Urinary Nephrin as a biomarker of diabetic nephropathy in patients with type 2 diabetes mellitus

Thesis

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السكري في مرضى النفرين البولي كمؤشر بيولوجي لإعتلال الكلى البول السكري من النوع الثاني

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توطئة للحصول علي درجة الماجستير في الباطنة العامة

مقدمة من

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Dedication

I want to dedicate this work for my father who was there for me through all the difficult times.

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Finally, I could not forget my mother, the most precious person in my life, who had been wishing always of this moment.

With deep thanks

Contents

List of Abbreviations

8-OHdG	8-Hydroxy-2′-deoxyguanosine
8-oxodG	8-oxo-7,8-dihydro-2′-deoxyguanosine
ACCORD	Action to Control Cardiovascular Risk in Diabetes
ACEi	angiotensin converting enzyme inhibitors
ACR	Albumin Creatinine Ratio (alb/cr ratio)
AER	Albumin Excretion Rate
AGES	Advanced Glycosylation End Products
AGT	Angiotensinogen
ARBs	Angiotensin-II Receptor Blockers
AT- II	Angiotensin-II
CKD	Chronic Kidney Disease
CrCl	Creatinine Clearance
CTGF	Connective Tissue Growth Factor
DCCT	The Diabetic Control and Complication Trial
DM	Diabetes Mellitus
DN	Diabetic Nephropathy
EDIC	Epidemiology of Diabetes Interventions and Complications
ELISA	Enzyme-Linked Immunosorbent Assay
ESRD	End Stage Renal Disease
FSGS	Focal Segmental Glomerulosclerosis

GAG	Glycosaminoglycan
GBM	Glomerular Basement Membrane
GFR	Glomerular Filtration Rate
HbA1C	Hemoglobin A1C
HD	Hemodialysis
HIV	Human Immunodeficiency Virus
KDIGO	Kidney Disease Improving Global Outcomes
KDOQI	The Kidney Disease Outcomes Quality Initiative
KIM-1	Kidney Injury Molecule-1
L-FABP	Liver-Type Fatty Acid–Binding Protein
LVH	Left Ventricular Hypertrophy
MAPK	Mitogen-Activated Protein Kinase
MCD	minimal change disease
miRNA	microRNA
MMP	Matrix Metalloproteinase
MN	Membranous Nephropathy
MPGN	Mesangioproliferative Glomerulonephritis
NAG	N-Acetyl-beta-Glucosaminidase
NGAL	Neutrophil Gelatinase-Associated Lipocalin
PT	Proximal Tubule
PTC	Proximal Tubule Cell
RAAS	Renin-Angiotensin-Aldosterone System

RBP	Retinol Binding Protein
SD	The Slit Diaphragm
TGF-β	Transforming Growth Factor-β
TGF-β	Transforming growth factor
TNF-α	Tumor Necrosis Factor-alpha
UKPDS	United Kingdom Prospective Diabetes Study
VEGF	Vascular Endothelial Growth Factor
VEGF-A	Vascular Endothelial Growth Factor-A
WT1	Wilm's Tumor-1

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ABSTRACT

Background: Our study was a cross sectional study aimed to assess the role of urinary nephrin as an early biomarker for diabetic nephropathy in patients with type 2 diabetes mellitus. We measured urinary nephrin in 75 patients with type 2 DM. Patients were divided according to albumin/ creatinine ratio into 3 groups (25 normoalbuminuric patients, 25 microalbuminuric patients, 25 macroalbuminuric patients) and they were compared to 15 healthy control subjects.

Objective: To evaluate the role of urinary nephrin as an early biomarker for diabetic nephropathy in patients with type 2 diabetes mellitus.

Patients and Methods: We compared those three groups (normoalbuminuric, microalbuminuric and macroalbuminuric groups) as regard demographic data, laboratory results and clinical parameters. We excluded patients with other causes of proteinuria or podocytopathy rather than diabetic nephropathy.

Results: Our results show that there was no significant difference between study groups as regard sex, age and blood pressure. We found in our study that urinary nephrin was higher in all patients groups than control group, with macroalbuminuric group had the highest level, and normoalbuminuric group has the lowest level in patients group, but still significantly higher than control group. We found also that there was a positive correlation between urinary nephrin levels and the degree of albuminuria in all patients and in different groups including normoalbuminuric group.

Conclusion: We also compared between different study groups as regard estimated glomerular filtration rate (eGFR) (using MDRD and COCKCRAFT), this showed that macroalbuminuric group had lower eGFR than normoalbuminuric group, while there was no significant difference in eGFR between microalbuminuric group and the other two groups. *(Why writing the last part with conclusion NOT with results???)*

Keywords: Diabetes Mellitus – Chronic Kidney Disease - Diabetic Nephropathy - Albumin Excretion Rate

Introduction

Approximately 366 million people were diagnosed with diabetes mellitus (DM) worldwide in 2011 and this is expected to increase to 552 million by 2030 ***(Zimmet et al., 2014).***

Diabetes is the leading cause of chronic kidney disease (CKD) in many developed countries and is also rapidly becoming the leading cause in developing countries as a consequence of the global increase in type 2 diabetes and obesity ***(Hojs et al., 2015).***

Diabetic nephropathy occurs in up to 40% of people with type 1 or type 2 diabetes. People with diabetic nephropathy are not only at significant risk of progression to end-stage renal disease (ESRD), but there is also a concomitant increase in cardiovascular morbidity and mortality. Hence, it is important to identify patients at risk of diabetic nephropathy and also those at high risk of progression to ESRD ***(Hojs et al., 2015)***

Diagnostic marker to detect diabetic nephropathy (DN) at early stage is important as early intervention can slow the loss of kidney function and reduce adverse outcomes. Microalbuminuria has been accepted as the earliest marker for development of DN ***(Fiseha, 2015).***

However, a proportion of patients with either type 1 or type 2 diabetes does not follow classical albuminuric