

Does Medical Insurance Matter in the Progression to Endstage Renal Disease Among Patients with Lupus Nephritis?



Lupus nephritis may affect up to 60% of patients with systemic lupus erythematosus (SLE) over time¹ and may lead to the development of endstage renal disease (ESRD) in 20% to 25% of those with lupus nephritis, even if properly treated²⁻⁴. Indeed, the incidence of ESRD due to lupus nephritis, like that due to all other causes, has increased over the last few decades⁵, which may reflect the dissociation between clinical trial data and clinical practice data, the fact that even properly treated patients go on to develop ESRD^{2,4,6}, and/or the fact that these data cannot possibly reflect the therapeutic advances made over the last 10–15 years. Several demographic, clinical, and histopathological features have been associated with an increased risk of ESRD among these patients; they include male gender, Hispanic and African American ethnicity, hypertension, anemia, nephrotic syndrome, persistently elevated serum creatinine levels, diffuse proliferative histopathological forms, high chronicity index, treatment noncompliance, and diagnostic and therapeutic delays^{2,6-12}. Even a delay between the onset of renal abnormalities and securing a renal biopsy has been shown to be a powerful predictor of ESRD in these patients¹⁰. These data taken together suggest that access to care may play a crucial role in the outcome of renal disease in patients with SLE.

In this issue of *The Journal*, Ward¹³ examines the association between insurance status and age of onset of ESRD. This cross-sectional study of the 1996-2004 national population-based registry [the United States Renal Data System (USRDS)] of all incident cases of ESRD¹⁴ due to lupus nephritis ($n = 7971$), shows that the uninsured (or those with limited insurance) evolve to ESRD faster, that is, they develop it at a younger age, than those with private insurance. Of importance, it was the medical insurance rather than the socioeconomic status (SES) that accounted for these findings, except for non-Hispanic White patients ($n = 2590$), in whom SES was also significant, albeit less importantly. Of course the assumption here is that the onset of lupus nephritis is unrelated to medical insurance status.

The data presented by Ward¹³ corroborate the importance of insurance status in influencing the course and outcome of SLE, as has been shown by Karlson, *et al*¹⁵ and others^{11,16} over the years. Perhaps the finding most deserving of special comment relates to the fact that the uninsured and those with Medicaid performed similarly in these analyses. We know, however, that medical insurance status is not stable¹⁵. Thus, it is entirely possible that patients on Medicaid at the time they entered the registry were uninsured when lupus or renal involvement first ensued; like the uninsured patients, they may have had limited access to proper care and adequate treatment prior to the onset of ESRD. Indeed, in a relatively small study conducted by Barr, *et al* among African American, Hispanic, and White patients with focal and diffuse proliferative lupus nephritis, Medicare (but not Medicaid) was found to be an independent predictor of doubling of serum creatinine¹⁶.

Of course, it is possible that factors otherwise not explored by Ward could have accounted for the differences observed in the occurrence of ESRD at a younger age among the uninsured. Although comorbid conditions (and SES) were adjusted for in the analyses, we know that genetic factors [HLA-DRB1*1503 and polymorphisms of FCGR3A (FCGR3A*GG)] may predispose patients with lupus nephritis to worsening proteinuria that often precedes the onset of ESRD^{12,17,18}, yet such data were not available in the registry. There is no reason to believe, however, that the distribution of these alleles would have been different among patients with and those without medical insurance.

This study has several strengths. The most important is the source of information, the USRDS, which includes all US patients with ESRD; thus, the data are representative of the entire nation; second, although an individual measure of SES was not available in the registry, the author used an area-based measure of SES, which has been found to be moderately to highly correlated with individual SES¹⁹. Third, the consistency of the results across all ethnic groups studied reinforces the validity of the findings.

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A few limitations are worth pointing out, however. First, details about the patients' diagnosis and course prior to the occurrence of ESRD are unavailable, including the actual diagnosis of lupus nephritis; nevertheless, it has been shown that the vast majority of patients with lupus in whom a renal biopsy is performed have lupus nephritis in contrast to other pathology to explain their renal abnormalities²⁰. In this context, the assumption that ESRD, as per the registry, was indeed the result of lupus nephritis seems entirely appropriate. Second, knowing that medical insurance status is unstable, it would have been better to have this information at onset of disease or renal involvement rather than at the time ESRD ensued and patients entered the registry; however, patients are more likely to lose their private insurance as a function of changes in their work status, rather than to acquire it as they become ill²¹. This "misclassification" may have attenuated the differences found, but it does not abrogate them.

Despite these drawbacks, we think the study by Ward¹³ conveys a very powerful message. Medical insurance status emerges as a risk factor associated with the occurrence of ESRD at a younger age. Limited or no medical insurance is strongly associated with inadequate medical care, resulting in diagnostic and treatment delays that in turn are strong predictors of the occurrence of ESRD. As Ward points out, the cost of insurance, and therefore of timely and adequate diagnosis and treatment, is far less than the high cost of renal replacement therapy (dialysis and transplantation). This is but one more reason to advocate for a much wider (universal) insurance coverage in the US than the one currently available²²; less wealthy countries enjoy such a privilege. It is about time we do too, if the ravages of diseases such as lupus and other chronic diseases are to be significantly curtailed.

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REFERENCES

1. Cameron JS. Lupus nephritis. *J Am Soc Nephrol* 1999;10:413-24.
2. Neumann K, Wallace DJ, Azen C, et al. Lupus in the 1980s: III. Influence of clinical variables, biopsy, and treatment on the outcome in 150 patients with lupus nephritis seen at a single center. *Semin Arthritis Rheum* 1995;25:47-55.
3. Ward MM, Studenski S. Clinical prognostic factors in lupus nephritis. The importance of hypertension and smoking. *Arch Intern Med* 1992;152:2082-8.
4. Austin HA3, Klippel JH, Balow JE, et al. Therapy of lupus nephritis. Controlled trial of prednisone and cytotoxic drugs. *N Engl J Med* 1986;314:614-9.
5. Ward MM. Changes in the incidence of end-stage renal disease due to lupus nephritis, 1982-1995. *Arch Intern Med* 2000;160:3136-40.
6. Dooley MA, Hogan S, Jennette C, Falk R. Cyclophosphamide therapy for lupus nephritis: poor renal survival in black Americans. Glomerular Disease Collaborative Network. *Kidney Int* 1997;51:1188-95.
7. 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;23:547-54.
8. Lupus nephritis: prognostic factors and probability of maintaining life-supporting renal function 10 years after the diagnosis. Gruppo Italiano per lo Studio della Nefrite Lupica (GISNEL). *Am J Kidney Dis* 1992;19:473-9.
9. Contreras G, Pardo V, Cely C, et al. Factors associated with poor outcomes in patients with lupus nephritis. *Lupus* 2005;14:890-5.
10. Fauschou M, Starklint H, Halberg P, Jacobsen S. Prognostic factors in lupus nephritis: diagnostic and therapeutic delay increases the risk of terminal renal failure. *J Rheumatol* 2006;33:1563-9.
11. Petri M, Perez-Gutthann S, Longenecker JC, Hochberg M. Morbidity of systemic lupus erythematosus: Role of race and socioeconomic status. *Am J Med* 1991;91:345-53.
12. Alarcon GS, McGwin G Jr, Petri M, et al. Time to renal disease and end-stage renal disease in PROFILE: a multiethnic lupus cohort. *PLoS Med* 2006;3:e396.
13. Ward MM. Medical insurance, socioeconomic status and age of onset of end-stage renal disease in patients with lupus nephritis. *J Rheumatol* 2007;34:2024-7.
14. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. USRD 2005 annual data report: Atlas of end-stage renal disease in the United States. Minneapolis, MN: United States Renal Data System; 2005.
15. Karlson EW, Daltroy LH, Lew RA, et al. The independence and stability of socioeconomic predictors of morbidity in systemic lupus erythematosus. *Arthritis Rheum* 1995;38:267-73.
16. Barr RG, Seliger S, Appel GB, et al. Prognosis in proliferative lupus nephritis: the role of socio-economic status and race/ethnicity. *Nephrol Dial Transplant* 2003;18:2039-46.
17. Bastian HM, Alarcon GS, Roseman JM, et al, LUMINA Study Group. Systemic lupus erythematosus in a multiethnic US cohort (LUMINA) XLII: Factors predictive of new or worsening proteinuria. *Rheumatology Oxford* 2007;46:683-9.
18. Bastian HM, Alarcon GS, McGwin G Jr, et al. FCGR3A*GG alleles are associated with the development of end stage renal disease (ESRD) in systemic lupus erythematosus (SLE) patients with biopsy-proven lupus nephritis (LN) [abstract]. *Arthritis Rheum* 2006;54 Suppl:S824.
19. Diez-Roux AV, Kiefe CI, Jacobs DR Jr, et al. Area characteristics and individual-level socioeconomic position indicators in three population-based epidemiologic studies. *Ann Epidemiol* 2001;11:395-405.
20. Baranowska-Daca E, Choi YJ, Barrios R, Nassar G, Suki WN, Truong LD. Nonlupus nephritides in patients with systemic lupus erythematosus: a comprehensive clinicopathologic study and review of the literature. *Hum Pathol* 2001;32:1125-35.
21. Holahan J, Cook A. Changes in economic conditions and health insurance coverage, 2000-2004. *Health Aff (Millwood)* 2005;Suppl Web Exclusives:W5-498-508.
22. US Census Bureau. Income, poverty, and health insurance coverage in the United States: 2005. Internet. Available at: http://www.tribal-institute.org/download/2000_income.pdf. Accessed July 30, 2007.