

Systemic Lupus Erythematosus

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*Lupus reflects a wide spectrum of syndromes that share many clinical, inflammatory, immunological and genetic features. These syndromes comprise latent lupus, drug-induced lupus, discoid lupus, systemic lupus erythematosus (SLE), advanced lupus and anti-phospholipid syndrome. The disease is potentially fatal when left untreated or inadequately treated.*¹

Over the past 4 decades, the incidence of SLE has nearly tripled, from 51/100,000 to between 122 and 124/100,000 population.²⁻⁴ This is due to better recognition of its mild form, use of the ANA test and improved survival. The higher incidence may also be associated with ultraviolet light, long-term use of oral contraceptives and oestrogen replacement therapy.⁵⁻⁷

Clinical and Immunological Manifestations

Although incidences of fever, photosensitivity and facial rash of SLE are higher in the East than in the West,⁸ the various clinical manifestations of SLE expressed as a percentage of all cases are similar.⁹⁻¹³ Autoantibody profiles of patients with SLE (in different countries and of different races) have been shown to be similar, but with varying degrees of severity and rates of mortality.¹³

Causes of Mortality

The negative effect of renal involvement on prognosis has been confirmed by numerous studies.^{9,10,13-15} It is considered the primary cause of mortality in patients with SLE.

Nosocomial infections are common in hospitalised patients with SLE.¹⁵⁻²⁰ These are associated with an overall increase in disease activity. Infection is the second most significant cause of death in patients with SLE.

Herpes zoster infection results in significant morbidity and occurs more frequently in patients with SLE than the general population. This is probably due to the patients' defective cellular immunity.²¹ Individuals who have had severe manifestations of lupus are at greatest risk of infection from *Herpes zoster*.²²

Cardiovascular disease is the third most common cause of mortality, especially those receiving long-term corticosteroid therapy.^{23,24}

Other less frequent, but potentially fatal complications, of disease activity include cerebral lupus²⁵⁻²⁷ and pulmonary manifestations of lupus.²⁸⁻³⁰ Haematological manifestations may reduce life expectancy in some patients.³¹ For example, some manifestations of antiphospholipid syndrome (eg. thrombocytopenia or thrombosis) increase mortality in patients with SLE.³²

Damage Index

Damage indices have been devised to predict life expectancy in patients with SLE. These take into consideration the organ systems that have been affected or damaged by SLE.^{16,33-35} Renal

and pulmonary involvement, in particular, are predictors of worst outcomes. The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index indicates that damage to the pulmonary system results in death within 10 years of diagnosis.

Therapy

Hydroxychloroquine is effective as an initial therapy for mild lupus. It may be indicated for the prevention of disease or treatment-induced complications including hyperlipidaemia, diabetes mellitus, liver function test elevation and thrombosis.^{36,37}

For single drug therapy, methylprednisolone,³⁸ methotrexate,³⁹ cyclophosphamide,⁴⁰ and cyclosporin⁴¹ are effective. The use of immunosuppressants as monotherapy may induce severe adverse effects that influence the disease outcome and are potentially fatal if not promptly attended to. It has been reported that use of pulse intravenous (PIV) single immunosuppressants resulted in remission of SLE on maintenance therapy, but not treatment-free remission.⁴²⁻⁴⁶

Severe disease activity requires immediate intensive treatment. A combination of corticosteroid with low dose selective immunosuppressants can be used. Examples of low dose selective immunosuppressants include: immunosuppressive dose of PIV methylprednisolone; methotrexate; cyclophosphamide; and oral cyclosporine. Treatment of lupus nephritis, lupus nephrotic syndrome, lupus vasculitis and other severe complications with PIV combination of selective low dose immunosuppressants achieved remission.⁴⁷ Favourable results have been obtained with maintenance therapy of prednisone and azathioprine following an initial course of oral cyclophosphamide until complete or partial remission of lupus nephritis has occurred.¹ Azathioprine is a renowned steroid-sparing agent.⁴⁸

Survival

Many factors contribute to outcome in SLE, and these include: age; gender; race (genetic); behavioural; psychological; socioeconomic; immunological; immunogenetic variables; disease activity; infection; specific organ system involvement; and specific organ damage.^{10,11,14,15,18,20,22} Over the last 50 years, the survival rate of patients with SLE has risen significantly. This is as a result of better approaches to existing therapy, such as the prompt and improved treatment of disease complications and drug toxicity.⁶ Five-year survival was 50% in 1950, but had increased to 80 to 90% in the 1990s.^{49,50}

Treatment-free Remission

Several studies have reported treatment-free remission in patients with SLE using a variety of treatment regimens.^{42,51,52} ([Table](#)) Treatment-free control of severe lupus was achieved by plasmapheresis in a sterile ward, followed by pulse cyclophosphamide.⁵¹ Intravenous immunoglobulins were effective for treating recurrent infection.⁵³ These included patients that had severe, but reversible, organ involvement.

SLE is generally more responsive to therapy when treated before irreversible organ damage has occurred. In primary rheumatology centres, the majority of cases that fulfil the ACR classification criteria for lupus are mild.^{54,55} These cases tend to result in treatment-free

remission, even in a developing country.⁴² The intractable and chronic patients with SLE are usually referred to tertiary rheumatology care centres and are unlikely to attain treatment-free remission.

Conclusion

Fifty years ago, SLE was a potentially fatal disorder for most patients. Today, it can be treated, and in the vast majority of cases, long-term treatment-free remission can be expected.

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Competing Interests: none declared.

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