What impact do race and ethnicity have on lupus mortality?

“Behavioral, psychosocial factors and co-morbidities (for instance, obesity) are highly correlated and participate as mediators of health outcomes as well as confounders.”

Keywords: disparities • ethnicity • mortality • outcome • race • systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is a complex autoimmune disease that affects predominantly women of childbearing age, with protean clinical manifestations involving virtually any organ including vital organs such as the heart, kidneys and CNS [1].

It is well recognized that some US minorities such as African–Americans, Hispanics and Asians have a worse disease course (e.g., a higher incidence of renal disease) [2]. These minorities have also been found to have a greater likelihood of progression to end stage renal disease (ESRD), and ultimately a higher damage accrual [3].

Several studies have also reported higher mortality rates (MRs) among non-Caucasian patients, with mortality rates two- to threefold higher among African–Americans [4–8]. The US Centers for Disease Control reported significant differences by age and race in MRs among SLE patients ≥15 years old, between 1979 and 1998. MRs were highest among African–Americans and patients >45 years old [9].

In a study conducted in South Carolina that included 6521 admitted SLE patients, Anderson and colleagues [7] reported that African–American patients had a 15% higher risk of mortality than white patients, after adjusting for health insurance, socioeconomic status, length of stay and co-morbidity index. The leading cause of death in African–American patients was SLE (20%). In a subgroup analysis, African–American patients younger than 50 years of age were less likely to die of malignancy than white patients, and more likely to die of infections.

Some, but not all studies, have reported higher MRs among residents in the USA of Asian descent [4]. Other studies conducted in Asian countries reported specific differences among Asian SLE patients based on their origin. For example, Wang demonstrated a reduced survival among Asian Indian patients compared with Chinese and Malay patients in Malaysia [10]. It is important to bear in mind that mortality studies in SLE are often difficult to compare since they are composed of different ethnic populations at various stages of disease.

Most of the studies conducted in US minorities share some limitations regarding the misclassification of Hispanic patients as a unique group, regardless of their origin. Asians patients are often misclassified as well, without distinguishing patients from the Middle East, Southeast or Pacific Islands.

Ethnicity is a complex sociological term that involves several factors including ancestral genes, regions of residence, socioeconomic and cultural factors. Thus, it is not a simple task to label a heterogeneous group such as Hispanics as a unique group that shares Spanish as their primary language as its main characteristic given the wide range of genetic, socioeconomic and biological differences [11].

For these reasons, a subgroup analysis is recommended in studies analyzing Hispanic populations. For example, the LUMINA study reported higher MRs among Texan Hispanics than in Puerto Rican Hispanics, but those differences disappear after adjusting socioeconomic status [12].
The GLADEL (Grupo LatinoAmericano De Estudio de Lupus, Latin American Group for the Study of Lupus) cohort is a well-defined group of more than 1200 Latin American patients with SLE from nine countries with a disease diagnosis of at least 2 years at entry [13]. When authors analyzed mortality among groups, there were no significant differences in survival rates between whites and non-whites (Mestizos and African–Latin Americans).

There is enough evidence that African–Americans have the worst prognosis among SLE patients, including more organ damage and higher mortality. However, data from Hispanic and Asian populations with SLE living in the USA are inconclusive. We recently reported two studies in patients with ESRD due to lupus nephritis (LN) [14] and in Medicaid population with SLE [15] and with some unexpected results. Hispanic and Asian patients had a better survival rate than their counterparts, despite a higher burden of cardiovascular risk factors. These unexpected results are discussed briefly in the current editorial.

Mortality in patients with ESRD due to lupus nephritis

It is well known that SLE patients who reach ESRD have a higher mortality risk. In addition, some differences between races and ethnicities have been described in patients with ESRD. Those differences can be explained in part by disparities in accessing healthcare among races/ethnicities. African–American patients are less likely to use peritoneal dialysis or preemptive transplant as initial renal replacement therapies [16], and have an increased risk of graft loss [17].

Recently, we reported a more favorable outcome in Hispanic and Asian patients in terms of cardiovascular events, and mortality in patients with ESRD due to LN [14]. We conducted a retrospective study using data from the US Renal Data System, the national registry of patients with ESRD. We were able to identify over 12,000 patients with ESRD with diagnosis of SLE as the main cause of ESRD from 1995 to 2008.

In crude analysis (unadjusted) and taking competing risks (kidney transplantation and loss to follow-up), Asians (vs whites) and Hispanics (vs non-Hispanics) with LN-associated ESRD patients had a 30 and 21% lower risk of mortality, respectively. Conversely, African–American patients experienced higher mortality with a 27% higher risk of death than white patients (95% CI: 1.18–1.36).

We also performed an age-stratified analysis, and differences according to race/ethnicity persisted. African–American LN-associated ESRD patients <40 years had an almost 70% higher risk of death than white patients. In the group between 40 and 59 years, African–American patients had a 26% higher risk than their white counterparts. Hispanic patients between 40 and 59 years and ≥60 years, had 22 and 24% respectively, lower adjusted mortality than non-Hispanics.

Other groups, reported recent similar results in patients with all-cause ESRD [18] and in patients with LN-associated ESRD [19]. Sexton and colleagues [19] reported that African–American and non-Hispanic patients had a higher mortality risk. Additionally, other factors related with worse prognosis were older age, smoking, diabetes and peripheral vascular disease. At the same time, differences in MRs by age were also recently reported in a large observational study that included patients with all-cause ESRD in the USA [20]. African–American patients ≤50 years had increased MRs compared with white patients.

Mortality in Medicaid recipients with SLE

Medicaid has become the main public health insurance program in the USA for the low-income population, covering over 62 million Americans. It is also the predominant source of coverage and financing of long-term care services for the elderly and individuals with disabilities. Medicaid covers one in five Americans and covers more than one in three children [21].

We analyzed data between the years 2000 and 2006 from the administrative Medicaid database, identifying 42,221 prevalent cases of SLE. Among the cases, 8191 had LN [15].

Co-morbidities included hypertension in 31%, diabetes in 24%, atherosclerosis in 16% and angina in 12%. The analysis adjusted for SLE-specific co-morbidities including pericarditis, thrombocytopenia, seizures and hemolytic anemia, using a risk adjustment index described by Ward [22].

During a mean follow-up of 2.6 years, there were 2058 deaths in the overall cohort, for an unadjusted mortality rate of 19.07 (95% CI: 18.36–19.91) per 1000 person-years. Among the subgroup with LN, there were 774 deaths, for a mortality rate of 44.64 (95% CI: 41.60–47.90) per 1000.
In a model that adjusted only for age and sex, Hispanic and Asian patients had MRs less than half than those of whites (hazard ratios: 0.41, 95% CI: 0.34–0.50 and 0.30, 95% CI: 0.21–0.43), while African–Americans and native Americans had higher rates (hazard ratios: 1.36, 95% CI: 1.24–1.49 and 1.43, 95% CI: 1.06–1.92).

The final model also adjusted for cardiovascular and lupus-related co-morbidities, and resulted in somewhat attenuated, though still significant, between-group differences. For instance, the 36% higher mortality risk among African–Americans decreased to 21% in the fully adjusted model.

Despite the fact that we had a relatively short follow-up (<3 years of average), we found a great disparity in MRs and adjusted hazard ratios among Medicaid recipients with SLE according to patients’ race/ethnicity.

**Conclusion & future perspective**

The relationships of race/ethnicity to socioeconomic status, lifestyle factors and co-morbidities, all of which are related to SLE outcomes as well, are extremely complex. Behavioral, psychosocial factors and co-morbidities (for instance, obesity) are highly correlated and participate as mediators of health outcomes as well as confounders. It is difficult to draw definitive conclusions owing to difficulties in investigating mediation, the presence of unmeasured confounders and the likely bidirectional relationships between psychosocial, behavioral factors and co-morbidities over time.

Despite this complexity and interrelation, we described higher MRs among African–Americans, and lower MRs among Hispanics and Asians living in the USA in two different SLE populations (patients from Medicaid and patients with LN-related ESRD), reflecting the importance of race and ethnicity as critical independent factors for mortality in patients with SLE.

Further studies are needed in different populations in order to elucidate the specific weight of race/ethnicity over MRs. In addition, new studies evaluating ethnic subgroups are necessary with some other relevant clinical parameters such as disease activity and treatment.

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Commentary

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