

**PREVALENCE AND RISK FACTORS FOR  
PULMONARY ARTERIAL HYPERTENSION IN  
PATIENTS WITH SYSTEMIC LUPUS  
ERYTHROMATOSIS**

*Thesis*

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*By*

**Nermine Noshay Aziz**  
(M.B., Ch, M.Sc.)

*Supervised by*

**Prof. Dr. Mohamed Salah Eldin Abdel Baki**

Professor of Internal Medicine  
Faculty of Medicine - Ain Shams University

**Prof. Dr. Reem Abdel Moneim Habib**

Professor of Internal Medicine  
Faculty of Medicine - Ain shams University

**Dr. Noha Hussien Shedid**

Assistant Professor of Internal Medicine  
Faculty of Medicine - Ain shams University

**Dr. Caroline Samy Morad**

Lecturer of Internal Medicine  
Faculty of Medicine - Ain shams University

**Dr. Wael Mahmoud El Kilany**

Lecturer of Cardiology  
Faculty of Medicine - Ain shams University

Faculty of Medicine  
Ain Shams University

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## List of Abbreviations

<b>ACEi</b>	.....Angiotensin inhibitors
<b>ACL IgG</b>	.....Anticardiolipin IgG
<b>ACL IgM</b>	.....Anticardiolipin IgM
<b>AECA</b>	.....Antiendothelial cell antibodies
<b>ALP</b>	.....Alkaline Phosphatase
<b>ALT</b>	.....Alanine Transaminase
<b>ANA</b>	.....Antinuclear Antibody
<b>anti-CCP</b>	.....Anti-Citrulline Containing Peptide
<b>anti-dsDNA</b>	.....Anti-Double Stranded DNA
<b>anti-ENA</b>	.....Anti-Extractable Nuclear Antigen
<b>APL</b>	.....Antiphospholipid
<b>APS</b>	.....Antiphospholipid Syndrome
<b>ARBs</b>	.....Angiotensin Receptor Blockers
<b>AST</b>	.....Aspartate Transaminase
<b>AVN</b>	.....Avascular Necrosis
<b>AZA</b>	.....Azathioprine
<b>BILAG</b>	.....British Isles Lupus Activity Group
<b>BUN</b>	.....Blood Urea Nitrogen
<b>CBC</b>	.....Complete Blood Picture
<b>CCB</b>	.....Calcium Channel Blockers
<b>CLE</b>	.....Cutaneous Lupus Erythematosus
<b>CMR</b>	.....Cardiac Magnetic Resonance
<b>Cox-2</b>	.....Cyclo-Oxygenase-2
<b>CRP</b>	.....C-reactive Protein
<b>CT</b>	.....Computed Tomography
<b>CTDs</b>	.....Connective Tissue Diseases
<b>CXR</b>	.....Chest X-ray

## List of Abbreviations (Cont.)

<b>CYC</b> .....	Cyclophosphamide
<b>DLCO</b> .....	Diffuse Lung Capacity of Carbon Monoxide
<b>DLE</b> .....	Discoid Lupus Erythematosus
<b>ECG</b> .....	Electrocardiogram
<b>ECLAM</b> .....	European Consensus Lupus Activity Measurement
<b>ER <math>\alpha/\beta</math></b> .....	Estrogen Receptors Alpha and Beta
<b>ERA</b> .....	Endothelin Receptor Antagonists
<b>ESR</b> .....	Erythrocyte Sedimentation Rate
<b>ESRD</b> .....	End-Stage Renal Disease
<b>ETRA</b> s .....	Endothelin Receptor Antagonists
<b>EULAR</b> .....	European League against Rheumatism
<b>Fc<math>\gamma</math>R</b> .....	Fc Gamma Receptor
<b>hpf</b> .....	High-Power Field
<b>HRCT</b> .....	High-resolution computed tomography
<b>IC</b> .....	Immune Complex
<b>IFN<math>\alpha</math></b> .....	Interferon-Alpha
<b>IL</b> .....	Interleukin
<b>iNO</b> .....	Inhaled Nitric Oxide
<b>IPAH</b> .....	Idiopathic Pulmonary Arterial Hypertension
<b>ISN/RPS</b> .....	International Society of Nephrology / Renal Pathology Society
<b>IV</b> .....	Intravenous
<b>IVIG</b> .....	Intravenous Immunoglobulin
<b>LAC</b> .....	Lupus Anticoagulant

## List of Abbreviations (Cont.)

<b>LN</b>	.....Lupus Nephritis
<b>LP</b>	.....Lupus Pancreatitis
<b>MMF</b>	.....Mycophenolate Mofetil
<b>MP</b>	.....Methylprednisolone
<b>MRA</b>	.....Magnetic Resonance Angiography
<b>NPSLE</b>	.....Neuropsychiatric Syndromes of Systemic Lupus Erythematosus
<b>NSAIDS</b>	.....Nonsteroidal Anti-Inflammatory Drugs
<b>PAH</b>	.....Pulmonary Arterial Hypertension
<b>PASP</b>	.....Pulmonary Artery Systolic Pressure
<b>pDCs</b>	.....Plasmacytoid Dendritic Cells
<b>PDE-5-I</b>	.....Phosphodiesterase-5-inhibitors
<b>PFTs</b>	.....Pulmonary Function Tests
<b>PH</b>	.....Pulmonary Hypertension
<b>PLGE</b>	.....Protein-losing gastroenteropathy
<b>RBCs</b>	.....Red Blood Cells
<b>RHC</b>	.....Right Heart Catheterization
<b>RTX</b>	.....Rituximab
<b>sGC</b>	.....Soluble Guanylate Cyclase
<b>SLAM</b>	.....Systemic Lupus Activity Measure
<b>SLE</b>	.....Systemic Lupus Erythematosus
<b>SLE-aPAH</b>	.....SLE-associated PAH
<b>SLEDAI</b>	.....Systemic Lupus Erythematosus Disease Activity Index
<b>SLICC/ACR-DI</b>	.....Systemic Lupus International Collaborating Clinics / American College of Rheumatology-damage Index

## **List of Abbreviations (Cont.)**

<b>sPAP</b> .....	Systolic Pulmonary Artery Pressure
<b>TLR7/9</b> .....	Toll-Like Receptor 7/9
<b>TTP</b> .....	Thrombotic Thrombocytopenic Purpura
<b>UV</b> .....	Ultraviolet
<b>WBCs</b> .....	White Blood Cells
<b>WHO</b> .....	World Health Organization

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## Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune connective tissue disorder that primarily affects women of childbearing age (*Ko et al., 2011*). It may involve many different tissues and organs, producing a broad spectrum of signs and symptoms (*Cervera et al., 2003*).

SLE is characterized by some combination of inflammation and fibrosis, and the clinical phenotype is dictated by the relative contributions of each of the organs affected. Tissue injury appears to be mediated by characteristic autoantibody production, immune complex formation, and their organ-specific deposition. As expected in a multisystem disease, the entire pulmonary system is vulnerable to injury. Any of its compartments—airways, lung parenchyma, vasculature, pleura, or the respiratory musculature—may be independently or simultaneously affected (*Swigris et al., 2008*).

Pulmonary involvement in SLE is relatively frequent in adult patients rather than children. Pulmonary hypertension (PH) is the most severe form of lupus associated pulmonary involvement (*Kamel et al., 2011*). Pulmonary arterial hypertension (PAH) is a subset of PH that results from increased vascular resistance in the pulmonary arteries and may ultimately result in right heart failure (*Simonneau et al., 2009*). The prevalence of PAH in patients with lupus is largely unknown, but has been

reported to approximate 6%-15% in adult patients, in whom it is most commonly associated with Raynaud's phenomenon (*Swigris et al., 2008*).

Although several mechanisms are involved in pathogenesis of pulmonary hypertension in SLE, the real causes are yet unknown. The hypothesis of pulmonary vasculitis, with deposits of immunocomplexes and complements on the pulmonary artery walls, thromboembolic blockage in pulmonary vessels, possibly related to antibodies (anticardiolipin antibody and lupus anticoagulant), and vasospasms, are suggested by a greater frequency of Raynaud's phenomenon in these patients involvement (*Kamel et al., 2011*).

The non-specific nature of symptoms such as dyspnea, palpitations, fatigue and syncope associated with PAH could lead to a delay in the diagnosis of PAH in patients with SLE. This suggests a need for appropriate screening methods to identify PAH. Although the gold standard test to diagnose PAH is right heart catheterization, this is an invasive and expensive test which makes it unsuitable for use as a screening tool (*Prabu et al., 2009*). Doppler echocardiography currently is considered the non-invasive screening test of choice for evaluating pulmonary hypertension (*Kamel et al., 2011*).

## **Aim of the Work**

This study aims to estimate the frequency of PAH and identify risk factors for PAH in a large cohort of SLE patients (Ain Shams Lupus cohort).