Insulin resistance during pregnancy and a limitation in the pancreatic β-cell reserve contribute to the development of GDM. Furthermore, adipocyte secreted factors - so-called adipokines - influence insulin sensitivity hence might play an important role in the pathogenesis of GDM ***(Ranheim et al., 2009).***

Adipocyte-specific fatty acid–binding protein (A-FABP) has recently been described as a novel adipokine associated with insulin resistance. It belongs to the fatty acid-binding protein super-family whose members have relative molecular

masses of ~15 kDa and it is highly expressed in adipose tissue. A-FABP is a predominant cytosolic protein of mature adipocytes, accounting for ~6% of total cellular proteins. This protein may be an important regulator of systemic insulin sensitivity and lipid and glucose metabolism ***(Makowski and Hotamisligil, 2004).***

A-FABP serum levels were significantly increased in overweight and obese subjects as compared to lean controls and correlated positively with waist circumference, blood pressure, and insulin resistance. Higher baseline levels of circulating A-FABP independently predicted the risk to develop a metabolic syndrome during a follow up of 5 years ***(Xu et al., 2007).*** Similarly, baseline A-FABP concentrations were predictive of type 2 DM independent of obesity, insulin resistance, or glycemic indexes ***(Tso et al., 2007).*** Moreover, A-FABP might have a central role in the development of metabolic and cardiovascular disease ***(Yeung et al., 2007).*** In addition, many researchers suggest the alteration of A-FABP levels in cases of GDM ***(Kralisch et al., 2009).***

AIM OF THE WORK

The aim of the present study was to demonstrate the clinical utility of adipocyte fatty acid binding protein (A-FABP) as a novel adipokine related to gestational diabetes mellitus and to study its correlation with the metabolic and cardiovascular risk of the disease.