An assessment of renal failure in an SLE cohort with special reference to ethnicity, over a 25-year period

M. Adler, S. Chambers, C. Edwards, G. Neild and D. Isenberg

**Objectives.** Although the prognosis for patients with renal lupus has improved, a small number still progress to renal failure. Studies from the USA have found it difficult to distinguish whether the higher rate of renal failure in African-Americans is due to genetic or socio-economic factors. Our aim was to identify ethnic and other factors in a UK lupus cohort that contribute to renal failure.

**Methods.** The University College London (UCL) Hospitals lupus cohort of 401 patients (Whites 64%, Blacks 19%), followed since 1978, has 127 patients with renal disease, of whom 21 have gone into renal failure. We determined the characteristics and possible causes of renal failure in this group. Black patients were disproportionately represented in the renal failure group (62% vs 19% for Whites).

**Results.** Those in the renal failure group had persistently low C3 compared with the renal disease cohort. A high proportion of patients in the renal failure group were felt to be non-adherent to treatment.

**Conclusions.** Given that health-care for patients in the UK is free at the point of delivery, we postulate that in our cohort genetic factors rather than socio-economic status are likely to be more significant in causing renal failure. However, there may be cultural and other reasons for this, which requires further study.

**Key words:** Systemic lupus erythematosus, End-stage renal failure, Ethnicity.
### Results

Of the 401 patients in this cohort, 127 had lupus nephritis and 21 of these developed ESRF. Baseline creatinine in all patients who went on to develop lupus nephritis was normal except in two patients who actually presented in acute renal failure. The mean age of ESRF was 33.4 yr (range 17–58) and eight of the 21 patients received a kidney transplant, three of which failed. Table 1 shows the WHO class of nephritis in the renal group as a whole and in those in ESRF. Table 2 illustrates, in more detail, various socio-economic, follow-up and mortality data of Black, White and Asian patients with WHO class III, IV and V renal disease. We have not included patients of Chinese origin or mixed race in the analysis as the numbers are very small. The mean duration of follow-up since diagnosis of SLE was 8.9 yr for Blacks, 15.1 yr for Whites and 14.2 yr for Asians ($P < 0.001$, Blacks compared with the other two groups). There was no statistically significant difference in time from diagnosis of SLE to development of renal involvement in the three groups. There were 19 deaths in the renal lupus cohort as a whole and 12 of the patients in ESRF died, although not all deaths were attributed to SLE alone.

The treatment protocols used in the patients with lupus nephritis were standardized as previously published and are not further described here in detail [7], with the exception that in the past 2 yr we have increasingly prescribed mycophenolate mofetil in preference to cyclophosphamide. Nineteen patients who developed ESRF received at least 6 months of azathioprine at an average dose of 2 mg/kg and five had received mycophenolate mofetil up to the maximum tolerated dose, ranging from 2 to 3 g per day. Seventeen of the 21 ESRF patients were treated with at least three infusions of cyclophosphamide, generally 750 mg per infusion.

Only six patients with ESRF had immunoglobulin G (IgG) anticardiolipin antibodies and only one had a positive lupus anticoagulant (data not shown). Table 3 illustrates the differences in ethnicity between the renal and non-renal groups as well as those in ESRF. In the cohort, 44% (33/74) of Blacks developed lupus nephritis whereas only 22% (58/258) of Whites and 47% (18/38) of Asians did. This difference between Blacks and Whites was statistically significant ($P = 0.003$) but there was no significant difference between Asians and Whites ($P = 0.63$). Table 4 shows that our Black patients were particularly likely to have lupus nephritis associated with persistently high levels of dsDNA antibody (defined as twice the upper limit of normal on three occasions) and low C3 levels (defined as being below normal on three occasions) and this was statistically significant. Our data also shows that Blacks were also more likely to progress to ESRF ($P < 0.001$) and that, irrespective of ethnicity, once lupus nephritis occurred, low C3 levels were associated with progression to ESRF ($P = 0.018$). In the lupus nephritis cohort, age at diagnosis of nephritis was not associated with ESRF ($P = 0.932$) or with persistently raised levels of dsDNA ($P = 0.914$). The mean time from SLE diagnosis to development of lupus nephritis was 34 months (s.d. 59), whereas for those who progressed to ESRF the mean time from SLE diagnosis to onset of renal involvement...
Discussion

To the best of our knowledge this is the first long-term follow-up study of patients with lupus nephritis who have gone into renal failure outside of North America. African-American patients are known to have more aggressive lupus and renal disease despite treatment with cyclophosphamide [1]. Our data concur with the American findings—the patients progressing to end-stage renal disease were much more likely to be Black than White or Asian. No differences in follow-up of patients from the various ethnic groups were observed in our study.

<table>
<thead>
<tr>
<th>Ethnic group</th>
<th>Total number</th>
<th>Lupus nephritis (%)</th>
<th>ESRF (%)</th>
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<tbody>
<tr>
<td>Caucasian (White)</td>
<td>258 (64%)</td>
<td>58 (46%)</td>
<td>4 (19%)</td>
</tr>
<tr>
<td>Black</td>
<td>75 (19%)</td>
<td>33 (26%)</td>
<td>13 (62%)a</td>
</tr>
<tr>
<td>Asian (Indian subcontinent)</td>
<td>38 (9%)</td>
<td>18 (14%)</td>
<td>2 (9%)</td>
</tr>
<tr>
<td>Other</td>
<td>30</td>
<td>18</td>
<td>2</td>
</tr>
</tbody>
</table>

*P ≤ 0.001 (χ² test).

Table 4. Comparison of serological features in the Black SLE patients compared with the total cohort, with and without renal disease

<table>
<thead>
<tr>
<th>Total cohort (n = 401)</th>
<th>Non-renal (n = 274)</th>
<th>Lupus nephritis (total) (n = 127)</th>
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</thead>
<tbody>
<tr>
<td>Black (n = 75)</td>
<td>42 (15)</td>
<td>33 (26)</td>
</tr>
<tr>
<td>High dsDNA (n = 244)</td>
<td>139 (51)</td>
<td>105 (83)</td>
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<tr>
<td>Low C3 (n = 160)</td>
<td>69 (25)</td>
<td>91 (72)</td>
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<tr>
<th></th>
<th>n (%)</th>
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<tr>
<td>Black</td>
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<td>Low C3</td>
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mofetil was more effective than intravenous cyclophosphamide in inducing remission of lupus nephritis, and was associated with less toxicity [19]. Studies are currently in progress to determine the most effective strategy for maintaining disease remission. Relatively few of our patients were re-biopsied (n = 11), though in the main azathioprine was only stopped if it was obvious that it was no longer effective or causing side-effects.

A very recent North American study with a large number of Hispanics and African-Americans has shown that these two ethnic groups, as well as other factors (baseline hypertension, raised serum creatinine and high chronicity index on biopsy), are associated with poor outcome in lupus nephritis [20]. However, they did not try to assess the affect of patient compliance on outcome. We conclude that Blacks with SLE have a significantly poorer outcome with respect to renal involvement than the white population in the UK. Given the diverse socio-economic and cultural background of our black lupus patients (some born in Africa, some in the West Indies, others in the UK), the similar proportions of each group in the cohort as a whole and amongst those in renal failure is notable (Table 5). It seems to us that this observation supports the idea of a significant contribution of genetics to prognosis in renal lupus. Further studies are needed to determine whether race is a truly independent risk factor for poor outcome, or whether social factors remain more important.

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References