Prevalence and risk factors for pulmonary arterial hypertension in patients with Systemic Lupus Erythromatosis

Thesis

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List of Abbreviations

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

List of Abbreviations (Cont.)

CYC .....Cyclophosphamide

DLCO.....Diffuse Lung Capacity of Carbon Monoxide

DLE .....Discoid Lupus Erythematosus

ECG.....Electrocardiogram

ECLAM .....European Consensus Lupus Activity Measurement

ER α/β.....Estrogen Receptors Alpha and Beta

ERA .....Endothelin Receptor Antagonists

ESR .....Erythrocyte Sedemintation Rate

ESRD.....End-Stage Renal Disease

ETRAs .....Endothelin Receptor Antagonists

EULAR.....European League against Rheumatism

FcγR.....Fc Gamma Receptor

hpf.....High-Power Field

HRCT.....High-resolution computed tomography

IC.....Immune Complex

IFNα .....Interferon-Alpha

IL.....Interleukin

iNO .....Inhaled Nitric Oxide

IPAH.....Idiopathic Pulmonary Arterial Hypertension

ISN/RPS.....International Society of Nephrology / Renal Pathology Society

IV.....Intravenous

IVIG.....Intravenous Immunoglobulin

LAC.....Lupus Anticoagulant

List of Abbreviations (Cont.)

LN.....Lupus Nephritis

LP.....Lupus Pancreatitis

MMF.....Mycophenolate Mofetil

MP.....Methylprednisolone

MRA.....Magnetic Resonance Angiography

NPSLE.....Neuropsychiatric Syndromes of Systemic Lupus Erythematosus

NSAIDS.....Nonsteroidal Anti-Inflammatory Drugs

PAH.....Pulmonary Arterial Hypertension

PASP.....Pulmonary Artery Systolic Pressure

pDCs.....Plasmacytoid Dendritic Cells

PDE-5-I.....Phosphodiesterase-5-inhibitors

PFTs.....Pulmonary Function Tests

PH.....Pulmonary Hypertension

PLGE.....Protein-losing gastroenteropathy

RBCs.....Red Blood Cells

RHC.....Right Heart Catheterization

RTX.....Rituximab

sGC.....Soluble Guanylate Cyclase

SLAM.....Systemic Lupus Activity Measure

SLE.....Systemic Lupus Erythematosus

SLE-aPAH.....SLE-associated PAH

SLEDAI.....Systemic Lupus Erythematous Disease Activity Index

SLICC/ACR-DI.....Systemic Lupus International Collaborating Clinics / American College of Rheumatology-damage Index

List of Abbreviations (Cont.)

sPAP .....Systolic Pulmonary Artery Pressure

TLR7/9 .....Toll-Like Receptor 7/9

TTP.....Thrombotic Thrombocytopenic Purpura

UV.....Ultraviolet

WBCs.....White Blood Cells

WHO .....World Health Organization

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Introduction

Systemic lupus erythromatosis (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).