ISSN 2664-4169 (Print) & ISSN 2664-7923 (Online)
South Asian Research Journal of Biology and Applied Biosciences
Abbreviated Key Title: South Asian Res J Bio Appl Biosci

| Volume-6 | Issue-3 | May-Jun -2024 | **DOI: 10.36346/sarjbab.2024.v06i03.002**

Review Article

The Effect of Human Leukocyte Antigen in Development of Systemic Lupus Erythematosus in Patients

Israa Mohammad Abd AL-Khaliq[1*]

[1]HLA Typing Unit, Al-Kindy College of Medicine, Baghdad University, Baghdad, Iraq

***Corresponding Author:** Israa Mohammad Abd AL-Khaliq
HLA Typing Unit, Al-Kindy College of Medicine, Baghdad University, Baghdad, Iraq

Article History
Received: 02.03.2024
Accepted: 08.04.2024
Published: 10.05.2024

Abstract: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by the production of autoantibodies against nuclear antigens and a systemic inflammation that can damage a broad spectrum of organs. SLE patients suffer from a wide variety of symptoms, which can affect virtually almost any tissue. As lupus is difficult to diagnose, the worldwide prevalence of SLE can only be roughly estimated to range from 10 and 200 cases per 100,000 individuals with dramatic differences depending on gender, ethnicity, and location. Although the treatment of this disease has been significantly ameliorated by new therapies, improved conventional drug therapy options, and a trained expert eye, the underlying pathogenesis of lupus still remain widely unknown. The complex etiology reflects the complex genetic background of the disease, which is also not well understood yet. However, in the past few years advances in lupus genetics have been made, notably with the publication of genome wide association studies in humans.

Keywords: Systemic lupus erythematosus, autoimmunity, HLA, genetic factor.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune rheumatic disease in which disease flares are interspersed with episodes of remission. In contrast to organ specific autoimmune diseases, SLE comprises a constellation of signs and symptoms that can affect multiple organ systems. This diversity of presentation, changing clinical features and fluctuating disease course often presents challenges in diagnosis and management. The prevalence of SLE is variable, dependent on ethnic origin and ranges from 40–200 per 100,000 of population. SLE is more common in those of African and Asian ancestry than in Europeans. It is predominantly a disease of females, with a female to male ratio of 9:1 [1]. Non-European patients with SLE tend to have a younger onset of disease and greater incidence of serious organ involvement, reflective of a more severe clinical phenotype. The broad spectrum of clinical presentations includes mucocutaneous, musculoskeletal, haematological, cardiopulmonary, renal and central nervous system manifestations. Lupus nephritis and neuropsychiatric lupus are considered the most severe forms of organ involvement and can result in significantly reduced life expectancy [2]. This has led to recognition of the need for early intensive immunosuppression. Current treatment regimens consist of antimalarial drugs, corticosteroids, conventional disease-modifying anti-rheumatic drugs, cyclophosphamide and biologics. However, conventional therapies fail to adequately suppress disease activity in a significant proportion of patients and newer targeted therapies are being developed [3].

The HLA, as per almost all the ADs, has been shown to exert the strongest genetic association and effect on SLE to date. The top association was found at HLA-DRB1. Studies examining HLA class II have consistently replicated the HLA-DR2 (DRB1*15:01), HLA-DR3 (DRB1*03:01), HLA-DRB1*08:01, and HLA-DQA1*01:02 alleles associated with the disease in American and European populations with a twofold RR conferred by each allele [4, 5]. The extended HLA 8.1 AH (ancestral haplotype) is considered a common European haplotype implicated in SLE susceptibility. In both European and Asian populations has shown that the strongest contribution to risk for SLE resides in the HLA region and consists of multiple genetic effects [6]. The long-range LD within the HLA region has made assessing the relative contribution of each component gene to disease susceptibility difficult. However, the available evidence suggests that

genetic variants such as HLA-DR2 and HLA-DR3, HLA-DPB1, HLA-G, and class III (such as MSH5 and SKIV2L) genes, in particular, predispose an individual to SLE [7].

Moreover, the role of SLE-associated HLA class II alleles in initiating SLE-relevant autoantibody responses has been demonstrated in humanized mice expressing the HLA-DR3 transgene but no other DR or DQ alleles [8]. Microarray studies done on SLE patients have revealed that the MHC class I genes are under expressed when compared with controls [9]. The MHC class I region is required for the detection of intracellular pathogens by $CD8^+$ T cells, and its absence seems to lead to a failure to defend against such pathogens. A certain gene transcription signature in $CD8^+$ T cells has been linked to SLE disease prognosis [10].

REFERENCES

1. Lim, S. S., Bayakly, A. R., Helmick, C. G., Gordon, C., Easley, K. A., & Drenkard, C. (2014). The incidence and prevalence of systemic lupus erythematosus, 2002–2004: the Georgia Lupus Registry. *Arthritis & rheumatology*, *66*(2), 357-368.
2. Feldman, C. H., Hiraki, L. T., Liu, J., Fischer, M. A., Solomon, D. H., Alarcón, G. S., ... & Costenbader, K. H. (2013). Epidemiology and sociodemographics of systemic lupus erythematosus and lupus nephritis among US adults with Medicaid coverage, 2000–2004. *Arthritis & Rheumatism*, *65*(3), 753-763.
3. Somers, E. C., Marder, W., Cagnoli, P., Lewis, E. E., DeGuire, P., Gordon, C., ... & McCune, W. J. (2014). Population-based incidence and prevalence of systemic lupus erythematosus: the Michigan Lupus Epidemiology and Surveillance program. *Arthritis & rheumatology*, *66*(2), 369-378.
4. Fernando, M. M. A., Stevens, C. R., Sabeti, P. C., Walsh, E. C., McWhinnie, A. J. M., Shah, A., ... & Vyse, T. J. (2007). Identification of two independent risk factors for lupus within the MHC in United Kingdom families. *PLoS genetics*, *3*(11), e192.
5. Bronson, P. G., Komorowski, L. K., Ramsay, P. P., May, S. L., Noble, J., Lane, J. A., ... & Barcellos, L. F. (2010). Analysis of maternal–offspring HLA compatibility, parent-of-origin effects, and noninherited maternal antigen effects for HLA–DRB1 in systemic lupus erythematosus. *Arthritis & Rheumatism*, *62*(6), 1712-1717.
6. Guerra, S. G., Vyse, T. J., & Cunninghame Graham, D. S. (2012). The genetics of lupus: a functional perspective. *Arthritis research & therapy*, *14*, 1-12.
7. Fernando, M. M., Freudenberg, J., Lee, A., Morris, D. L., Boteva, L., Rhodes, B., ... & Vyse, T. J. (2012). Transancestral mapping of the MHC region in systemic lupus erythematosus identifies new independent and interacting loci at MSH5, HLA-DPB1 and HLA-G. *Annals of the rheumatic diseases*, *71*(5), 777-784.
8. Jiang, C., Deshmukh, U. S., Gaskin, F., Bagavant, H., Hanson, J., David, C. S., & Fu, S. M. (2010). Differential responses to Smith D autoantigen by mice with HLA-DR and HLA-DQ transgenes: dominant responses by HLA-DR3 transgenic mice with diversification of autoantibodies to small nuclear ribonucleoprotein, double-stranded DNA, and nuclear antigens. *The journal of immunology*, *184*(2), 1085-1091.
9. Chaussabel, D., Quinn, C., Shen, J., Patel, P., Glaser, C., Baldwin, N., ... & Pascual, V. (2008). A modular analysis framework for blood genomics studies: application to systemic lupus erythematosus. *Immunity*, *29*(1), 150-164.
10. McKinney, E. F., Lyons, P. A., Carr, E. J., Hollis, J. L., Jayne, D. R., Willcocks, L. C., ... & Smith, K. G. (2010). A CD8+ T cell transcription signature predicts prognosis in autoimmune disease. *Nature medicine*, *16*(5), 586-591.