AIN SHAMS UNIVERSITY
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Evalution of circulating fibroblast growth factor 21 in Type 2 diabetic patients with nephropathy

A Thesis

Submitted for the degree of Master of Science

As a partial fulfillment for requirements of the master of Science

Biochemistry

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2019


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١٤٣٥

Acknowledgement

First and foremost cordial thanks to Allah, the most Merciful, to whom I owe support and success in my whole life.

No words could express my deep gratitude and sincere appreciation to Prof. Dr. Azza Ahmed Atef, professor of biochemistry, faculty of Science, Ain Shams University, for her great effort exerted, endless help, close supervision, creative thinking, valuable suggestions and advice for this work.

I wish to express my good indebtedness and sincere gratitude to Prof. Dr. Magda Kamal Ezz, Professor of Biochemistry, Biochemistry Department, Faculty of Science, Ain Shams University for her kind guidance, patience, sincere encouragement, valuable advice and strong Co-operation.

I would like to express my deepest gratefulness to Prof. Dr. Mohamed Hesham Mohamed Mahfouz, Professor of Biochemistry, Biochemistry department, National Institute of Diabetes and Endocrinology (NIDE) for his perpetual guidance, creative thinking and tremendous concern.

Declaration

This thesis has not been submitted for a degree at this or any other university

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I dedicate this thesis to

The memory of my father and my mother whom I still miss every day.

My mother who had a great virtue to reach my situation nowadays, she was the motivator and supporter for my dreams to become true.

I also dedicate this thesis to my small family, my husband and lovely daughters for their help, encouragement, patience, care and support.

My sisters for their valuable advice, unlimited help and cooperation, They gave me the love for my great family.

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Abstract

Background: Microalbuminuria is often cited as a sensitive early marker for diabetic kidney disease and is thought to precede the more detrimental events seen in advanced stages of diabetic nephropathy .

Aim: The aim of this study was to evaluate the levels of Fibroblast growth factor 21, a modulator of cellular activities, in the different stages of diabetic albuminuria in an attempt to examine the possibility of considering FGF21 as a predictor marker of diabetic nephropathy in Type 2 diabetic patients whom at risk of that disease.

Subjects and Methods: Eighty subjects were enrolled in this study: 20 normal controls were age and sex matched with 60 Type 2 diabetics. Diabetic groups were classified according to albumin/creatinine ratio (A/C ratio) into diabetic group with normoalbuminuria (A/C ratio<30 mg/g), with microalbuminuria (A/C ratio =30-299 mg/g) and with macroalbuminuria (A/C ratio ≥ 300 mg/g). Serum FGF21, diabetic biomarkers, lipid profile, kidney functions and serum albumin were evaluated in this study.

Results: Serum FGF21 showed a progressive increase in the diabetic groups parallel to the degree of albuminuria. In Type2 diabetic normo, micro and macroalbuminuria groups, there were significant increases (P<0.001) in the levels of fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), serum insulin, HOMA-IR, total cholesterol (TC), triacylglycerols (TAGs), low density lipoprotein-cholesterol (LDL-C), very low density lipoprotein-cholesterol (vLDL-C), atherogenic index 1 and 2, while, serum high-density lipoprotein-cholesterol (HDL-C) showed a significant decrease (P<0.001) as compared to the control group. Serum levels of FGF21 as well as kidney function tests (s. cyctatin C, s. creatinin, s. urea, BUN) primarily cyctatin C were progressively increased (P<0.001) parallel to the degree of albuminuria as

compared with the normal controls. Furthermore, in diabetic macroalbuminuria group serum albumin levels showed a significant decrease (P<0.05) whereas, in diabetic micro and macroalbuminuria groups creatinine in urine and estimated glomerular filtration rate (eGFR) showed significant decreases (P<0.001) and microalbumin in urine and A/C ratio showed significant increases (P<0.001) as compared to the control group. There were significant positive correlations between FGF21 from one hand and FPG and cystatin C, while it showed significant negative correlation with eGFR in all diabetic groups. Furthermore, FGF21 showed significant positive correlations with s. creatinine, urea and BUN, while it showed significant negative correlation with serum albumin in diabetic microalbuminuia and macroalbuminuria diabetic patients. However, FGF21 showed significant positive correlations with insulin and HOMA-IR in macroalbuminuria diabetic patients.

Conclusion: These results concluded that FGF21 found to be associated with the degree of hyperglycemia and s. cystatin in Type 2 diabetic patients with different degree of albuminuria and can be used as a biomarker for predicting microalbuminuria and macroalbuminuria in Type 2 diabetic patients.

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List of Abbreviations

Acetyl CoA	Acetyl coenzyme A
ACOG	American council of Obstetricians and Gynecologists
A/C	Albumin/creatinine
ADA	American Diabetes Association
AKT	v-akt murine thymoma viral oncogene homolog
AP-1	Activating protein-1
BAT	Brown adipose tissue
BMI	Body mass index
BUN	Blood urea nitrogen
CAD	Coronary artery disease
CAL	Calibration
CAP	Cb1-associated protein
CKD	Chronic kidney disease
CNS	Central nervous system
Conc	Concentration
CVD	Cardiovascular disease
D2M	Type two diabetes
DKD	Diabetic kidney disease
DM	Diabetes mellitus
eGFR	estimated glomerular filtration rate
ELIZA	Enzyme-linked immunosorbent assay
ERK	Extracellular regulated kinase
ESRD	End stage renal disease
FATP-1	Fatty acid –transport protein 1
FFAs	Free fatty acids
FGF	Fibroblast growth factor