

# Autoimmune Diseases in Low and Middle Income Countries: A Neglected Issue in Global Health

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**S**ystemic and organ-specific autoimmune diseases include more than 100 conditions and are estimated to affect at least 5% of the world population, causing significant morbidity and mortality [1]. The vast majority of studies on these diseases are performed in high income countries, and the general impression is that autoimmune diseases are of little relevance to middle and low income countries. Strachan's hygiene hypothesis has added weight to this impression. However, autoimmune diseases are highly relevant to developing countries and should be given the attention they deserve. The prevalence of systemic lupus erythematosus (SLE), the prototype severe systemic autoimmune disease, ranges from 0.02% to 0.15%, but incidence and prevalence rates are two to three times higher in people of Asian or African origin than in Caucasians [2,3]. SLE is also more frequent among Aboriginal than non-Aboriginal Australians. African-American and Asian patients have more hematologic, neurologic and renal manifestations [2] and accumulate more damage over time at a faster rate than Caucasians [2]. Patients of Black African descent in Europe show greater disease activity compared to Caucasian patients [4].

The epidemiology of SLE in high income countries is known through regis-

tries and cohorts while similar data are unavailable in developing countries, giving the impression that the disease is of little importance there. However, where epidemiological studies have been done, the occurrence of SLE was found to be considerable and sometimes even higher than in developed countries. For instance, the annual incidence has been calculated to be 8.7/100,000 in a Brazilian urban area [5], and prevalence rates of 12.2/100,000 in South African blacks [6], 19.3/100,000 in Saudis [7], and 159/100,000 in Puerto Ricans [8] have been reported. Antinuclear antibody-positive autoimmune diseases are on the increase in India, and the long-held view that the incidence of SLE is low in Africa has recently been challenged and attributed to under-diagnosis and under-reporting [9,10].

Other autoimmune diseases are not uncommon in low and middle income countries: the prevalence of rheumatoid arthritis ranges from 0.12 to 0.90% as compared to 0.5%–1.1% in North America and Northern Europe [11], and the mean age of onset is 8–10 years earlier than in Caucasians for both Latin American Hispanics and South African blacks. Multiple sclerosis is increasing in developing countries, and the incidence of Graves' disease is growing in urban southern African blacks, possibly due to increased dietary iodine intake. African-Americans have a higher incidence of scleroderma than white Americans and the disease is not infrequent in South African blacks. Pulmonary arterial hypertension is a severe associated feature in black patients.

Hence, autoimmune diseases most likely affect well over 100 million people in low and middle income countries

where they are also often more severe, occur in younger patients, and lead to higher mortality, as shown for SLE in studies from South Africa [12], Iran [13] and the Philippines. The burden of health care costs and costs associated with work loss and reduced productivity is considerable [14].

Unfortunately, many patients in developing countries do not receive appropriate medical care, and autoimmune diseases are either unrecognized or inappropriately treated. In most of these countries access to health care services is problematic due to financial constraints, there is a shortage of skilled nurses and physicians, rheumatologists are rare, and immunological diagnostic services non-existent. Even when autoimmune diseases are suspected or diagnosed, the lack of patients' education and the use of traditional medicine delay the initiation of treatment which is often too costly.

Attention has to be raised so that improvement in diagnostic (including pathology) and therapeutic services along with increased awareness and recognition of autoimmune diseases by patients and health care workers can occur. Diagnostic delays indeed have a highly negative impact on the prognosis of the most severe autoimmune diseases. Epidemiologic, demographic and clinical data must be collected in developing countries to enable a better understanding of the peculiarities of the various diseases and of possible variance with developed countries. A huge gap in knowledge exists, as evidenced by a study of the literature on SLE research between 2002 and 2011 which indicated that less than 20% of the publications come from developing countries (12% if China is

excluded) and a search for data in autoimmune geoepidemiology has shown that the vast majority of studies come from Europe and the United States [15].

Issues that need urgent attention are endemic infections such as human immunodeficiency virus (HIV), hepatitis B, human papillomavirus and tuberculosis, as well as the development of cost-effective and affordable strategies for the management of autoimmune diseases. HIV infection can mimic autoimmune diseases (particularly SLE) clinically and can sometimes be difficult to distinguish [9].

Infections are responsible for 58% of SLE deaths in Brazil [16] and up to 80% in Asia [17]. Risk factors for infections in patients with SLE are disease activity, nephritis, low socioeconomic status (all more prevalent in patients from low and middle income countries) and the use of high doses of methylprednisolone or cyclophosphamide – drugs largely employed due to the greater gravity of disease in developing countries and the higher costs of other drugs [18]. Tuberculosis is of particular importance in patients living in these countries, and tuberculosis screening should be systematically performed and isoniazid prophylaxis considered for patients in low and middle income countries.

The risk of high grade cervical squamous intraepithelial lesions is increased in patients with SLE [19], and screening for such lesions should be performed regularly in all patients.

Replacement of corticosteroids whenever possible with hydroxychloroquine, methotrexate, cyclophosphamide, azathioprine and mycophenolate mofetil is an

important strategy in severe autoimmune diseases. Hence, it is vital that fairly cheap generics become available in developing countries to facilitate the use of these drugs [18]. Other drugs, such as rituximab [20], could also be made available for severe conditions through agreements and partnerships with drug companies.

It is time to finally recognize the importance of autoimmune diseases in low and middle income countries and to improve the outlook for affected patients. Both private and government sectors must realize the burden of these diseases, join efforts and address the numerous challenges.

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