# 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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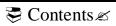
Last but not least, sincere gratitude to My Family for their continuous encouragement and spiritual support.

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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

#### List of Abbreviations

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

**SETM** Serum thrombomodulin

**TNF-\alpha**: Tumor necrosis factor-alpha

**VEGF** : Vascular endothelial growth factor

**VEGFRs**: Vascular endothelial growth factor receptors

**WBCs**: White blood cells

**WHO**: World Health Organization

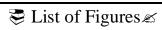
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## **Introduction**

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).