HAEMODYNAMIC FLOW TO THE HIP IN FEMALE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CORRELATION WITH RISK FACTORS OF OSTEONECROSIS

Thesis

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DEDICATION

To my parents who taught me everything I know, for their love, care and advise which were always there to support and encourage me in every moment of my life.

To my husband, daughter and son for their great tolerance, strong support and persistant understanding.

To my brother for his care and support.

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NAHLA NAEEM

Abstract

Osteonecrosis is strongly associated with systemic lupus erythematosus. The hip, and in particular the femoral head, is the most commonly encountered type. Glucocorticoids as well as disease associated factors have been proposed to enhance the risk for osteonecrosis development. This study aims to evaluate haemodynamic changes in the femoral head in patients with SLE before the development of osteonecrosis and determine the effect of the various risk factors of osteonecrosis on haemodynamic flow. This study was conducted on fourty consecutive female patients with systemic lupus erythematosus and twenty healthy volunteers, whom underwent clinical assessment, laboratory investigations as well as colour & power doppler ultrasound of the blood vessels (medial & lateral circumflex femoral arteries) supplying the femoral head bilaterally. From this study we concluded that hemodynamic flow to the hip is already altered in SLE patients without ON, and the presence of associated risk factors of ON contribute to more haemodynamic flow alteration.

Key words:

Systemic Lupus Erythematosus, Osteonecrosis, Hip joint, Risk factors.

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LIST OF ABBREVIATIONS

ACE	Angiotensin Converting Enzyme
ACR	American College of Rheumatology
ALT	Alanine Transaminase
ANA	Anti Nuclear Antibody
ANCA	Anti Neutrophil Cytoplasmic Antibody
Anti ds-DNA	Anti double stranded deoxyribonucleic acid
Anti- Sm	Anti Smith
APL	Antiphospholipid antibodies
APS	Antiphospholipid Syndrome
APTT	Activated partial thromboplastin time
ARCO	Association of Research Circulation Osseous
ASIS	Anterior Superior Illiac Spine
AST	Aspartate Transaminase
AVN	Avascular Necrosis
CAD	Coronary Artery Disease
CBC	Complete Blood Count
CCD	Caput Collom Diaphyseal
CLE	Cutaneous Lupus Erythematosus
CNS	Central Nervous System
CRP	C- reactive protein
CS	Corticosteroids
CT	Computed Tomography
CVA	Cerebrovascular Accident
DC	Dendritic Cells
DJD	Degenerative Joint Disease
DMARDS	Disease Modifiying Anti Rheumatic Drugs
DNA	Deoxyribonucleic acid
EBV	Ebstein Barr Virus

ECG	Electrocardiogram
EDV	End Diastolic Velocity
ELISA	Enzyme Linked Immunosorbant Assay
ENA	Extractable Nuclear Antigen
ESR	Erythrocyte Sedimentation Rate
EULAR	European League Against Rheumatism
FDA	Food and Drug Administration
FDC	Follicular Dendritic Cells
GC	Germinal Centres
HDL	High Density Lipoprotein
HIV	Human immunodeficiency virus
HLA	Human Leucocyte Antigen
HMGB1	High Mobility Group Box 1
Ig G	Immunoglobulin G
Ig M	Immunoglobulin M
IVIG	Intravenous Immunoglobulin
LCF	Lateral Circumflex Femoral
LDL	Low Density Lipoprotein
LEVs	Lateral Epiphyseal Vessels
Max	Maximum
MCF	Medial Circumflex Femoral
mg	milligrams
MHC	Major Histocompatibility Complex
Min	Minimum
MRA	Magnetic Resonance Angiograohy
MRI	Magnetic Resonance Imaging
NSAIDs	Non steroidal anti-inflammatory drugs
ON	Osteonecrosis
Op-1	Osteogenic protein-1
PI	Pulsatility Index

PSV	Peak Systolic Velocity
RBCs	Red Blood Cells
rhBMP-2	Recombinant human Bone Morphogenetic Protein-2
RI	Resistivity Index
RNP	Ribonucleoprotein
ROM	Range of Motion
S/D	Systolic to Diastolic ratio
SCD	Sickle Cell Disease
SD	Standard Deviation
SLE	Systemic Lupus Erythematosus
SLEDAI	Systemic Lupus Erythematosus Disease Activity Index
SLICC/ACR	Systemic Lupus International Collaboration Clinics/ACR damage index
SPECT	Single Photon Emission Computed Tomography
TB	Tuberculosis
TBMs	Tingible Body Macrophages
TGs	Triglycerides
THA	Total Hip Arthroplasty
TNF	Tumour Necrosis Factor
TTP	Thrombotic thrombocytopenic purpura
US	Ultrasound
UV	Ultraviolet
WBCs	White Blood Cells

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INTRODUCTION

Osteonecrosis (ON) is a clinical entity of an unclear pathogenisis characterized by death of the bone marrow and the trabecular bone. It often results in the collapse of the architectural bone structure, leading to joint pain and loss of function. Circulatory impairment of the affected bone has been postulated to be the common denominator for all cases of ON **(Filaho *et al.*, 2007).**

The term "avascular necrosis" describes the occurance of osteonecrosis in the epiphysis. When the same process involves the metaphysis or diaphysis the term "bone infarct" is applied **(Watson *et al.*, 2004).** Avascular necrosis occurs in a number of conditions usually involving the epiphysis of long bones, such as the femoral and humeral heads and the femoral condyles, but small bones and the vertebrae can also be affected. The anterolateral aspect of the femoral head, the principle weightbearing region and the site of greatest mechanical stress, typically is involved, but no region of the femoral head is necessarily spared **(Sharma *et al.*, 2003).**

Osteonecrosis may be due to a traumatic insult with interruption of the vascular supply or non-traumatic in conditions that result in vascular occlusion or increased intraosseous pressure **(Aranow *et al.*, 1997)**. The pathogenesis of non-traumatic ON of the femoral head has been suggested by vascular occlusion, thrombophilia, altered fat metabolism and fat emboli, elevated intracortical pressure, inhibition of angiogenesis, intramedullary haemorrhage, mechanical stress and primary cell death **(Abu-Shakra *et al.*, 2003).**

Among the rheumatic diseases, ON is strongly associated with systemic lupus erythematosus (SLE). Most investigators have found the use of glucocorticoids to be a major risk factor for ON in SLE **(Nagasawa *et al.*, 2005)**. Osteonecrosis of the hip, and in particular the femoral head, is the most commonly encountered type in clinical practice

(Steinberg, 1999). In SLE symptomatic ON has been reported in 10-12% of patients **(Gladman *et al.*, 2001)**. It has been reported to occur within four years of diagnosis in at least 80% of cases **(Park *et al.*, 2007)**. However, ON has also been reported in lupus patients whom have never received therapy with this drug **(Zonana *et al.*, 2000)** Moreover, a significant lower frequency of ON has been reported in other clinical conditions requiring chronic corticosteroid therapy **(Zizic, 1990).** Alternatively, disease associated factors have been proposed to enhance the risk for ON development, such as: disease activity, vasculitis, Raynaud`s phenomenon, thrombophlebitis, antiphospholipid antibodies or syndrome, thrombophilia and hypofibrinolysis **(Tektoniolou *et al.*, 2003)**. Among these, disease activity is perhaps the most difficult to elucidate, since most studies have not used standard instruments of measurement, and more importantly they have not evaluated flares at the time of or close to the clinical onset of ON **(Gladman *et al.*, 2005)**

Since joint preservation measures have a much better prognosis when the diagnosis of ON is made early in the course of the disease, and since the results of joint replacement therapy are poorer in younger age groups, diagnosing ON as early as possible is critical to prevent or delay progression of the disease **(Sharma *et al.*, 2003).**

During the last years, magnetic resonance imaging (MRI) has proven to be the single method for the early diagnosis of ON. It is a very safe technique and is both very sensitive and very specific for ON **(Aiello *et al.*, 2004).** MRI and bone scintigraphy are helpful for diagnosing early ON of the femoral head. However, no predictive test is known to detect ON **(Lee *et al.*, 2007).**

Evaluation of haemodynamic flow to the femoral head is important in understanding how blood flow is closely related to intraosseous pressure and the pressure of the joint cavity **(Launder *et al.*, 1981)**.