LUPUS AROUND THE WORLD

Ricard Cervera, Gerard Espinosa*

Systemic lupus erythematosus (SLE) is the most diverse of the autoimmune diseases because it may affect any organ of the body and display a broad spectrum of clinical and immunological manifestations. Although previously considered a rare disease, it now appears to be relatively common in certain population groups. This is probably due to the development of several immunological tests that have allowed the description of many atypical or benign cases that otherwise might not have been diagnosed. Furthermore, with the introduction since 1982 of a set of more sensitive criteria for SLE classification, more cases can nowadays be detected. Several descriptive epidemiological studies on SLE have been conducted worldwide; however, the most extensive available data comes from the European Union (EU) and the United States of America (USA).

The incidence of SLE in the general population varies according to the characteristics of the population studied, i.e. age, gender, race, ethnic/national origin or period of time studied, but also depending on changes in diagnostic criteria. In the EU, the annual incidence that has been described ranges between 3.3 cases per 100,000 persons per year in Iceland[1] and 4.8 cases per 100,000 persons per year in Sweden.[2] In the USA, the annual incidence of SLE has been estimated in several studies, with incidence rates ranging from 1.8 to 7.6 cases per 100,000 persons per year.[3-7] According to Rochester data, the rates increased by a factor of 2.5 from the years 1950-1954[6] to the years 1975-1979.[7] In Okinawa, Japan, Iseki et al.[8] reported 566 newly diagnosed cases of SLE from 1971 to 1991, corresponding to an average annual incidence rate of 3.0 per 100,000 persons per year. On the Island of Curacao, incidence rate from 1980 to 1989 was 4.6 per 100.000 persons per year.[9]

The different studies on prevalence in general population also show marked differences. In the EU, the study of Hochberg et al.[10] in England and Wales reported in 1982 a prevalence of 12.5 cases per 100,000 women of all ages that increased to 17.7 in women of 15 to 64 years. More recent studies by Hopkinson et al.[11] indicate a prevalence of 25 cases per 100,000 persons in Nottingham and those of Johnson et al.[12] a prevalence of 28 cases per 100,000 persons. The greater prevalence in Europe has been described in Sweden where there were registered 39 cases per 100,000 persons.[2] The overall prevalence in the USA has been reported to range between 14.6 and 50 cases per 100,000 persons (including white and black people).[3-7] In New Zeland, Australia and Japan, the SLE prevalence observed was of 15, 52 and 21 cases per 100,000 persons, respectively.[13-15]

A greater incidence and prevalence of SLE has consistently been found in blacks than in whites.[3] A study in Birmingham, England, found a higher age-adjusted incidence and prevalence in Afro-Caribbeans than in whites.[12] Incidence rates (age--adjusted) were 25.8 and 4.3 per 100,000 persons per year in Afro-Caribbeans and whites, respectively, and prevalence rates were 112 and 21 per 100,000 persons. In this study, the age distribution of incident cases differed significantly, with a younger median age in Afro-Caribbean females of 34.5 years, compared with 41 years in white females. Some data exist also regarding excess prevalence of SLE among Asians compared with whites. In Birmingham,[12] the age-adjusted incidence and prevalence rates of SLE in Asians were 20.7 and 46.7 per 100,000 persons compared with 4.3 and 20.7 per 100,000 persons in whites, respectively.

However, the cases described in Africa until the last decade were very scarce. Although there are no good epidemiological studies, currently it is considered that these differences could be attributed to the associated socio-economic conditions that favor or hinder the diagnosis and correct treatment. For example, since this disease affects fundamentally young women with an age at onset between 15 and 40 years, it is possible that the incidence will be greater in countries with a rapid growth of their population. Also, in the countries and social groups with worse socio-economic conditions, a more severe clinical presentation could be more frequent.[16]

An important question that has been raised by

*Department of Autoimmune Diseases, Hospital Clínic, Barcelona, Catalonia Spain.

several authors is whether the age at onset of the disease or the gender can modify the disease expression and define some specific SLE subsets. An important amount of information of this topic comes from the studies performed with the «Euro--Lupus» cohort. This cohort is composed by 1,000 patients with SLE from seven European countries that have been followed prospectively since 1991.[17]

SLE can appear in all ages. However, in most of the patients, the SLE symptoms appear between 15-40 years, with an average between 29-32 years.[17] In some studies carried out recently,[1,5,18] the mean age of appearance of symptoms has increased up to 41 to 47 years. Nevertheless, SLE can appear before 15 years of age in 8-15% of the patients and in a similar percentage in elderly ages (above 55 years-old). In the «Euro-Lupus» cohort,[17] 76 out of the 1,000 patients with SLE (8%) developed the disease before the age of 14. Female/male ratio (7/1) was not as pronounced as in the general SLE population (10/1). In addition, childhood onset patients more often showed severe organ involvement as a presenting manifestation, nephropathy being a prominent feature. On the other hand, it was found in the «Euro-Lupus» cohort that 90 patients (9%) developed the disease after the age of 50 and typical SLE manifestations, such as malar rash, photosensitivity, arthritis or nephropathy, were less common than in the younger patients. In contrast, sicca syndrome was very frequently found.[17] Although the explanation for this apparent age-related variability in the expression of the disease is still unclear, it has been speculated that older and younger patients may have different genetic determinants of disease and respond to different triggering mechanisms. Alternatively, the less exuberant expression of SLE both clinically and immunologically in older patients may reflect senescence of the immune system.

Clinical studies have consistently demonstrated a female predominance. Thus, in the greater American series, which included 1,103 patients,[19] 88% were females and in the greater European series,[16] with 1,000 patients, 91% were females. This excess of females is especially noteworthy in the 15 to 64 year age group, where ratios of age and sex specific incidence rates show a six to tenfold female excess. No such excess was noted in the 14 and younger and in the 65 and older age groups. These age-related differences in the female/male ratios have been considered to be related to hormonal changes. In the «Euro-Lupus Cohort»,[17] 92 out of the 1,000 (9%) patients with SLE were men and a higher prevalence of serositis was found in these patients as a presenting manifestation. This atypical presentation is of paramount importance because it can lead to a delay in establishing the correct diagnosis.

In summary, epidemiologic studies on SLE have been performed in many parts of the world and the excellent original article in this issue of *Acta Reumatológica Portuguesa* by Santos et al.[20] describing a Portuguese SLE cohort is an additional example. This has enabled to know the approximate incidence and prevalence of this disease in the general population and the differences on the patterns of disease expression in specific SLE subsets. Furthermore, this can have a better impact on overall health status of SLE patients.

Correspondence to:
Ricard Cervera
Servei de Malalties Autoimmunes
Hospital Clínic
C/Villarroel 170
08036-Barcelona, Catalonia, Spain
e-mail: rcervera@clinic.ub.es

References

1. Gudmundsson S, Steisson K. Systemic lupus erythematosus in Iceland 1975 through 1984. A nationwide epidemiological study in an unselected population. J Rheumatol 1990; 17: 1162-1167.
2. Nived O, Sturfelt G, Wolheim F. Systemic lupus erythematosus in an adult population in southern Sweden: incidence/prevalence and validity of ARA revised criteria. Br J Rheumatol 1985; 24: 147-154.
3. Siegel M, Lee SL. The epidemiology of systemic lupus erythematosus. Semin Arthritis Rheum 1973; 3: 1-54.
4. Fessel WJ. Systemic lupus erythematosus in the community: incidence, prevalence, outcome and first symptoms; the high prevalence in black women. Arch Intern Med 1974; 134: 1027-1035.
5. Hochberg MC, Perlmutter SL, Medsger TA et al. Prevalence of self-reported physician-diagnosed systemic lupus erythematosus in the USA. Lupus 1995; 4: 454-456.
6. Michet CJ, McKenna CH, Elveback LR, Kaslow RA, Kurland LT. Epidemiology of systemic lupus erythematosus and other connective tissues disease in Rochester, Minnesota, 1950 through 1979. Mayo Clin Proc 1985; 60: 105-113.
7. Uramoto KM, Michet CJ, Thumboo J, et al. Trends in the incidence and mortality of systemic lupus erythematosus (SLE) 1950-1992. Arthritis Rheum 1997; 40 (suppl 9): S161.
8. Iseki K, Miyasato F, Oura T, Uehara H, Nishime K, Fukiyama K. An epidemiologic analysis of end-stage lupus nephritis. Am J Kidney Dis 1994; 23: 547-554.

9. Nossent JC. Systemic lupus erythematosus on the Caribbean island of Curacao: an epidemiological investigation. Ann Rheum Dis 1992; 51: 1197-1201.
10. Hochberg M. Prevalence of systemic lupus erythematosus in England and Wales, 1981-2. Ann Rheum Dis 1987; 46: 664-666.
11. Hopkinson ND, Doherty M, Powell RJ. Clinical features and race-specific incidence/prevalence rates of systemic lupus erythematosus in geographically complete cohort of patients. Ann Rheum Dis 1994; 53: 675-680.
12. Johnson AE, Gordon C, Palmer RG, Bacon PA. The prevalence and incidence of systemic lupus erythematosus in Birmingham, England. Arthritis Rheum 1995; 38: 551-558.
13. Meddings J, Grennan MD. The prevalence of systemic lupus erythematosus (SLE) in Dunedin. N Z Med J. 1980; 91: 205-206.
14. Anstey A, Bastian I, Dunckley H, Currie BJ. Systemic lupus erythematosus in Australian aborigines: high prevalence, morbidity and mortality. Aust N Z J Med 1993; 23: 646-651.
15. Fukase M. The epidemiology of systemic lupus erythematosus in Japan. In: Fukase M (Ed). Systemic lupus erythematosus. University Park Press, Baltimore 1980; pg. 3-10.
16. Symmonds DPM. Frequency of lupus in people of African origin. Lupus 1995; 4: 176-178.
17. Cervera R, Khamashta MA, Font J, et al. Systemic lupus erythematosus: Clinical and imunological patterns of disease in a cohort of 1000 patients. Medicine (Baltimore) 1993; 72: 113-124.
18. Johnson H, Nived O. Estimating the incidence of systemic lupus erythematosus in a defined population using multiple sources of retrieval. Br J Rheumatol 1990; 29: 185-188.
19. Ginzler EM, Diamond HS, Weiner M, et al. A multicenter study of outcome in systemic lupus erythematosus. Arthritis Rheum 1982; 25: 601-617.
20. Santos MJ, Capela S, Figueira R et al. Caracterização de uma população portuguesa de doentes com lúpus eritematoso sistémico. Acta Reum Port 2007;32:153--161.