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**Review Article**

# A role of biomarkers in systemic lupus erythematous: a comprehensive review

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## ABSTRACT

Systemic lupus erythematous (SLE) is an auto immune disease that can involve almost all body organs. Lupus erythematous may be classified in to several subtypes according to clinical features including systemic and cutaneous lupus erythematous, drug induced lupus and neonatal lupus. SLE progression includes in the immune system. Pathological manifestation of SLE are due to antibody formation and deposition of immune complexes in different organs of the body. Due to formation or disposition of immune complex in different body tissues and vessels, which may lead to complement activation and more organ damage. Other factors include genetic factors, hormonal abnormalities and environmental factors. There is a challenge in establishing a diagnosis, determining disease activity. Therefore, an important needs is a repertoire of biomarkers that can accurately with prediction, diagnosis, and disease, activity monitoring and stratifying patient. SLE can be diagnosed by using different biomarkers as anti-smith antibodies (ANAS), antibodies to double stand deoxyribonucleic acid (DNA) and level of complement components C3 C4, and CH50. More immunological biomarkers are needed to be better understanding of disease SLE. SLE is an autoimmune disease which can travel to any organ or a system i.e. biomarkers for cardiovascular involvement in SLE, biomarkers for respiratory involvement in SLE, biomarkers for lupus arthritis.

**Keywords:** Systemic lupus erythematous, Biomarkers, Diagnosis, Disease activity

## INTRODUCTION

Systemic lupus erythematous (SLE) is an autoimmune disease that can involve all body organs, it may be classified in to several sub types such as systemic lupus erythematous, cutaneous lupus erythematous, Drug induced lupus erythematous and neonatal lupus, it involves in the immune system. SLE usually begins with mild symptoms such as fatigue, fever and skin rashes. Without treatment it may end with organ failure or organ damage the patients may have positive history of lupus, skin rashes, arthritis and fatigue which may leads to SLE (Figure 1 and 2).[1] SLE is a chronic auto immune inflammatory disease with a wide spectrum of clinical and serological manifestation caused by auto antibody production, complement activation and immune complex deposition. The etiopathogenesis of SLE is not completely clear, but it results in the complex formation between genetic and hormonal factors and environmental exposure.[2]

Biomarkers are defined as a characteristic that is objectively measured and evaluated as indicator of normal biological process, pathogenic process or pharmacological process, pathogenic process and therapeutic interventions SLE was mainly diagnosed by clinical features and lab findings. Biomarkers widely used for SLE diagnosis include anti nucleal antibodies (ANAS), anti-smith antibodies, antibodies to double strand DNA and level of serum complement components C3, C4, and CH50. ANAS have high sensitivity and have very little positive predictive to SLE and anti-smith antibodies and double strand DNA have low sensitivity and have high positive predictive to SLE.[3]

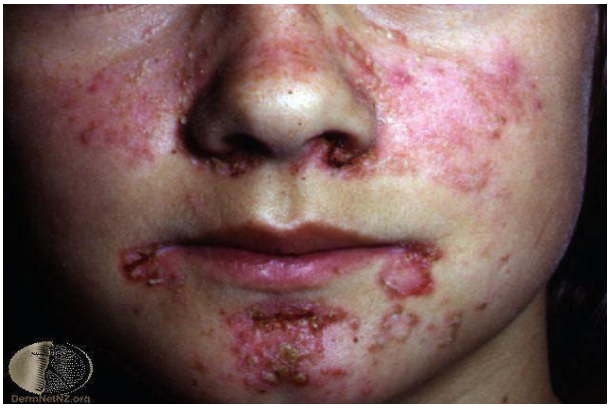

**Figure 1: Systemic lupus erythematosus symptoms.**

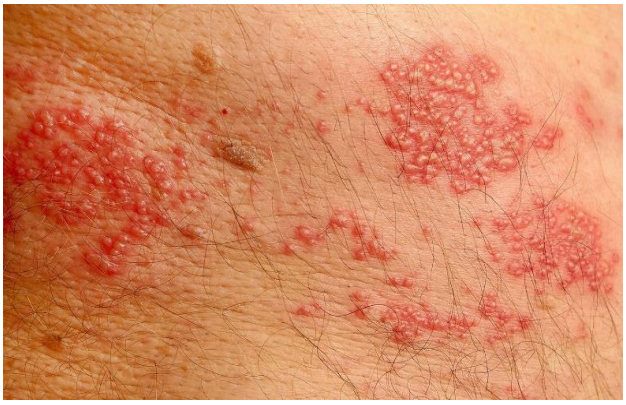

**Figure 2: Hallmarks of systemic lupus erythematosus.**

## NON-ORGANIC SPECIFIC BIOMARKERS FOR SLE

### *Serum ANAS*

ANAS detected by indirect immune fluorescence on HEP-2 cells has long been regarded as a pivotal immunological biomarker in serum for patient with SLE, eligibility for SLE ANAS include in acr-1997, SLICC-2012, EULAP-2019 criteria, if these is positive for ANA, further testing for ds DNA, SSA Sjogren's syndrome antigen B, SM, ribonucleic protein should be done.[4,5] ANA is unique test for SLE. But it has low specificity as they can occur in 5-10% of healthy controls, more in older patients (30).[6]

### *Serum complements 3 (C3) and complement 4 (C4)*

Serum complements 3 (C3) and complements 4 (C4) are widely used to assess the presence of biologically active immune complex and monitor disease activity.[7] Low serum level of C3 and C4 are considered in the slicc-2012 SLE classification criteria. Patient with both low level of C3 and C4 are readily diagnosed with SLE patient either low C3 or C4 together with a positive ANA test showed 99.3% specificity for an SLE diagnosis.[8] Furthermore, decreased level of C3 and C4 have clinically evident flare and positively with SLE disease activity.[9]

### *Antinucleosome*

The prevalence of antinucleosome, AN4A in SLE differ from 50% to 100%, AN4A can combine with other clinical findings and other lab test for diagnosing SLE and drug induced lupus.[10]

### *Sedimentation rate of erythrocytes and C-reactive protein*

High erythrocyte edimentation rate (ESR) value and low C-reactive protein (CRP) level is key sign of inflammation in SLE and also used in monitoring SLE disease activity.[11] Both ESR and CRP values are increased. SLE patients with serositis and arthritis.[12]

### *Organ-specific SLE biomarkers*

*Anti-ds DNA anti bodies*

Associated with SLE disease activity and can predict the development of LN, high specificity ranges in 96% and low diagnostic sensitivity ranges in 52-70%.[13]

*Anti-SM antibodies*

It has a highly specific diagnostic biomarker for SLE with specificity of 99% but with a low sensitivity of 5-30%.[14]

*Anti-c1q antibodies*

Increased anti c1q antibody used in predict in the renal flares in lupus nephritis with ranges of an 81-97% sensitivity and a 71-95% specificity. Standardized laboratory assay has not been established.[15]

### *Lupus in arthritis*

Joint involvement is one of the common symptom in systemic lupus erythematous, with a frequency ranging from 69 to 95%.

This feature significantly influences the patient's quality of life, possibly leading to disability and impaired functional performances inn daily activities.

Auto antibodies associated with inflammatory arthritis such as rheumatoid arthritis (RA), have also been shown to play a role in SLE arthritis.

Anti-citrullinated peptide antibodies are a serological marker for rheumatoid arthritis. Recently anti-carbamylated protein antibodies have been indented in RA.

By these antibodies and phenotypes SLE patients also developing erosive arthritis similar to that RA.[16] Recent survey studies shows that if a patient is having high levels of anti-cyclic citrullinated peptide (CCP) paper to be one important marker in SLE patients.

If anti CCP/anti CAP ratios more than 2 then it is indented as deforming arthritis.[17]

***Lupus in respiratory***

SLE is an autoimmune inflammatory disease, it may lead damage if other organs as respiratory for detection of an oxidative stress. All biomolecules (lipids, protein and DNA) can damage by excessive production of reactive oxygen species (ROS), the product of these cause modifications in the biological fluid with disease activity of SLE, it suggests the oxidative modification of biomarkers, increased malondialdehyde (MDA) modified protein, anti-SOB and anti-catalase antibodies, albumin modification by 9-hydroxy-2-nonenal (HNE) in sera of patients it shows activity of the SLE disease.[18]

***Biomarkers for cardiovascular involvement in SLE***

Cardiovascular disease (CVD) is one of the most important complication of SLE.

The monocyte to high density lipoprotein cholesterol ratio and low-density granulocytes to high density lipoprotein cholesterol ratio are high in SLE patients, the biomarkers for identifying CVD risk in SLE patients.[19] Dysfunctional high-density lipoprotein is a key biomarkers of arthero sclerosis in lupus and biomarkers for SLE patient with CVD, high troponin T identified biomarker event in SLE patient.[20] Serum levels of Ig G anticardiolipin antibodies and E-selection are associated with EVD in lupus.[21]

## CONCLUSION

SLE is an auto immune disease it can travel to any organ or a system which lead to damage of tissue. Biomarkers play a crucial role in diagnosis of SLE by the use of biomarkers we can detect the stages in SLE. More immunological biomarkers are needed to better understanding of disease SLE including organic and non-organic SLE biomarkers. No single biomarker is sensitive and specific enough for SLE. Still ongoing investigations are going on biomarker studies hence we can't interpretative the exact evidence and research on SLE biomarkers don't progress to studies on practical application.

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