SERUM LEVEL OF FETUIN-A IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) : RELATION TO DISEASE ACTIVITY AND ACCELERATED ATHEROSCLEROS+IS

Thesis

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Dedicated To

My Father
My Mother

My Wife,

My Son &
My Sister

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LIST OF ABBREVIATIONS

ASVD	**:**	Atherosclerotic vascular disease .
AHSG	**:**	Alpha 2-Heremans-Schimd glycoprotein .
Bcl-2	**:**	B-cell leukemia/lymphoma 2 .
BRC	**:**	bromocriptine .
BVSMC	**:**	Bovine vascular smooth muscle cells .
CTLA4	**:**	Cytotoxic T-lymphocyte-associated protein 4.
CaMKIV	**:**	Ca^{2+}-calmodulin kinase IV.
CVD	**:**	Coronary vascular disease.
CVC	**:**	Cardiovascular calcification .
DHT	**:**	Dihydrotestosterone .
DHEA	**:**	Dehydroepiandrosterone .
DNA	**:**	Deoxy ribonucleic acid .
Fcγ Rs	**:**	Fc gamma receptors .
GnRH hormone	**:**	Gonadotropin-releasing
HD	**:**	Hemodialysis .
HLA	**:**	Human leukocyte antigen .
HPA	**:**	Hypothalamic-pituitary adrenal axis .
HPG	**:**	Hypothalamic-pituitary gonadal axis .
IL-2	**:**	Interleukin -2 .
INF-γ	**:**	Interferon gamma .
IMT .	**:**	Intimal media thickness
MHC I	**:**	Major histocompatbility complex I .
MHC II	**:**	Major histocompatbility complex II .
MBL	**:**	Mannose-binding lectin .
NSAID	**:**	Non-steroidal anti-inflammatory drugs
OxLDL	**:**	Oxidized low density lipoprotein .
PBMC	**:**	Peripheral blood mononuclear cell .
PRL	**:**	Prolactin .
SLE	**:**	Systemic lupus erythematosus .
SLEDAI	**:**	Systemic lupus erythematosus activity index .
TNF factor	**:**	Tumor necrosis
TNFRs	**:**	Tumor necrosis factor receptors .
Th1	**:**	T-helper cell type 1 .
Th2	**:**	T-helper cell type 2 .
TGF-ß	**:**	Transforming growth factor- beta .
UV	**:**	Ultraviolet .
VSMC	**:**	Vascular smooth muscle cells .
ANA	**:**	Anti-nuclear antibody .

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INTRODUCTION

History of Systemic lupus erythematosus

The history of lupus can be divided into three periods: the classical period which shows the description of the cutaneous disorder, the neoclassical period which shows the description of the systemic or disseminated manifestations of lupus and the modern period which was heralded by the discovery of the lupus erythematosus (LE) cell.[1]

The history of lupus during the classical period was reviewed by Smith and Cyr in 1988.[2] The derivation of term lupus and clinical descriptions of cutaneous lesions of lupus vulgaris, lupus profundus, discoid lupus and photosensitive nature of malar or butterfly rash.[2]

The Neoclassical era of the history of lupus began in 1872 when Kaposi [3], first described the systemic nature of the disorder. The sentinel event in the mid 1900s, which heralded the modern era was the discovery of LE cell by Hargraves and colleagues in 1948.[4] The investigators observed these cells in the bone marrow of patients with acute disseminated lupus erythematosus. This discovery ushered in the present era of the application of immunology to the study of lupus erythematosus.[4]

Since 1954, various unusual proteins (antibodies) that act against the patients' own tissues have been found to be associated with systemic lupus erythematosus (SLE). Detection of these abnormal proteins has been used to develop more sensitive tests for SLE like anti-nuclear antibody (ANA), anti-DNA antibody and anti-smith antibody. The presence of these antibodies may be the result of factors other than SLE.[5]

Systemic lupus erythematosus

SLE is an autoimmune disease in which immune system attacks the body cells and tissues, resulting in inflammation and tissue
damage. SLE can affect any part of the body, but often harms the heart, joints, skin, kidney, lungs, blood vessels and central nervous system.[6]

SLE reflects a general defect in immune regulation that results in hyperactive T cells and B cells. The role of vascular injury in the pathogenesis of SLE is due to circulating immune complexes of autoantibodies and self antigens are deposited in the vascular wall of SLE patients and activate the complement pathway that initiate inflammatory response.[7]

It is also a disease of unknown cause that may cause variable combinations of fever, rash, hair loss, arthritis, pleuritis, pericarditis, nephritis, anemia, leukopenia, thrombocytopenia and central nervous system diseases. The clinical course of SLE is characterized by periods of remissions and acute or chronic relapses.[8]

Epidemiology

The reported prevalence of SLE in the population is 40 to 150 cases per 100,000 due to improved detection of mild disease, the incidence has nearly tripled in the last 40 years.[9] Estimated incidence rates in North America, South America, Europe and Asia range from about 15 to 254 per 100,000 per year.[10] In the United

States, data from two states with large urban and minority populations, the prevalence was 104 to 170 per 100,000 women, with prevalence in
Afro- American women 2.5 to three-fold higher than in Caucasian women.[11]

SLE is up to 10 times more common in women than men and typically has a predilection for women in their childbearing years.[12]

The prevalence of SLE is higher among Asians, Afro-Americans, Afro-Caribbeans and Hispanic Americans compared to Americans of European descent in the United States and among Asian Indians compared to Caucasians in Great Britain but is seem infrequently in Blacks in Africa.[13]

Sixty-five percent of patients with SLE have disease onset between the ages of 16 and 55. The remaining 20 percent present before age 16 and 15 percent after age 55. Median ages at diagnosis for white females range from 37 to 50 years, in white males from 50 to 59, in black females from 15 to 44 and in black males from 45 to 64.[14]

Diagnostic criteria

The diagnosis of SLE is facilitated by determining whether the patient has 4 of 11 clinical and/or laboratory criteria developed for the classification of SLE (Table I).[15,16]

Table (I): Criteria for classification of Systemic Lupus erythematosus.[15,16]

Criterion	Definition / Example
1- Malar rash	Fixed erythema over the malar eminences / tending to spare the national folds.
2- Discoid rash	Erythematosus raised patches and may scares.
3- Photosensitivity	Skin rash as result of unsual reaction to sunlight.
4- Oral ulcer	Usually painless.
5- Arthritis	Non–erosive : Jaccoud's arthropathy.
6- serositis	a) Pleuroitis (Pleuritic pain, Pleural rub, Pleural effusion). b) Pericarditis (ECG changes, Rup, Pericardial effusion).
7- Renal disorder	a) Proteinuria (> 3 + or 0.5 g / day). b) Cellular casts in urine.
8- Neurological disorders	a) seizures. b) Psychosis.
9- Haematological disorders	a) Haemolytic anemia. b) Leukopenia. c) lymphopenia. d) Thrombocytopenia.
10- Immunological	a) Anti-DNA antibodies. b) Anti-sm antibodies. c) Anti-phopholipid antibodies.
11- Anti-nuclear antibody (ANA)	Exclude drug causes.