Renal Expression of Vascular Endothelial Growth Factor in Lupus Nephritis

Thesis
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تحديد مستوي معامل النمو للخلايا المبطنة للأوعية الدموية بالكلي عند الأطفال المصابين بمرض الذئبة الحمراء

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Marwa Salah Abbass

بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم

صدق الله العظيم

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List of Abbreviations

ACR	**:**	American college of Rheumatology
ADPKD	**:**	Autosomal dominant polycytic kidney disease
ANAs	**:**	Antinuclear antibodies
Anti- dsDNA	**:**	Antidouble Stranded deoxyribonucleic acid
BILAG	**:**	British Isles Lupus Assessment Group
BLYS	**:**	B lymphocyte stimulator
BUN	**:**	Blood urea nitrogen
C	**:**	Complement
CBC	**:**	Complete blood count
CRP	**:**	C-reactive protein
DPLN	**:**	Diffuse proliferative lupus nephritis
ESR	**:**	Erythrocyte sedimentation rate
ESRD	**:**	End stage renal disease
GBM	**:**	Glomerular basement membrane
GFR	**:**	Glomerular filtration rate
GN	**:**	Glomerulonephritis
Ig	**:**	Immunoglobulin
IL	**:**	Interleukin
INF-γ	**:**	Interferon gamma
ISN/RPS	**:**	International Society of Nephrology/ Renal Pathology Society
LN	**:**	Lupus Nephritis

MCP-1	**:**	Monocyte chemo-attractant protein-1
mEPCR	**:**	Membrane expression of endothelial protein C receptor
MMF	**:**	Mycophenolate mofetil
NGAL	**:**	Nentrophil gelatinase associated lipocalin
NP	**:**	Neuro-psychiatric
PAF	**:**	Platelet activating factor
PDGF	**:**	Platelet derived growth factor
PTCs	**:**	Peritubular Capillaries
PTECs	**:**	Proximal tubular epithelial cells
RBCs	**:**	Red Blood cells
SD	**:**	Standard Deviation
sF1T 1	**:**	Soluble form of VEGF receptor-1
SLE	**:**	Systemic lupus erythematosus
SLEDAI	**:**	Systemic Lupus Erythmatosus Disease activity Index
SLICC/ACR	**:**	Systemic Lupus International Collaborating Clincs/American College of Rheumatology
STAT-1	**:**	Signal transducer and activator of transcription-1
sTM		Serum thrombomodulin
TNF-α	**:**	Tumor necrosis factor-alpha
VEGF	**:**	Vascular endothelial growth factor
VEGFRs	**:**	Vascular endothelial growth factor receptors
WBCs	**:**	White blood cells
WHO	**:**	World Health Organization

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Introduction

Systemic lupus erythromatosus is an autoimmune disease characterized by acute and chronic inflammation of various tissues of the body. The antibodies and accompanying cells of inflammation can affect tissues anywhere in the body. Lupus has the potential to affect a variety of areas. SLE most often harms the skin, heart, lungs, kidneys, joints and /or nervous system. The course of the disease is unpredictable with periods of illness (called flares) alternating with remission ***(Anisur et al., 2008).***

The precise reason for the abnormal autoimmunity that causes lupus is not known (inherited genes, viruses, ultraviolet light, and certain medications) may all play some role ***(D'Cruz et al., 2007).*** Kidney disease is one of the commonest and the most serious manifestation of (SLE). Despite improvement in the medical care of SLE in the past two decades the prognosis of lupus nephritis remains unsatisfactory. Up to 25% of patients still develop end stage renal failure 10 years after onset of renal disease ***(Mok, 2006).***

Renal biopsy is the gold standard for providing information on the histological classes of lupus nephritis and the relative degree of activity and chronicity in the glomeruli ***(Mok, 2006).***

There is different tissue markers that has been associated with histological classes or renal functions deterioration in lupus nephritis. Intrarenal vascular endothelial growth factor mRNA expression predicts the deterioration of renal functions (VEGF expression) ***(Avihingsanon et al., 2009).*** Vascular endothelial growth factor (VEGF) has been shown to stabilize kidney functions in animal model of thrombotic microangiopathy ***(Kim et al., 2000)***.

The protective actions were principally mediated through preserved glomerular and peritubular capillary structures. This may help to preserve glomerular filtration rate by maintaining glomerular capillary filtration surface area as well as preventing tubulointerstitial fibrosis ***(Kang and Johnson, 2003).*** Hence patients with proliferative LN who had decreased intrarenal VEGF expression are at risk for a rapid decline of renal functions at the time of renal flare. The combination of renal pathology such as class III/ IV LN and reduced VEGF expression could predict poor renal survival ***(Shulman et al., 1996).*** VEGF plays a crucial role in the preservation of renal functions and may also serve as a useful biomarker in monitoring the progression of lupus nephritis ***(Lemos et al., 2003).***

Aim of the Work

The aim of the present study is to try to correlate VEGF expression in the kidney with renal histopathology and prognosis of lupus nephritis.

Lupus Nephritis

Systemic lupus erythromatosus

Childhood systemic lupus erytheromatosus generally presents between the ages of 3 and 15 years, with girls out numbering boys 4: 1. SLE most often harms the skin, heart, lungs, kidneys, joints and/or nervous system. The clinical presentation of SLE is a function of its immunopathology ***(Frieri et al., 2012).***

As many as 30% of sufferers have some dermatological symptoms (and 65% suffer such symptoms at some point), with 30% to 50% suffering from the classic malar rash (or butterfly rash) associated with the disease. Some may exhibit thick, red scaly patches on the skin (referred to as discoid lupus). Alopecia; mouth, nasal, and vaginal ulcers; and lesions on the skin are also possible manifestations ***(James et al., 2005).***

The most commonly sought medical attention is for joint pain, with the small joints of the hand and wrist usually affected, although all joints are at risk. The Lupus Foundation of America estimates more than 90 percent of those affected will experience joint and/or muscle pain at some time during the course of their illness ***(Hemminki et al., 2009).***