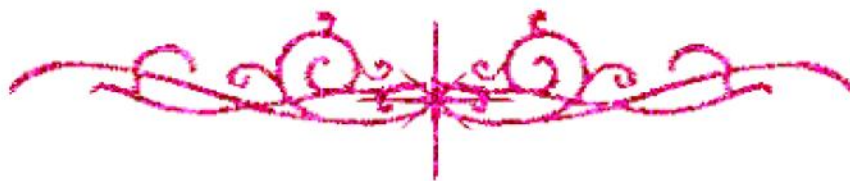


بسم الله الرحمن الرحيم





شبكة المعلومات الجامعية التوثيق الالكتروني والميكرو فيلم



جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



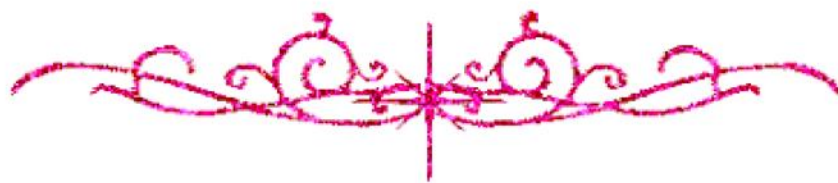


بعض الوثائق الأصلية تالفة





بالرسالة صفحات
لم ترد بالأصل





Role of Fibroblast growth factor 21 (FGF-21) as a prognostic marker for fetal and maternal complications in patients with gestational diabetes mellitus

Thesis

*Submitted for Partial Fulfilment of Master Degree in
Internal Medicine*

By

Ola Mohamed Mostafa Shaheen

M.B.B.CH., Ain Shams University, 2015

Under the Supervision of

Prof. Dr. Mohamed Reda Halawa

*Professor of Internal medicine and Endocrinology
Faculty of Medicine – Ain Shams University*

Prof. Dr. Magdy Hassan Kolaib

*Professor of Obstetrics and Gynecology
Faculty of Medicine – Ain Shams University*

Dr. Salah Hussein El-Halawany

*Lecturer of Internal Medicine and Endocrinology
Faculty of medicine – Ain Shams University*

Dr. Dina Ahmed Marwan

*Lecturer of Internal Medicine and Endocrinology
Faculty of Medicine – Ain Shams University*

*Faculty of Medicine
Ain Shams University*

2020

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا انك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٢٢

Acknowledgment

*First and foremost, I feel always indebted to **ALLAH**, the Most Kind and Most Merciful.*

*I'd like to express my respectful thanks and profound gratitude to **Prof. Dr. Mohamed Reda Halawa**, Professor of Internal Medicine and Endocrinology, Faculty of Medicine – Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

*I am also delighted to express my deepest gratitude and thanks to **Prof. Dr. Magdy Hassan Kolaib**, Professor of Obstetrics and Gynecology, Faculty of Medicine – Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

*I am deeply thankful to **Dr. Salah Hussein El-Halawany**, Lecturer of Internal Medicine and Endocrinology, Faculty of medicine – Ain Shams University, for his great help, active participation and guidance.*

*I wish to introduce my deep respect and thanks to **Dr. Dina Ahmed Marwan**, Lecturer of Internal Medicine and Endocrinology, Faculty of Medicine – Ain Shams University, for her kindness, supervision and cooperation in this work.*

I would like to express my deep gratitude and thankfulness to the patients and control subjects included in this study for their cooperation. Finally, I would like to thank Clinical pathology department and Ain Shams University hospitals laboratories for their great efforts throughout the study

Ola Mohamed

List of Contents

Title	Page No.
List of Abbreviations.....	I
List of Tables	IV
List of Figures	VI
Introduction	1
Aim of the Study	3
Review of Literature	
Gestational Diabetes	4
Fibroblast Growth Factor 21	33
Fibroblast Growth Factor in Gestational Diabetes	45
Patients and Methods.....	49
Results	62
Discussion	86
Summary	92
Conclusion	94
Recommendations	96
References	97
Arabic Summary	—

List of Abbreviations

Abb.	Full term
2hpp.....	2 hour postprandial
Ab.....	Antibody
ACOG	American College of Obstetricians and Gynecologists
ADA	American Diabetes Association
ADA	American Diabetes Association
AGEs.....	Advanced Glycation End products
AUC	Area under curve
BAT.....	Brown Adipose Tissue
BMI.....	Body Mass Index
Cr.....	Creatinine
CS	Cesarean section
CVD	Cardiovascular disease
DM	Diabetes Mellitus
EDTA.....	Ethylenediaminetetraacetic acid
ELISA.....	Enzyme-linked immunosorbent assay
ERK	Extracellular signal Regulated Kinase
FBS	Fasting blood sugar
FDA	Food and Drug Administration
FGF21.....	Fibroblast growth factor 21
FGFR.....	Fibroblast Growth Factor Receptors
FPG.....	Fasting Plasma Glucose
FRS2.....	Fibroblast Growth Factor Receptors substrate 2
GDM	Gestational diabetes mellitus
Grb2.....	Growth factor receptor-bound protein 2
Hb A1c.....	Hemoglobin A1c
hCG.....	Human Chorionic Gonadotrophin
HDL.....	High Density Lipoproteins

List of Abbreviations Cont...

Abb.	Full term
HELLP	Hemolysis, Elevated Liver enzymes, Low Platelets
HFD	High Fat Diet
hPL	Human Placental Lactogen
HRP	Horseradish Peroxidase
HS	Highly significant
IADPSG	International Association of Diabetes In Pregnancy Study Groups
IDF	International Diabetes Federation
IL	Interleukin
IQR	Inter-quartile range
IR	Insulin Resistance
JNK	c-Jun N-terminal kinase
KLB	β klotho
LDL	Low Density Lipoproteins
MedDiet	Mediterranean Diet
MetS	Metabolic Syndrome
miRNA	Micro Ribonucleic Acid
MNT	Medical Nutrition Therapy
mtDNA	Mitochondrial Deoxyribonucleic Acid
NAFLD	Non Alcoholic Fatty Liver Disease
NGT	Normal Glucose Tolerance
NICE	National Institute for Health and Care Excellence
NPV	Negative predictive value
NS	Non significant
OD	Optical density
OGTT	Oral Glucose Tolerance Test

List of Abbreviations Cont...

Abb.	Full term
PG	Plasma Glucose
PPV	Positive predictive value
RCT.....	Randomized Controlled Trial
ROC	Receiver operating characteristic
S.....	Significant
SMBG	Self Monitoring Blood Glucose
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 diabetes mellitus
TC	Total Cholesterol
TG	Triglycerides
TNF	Tumor Necrosis Factor
TNFR-1.....	Tumor Necrosis Factor Receptor 1
UCP-1	Uncoupling protein-1
UK	United Kingdom
VLDL.....	Very Low-Density Lipoprotein
WAT.....	White Adipose Tissue
WHO	World Health Organization
ZDF.....	Zucker Diabetic Fatty
ZO	Zonulin

List of Tables

Table No.	Title	Page No.
Table (1):	Threshold levels in venous plasma after 75 OGTT according to IADPSG consensus recommendations.....	16
Table (2):	IADPSG recommendations for detection of Diabetes during pregnancy.....	17
Table (3):	Various criteria for gestational diabetes mellitus (GDM) diagnosis using oral glucose tolerance test (OGTT).....	18
Table (4):	Demographic and Laboratory data of control group.....	62
Table (5):	Demographic and Laboratory data of patient group.	64
Table (6):	Demographic data of the patients and control group.	67
Table (7):	Laboratory data of the patients and control group.	69
Table (8):	Fetal outcome in patient and control group.	72
Table (9):	Maternal outcome in patients and control groups.	74
Table (10):	FGF 21 levels in patient and control groups.	76
Table (11):	Correlation between serum FGF 21 levels and demographic and laboratory data in both groups.....	77
Table (12):	Correlation between serum FGF 21 levels and fetal outcome in both study groups.	80

List of Tables Cont...

Table No.	Title	Page No.
Table (13):	Correlation between serum FGF 21 levels and maternal outcome in both study groups.	85
Table (14):	Realtion between fetal and maternal complications in patients with GDM and demographic data of the patients.	77
Table (15):	ROC curve analysis of FGF 21 levels in patients and control group.....	79

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Phylogenetic relationship of the FGFs based on amino acid sequence	33
Figure (2):	Mechanism of FGF21 action	35
Figure (3):	Mechanisms by which FGF21 improves glycaemic control in mouse and in vitro cell culture models.....	37
Figure (4):	FGF21 transmits a negative feedback signal to decrease further sugar consumption.....	39
Figure (5):	BMI in both study groups.....	68
Figure (6):	HbA1C levels in both study groups.....	70
Figure (7):	Fasting and 2 hr postprandial blood glucose levels in both study groups.	70
Figure (8):	Lipid profile in both study groups.	71
Figure (9):	Fetal outcome in both study groups.....	73
Figure (10):	Maternal outcome in both study groups.	75
Figure (11):	FGF 21 levels in both study groups.	76
Figure (12):	Correlation between FGF 21 levels and maternal BMI in both study groups.	78
Figure (13):	Correlation between FGF 21 levels and HbA1C in both study groups.	78
Figure (14):	Correlation between FGF 21 levels and fasting blood glucose levels in both study groups.....	79
Figure (15):	Correlation between FGF 21 levels and 2 hr post prandial blood glucose levels in both study groups.	79