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Challenges for lupus management in emerging countries

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Summary

In emerging countries, systemic lupus erythematosus (SLE) has been associated with several unfavorable outcomes including disease activity, damage accrual, work disability and mortality. Poor socioeconomic status (SES) and lack of access to healthcare, especially in medically underserved communities, may be responsible for many of the observed disparities. Diagnostic delay of SLE or for severe organ damages (renal involvement) have a negative impact on those adverse outcomes in lupus patients who either belong to minority groups or live in emerging countries. Longitudinal and observational prospective studies and registries may help to identify the factors that influence poor SLE outcomes in emerging countries. Infection is an important cause of mortality and morbidity in SLE, particularly in low SES patients and tuberculosis appears to be frequent in SLE patients living in endemic areas (mainly emerging countries). Thus, tuberculosis screening should be systematically performed and prophylaxis discussed for patients from these areas. SLE treatment in the developing world is restricted by the availability and cost of some immunosuppressive drugs. Moreover, poor adherence has been associated to bad outcomes in lupus patients with a higher risk of flares, morbidity, hospitalization, and poor renal prognosis. Low education and the lack of money are identified as the main barrier to improve lupus prognosis. Newer therapeutic agents and new protocols had contributed to improve survival in SLE. The use of corticoid-sparing agents (hydroxychloroquine, methotrexate, azathioprine and mycophenolate mofetil) is one of the most useful strategy; availability of inexpensive generics may help to optimize access to these medications.

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by wide-ranging symptoms and multiple organ system impairments, predominantly affecting young women during the childbearing years. It is a chronic relapsing inflammatory illness causing accrual of organ damage over time as well as increased morbidity and mortality.

Advances in therapy and management in recent decades have dramatically improved patient survival in SLE, from 50% in the 1950s to over 90% currently. As a consequence, disease- and

treatment-related (particularly glucocorticoid) complications are expected to rise. Increased understanding of the molecular mechanisms underlying the pathogenesis of autoimmune rheumatic diseases has led to the development of new drugs that improve disease control and quality of life and reduce both accrued damage and glucocorticoid usage. But many other aspects of SLE remain challenging, including prompt diagnosis, disease monitoring, management of refractory disease, quality of life (QoL), and, in patients with long-standing disease, accelerated complications of atherosclerosis [1].

How do emerging countries deal with these difficulties? Few data are available from those areas, but worse outcomes are generally associated with ethnic minorities, low socioeconomic status (SES), and low educational levels. In SLE, poor SES has been associated with several unfavorable outcomes including disease activity and severity, damage accrual, work disability, and mortality [2–4].

Emerging countries are currently facing a dichotomy in healthcare demand: they must attempt to provide adequate care to cure and prevent communicable diseases at the same time as they must deal with the growing prevalence of chronic illnesses (such as diabetes, hypertension, cardiovascular diseases, cancer, and rheumatic diseases). Growing disparities in healthcare access and delivery characterize these nations. Many factors besides the very low percentage of people covered by health insurance may explain these disparities; some are individual factors (poverty, malnutrition, unhealthy behaviors, lack of adherence to medical advice), while others concern the healthcare system (lack of access to specialized facilities, geographic isolation, and barriers) and the society (poor gross-domestic product, inadequate health policies, lack of social support) [5]. The SLE challenges discussed above are still more difficult in emerging countries, especially because they must also deal with other crucial needs, including long delays in access to diagnosis, especially immunological diagnostic services, more severe presentation, end-stage organ damage, infectious complications, healthcare access, and the cost of treatment.

Our goals in this review are two-fold. First, we will report the differences and specificities of lupus patients and management in emerging countries. We will then discuss the perspectives for improving SLE outcomes there.

Methods

Published studies were searched by querying PubMed, Medline, Embase, and Cochrane. The search process used the following keywords: systemic lupus erythematous, epidemiology, registry, diagnosis, treatment, prognosis, trials, emerging countries, and developing countries, challenges, with a specific look at publications from Africa, Asia, and Latin America. The search was performed with no date limit, and then focused on the last 20 years. The populations of the emerging countries were likened to minorities living in developed countries because they often share socioeconomic characteristics.

Results

Epidemiology

SLE has been reported all over the world. Many epidemiological studies have detailed its incidence, prevalence, and mortality rates and their distribution according to gender, age, race, and disease presentation.

However, the epidemiology of SLE in developing countries remains largely unknown and probably underestimated, while that in developed countries is known through registries and cohorts. Some of these have contributed substantially to lupus research, especially on the differences in presentations and outcome according to ethnicity. Thus, the LUMINA cohort (Lupus in Minorities: Nature versus nurture) compared SLE in three different ethnic groups in the United States: Hispanics, African-American, and whites [3]. The GLADEL registry (Grupo LatinoAmerican De Estudio del Lupus) includes patients from different Latin American countries [6]. The Euro-Lupus project [7], the Johns Hopkins cohort [8], the Canadian multiethnic cohort [9], and data from the UK [10] have also helped to highlight the epidemiological differences among lupus patients. Analysis of racial origins suggests a higher prevalence of SLE among black Americans, Afro-Caribbeans, and Asian groups than among whites [2,4,9,11,12]. A similar pattern has been reported in the aboriginal populations of Australia, whose SLE prevalence is higher among whites [13]. In contrast to the high prevalence of SLE in those of African ancestry reported in USA registries [11], the incidence of SLE on the African continent itself seems low. This is likely largely due to the paucity of published data and underdiagnosis [14]. The mean age of disease onset seems low, and the female preponderance appears to be higher in several developing countries than in developed countries [15–25] (*table I*).

Clinical features and outcomes

The clinical manifestations of SLE show substantial geographical and ethnic variation between populations. In emerging countries and in minorities, SLE tends to be more severe, have more clinical manifestations, entail more prevalent and more severe nephritis, have higher rates of disease activity, and finally lead to more rapid accumulation of organ damage and higher mortality [3,26–28]. These points have been well described in different cohorts [15–25] and are illustrated in *tables II and III*.

Different cohorts have found lupus nephritis to be two to three times more prevalent among African-Americans and Hispanics (62%) than whites (26%) [3,10,15,28–30]. Afro-Caribbeans have high lupus nephritis rates and higher damage scores than other Canadian ethnic groups [9], and in the GLADEL cohort African-Latin Americans and mestizos both have higher