

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

Thesis

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# الأهمية الأكلينيكية للبروتين الرابط للأحماض الدهنية ذات الخلايا الشحمية فى مرضى سكر الحمل

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توطئة للحصول على درجة الماجستير  
فى الباثولوجيا الأكلينيكية

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# LIST OF ABBREVIATIONS

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

## LIST OF ABBREVIATIONS (Cont...)

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

## LIST OF ABBREVIATIONS (Cont...)

Abbrev.	Full term
<b>T2DM</b>	Type 2 Diabetes Mellitus.
<b>TG</b>	Tri Glyceride
<b>TH</b>	T-Helper cell.
<b>TMB</b>	Tetra Methyl Benzidine.
<b>TNF<math>\alpha</math></b>	Tumor Necrosis Factor Alpha.
<b>UK</b>	United Kingdom.
<b>VLDL</b>	Very Low Density Lipoprotein.
<b>WHO</b>	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  $\beta$ -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.