Laboratory Abnormalities at the Onset of Treatment of End-Stage Renal Disease

Are There Racial or Socioeconomic Disparities in Care?

Michael M. Ward, MD, MPH

Background: Laboratory abnormalities at the start of treatment of end-stage renal disease (ESRD) have been reported as worse in racial/ethnic minorities than in white patients, suggesting racial disparities in care. It is not known whether these differences are attributable to racial/ethnic differences in socioeconomic status (SES).

Methods: We tested associations between race/ethnicity, SES, and type of medical insurance and serum creatinine level, estimated glomerular filtration rate, serum albumin level, and hematocrit at the start of treatment of ESRD and use of epoietin before ESRD treatment in a large national population-based sample. Data on 515,561 patients beginning ESRD treatment between January 1, 1996, and June 30, 2004, were obtained for this cross-sectional survey from the United States Renal Data System.

Results: Race/ethnicity had a much stronger association than SES with each laboratory measure. Adjusted mean serum creatinine levels were lowest in white patients (7.5 mg/dL [663.0 µmol/L]; 95% confidence interval [CI], 7.45-7.49) and highest in black patients (8.9 mg/dL [786.7 µmol/L]; 95% CI, 8.92-8.97) (P < .001 across racial/ethnic groups). Adjusted mean hematocrit for white patients (29.5%; 95% CI, 29.4%-29.6%) was significantly higher and for black patients (28.3%; 95% CI, 28.2%-28.4%) significantly lower than that of all other racial/ethnic groups (P < .001 across racial/ethnic groups). Less marked differences were present for estimated glomerular filtration rate and serum albumin level. In contrast, predialysis use of epoietin was associated with race/ethnicity (black vs white: odds ratio, 0.80; 95% CI, 0.78-0.81; Hispanic vs white: odds ratio, 0.87; 95% CI, 0.85-0.89) and showed a graded decrease with decreasing SES (odds ratio for the lowest vs highest socioeconomic quartile 0.68; 95% CI, 0.67-0.70). Patients without medical insurance had more abnormal laboratory values than those with insurance, but these associations were weaker than those of race/ethnicity.

Conclusions: Minorities, particularly black patients, had more severe laboratory abnormalities at the start of ESRD treatment than white patients. These differences were not readily attributable to SES differences. Absence of medical insurance, SES, and race/ethnicity were associated with the likelihood of predialysis use of epoietin.

Arch Intern Med. 2007;167:1083-1091
ted differences in laboratory measures at the start of dialysis can be accounted for by differences in SES or medical insurance status. Predialysis use of epoietin is also examined as a measure of disparities in the treatment of patients with chronic kidney disease.

DATA AND PATIENTS

Information on patients with incident ESRD was obtained from the United States Renal Data System (USRDS), a national population-based registry of all patients with ESRD. Patients are enrolled in the USRDS after being certified as needing long-term renal replacement therapy by their nephrologist. The USRDS includes patient demographic and clinical characteristics and selected laboratory test values at the start of renal replacement therapy, types of renal replacement therapy, and outcomes. The study protocol was exempted from human subjects review by the National Institutes of Health Office of Human Subjects Research.

Data were abstracted on all patients with incident ESRD between January 1, 1996, and June 30, 2004, who resided in 1 of the 50 states or the District of Columbia (N=779,918). We excluded 2001 patients with missing data on age, sex, or race and 20,641 (2.65%) with missing or invalid ZIP codes, leaving 757,276 patients. We then limited the analysis to the 747,356 patients who were 20 years or older to minimize confounding by age-associated differences in laboratory values and patterns of care. We also excluded 12,854 patients who had undergone renal transplantation within 30 days of beginning ESRD treatment because these patients are generally healthier and wealthier than those treated with dialysis. Last, we excluded 219,141 patients who had missing values for serum creatinine or whose reported values were obtained more than 45 days before or more than 1 day after the start of dialysis. The final sample consisted of 515,561 patients.

STUDY VARIABLES

Four laboratory values were studied as dependent variables: serum creatinine, serum albumin, hematocrit, and estimated glomerular filtration rate (GFR). The GFR was calculated using the 4-variable model of the Modification of Diet in Renal Disease study. We also examined predialysis use of epoietin.

The independent variables of interest were race/ethnicity, SES, and medical insurance status. Medical insurance before renal replacement therapy was categorized as none, Medicare only, Medicaid with or without Medicare, and private insurance with or without Medicare. The USRDS does not include patient-level measures of SES. Therefore, we developed a composite measure of SES and assigned an SES score to each patient based on the characteristics of their ZIP code of residence. We first abstracted data from the 2000 US Census on income, wealth, education, and occupation according to ZIP code tabulation area. By using principal components analysis we identified 7 census measures to include in the SES measure. Each of these measures loaded strongly on a single factor, with all factor loads being greater than 0.75, and together they explained 70% of the variance across ZIP codes. We then computed z scores for each ZIP code for each measure. The composite SES score was then computed as the sum of the z scores for all 7 measures.

To validate this measure, we compared SES scores across educational levels in 2394 patients who participated in the USRDS Dialysis Morbidity and Mortality Wave II substudy, which collected information on educational attainment. Mean SES scores were 0, 0.80, 1.35, and 2.85 for those with fewer than 12 years of school, high school graduates, some college, and college graduates, respectively (P<.001 for linear trend). Covariates included patient age, sex, each of 11 comorbid conditions, employment status, and functional status. Employment was coded as present if the patient was employed full-time or part-time at the start of renal replacement therapy. Inability to ambulate and inability to transfer were used to measure functional status.

STATISTICAL ANALYSIS

Values of serum creatinine and GFR were log-transformed for analysis and then transformed back to natural units for presentation. The SES scores were categorized into quartiles to allow for nonlinear associations with the laboratory values and epoietin use. Because ESRD occurs more commonly among those of lower SES, the SES categories do not define quartiles of patients.

Univariable comparisons of laboratory values among racial/ethnic groups, SES score quartiles, and patients with different types of insurance coverage were performed using analysis of variance. Comparisons of predialysis epoietin use were performed using logistic regression analysis. Multivariate models included the covariates of patient age, sex, comorbid conditions, employment, and functional status. The interactions between race/ethnicity and SES score quartile and between race/ethnicity and insurance type were also tested. The magnitude of association between race/ethnicity, SES score, and type of medical insurance and each laboratory measure was assessed using $\omega^2$, a measure of effect size that represents the proportion of the dependent variance accounted for by an independent variable in the population. Although $\omega^2$ has a theoretical range of 0 to 1, values greater than 0.1 are uncommon, and values of 0.05 are considered to represent moderate effects. Analyses were first performed in the subgroup of patients who participated in the USRDS Dialysis Morbidity and Mortality Wave II study using either educational level or the composite SES score as the measure of SES. The main analysis used the SES score and included all patients with available laboratory data. Because considerations for initiating renal replacement therapy differ among primary renal diseases, we also tested associations in patients with ESRD due to diabetes mellitus, for whom treatment often begins at higher levels of renal function than for those with other causes of ESRD and those with ESRD due to lupus nephritis, a large proportion of whom are racial/ethnic minorities. All the analyses were performed using SAS programs (SAS Institute Inc, Cary, NC). All hypothesis testing was 2-tailed. Because of the large sample, most $P$ values were small, and effect sizes ($\omega^2$) were considered more relevant for comparison.

RESULTS

ASSOCIATIONS IN THE DIALYSIS MORBIDITY AND MORTALITY WAVE II STUDY PARTICIPANTS

Of the 2394 patients (mean±SD age, 57.5±15.3 years; 53.05% men) who had values for serum creatinine and estimated GFR at the start of renal replacement therapy, 1883 (78.65%) also had values for serum albumin and 2169 (90.60%) also had hematocrit recorded in the same time frame. There were significant differences among racial/ethnic groups in serum creatinine values but no differences by level of education (Table 1). In the multivariate-adjusted model, white patients had significantly lower mean serum creatinine values than black patients.
(P < .001), Hispanic patients (P < .001), or American Indians (P = .04). Mean GFRs differed among racial/ethnic groups but not by educational level. Serum albumin levels did not vary significantly by race/ethnicity or educational level. Hematocrit readings were significantly higher in white patients than in black patients and Hispanic patients (P < .001 for both) but did not differ by educational level. Mean serum creatinine values were higher...
and mean GFR and hematocrit readings were lower in patients without medical insurance than in those with insurance (P<.05 for all) but did not differ among those with different types of insurance. There were no interactions between race/ethnicity and educational level or type of medical insurance (P=.20 for all). Comparison of ω² values confirmed that race/ethnicity was more strongly associated with variations in each laboratory test than with educational level or medical insurance.

Adjustment using the composite SES score resulted in mean values for each racial/ethnic group that were similar to those based on adjustment using educational level as the measure of SES, supporting the validity of the composite SES score.

ASSOCIATIONS IN THE MAIN SAMPLE

The main sample (n=515 561) included 271 390 white patients, 158 886 black patients, 58 701 Hispanic patients, 18 394 Asian/Pacific Islanders, 5587 American Indians, and 2603 persons of other race/ethnicity. Their mean±SD age was 61.3±15.3 years, and 54.03% were men. Of the sample, 69.42% had serum albumin values recorded in the 45 days before dialysis (n=357 933), and 88.45% had hematocrit readings recorded (n=456 010).

Compared with patients included in the study, those who were excluded because serum creatinine values were missing or were outside the required time frame were older (mean±SD age, 67.6±14.2 years), had higher mean SES scores (0.9 vs 0.8), and included slightly fewer men (52.22%) and more white patients (69.82%).

Variations in serum creatinine levels were much greater for race/ethnicity (ω²=0.021) than for SES (ω²=0.0001) (Figure 1A) and type of medical insurance (ω²=0.006) (Figure 2A). Multivariate-adjusted mean serum creatinine levels were lowest in white patients (7.5 mg/dL [663.0 µmol/L]) and highest in black patients (8.9 mg/dL [786.7 µmol/L]). Mean serum creatinine levels were highest in those without medical insurance and those with missing data on insurance in each racial/ethnic group (Figure 2A).
Estimated GFRs at the onset of dialysis varied weakly with race/ethnicity ($\omega^2=0.003$) (Figure 1B and 2B) and type of medical insurance ($\omega^2=0.0026$) (Figure 2B) but were not associated with SES (Figure 1B). Multivariate-adjusted rates were highest in white patients (8.9 mL/min per 1.73 m$^2$) and black patients (8.8 mL/min per 1.73 m$^2$) and lowest in Asian/Pacific Islanders (7.6 mL/min per 1.73 m$^2$). Estimated GFRs were lowest in those without medical insurance and in those with missing data on insurance in each racial/ethnic group.

Serum albumin levels varied significantly with race/ethnicity, SES (Figure 1C), and type of medical insurance (Figure 2C), but all associations were weak. White patients had the highest multivariate-adjusted levels (3.2 g/dL), and American Indians had the lowest levels (3.0 g/dL). Levels increased slightly with higher SES.

Hematocrit readings at the start of dialysis were also more strongly associated with race/ethnicity ($\omega^2=0.006$) than with SES ($\omega^2=0.00004$) (Figure 1D) or type of medical insurance ($\omega^2=0.0029$) (Figure 2D). The multivariate-adjusted mean hematocrit of white patients (29.5%) was significantly higher than that of all other racial/ethnic groups, and the value for black patients (28.3%) was significantly lower ($P<.001$ for all). Adjusted mean hematocrit increased slightly with increasing SES scores, from 28.6% in the lowest SES group to 29.0% in the highest SES group. Mean hematocrit readings were lowest in patients without medical insurance and those with missing data on insurance in each racial/ethnic group.

White-black differences in serum creatinine values and estimated GFRs at the start of dialysis were fairly uniform across ESRD networks. There was greater regional heterogeneity in white-Hispanic differences, which ranged from an adjusted mean difference in serum creatinine values of −0.1 mg/dL (−8.8 µmol/L) in network 9 (Indiana, Kentucky, and Ohio) to −1.24 mg/dL (−109.6 µmol/L) in network 6 (North Carolina, South Carolina, and Georgia) and an adjusted mean difference in estimated GFRs of 0.4 mL/min per 1.73 m$^2$ in network 18 (southern California) to 1.37 mL/min per 1.73 m$^2$ in network 10 (Illinois). There was also regional heterogeneity in hemat-
ocrit readings at the start of dialysis. White-black differences in hematocrit ranged from 0.7% in network 18 (southern California) to 1.5% in network 2 (New York), and white-Hispanic differences ranged from 0.1% in network 9 (Indiana, Kentucky, and Ohio) to 1.3% in network 13 (Arkansas, Louisiana, and Oklahoma).

Racial/ethnic differences in serum creatinine levels, estimated GFRs, and serum albumin levels remained stable across various patient subsets.
across time. For example, adjusted mean white-black differences in serum creatinine levels were −1.6 mg/dL (−141.4 µmol/L) in 1996-1998 and −1.4 mg/dL (−123.7 µmol/L) in 2002-2004. White-black differences in hematocrit decreased slightly from 1.3% in 1996-1998 to 0.9% in 2002-2004, but white-Hispanic differences did not change.

**SUBGROUPS WITH ESRD DUE TO DIABETES MELLITUS OR LUPUS NEPHRITIS**

The timing of ESRD treatment and the racial/ethnic composition of patients may differ for primary renal diseases, which could confound associations among race/ethnicity, SES, and laboratory values. To control for this possibility we examined associations among patients with ESRD due to diabetes mellitus or lupus nephritis. Associations in patients with ESRD due to diabetes mellitus (n=208 266; mean±SD age, 63.1±11.7 years; 49.85% men) were similar to those in the main analysis (Table 2).

White patients had higher mean serum creatinine values, and black patients had lower values, than those in other racial/ethnic groups. Estimated GFRs were highest in white patients and lowest in American Indians. Hematocrit readings varied more strongly by race/ethnicity than SES. Type of medical insurance was weakly associated with each laboratory measure.

Among patients with ESRD due to lupus nephritis (n=6018; mean±SD age, 41.8±14.2 years; 82.49% women), results were again similar to those in the main analysis (Table 2). In this smaller sample, there was no association between SES and any laboratory value or between race/ethnicity and estimated GFR. Serum creatinine values were lowest in white patients and highest in black patients. Black patients had lower hematocrit readings than the other groups. Mean serum creatinine values were higher and mean GFRs and hematocrit readings were lower in patients without medical insurance.

**USE OF EPOIETIN**

Racial/ethnic and SES differences in hematocrit readings may be related to variations in the use of epoietin in the period before dialysis. There was a graded decrease in the likelihood of epoietin use with decreasing SES score, even with adjustment for medical insurance status (Table 3). Compared with white patients, epoietin use was slightly more likely among Asian/Pacific Islanders and less likely among other racial/ethnic groups. Similar findings were present in patients with a predialysis hematocrit less than 30%.

**COMMENT**

In this large study, mean serum creatinine levels at the start of dialysis were approximately 1.5 mg/dL (132.6 µmol/L) lower in white patients than in black patients, 1.0 mg/dL (88.4 µmol/L) lower in white patients than in Asian/Pacific Islanders, and 0.5 mg/dL (44.2 µmol/L) lower in white patients than in Hispanic patients and American Indians. Mean hematocrit readings were greater than 1% higher in white patients than in black patients and slightly less than 1% higher in white patients than in Hispanic patients, Asian/Pacific Islanders, and American Indians. These differences were present despite adjustment for SES and type of medical insurance. Measures of SES were only weakly associated with laboratory val-

---

**Table 3. Association of Race/Ethnicity, SES, and Type of Medical Insurance With Epoietin Use Before Dialysis in All Patients and in the Subgroup With Hematocrit Readings Less Than 30%**

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Patients (n = 515 184)</th>
<th>Patients With Hematocrit Readings &lt;30% (n = 296 183)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epoietin Use, %</td>
<td>Odds Ratio (95% CI)*</td>
<td>Odds Ratio (95% CI)*</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>33.39 [Reference]</td>
<td>29.47 [Reference]</td>
</tr>
<tr>
<td>Black</td>
<td>25.90 (0.78-0.81)</td>
<td>22.20 (0.77-0.81)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>27.49 (0.85-0.89)</td>
<td>23.77 (0.87-0.93)</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>35.69 (1.03-1.11)</td>
<td>30.25 (1.01-1.11)</td>
</tr>
<tr>
<td>American Indian</td>
<td>29.23 (0.83-0.95)</td>
<td>25.23 (0.82-0.98)</td>
</tr>
<tr>
<td>Other</td>
<td>27.73 (0.78-0.94)</td>
<td>24.22 (0.78-0.91)</td>
</tr>
<tr>
<td>SES score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 4 (high)</td>
<td>36.81 [Reference]</td>
<td>32.06 [Reference]</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>32.90 (0.84-0.89)</td>
<td>28.21 (0.83-0.89)</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>29.79 (0.74-0.78)</td>
<td>25.72 (0.75-0.80)</td>
</tr>
<tr>
<td>Quartile 1 (low)</td>
<td>26.47 (0.67-0.70)</td>
<td>22.94 (0.68-0.73)</td>
</tr>
<tr>
<td>Type of medical insurance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicare alone</td>
<td>29.10 [Reference]</td>
<td>25.27 [Reference]</td>
</tr>
<tr>
<td>Private insurance, with or without Medicare</td>
<td>34.17 (1.18-1.23)</td>
<td>29.82 (1.17-1.25)</td>
</tr>
<tr>
<td>Medicaid, with or without Medicare</td>
<td>27.19 (0.97-0.99)</td>
<td>23.82 (0.93-1.00)</td>
</tr>
<tr>
<td>None</td>
<td>17.30 (0.57-0.61)</td>
<td>15.71 (0.58-0.64)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; SES, socioeconomic status.
*Based on logistic regression analysis with the covariates of age, sex, comorbid conditions, employment status, ability to ambulate, and ability to transfer.
ues. The effect sizes for race/ethnicity, although small, were much larger than those for SES and type of medical insurance, indicating the predominance of race/ethnicity in this relationship. These findings extend previous research that reported racial/ethnic differences in laboratory abnormalities at the start of dialysis but that did not include measures of SES or that examined insurance status only.

Racial/ethnic differences in laboratory values may have several different causes. The spectrum of primary renal diseases may differ among racial/ethnic groups. Diseases that are either asymptomatic, and, therefore, undetected, or rapidly progressive may occur more commonly in racial/ethnic minorities. However, results were similar among patients with ESRD due to diabetes mellitus or lupus nephritis, suggesting that differences in the distribution of primary diseases among racial/ethnic groups is not responsible for the racial/ethnic differences observed. Once chronic kidney disease is diagnosed, cultural differences in trust in physicians or the health care system may lead to delays in treatment. Differences in quality of care may also have a role. Deficiencies in patient-physician communication, patient education, and follow-up may contribute to racial/ethnic differences in laboratory abnormalities at the start of ESRD treatment. Uremic symptoms are a major indication for dialysis, and black patients may be less likely than white patients to develop uremic symptoms at a given level of residual renal function. However, anemia and hypoalbuminemia belie the severity of chronic renal failure at the start of dialysis in black patients.

More specific evidence of racial/ethnic disparities in quality of care was the difference in predialysis use of epoietin. Black patients were 20% less likely and Hispanic patients and American Indians were 11% to 13% less likely than white patients to be treated with epoietin after adjustment for SES and medical insurance. Differences in the use of epoietin may contribute to differences in complications, exercise tolerance, and quality of life. Lower SES and the absence of medical insurance were also associated with lower likelihoods of predialysis use of epoietin, consistent with expectations for measures of access to quality care.

White-black differences in serum creatinine levels and estimated GFRs showed limited regional variation, but there was substantial regional variation in hematocrit readings. There were also wide regional variations in white-Hispanic differences. This heterogeneity suggests that the factors responsible for racial/ethnic differences in laboratory abnormalities are not intrinsic cultural factors or related to minorities more likely declining treatment but rather that the factors are extrinsic and related to variations in quality of care. Studies that contrast processes of care across networks would be helpful in identifying ways to reduce these disparities. White-black differences in mean hematocrit readings decreased from 1996-1998 to 2002-2004, but few other changes indicated a decrease in racial/ethnic disparities across time.

The strengths of this study include the large population-based sample, testing for regional and temporal variations, and replication of results in 2 selected diseases. The study is limited in that personal measures of SES were not available for all patients. The main analysis used an area-based measure, which may misclassify patients. However, results were similar in the subgroup of patients for whom data on educational attainment were available. Data on laboratory values at the start of ESRD treatment were missing or outdated for some eligible patients, who were more likely to be older and white. This could bias the results if the missing values systematically differed from the values that were available, but this seems unlikely.

The results of this study indicate that the differences that exist among racial/ethnic groups in laboratory abnormalities at the start of ESRD treatment are likely not due to confounding by SES. Black patients had more abnormal values than patients of other racial/ethnic groups on several measures. Predialysis use of epoietin was lower among black patients, Hispanic patients, and American Indians; those of lower SES; and those without medical insurance. These differences, when considered in the context of previous evidence of late referral to nephrologic care, and historical differences in hemodialysis dose and in access to renal transplantation suggest racial/ethnic disparities in the quality of care of patients beginning renal replacement therapy. Understanding differences in the processes of care during this clinical transition may provide explanations for the origins of the disparity and may offer solutions.

Accepted for Publication: February 5, 2007.

Correspondence: Michael Ward, MD, MPH, Intramural Research Program, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, 10 Center Dr, Bldg 10 CRC, Room 4-1339, MSC 1468, Bethesda, MD 20892 (wardm1@mail.nih.gov).

Author Contributions: Dr Ward had full access to all the data in the study and takes full responsibility for the integrity of the data and the accuracy of the data analysis.

Financial Disclosure: None reported.

Funding/Support: This research was supported by the Intramural Research Program of the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health.

Role of the Sponsor: The funding agency had no role in the design and conduct of this study; collection, management, analysis, and interpretation of the data; or preparation, review, or approval of the manuscript.

Disclaimer: The interpretation and reporting of these data are the responsibility of the author and in no way should be seen as an official policy or interpretation of the US federal government.

Acknowledgment: The data reported herein were supplied by the USRDS.

REFERENCES


