Faculty of Science
Biochemistry Department

Evaluation of the role of cytokine gene polymorphisms in diabetic nephropathy among Kuwaiti patients with type 2 diabetes mellitus

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Submitted by
Ashraf EL-Said Hafez EL-Helaly

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Under the supervision of

Prof. Dr. Shadia A. Fathy

Professor of Biochemistry
Faculty of Science
Ain Shams University

Prof. Dr. Mohamed R. Mohamed

Professor of Biochemistry & Molecular Biology
Faculty of Science
Ain Shams university

Dr. Mohamed A. M. Ali

Assistant Professor of Biochemistry
Faculty of Science
Ain Shams university

Dr. Abdulnabi T. Alattar

Consultant & Physician Diabetologist
Internal Medicine Department
Amiri Hospital, Kuwait city, Kuwait

Faculty of Science
Ain Shams University
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This thesis has not been submitted
to this or any other university

Ashraf Elsaid Hafez Elhelaly

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List of abbreviations

Abbreviation	Full name
Alb	Albumin
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AUC	Area under the curve
BMI	Body mass index
BUN	Blood urea nitrogen
Ca	Calcium
CAD	Coronary artery disease
CCD	Charge coupled device
cDNA	complementary DNA
CE	Capillary electrophoresis
CHF	Congestive heart failure
CI 95%	Confidence interval 95%
Cl	Chloride
Cr	Creatinine
CRP	C-reactive protein
CVDs	Cardiovascular diseases
CVS	Cardiovascular system
DCCT	Diabetes control and complications trial
DCs	Dendritic cells
DKA	Diabetic ketoacidosis
DKD	Diabetic kidney disease
DM	Diabetes mellitus
DN	Diabetic nephropathy
EDIC	Epidemiology of diabetes interventions and complications study
EDTA	Ethylenediaminetetraacetic acid
eGFR	Estimated glomerular filtration rate

ELISA	Enzyme-linked immunosorbent assay
ESRD	End-stage renal disease
FP	Forward primer
FPG	Fasting plasma glucose
GDM	Gestational diabetes mellitus
GFR	Glomerular filtration rate
HbA1c	Hemoglobin A1c
HDL-C	High-density lipoprotein cholesterol
HLA	Human leucocyte antigens
HRP	Horseradish peroxidase
HTN	Hypertension
HWE	Hardy-Weinberg equilibrium
IFG	Impaired fasting glucose
IFN-γ	Interferon gamma
IGH	Impaired glucose homeostasis
IGH	Impaired glucose homeostasis
IGT	Impaired glucose tolerance
IL-10	Interleukin-10
IL-12	Interleukin-12
IL-13	Interleukin-13
IL-2	interleukin-2
IL-4	Interleukin-4
IL-5	Interleukin-5
IL-6	Interleukin-6
IQR	Interquartile range
K	Potassium
LA	Lactic acidosis
LD	Linkage disequilibrium
LDL-C	Low-density lipoprotein cholesterol
MA	Microalbumin
MGB	Minor groove binder
MHC	Major histocompatibility complex
MI	Myocardial infarction

mRNA	Messenger RNA
Na	Sodium
NFQ	Non-fluorescent quencher
NK	Natural killer cells
NPDR	Non- proliferative diabetic retinopathy
NPV	Negative predictive value
OD	Optical density
OGTT	Oral glucose tolerance test
P	Phosphorous
PAF	platelet activating factor
PCR	Polymerase chain reaction
PDR	Proliferative diabetic retinopathy
POP	Performance optimized polymers
PPV	Positive predictive value
ROC	Receiver operating characteristic
ROS	Reactive oxygen species
RP	Reverse primer
SD	Standard deviation
SDS	Sequence detection system
SLE	Systemic lupus erythematosus
SNPs	Single nucleotide polymorphisms
SPSS	Statistical package for the social sciences
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus
TAE	Tris-Acetate-EDTA-Na_2
Taq	*Thermus aquaticus*
TB	Total bilirubin
TC	Total cholesterol
TG	triglycerides
TH1	T-lymphocyte helper cell type 1
Th2	T-lymphocyte helper cell type 2
TMB	3,3',5,5'-tetramethylbenzidine
TNF-α	Tumor necrosis factor alpha

TP	Total protein
UACR	Urinary albumin–to– creatinine ratio
UAE	Urinary albumin excretion

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ABSTRACT

Abstract

Background: Data from previous studies on the role of inflammatory cytokines as biomarkers for diabetic kidney disease (DKD) are contradictory. The association of a particular inflammatory cytokine single nucleotide polymorphism (SNP) with susceptibility to DKD has not been consistently replicated. We aimed to investigate the utility of inflammatory cytokines as biomarkers for DKD in type 2 diabetes mellitus (T2DM) patients. Association of inflammatory cytokine gene SNPs with the development of DKD was also explored. **Subjects & Methods:** One hundred and fifty-nine Kuwaiti subjects were recruited in this study, including 50 T2DM patients without DKD, 67 diabetic DKD patients and 42 healthy subjects. Plasma levels of interleukin-6 (IL-6), IL-10, interferon gamma (IFN-γ) and tumor necrosis factor alpha (TNF-α) were measured by enzyme-linked immunosorbent assays. Nine SNPs, including 2 SNPs in *IL-6*, 3 SNPs in *IL-10*, 1 SNP in *IFN-γ* and 3 SNPs in *TNF-α*, were genotyped using TaqMan SNP genotyping assays. **Results:** Diabetic DKD patients showed higher IL-6, IL-10, IFN-γ and TNF-α levels than those without DKD. Diabetic DKD patients had a significantly higher frequency of *IL-10* −1082A allele than those without DKD (P=0.001). No significant association of *IL-6* −174/−597 haplotypes with DKD risk was detected (P=0.188). Distribution of *IL-10* −592/−819/−1082 haplotypes differ significantly between T2DM patients with/without DKD (P=0.014). Diabetic DKD patients had a significantly lower frequency of *IL-10* −592C/−819C/−1082G haplotype than those without DKD (P=0.002). **Conclusion**: Although inflammatory cytokine genotypes and, more importantly, haplotypes may have the potential to identify those patients at risk of DKD, hence, improving DKD predisposition prediction, further investigations regarding their real clinical significance is warranted in a large cohort of patients.