# *RELATIONSHIP BETWEEN SEROLOGICAL MARKERS AND CLINICAL MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS*

*Thesis*

Submitted for Partial Fulfillment of
the Master Degree in
Internal Medicine



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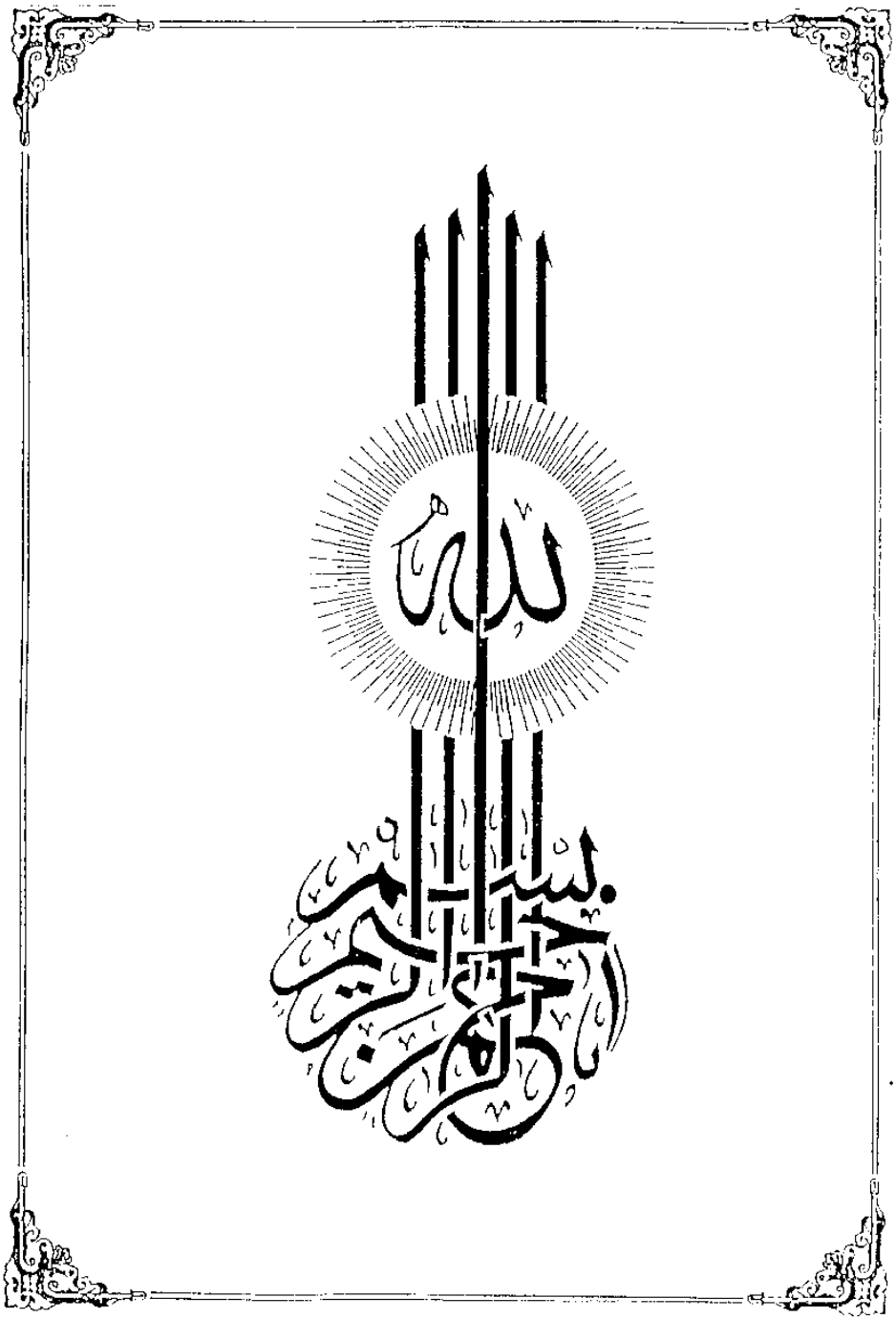

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*AHMED ELSEBAAIE*

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# LIST OF ABBREVIATIONS

| | | |
|---|---|---|
| aCL | : | anticardiolipin |
| ANA | : | antinuclear antibody |
| ANA's | : | antinuclear antibodies |
| ANF | : | antinuclear factor |
| Anti-Sm | : | anti-smith |
| APL | : | anti-phospholipid |
| ARA | : | American Rheumatism Association |
| $C_3$, $C_4$ | : | Complement No. 3, Complement No. 4 |
| CREST | : | (C) calcinosis, (R) Raynaud's, (E) esophageal stenosis, (S) Sclerodactyly, (T) Telangiectasia |
| ds-DNA | : | double stranded DNA |
| LAC | : | Lupus anticoagulant |
| NLE | : | Neonatal lupus erythematosus |
| PSS | : | Progressive Systemic Sclerosis |
| SLE | : | Systemic lupus erythematosus |
| Sn RNP | : | Small nuclear ribonucleoprotein |
| SSA | : | Sjogren's Syndrome A |
| SSB | : | Sjogren's Syndrome B |
| SS-DNA | : | Single Stranded DNA |

# INTRODUCTION AND AIM OF THE WORK

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Systemic lupus erythemotosus (S.L.E.) is a chronic inflammatory disease of unknown cause that may affect the skin, joints, kidneys, lungs, nervous system, serous membranes and other organs of the body.

Patients with S.L.E. develop distinct immunologic abnormalities especially anti-nuclear antibodies. The clinical course of S.L.E. is characterized by period of remission and chronic or acute relapses, (**Kelley et al., 1993**).

Anti-double stranded-DNA antibodies are rather specific for S.L.E. and are observed at high frequency in patients with active disease (75% to 95%) (**Beufils et al, 1983**). The presence of autoantibodies in the circulation explains at least some of the manifestations of S.L.E. Thus there is strong evidence that the renal disease of S.L.E. results from the deposition of immune complexes, with anti-DNA antibodies as an important components. In many patients, anti-DNA rises with activity of the renal disease and anti-DNA antibodies can be isolated from affected kidneys.

Reflecting the deposition of immune complexes, there is activation of the complement system with serum hemolytic complement falling in active disease. There are patients with abnormal serologies without renal disease, so the discrepence between serologic abnormalities and clinical events suggests that only some autoantibodies play a pathogenetic role. Serological data, therefore need not be viewed as absolutely predictive of active S.L.E. Since some serologic abnormalities may occur in the setting of clinicaly quiescent disease (**Snyderman R. et al., 1986**). Therefore, this work was designed to study relationship between serological markers and clinical manifestations in 30 patients with S.L.E.

# REVIEW OF LITERATURE

# SYSTEMIC LUPUS ERYTHEMATOSUS

*Definition:*

Systemic lupus erythematosus is a multisystem inflammatory disorder characterized by autoantibodies production.

In the last decade, there have been significant advances in the understanding of disease mechanism in SLE reflecting the interest in SLE as a protype for autoimmunity and spectacular growth of the field of immunology (**Pisetesky, 1986**).

*Historical perspective:*

Lupus, which is latin for wolf, has been used about 1230 to describe cutaneus conditions which resemble the malar erythema of a wolf. Numerous publications in the nineteenth century by Beteman, Hebra, Kaposi and others described what we know now as a lupus of the skin (**Kaposi, 1972**). In 1852, Cazenava and Talbot first used the term "lupus erythematosus" (**Cazenava and Talbot, 1974**). **Kaposi, in (1872)** noted the systemic involvement in lupus, and that the rash resembled a butterfly.

Theories on the nature of the immune system and on its failure was studied by "Froui and Coworkers" in 1953, gave the experimental basis for "Immunological tolerance", which has contributed substantially to the concept of "autoimmune disease" **(Froui, 1957)**.

*Incidence and prevalence:*

Recent epidemiologic studies suggest a far greater frequency of disease than was revealed by surveys of previous decades. The incidence of SLE is currently estimated to be 50 to 70 new cases per year per million population, it has a prevalence of approximately 500 patient per million. The frequency of SLE is substantially increased in several segments of the population. females, particularly during the reproductive years are at greater risk for SLE thMw males, the female to male sex ratio is about 9:1 **(Kleppel and Decker, 1983)**. The increased frequency of SLE among females is thought to be due to unknown hormonal effect **(Lahita et al., 1983)**. There appears to be an increase in the frequency of SLE in certain racial groups, including American blacks, American indians and orientals **(Kleppel and Decker, 1983)**. The disease is also common in HLA-$B_8$ and $DR_3$ patients **(Winchester and Nuonez, 1982)**.

*Aetiology:*

Despite intensive efforts, no etiology has yet been found for SLE. A variety of factors have been proposed to be etiologic for SLE, including viral, genetic, environmental, hormonal and immunological influences. It is probable, however that none of these factors operate independently in the production of clinical disease. Rather, the development of SLE probably requires a modification in the complex interelationship between the host, the pathogen and the environment (**Wallace and Dubois, 1987**).

*Drug induced lupus:*

Drugs have been incriminated in precipitating or exacerbating SLE especially in females who are $HLADR_4$. The drugs which may give lupus like syndrome can be classified as those where the association is definite including hydralazine, procainamide and isoniazide, although with isoniazide the studies confirm serologic conversion and not symptoms, or those where the association is very possible including phenytoin, chlorpromazine, methyl dopa, penicillamine, quinidine, beta blockers, propyl thiouracil, lithium carbonate and nitrofurantoin (**Hess, 1982**). The features suggesting that SLE is drug induced are the frequent presence of

anti-histones antibodies, the absence of anti-DNA antibodies, the normal serum complement, the infrequent involovement of renal and central nervous system, the frequent occurence in an older age group, and the disease is uncommon in blacks (**Epstein and Barland, 1985**).

*Clinical picture:*

The classical picture of a patient with well advanced lupus is that of a young female with fever, weight loss, arthralgia, butterfly rash, pleural effusion, and nephritis. The course of the disease is characterized by periods of remission and activity (**McCarty, 1982**). The major clinical manifestations during the course of the disease are described in the following:

*1. General Symptomatology:*

There is no characteristic pattern for the clinical features at the onset of SLE nor any consistency in the course of the illness (**Reeves and Lahita, 1987**).

Constitutional symptoms include: fatigue (in 80-100 percent of patients) weight loss, fever (in over 80% of SLE patients), hair loss, generalized body aches, haedache, and easy bruising **(Rothfield, 1981)**.

2. *Muscloskeletal manifestations:*

Most patients complain of arthralgia rather than arthritis. fingers, hands, wrists, knees, and elbows are commonly affected. Skeletal muscle are clinicaly affected in up to 50% of patients. Myalgia, proximal muscle weakness and carpal tunnel have all been reported. 15% of patients show atrophy and extreme muscle weakness **(Oxenhandler, et al, 1982)**.

3. *Mucocutaneous manifestation:*

The skin and mucous membrane are symptomatically involved in over 8% of patients **(Gillians, 1987)**. Photosensetivity occurs in up to 58%, butterfly rash appears in approximately 50%, and alopecia is generaly seen during exacerbations of the disease, **(Provost and Dore, 1983)** **(Dubois and Wallace, 1987)**. Vascular lesions including periungal erythema, Raynaud's phenomenon and various form of vasculitis occur in about 50% of patient **(Gilliam, 1987)**.