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# Racial and ethnic disparities in pediatric renal allograft survival in the United States

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This study was undertaken to describe the association of patient race/ethnicity and renal allograft survival among the national cohort of pediatric renal allograft recipients. Additionally, we determined whether racial and ethnic differences in graft survival exist among individuals living in low- or high-poverty neighborhoods and those with private or public insurance. Among 6216 incident, pediatric end-stage renal disease patients in the United States Renal Data System (kidney transplant from 2000 through September, 2011), 14.4% experienced graft failure, with a median follow-up time of 4.5 years. After controlling for multiple covariates, black race, but not Hispanic ethnicity, was significantly associated with a higher rate of graft failure for both deceased and living donor transplant recipients. Disparities were particularly stark by 5 years post transplant, when black living donor transplant recipients experienced only 63.0% graft survival compared with 82.8 and 80.8% for Hispanics and whites, respectively. These disparities persisted among high- and low-poverty neighborhoods and among both privately and publicly insured patients. Notably profound declines in both deceased and living donor graft survival rates for black, compared with white and Hispanic, children preceded the 3-year mark when transplant Medicare eligibility ends. Further research is needed to identify the unique barriers to long-term graft success among black pediatric transplant recipients.

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Kidney transplantation is the preferred treatment for end-stage renal disease (ESRD) patients owing to its improved patient survival, quality of life, reduced morbidity, and economic savings compared with dialysis.<sup>1</sup> In pediatric ESRD, children who receive kidney transplants also show improved growth.<sup>2</sup> However, transplantation is not a cure; for children with ESRD, conditional on surviving the first year with a functioning transplant, the current graft half-life is estimated at 12 years for deceased donor (DD) transplants and 15 years for living donor (LD) transplants.<sup>3</sup> Transplant maintenance requires diligent medication adherence, frequent laboratory monitoring, and clinic visits.

In the United States, racial, sociocultural, and socioeconomic differences have been shown to compound the challenges of maintaining long-term function of a kidney transplant.<sup>4</sup> Among renal allograft recipients, studies have reported worse short- and long-term allograft survival for African-American patients in both adults and children.<sup>5–9</sup> In the pediatric population, the rate of graft failure among black patients has been reported as nearly twice the rate of graft failure of white patients.<sup>10–12</sup> Several studies have documented racial disparities in access to kidney transplantation among blacks and Hispanics versus white pediatric patients,<sup>13</sup> including decreased rates of waitlisting,<sup>14,15</sup> reduced rates of preemptive transplantation,<sup>15</sup> lower LD rates, and poorer human leukocyte antigen (HLA) matches.<sup>16</sup> Pediatric ESRD patients who receive a preemptive transplant<sup>11</sup> or LD (vs. DD) kidney transplant<sup>17</sup> have improved graft survival.

The reasons for these disparities are likely multifactorial in nature, and low socioeconomic status (SES) is an important risk factor for poor health outcomes among pediatric ESRD patients.<sup>18</sup> Although prior studies have adjusted for some SES factors, the presence of racial disparities in renal allograft survival across levels of SES has not been previously described among the US pediatric kidney allograft recipient population. Furthermore, Hispanics have often been overlooked in pediatric studies of renal allograft survival, although they comprise a growing proportion of the pediatric ESRD population.<sup>19</sup> One single-center study by Muneeruddin

*et al.*<sup>20</sup> suggested that Hispanics had improved DD graft survival but similar LD graft survival compared with African Americans. Notably, in the Muneeruddin *et al.*<sup>20</sup> study, Hispanics were of similar SES to whites. Finally, previous research examining racial and ethnic differences in pediatric allograft survival has not examined interactions between SES and donor source. The purpose of our study was to describe the association of patient race/ethnicity and renal allograft survival among the national cohort of pediatric renal allograft recipients, and to determine whether racial and ethnic differences in LD and DD allograft survival exist among individuals living in low- versus high-poverty neighborhoods and those with private versus public insurance.

## RESULTS

### Demographic and clinical characteristics of the study population

Among the 6216 pediatric DD or LD recipients included in this analysis, 893 patients (14.4%) experienced graft failure owing to any cause over a median follow-up period of 4.5 years, and an additional 307 pediatric transplant recipients (4.9%) died with a functioning graft. Demographic and clinical characteristics of the study population by race/ethnicity are presented in Table 1. The mean age at the time of transplant was  $10.9 \pm 5.2$  years, 58.5% were male, 21.1% were black, and 26.7% were Hispanic. Racial differences in demographic and clinical characteristics of the pediatric transplant recipients were apparent. On average, white patients were younger (10.3 years) compared with Hispanic (11.3 years) and black patients (11.8 years). Compared with white patients, blacks were more likely to have a body mass index >85th percentile (19.0% vs. 11.6%). Compared with whites, a greater proportion of both Hispanic and black patients had public insurance (71.5 and 68.8% vs. 42.5%, respectively) and lived in impoverished neighborhoods (32.9 and 38.2% vs. 13.6%) (Table 1).

### Transplant and donor characteristics of the study population by race

Both Hispanic and black patients were less likely to receive an LD transplant (33.3 and 25.5% vs. 58.6%), to be preemptively transplanted (14.2 and 8.7% vs. 27.4%, respectively), and more likely to spend  $\geq 1$  year on dialysis before transplant (59.4 and 56.5% vs. 36.5%, respectively) compared with whites. Longer donor cold ischemia time (>24 h) was more common among black DD recipients compared with whites and Hispanics (11.8% vs. 9.0% vs. 8.8%, respectively). Donor age was higher among whites compared with minorities, and whites had fewer HLA mismatches. The majority of patients (77.5%) were prescribed a tacrolimus-based immunosuppression regimen at discharge, followed by a cyclosporine-based regimen (11.7%), and a higher proportion of black and Hispanic patients were prescribed tacrolimus- versus cyclosporine-based regimens compared with whites (81.7 and 79.9% vs. 74.9%,  $P < 0.0001$ ). Delayed graft function was more common among black DD transplant recipients

(11.2%), compared with whites (5.4%) and Hispanics (5.9%) (Table 1).

### Graft survival (crude analyses)

Among pediatric kidney transplant recipients in the United States, overall 1-year graft survival was 95.2% (95% confidence interval (CI): 94.4–95.9) among DD transplant recipients and 97.9% (95% CI: 97.3–98.3) among LD transplant recipients (Figure 1). Overall graft survival rates were lower for blacks compared with both Hispanics and whites throughout the follow-up period ( $P < 0.0001$ ), with racial/ethnic differences more pronounced in long-term graft survival (Figure 1). Among DD transplant recipients, the 2-year graft survival was 91.5% for whites and 93.7% for Hispanics, but only 86.4% for blacks. Among LD transplant recipients, the 2-year graft survival was 96.8% for whites, 96.7% for Hispanics, and 93.0% for blacks. These racial differences were notably greater in 5-year graft survival. At 5 years, black LD recipient overall graft survival was 78.9% (vs. 90.8% for Hispanics; 92.2% for whites) and black DD recipient graft survival was 63.0% (vs. 82.8% for Hispanics; 80.8% for whites).

In crude Cox analyses for DD transplant recipients, Hispanics had similar rates of graft failure as white DD recipients at any given time during follow-up (hazard ratio (HR) = 0.90; 95% CI: 0.74–1.09), and the rate of graft failure for blacks was twice as high as that for whites (HR = 2.00; 95% CI: 1.70–2.36). Among LD transplant recipients, the disparity was higher among blacks compared with whites (HR = 2.65; 95% CI: 2.03–3.45), and similar among Hispanics and whites (HR = 1.06; 95% CI: 0.78–1.43) (Table 2).

Of the known causes of graft failure (71% of graft failures), the most common reasons included chronic rejection (37.7% of graft failures), acute rejection (23.3%), recurrent disease (10.8%), other (10.4%), and noncompliance (9.5%). Less common reasons included primary failure (3.0%), graft thrombosis (2.1%), infection (1.7%), BK virus (1.3%), and urologic complications (0.5%). Racial/ethnic differences in causes of graft failure did exist, where a greater proportion of black patients (27.0%) had acute rejection compared with whites (21.7%) and Hispanics (19.0%). Whites also had a higher rate of recurrent disease (14.5%) compared with Hispanics (10.4%) and blacks (7.5%). In addition, noncompliance was reported as the cause of graft failure more commonly for black (11.4%) versus white (8.3%) and Hispanic (7.9%) patients.

### Multivariable-adjusted graft failure

The final, multivariable, donor type-stratified Cox models examining the effect of race/ethnicity on graft survival adjusted for age, sex, insurance status, neighborhood poverty, etiology of ESRD, peak panel reactive antibody, body mass index >85%, blood type, receipt of a preemptive transplant, immunosuppression regimen at discharge, induction therapy, Share 35 cohort era (i.e., post-2005 implementation of the Share 35 allocation policy that preferentially allocated

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