Assessment of the Potential Role of Some Inflammatory Cytokines and Chemokines in Lupus Nephritis Patients

A Thesis
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By

Dina Samir Elsaid Said Ahmed

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Under supervision of

Prof. Dr. Kamal Ali Shalaby
Professor of Biochemistry, Biochemistry Departement
Faculty of Science, Ain Shams University

Prof. Dr. Rasha Ali Abdel Noor
Assistant Professor of Internal Medicine & Rheumatology
Faculty of Medicine,Tanta University

Dr. Riham Abdel Hamid Haroun
Lecturer of Biochemistry, Biochemistry Departement
Faculty of Science, Ain Shams University

Biochemistry Department
Faculty of Science
Ain Shams University

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Abstract

Dina Samir El-said Said Ahmed. Assess the potential role of urinary TWEAK and urinary MCP-1 in systemic lupus erythematosus patients and determine their correlation with lupus nephritis activity in Egyptian patients. Biochemistry Department, Faculty of Science, Ain Shams University.

Background: There is no single biomarker to detect lupus nephritis activity. Renal biopsy is still the gold standard method but it's invasive and mainly used in the initial assessment of the patients. Urinary tumor necrosis factor-like weak inducer of apoptosis (uTWEAK), and urinary monocyte chemoattractant protein-1 (uMCP-1) can be secreted in urine of active lupus nephritis.

Patients and Methods: This is a case control study conducted on a total of 114 subjects; 92 SLE patients and 22 healthy volunteers. The patients were recruited from rheumatology unit at internal medicine department, Tanta university hospital, Tanta, Egypt. The patients and controls were subjected to full history taking, complete clinical examination, routine laboratory tests, Urinary TWEAK and urinary MCP-1 measurement, assessment of the disease activity using SLE Disease Activity Index (SLEDAI) and renal SLEDAI (r-SLEDAI) scores.

Results: Urinary TWEAK and uMCP-1 levels were higher in SLE with active nephritis group than those of other SLE groups and controls. There was a significant positive correlation between urinary TWEAK and urinary MCP-1 levels in lupus patients and proteinuria, anti-ds DNA, SLEDAI and r-SLEDAI and negatively with C3 and C4. TWEAK showed a sensitivity of 80.43% &100 % and specificity of 50%& 100% in detecting lupus activity and lupus nephritis activity respectively. Also uMCP-1 showed a sensitivity of 82.6% &100 % and specificity of 50%& 100% in detecting lupus activity and lupus nephritis activity respectively.

Conclusions: Urinary TWEAK and uMCP-1 are new, easily obtained, accurate markers with high sensitivity and specificity in detection of lupus nephritis activity.

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✍ *Dina Samir Elsaid Said Ahmed*

Dedication

Every challenging work needs self efforts as well as guidance of elders especially those who were very close to our heart.

My humble effort I dedicate to my sweet and loving.

To my mother my first person in my life.

&

To my father without him I'm nothing.

Whose affection, love, encouragement and prays of day and night make me able to get such success and honor.

✍ Dina Samir Elsaid Said Ahmed

Declaration

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

Dina Samir Elsaid Said Ahmed

List of Abbreviations

aa	amino acids
ACL	Anticardiolipin
ACR	American College of Rheumatology
Alb	Albumin
ALT	Alanine transferase
ANAs	Antinuclear Antibodies
AP-1	Activator protein 1
APRIL	A proliferation-inducing ligand
APS	Antiphospholipid antibody
AST	Aspartate transferase
AUC	Area under the curve
BCMA	B-cell maturation antigen
BILAG	British Isles Lupus Assessment Group
BUN	Blood urea nitrogen
(ds) DNA	Double strand deoxyribonucleic acid
C3	Complement 3

List of Abbreviations (Cont.)

C4	Complement 4
CBC	Complete blood count
CCL2	Chemokine ligand 2
CD	Cluster of differentiation
CNS	Central nervous system
CRP	C- reactive protein
CVA	Cerebrovascular accident
D.BIL	Direct Bilirubin
DILE	Druge Induced SLE
DNA	Deoxyribonucleic acid
EBV	Epstein–Barr virus
ECLAM	European Consensus Lupus Activity Measurement Index
EDTA	Ethylenediaminetetraacetic acid
eGFR	Estimated glomerular filtration rate
ESR	Erythrocyte sedimentation rate
FBS	Fasting plasma glucose

List of Abbreviations (Cont.)

ENA	Extractable nuclear antigens
ERK	Extracellular-signal-regulated kinase
ESRD	End-stage renal disease
EULAR	European League Against Rheumatism
Fn14	Fibroblast growth factor inducible 14
GN	Glomerulonephritis
HB	Hemoglobin
HHV 8	Human herpes virus 8
HLA	human leukocyte antigen
HPV	Human papilloma virus
IAPP	Immunoadsorption plasmapheresis
IAS	Immunoadsorption
ICs	Immune complexs
INF- α	Interferon-alpha
IFN-γ	Interferon-gamma
INR	International normalized ratio

List of Abbreviations (Cont.)

IQR	Interquartile Range
IgG	Immunoglobulin G
IL	Interleukin
IP-10	Induced protein 10
IRF5	Interferon regulatory factor 5
JAK	Janus kinase
JNK	Jun N-terminal kinases
LAC	Lupus anticoagulant
LDH	Lactate Dehydrogenase
LN	Lupus Nephritis
MAPKs	Mitogen-activated protein kinase
MAX	Maximum
MCP-1	Monocyte chemoattractant protein-1
MIN	Minimum
NF-kB p65	Nuclear factor kappa-light-chain-enhancer of activated B cells
NK	Natural killer cells

List of Abbreviations (Cont.)

NSAIDs	Non- steroidal anti-inflammatory drug
P 38	Protein 38
PDCD1	Programmed cell death 1
PDGF	Platelet-derived growth factor
PI3K	Phosphoinositide 3-kinase
PKB or Akt	Protein kinase B
PKC	Protein kinase C
PLAT	Platelets
PMA	Phorbol myristate acetate
PT	Prothrombin time
PTPN22	Protein Tyrosine Phosphatase, Non-Receptor Type 22
RANTES	Regulated on Activation, Normal T Cell Expressed and Secreted
RBCs	Red blood cells
RNP	Ribonucleoprotein
ROC	Receiver operating characteristic
r-SLEDAI	Renal SLEDAI score

List of Abbreviations (Cont.)

SD	Standard Deviation
SLAM	Systemic Lupus Activity Measure
SLE	Systemic lupus erythematosus
SLEDAI	Systemic Lupus Erythematosus Disease Activity Index
SLICC	Systemic Lupus International Collabration Criteria
Sm	Smith antigen
SNP	Single nucleotide polymorphism
SS	Single strand
STAT4	Signal transducer and activator of transcription 4
TCR	T-cell receptor
T.BIL	Total Bilirubin
TNF	Tumor necrosis factor
TMB	Tetramethylbenzidine
TP	Total Protein
TREX1	Three prime repair exonuclease 1

List of Abbreviations (Cont.)

TWEAK	Tumor necrosis factor–like weak inducer of apoptosis
uMCP-1	Urinary Monocyte chemoattractant protein-1
uTWEAK	Urinary tumor necrosis factor –like weak inducer of apoptosis
UV	Ultraviolet light
WBCs	White blood cells
WHO	World Health Organization

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