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Audrey Martyn Date

The Role of Socioeconomic Status on Development of End-Stage Renal Disease for those with Lupus Nephritis

By

Audrey Martyn
MPH

Epidemiology

_____

David Kleinbaum, PhD
Committee Chair

_____

S. Sam Lim, MD, MPH
Committee Member

_____

Cristina Drenkard, MD, PhD
Committee Member

The Role of Socioeconomic Status on Development of End-Stage Renal Disease for those with Lupus Nephritis

By

Audrey Martyn

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Thesis Committee Chair: David Kleinbaum, PhD

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Abstract

The Role of Socioeconomic Status on Development of End-Stage Renal Disease for those with Lupus Nephritis

By Audrey Martyn

Background: Systemic lupus erythematosus (SLE) is a potentially fatal chronic autoimmune disease that can affect multiple systems of the body. SLE causes inflammation to the kidneys in up to 60% of cases, leading to lupus nephritis. Lupus nephritis is a serious condition that can lead to end-stage renal disease (ESRD) which is treated with dialysis or a renal transplant. African Americans have poorer outcomes with lupus nephritis compared to whites. This difference cannot be fully explained by biologic or genetic factors. The aim of this study was to determine if there is an association between socioeconomic status (SES) and progression of ESRD for those with lupus nephritis.

Methods: 558 African American and White Patients with lupus nephritis were identified from The Georgia Lupus Registry, a population-based registry of patients with lupus in a large Metropolitan area of Atlanta. ESRD status was gathered from the Centers for Medicare & Medicaid Services (CMS) Medical Evidence Report (Form CMS-2728), which is filled out for patients receiving ESRD treatment. SES was determined using a social deprivation index, which examined a patient's neighborhood environment, using the 2000 U.S. Census tract information corresponding to the patient's home address between 2002 and 2004. Univariate and Multivariate logistic regression was performed to determine the association between SES and developing ESRD.

Results: Multivariate analysis did not reveal an association between SES and the development of ESRD in those with lupus nephritis. In particular, there was no difference between the second quartile and first quartile (aOR 1.44 (95% CI 0.74-2.78)), between the second quartile and third quartile (aOR 1.23 (95% CI 0.66-2.28)), and between the second quartile and fourth quartile (aOR 1.70 (95% CI 0.93-3.08)).

Conclusion: SES, derived from the social deprivation index, was not associated with increased risk of developing ESRD among those with lupus nephritis. Nevertheless, since SES was measured at the neighborhood level, it is possible that SES may be associated with developing ESRD if SES is measured at the individual level.

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BACKGROUND:

Systemic Lupus Erythematous

Systemic lupus erythematous (SLE) is a potentially fatal chronic inflammatory autoimmune disease that affects multiple systems of the body [1-3]. The disease is episodic, characterized by flares and remission [4]. Flares occur when a person experiences new signs and symptoms of inflammation or worsening organ involvement. The disease manifests in many forms including skin rashes, photosensitivity, involvement of internal organs including the kidneys and heart, arthritis, neurologic problems, and hematologic disorders. It is assumed that a person develops the disease from a combination of genetic, hormonal, and environmental factors [5]. Lupus inflammatory manifestations are treated with anti-inflammatory and immunosuppressive drugs, which have a wide range of potential side effects [3, 5]. These consequences include organ and tissue damage and comorbid conditions.

Distribution of Systemic Lupus Erythematous

There are age, gender and race disparities in the incidence, prevalence, and health outcomes of SLE [3]. It is not clearly understood why these disparities exist. Nonwhite people are more likely to develop the disease at younger ages, have higher mortality rates, more renal involvement and worse outcomes [3, 6]. The incidence of SLE is three to four times higher for Black women compared to white women. Lupus disproportionately affects nonwhite women in their child bearing years; this group is more likely to experience higher mortality and a more "active" form of the disease [7, 8]. Men are less likely to develop SLE [3, 9].

Disparities are also found in the poor, those with limited access to health care, and those with limited education. Studies have indicated that these groups are at increased risk of developing SLE and having poorer health outcomes. Biological and genetic features have been considered to explain these differences but these alone do not explain the "socioeconomic 'gap'" that is continuing to widen over time [3].

Incidence and Prevalence of Systemic Lupus Erythematous

The distribution and determinants of lupus are not fully understood. Consequently, the incidence and prevalence of lupus has not been adequately determined. There is wide variability in the estimates of the incidence and prevalence of SLE due to different methodology between studies, including but not limited to: different case definitions, limited resources, varying demographic groups targeted in assessment, lack of reliability from data and diagnosis, and limited contact with those who are at risk due to lack of health care [10]. Although the exact incidence is not known, there is evidence to show that it has been increasing over the past four decades [3].

Lupus Nephritis

Systemic lupus erythematosus affects multiple systems of the body [1, 2]. When SLE causes inflammation of the kidneys, it is called lupus nephritis [11]. This is a serious manifestation of SLE and could lead to end-stage renal disease (ESRD) [6]. Lupus nephritis is heterogeneous, meaning that the disease does not progress the same way or even follow similar paths in all patients. The pathology of this disease ranges from "silent" with little to no symptoms to forms that rapidly evolve into ESRD [11].

The American College of Rheumatology notes that lupus nephritis impacts the majority of people, up to 60%, who have SLE [12]. This number is lower in European cohorts [2]. The progression typically happens rapidly, most likely developing within the first years of diagnosis of SLE, however some patients progress to lupus nephritis later in the course of their disease. It is important that all patients who are believed to have lupus nephritis undergo a renal biopsy to confirm the disease as well as to help identify the proper treatment [13]. Of all people who received a renal biopsy, 90% of patients had abnormal results [13].

End-Stage Renal Disease

Overall 20% to 30% of those with lupus nephritis develop ESRD [12, 14], with 4% to 20% developing ESRD within the first ten years [2, 15], and 10% to 30% developing ESRD within the first 15 years [16].

Patients with lupus nephritis are given immunosuppressive therapies to treat their illness and prevent further deterioration of their kidneys. Patients may progress to ESRD due to limited treatment. [12, 15, 17, 18]. However, even those with optimal care and treatment may still progress to ESRD. Ten to thirty percent of lupus nephritis patients receiving proper treatment will progress to ESRD. Once a person develops ESRD their treatment includes dialysis and/or a renal transplant [1, 15]. SLE patients with kidney involvement are at increased risk for poor health outcomes [19]. A retrospective study indicated that those who were diagnosed with lupus nephritis had a 5-year survival rate of 90% and a 10-year survival rate of 75% to 85% [1].

Predictors of End-Stage Renal Disease

Predictors associated with increasing the risk of ESRD among those with lupus nephritis include, but are not limited to: male gender, Hispanic ethnicity, and African American race. Men have more severe forms of lupus nephritis [11]. Other factors include disease duration, the number of American College of Rheumatology (ACR) criteria, comorbidities such as hypertension and diabetes mellitus, the histological extension and location of inflammatory and scaring changes in the renal tissue, and elevated serum creatinine levels [6, 14]. It is possible that genetics may make some people more susceptible to renal involvement [3, 6]. Literature has shown that area based factors such as neighborhood poverty level, employment, educational level, and family size can affect the outcomes of ESRD for people with SLE [3].

Incidence of End-Stage Renal Disease

Over the last 15 years, the incidence of ESRD among those with lupus nephritis has not decreased despite the vast improvements in medical technology and the introduction, between 1982 and 1995, of efficacious treatments [15, 18, 20]. In fact, some research has shown that the incidence has increased over the last few decades [12]. However, between 1995 and 2004 the incidence of ESRD secondary to lupus nephritis appeared to be constant [18].

Disparities of Lupus Nephritis

The disparities found with SLE are also found in those with lupus nephritis with and without ESRD [3, 6]. Additionally, literature has shown that African Americans have poorer outcomes with lupus nephritis than whites [21]. Demas [3] describes a "socioeconomic 'gap'" found in the incidence, prevalence, and health outcomes of SLE that is not completely explained by biologic and genetic factors.

Faurschou [2] examined data from the National Institutes of Health spanning two decades in the article *Long-Term Mortality and Renal Outcome in a Cohort of 100 Patients With Lupus Nephritis*. This study found that black patients were more likely than other races to develop problems with their kidneys.

Ward [9] states in an editorial that the disparities seen with SLE patients are due to psychosocial factors such as social support, access to health care, and coping mechanisms. He states that socioeconomic status (SES) and race are proxies for determining the psychosocial differences.

Socioeconomic Status

Research has shown that between 1995 and 2004 the incidence of ESRD secondary to lupus nephritis was constant [18]. During this time a social gradient effect was observed between the highest and lowest social classes when separated into quartiles. Those in the lowest SES quartile experienced the highest risk of ESRD, and the risk decreased by improved social class. These findings suggest that improved SES could decrease the risk of progression to ESRD in those with lupus nephritis [18].

SES is a dynamic variable that indicates an individual's social and economic resources [1], which may influence access to healthcare, medical understanding, and timeliness of receiving care. The reason SES may influence these problems may be education, income, medical insurance, social support, and area-based measures based on residence [3].

The previously mentioned "socioeconomic gap" described by Demas [3] has been found consistently among relevant literature. Another study that used patients from two hospitals in

New York, determined that the poorer outcomes experienced by African Americans was associated with SES independent of race or ethnicity [21]. Indicating SES may be the issue rather than biological or genetic differences. However, both race/ethnicity and socioeconomic status are important predictors [11, 21, 22]. This study used neighborhood poverty, education, and insurance to determine a patient's SES.

Demas [3] reviewed studies that examined the disparities found with the incidence, prevalence, and health outcomes of those with SLE. SES was measured by income, education, wealth, medical insurance, and other area based measures. It found that those with lower SES had higher incidences of SLE and more severe forms of the disease.

An association between SES and progression to ESRD for those with lupus nephritis was found in the study described in *Socioeconomic status and the incidence of ESRD* [17]. This study gathered patient data from the United States Renal Data System (USRDS) and used zip codes and data from the 2000 U.S. Census to determine a patient's SES at the neighborhood level. The SES measure was a validated composite variable, which included information such as education, income, area poverty, and house value. The results were stratified by sex and race to account for the different prevalence's. "The incidence of ESRD caused by lupus nephritis was significantly greater in those in the lowest SES quartile relative to those in the highest SES quartile for white women, white men, black women, Asian/Pacific-Islander women, and Hispanic women, but not black or Hispanic men." Data obtained from the U.S. Census at the zip code level is not as accurate as data found at the census tract and/or block group level. Census tract and block groups provide a better measurement of a patient's immediate physical neighborhood [1].

Research, determining SES from the census block group level, described that the quantity of health care delivery systems in place and the SES of the neighborhood influence the number of physician visits [22]. A criticism of this research is that severity of SLE was measured by the patients self-report.

Being in a lower SES bracket may impact a patient's ability to access quality health care, visit doctors, or adequately comply with treatments [1, 21]. Disenfranchised groups such as the elderly and poor are more likely to experience avoidable hospital visits and have less access to specialist care [22]. Unfortunately those patients who have the most severe symptoms do not have access to care, capable doctors, and do not get a diagnosis in a timely manner [7]. It has been found that limited access to care has led to developing ESRD more quickly. Education has been seen as a predictor of SLE outcomes and is important aspect of SES [3]. The theory is that the more educated a person is the more capable they are to advocate for their own health.

It has been shown that those who lack insurance or have poor insurance develop ESRD at earlier ages than those with medical insurance [12, 15]. It should be noted that insurance is not a good proxy for SES because it fails to account for those patients who receive assistance from the government (Medicaid or Medicare) due to their illness [21]. The association between lack of access to medical care and increased risk of ESRD secondary to SLE was found in a population-based ecological study in California between 1999 and 2004 [3, 15].

Purpose of Thesis

There is limited knowledge on the role of SES in the progression to ESRD in those with SLE or lupus nephritis, despite the research that has been performed in this area [16].

A criticism of previous research is that subjects were not derived from a population-based lupus registry and for that reason results may not be generalizable to all people with lupus nephritis [1, 5, 6, 15, 18, 21, 23]. Additionally, previous studies have used data from the USRDS, which does not include information to validate the diagnosis of SLE, or clinical data prior to their progression to ESRD [12, 18].

The benefit of this study is that it used validated SLE cases with lupus nephritis from a large population-based registry to compare those who have lupus nephritis without ESRD to those who progressed to ESRD. The benefit of using a population-based registry is that it contains a relatively large group of patients and accurately represents the real world population

[5]. Specifically for this population it contains a large proportion of African Americans, one of the racial groups at highest risk of developing SLE with severe complications. For these reasons, the analysis will add to existing knowledge in the area, contributing to understanding racial disparities in lupus outcomes.

Additionally, the majority of previous research attempting to determine the role of SES on the development of ESRD in those with lupus nephritis, defined the SES variable by using neighborhood information from a patient's zip code of residence [1, 17, 18]. Using a patient's census tract and block group is more accurate than using a patient's zip code to determine their neighborhood environment and establish their SES [1]. This study determined a patient's SES by their census tract and poverty level from the block group, and therefore examining SES more accurately.

The purpose of this is study is to determine the role of socioeconomic status and neighborhood poverty as predictors of ESRD in SLE patients with lupus nephritis.

METHODS:

Hypothesis

This study hypothesized that socioeconomic status was a predictor of developing end-stage renal disease among those diagnosed with lupus nephritis. It was also hypothesized that poverty alone was a predictor of developing end-stage renal disease among those diagnosed with lupus nephritis. Finally it was hypothesized that models containing both African Americans and Whites would yield different results than models that only included African Americans.

Study Design and Participants

IRB protocol was reviewed and approved by the IRB at Emory University and the Georgia Department of Community Health.

Participants in this analysis were selected from The Georgia Lupus Registry (GLR), a population-based registry of lupus that aims to estimate the incidence and prevalence of lupus in a well-defined metropolitan area of Atlanta. To maximize case ascertainment, the GLR used multiple sources. Potential lupus cases were ascertained and abstracted from health care providers, hospitals, commercial laboratories, community organizations, lupus research databases, and population data such as Medicaid claims. Administration databases were searched using the International Classification of Diseases, Ninth Revision (ICD-9). Those with the Clinical Modification billing code 710.0 (systemic lupus erythematosus (SLE) and 695.4 (discoid lupus) were searched as potential lupus cases from administrative databases. Also those with certain conditions that may develop into SLE or are related to SLE were included, such as billing code 710.8 (other specified connective tissue disease) and 710.9 (unspecified connective tissue disease) [10].

The primary purpose of the population-based Georgia Lupus Registry is to determine the prevalence of SLE in 2002 and the incidence in 2002-2004 in Fulton and DeKalb Counties in Georgia [10]. It is a competitively funded by a grant through the Centers for Disease Control and Prevention (CDC).

Only patients found to be in the GLR that had a validated diagnosis of SLE were included in this analysis. To be considered a validated case, a patient must meet four or more of the criteria determined by the revised 1982 American College of Rheumatology (ACR) criteria [24]. Patients who fulfilled three ACR criteria with a final diagnosis of SLE by a rheumatologist were also considered validated [10].

Of those validated cases of SLE, only those with lupus nephritis were included in the final analysis of this study. A patient was determined to have lupus nephritis if they had one or more of the following: 24-hour proteinuria greater than 500 mg on at least one occasion, semi-quantitative proteinuria greater than 300 mg/dl on at least one urinalysis, protein to creatinine ratio greater than 0.5 on at least one random urine collection, cellular casts on microscopic analysis of urine sediment, or a renal biopsy with a WHO class greater than two.

Patients were included in the analysis provided they had a home address at the GLR catchment period (years 2002 to 2004) on record.

End-Stage Renal Disease

Once a patient begins end-stage renal disease (ESRD) treatment, such as dialysis or a renal transplant, medical renal providers fill out the Centers for Medicare & Medicaid Services (CMS) Medical Evidence Report (Form CMS-2728)[25]. This form is sent to the CMS databases to identify a patient as eligible for Medicare or to reclassify current Medicare recipients as ESRD patients [16]. Information for ESRD patients is included with the Form CMS-2728 regardless of Medicare eligibility. Information from the Form CMS-2728 is found in the US Renal Data System (USRDS) a 'national population based registry that contains all patients with ESRD' [16]. Data from the USRDS was merged with the GLR database if a patient's ICD-9, Clinical Modification billing code, indicated that their primary disease was lupus.

If a patient had a CMS-2728 form indicating that they had received ESRD services and they were previously in the GLR database they were coded to have the outcome, ESRD, for this analysis.

Exposure Variables

Participant's addresses were obtained for the years 2002, 2003, and 2004 using a patient's medical record, administrative data, or the internet database Lexis-Nexis. These addresses were geocoded to find the corresponding 2000 U.S. Census tract group and block group number. The earliest geocoded address per participant was used to determine the appropriate tract group and block group number. Census tract groups and block groups were used to determine a patient's socioeconomic status variable as well as the participant's poverty variable.

Socioeconomic Status:

Socioeconomic status for this analysis was calculated by using a neighborhood deprivation index that corresponds to a participant's census tract group number. Previous research has shown that social indicators such as partner violence and economic markers that identify those who are economically underprivileged are clustered at the neighborhood level [26]. For this reason, census tracts were used when creating the social deprivation index. A standardized index made up of eight variables were compiled to create the social deprivation index including: 'percent of males in management and professional occupations, percent of crowded housing, percent of households in poverty, percent of female headed households with dependents, percent of households on public assistance and households earning $30,000 per year estimating poverty, percent earning less than a high school education, and the percent unemployed'[26]. The higher the standardized social deprivation index, the more deprived is the neighborhood at the tract level. Information for this variable came from the 2000 U.S. Census.

A dataset containing the social deprivation index for all tract groups in Georgia was merged with a dataset containing patients from the GLR, by tract group number. This continuous standardized social deprivation index was divided into quartiles; the first quartile being the least deprived and the fourth quartile being the most deprived. The second quartile was chosen as the reference group in our analysis.

Poverty:

A separate model was run to determine the impact of poverty alone. Poverty was determined using the 2000 U.S. Census data at the block group level. The block group is a subset of the tract group and the smallest meaningful geographic area where data is collected and tabulated by the U.S. Census [27]. The purpose of using the block group data was to obtain the smallest area associated with a patient's geographic neighborhood. Poverty was calculated by dividing the total number of people whose income in 1999 was below the poverty level by the total number of people for which poverty was determined.

A dataset containing the poverty variable for block groups in Fulton and DeKalb County was merged with the GLR participants by block group number. This continuous variable was divided into quartiles the first quartile being the least impoverished area and the fourth quartile being the most impoverished area. The second quartile was chosen as the reference group in our analysis.

Confounding Variables

For the model that contained both African Americans and Whites, race was controlled for as a dichotomous variable, using whites as the reference group. All four models controlled for sex, number of ACR criteria, age at the time of SLE diagnosis, and duration of the disease. Sex was controlled for in the model as a dichotomous variable, using males as the reference group. The number of ACR Criteria was included in the model as a continuous variable. The value ranged from a total of four ACR Criteria to all eleven ACR criteria. If a person had three ACR criteria with a final diagnosis of SLE by a rheumatologist, they were categorized as having 4 ACR criteria. Age at diagnosis of systemic lupus erythematosus was controlled for in the models as a continuous variable. Lastly, duration of disease was controlled for in the model. For those who were classified as having ESRD, duration of disease was calculated as time between the date of SLE diagnosis and first date of ESRD treatment. For those who did not have ESRD, duration of diagnosis was calculated as time between date of SLE diagnosis and date of their last physician visit. Duration of disease was a continuous variable in the model.

Interaction Variables

All initial models contained interaction terms involving products of the exposure variable (either SES or Poverty level) with each covariate that was identified as potential confounders.

Modeling Analyses

Logistic regression models were used for analysis to calculate odd ratio estimates of the exposure variable (either SES or Poverty level) to ESRD, controlling for potential confounding and effect modification. Two models were run to determine the association between SES and the risk of developing ESRD for those diagnosed with lupus nephritis. Additionally, two models were run to determine the association between poverty levels and the risk of developing ESRD for those diagnosed with lupus nephritis.

Model 1: Examined the association between SES and ESRD status for both African Americans as well as whites.

Model 2: Examined the association between poverty level and ESRD status for both African Americans and Whites.

Model 3: Examined the association between SES and ESRD status for African Americans only.

Model 4: Examined the association between poverty level and ESRD status for African Americans only.

Testing Collinearity:

Collinearity was tested on all models using a Macro developed at CDC and Emory University [28]. A high condition index (CI), roughly greater than 30, indicated collinearity provided at least two variance decomposition proportions (VDP) on variables other than the intercept were also high, i.e., roughly greater than 0.5. [28]. The interaction variable with the highest variance decomposition proportions (VDP) corresponding to the highest CI was dropped. The model was rerun without the dropped variable and reexamined for collinearity. This process was repeated until there were no more condition indices above the rough cut-point of 30.

Testing Interaction:

A Likelihood Ratio Test (LRT) was performed on all remaining interaction terms that were not dropped due to collinearity. Interaction terms were tested together in a "chunk test." If the LRT yielded a non-significant p-value (<0.05), then backwards elimination (BWE) was performed to see if some individual interaction terms should remain in the model. If as a result of both the chunk test and the BWE approach, no interaction terms were found to be significant at a p-value of 0.05, and then all interaction terms were removed.

Assessing Confounding:

Confounding was examined for all four models. All possible subsets of confounders were considered in addition to the full (i.e., gold standard) model. A 10% rule was used to determine if a reduced model (obtained by dropping potential confounders), controlled for confounding by yielding an OR estimate within 10% of the gold standard (GS) model. For those (candidate) subsets that controlled for confounding, we then obtained 95% confidence intervals for the OR to determine whether any such subset gained meaningful precision when compared to the precision obtained for the GS OR estimate. The reduced model that gained the most precision was determined to be the best model, although if no reduced model gained meaningful precision, the gold standard (initial) model was chosen as best.

SAS statistical software 9.2 was used for the data analysis. Hypothesis testing was 2-tailed. P-values <0.05 were considered to be significant.

Initial Model 1: logit P(ESRD=1|X) = β_1SES1+ β_2SES3+ β_3SES4+ β_4RACE+ β_5SEX+ β_6ACRCRIT+ β_7AGESLEDIAG+ β_8DUROFDIAG+ β_{14}SES1*RACE+ β_{24}SES3*RACE+ β_{34}SES4*RACE+ β_{15}SES1*SEX+ β_{25}SES3*SEX+ β_{35}SES4*SEX+ β_{16}SES1*ACRCRIT+ β_{26}SES3*ACRCRIT+ β_{36}SES4*ACRCRIT+ β_{17}SES1*AGESLEDIAG+ β_{27}SES3* AGESLEDIAG + β_{37}SES4* AGESLEDIAG + β_{18}SES1*DUROFDIAG+ β_{28}SEX3*DUROFDIAG+ β_{38}SES4*DUROFDIAG

Initial Model 2: **logit P(ESRD=1|X)**= β_1POV1+ β_2POV3+ β_3POV4+ β_4RACE+ β_5SEX+ β_6ACRCRIT+ β_7AGESLEDIAG+ β_8DUROFDIAG+ β_{14}POV1*RACE+ β_{24}POV3*RACE+

β_{34}POV4*RACE+ β_{15}POV1*SEX+ β_{25}POV3*SEX+ β_{35}POV4*SEX+ β_{16}POV1*ACRCRIT+ β_{26}POV3*ACRCRIT+ β_{36}POV4*ACRCRIT+ β_{17}POV1*AGESLEDIAG+ β_{27}POV3*AGESLEDIAG+ β_{37}POV4*AGESLEDIAG+ β_{18}POV1*DUROFDIAG+ β_{28}POV3*DUROFDIAG+ β_{38}POV4*DUROFDIAG

Initial Model 3: **logit P(ESRD=1|X) =** β_1SES1+ β_2SES3+ β_3SES4+ β_4SEX+ β_5 ACRCRIT + β_6AGESLEDIAG + β_7DUROFDIAG+ β_{14}SES1*SEX+ β_{24}SES3*SEX+ β_{34}SES4*SEX+ β_{15}SES1*ACRCRIT+ β_{25}SES3*ACRCRIT+ β_{35}SES4*ACRCRIT+ β_{16}SES1*AGESLEDIAG+ β_{26}SES3*AGESLEDIAG+ β_{36}SES4*AGESLEDIAG + β_{17}SES1*DUROFDIAG+ β_{27}SEX3*DUROFDIAG+ β_{37}SES4*DUROFDIAG

Initial Model 4: logit P(ESRD=1|X) = β_1POV1+ β_2POV3+ β_3POV4+ β_4SEX+ β_5 ACRCRIT + β_6 AGESLEDIAG + β_7DUROFDIAG+ β_{14}POV1*SEX+ β_{24}POV3*SEX+ β_{34}POV4*SEX+ β_{15}POV1*ACRCRIT+ β_{25}POV3*ACRCRIT+ β_{35}POV4*ACRCRIT+ β_{16}POV1*AGESLEDIAG+ β_{26}POV3*AGESLEDIAG+ β_{36}POV4*AGESLEDIAG+ β_{17}POV1*DUROFDIAG+ β_{27}POV3*DUROFDIAG+ β_{37}POV4*DUROFDIAG

RESULTS:

Model 1 (Exposure variable = SES level, Dataset contains African Americans and Whites)

Descriptive Statistics:

The original cohort of validated systemic lupus erythematosus (SLE) cases who were diagnosed with lupus nephritis consisted of 558 patients who were either African American or White. The cohort included in analysis consisted of 522 patients. Thirty one patients were not included because there was no available address for any year between 2002 and 2004. Only those with complete information for socioeconomic status, race, sex, number of ACR criteria, age at time of SLE diagnosis, and duration of disease were included for analysis; five patients were excluded due to these criteria. Two patients were missing SES, three patients were missing the age of SLE diagnosis, and three patients were missing duration of diagnosis.

The racial distribution for this model was African American 445 (85%) and White 77 (15%). The data consisted of women 443 (85%) and men 79 (15%). The number of ACR criteria a person can have in this cohort ranges from four to eleven, the distribution of the number of ACR criteria is as followed: 4 (17%), 5 (21%), 6 (25%), 7 (17%), 8 (11%), 9 (6%), 10 (2%), and 11 (1%). The average age at diagnosis of SLE is 32 years old ±14 years and the average duration of disease is 9 years ± 8 years. Of the 522 patients included in analysis 115 (22%) had the outcome of end-stage renal disease. These data are shown in Table 1.

Univariate analysis:

Using univariate analysis, we found that race, the number of ACR criteria, and age at diagnosis of SLE (but not socioeconomic status, sex, and duration of disease) were significantly associated with developing ESRD among those with lupus nephritis.

Multivariate Analysis:

Using a hierarchical BW elimination approach [28], we found no evidence of interaction. Also, using the guideline of 10%, no reduced model gained precision by dropping any subset of the confounders; for this reason, all potential confounders (i.e., race, sex, age at diagnosis of SLE,

the number of ACR criteria, and duration of disease) remained in the model. Using the 2nd quartile as a reference group, socioeconomic status was not significantly associated with developing ESRD in those with lupus nephritis when controlling for all potential confounders, namely, race, sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Compared to those in the second highest socioeconomic group (quartile 2), those in quartile 1 were 1.44 (95% CI 0.74-2.78) more likely to have ESRD when controlling for race, sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Compared to those in the second highest socioeconomic group (quartile 2), those in quartile 3 were 1.23 (95% CI 0.66-2.28) more likely to have ESRD when controlling for race, sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Compared to those in the highest socioeconomic group (quartile 2), those in quartile 4 were 1.70 (95% CI 0.93-3.08) more likely to have ESRD when controlling for race, sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Reduced and Final Model 1: logit P(ESRD=1|X) = β_1SES1+ β_2SES3+ β_3SES4+ β_4RACE+ β_5SEX+ β_6ACRCRIT+ β_7AGESLEDIAG+ β_8DUROFDIAG

Model 2 (Exposure variable = Poverty level, Dataset contains African Americans and Whites)

Descriptive statistics:

The original cohort of validated SLE cases who were diagnosed with lupus nephritis consisted of 558 patients who were either African American or White. The cohort included in analysis consisted of 504 patients. Thirty one patients were not included because there was no available address for any year between 2002 and 2004. Only those with complete information for poverty level, race, sex, number of ACR criteria, age at time of SLE diagnosis, and duration of disease were included for analysis. Twenty three patients were excluded due to these criteria. Three patients were missing the age of SLE diagnosis, twenty patients lacked information for poverty at the block group level, and three patients were missing duration of diagnosis.

The racial distribution for this model was African American 430 (85%) and Whites 74 (15%). The data consisted of women 430 (85%) and men 74 (15%). The number of ACR criteria a person can have in this cohort ranges from four to eleven, the distribution of the number of ACR criteria is as followed: 4 (17%), 5 (20%), 6 (25%), 7 (18%), 8 (11%), 9 (6%), 10 (2%), and 11 (1%). The average age at diagnosis of SLE is 32 years old ±14 years and the average duration of disease is 9 years ± 8 years. Of the 504 patients included in analysis 112 (22%) had the outcome of ESRD. These data are shown in Table 2.

Univariate Analysis:

Using univariate analysis, we found that race, number of ACR criteria, and age at diagnosis of SLE (but not proportion of people living in poverty at the block group level, sex, and duration of disease) were significantly associated with developing ESRD among those with lupus nephritis.

Multivariate Analysis:

As in the previous analysis involving SES rather than Poverty level as the exposure, we found no evidence of interaction, and we controlled for all potential confounders. Using the 2nd quartile as a reference group, poverty status was not significantly associated with developing ESRD in those with lupus nephritis when controlling for race, sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Compared to those in the second least impoverished group (quartile 2), those in least impoverished areas (quartile 1) were 0.95 (95% CI 0.51-1.78) less likely to have ESRD when controlling for race, sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Compared to those in the second least impoverished group (quartile 2), those in quartile 3 were 0.91 (95% CI 0.50-1.65) less likely to have ESRD when controlling for race, sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Compared to those in the second least impoverished group (quartile 2), those in quartile 4 were 1.03 (95% CI 0.56-1.87) more likely to have ESRD when controlling for race, sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Reduced and Final Model 2: **logit P(ESRD=1|X)** = β_1POV1+ β_2POV3+ β_3POV4+ β_4RACE+ β_5SEX+ β_6ACRCRIT+ β_7AGESLEDIAG+ β_8DUROFDIAG

Model 3 (Exposure variable = SES level, Dataset contains African Americans only)

Descriptive Statistics:

The original cohort of validated SLE cases who were diagnosed with lupus nephritis consisted of 476 patients who were African American. The cohort included in this analysis consisted of 445 patients. Twenty six patients were not included because there was no available address for any year between 2002 and 2004. Only those with complete information for SES, sex, number of ACR criteria, age at time of SLE diagnosis, and duration of disease were included for analysis. Five patients were excluded due to these criteria. Two patients were missing SES, three patients were missing the age of SLE diagnosis and three patients were missing duration of diagnosis. Of the 445 patients included in analysis 110 (25%) had the outcome of ESRD.

The gender distribution of sex was women 381 (86%) and men 64 (14%). The number of ACR criteria a person can have in this cohort ranges from four to eleven, the distribution of the number of ACR criteria is as followed: 4 (16%), 5 (21%), 6 (25%), 7 (18%), 8 (12%), 9 (6%), 10 (1%), and 11 (1%). The average age at diagnosis of SLE is 31 years old ±14 years and the average duration of disease is 9 years ± 8 years. Of the 445 patients included in analysis 110 (25%) have the outcome of ESRD. These data are shown in Table 3.

Univariate Analysis:

Using univariate analysis, we found that age at diagnosis of SLE and the number of ACR criteria (but not socioeconomic status, sex, and duration of disease) were significantly associated with developing ESRD among those with lupus nephritis.

Multivariate Analysis:

As in the previous analysis involving SES and both African Americans and Whites, we found no evidence of interaction, and we controlled for all potential confounders. Using the 2nd quartile as a reference group, poverty status was not significantly associated with developing ESRD in those with lupus nephritis when controlling for sex, age at the diagnosis of SLE, the number of ACR criteria, and duration of disease.

Compared to those in the second highest socioeconomic group (quartile 2), those in quartile 1 were 1.31 (95% CI 0.69-2.50) more likely to have ESRD when controlling for sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Compared to those in the second highest socioeconomic group (quartile 2), those in quartile 3 were 1.49 (95% CI 0.79-2.82) more likely to have ESRD when controlling for sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Compared to those in the highest socioeconomic group (quartile 2), those in quartile 4 were 1.55 (95% CI 0.81-2.95) more likely to have ESRD when controlling for sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Reduced and Final Model 3: logit P(ESRD=1|X) = β_1SES1+ β_2SES3+ β_3SES4+ β_4SEX+ β_5ACRCRIT + β_6 AGESLEDIAG + β_7DUROFDIAG

Model 4 (Exposure variable = Poverty level, Dataset contains African Americans only)

Descriptive Statistics:

The original cohort of validated SLE cases who were diagnosed with lupus nephritis consisted of 476 patients who were African-American. The cohort included in this analysis consisted of consisted of 430 patients. Twenty six patients were not included because there was no available address for any year between 2002 and 2004. Only those with complete information for poverty level, sex, age at time of SLE diagnosis, number of ACR criteria, and duration of disease were included for analysis. Twenty patients were excluded due to these criteria. Seventeen patients are missing poverty level, three patients were missing the age of SLE

diagnosis, and three patients were missing duration of disease. Of the 430 patients included in analysis 107 (25%) had the outcome of ESRD.

The gender distribution of sex was women 369 (86%) and men 61 (14%). The number of ACR criteria a person can have in this cohort ranges from four to eleven, the distribution of the number of ACR criteria is as followed: 4 (16%), 5 (20%), 6 (25%), 7 (19%), 8 (12%), 9 (6%), 10 (1%), and 11 (1%). The average age at diagnosis of SLE is 31 years old ±14 years and the average duration of disease is 9 years ± 8 years. Of the 430 patients included in analysis 107 (25%) have the outcome of ESRD. These data are shown in Table 4.

Univariate Analysis:

Using univariate analysis the number of ACR criteria and age at diagnosis of SLE (but not proportion of people living in poverty, sex, and duration of disease) were significantly associated with developing ESRD among those with lupus nephritis.

Multivariate Analysis:

As in the previous analysis involving SES rather than poverty level as the exposure, we found no evidence of interaction, and we controlled for all potential confounders. Using the 2nd quartile as a reference group, poverty status was not significantly associated with developing ESRD in those with lupus nephritis when controlling for sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Compared to those in the second least impoverished group (quartile 2), those in quartile 1 were 0.85 (95% CI 0.46-1.57) less likely to have ESRD when controlling for sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Compared to those in the second least impoverished group (quartile 2), those in quartile 3 were 0.70 (95% CI 0.37-1.32) less likely to have ESRD when controlling for sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Compared to those in the second least impoverished group (quartile 2), those in quartile 4 were 0.87 (95% CI 0.47-1.60) less likely to have ESRD when controlling for sex, age at diagnosis of SLE, number of ACR criteria, and duration of disease.

Reduced and Final Model 4: **logit P (ESRD=1|X)** = β_1POV1+ β_2POV3+ β_3POV4+ β_4SEX+ β_5ACRCRIT + β_6 AGESLEDIAG + β_7DUROFDIAG

DISCUSSION:

The primary purpose of this study was to determine if there was an association between a patient's socioeconomic status or poverty level and the development of end-stage renal disease for those with lupus nephritis. Socioeconomic status and poverty level were run in separate models. Each exposure variable was tested using a model with both African Americans and Whites and a model with only African Americans.

Previous research [16] had found that compared to those with Medicaid or no insurance, those with private health insurance develop ESRD at an older age. The authors of that study hypothesized that patients have a slower progression to ESRD when they have better access to care.

Another study[15] found that people with SLE living in zip codes that have a higher proportion of avoidable hospital visits, have higher incidences of ESRD. The author believed this may be due to educational and organizational barriers that lead to worse health outcomes.

Ward [17] examined socioeconomic status and the incidence of ESRD among those with lupus nephritis. Using a validated SES variable divided into quartiles he found a gradient effect. Those in the lowest socioeconomic status quartile had an increased risk of developing ESRD when compared to those in the highest socioeconomic quartile.

These studies indicate that those with a higher socioeconomic status have a lower risk of developing ESRD. This may be due to access to health care, education, or a combination of variables.

A major finding of this study was that SES was not a statistically significant predictor of developing ESRD among those with lupus nephritis. This result was not consistent with previous research.

However, the social gradient effect described by Ward was weaker for African Americans compared to other racial groups [17]. African Americans may have physiological differences or worse quality of health care due to discrimination that reduces the effect of SES.

Ward also hypothesized that measuring SES at the neighborhood level was not appropriate for African Americans, because there is greater heterogeneity for this group [17]. This may explain why SES at the neighborhood level was not a significant predictor of developing ESRD in this analysis.

The second major finding of this study was that the proportion of poverty in a patient's neighborhood is not a statistically significant predictor of developing ESRD among those with lupus nephritis. It is possible that poverty alone does not account for a patient's inability to access to care.

Strengths:

The strengths of the study include the population-based registry for which the patients were abstracted. Using a population-based registry mirrors the actual population of disease and provides a large number of participants [5]. For this reason, the results from this analysis could be generalizable to SLE patients of similar demographic characteristics in the US.

Previous studies examining SES as a predictor of ESRD for those with lupus nephritis or SLE, used data from the United States Renal Data Systems (USRDS), or non-population based cohorts [6, 17, 18]. The USRDS only includes patients who have started ESRD treatment, meaning only cases with the outcome are included in the analysis. The benefit of using The Georgia Lupus Registry is that it contains patients who have lupus nephritis with and without ESRD. For this reason the study was able to identify the odds of developing ESRD.

Addresses were available for 536 (96%) of the original cohort for either one or more of the years between 2002 and 2004. These addresses were geocoded to get accurate information for the patient's census tract and block group to determine SES. Previous studies have used zip codes or zip code tabulation areas to determine a patient's SES [1, 15, 17, 18]. Census tract and block group measures have been found to be better predictors of SES compared to zip codes because it better represents the neighborhood [1].

Lastly, the study examined poverty level in a patient's neighborhood. The purpose of this analysis was to determine if poverty alone increased the risk of ESRD among those with lupus nephritis. This analysis provides knowledge that poverty at the block group level is not an indicator of developing ESRD in this population. If SES is a predictor of ESRD it is reasonable to conclude that income alone does not explain the differences found between social groups.

Weaknesses:

The socioeconomic status variable used in this study came from the social deprivation index described in the article by Messer [26]. The social deprivation index has been validated in populations examining perinatal outcomes. The eight variables making up the social deprivation index (percent of males in management and professional occupations, percent of crowded housing, percent of households in poverty, percent of female headed households with dependents, percent of households on public assistance and households earning $30,000 per year estimating poverty, percent earning less than a high school education, and the percent unemployed) may not be an accurate predictor of SES for this population. Ward [17] has created a SES variable validated for patients with lupus nephritis while testing the outcome ESRD. It is probable that the use of Ward's SES variable would yield significant results if used in this analysis. Also, using individual identifiers for SES for African Americans may have been more appropriate for this population, but that information was not available in the GLR.

Patient's addresses were only available for the years 2002 to 2004. A majority of patients were diagnosed with SLE prior to 2002; with 464 (83%) diagnosed in 2001 or earlier, 36 (6%) diagnosed in 2002, 30 (5%) diagnosed in 2003, 25 (5%) diagnosed in 2004, and 3 (1%) diagnosis date unknown. Not having the address of a patient at the time of diagnosis could lead to an inaccurate measure of SES. It is possible that a patient moved into a neighborhood associated with lower SES due to their diagnosis or a patient had a condition based on their surroundings.

Lastly, this study failed to control for comorbidities such as hypertension and diabetes mellitus which have previously been identified as possible confounders [16]. The GLR does not collect information on these comorbidities, making it impossible to control for them.

Conclusion:

This study has added to the existing knowledge on the role of SES in the progression to ESRD in those with lupus nephritis. The results are generalizable to lupus nephritis patients of similar demographic characteristics in the US because validated subjects were extracted from a large population-based lupus registry.

There was no association found between either SES or poverty in the development of ESRD among those with lupus nephritis. Indicating that these disparities could be explained by biologic or genetic differences or there is another factor, not yet identified. It is also probable that the study did not adequately measure SES or poverty for this population. Results may have been different if SES was measured using a separate validated index or SES was measured on the individual level. Additional information could be gained from rerunning analysis with a different indicator of SES using the same source of data, the large population-based registry.

More must be done to identify the reason disparities exist in those with SLE and lupus nephritis to prevent poorer outcomes experienced by certain individuals.

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Table 1. Baseline Demographic Information For Patients in Model 1

	ESRD (N=115)	Total (N=522)	p-Value
Race			<0.01
White	5 (4%)	77 (15%)	
African American	110 (96%)	445 (85%)	
Sex			0.64
Male	19 (17%)	79 (15%)	
Women	96 (83%)	443 (85%)	
Number of ACR Criteria			0.02
4	15 (13%)	89 (17%)	
5	21 (18%)	108 (21%)	
6	27 (23%)	130 (25%)	
7	24 (21%)	92 (17%)	
8	14 (12%)	60 (11%)	
9	9 (8%)	31 (6%)	
10	3 (3%)	8 (2%)	
11	2 (2%)	4 (1%)	
Age of SLE Diagnosis (years), Mean (SD)	29 (13)	32 (14)	0.01
Duration of Disease (years), Mean (SD)	8 (7)	9 (8)	0.32

Table 2. Baseline Demographic Information For Patients in Model 2

	ESRD (N= 112)	Total (N=504)	p-Value
Race			<0.01
White	5 (4%)	74 (15%)	
African American	107 (96%)	430 (85%)	
Sex			0.64
Male	18 (16%)	74 (15%)	
Female	94 (84%)	430 (85%)	
Number of ACR Criteria			0.02
4	14 (12%)	86 (17%)	
5	20 (18%)	102 (20%)	
6	27 (24%)	124 (25%)	
7	24 (21%)	92 (18%)	
8	13 (12%)	57 (11%)	
9	9 (8%)	31 (6%)	
10	3 (3%)	8 (2%)	
11	2 (2%	4 (1%)	
Age of SLE Diagnosis (years), Mean (SD)	28 (13)	32 (14)	0.01
Duration of Disease (years), Mean (SD)	8 (7)	9 (8)	0.36

Table 3. Baseline Demographic Information For Patients in Model 3

	ESRD (N= 110)	Total (N=445)	p-Value
Sex			0.50
Male	18 (16%)	64 (14%)	
Female	92 (84%)	381 (86%)	
Number of ACR Criteria			0.05
4	15 (13%)	70 (16%)	
5	20 (18%)	91 (21%)	
6	25 (23%)	113 (25%)	
7	23 (21%)	82 (18%)	
8	14 (13%)	53 (12%)	
9	8 (7%)	27 (6%)	
10	3 (3%)	5 (1%)	
11	2 (2%)	4 (1%)	
Age of SLE Diagnosis (years), Mean (SD)	28 (13)	31 (14)	0.01
Duration of Disease (years), Mean (SD)	8 (7)	9 (8)	0.89

Table 4. Baseline Demographic Information For Patients in Model 4

	ESRD (N= 107)	Total (N=430)	p-Value
Sex			0.56
Male	17 (16%)	61 (14%)	
Female	90 (84%)	369 (86%)	
Number of ACR Criteria			0.05
4	14 (13%)	68 (16%)	
5	19 (18%)	85 (20%)	
6	25 (23%)	109 (25%)	
7	23 (22%)	82 (19%)	
8	13 (12%)	50 (12%)	
9	8 (7%)	27 (6%)	
10	3 (3%)	5 (1%)	
11	2 (2%)	4 (1%)	
Age of SLE Diagnosis (years), Mean (SD)	28 (13)	31 (14)	0.01
Duration of Disease (years), Mean (SD)	9 (7)	9 (8)	0.93

Table 5: Logistic Regression Final Model 1

Variable	Parameter Estimate	Standard Error	Odds Ratio	95% Confidence Interval
SES1	0.36	0.34	1.44	0.74-2.78
SES3	0.21	0.31	1.23	0.66-2.28
SES4	0.53	0.30	1.70	0.93-3.08
Sex	-0.13	0.30	0.88	0.49-1.58
Race	1.48	0.50	4.41	1.65-11.84
ageSLEdiag	-0.02	0.01	0.98	0.97-1.00
ACRcrit	0.11	0.07	1.11	0.97-1.28
durofdiag	-0.02	0.01	0.99	0.96-1.01

Table 6: Logistic Regression Final Model 2

Variable	Parameter Estimate	Standard Error	Odds Ratio	95% Confidence Interval
POV1	-0.05	0.32	0.95	0.51-1.78
POV3	-0.10	0.31	0.91	0.50-1.65
POV4	0.03	0.31	1.03	0.56-1.87
Sex	-0.12	0.31	0.88	0.49-1.61
Race	1.41	0.49	4.10	1.58-10.68
ageSLEdiag	-0.02	0.01	0.98	0.96-1.00
ACRcrit	0.11	0.07	1.12	0.97-1.28
durofdiag	-0.01	0.01	0.99	0.96-1.01

Table 7: Logistic Regression Final Model 3

Variable	Parameter Estimate	Standard Error	Odds Ratio	95% Confidence Interval
SES1	0.27	0.41	1.31	0.69-2.50
SES3	0.40	0.22	1.49	0.79-2.82
SES4	0.44	0.18	1.55	0.81-2.95
Sex	-0.13	0.66	0.87	0.48-1.60
ageSLEdiag	-0.02	0.03	0.98	0.96-1.00
durofdiag	0.09	0.21	1.10	0.95-1.27

Table 8: Logistic Regression Final Model 4

Variable	Parameter Estimate	Standard Error	Odds Ratio	95% Confidence Interval
POV1	-0.16	0.31	0.85	0.46-1.57
POV3	-0.36	0.32	0.70	0.37-1.32
POV4	-0.14	0.31	0.87	0.47-1.60
ageSLEdiag	-0.13	0.32	0.88	0.47-1.64
ACRcrit	-0.02	0.01	0.98	0.96-1.00
durofdiag	0.10	0.07	1.10	0.95-1.28