

Study of the Relation between Inflammatory and Fibrogenic Cytokines in Diabetic Nephropathy

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(Biochemistry)

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"دراسة العلاقة بين السيستوكينات المسببة للإلتهاب والتليف فى الإعتلال الكلوى السكرى"

كمطلب جزئى لإستيفاء الحصول على درجة الماجستير فى العلوم الصيدلية
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من الصيدلانية

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Summary and Conclusion

Diabetic nephropathy (DN) is a serious microvascular complication of diabetes mellitus (DM). Though the progression of DN is very slow, many of diabetic patients develop ESRD. Chronic hyperglycemia is considered as the major initiator of diabetic kidney disease, either by hemodynamic or metabolic pathways leading to induction of growth factors and cytokines.

The present study was undertaken to assess whether transforming growth factor beta 1 (TGF- β_1), connective tissue growth factor (CTGF), monocyte chemoattractant protein-1 (MCP-1) and fibronectin (FN) levels in type 2 diabetic patients are associated with diabetic kidney disease as reflected by their albumin excretion rate (AER).

In order to fulfill our aim in this study, it was conducted on 82 subjects divided into two groups: group I: consists of 17 healthy volunteers served as control group, group II: consists of 65 diabetic patients subdivided into three subgroups: group II_a: consists of 18 diabetic patients with normoalbuminuria, group II_b: consists of 22 diabetic patients with microalbuminuria and group II_c: consists of 25 diabetic patients with macroalbuminuria.

Fasting plasma glucose, glycated hemoglobin (HbA_{1c}) %, fasting serum insulin, serum creatinine, creatinine clearance, TGF- β_1 , plasma CTGF, MCP-1 and FN were determined. Also, urinary albumin, creatinine, albumin/creatinine ratio and N-Acetyl-D-glucosaminidase (NAG) were determined in the different studied groups. Then, the correlations among these parameters were examined statistically to gain more insight into our results.

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا
إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ

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List of Contents

Subjects	Page
List of Abbreviations	i
List of Tables	vi
List of Figures	vii
Introduction and Aim of the Work	1
Review of Literature	3
Complications of diabetes mellitus	5
Diabetic nephropathy	6
Structural and functional abnormalities in diabetic nephropathy	8
Microalbuminuria	10
Risk factors of diabetic nephropathy	13
Pathogenesis of diabetic nephropathy	15
Hemodynamic pathways	16
Metabolic pathways	17
Transforming growth factor beta-1 (TGF- β_1)	23
Connective tissue growth factor (CTGF)	26
Monocyte chemoattractant protein-1 (MCP-1)	29
Fibronectin (FN)	31
Subjects and Methods	33

List of Contents

Results	69
Discussion	85
Summary and Conclusion	97
References	99
Appendix	I - IV
Arabic Summary	

List of Abbreviations

ADA	American Diabetes Association
AER	Albumin excretion rate
AGEs	Advanced glycation end products
Akt	Serine/threonine protein kinase
AR	Aldose reductase
BMI	Body mass index
BMPs	Bone morphogenetic proteins
CAD	Coronary artery diseases
CCL2	Chemokine [C-C motif] ligand 2
CCN	Cysteine-rich 61 /CTGF/ nephroblastoma overexpressed protein
CCR2	Chemokine receptor 2
cFN	Cellular fibronectin
CIg	Cold-insoluble globulin
CKD	Chronic kidney disease
CR	Chordin-like cysteine-rich
CTGF	Connective tissue growth factor
DAG	Diacylglycerol
DG	Deoxyglucosone
DHAP	Dihydroxyacetone phosphate

DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
DN	Diabetic nephropathy
ECM	Extracellular matrix
eGFR	Estimated glomerular filtration rate
EGFR	Epidermal growth factor receptor
EMT	Epithelial–mesenchymal transformation
ERK	Extracellular signal-regulated kinase
ESRD	End-stage renal disease
FBG	Fasting blood glucose
FN	Fibronectin
GAG	Glycosaminoglycans
GBM	Glomerular basement membrane
GDM	Gestational diabetes mellitus
GFAT	Glutamine: fructose-6 phosphate amidotransferase
GFR	Glomerular filtration rate
GOD	Glucose oxidase
GSH	Reduced glutathione
GSSG	Oxidized glutathione
HbA_{1c}	Glycated hemoglobin
IDDM	Insulin dependent diabetes mellitus
IGFBP	Insulin-like growth factor binding

	protein
IL-8	Interleukin-8
JNK	c-Jun N-terminal kinase
K/DOQI	Kidney Disease Outcomes Quality Initiative
LAP	Latency associated peptide
LLC	Large latent complex
LTBP	Latent TGF- binding protein
MAbs	Monoclonal antibodies
MAPK	Mitogen activated protein kinase
MCP-1	Monocyte chemoattractant protein-1
MG	Methylglyoxal
MMP-2	Matrix metalloproteinase-2
MNP-GlcNAc	2-methoxy-4-(2' nitrovinyl) phenyl 2-acetamido-2-deoxy- -D-glucopyranoside
NAD⁺	Nicotinamide adenine dinucleotide
NADP⁺	Nicotinamide adenine dinucleotide phosphate
NADPH	Reduced nicotinamide adenine dinucleotide phosphate
NAG	N-Acetyl- -D-glucosaminidase
NF- B	Nuclear factor-kappa beta
NIDDM	Non insulin dependent diabetes mellitus
NO[•]	Nitric oxide
NOV	Nephroblastoma overexpressed protein

O₂^{•-}	Superoxide anion
OHAs	Oral hypoglycemic agents
ONOO⁻	Peroxynitrite
PAP	Para-aminophenazone
pFN	Plasma fibronectin
PI3K	Phosphoinositide-3-OH kinase
PKB	Protein kinase B
PKC	Protein kinase C
POD	Peroxidase
RAGEs	Receptors of advanced glycation end products
RER	Rough endoplasmatic reticulum
ROS	Reactive oxygen species
R-Smad	Receptor Smads
SDH	Sorbitol dehydrogenase
SGK-1	Serine/threonine glucocorticoid kinase-1
SLC	Small latent complex
SP	Signal peptide
TAK-1	TGF- β -activated kinase 1
TGF-β₁	Transforming growth factor beta-1
TIMP-2	Tissue inhibitor of metalloproteinase-2
TMB	Tetra methyl benzidine

List of Abbreviations

UAE	Urinary albumin excretion
UDPGlcNAc	Uridine diphosphate N-acetyl glucosamine
VEGF	Vascular endothelial growth factor
vWC	Von Willebrand factor type C

List of Tables

Table No.	Table Title	Page
1	Different stages of diabetic nephropathy	7
2	Measurement and significance of albumin excretion rate (AER)	11
3	Demographic characteristics of studied groups	70
4	Diabetic markers of studied groups	71
5	Kidney function tests of studied groups	74
6	TGF- 1, CTGF, MCP-1 and FN of studied groups	77
7	Summary of the results of the studied parameters	84
8	Individual data of healthy control group I	I
9	Individual data of diabetic normoalbuminuric group II _a	II
10	Individual data of diabetic microalbuminuric group II _b	III
11	Individual data of diabetic macroalbuminuric group II _c	IV

List of Figures

Figure No.	Figure Title	Page
1	Various defects leading to hyperglycemia and type 2 DM	5
2	Renal biopsy specimen from a T2DM patient	9
3	Structural abnormalities have an effect on albuminuria	12
4	Interaction of hemodynamic and metabolic pathway, cytokines and intracellular signalling molecules mediating diabetic nephropathy	16
5	Metabolic pathways associated with diabetic nephropathy	18
6	Hyperglycemia increases flux through the polyol pathway	19
7	Hyperglycemia increases flux through the hexosamine pathway	20
8	Schematic representation of various biological targets of PKC activation leading to diabetic nephropathy	21
9	Posttranslational processing of TGF- 1	25
10	Role of transforming growth factor- 1 and connective tissue growth factor in diabetic nephropathy pathogenesis	26
11	Structure of CCN family members	27
12	Role of MCP-1 in diabetic nephropathy	30
13	The modular structure of fibronectin and its binding domain	32
14	Insulin Calibration Curve	45
15	Albumin Calibration Curve	48
16	TGF- 1 Calibration Curve	56
17	CTGF Calibration Curve	60
18	MCP-1 Calibration Curve	64

19	Fibronectin Calibration Curve	67
20	Plasma glucose levels in healthy control subjects (group I), diabetic patients with normoalbuminuria (group II _a), diabetic patients with microalbuminuria (group II _b) and diabetic patients with macroalbuminuria (group II _c)	72
21	Blood HbA _{1c} levels in healthy control subjects (group I), diabetic patients with normoalbuminuria (group II _a), diabetic patients with microalbuminuria (group II _b) and diabetic patients with macroalbuminuria (group II _c)	72
22	Serum TGF -1 levels in healthy control subjects (group I), diabetic patients with normoalbuminuria (group II _a), diabetic patients with microalbuminuria (group II _b) and diabetic patients with macroalbuminuria (group II _c)	78
23	Correlation of FBG with (a) AER, (b) eGFR, (c) TGF -1, (d) CTGF, (e) MCP-1 and (f) FN.	79
24	Correlation of AER with (a) TGF -1, (b) CTGF, (c) MCP-1 and (d) FN.	80
25	Correlations of (a) TGF -1 with CTGF, (b) TGF -1 with MCP-1, (c) TGF -1 with FN, (d) CTGF with MCP-1, (e) CTGF with FN, and (f) MCP-1 with FN	81