Low Socioeconomic Status Is Associated with Cardiovascular Risk Factors and Outcomes in Systemic Lupus Erythematosus

JANET W. MAYNARD, HONG FANG, and MICHELLE PETRI

ABSTRACT. Objective. Accelerated atherosclerosis is a major cause of death in systemic lupus erythematosus (SLE), yet little is known about the effect of socioeconomic status. We investigated whether education or income levels are associated with cardiovascular risk factors and outcomes in SLE.

Methods. Our study involved a longitudinal cohort of all patients with SLE enrolled in the Hopkins Lupus Cohort from 1987 through September 2011. Socioeconomic status was measured by education level (≥ 12 years or < 12) and income tertiles (> $60,000, $25,000–$60,000, or < $25,000).

Results. A total of 1752 patients with SLE were followed prospectively every 3 months. There were 1052 whites and 700 African Americans. Current smoking, obesity, hypertension, and diabetes mellitus were more common in African Americans (p < 0.01 for all), but there was no statistical difference in the frequency of myocardial infarction or stroke. In multivariate analyses stratified by ethnicity, low income was strongly associated with most traditional cardiovascular risk factors in whites, but only with smoking and diabetes in African Americans. In whites, low income increased the risk of both myocardial infarction (OR 3.24, 95% CI 1.41–7.45, p = 0.006) and stroke (OR 2.85, 95% CI 1.56–5.21, p = 0.001); in African Americans, these relationships were not seen. Low education, in contrast, was associated with smoking in both ethnic groups.

Conclusion. Low income, not low education, is the socioeconomic status variable associated with cardiovascular risk factors and events. This association is most clearly demonstrable in whites.

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Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS SOCIOECONOMIC STATUS EDUCATION INCOME CARDIOVASCULAR DISEASE MYOCARDIAL INFARCTION

Cardiovascular disease is a leading cause of death among patients with systemic lupus erythematosus (SLE). Previous research has demonstrated a 9-fold increase in the myocardial infarction rate in Swedish patients with SLE and a > 50-fold increase in risk in women between 35 and 44 years of age in Pittsburgh, PA, USA. Cerebrovascular events account for 20% to 30% of deaths in patients with SLE.

Numerous studies have shown that socioeconomic status is inversely associated with the prevalence of cardiovascular risk factors and poor cardiovascular outcomes in the general population. However, this relationship is complicated by biological and ethnic factors, because even after controlling for socioeconomic status, hypertension and other cardiovascular risk factors and outcomes are more common in African Americans.

SLE occurs with a greater incidence and prevalence in African Americans. Worse outcomes are found in minorities, both African Americans and Hispanic Americans. Socioeconomic factors are possible confounders of these ethnic differences.

Although there is an increased risk for atherosclerotic cardiovascular diseases in patients with SLE, it is not clear whether socioeconomic status affects cardiovascular risk factors or cardiovascular outcomes and whether this relationship is confounded by ethnicity. In our study, we used the Hopkins Lupus Cohort, the largest longitudinal cohort of patients with SLE, followed by 1 provider since 1987. We examined the hypothesis that socioeconomic status, as measured by income and education level, is inversely associated with cardiovascular risk factors, myocardial infarction, and cerebrovascular accident in SLE. The large cohort size allowed for ethnicity stratification and assessment for effect modification. Thus, we evaluated whether the effect of socioeconomic status on cardiovascular risk factors and outcomes differs in whites and African Americans. In addi-
tion, we evaluated whether ethnicity itself is a risk factor for cardiovascular risk factors and outcomes.

MATERIALS AND METHODS

Patient selection. The longitudinal cohort included all patients with SLE who enrolled in the Hopkins Lupus Cohort from 1987 through September 2011, as described. Inclusion in the cohort was based on the clinical diagnosis of SLE by the principal investigator (MP). Our study was approved by the Johns Hopkins University School of Medicine Institutional Review Board. All patients gave informed consent.

Database. Since initiation of the cohort study in 1987, clinical and laboratory data have been prospectively collected at each clinic visit in a systematic fashion, according to the Hopkins Lupus Cohort protocol. At cohort entry, basic demographic characteristics (date of birth, age at SLE onset, ethnicity, sex, years of education, combined annual household income) and presenting clinical manifestations were recorded. Clinical manifestations within the first year after diagnosis of SLE were assessed directly for those who entered the cohort within a year of diagnosis and by chart review for those who entered later. Patients were seen at regular intervals of 3 months, or more frequently if medically indicated. At each patient visit, a complete history, physical examination, and routine laboratory testing were performed. Damage was assessed with the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index.

Measures of cardiovascular disease risk factors and outcomes. Data regarding basic demographic and socioeconomic factors (age, sex, ethnicity, body mass index (BMI), education level, combined annual household income, insurance coverage, marital status, and smoking status) were obtained from the Hopkins Lupus Cohort database. Cardiovascular risk factors that were evaluated in this analysis included tobacco use, obesity, hypertension, hyperlipidemia, and diabetes mellitus. Smoking was categorized as current or past use of tobacco. Obesity was defined as BMI > 27.8 kg/m² for men and > 27.3 kg/m² for women. Hypertension was defined as use of medications to treat hypertension or blood pressure > 140/90 mm Hg. Hyperlipidemia was defined as cholesterol level > 200 mg/dl. Diabetes mellitus was defined according to the American Diabetes Association criteria. The cardiovascular and cerebrovascular outcomes of interest were myocardial infarction and cerebrovascular accident, defined using the SLICC/ACR Damage Index. A subject was considered to have a cardiovascular risk factor if it occurred at any time during followup.

Measures of socioeconomic status. Two variables were used to measure socioeconomic status: combined annual family income and years of education. These variables were recorded at cohort entry. Income was categorized into tertiles: < $25,000 per year, $25,000 to $60,000 per year, or > $60,000 per year. Education was categorized as < 12 years, or ≥ 12 years.

Statistical analysis. Data were analyzed using Stata 10.0 (Stata Corp., College Station, TX, USA). Baseline sociodemographic and clinical features were compared between whites and African Americans. Patients of other ethnicities were rare and were excluded from the analysis. Characteristics were compared using Pearson’s chi-square for categorical variables and t tests for continuous variables.

Univariate analyses were performed using logistic regression to evaluate the unadjusted relationship between socioeconomic status and cardiovascular risk factors, myocardial infarction, and cerebrovascular accident. Multivariate logistic regression was used to examine the relationship between socioeconomic status and cardiovascular risk factors, myocardial infarction, and cerebrovascular accident adjusting for age at SLE onset, sex, and income or education level. Additional multivariate models controlled for other cardiovascular risk factors, including antiphospholipid antibody status and prednisone use. Models were explored using likelihood ratio testing and forward and backward model selection. The final model selection was based on knowledge of clinically relevant variables. We evaluated for effect modification of ethnicity on the relationship between socioeconomic status and cardiovascular outcomes by stratifying the participants on the basis of ethnicity. Additionally, univariate and multivariate analyses evaluated whether ethnicity itself is associated with cardiovascular risk factors and outcomes. These multivariate models adjusted for age of SLE onset, sex, income, and education. In all models, education level was dichotomized rather than divided into 3 categories due to improved model fit with the variable when it was dichotomized. There was no evidence of interaction between ethnicity and education or income levels.

RESULTS

From 1987 to September 2011, 1909 participants were enrolled in the Hopkins Lupus Cohort. This analysis was restricted to African American and white participants, excluding 157 patients from the study population. Therefore, 1752 patients were included in the current study, with the following characteristics: 92.4% were female and 40.0% African American (Table 1). The mean age at SLE onset was 29.9 years (SD 13.5) for whites and 29.4 years (SD 11.8) for African Americans (p = 0.47).

Significant differences were found in education and income levels of whites and African Americans. The median income level for whites was $50,000 (interquartile range [IQR] $38,000), compared with $23,000 (IQR $38,400) for African Americans. The mean education level was 14.4 years (SD 2.8) for whites, versus 13.3 years (SD 2.8) for African Americans (p < 0.001).

Association of income levels with cardiovascular risk factors, myocardial infarction, and cerebrovascular accident. In both whites and African Americans, individuals in the lowest income category had the highest frequency of current or past smoking and cerebrovascular accident (p < 0.05 for each; Table 2). In whites, but not African Americans, individuals in the lowest income category had a higher frequency of obesity (p < 0.001) and myocardial infarction. In African Americans, but not whites, individuals in the lowest income category had a higher frequency of hyperlipidemia (p = 0.04).

In univariate analyses, whites in the lowest income category (< $25,000) had an increased risk of current or past smoking, obesity, hypertension, diabetes mellitus, myocardial infarction, and cerebrovascular accident compared with individuals in the highest income category (> $60,000; data not shown). This association was also seen for individuals in the second-lowest income category ($25–$60,000) for obesity. There was a significant, graded relationship between income and the odds of each cardiovascular risk factor, myocardial infarction, and cerebrovascular accident (p for trend < 0.001 for current smoking, past smoking, obesity, hypertension, hyperlipidemia, diabetes mellitus, myocardial infarction, and cerebrovascular accident). In contrast, African Americans in the lowest income category (< $25,000) had an increased risk only of current or past smoking and diabetes mellitus. There was a significant graded relationship between income and the odds of these variables, in addition to hyperlipidemia and cerebrovascular accident.
In multivariate analyses in whites, there was minimal attenuation of the relationship between current smoking, obesity, hyperlipidemia, diabetes mellitus, myocardial infarction, and cerebrovascular accident and the lowest income category (Table 3). Similarly, individuals in the second-lowest income category had > 1.5 increased odds of...
obesity compared with individuals in the highest income category (obesity: OR 1.65, 95% CI 1.22, 2.22, p = 0.001), even after control for confounders, including education level. There was a significant, graded relationship between income category and current smoking (p for trend = 0.001), obesity (p for trend < 0.001), hypertension (p for trend = 0.02), hyperlipidemia (p for trend = 0.05), diabetes mellitus (p for trend = 0.02), myocardial infarction (p for trend = 0.006), and cerebrovascular accident (p for trend = 0.001).

In multivariate analyses in African Americans, the association between current smoking and diabetes mellitus and the lowest income category remained significant; however, there was no relationship between obesity, hypertension, hyperlipidemia, myocardial infarction, or cerebrovascular accident and income. Similarly, there was no evidence of a graded relationship between obesity, hypertension, hyperlipidemia, or myocardial infarction and income in African Americans. In addition, African Americans did have an association between the lowest income category and past smoking (OR 2.70, 95% CI 1.59, 4.60) that was not seen in whites.

Association of income levels with cardiovascular risk factors, myocardial infarction, and cerebrovascular accident. After adjustment for additional cardiovascular risk factors, including antiphospholipid antibody status and prednisone use, there was attenuation of the relationship between income and hypertension, hyperlipidemia, and diabetes mellitus in whites. In contrast, in whites, the relationship between obesity, myocardial infarction, and cerebrovascular accident and the lowest income category remained even after adjustment for other cardiovascular risk factors (obesity: OR 1.94, 95% CI 1.32, 2.84; myocardial infarction: OR 2.59, 95% CI 1.10, 6.09; cerebrovascular accident: OR 2.53, 95% CI 1.36, 4.69). In African Americans, the relationship between diabetes mellitus and the lowest income category remained after adjustment for other cardiovascular risk factors (OR 2.72, 95% CI 1.21, 6.09).

Association of ethnicity with cardiovascular risk factors, myocardial infarction, and cerebrovascular accident. After control for comorbidities and socioeconomic status, ethnicity was not significantly associated with current or past smoking, hyperlipidemia, diabetes mellitus, myocardial infarction, or cerebrovascular accident (Table 5). African American ethnicity was associated with obesity (OR 1.39, 95% CI 1.19, 1.60).
DISCUSSION

Our longitudinal study found that education and income level, although both are used as markers of socioeconomic status, acted differently. Both income and education were associated with cardiovascular risk factors and outcomes. However, education and income levels were associated with different cardiovascular risk factors and this relationship was modified by ethnicity. In addition, income levels were associated with poor cardiovascular outcomes, even after adjustment for other comorbidities and education level.

The hazardous effects of lower income levels were different in whites and African Americans. In whites, low income was associated with all the cardiovascular risk factors and outcomes, except past smoking. In contrast, in African Americans, only current or past smoking and diabetes mellitus were associated with low income. Similarly, after adjustment for potential confounders, low education was associated with current or past smoking in both ethnic groups, but was associated only with hypertension in African Americans.

Lower income levels were associated with a greater number of cardiovascular risk factors than lower education levels in whites. The association of income with cardiovas-

Table 4. Ethnicity-stratified univariate and multivariate analyses of the effect of lower education levels on cardiovascular risk factors, myocardial infarction, and cerebrovascular accident in the Hopkins Lupus Cohort. High education: ≥ 12 years (reference); low education: < 12 years. Significant results are shown in bold type.

<table>
<thead>
<tr>
<th>Group</th>
<th>Univariate</th>
<th>Multivariate*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>Whites</td>
<td></td>
<td></td>
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<tr>
<td>Current Smoking</td>
<td>4.49 (1.67, 7.57)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Past smoking</td>
<td>3.11 (1.85, 5.23)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Obesity</td>
<td>1.47 (0.90, 2.42)</td>
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<tr>
<td>Hypertension</td>
<td>1.12 (0.68, 1.84)</td>
<td>0.65</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1.28 (0.77, 2.13)</td>
<td>0.35</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.30 (0.58, 2.95)</td>
<td>0.52</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>3.13 (1.40, 6.70)</td>
<td>0.005</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>1.32 (0.59, 3.00)</td>
<td>0.50</td>
</tr>
<tr>
<td>African Americans</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoking</td>
<td>4.09 (2.63, 6.35)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Past smoking</td>
<td>4.24 (2.72, 6.62)</td>
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<tr>
<td>Obesity</td>
<td>1.10 (0.72, 1.67)</td>
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<tr>
<td>Hypertension</td>
<td>1.99 (1.23, 3.21)</td>
<td>0.005</td>
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<tr>
<td>Hyperlipidemia</td>
<td>1.52 (0.98, 2.35)</td>
<td>0.06</td>
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<tr>
<td>Diabetes mellitus</td>
<td>2.43 (1.47, 4.02)</td>
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<tr>
<td>Myocardial infarction</td>
<td>2.58 (1.26, 5.28)</td>
<td>0.01</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>1.92 (1.08, 3.43)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

* Adjusted for age at SLE onset, sex, and income. SLE: systemic lupus erythematosus.

Table 5. Association of ethnicity with cardiovascular risk factors, myocardial infarction, and cerebrovascular accident in the Hopkins Lupus Cohort. Reference group is white ethnicity. Significant results are shown in bold type.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Multivariate*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>African American</td>
<td>(95% CI)</td>
</tr>
<tr>
<td>Current Smoking</td>
<td>1.34 (1.05, 1.72)</td>
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<tr>
<td>Past smoking</td>
<td>0.99 (0.82, 1.21)</td>
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<td>Obesity</td>
<td>1.79 (1.47, 2.17)</td>
<td>&lt; 0.001</td>
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<tr>
<td>Hypertension</td>
<td>2.27 (1.87, 2.77)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1.08 (0.89, 1.31)</td>
<td>0.43</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.91 (1.40, 2.60)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1.26 (0.82, 1.95)</td>
<td>0.29</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>1.29 (0.94, 1.79)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

* Adjusted for age of SLE onset, sex, income, and education. SLE: systemic lupus erythematosus.

95% CI 1.27, 2.00, p < 0.001) and hypertension (OR 2.13, 95% CI 1.69, 2.68, p < 0.001).

The hazardous effects of lower income levels were different in whites and African Americans. In whites, low income was associated with all the cardiovascular risk factors and outcomes, except past smoking. In contrast, in African Americans, only current or past smoking and diabetes mellitus were associated with low income. Similarly, after adjustment for potential confounders, low education was associated with current or past smoking in both ethnic groups, but was associated only with hypertension in African Americans.

Lower income levels were associated with a greater number of cardiovascular risk factors than lower education levels in whites. The association of income with cardiovas-
cular risk factors and outcomes remained even after adjustment for education levels. In multivariate analysis in whites that controlled for the other measure of socioeconomic status, lower income levels were associated with current smoking, obesity, hypertension, hyperlipidemia, diabetes mellitus, myocardial infarction, and cerebrovascular accident, whereas education levels were associated only with current or past smoking. This suggests that income level is a more important factor than education level in determining cardiovascular risk factors in whites. However, there was attenuation of this relationship after adjustment for additional cardiovascular risk factors, suggesting that this relationship may be confounded by other factors.

The Lupus in Minorities: Nature versus Nurture (LUMINA) study also found no statistically significant difference in the number of vascular events based on education level. There were increased vascular events in lower income participants in univariate analyses in the LUMINA study, and this approached statistical significance (p = 0.052). However, further multivariate analyses were not performed. In addition, the LUMINA analyses dichotomized participants based on the US government’s definition of poverty, rather than evaluating for a dose response between income levels and cardiovascular risk factors, myocardial infarction, and cerebrovascular accident.

Socioeconomic status influences cardiovascular risk factors and outcomes through complicated mechanisms. Previous research suggested that socioeconomic status, measured by income, education, and occupation, acts directly to increase cardiovascular risk factors, and also through modifiers, such as behavioral factors, including decreased physical activity. Additionally, living in a disadvantaged neighborhood and exposure to psychological hazards in neighborhoods are independent risk factors for cardiovascular disease. Thus, it is possible that income and education level are proxies for environmental or neighborhood factors that increase the risk of cardiovascular risk factors and outcomes.

Socioeconomic status and ethnicity may affect underlying inflammatory pathways. An analysis of the Hopkins Lupus Cohort found that high sensitivity C-reactive protein (hsCRP) was negatively correlated with years of education and income level. Also, hsCRP levels were significantly higher in African Americans than in whites.

We found that African American ethnicity was not associated with myocardial infarction in SLE. A previous evaluation of the Hopkins Lupus Cohort also found that coronary artery disease (defined as angina pectoris, myocardial infarction, or cardiac sudden death) was not associated with black ethnicity in univariate analyses. An additional study found that carotid plaque and intima-media wall thickness measured by B-mode ultrasound did not vary by ethnicity in SLE. The LUMINA study found that ethnicity was not an independent contributor to the occurrence of cardiovascular, cerebrovascular, and peripheral vascular events in SLE.

In our study, ethnicity was associated with obesity and hypertension, which is similar to the findings of the Atherosclerosis Risk in Communities (ARIC) study, a population-based study in the United States. However, unlike the ARIC study, we did not observe a relationship between ethnicity and diabetes mellitus.

Measuring socioeconomic status is difficult and requires the use of proxy measures. Income and employment status may vary over time. Research by Karlson, et al. found that the most stable measure of socioeconomic status appears to be the level of education, because most patients have completed their education prior to onset of disease. In addition, education was found to be highly correlated with other socioeconomic factors. In the current analyses, longitudinal data regarding career changes were not available. This is a potential limitation, as disease activity may lead to changes in socioeconomic status. In addition, a survival analysis was not used, nor was it possible to adjust for cumulative damage or disease activity, as the study group was not an inception cohort. Another potential limitation is that the presence of cardiovascular risk factors, such as hypertension and obesity, and the proxy measures of socioeconomic status could vary over time. The current analysis focused on the association between baseline socioeconomic status and cardiovascular risk factors and outcomes, rather than addressing how SLE activity related to changes in socioeconomic status. Another potential limitation of our analysis is that data for disease activity prior to cohort entry were not available. This is unlikely to influence the association of socioeconomic factors with cardiovascular risk factors. We studied both education and income levels and found that low household income level was the most informative measure of socioeconomic status in whites.

As many cardiovascular risk factors, including smoking and obesity, are potentially modifiable, we advocate that these risk factors be aggressively treated in patients with SLE. While ethnicity appears to modify the relationship between socioeconomic status and cardiovascular risk factors and outcomes, there was an association in both whites and African Americans. These data suggest that comprehensive care programs for all SLE patients of lower socioeconomic background need to target traditional cardiovascular risk factors.

There are many strengths of the Hopkins Lupus Cohort, including the prospective ascertainment of risk factors in all cohort patients, and the use of 1 provider for all followup visits. However, it should be noted that our subjects were recruited from Baltimore and the results may not be generalizable to all patients with SLE.

Our study demonstrates that socioeconomic status plays an important role in traditional cardiovascular risk factors in a cohort of patients with SLE. This relationship appears to be modified by ethnicity. High family income appears to be
protections against myocardial infarction in whites, while high education in either ethnic group was not. Future studies should attempt to address these markers of socioeconomic status in cardiovascular disease in patients with SLE in other centers and nations to help improve our understanding of their role in cardiovascular disease, the primary cause of death in SLE in the developed world.

REFERENCES